22ND INTERNATIONAL WORKSHOP OF THE INTERNATIONAL SOCIETY FOR THE STUDY OF VASCULAR ANOMALIES

29 May - 1 June 2018

Muziekgebouw aan 't IJ
Amsterdam, the Netherlands

Program and Abstracts

ISSVA

www.issva2018.org

INDEX

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Welcome Letter
(from the ISSVA President)

Dear Colleagues and Friends,

On behalf of the Board of the International Society for the Study of Vascular Anomalies (ISSVA), I am happy to welcome you to the 22nd ISSVA Workshop in the beautiful city of Amsterdam in the Netherlands. Your outstanding commitment to vascular anomalies and our Society is exemplified by the record number of abstract submissions and participant registration.

I am thrilled to see how the various modifications we have made to the meeting agenda will develop your learning experience and networking possibilities. We modified the Primer Course to keep it basic and therefore more adapted to beginners in the field of vascular anomalies. On the other hand, we developed a number of Advanced Specialty Workshops that run in parallel to the basic course to enable discussion of specific questions in selected specialties.

I would like to express my gratitude to Dr Francine Blei, Chair of the ISSVA Scientific Committee, and all of its members, for their tremendous work in going through all the submitted abstracts and preparing this outstanding program.

Finally, I am also very grateful to the local organizing committee, which in collaboration with the Board and staff, set up this 22nd ISSVA workshop, which I am certain will be an outstanding meeting!

Sincerely Yours,

Laurence M Boon, MD, PhD
2018 ISSVA President

Welcome Letter
(from the Local organising committee)

Dear Colleagues and friends,

On behalf of the local Organising Committee, we would like to welcome you to Amsterdam for the 22th International Congress on Vascular anomalies.

We are indebted to the members of the Executive board and the scientific Committee of the society for their hard work putting an excellent scientific program together.

On Tuesday we will start with the Primer Course venue: Academic Medical Centre which serves as an introduction to those in training or new in the field. New are the advanced courses intended to enhance and share knowledge in the different specialist groups.

The meeting venue (Muziekgebouw aan het IJ) is beautifully located along the river, just minutes walk from the center of Amsterdam and the Central Station. It creates together with the social events an ideal atmosphere for informal and relaxing opportunities for networking and exchanging ideas.

We are proud to welcome you in Amsterdam, an exciting and vibrant city which we hope you all will enjoy.

Leo Schultze Kool
Chantal van der Horst

INTRODUCTION ISSVA

About the International Society for the Study of Vascular Anomalies (ISSVA)

The International Society for the Study of Vascular Anomalies (ISSVA) is the formalization of prior biennial international workshops, which were started in 1976 by Drs. John Mulliken and Anthony Young, of specialists interested in the diagnosis, management and investigation of these disorders. ISSVA was officially founded in 1992, two years after its first International Workshop held in 1990 in Amsterdam. The basic concepts behind the workshops has been maintained over the years as the field burgeoned around the original classification of vascular anomalies developed, revised and codified by ISSVA.

Today, the ISSVA workshops, held all over the world, gather hundreds of international specialists of various medical disciplines involved in the treatment of patients afflicted with vascular anomalies. These biennial workshops have fostered time proven personal contacts, collaboration, and informal exchange of scientific knowledge concerning vascular anomalies. The ISSVA membership is comprised of the dedicated physicians, scientists, and nurses who attend the workshops and support the fundamental mission of the organization to improve the lives of patients with vascular anomalies.

Vascular anomalies are a group of common and rare disorders of blood vessel growth leading to identifiable vascular lesions and their associated deformities. The official language of the Society is English and the Society is governed by the law of the United States of America.

COMMITTEES

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Scientific Committee

Scientific Committee Chair	Francine Blei	United States
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	Tony Penington	Australia
	Jonathan Perkins	United States
	Carsten Philipp	Germany
	Julie Powell	Canada
	Julie Prendiville	Canada
	Kristina Rosbe	United States
	Michel Wassef	France
	June Wu	United States

Local Organising committee	Leo Schultze Kool	the Netherlands
	Chantal van der Horst	the Netherlands
	Frédérique Bouwman,	the Netherlands
	Viviane van de Crommert	the Netherlands
	Mark Koelemaij	the Netherlands
	Pina Middelkamp	the Netherlands
	Jim Reekers	the Netherlands
	Dietmar Ulrich	the Netherlands
	Bas Verhoeven	the Netherlands
	Carine van der Vleuten	the Netherlands
	Allard van de Wal	the Netherlands

INTRODUCTION TO THE SCIENTIFIC PROGRAM

Oral presentations
These sessions are composed out of submitted abstracts.
Oral presentations are indicated by the prefix: O

Poster sessions
All poster boards are situated in the Atrium of the Muziekgebouw aan 't IJ.
The poster exhibition is open to all participants during the entire congress.
The numbers on the poster boards correspond with the abstract numbers in the program and abstract book.
All posters are indicated by the prefix: P

Intructions for presenters and chairs

Information for speakers
The meeting room is equipped with a data projector. Please bring your presentation on memory stick to the Speaker Slide Center in the break before the start of your session. Technicians will assist you loading your presentation. It is not allowed to use your own laptop. Please make sure your presentation is suitable for Microsoft PC (no Macintosh). The conference program is very tight, with not much free time between sessions. Please respect the allotted time for presentation to ensure that your session stays on track.
Arrive at the meeting room ten minutes before the session starts. Become familiar with the operation of the audiovisual equipment. Greet the chairs who will explain how they would like to run the session.

Information for session chairs
Thank you for accepting to chair a session. Your contribution is very important to ensure that sessions run smoothly, and to stimulate discussion. The conference program is very tight, with not much free time between sessions. Part of your contribution as a chair will be to ensure that your session stays on track.
We kindly ask you to arrive in the room ten minutes before the session starts to become familiar with the operation of the audiovisual equipment. Please explain to the presenters how you would like to run the session. The presenters are asked to bring their presentation on memory stick to the Speaker Slide Center, latest in the break before the start of the session. Technicians will assist chairs and presenters in the meeting room. It is not allowed to use own laptops.

Poster presentations
All posters are situated at the poster area, Atrium. The poster area is open to all participants during the entire congress. The numbers on the poster panels correspond with the abstract numbers in this abstract book.

Poster mounting
Tuesday, 29 May 2018 18:00 - 19:30
Wednesday, 30 May 2018 08:30 - 12:00

Poster Presentation Times
Please note that the poster presenters will be at their posters to answer questions at the following days and times:

Wednesday, 30 May: 12:15 - 13:45
Posters P001-P058; P145-P156; & P191-219

Thursday, 31 May: 12:00 - 13:30
Posters P059-P144 & P157-P190

Friday, 1 June 12:05 - 13:30 - poster viewing

Poster removal
Friday, 1 June from 13:30 to 15:30 hrs. Posters that not have been removed by the authors/presenters after this time slot are removed and disposed of by the congress staff.

SCIENTIFIC PROGRAM

Tuesday, 29 May 2018

Primer Course

Location AMC – College Room 4

08:00 - 08:05 ***Welcome***
Laurence Boon

Session 1: Hemangiomas and other Vascular Tumors
Moderators: Rod Phillips and Anne Dompmartin

08:05 **Vascular Anomalies Classification**
Laurence Boon

08:25 **Infantile Hemangiomas: Clinical Features, Risk Stratification, and Diagnosis**
Carine van der Vleuten

08:45 **PHACES and LUMBAR Syndromes: Structural and Associated Anomalies**
Maria Garzon

09:05 **Pathology of Hemangiomas**
Paula North

09:25 **Medical Treatments for Infantile Hemangioma**
Christine Léauté-Labrèze

09:45 **Role of Laser and Surgery for Infantile Hemangiomas**
Chantal van der Horst

10:05 **Differential Diagnosis of Hemangiomas and Other Vascular Tumors**
Julie Powell

10:25– 10:40 ***Break***

Session 2: Vascular Malformations
Moderators: Gulraiz Chaudry and Juan Carlos López Gutiérrez

10:40 **Vascular Malformations –Clinical Features, Risk Stratification and Diagnosis**
Juan Carlos López Guttiérez

11:00 **Coagulopathies in Vascular Malformations: Diagnosis and Treatment**
Leo Brandao

11:20 **Imaging Characteristics of Vascular Malformations**
Philip John

11:40 **Interventional Radiology for Vascular Malformations**
Pat Burrows

12:00 **Pathology of Vascular Malformations**
Michel Wassef

12:20 **Surgical Approaches to Vascular Malformations**
Dov Goldenberg

12:40 **Genetic Basis of Vascular Malformations**
Miikka Vikkula

13:10– 14:00 ***Lunch***

Session 3 Genetics and other topics in Vascular Anomalies
Moderators: Ana Giachetti and Raoul C.M. Hennekam

14:00 **Medical Management of Vascular Malformations**
Cameron Trenor

14:25 **Vascular Malformations: When and Why to Refer to Genetic Counseling and Testing**
Nicole Revencu

14:50 **Lymphedema and Lymphedema Syndromes**
Sahar Mansour

15:15 **Tips and Tricks for Building and Sustaining a Vascular Anomalies Clinic?**
Aimee Smidt

15:35 **Things You Don't Want to Miss/Summary – Pearls**
Francine Blei

15:50 ***Quiz: Case Presentations & Audience Participation***

Advanced Specialty Workshops

14:00 - 17:00 Genetics/Genomics and Translations to Possible Therapeutics

Location AMC - Room G4-123

14:00 **Era of Precision Medicine. It's All About the Genes**
Miikka Vikkula
14:30 **Steps to Translation. It's Not a Simple Task**
Les Biesecker
15:00 **The Power of One. Rare Diseases: Success with Limited Knowledge – The Sirolimus Story**
Maroeska te Loo
15:30 **Where Do We Go From Here? Therapeutic Strategies and Clinical Design**
Denise Adams
16:00 **ISSVA- Next steps**
All

14:00 - 17:00 Interventional Radiology

Location AMC - Room De Ziedses, B1-120

14:00-14:50 *Leo Schultze Kool, moderator*
14:00-14:30 **The confusing types of central conducting lymphatic disorders**
Highlights on differentiation, treatment and management
Max Itkin
14:30-14:50 **Discussion with attendees and cases review**
15:00-16:00 *Jim Reekers, moderator*
Debates, awareness, consensus and other sclerosing agents
15:00-15:10 **Toxicity of Bleomycin**
Josee Dubois
15:10-15:40 **What are your preferences and/or indications for LM and VM**
Pat Burrows, Jim Reekers, Leo Schultze Kool, Josee Dubois
15:40-16:00 **Discussion with attendees and cases review**
16:00-17:00 *Josee Dubois, moderator*
How to do it: AVM (approach: endovascular, arterial and/or venous side, percutaneous agents, when)
Patricia Burrows, Wayne Yakes
Two cases presentations with the approach
Patricia Burrows, Wayne Yakes

14:00 - 17:00 Surgery

Steven Fishman, Anthony Penington, Gresham Richter, Chantal van der Horst
Location AMC - Room Vrijzaal

14:00 - 17:00 *Surgery Chair: Chantal van der Horst*

14:00 **Welcome and introduction**
Chantal van der Horst
14.05 **Update on surgical management of Klippel-Trenaunay syndrome**
Steve Fishman
14.30 **Case based discussion CVLM**
Panel: Steve Fishman; Dov Goldenberg; Raul Mattass (Chair Chantal van der Horst)
15.00 **Algorithm for LM surgery in the head and neck**
Gresham Richter
15.20 **Case based discussion LM and other head and neck vascular anomalies**
Panel: Gresham Richter; Jon Perkins; Milton Waner; (Chair Tony Penington)
16.00 **My approach to AVM surgery**
Tony Penington
16.15 **My approach to AVM surgery**
James Suen
16.30 **Case based discussion, challenging AVM**
Panel: Tony Penington; James Suen; Arin Greene; (Chair Bas Verhoeven)
17.00 **Close**

14:00 - 17:00 Pathology

Location AMC - Room Patology, building M

14:00 **Diagnosis of PHOST and FAVA**
Harry Kozakewich
14:20 **Hyperkeratotic vascular anomalies**
Isabel Colmenero
14:40 **Small vessel-rich AVM**
Paula North
14:55 **Profuse vascular proliferations in congenital malformation**
Allard van der Wal
15:10 **Spindle-cell hemagioma**
Uta Flucke
15:25 **A glomus tumor case**
Louis Libbrecht

15:35 ***Break***

16:00 **Acquired vascular tumors resembling CH**
Michel Wassef
16:10 **Lobular mixed lymphatic-venous malformations of the subcutis**
Paula North
16:20 **Kaposiform lymphangiomatosis**
Harry Kozakewich
16:30 **Outcome of angiosarcoma with lymphatic differentiation**
Paula North
16:40 **A series of unusual nodular vascular malformations**
Michel Wassef
16:50 **Supplemental paper or cases for diagnosis…**

Patient Organizations Course

Location to be announced

14:00 - 14:30 ***Meet and greet***

14:30 - 14:45 ***Welcome by Patient organisation Hevas***

14:45 - 15:15 **The role of Patient Advocacy Organizations in the USA as educators**
Dr. Linda Rozell-Shannon, Vascular Birthmark Foundation USA

15:15 - 15:45 **European Reference Network and role Patient Organisations**
Matt Boltz-Johnson MA, EURORDIS

15:45 - 16:00 ***Break***

16:00 - 16:30 **Shared decision making**
Sophie E.R. Horbach MD, AMC The Netherlands

16:30 - 17:00 **Discussion guided by Matt Boltz-Johnson**

18:00 - 19:30 ***Welcome Reception at the Muziekgebouw aan 't IJ***

ISSVA WORKSHOP

Wednesday, 30 May 2018

08:00 ***Opening remarks***

Scientific Session 1: Updates in Vascular Anomalies, Bench and Bedside
Moderators: Ilona Frieden & Steven Fishman

08:15 O001 **Patient-reported outcomes of bleomycin sclerotherapy for low flow vascular malformations and predictors of improvement.**
Sophie E.R. Horbach, Joost S. van de Ven, Pythia T. Nieuwkerk, Phyllis I. Spuls, Chantal M.A.M. van der Horst and Jim A. Reekers

08:24 O002 **Efficacy and Safety of Pre-Operative Glue Embolization in Treatment of Head and Neck Venous Malformations**
Jonathan Perkins

08:33 O003 **Embryonic Stem Cell-like Subpopulations in Venous Malformation**
Elysia Tan, Sam Siljee, Helen Brasch, Jennifer de Jongh, Susana Enriquez, Swee Tan and Tinte Itinteang

08:42 O004 **CD133+ cells isolated from venous malformation recapitulate the clinical phenotype in a mouse model**
Peter Grzesik, Michael Schonning, Seung Koh, Ravi Sun, Andrew K. Edwards, Alison Kitajewski, Gresham T. Richter, Carrie J. Shawber and June Wu

08:51 O005 **Retrospective Study of Hematologic Complications in Patients with Localized Intravascular Coagulopathy Undergoing Sclerotherapy**
Kiersten Ricci, Adrienne Hammill, Carol Chute, Paula Mobberley-Schuman, Roshni Dasgupta and Manish Patel

09:00 O006 **Venous malformations and blood coagulation in children**
Johanna Aronniemi, Katariina A. Mattila, Anne Mäkipernaa, Päivi Salminen, Anne Pitkäranta, Johanna Pekkola and Riitta Lassila

09:08 O007 **Effect of Sirolimus on Coagulopathy of Slow-flow Vascular Malformations**
Bethany Verkamp, Joana Mack, Gresham Richter, Kelly Stewart and Shelley Crary

09:18 O008 **Efficacy and Safety of Sirolimus in Vascular Malformations Refractory to Standard Care: Preliminary Results of a Phase III Clinical Trial VASE**
Emmanuel Seront, Jennifer Hammer, An Van Damme, Anne Dompmartin, Marie Antoinette Sevestre, Jochen Rössler, Annouk Bisdorff Bresson, Isabelle Quere, Sandra Schmitz, Philippe Clapuyt, Frank Hammer, Catherine Legrand, Miikka Vikkula and Laurence Boon

09:27 O009 **ABL kinase inhibitor Ponatinib combined with rapamycin causes regression of murine Venous Malformation**
Xian Li, Yuqi Cai, Jillian Goines, Patricia Pastura, Paula Mobberley-Schuman, Megan Metcalf, Adrienne Hammill, Denise Adams, Tim LeCras and Elisa Boscolo

09:36 O010 **Initial Experience of Intravascular Sclerotherapy with C-arm Scan under the Guidance of Computer Navigation for Low-flow Vascular Malformations in the Complicated Anatomic Regions of Head and Neck: Report on 8 Procedures**
Hao Gu, Hui Chen, Zimin Zhang, Yunbo Jin, Xi Yang, Li Hu, Yongying Wang and Lin Xiaoxi

09:45 O011 **Sclerotherapy For Intramuscular Vascular Malformations: A Single Center Experience**
Federico Scorletti, Manish Patel, Adrienne Hammill, Kiersten Ricci, Charles Myers and Roshni Dasgupta

09:54 O012 **Venous Malformations are Proliferative: Clinical Implications**
Michael Schonning, Ajit Muley, Seung Koh, Peter Grzesik, Carrie J. Shawber and June Wu

10:03 O013 **The European Reference Network (ERN) for rare vascular diseases (VASCERN): VASCA-working group - towards better management of vascular anomaly patients**
Miikka Vikkula, Leo Schultze Kool, Alan Irvine, Päivi Salminen, Nader Ghaffarpour, Andrea Diociaiuti, Jochen Rössler, C.T. van den Bosch, Eulalia Baselga, Anne Dompmartin and Laurence Boon

10:12 O014 **Outcome measurement instruments for peripheral vascular malformations (OVAMA project)**
Amber P. Rongen, Sophie E.R. Horbach, Roy G. Elbers, Chantal M.A.M. van der Horst, Cecilia A.C. Prinsen, Phyllis I. Spuls and OVAMA consensus group

10:20 ***Coffee Break***

Summary Advanced Specialty Sessions

10:45 **Interventional Radiology**

10:56 **Surgery**

11:07 **Pathology**

11:18 **Medical/Genetics**

11:30 **Keynote: Lessons learned from our patients: Questions, Investigation, Solutions**
Steven FIshman, Boston Children's Hospital, Boston, USA

12:15 ***Lunch & Poster Viewing***

Difficult Cases 1
Moderators: Alejandro Berenstein & Julie Prendiville

13:45 O015 **Fœtal pulmonary and cerebral arterio-venous malformations as presenting signs of RASA-1 CM-AVM syndrome**
Julie Powell, Aspasia Karalis, Sandrine Essouri, Denis Bérubé and Josee Dubois

13:56 O016 **Cerebral Proliferative Angiopathy associated with Multiple Capillary Malformations: A new Rasopathy?**
Anne Dompmartin

Scientific Session 2: Vascular Malformations 1
Moderators: Douglas Marchuk & Annouk Bisdorff-Bresson

14:11 O017 **Wall shear stress in the feeding artery of a superficial arteriovenous malformation is an early and reliable marker of progression.**
Imane El Sanharawi, Didier Salvan, Gabrielle Mangin Mangin, Adrien Cogo, Stephanie Lenck, Olivier Baillart, Nathalie Kubis, Annouk Bisdorff Bresson and Philippe Bonnin

14:20 O018 **The use of Bleomycin and a Thrombin –Gelatin Hemostatic Matrix in the Treatment of Recurrent or Residual High Flow Arteriovenous Malformations of the Head and Neck**
Alejandro Berenstein

14:29 O019 **Efficacy of an AVM Classification System that Directs Endovascular Therapies Accurately**
Wayne Yakes

14:38 O020 **Extracranial artreriovenous malformations: a classification based on clinical, surgical and endovascular features.**
Giacomo Colletti, Margherita Dessy, Laura Moneghini, Anna Ierardi, Raul Mattassi and Federico Biglioli

14:47 O021 **Germline Loss-of-Function Mutations in EPHB4 cause a Second Form of Capillary Malformation Arteriovenous Malformation (CM-AVM2) deregulating RAS-MAPK signaling**
Nicole Revencu, Mustapha Amyere, Raphaël Helaers, Eleonore Pairet, Eulalia Baselga, Maria Cordisco, Wendy Chung, Josee Dubois, Jean-Philippe Lacour, Loreto Martorell, J uliette Mazereeuw-Hautier, Reed E. Pyeritz

14:56 O022 **Expanding the phenotypic spectrum of cases with an EPHB4 mutation**
Whitney Wooderchak-Donahue, Gulsen Akay Tayfun, Jamie McDonald, Kevin Whitehead, David Stevenson and Pinar Bayrak-Toydemir

15:03 O023 **EPH-B4 Regulates Venous Adaptive Remodeling in Arteriovenous Fistulas via an AKT1-Dependent Mechanism**
Naiem Nassiri and Alan Dardik

15:10 O024 **Genetic Testing in the Diagnostic Workup of Vascular Anomalies**
Miikka Vikkula, Nicole Revencu, Anne Dompmartin, Elsa Khoury, Antonella Mendola, Nisha Limaye, Raphaël Helaers, Elodie Fastré, Matthieu Schlögel, Nassim Homayun, Pascal Brouillard and Laurence Boon

15:19 O025 **Clinical Utility of a NGS panel in the Diagnosis of Vascular Malformations Syndromes**
Whitney Wooderchak-Donahue, Gulsen Akay-Tayfun, Peter Johnson, Jamie McDonald, J. Fredrik Grimmer, Gresham Richter, Marcie Steeves, Angela Lin, David Stevenson and Pinar Bayrak-Toydemir

15:26 O026 **Molecular Diagnosis of Mosaic Skin Development Disorders using Next Generation Sequencing.**
Virginie Carmignac, Paul Kuentz, Arthur Sorlin, Martin Chevarin, Thibaud Jouan, Charlotte Poë, Yannis Duffourd, Frédéric Tran Mau Them, Christel Thauvin, Christophe Philippe, Jean-Baptiste Rivière, Laurence Faivre, Pierre Vabres and Investigators MUSTARD

15:33 O027 **ISSVA Classification of Vascular Anomalies. 2018 Update Proposal.**
Michel Wassef, Eulalia Baselga, Gulraiz Chaudry, Maria Garzon, Dov Goldenberg, Juan-Carlos Lopez-Gutierrez, David Lord, Tony Penington, Julie Prendiville, June Wu and Francine Blei

15:45 ***Coffee Break***

16:00 **General Assembly**

Thursday, 31 May 2018

Scientific Session 3: Vascular Malformations 2
Moderator: Miikka Vikkula

08:00 O028 **Endothelial Cell Lineage Tracing in Cerebral Cavernous Malformations: A Modification of the "Two-Hit" Mutation Model of CCM Pathogenesis.**
Matthew Detter and Douglas Marchuk

08:09 O029 **Rapamycin not shown to inhibit LM growth in a mouse xenograft model.**
Tony Penington, Zerina Lokmic and Nerida Sleebs

08:18 O030 **Activation Of AKT In Tissue Endothelial Cells & Elevated Serum ANG-2 levels in Patients With Capillary Lymphatic Venous Malformations**
Tim LeCras, Jillian Goines, patricia pastura, Paula Mobberley-Schuman, Megan Metcalf, Denise Adams, Adrienne Hammill and Elisa Boscolo

08:27 O031 **Laser Ablation of Lymphatic Malformation Using Nanoparticle Targeted Therapy**
Ravi Sun, Ekaterina Galanzha, Dmitry Nedosekin, Haihong Zhang, Ting Wei, Zerina Lokmic, June Wu, Tony Penington, Vladimir Zharov and Gresham Richter

08:36 O032 **Excessive PI3K/mTOR signaling causes lymphatic hyperplasia and dysfunction in mice**
Devon Hominick, Noor Khurana, Lara Rodriguez-Laguna, Noelia Agra, Gema Gordo, Pablo Lapunzina, Juan C. Lopez-Gutierrez, Victor Martinez-Glez and Michael Dellinger

08:43 O033 **Gene Expression Detected in Peripheral Blood of Patients with Lymphatic Malformation**
Joyce Teng, Kavita Sarin, Taehan Kim, Ramie Lekwuttikan, Elidia Tafoya and Malcolm Chelliah

08:50 O034 **Superficial Cutaneous Vascular Malformations and Other Skin Manifestations of the PIK3CA-Related Overgrowth Spectrum (PROS)**
Justine Pasteur, Paul Kuentz, Yannis Duffourd, Arthur Sorlin, Laurence Faivre, Christelle Thauvin, Jean-Baptiste Rivière, Pierre Vabres and Investigators of MUSTARD Cohort

08:57 O035 **The full spectrum of post-zygotic PIK3CA mutations in non-syndromic lymphatic malformations**
James Bennett, Chi Cheng, Dana Jensen, Andrew Timms, Sheila Ganti, Giri Shivaram, Randall Bly, Andrew Kirsh, William Dobyns, Mark Makesky and Jonathan Perkins

09:04 O036 **Activating mutations in PIK3CA are specifically localized in lymphatic malformation-derived lymphatic endothelial cells of young children: therapeutic implications**
Jochen Rössler, Hannah Blesinger, Juergen Becker, Silke Kaulfuss and Jörg Wilting

09:11 O037 **Safety and Efficacy of Low Dose Sirolimus in Patients with PIK3CA-Related Overgrowth**
Victoria Parker, Kim M. Keppler-Noreuil, Pierre Vabres, Leena De Silva, Julie C. Sapp, Maxime Luu, Marjorie J. Lindhurst, Elodie Gautier, Marc Bardou, Laurence Faivre, Robert Semple and Leslie G. Biesecker

09:18 O038 **Segmental Overgrowth in Syndromic Vascular Anomalies: Towards a Pharmacogenetic Therapy with Rapamycin**
V. Baraldini, L. Spaccini , E. Cattaneo , D. Graziani, L. Moneghini, G. Bulfamante

09:25 O039 **"PTEN hamartoma of soft tissue" may also be related to PIK3CA mutations.**
Olivia Boccara, Louise Galmiche-Rolland, Bérengère Dadone, Stéphanie Pannier, Véronique Soupre, Florence Pedeutour and Sylvie Fraitag

09:32 O040 **How to build a multi-disciplinary vascular anomalies clinic from scratch: Lessons learned from a large, tertiary-care American children's hospital**
C. Matthew Hawkins, Steven Goudy, Michael Briones, Rachel Swerdlin, Jonathan Meisel, Sarah Milla, Magdalena Soldanska and Leslie Lawley

09:39 O041 **A FAIR compliant registry for the vascular malformation centres within the European Reference Networks. How it was done**
Leo Schultze Kool, Alan IRVINE, Päivi Salminen, Nader Ghaffarpour, Andrea Diociaiuti, Jochen Rössler, C.T. van den Bosch, Eulalia Baselga, Anne Dompmartin, Laurence Boon, Miikka Vikkula, Luiz Bonino, Mark Thompson, Annika Jacobsen, David van Enckevort and Marco Roos

09:46 O042 **The European Reference Network (ERN) criteria for multidisciplinary vascular anomaly clinics (VASCA) in the VASCERN**
Jochen Rössler, Eulalia Baselga, Laurence Boon, Andrea Diociaiuti, Anne Dompmartin, Nader Ghaffarpour, Alan D Irvine, Paivi Salminen, Leo SchultzeKool, Caroline van den Bosch and Miikka Vikkula

09:54 O043 **Patient involvement on vascular anomalies in the European Reference Network VASCERN**
C.T. van den Bosch, Matt Bolz-Johnson, Miikka Vikkula, Leo Schultze Kool, Jochen Rössler, Eulalia Baselga, Laurence Boon, Andrea Diociaiuti, Anne Dompmartin, Nader Ghaffarpour, Alan Irvine, Päivi Salminen, Maria Barea, Ange van der Velden and Petra Borgar

10:00 ***Coffee Break***

Difficult Cases 2
Moderators: Juan Carlos Lopez-Guttierez & Denise Adams

10:30 O044 **Syndromic segmental arterio-venous malformation: a therapeutic challenge**
Olivia Boccara, Annouk Bisdorff Bresson, Diala Khraiche, Olivier Naggara, Timothée de Saint-Denis, Paul Kuentz, Smail Hadj-Rabia, Francis Brunelle and Stéphanie Pannier

10:39 O045 **A difficult case of upper limb venous malformation with intolerance to oral sirolimus**
Mei-Yoke Chan, Luke Toh and Mark Koh

10:48 O046 **Management challenges of a complex CLOVES Syndrome patient with severe scoliosis and lipomatous overgrowth**
Wesley Barry, Donna Nowicki, Minnelly Luu, Chadi Zeinati, Lori Howell and Dean Anselmo

10:57 O047 **Case Report: Management of Menorrhagia in a Young Woman with Blue Rubber Bleb Nevus Syndrome: Failures and Successes**
Carrie Terrell, Sheilagh Maguiness and Brenda Weigel

Scientific Session 4: Vascular Malformations 3
Moderators: Gerald M. Legiehn & David Lord

11:10 O048 **Prevalence of Cardiac Failure in Patients with Arteriovenous Malformations**
Megan Gaffey, Megan Scarbrough, Ravi Sun, Joseph Deloach, James Suen and Gresham Richter

11:19 O049 **PET/CT imaging of angiogenesis in arteriovenous malformations**
Daphne Lobeek, Mark Rijpkema, Miikka Vikkula, Laurence Boon, Frédérique Bouwman, Willemijn Klein, Erik Aarntzen and Leo Schultze Kool

11:26 O050 **Melorheostosis and vascular anomalies caused by somatic mosaicism of KRAS**
Minia Campos-Domínguez, Víctor Martínez-Glez, Verónica Seidel, Teresa Martínez-Menchón, Belén Ferri Ñiguez, Antonio Cervantes Pardo, Ángel Lancharro-Zapata, Yolanda Ruiz-Martín, Antonio Salcedo-Posadas, Jorge Huerta-Aragonés, Carmen Garrido-Colino, Beatriz Berenguer-Fröhner, Elena De Tomás-Palacios, Concepción Lorca-García and Rosario García-Pajares

11:33 O051 **Extracranial Arteriovenous Malformations (AVMs) Are Caused by Activating MAP2K1 Mutations In Endothelial Cells**
Javier A. Couto, August Yue Huang, Patrick J. Smits, Dennis J. Konczyk, Jeremy A. Goss, Steven J. Fishman, John B. Mulliken, Matthew L. Warman, Arin K. Greene

11:43 O052 **Mosaic RAS/MAPK variants cause sporadic vascular malformations which respond to targeted therapy**
Satyamaanasa Polubothu, Mary Glover, Lara Al-Olabi, Katherine Dowsett, Katrina Andrews, Paulina stadnik, Agnel P Joseph, Rachel Knox, Alan Pittman, Graeme Clark, William Baird, Neil Bulstrode, Kristiana Gordon, Darren Hargrave, Sue Huson, Thomas Jacques, Gregory James, Hannah Kondolf, Loshan Kangesu, Kim Keppler-noreuil, Amjad Khan, Marjorie Lindhurst, Mark Lipson

11:52 O053 **The Role of Notch Pathway Components in Extracranial Arteriovenous Malformations**
Ting Wei, Haihong Zhang, Ravi Sun and Gresham Richter

12:00 ***Lunch & Poster Viewing***

Scientific Session 5: Hemangiomas and Vascular Tumors
Moderators: Eulalia Baselga & Maria Garzon

13:30 O054 **Source of Elevated AFP Levels in Infantile Haemangioma**
Tinte Itinteang, Matthew Munro, Bede van Schaijik, Jennifer de Jongh, Erin Paterson, Reginald Marsh and Swee Tan

13:37 O055 **Resistance Index (RI) in Colour Coded Duplex Sonography (CCDS) Easy Use and Reliable Results in the Determination of Activity in Infantile Hemangiomas**
Peter Urban

13:44 O056 **Non-involuting congenital hemangiomas (NICH) with post-natal atypical growth: a case series**
Maria Cossio, Josee Dubois, Catherine McCuaig, Danielle Marcoux, Sandra Ondrejchak and Julie Powell

13:51 O057 **Tardive Expansion Congenital Hemangioma: a variation of NICH or a new hemangiomatous entity?**
Chen Hua, Yunbo Jin, Lizhen Wang, Hui Chen, Gang Ma, Yajing Qiu and Lin Xiaoxi

13:58 O058 **Use of the Hemangioma Severity Scale to facilitate treatment decisions for infantile hemangiomas**
Carine Van der Vleuten and Andre Moyakine

14:07 O059 **Multiple cutaneous and visceral GLUT-1 positive congenital vascular tumors: a novel entity or a variant of multifocal infantile hemangiomatosis.**
Esperanza Mantilla-Rivas, Pamela Tan, Jocelyn C Zajac, Alexandra Tilt, Nancy Bauman, Philip Guzzetta, Gina Krakovsky, Bhupender Yadav, Ana Yasmine Kirkorian and Albert Oh

14:14 O060 **Systemic Timolol Exposures Following Topical Application to Infantile Hemangiomas**
Beth Drolet, Felix Boakye-Agyeman, Sarah Chamlin, Scott Denne, Anita Haggstrom, Barrie Harper, Kristen Holland, Jan Hau Lee, Hui Min Liew, Andrew Lewandowski, Casey Gelber, Anthony Mancini, Dawn Siegel, Nicole Stefanko, Rami Yogev and Chiara Melloni

14:23 O061 **Efficacy and Safety of Topical Timolol Maleate 0.5% Solution for Infantile Hemangioma in Early Proliferative Phase. A Randomized Clinical Trial**
Fania Muñoz Garza, Mónica Ríos Varela, Esther Roé Crespo, Lluis Puig Sanz, José Bernabeu Wittel and Eulalia Baselga Torres

14:32 O062 **Utility of Prolonged Monitoring During Initiation of Oral Propranolol for Infantile Hemangioma**
Leanna Hansen, Denise Adams, Eulalia Baselga Torres, Sarah Chamlin, Kristen Corey, Flora Frascari, Ilona Frieden, Peter Frommelt, Eloise Galligan, Maria Garzon, Kimberly Horii, Justyna Klajn, Christine Lauren, Anthony Mancini, Diana Mannschreck, Erin Mathes, Anelah McGinness, Brandon Newell, Henry Nguyen, Amy Nopper, Tola Oyesanya, Kate Puttgen, Megan Reynolds, Dawn Siegel, Nicole Stefanko, Megha Tollefson and Beth Drolet

14:39 O063 **AQP1 plays a key role in propranolol response in vivo**
Francois Moisan, Priscilla Kaulanjan, Sorilla Prey, Maya Loot, Christine Léauté Labreze, Alain Taieb and Hamid Rezvani

14:46 O064 **Propranolol treatment does not affect growth and development of children with infantile hemangioma**
Andre Moyakine

14:53 O065 **Hemangioma Sequelae In Infantile Hemangiomas Treated With Propranolol**
Eulalia Baselga, may el hachem, Andrea Diociaiuti, Claudia Carnevale, Camila Downey, Esther Roe, Iria Neri, Miriam Leuzzi, Jose Bernabeu-Wittel, M Teresa Montserrat-Garcia, Alejandro Ortiz-Prieto, antonio torrelo, Nicole Knopfel, Nadia Vercellino, Francesca Manunza, M Antonia Gonzalez-Enseñat, M Asuncion Vicente-Villa and ignasi Gich

15:00 O066 **The positive predictive value of hemangioma location for risk of PHACE syndrome: a retrospective analysis**
Colleen Cotton, Jusleen Ahluwalia, Ilona Frieden, Leslie Castelo-Soccio, Elena Pope, Dawn Siegel, Esteban Fernandez-Faith, Kim Morel, Christine Lauren, Maria Garzon, Anthony Mancini, Sarah Chamlin, Anita Haggstrom, Megha Tollefson, Marilyn Liang, Sharon G

15:07 O067 **Sternal/Midline Anomalies in PHACE Syndrome**
Nicole Stefanko, Beth Drolet, Olayemi Sokumbi, Ilona Frieden, Renee Howard, Juan Carlos Lopez Gutierrez, Maria Garzon, Eloise Galligan, Denise Metry, Francine Blei, Janet Fairley, Deborah Goddard and Dawn Siegel

15:15 ***Coffee Break***

Difficult Cases 3
Moderators: Beth Drolet & Lisa Weibel

15:45 O068 **Necrotizing Infection of an Infantile Hemangioma: An Uncommon Complication of a Common Disorder**
Bridget Shields, Lauren Brin Hermans, Beverly Aagaard-Kienitz, David Wargowski, Darya Buehler, Jason Pinchot, Carrie Kovarik, Lisa Arkin and Catharine Garland

15:54 O069 **Primary Hepatic Angiosarcoma in a 3 year-old Child Complicated by Consumptive Hypothyroidism: A Case Report**
Lara Mrak, Michael Woods, Carol Diamond, Jason Pinchot, Beverly Aagaard Kienitz, Lisa Arkin, Paula North, Darya Buehler and Kara Gill

16:03 O070 **Controversy RICH or KHE? What constitutes a true Kasabach Merritt syndrome? Necrotizing fasciitis in vascular anomalies: Seeking other centers experience, prevention?**
Catherine McCuaig, Michele David, Patricia Bortoluzzi, Louise Laberge, Elizabeth Rousseau, Afshin Hatami, Sandra Ondrejchak and Josée Dubois

16:12 O071 **Fatal hemorrhage from a rapidly involuting congenital hemangioma in an infant**
Aicha Salhi, Warda Drali, Nora Cheddani, Toufik Tounsi, Assya Djeridane, Abdelhamid Aitbenamar, Zoheir Belkaid and Ismail Benkaidali

Friday, 1 June 2018

Scientific Session 6: Lymphedema and Lymphatic Malformations
Moderators: Michael Dellinger & Tony Pennington

08:00 O072 **Lymphoscintigraphic Evaluation of Systemic Tracer Uptake in Patients with Primary Lymphedema and Establishment of an Evidenced-Based Protocol**
Arin Greene, Aladdin Hassanein, David Zurakowski, Frederick Grant, Stephan Voss and Reid MacIlellan

08:09 O073 **Proliferative Cells Resembling Mesenchyme Stem Cell-like Pericytes Derived from Kaposiform Hemangendothelioma and Kaposiform Lymphangiomatosis Lesions**
Kathryn Glaser, Peter Dickie, Denise Adams and Belinda Dickie

08:18 O074 **Kaposiform Lymphangiomatosis Caused by a Somatic NRAS Mutation**
Daniel M Balkin, Carol Nelson-Williams, Kristin Shimano, Tippi MacKenzie, Jessica L Davis, William Y Hoffman, Richard P Lifton and Ilona J Frieden

08:25 O075 **Generalized Lymphatic Anomaly Is Caused By Somatic Activating PIK3CA Mutations**
Lara Rodriguez Laguna, Noelia Agra, Gema Gordo Trujillo, Noor Khurana, Devon Hominick, Pablo Lapunzina, Juan Carlos Lopez-Gutierrez, Michael Dellinger and Victor Martinez-Glez

08:32 O076 **Lobular Capillary-Lymphatic Malformation of Subcutis: a Newly Recognized Entity with Distinctive Histological and Clincial Features**
Paula North and Valerie Salato

08:41 O077 **Prenatally diagnosed lymphatic malformations: clinical characteristics and outcomes**
Nancy Wang, Isabelle Chumfong, Lan Vu, Ilona Frieden, Kristina Rosbe and Josephine Czechowicz

08:48 O078 **ADAMTS3 Mutations cause Hennekam Lymphangiectasia-Lymphedema Syndrome 3**
Miikka Vikkula, Pascal Brouillard, Laura Dupont, Raphaël Helaers, Richard Coulie, George E. Tiller, Joseph Peeden and Alain Colige

08:55 O079 **Somatic NRAS mutation in patient with Generalized Lymphatic Anomaly**
Eugenia Manevitz-Mendelson, Gil S. Leichner, Ortal Barel, Inbal Davidi-Avrahami, Limor Strasser Ziv, Eran Eyal, Itai Pessach, Uri Rimon, Aviv Barzilai, Ninette Amariglio, Gideon Rechavi, Karina Yaniv and shoshana Greenberger

09:02 O080 **Kaposiform hemangioendothelioma: clinical features, complications and risk factors for Kasabach-Merritt phenomenon**
Yi Ji, Siyuan Chen and Bo Xiang

09:09 O081 **Dynamic contrast enhanced MR lymphangiography in patients with lymphatic anomalies.**
Maxim Itkin and Gregory Nadolski

09:18 O082 **A feasibility study to demonstrate the use of Near Infrared Fluorescent Lymphatic Imaging (NIRFLI) to diagnose and direct treatment in pediatric patients with lymphatic anomalies**
Rodrick Zvavanjanja, John Rasmussen, Adelaide Hebert, Eva Sevick and Matthew Greives

09:25 O083 **Differences in clinical findings and plasma cytokine profiles between generalized lymphatic anomaly and kaposiform lymphangiomatosis**
Michio Ozeki, Akifumi Nozawa, Norio Kawamoto, Akihiro Fujino, Satoshi Hirakawa and Toshiyuki Fukao

09:34 O084 **Lymphatic malformations treated by venous anastomosis technique based on flow assessment.**
Motoi Kato, Shoji Watanabe and Azusa Watanabe

09:43 O085 **Phase II Study of Sirolimus and Complicated Vascular Anomalies: Long term outcomes in Kaposiform Hemangioendothelioma**
Denise Adams, Cameron Trenor, Kiersten Ricci, Manish Patel, Gulraiz Chaudry, Megan Metcaff, Paula Mobberley-Schuman, Justyna Klajn, Anita Gupta, Carol Chute, Arnold Merrow, Roshni Dasgupta, Belinda Dickie and Adrienne Hammill

09:52 O086 **A Multidisciplinary Team Approach to Effectively Treat Abdominal Lymphatic Malformations**
Wesley Barry, Donna Nowicki, Minna Wieck, Kathy Schall, Minnelly Luu, Lori Howell, Chadi Zeinati and Dean Anselmo

10:00 ***Coffee Break***

Difficult Cases 4
Moderators: Jochen Roessler & Adrienne Hammill

10:30 O087 **Generalised Lymphatic Anomaly Treated with Sirolimus and Bevacizumab**
Tamás Bűdi (Semmelweis University, 2nd Dept. of Paediatrics); Zsuzsa Nagy (Semmelweis University, Budapest); Edit Varga (Semmelweis University, Budapest); György Balázs (Semmelweis University, Budapest); Zoltán Jenővári (Semmelweis University, Budapest)

10:39 O088 **Difficult case of a lymphedema patient with deteriorating venous outflow of lower limbs**
Tamás Budi, Zsuzsa Nagy, Edit Varga, György Balázs and Zoltán Jenovári

10:48 O089 **Case of Multifocal Lymphangioendotheliomatosis with Thrombocytopenia (MLT)…without thrombocytopenia and with minimal cutaneous involvement**
Priya Mahajan, Judith Margolin and Ionela Iacobas

10:57 O090 **Diagnostic and Management Dilemma in a Neonate**
Ionela Iacobas, Priya Mahajan, Sudhen Desai, Judith Margolin, Tara Rosenberg and Sheena Pimpalwar

Scientific Session 7: Vascular Malformations Surgery, Interventional Radiology, and Imaging
Moderators: David Darrow & Patricia Burrows

11:10 O091 **Facial reanimation in patients with flaccid facial paralysis after excision of facial vascular anomalies**
Teresa O, Milton Waner and Ho Yun Chung

11:19 O092 **Three Thousand Sclerotherapy Treatments of Vascular Anomalies with Intralesional Bleomycin Injection**
Tobian Muir, Sri Murugan, Gareth Kessell, Raj Jayaraj, Sheamus Fitzgerald and Rajeev Padmanhaban

11:28 O093 **Operative treatment of lower extremity venous malformations**
Pia Vuola, Jussi Repo, Päivi Salminen, Johanna Aronniemi, Kimmo Lappalainen and Erkki Tukiainen

11:37 O094 **Effectiveness and safety of balloon-assisted sclero-embolotherapy for subcutaneous arteriovenous malformations**
Shigeki Imai and Tomomi Sato

11:44 O095 **Ethylene vinyl alcohol copolymer in the treatment of high flow arteriovenous vascular malformations: Long- term results and histology**
Antoinette Gomes, Phillip Monteleone, Alison Vasan , James Sayre and Susan Bukata

11:51 O096 **Ethanol embolization combined or not with surgery and close clinical follow-up can effectively control extracranial arterio-venous malformations (AVMs)**
Jean Nicolas Racicot, Josee Dubois, Patrick Gilbert, Patricia Bortoluzzi, Julie Powell, Alain Danino, Marie-France Giroux and Gilles Soulez

11:55 O097 **Efficacy of flow related color-coded DSA in direct puncture treatment of arteriovenous malformations.**
Kunie Ohuchi, Shiro Onozawa, Yoshiaki Katada, Goro Takada and Rintaro Akimoto

12:05 ***Lunch & Poster Viewing***

12:30 ***Lunch Symposium (company sponsored - non-CME) (more information on page 21)***

Scientific Session 8: Vascular Malformations Potpourri
Moderators: Gilles Soulez & Chantal van der Horst

13:30 O098 **Hormone Receptors Expression in Microvascular Proliferation of Arteriovenous Malformation**
Amalia Mulia Utami, Onno J. de Boer, Dara R. Pabittei, Claire Mackaaij and Allard C. van der Wal

13:39 O099 **Electrosclerotherapy as a novel treatment option for hypertrophic capillary malformations: proof of concept**
Sophie E.R. Horbach, Albert Wolkerstorfer, Folkert Jolink, Paul R. Bloemen and Chantal M.A.M. van der Horst

13:48 O100 **Bleomycin Electrosclerotherapy (EST); an Exciting Emerging Treatment in the Management of Vascular Malformations**
Tobian Muir, Liam McMorrow, Sri Murugan, Gareth Kessell and Raj Jayaraj

13:57 O101 **Pregnancy in Women with Klippel-Trenaunay Syndrome: Report of a Complicated Case and Proposal for Standardized Care**
Max M. Lokhorst, Sophie E.R. Horbach, J.W. Ganzevoort, S. Middeldorp, CE Oduber and C.M.A.M. van der Horst

14:06 O102 **Chitosan-doxycycline hydrogel: An MMP inhibitor/sclerosing embolizing agent as a new approach to treat AVMs and LM.**
Gilles Soulez, Fatemeh Zehtabi, Pompilia Ispas-Szabo, Djahida Djerir, Lojan Sivakumaran, Mircea Alexandru Mateescu and Sophie Lerouge

14:15 O103 **Pre-operative percutaneous n-BCA glue embolization of truncal and extremity venous malformations: technique, safety, and clinical outcomes**
Giridhar Shivaram, Eric Monroe, Rush Chewning, Antoinette Lindberg, Kevin Koo, Randall Bly and Jonathan Perkins

14:22 O104 **INTRAMUSCULAR VENOUS MALFORMATIONS OF THE CALF: SURGICAL TREATMENT OUTCOME OF 57 PATIENTS**
Claude Laurian, Veronique Marteau, Claudine Massoni, Pierre Cerceau, Akli Zetchi, Nikos Paraskevas, Emmanuel Houdart and Annouk Bisdorff Bresson

14:29 O105 **In the Age of B-Blockers Is There A Role For Surgery To Manage Infantile Hemangioma in Sensitive Facial Anatomical Regions?**
Jugpal Arneja

14:38 O106 **Comparison of two generation photosensitizers of PsD-007 and HMME photodynamic therapy for treatment of port-wine stain: a retrospective study.**
Gang Ma, Yue Han, Wenxin Yu, Jiafang Zhu, Yajing Qiu, Hui Chen, Yunbo Jin and Lin Xiaoxi

14:47 O107 **Diagnosis and Treatment of Hepatic Venous Malformations**
Wayne Yakes

14:55 O108 **Imaging of Epithelioid Hemangioendothelioma**
Yan Epelboym, Frederic Thomas-Chausse, Ahmad Alomari, Cameron Trenor, Denise Adams and Gulraiz Chaudry

15:00 ***Coffee Break***

Difficult Cases 5
Moderators: Milton Waner & Gresham Richter

15:30 O109 **Management of a massive right lower extremity and buttock venous malformation requiring abdominoperineal resection**
Wesley Barry, Donna Nowicki, Chadi Zeinati, Minnelly Luu, Lori Howell and Dean Anselmo

15:39 O110 **Unclear Diagnosis and Management of A Congenital Nasal Vascular Lesion**
Nancy Bauman, Gina Krakovsky, Phillip Guzzetta, Bhupender Yadav, Albert Oh, Yasmine Kirkorian, Monica Pearl, Christopher Rossi, Bernard Cohen and Amir Dorafshar

15:48 O111 **Transvenous and image-guided embolization techniques combined with surgical reconstruction for difficult AVMS of the head and neck.**
Alejandro Berenstein, Milton Waner, Priya Kesarwani And Teresa O

15:57 O112 **Complex bilateral cervicofacial lymphatic malformation mandibular deformity in pediatric patient**
Tara Rosenberg, Ionela Iacobas, Priya Mahajan, Judith Margolin, Raphael J. Yoo and Sheena Pimpalwar

16:05 ***Award Ceremony & Closing***

SOCIAL PROGRAM

Welcome reception

Right after the end of the first day's scientific program, we would like to invite you to our Welcome reception! Meet fellow congress attendees, speakers and exhibitors by enjoying drinks and several delicious bites. This welcome reception is kindly offered to all registered delegates free of charge.
Tuesday 29 May 18:00 - 19:30

Location: Muziekgebouw aan 't IJ, at the exhibition

Canal boat tour

Besides providing a stunning backdrop to the city's historical centre, floating down Amsterdam's canals is one of the most memorable ways to discover the city's sights and attractions. Whether you're a first-time or frequent visitor, everything in Amsterdam seems a bit more magical when viewed from a boat.

Delegates will receive a ticket for a boat tour (1 hour) with their registration package. On Wednesday 30th May, delegates have the opportunity to take a boat tour. The tickets will be valid all days of the workshop. The boat tour is offered by the community of Amsterdam

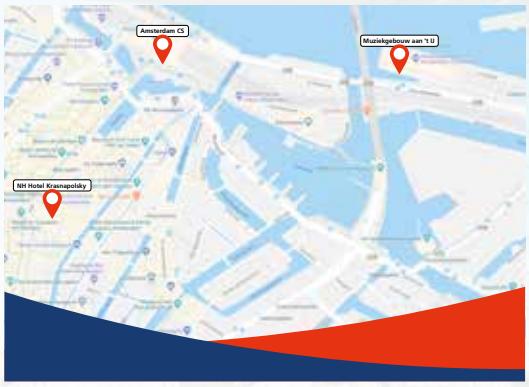
The boat tour is included in the conference fee.

Congress dinner party

The Congress Dinner Party on Thursday 31 May will be held at the Grand Hotel Krasnapolsky - Wintertuin (Winter Garden), Damsquare, City Center.

Tickets at €100 to be ordered in advance.

Directions
Amsterdam Central Station: It's a 12 minute walk to the hotel.From the main exit walk straight across the Stationsplein square. At the traffic lights, head straight towards Dam Square. You will see the hotel on the left side of the square. If walking is not an option take tram line 1, 2, 5, 13 or 17 to the Dam Square stop. You will see the hotel on the left hand side of the Dam.



Dress code - Smart casual

Farewell reception

Join us for drinks, while we look back to a succesfull meeting, on Friday 1 June, 16:15.

GENERAL INFORMATION

Venues

Basic Primer Course & Advanced Specialty Workshops, 29 May
Academic Medical Center (AMC)
Meibergdreef 9
1105 AZ Amsterdam

ISSVA Workshop, 30 May-1 June
Muziekgebouw aan 't IJ, Amsterdam
Piet Heinkade 1
1019 BR Amsterdam

Route description

Route description from Amsterdam Medical Center (AMC) to the Muziekgebouw aan 't IJ, via Amsterdam Central Station
metro #54 will bring you from station HOLENDRECHT to Amsterdam Central Station, in approx. 20 minutes.

From the northern exit of the Central Station, the venues' typical architecture can be seen at a distance of approximately one kilometer, eastwards on the IJ. It's a 10 minute walk from the back side of the station (Noord). Go to the right and walk along the water. Walk up the bridge and you will find the Bimhuis/Muziekgebouw aan 't IJ on you left hand side where you can take the passengers bridge to the entrance. In short: out of the station (Noord), to the right and up the bridge.

By tram
Line 26 Centraal Station / IJburg also stops directly in front of the venues (the stop is called Muziekgebouw / Bimhuis and is the first stop coming from Central Station direction IJburg).

Registration fee onsite

Late registration fee and onsite (After 1 May 2018)

ISSVA Workshop	750 EUR
ISSVA Workshop for Residents /Nurses/Trainees*	525 EUR
ISSVA Workshop day registration	350 EUR
ISSVA Workshop day registration for Residents/Nurses/Trainees*	175 EUR

* Residents have to provide a written certification by head of department

The registration fee includes the following
Admission to the meeting, welcome reception, program and abstract book, certificate of attendance, lunches and all coffee breaks.
The gala dinner is only available for registered participants.
Please check the registration desk for information on availability.

Opening hours registration/information desk

Location AMC

Tuesday 29 May	07:00-17:00

Location Muziekgebouw aan 't IJ

Tuesday 29 May	17:30-19:30
Wednesday 30 May	07:30-17:00
Thursday 31 May	07:30-17:00
Friday 1 June	07:30-17:00

Openings hours speakerslide center

Tuesday 29 May	17:30-19:30
Wednesday 30 May	07:30-17:00
Thursday 31 May	07:30-17:00
Friday 1 June	07:30-14:00

Cloakroom and luggage

Tuesday 29 May	17:30-19:30
Wednesday 30 May	07:30-18:00
Thursday 31 May	07:30-18:00
Friday 1 June	07:30-17:00

Namebadge

Participants should collect name badges from the conference registration desk. Since only registered participants will be permitted to attend the scientific sessions, the exhibition and poster areas, you are kindly asked to wear your badge when entering the congress venue.
Exhibitors will also receive badges to allow access to the respective areas.

WIFI

Free wireless internet is available for all congress delegates at the Muziekgebouw aan 't IJ.
Network: ISSVA Amsterdam
Password: ISSVA2018

ISSVA 2018 mobile app

This app can be downloaded in the App store (Apple) or in the Play Store (Android). In this app you will find a detailed overview of the scientific program, abstracts, posters and floor plan. For assistance and questions regarding the app please see the staff at the registration desk.

You can download the app in four simple steps:
1. Go to the appstore and search for 'Congress Care'
2. Instal and open the app on your phone or tablet.
3. Select the event ISSVA 2018 and click on 'install'
4. The app is now ready for use

ISSVA 2018 Twitter

ISSVA 2018 can be followed on Twitter, via @ISSVA. If you would like to share your tweets with other delegates following ISSVA 2018, please use #ISSVA2018.

Accreditation

Accreditation is applied for at the European Accreditation Council for Continuing Medical Education (EACCME). This accreditation will be endorsed by the European Union of Medical Specialists (UEMS) ensuring that the CME credits awarded to the participants are recognized by the national medical authorities who have agreed to co-operate in this European system. EACCME credits are recognized by the American Medical Association towards the Physician's Recognition Award (PRA).

Certificate of attendance

Certificates of attendance will be sent afterwards by email.

Congress language

The official Congress language will be English. No simultaneous translation will be available.

Insurance

In registering for ISSVA 2018, delegates agree that neither the organisation nor the congress agency Congress Care is responsible for individual medical, travel or personal insurance.
Delegates are requested to make their own travel and health insurance.
The organizers cannot assume liability for changes in the program due to external circumstances.

Sponsored Lunch Symposium

Pierre Fabre DERMATOLOGIE | SKIN EXPERTISE IN OUR DNA

Friday 01 June 2018 12:30 - 13:20

Infantile hemangiomas: new insights
Chair: Julie Powell, M.D.

10 years of propranolol: what have we learned?
Christine Léauté-Labrèze, M.D.

Another central mode of action of betablockers
Claude Knauf, Ph.D.

Early referral of infantile hemangioma: the next challenge
Carine Van der Vleuten, M.D.

Severe forms of infantile hemangioma (efficacy of propranolol, sequelae)
Eulalia Baselga, M.D.

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ABSTRACTS ORAL PRESENTATIONS

Scientific Session 1: Updates in Vascular Anomalies, Bench and Bedside

O001
Patient-reported outcomes of bleomycin sclerotherapy for low flow vascular malformations and predictors of improvement.

Sophie E.R. Horbach (Plastic and reconstructive surgery, Academic Medical Center (AMC) Amsterdam); Joost S. van de Ven (Plastic and recontructive surgery, Academic Medical Center, Amsterdam, the Netherlands); Pythia T. Nieuwkerk (Medical psychology, Academic Medical Center (AMC), Amsterdam, the Netherlands); Phyllis I. Spuls (Dermatology, Academic Medical Center, Amsterdam, the Netherlands); Chantal M.A.M. van der Horst (Plastic and reconstructive surgery, Academic Medical Center, Amsterdam, the Netherlands); Jim A. Reekers (Interventional Radiology, Academic Medical Center (AMC), Amsterdam, the Netherlands)

Purpose: There is paucity of data on patient-perceived outcomes of bleomycin sclerotherapy for congenital low-flow vascular malformations. In this study, the long-term outcomes of bleomycin sclerotherapy were investigated in terms of quality of life (QoL) and patient-perceived changes in health status.
Methods: A cohort of Dutch patients with vascular malformations undergoing bleomycin sclerotherapy between June 2010 and November 2015 completed questions about their disease symptoms, current QoL (Short Form 36-item Health Survey) and a retrospective assessment of baseline QoL, patient-perceived change in various health aspects(Global Rating of Change scales) and treatment satisfaction. QoL was analyzed relative to an age and sex-matched Dutch reference population. Predictive factors associated with QoL and patient-perceived improvement in overall health status were assessed using multivariable linear and logistic regression analyses, respectively.
Results: Seventy-seven patients, with a median follow-up of 22 months, were enrolled. Only 49.3% of the respondents indicated that they perceived (any form of) improvement in their overall health status. Most often improved were the specific health aspects 'pain' and 'overall severity of symptoms'. No factors were significantly predictive for patient-perceived overall improvement in health with respect to the vascular malformation. Impairment in work- or study-related activities prior to sclerotherapy was found to negatively impact physical QoL at follow-up.
Conclusion: Approximately half of patients with low-flow vascular malformations indicate an improvement in overall health status following bleomycin sclerotherapy, particularly concerning pain and severity of symptoms. However, most patients only perceived little to moderate improvement to their health and desire further treatment.

O002
Efficacy and Safety of Pre-Operative Glue Embolization in Treatment of Head and Neck Venous Malformations

Jonathan Perkins (Seattle Childrens Hospital)

Purpose: Purpose: Head and neck venous malformations (HNVMs) are difficult to eradicate. Single-stage, preoperative percutaneous embolization with n-butyl cyanoacrylate (n-BCA) glue followed by surgical excision ("GES"), in appropriate lesions, allows precise HNVM removal while preserving normal tissue and function. We describe advantages and contraindications of GES in HNVM treatment through a retrospective study of HNVMs evaluated between 2000 and 2016. We hypothesized that GES treatment outcomes improved compared to other treatment modalities.
Methods: Methods: Patients with localized HNVM and more than one year of follow-up were included. HNVM not amenable to GES, and comparison of these post-treatment complications between treatment modalities: symptom or lesion persistence, facial nerve injury, and skin ulceration were determined. Data was analyzed using descriptive statistics and Chi-square analysis.
Results: Results: Of 149 HNVMs identified, 136 were localized. The patients' age ranged from 0-49 (median 8.1 years), 79/136(58%) HNVMs were in female patients, and 62/136 (46%) were oral. Pre-2010 HNVMs: 25/61 (41%) were observed, 23/61 (38%) underwent excision, 12/61 (20%) received sclerotherapy, and one underwent GES. Post-2010 HNVMs: 35/75 (47%) were observed, 37/75 (50%) evaluated for GES or excision, and 3/75 (4%) had sclerotherapy. Of the HNVMs evaluated for GES: 24/37 (65%) had GES, 10 (27%) were not GES candidates due to high lesion outflow or superficial location, and were excised, GES was declined in 4 (11%) HNVMs. Post-2010, treatment complications decreased markedly, from 62% (23/37) pre-2010, to 20% (8/40) after 2010. GES comprised 15 of 16 oral-lesion interventions post-2010, with 20% (3/15) complication rate, vs. 78% (18/23) complication rate pre-2010 with other treatment methods (p = 0.001). Complication rates with GES (13%) were decidedly reduced compared to Excision (46%) and Laser/Sclerotherapy (93%). GES was not associated with skin ulceration or facial nerve injury.
Conclusion: Conclusions and Relevance: Localized HNVMs treated with GES have fewer complications compared to other treatment modalities.

O003
Embryonic Stem Cell-like Subpopulations in Venous Malformation

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Purpose: Venous malformation (VM) consists of a network of ectatic anomalous thin-walled venous channels. A role for an activating TIE2 mutation in the development of the dilated luminal vessels in VM, and its proposed involvement of embryonic stem cells (ESCs), led us to investigate the expression of ESC markers in subcutaneous VM (SCVM) and intramuscular VM (IMVM).
Methods: 4μm-thick formalin-fixed paraffin-embedded sections of SCVM from seven patients and IMVM samples from seven patients were analysed for the expression of Nanog, pSTAT3, OCT4, SOX2, SALL4, and CD44, using 3, 3-diaminobenzidine (DAB) immunohistochemical (IHC) staining. All these samples did not express lymphatic marker D2-40. NanoString and RT-PCR mRNA analyses were performed on snap-frozen SCVM (n=3) and IMVM (n=3) samples from the respective original cohorts of patients included in DAB IHC staining. To confirm co-expression of two proteins, immunofluorescence (IF) IHC staining on two representative samples of IMVM and SCVM each from the original cohorts of patients included for DAB IHC staining was performed. Cells derived from SCVM (n=4) were analysed using RT-qPCR for the expression of the same ESC markers.
Results: DAB IHC staining demonstrated expression of all above ESC markers in both SCVM and IMVM samples. IF IHC staining showed that these markers were localized to the endothelium within these lesions and that Nanog, pSTAT3, SOX2 and CD44 were also expressed by cells outside of the endothelium. NanoString mRNA analysis confirmed transcription activation of pSTAT3, OCT4 and CD44. RT-qPCR confirmed transcription activation of Nanog, SOX2 and SALL4 in both the tissues and cells.
Conclusion: Our findings support the presence of two ESC-like subpopulations, one within and one outside of the endothelium, of both SCVM and IMVM. Given that the endothelial ESC-like subpopulation expresses the more primitive marker, OCT4, it is exciting to speculate that they give rise to the non-endothelial subpopulation.

O004
CD133+ cells isolated from venous malformation recapitulate the clinical phenotype in a mouse model

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Purpose: Venous malformations (VMs) can cause disfigurement, and when combined with lymphatic malformations, life-threatening coagulopathy. Despite potential severe morbidities, treatment options are empirical including conservative management, sclerotherapy, and surgical de-bulking. Complications rates can be high (18-20%), and non-response (25%) or need for multiple treatments (28%) are common. Development of biologically-targeted therapy is limited as the pathophysiology of VMs is poorly understood. Recent studies have shown that VMs arise due to post-zygotic mutations. We hypothesize that a pathological cell population with progenitor characteristics contributes to VM pathobiology. The purpose of our study is to isolate and characterize cells from resected VMs.
Methods: Resected VM specimens were digested and cellssortedwithCD133-antibody coated beads. Isolated cells were analyzed by Fluorescence-Activated Cell Sorting and quantitative Reverse Transcriptase-PCR (qRT-PCR). In a mouse model, cells re-suspended in Matrigel were injected into nude mice and assessed by Doppler ultrasound weekly. After 3 weeks, mice were sacrificed and Matrigels harvest for histological and immunohistochemical analysis.
Results: Isolated CD133+ VM cells were positive for progenitor cell markers (CD34, CD90), endothelial cell markers (CD31, VE-CADHERIN, VEGFR2, CD146, VEGFR3). Expression of the progenitor gene, Nanog, was also observed by qRT-CR. Doppler able blood flow was detectable in VM cell implants by 2 weeks (Figure 2A). CD133+ cells formed clusters of dilated vascular channels lined by CD31+ endothelial cells, recapitulating the clinical phenotype of VMs.
Conclusions: A unique population of CD133+ endothelial cells that express progenitor genes were isolated from VMs (VMECs). TheseCD133+ cells were able to form dilated vascular channels phenocopying clinical specimen suggesting that this population of endothelial cells contributes to the pathogenesis of VMs. This novel mouse model can be used as a pre-clinical model to study potential therapeutics.

O005
Retrospective Study of Hematologic Complications in Patients with Localized Intravascular Coagulopathy Undergoing Sclerotherapy

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Purpose: Slow-flow vascular malformations (SFVMs), most commonly most multifocal or extensive venous (VM), venous-lymphatic (VLM) and capillary-lymphatic-venous malformations (CLVM), are associated with a consumptive coagulopathy, termed localized intravascular coagulopathy (LIC), characterized by elevated D-dimer, low fibrinogen, and/or mild thrombocytopenia. Affected individuals have an increased risk for hemorrhage, thrombosis, and progression to disseminated intravascular coagulopathy, particularly with manipulation of the abnormal endothelium of the malformation. In patients with SFVMs, hematologic complications of sclerotherapy and use of low molecular weight heparin (LMWH) as a preventative measure have not been well studied.
Methods: Retrospectively review hematologic complications and LMWH use in patients with SFVMs and LIC who underwent sclerotherapy.
Results: Thirty-nine of 300 vascular patients had SFVMs and LIC (24 with extensive VM/VLM, 9 with multiple VM/VLM, 4 with CLVM, 2 with localized VM/VLM) and underwent a total of 236 sclerotherapy procedures with 86% occurring in individuals under 18 years. All patients had elevated D-dimer; abnormal fibrinogen and platelet count were present in 28% and 25% respectively. LMWH was administered at 0.5mg/kg/dose once daily for 2 weeks before and after sclerotherapy in 85% of cases. No thrombotic complications occurred in children. One adult smoker with history of deep vein thrombosis (DVT) developed pulmonary emboli, presumably from DVT of treated extremity, while on LMWH. No significant pre- or post-operative bleeding events occurred. In 5 patients fibrinogen levels dropped below 100 mg/dL post-sclerotherapy for which cryoprecipitate was administered and no bleeding complications occurred. No intra-op bleeding or thrombotic events occurred.
Conclusion: Prophylactic LMWH use was common in this patient population and did not appear to increase the risk of significant bleeding before, during or after sclerotherapy. In children receiving LMWH, thrombotic complications after sclerotherapy appear rare but may still occur. Prospective studies evaluating peri-procedural LMWH are needed to determine benefit and optimal dosing.

O006
Venous malformations and blood coagulation in children

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Purpose: Venous malformations (VMs) are congenital low-flow lesions with a wide spectrum of clinical manifestations. Increasing number of studies links VMs to coagulation abnormalities, especially to decreased fibrinogen and elevated D-dimer. The condition, termed localized intravascular coagulopathy (LIC), may entail a risk for hematologic complications. However, detailed data on the laboratory variables for coagulation and fibrinolysis activity in VM patients are limited. We addressed this question by systematically analyzing the coagulation laboratory results in pediatric VM patients.
Methods: This retrospective study consisted of 62 pediatric VM patients with detailed laboratory tests for coagulation, fibrinolysis activity, and blood cell counts at a clinically steady phase. Using patient records and MRI we analyzed the clinical and imaging features of the malformations and calculated their correlations with laboratory variables, as well as evaluated coagulopathy related complications and effects of anticoagulant therapies on coagulation abnormalities.
Results: Clinically significant coagulation abnormalities were uncommon. Disseminated intravascular coagulopathy (DIC) did not occur, fibrinogen and platelets being generally normal. However, in addition to elevated D-dimer in 39% of the patients, leukopenia, decrease of FVII and FXIII, and elevation of antithrombin and FVIII were common. Decreased FXIII and elevated D-dimer were associated with large size, deep location, and diffuse and multifocal morphology, whereas elevated FVIII was associated with small size, superficial and confined location, discrete morphology, and less pain. Antithrombin was elevated in 55% of patients without associations with any of the clinical or laboratory variables.
Conclusion: We found novel and diverse associations between coagulation abnormalities and VMs. These findings are not consistent with previous reports and the theory of LIC. Further research exploring blood coagulation, angiogenesis, and genetic basis of VMs is necessitated.

O007
Effect of Sirolimus on Coagulopathy of Slow-flow Vascular Malformations

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Purpose: Stagnant blood flow in slow-flow vascular malformations (VM) can lead to localized intravascular coagulation (LIC) that is characterized by elevated D-Dimer levels, low fibrinogen and decreased platelet count. LIC can lead to localized thrombosis or bleeding which can result in pain and functional limitations. Patients with complex VM are frequently managed with sirolimus, an mTOR inhibitor, which can lead to clinical improvements. It is possible that some of these improvements from sirolimus could be secondary to improvement in the coexisting LIC. This study assessed the use of sirolimus to manage the coagulopathy seen in slow-flow VM.
Methods: Chart review of patients with VM started on sirolimus. Efficacy was objectively assessed through improvement of D-dimer, fibrinogen and platelet count. Three sets of lab values (pre-sirolimus, 1-3 months post-sirolimus, and most recent) were obtained for each patient when available.
Results: 35 patients had been prescribed sirolimus. 18 were excluded based on underlying condition other than slow-flow VM and 1 for inadequate records. 16 patients (13 combined vascular, 3 venous) were included in the study. All 16 had elevated D-dimer levels (median 2.99 mcg/mL FEU, range 0.83-14.65) prior to treatment. 2 patients had an associated low fibrinogen (below 175 mg/dL). With treatment, 14 (87.5%) patients showed an overall decrease in D-dimer levels with an average decrease of 1.52 mcg/mL FEU between pre- and post-sirolimus labs and 1.03 mcg/mL FEU between pre-sirolimus and most recent values. The two patients with low fibrinogen prior to treatment showed a decrease in D-dimer levels (mean decrease of 7.845 mcg/mL FEU) and normalization in fibrinogen (mean increase 83.95 mg/dL) after beginning sirolimus. No patient had thrombocytopenia.
Conclusion: Sirolimus was effective in improving coagulopathy associated with slow-flow VM. Long-term use of this medication in this population may decrease the bleeding and thrombotic complications that these patients experience, especially following invasive vascular procedures.

O008
Efficacy and Safety of Sirolimus in Vascular Malformations Refractory to Standard Care: Preliminary Results of a Phase III Clinical Trial VASE

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Purpose: In 2011, sirolimus was suggested to be efficacious in treatment of vascular anomalies with a lymphatic component. In a pilot study, we subsequently demonstrated efficacy on venous malformations (VMs). In 2016, we set up the VASE trial to assess the efficacy and safety of sirolimus in a large cohort of patients.
Methods: VASE is a prospective, multicentric European phase III cross over clinical trial. 250 patients (adults and infants) with various vascular malformations refractory to standard treatments are being enrolled. Sirolimus is administered continuously for 2 years. Evaluation includes clinical history and examination, Quality of life questionnaire, coagulation analysis, and MRI before and after one year of treatment. Genotyping of tissue biopsies is performed.
Results: Between January 2016 and October 2017, 44 patients (median age 44y; 2y-71y), including 31 VMs, 4 lymphatic malformations (LMs), 5 capillary-venous malformations (CVMs), 1 Klippel Trenaunay syndrome, 1 Blue Rubber Bleb Nevus Syndrome, 1 CLOVES Syndrome and 1 PHTS, were enrolled. Sirolimus was well tolerated with mostly mild and easily manageable side effects. Two patients developed grade 3 asthenia or grade 3 mucositis, and stopped definitively the treatment despite a clinical benefit, which was maintained. There was no complete response, but 89% of patients (n=39) presented a rapid clinical improvement with reduction of pain and/or coagulation abnormalities, decrease in size of lesions, and/or improvement in quality of life. Only 5 patients stopped sirolimus for lack of benefit. Currently, 29 patients have been treated with sirolimus for ≥12 months and 8 for ≥6 months. The 1-year radiological evaluation demonstrated VM reduction ≥10% in 45% of 21 evaluable patients.
Conclusion: Sirolimus showed impressive efficacy in slow-flow vascular malformations, reducing pain and improving functional restraint in the majority of patients. This underscores the results of our earlier pilot study on 20 VMs and other studies on LMs.

O009
ABL kinase inhibitor Ponatinib combined with rapamycin causes regression of murine Venous Malformation

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Purpose: Venous malformations (VMs) arise from developmental defects of the vasculature and are characterized by massively enlarged and tortuous venous channels. VMs grow commensurately leading to deformity, obstruction of vital structures, chronic swelling, bleeding and pain. Most VMs are associated with the activating mutation L914F in the endothelial cell tyrosine kinase receptor TIE2. Therapeutic options for VMs are limited and ineffective while targeted therapy with the mTOR inhibitor rapamycin shows moderate efficacy.
Methods: To identify novel therapeutic targets, we performed an unbiased screening of FDA-approved drugs in human umbilical vein endothelial cells expressing the TIE2-L914F mutation (HUVEC-TIE2-L914F).
Results: We identified three ABL kinase inhibitors that inhibited cell proliferation in HUVEC-TIE2-L914F. We show here that the common target of these inhibitors c-ABL is highly phosphorylated downstream of TIE2-L914F. The ABL kinase inhibitor Ponatinib, when combined with rapamycin, showed a synergistic anti-proliferative effect by promoting cell apoptosis in vitro and leading to vascular channel regression in a 3D fibrin gel assay. In vivo, treatment with Ponatinib combined with rapamycin caused lesion regression in a murine and patient-derived xenograft model of VM. Furthermore, reduced dose of the drug combination was effective in the murine VM model, and minimal side effects were recorded. Analysis of drug combination mechanism showed enhanced AKT inhibition and reduced ERK activity.
Conclusion: This is the first report of a combination therapy with Ponatinib and rapamycin for the treatment of VM.

O010
Initial Experience of Intravascular Sclerotherapy with C-arm Scan under the Guidance of Computer Navigation for Low-flow Vascular Malformations in the Complicated Anatomic Regions of Head and Neck: Report on 8 Procedures

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Purpose: The aim of this study was to report our initial experience combining C-arm scan and computer navigation in the treatment of low-flow vascular malformations in the complicated anatomic regions of head and neck, evaluating the feasibility and security while sharing our gain and loss.
Methods: The study included 8 procedures performed on 6 patients diagnosed as venous malformations (VMs) and lymphatic malformations (LMs), typical low-flow vascular malformations. Three of them presented with intraorbital lesions and the other three with pharyngeal ones. Navigation planning, reconstruction and simulation were performed based on CT and MR utilizing iPlan software. "Image fusion" was proceed to integrate two sets of image into a common model and optimize puncture approaches targeting the lesions while avoiding eloquent areas. Under the guidance of navigation, the accurate intravascular placement of needles, either percutaneous or transoral as planned, was accomplished and confirmed by C-arm scan, followed by delivery of sclerosants such as ethanol or polidocanol. Clinical outcomes, operating time, consistency of images of intraoperative and preoperative planning were analyzed.
Results: Placement of needles within lesions was performed successfully and confirmed in all procedures. Images from Intraoperative C-arm scanning and preoperative navigation simulation matched fundamentally in five procedures and partially in the other three. Operating time was dropped significantly after the first 3 procedures. No procedure-related complications were noted throughout the 3 months.
Conclusion: Intravascular sclerotherapy has been widely recognized as the first line treatment for low-flow vascular malformations. Computer navigation for such soft tissue lesions still relies on the adjacent position targeting on the basis of bones to a great extent. When it comes to the lesions in the complicated anatomic regions of head and neck, our preliminary results have proven computer navigation system with C-arm scan a feasible and relatively safe minimally-invasive technique.

O011
Sclerotherapy For Intramuscular Vascular Malformations: A Single Center Experience

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Purpose: Vascular malformations isolated to skeletal muscles are rare and often debilitating due pain and very challenging to treat. Multi-modal management options include compression garments, medical therapy, sclerotherapy and surgical resection.
The purpose of this study is to review the outcome of the sclerotherapy treatment for the isolated intramuscular vascular malformation in our institution.
Methods: Retrospective review of patients who underwent sclerotherapy for intramuscular venous malformations (IVM) between 2008-2016. Demographics, indications, and clinical follow-up were analyzed.
Results: 20 patients underwent sclerotherapy for IVM. 6 males and 14 females underwent 58 procedures. All patients presented with pain and were treated initially with compression garments. Median age at first treatment was 13 years (+/- 5.06 years). Initial protocol consisted of 2 sclerotherapy procedures with sodium tetradecyl sulfate (STS) within a 2-3 month interval. Median volume of the lesion was 40 cm3 (+/- 28.7), mostly located in the lower extremities (15/20). Median number of treatments was 2 (+/- 1.95). Treatment prior to puberty resulted in a median symptom-free time of 4 years (+/- 2.18) while after puberty resulted in a symptom-free time of 2 years (+/- 2.28). 2 patients had an underlying coagulopathy and were admitted for observation and peri-procedural Lovenox. No procedure related complications were noted with a median follow-up of 4 years (+/- 2.27).
Conclusion: IVMs are rare but can be incapacitating secondary to pain. Sclerotherapy is a useful minimally invasive procedure generally requiring at least two consecutive treatments. Treatment of patients prior to puberty appears to provide a more durable result and surgical resection may be avoided.

O012
Venous Malformations are Proliferative: Clinical Implications

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Purpose: Venous malformations (VMs) are proposed to be fully formed at birth and biologically quiescent. However, many VMs progressively enlarge, worsen over time, and recurrence can occur after treatment, suggesting VMs are biologically active. WehaveisolatedaCD133+ cell from VMs (VMECs) with progenitor and endothelial cell (CD31+/VE-CADHERIN+) characteristics that recapitulate the VM phenotype in a murine model. We hypothesize that VMs are hyperplastic lesions arising from a proliferative pool of VMECs.
Methods: Paraffin sections of VMs, control adult and neo-natal skin were immune stained for proliferative (Ki67) and EC (CD31) markers. EC proliferation (percentKi67+/CD31+ ECs) and average EC length were determined for fields/tissue. VMECs were compared to control human neo-natal dermal microvascular ECs (HMVEC). ERK activation was determined by Western blotting and immunofluorescent staining with antibodies against phospo-ERK (pERK) and total ERK. To determine proliferation, 4x 104VMECsand HMVECswereseededon6-welldishes in triplicate and grown in basal medium. Average cell number per well was determined by cell counter daily for 4 days. Statistical significance was determined by One-Way-ANOVA followed by pair-wise T-Test with p-value<0.05 considered significant.
Results: Relative to ECs in control skin, VMs had a significant increase in Ki67+ ECs ($p<0.0001$). Average EC length did not differ between VMs and controls (Figure1C). VMECs had increased ERK activation compared to HMVECs. VMECs grew significantly faster than control HMVECs at Days 3 and 4 ($p<0.05$).
Conclusions: Increased EC proliferation (not EC length) suggests that the dilated vessels in VMs arise due to EC hyperproliferation, not hypertrophy. VMECs had significantly increased EC proliferation compared to controls, possibly downstream of increased ERK activation. These results suggest that VMs are biologically active/proliferative. A strategy of using anti-proliferative medical therapy, such as MEK/ERK inhibitors, may be effective in treating VMs.

O013
The European Reference Network (ERN) for rare vascular diseases (VASCERN): VASCA-working group - towards better management of vascular anomaly patients

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Purpose: Rare diseases, including Vascular Anomalies, need multidisciplinary centers for quality management. It is essential for diagnosis, evaluation of prognosis and treatment options, and for clinical and translational research. The European Commission established 24 European Reference Networks for Rare Diseases in 2017. VASCERN is one of them, and vascular anomalies are the topic of one of its five disease-focused working groups (VASCA-WG). The ERN networks are set out to further improve access to diagnosis and treatment, and to improve research, including clinical trials.
Methods: The VASCA-working group currently includes 7 endorsed multidisciplinary Vascular Anomaly Centers and 2 Collaborating Centers. Work is mainly done by monthly virtual meetings and two annual face-to-face meetings. During 2017, the group focused on: 1) Nomenclature and codes (ICD11 and Orphanet), 2) Registry (FAIR principal), 3) Outcome measures, 4) Educational materials (including Dos and Don'ts documents and "patient pathways") and 5) Discussions on Difficult Cases.
Results: 1) Critical overview of currently widely used nomenclatures was performed, and suggestions to ICD11 and Orphanet are being developed, 2) A virtual registry using 16 minimal criteria is set up following FAIR principals, 3) Outcome measures were developed as part of the OVAMA study, 4) local patient materials (leaflets and on-line films) are being translated for distribution in all VASCA ERN countries, and visibility is guaranteed via VASCERN web-site (http://vascern.eu/), Facebook, YouTube and Twitter, and 5) a Clinical Patient Management System (CPMS) was set up by the EU allowing secured sharing of patient data between professionals for consultation and discussion.
Conclusion: The networking of Expert Centers via ERN already has tangible results for vascular anomaly patients. While further development of the aforementioned projects is continued, the VASCA-WG also aims to generate expert opinions on management, and foster collaborative (clinical) research in the area of vascular anomalies.

O014
Outcome measurement instruments for peripheral vascular malformations (OVAMA project)

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Purpose: The Outcome measures for VAscular MAlformations (OVAMA) group reached consensus on the core outcome domains for the core outcome set (COS) for peripheral vascular malformations (venous, lymphatic and arteriovenous malformations). However, it is unclear which instruments are available and suitable to measure these domains. The objective of this study was to identify all outcome measurement instruments for peripheral vascular malformations, and to evaluate their measurement properties.
Methods: With an initial literature search, we identified outcomes and outcome measurement instruments previously used in prospective studies on vascular malformations. In a second search, we retrieved studies on measurement properties of instruments that were either developed for vascular malformations, or used in prospective studies. If the latter instruments were not developed or validated for vascular malformations, we additionally searched for studies on measurement properties in clinically similar diseases (vascular or lymphatic diseases and benign tumors). We assessed the methodological quality of these studies according to the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) methodology, and evaluated the quality of the investigated measurement properties.
Results: The first search yielded twenty-seven prospective studies, none of these using disease-specific instruments for vascular malformations. The second search included twenty-two development and/or validation studies, concerning six instruments. Only the Lymphatic Malformation Function Instrument was developed specifically for vascular malformations. Other instruments were developed and/or partly validated for clinically similar diseases.
Conclusion: Additional research on measurement properties is needed to assess which instruments have the potential to be included in the COS. The results of this study inform the process of selection and/or development of these instruments.

Scientific Session 2: Vascular Malformations 1

O017

Wall shear stress in the feeding artery of a superficial arteriovenous malformation is an early and reliable marker of progression.

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Purpose: Blood pressure and flow are responsible for permanent remodeling aiming to adapt vessels to local hemodynamics. The wall shear stress (WSS) is the main stimulus of arterial remodeling responsible for adaptation to flow changes. Under stable physiological hemodynamic conditions, WSS is 8-10 dyne/cm², according to the size of conduit arteries. Superficial arteriovenous malformations (AVM) are characterized by abnormally developed vascular networks. We aimed to test in (AVM) the ability of WSS to be a vascular early and sensitive marker of tumor progression.
Methods: In a prospective blind study, 22 patients with AVM of the lower part of the face (12 stable, 10 progressive) were included and compared to 15 previously operated patients for AVM resection and 15 healthy controls. All patients had Doppler-ultrasound examination in the feeding arteries with WSS calculation in the internal, external carotid and facial arteries.
Results: (mean±SD) In the ipsilateral external carotid artery, WSS allowed us to distinguish between stable (9.2±1.4dynes/cm²) and progressive AVM (15.9±3.9dynes/cm², p<0.001), cut-off: 11.45dynes/cm² (sensitivity 90%, specificity: 100%). In the ipsilateral facial artery, WSS in stable AVM was 25.7±7.2dynes/cm² and progressive AVM 55.0±15.2dynes/cm² (p<0.001), cut-off: 31.05dynes/cm² (sensitivity 100%, specificity: 84%). In addition, the contralateral external carotid and facial arteries showed similar but lower modifications in active progressive AVM patients, due to the presence of numerous anatomic side to side anastomoses. Internal carotid arteries did not present any side to side or group difference.
Conclusion: A single Doppler-ultrasound measurement including WSS assessment in the feeding artery upstream from the AVM can predict progression.

O018

The use of Bleomycin and a Thrombin –Gelatin Hemostatic Matrix in the Treatment of Recurrent or Residual High Flow Arteriovenous Malformations of the Head and Neck

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Purpose: High flow AVMs have not been considered suitable for bleomycin embolization due to their high flow and therefore reduced contact time between bleomycin and the pathological endothelium of the nidus. We describe an embolization technique for recurrent and/or residual high flow AVMs using bleomycin mixed with a thrombin–gelatin hemostatic matrix (SurgifloTM) and contrast material that permits occlusion of the abnormal vessel and retains the bleomycin within the malformation.
Methods: Retrospective chart review of the clinic notes, photographs, previous and current angiographic studies, in patients with difficult recurrent and/or residual AVMs of the head and neck (H&N). To permit bleomycin to have sufficient contact time with the pathological endothelium, the nidus was accessed by direct percutaneous (DP) puncture of the venous outflow just beyond the nidus. Once the correct location was confirmed, a combination of SurgifloTM , bleomycin (1mg/cc, max dose 15 mg), and contrast material was injected in a retrograde fashion into the nidus. The SurgifloTM obstructed the nidus and outflow which permitted prolonged bleomycin exposure of the nidus endothelium.
Results: All twelve adult patients improved after treatment. A reduction of nidus size, healing of ischemic ulceration, decrease or elimination of bleeding episodes, decrease in pain, and improvement in angiographic appearance of the AVM were noted. In 2 patients, there was significant swelling which partially resolved in one patient. No other side effects such as ulceration, necrosis, or neuropathy were noted. There was an average of 3 sessions per patient. Average follow up was 27 months.
Conclusion: Preliminary results are very encouraging. This technique permits prolonged tissue contact with bleomycin in high flow AVMs permitting a biological effect as opposed to the purely mechanical occlusion which occurs with other embolic techniques. This technique opens up new therapeutic possibilities for otherwise incurable, and unmanageable high flow lesions.

O019
Efficacy of an AVM Classification System that Directs Endovascular Therapies Accurately

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Purpose: To determine if AVM angioarchitecture characteristics can be predictive and direct specific curative endovascular procedures accurately and consistently to treat high-flow malformations.
Methods: Angiographic analysis of high-flow vascular malformations determined 4 major angioarchitectures. Type I: Direct arterial/arteriolar to vein/venule connection; e.g., as commonly seen in pulmonary AVF, congenital renal AVF, etc. Type II: Arterial/arteriolar connections to a "nidus" that then have several out-flow veins with no intervening capillary beds in any of the vascular interconnections. Type IIIa: Arterial/arteriolar connections to an aneurysmal vein ("nidus" is the vein wall) that drains into a dominant out-flow vein with no intervening capillary bed in these connections. Type IIIb: Same angioarchitecture as Type IIIa, except that there are more than one (several) out-flow veins. Type IV: "Infiltrative" form of AVM whereby innumerable micro-arteriolar branches fistulize through a tissue (e.g., ear) totally infiltrating it, shunting into multiple out-flow veins. Capillary beds also exist in the tissue and are mixed with the innumerable AVFs. Without the capillaries the tissue could not be viable, therefore must be present.
Results: Type I: Can be effectively treated with mechanical devices; e.g., coils, Amplatzer Plugs, etc. Type II: Can be effectively treated with ethanol embolization. Type IIIa: Can be effectively treated by transcatheter ethanol, retrograde vein catheter access or direct puncture access of the aneurysmal vein and treatment with ethanol and coils, or even by coils alone. Type IIIb: Can be effectively treated as above, but can be more challenging by the vein route as more veins (not a single out-flow vein) require closure. Type IV: Can be effectively treated by transcatheter or direct puncture of the innumerable microfistulous AVFs by embolization with 50% -50% ethanol non-ionic contrast mixture.
Conclusion: This never before reported classification system has a direct impact on determining the curative endovascular and direct puncture embolization procedures and also determines the embolic agents that will successfully treat complex AVMS in the body.

O020
Extracranial artreriovenous malformations: a classification based on clinical, surgical and endovascular features.

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Purpose: Arterio-venous malformations (AVMs) show a clinical behavior that resembles that of neoplasms. It is crucial then to have a comprehensive staging system. This could allow a safe treatment planning and standardized communication between different specialists. The aim of the Authors is to provide a new staging system, encompassing clinical, surgical-anatomical and endovascular radiologic features.
Methods: We propose an original staging system for extracranial AVMs, named SECg. The staging system is divided in 3 sections, named S, E and C. "S" stays for Surgical-Anatomical. Here the physical features of the AVM and the involvement of different anatomical structures are described. "E" describes the endovascular characteristics of the AVM (ArterioVenous, ArterioloVenous, ArterioloVenular). "C" is used to address clinical features and-or local or general complications. Finally, "g" define if the malformation is growing or not, indicated respectively by g+ or g-.
Results: Following the S classification we can identify an AVM infiltrating or not noble or vital anatomical structures. Therefore we are able to define a curable or not curable patient and to predict an eventual morphological or functional damage following the surgery. With the E classification we can establish if an endovascular treatment is suitable or not in conjunction with surgery. Finally with the C and g classification, it can be defined the indication, relative to absolute, or the contra-indication to the treatment. The SECg staging system has been a valid mean for the treatment planning of all our AVMs patients.
Conclusion: We believe that a reliable and widely accepted staging system should allows to describe how far the disease has progressed, to drive for better treatment planning and to infer about prognosis. Then, importantly, it should enable adherent communication between clinicians of different specialties.

O021

Germline Loss-of-Function Mutations in EPHB4 cause a Second Form of Capillary Malformation–Arteriovenous Malformation (CM-AVM2) deregulating RAS-MAPK signaling

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Purpose: Most AVMs are localized and occur sporadically; however they also can be multifocal in autosomal dominant disorders, such as Hereditary Hemorrhagic Telangiectasia (HHT) and Capillary Malformation–Arteriovenous Malformation (CM-AVM). Previously, we identified RASA1 mutations in 50% of patients with CM-AVM. Herein we studied non-RASA1 patients to further elucidate the pathogenicity of CMs and AVMs.
Methods: We conducted a genome-wide linkage study on a CM-AVM family. Whole exome sequencing was also performed on 9 unrelated CM-AVM families. We identified a candidate-gene and screened it in a large series of patients. The influence of several missense variants on protein function was also studied in vitro.
Results: We found evidence for linkage in two loci. Whole-exome sequencing data unraveled four distinct damaging variants in EPHB4 in five families that co-segregated with CM-AVM. Overall, screening of EPHB4 detected 47 distinct mutations in 54 index patients: 27 lead to a premature stop codon or splice-site alteration, suggesting loss of function. The other 20 are non-synonymous variants that result in amino-acid substitutions. In vitro expression of several mutations confirmed loss of function of EPHB4. The clinical features included multifocal CMs, telangiectasias, and AVMs.
Conclusion: We found EPHB4 mutations in patients with multifocal CMs associated with AVMs. The phenotype, CM-AVM2, mimics RASA1-related CM-AVM1 and also HHT. RASA1 encoded p120RASGAP is a direct effector of EPHB4. Our data highlights the pathogenetic importance of this interaction and indicts EPHB4-RAS-ERK signaling pathway as a major cause for arterio-venous malformations.

O022

Expanding the phenotypic spectrum of cases with an EPHB4 mutation

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Purpose: Loss of function mutations in EPHB4 were recently shown to cause capillary malformation-arteriovenous malformation 2 (CM-AVM2). The CM-AVM2 phenotype was described as mimicking the RASA1-related disorders phenotype and also Hereditary Hemorrhagic Telangiectasia (HHT), as clinical features included multifocal CMs, telangiectasias, and AVMs. Several cases reportedly had recurrent epistaxis, another clinical feature that overlaps with HHT. Purpose: Based on the clinical overlap of CM-AVM2 and HHT, the goal of our study was to determine if patients with vascular malformations suspected to have HHT who tested negative for HHT causative genes (ENG, ACVRL1, and SMAD4) have an EPHB4 mutation.
Methods: Eighty-seven unrelated cases suspected to have HHT with negative HHT molecular diagnostic testing, were evaluated using exome sequencing or a custom next generation sequencing panel designed to capture the coding regions of EPHB4. Samples were sequenced using 2x100 PE reads on a HiSeq2500 instrument and data were analyzed.
Results: EPHB4 variants were identified in 10.3% (9/87) of cases suspected to have HHT. Seven cases had a novel pathogenic EPHB4 mutation that disrupted splicing or caused a stop codon. Two cases had an EPHB4 variant of uncertain significance. The majority of cases had epistaxis (8/9 cases) and telangiectasia (7/9 cases; some with a halo and in anatomical regions atypical for HHT). A family history of the disorder was reported in 4/9 cases. Two of nine cases (22.2%) had an AVM, which is similar to previous reports (18%). Clinical and molecular findings for these cases will also be presented to further expand the phenotype.
Conclusion: Our results highlight the importance of evaluating EPHB4 as part of the clinical differential for HHT and other vascular malformation syndromes and show that EPHB4 should be included in HHT panel testing to increase clinical sensitivity.

O023

EPH-B4 REGULATES VENOUS ADAPTIVE REMODELING IN ARTERIOVENOUS FISTULAS VIA AN AKT1-DEPENDENT MECHANISM

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Purpose: Arteriovenous malformations (AVM) and fistulas (AVF) lead to adaptive remodeling of the venous outflow in response to pathologic, fast-flow, arterialized shunts. These adaptive changes can propagate the shunt resulting in morbid venous hypertension, capillary steal, and cardiovascular overload. The molecular mechanisms that mediate venous remodeling can serve as potential therapeutic targets but are not currently well-understood. We hypothesized that the embryonic venous determinant Eph-B4 mediates adaptive remodeling of the venous outflow in response to pathologic arteriovenous shunts
Methods: We used a mouse aortocaval AVF model to determine the effects of Eph-B4 function on venous remodeling
Results: The remodeling vein was characterized by increased expression of both Eph-B4 as well as Ephrin-B2, the embryonic determinant of arteries. Stimulation of Eph-B-mediated signaling with Ephrin-B2/Fc showed augmented shunt patency with less venous wall thickness. Mutagenesis studies showed that tyrosine-774 is critical for Eph-B4 signaling and administration of inactive Eph-B4-Y774F diminished shunt patency via increased venous wall thickness. AKT1 expression was also increased in AVF; AKT1 knockout mice showed reduced fistula venous diameter and wall thickness. In AKT1 knockout mice, stimulation of Eph-B signaling with Ephrin-B2/Fc showed no effect on venous remodeling.
Conclusion: Venous remodeling in a fast-flow, arterialized shunt is associated with acquisition of dual arteriovenous identity; increased Eph-B activity stimulates shunt patency. Inhibition of AKT1 function abolishes Eph-B-mediated venous outflow remodeling suggesting that EphB4 regulates venous adaptation through an AKT1-mediated mechanism.

O024
GENETIC TESTING IN THE DIAGNOSTIC WORKUP OF VASCULAR ANOMALIES

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Purpose: Differential diagnosis of vascular malformations can be difficult. VMs may mimic GVMs, plaque-like GVMs CMs, CMs may be isolated lesions or part of CM-AVM, etc. The identification of genetic causes for many vascular malformations has opened the door for systematic genetic testing as an aide in clinical assessment of patients.
Methods: Genetic analyses were performed on >3500 patients. DNAs were collected from >2900 blood samples, and from >1800 vascular anomaly tissues obtained during surgical treatments or as biopsies. Mutations were screened for by sequencing. A panel approach allowing high coverage via NGS was used to identify low frequency somatic mutations in heterogeneous tissues samples. Clinical diagnosis was compared to the genetic results.
Results: A causative mutation was identified in >1200 samples. 750 were germline mutations and over 450 were somatic mutations identified in 37,5% (450/1200) of tissues. Germline mutations were identified in patients with family history and/or multifocal lesions, or primary lymphedema. Somatic mutations underscored sporadically occurring phenotypes. PIK3CA was the most frequently mutated: >80% of LMs, CLVMs, and CLOVES, and 20% of VMs. Somatic TIE2 mutation was identified in 60% of VMs, and GNAQ or GNA11 mutation in 70% of SWS and CMs. The genetic result fit with the clinico-radiologic diagnosis in most cases (+/- 1100/1200 = 92%), but resulted in revised diagnosis in others. It was helpful for differential diagnosis of lesions of small size, deeper localization and unusual presentation. Interestingly, series of lesions without a mutation were identified. They often clinically differed from those with a mutation.
Conclusion: Genetic testing has become a valuable clinical tool for management of vascular anomalies. It is useful to confirm and guide towards correct diagnosis, to recognise rare entities, and to identify persons with familial risk. Genetic testing also allows to identify unclassified entities, which need further clinico-genetic characterisation.

O025
Clinical Utility of a NGS panel in the Diagnosis of Vascular Malformations Syndromes

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Purpose: Vascular malformations are localized structural defects of the vasculature named for the type of vessel affected such as venous malformations (VM) and capillary malformations (CM) or a combination of two different vessels such as in arteriovenous malformations (AVMs). Inherited disorders featuring vascular malformations such as hereditary hemorrhagic telangiectasia (HHT) and capillary malformation-arteriovenous malformation (CM-AVM) syndrome often have overlapping phenotypes that can be difficult to distinguish clinically. Purpose: Because of the genetic complexity and phenotypic overlap of disorders featuring vascular malformations, we developed a custom designed next-generation sequencing (NGS) panel assay to rapidly identify mutations in 14 genes that cause vascular malformations (ENG, ACVRL1, SMAD4, GDF2, RASA1, PTEN, TIE2/TEK, GLMN, KRIT1/CCM1, CCM2, CCM3, BMPR2, CAV1, and KCNK3).
Methods: NGS hybridization capture and array-comparative genomic hybridization (aCGH) were used to interrogate 14 vascular malformation-causative genes in genomic DNA from a series of 122 patients with a vascular anomaly submitted for clinical testing.
Results: Twenty-five individuals had a pathogenic mutation of which 12 (48%) were novel. Twelve individuals had a variant of uncertain significance. Pathogenic mutations were most prevalent in RASA1 (10 cases) followed by GLMN (5 cases). Most cases with a RASA1 mutation were not diagnosed by the referring

physician as having CM-AVM, and three cases were "suspected to have HHT" instead. Two cases with suspected CM-AVM syndrome had a large RASA1 deletion, giving an overall deletion/duplication rate of 5.4% (2/37) among positive cases. The phenotypic spectrum of these disorders is expanded by the clinical and molecular delineation of several complex cases. For example, a patient with Parkes Weber syndrome (leg AVM/AVF and suspected lymphangioma) was found to have a pathogenic mutation in both RASA1 and PTEN.
Conclusion: Our data suggest that NGS multi-gene panel testing is beneficial for the molecular diagnosis of cases with complex vascular phenotypes.

O026
Molecular Diagnosis of Mosaic Skin Development Disorders using Next Generation Sequencing

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Purpose: Next Generation Sequencing (NGS) has allowed detection of low-level post-zygotic mutations in mosaic skin development disorders, mainly involving genes of the RAS-MAPK and PI3K-AKT-MTOR pathways amenable to treatment with targeted therapy such as MTOR inhibitors. We have developed an efficient molecular diagnostic approach to skin mosaic disorders using targeted sequencing and whole exome sequencing (WES) for negative cases.
Methods: We have collected DNA from 798 individuals with various mosaic skin development disorders in the M.U.S.T.A.R.D. (Mosaic Undiagnosed Skin Traits And Related Disorders) cohort. A total of 651 fresh skin biopsies were obtained. Depending on the clinical phenotype (overgrowth, vascular, epidermal, or pigmentary skin features), specimens underwent either a Targeted Ultra-Deep Sequencing search for mutations in candidates genes (TUDS; 1000-5000X; AKT1/2/3, PIK3CA, MTOR, GNA11, GNAQ, HRAS, KRAS, NRAS, KRT1, KRT10, TEK, FGFR1/2/3) or Whole Exome Sequencing (WES) using a pipeline tailored for detection of mosaic variations. For 42 patients without phenotypic clues to candidate genes and 25 with negative TUDS, WES (150-200X, n=26) was performed either pairwise (patient skin/blood) or on trios (patient skin/parents blood, n=41).
Results: After TUDS of 588 specimens, 310 patients (53%) were found to carry a post-zygotic mutations in affected tissue, mainly in the PIK3CA (66,4%) or GNAQ - GNA11 (14,3%) genes, always in patients affected with cutaneous vascular malformations or tumours. Analysis of 1 to 4 candidate genes was sufficient to detect a mutation in 94.4% of positive cases, whereas in TUDS-negative mosaic patients , WES as a second step found mutations in 5 novel genes so far.
Conclusion: Our results show a pretty good diagnostic performance for NGS in skin mosaic disorders, particularly with vascular component, and actual involvement of few candidate genes. Diagnostic efficacy strongly depends on accurate clinical appraisal of the phenotype. Proper location of skin biopsy on affected sites also appears as crucial, since biopsy on unaffected skin may explain false negative results.

O027
ISSVA Classification of Vascular Anomalies. 2018 Update Proposal.

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Purpose: The expanded ISSVA classification of vascular anomalies was adopted in Melbourne in 2014. Although many aspects of this classification have been implemented in clinical practice, it has also been criticized. Additionally, since 2014 there are newly recognized vascular anomalies and genetic information. We aim to present consensus changes and additions that could be included in the classification.
Methods: The ISSVA Scientific Committee and Board researched and reviewed any new data on vascular anomalies obtained from the literature as well as the criticisms received on the 2014 classification.
Results: The following topics were discussed: 1 the inclusion of a number of vascular tumors, mainly dermatologic, in the tumor section; 2 possible restriction of the use of the name "hemangioma" for infantile hemangioma; 3 inclusion of intramuscular hemangioma in the tumor, malformation, or provisional section; 4 inclusion of the geographic vs. reticular concept in the capillary malformations section; 5 capillary nature

of some telangiectasia; 6 inclusion of the so called acquired progressive lymphangioma in the lymphatic malformation section; 7 inclusion of "verrucous hemangioma" in the venous malformation section and the name to be used; 8 inclusion of the newly described familial intraosseous vascular malformation in the same section; 9 inclusion of fibroadipose vascular anomaly, sinusoidal hemangioma and acral arteriovenous "tumor" in the provisional section; 10 inclusion of the capillary malformation of the lower lip, lymphatic malformation of the face and neck, asymmetry and partial/generalized overgrowth (CLAPO) in the "associated with other anomalies" section; 11 the inclusion of newly described causal genes in the genetic appendix. While consensus was obtained on several topics, others still remain controversial.
Conclusion: We have addressed the major critiques of the 2014 ISSVA Classification, and we present this work for discussion of the controversial areas, in advance of a vote at the upcoming General Assembly, to adopt this newly revised version.

Thursday, 31 May 2018

Scientific Session 3: Vascular Malformations 2

O028
Endothelial Cell Lineage Tracing in Cerebral Cavernous Malformations: A Modification of the "Two-Hit" Mutation Model of CCM Pathogenesis.
Matthew Detter (Duke University); Douglas Marchuk (Duke University)

Purpose: Cerebral cavernous malformations (CCMs) are dilated, hemorrhagic capillaries that form multicavernous vascular lesions devoid of neural parenchyma within the central nervous system. CCMs can occur sporadically and also via an autosomal-dominant mode of inheritance, where evidence suggests that the malformations are seeded by a somatic mutation in the remaining wild-type copy of the gene mutated in the germline. However, this Knudsonian "tumor-supressor" model of lesion pathogenesis does not address whether the lesions consist entirely of a clonal expansion of the mutant cells, and whether more than one mutation is required for the complex multicellular architecture of the vascular malformation.
Methods: Using a Confetti (Brainbow) fluorescent protein expression construct and floxed alleles of the Ccm1 gene, we simultaneously generated mice with individual endothelial cell (EC) clones that have lost both copies of Ccm1 while expressing one of four different fluorescent proteins, thereby labeling the somatically mutated cells and all their descendants. Confocal imaging and 3D visualization/reconstruction of the resulting CCMs in isolated brain tissue identified the mutant cells descendent from the deletion (mutation) event.
Results: The predominant observation is that each CCM, or at least each cavern of each malformation, consists of ECs expressing a single color; thus, descendants of a single mutation event.
Conclusion: Individual CCM caverns appear to be clonal in that a single somatic mutation is found within the ECs lining the cavern. However, only a minority of the ECs lining the cavern harbor the initial somatic mutation. Thus, CCM pathogenesis includes both clonal events (a single mutation and some expansion) and recruitment or incorporation of wild-type ECs into the developing vascular malformation.

O029
Rapamycin not shown to inhibit LM growth in a mouse xenograft model.
Tony Penington (Royal Children's Hospital, Melbourne); Zerina Lokmic (School of Nursing, University of Melbourne); Nerida Sleebs (Murdoch Children's Research Institute)

Purpose: Rapamycin is increasingly used as a treatment for low flow vascular malformations. Many patients experience improvement in symptoms, but reduction in size of the lesion has been less commonly observed. It may be that early treatment, such as early in life or immediately post operatively would prevent growth of lymphatic malformation.
Methods: The effect of rapamycin treatment on the growth of lymphatic malformations was tested in a mouse xenograft model. Lymphatic malformation endothelial cells (LMECs) derived from three separate human lesions were seeded into mouse chambers in Matrigel. Tissue was harvested at three timepoints – 7, 14 and 28 days. Half of the animals were treated with rapamycin either at high dose or to human therapeutic levels for the duration of the study. The remaining animals were injected with saline only. Growth of lymphatic malformation was quantified by random point counting of histological sections from each chamber, expressed as the proportion of points in D2-40 positively stained vessels to total count. Data was analysed by multiway ANOVA with variables of cell source, timepoint and treatment versus control.
Results: D2-40 positive vessels were identified in most chambers but there was no significant reduction in the number of lymphatic structures in rapamycin treated mice compared to controls.
Conclusion: Although rapamycin suppresses the growth of LMEC in vitro at very low levels, no evidence was found to support an effect of rapamycin in supressing the growth of lymphatic malformation in vivo in this animal model. This is in a situation where lesions are actively growing, so the drug would be expected to be most effective. Although rapamycin can improve symptoms of lymphatic malformations, its effect at therapeutic levels in supressing growth may be limited. Alternative mechanisms by which rapamycin provides relief of symptoms may be more important.

O030
Activation Of AKT In Tissue Endothelial Cells & Elevated Serum ANG-2 levels in Patients With Capillary Lymphatic Venous Malformations

Tim LeCras (Cincinnati Children's Hospital); Jillian Goines (CCHMC); patricia pastura (CCHMC); Paula Mobberley-Schuman (Cincinnati Children's Hospital Medical Center); Megan Metcalf (CCHMC); Denise Adams (Boston Children's Hospital); Adrienne Hammill (Cincinnati Children's Hospital Medical Center); Elisa Boscolo (Cincinnati Children's Hospital)

Purpose: Capillary Lymphatic Venous Malformations (CLVM) occur in patients with Klippel-Trenaunay syndrome (KTS) and Congenital Lipomatous Overgrowth-Vascular malformation-Epidermal nevi-Spinal anomaly Syndrome (CLOVES). Mutations in the phosphatidylinositol-4,5-bisphosphate 3-kinase (PI3K), catalytic subunit alpha (PIK3CA) gene have been identified in tissue from KTS and CLOVES patients. Whether mutations are present in the endothelial cells (EC) of CLVM and if there is hyperactivation of the PI3K-Akt-mTOR pathway is unclear.
Methods: We isolated endothelial cells (EC) from tissue resected during debulking surgery or from fluid obtained by sclerotherapy procedure. Patient-derived EC were selected by CD31-conjugated immuno-magnetic beads and were passaged and stained for CD31 and lymphatic EC (LEC) marker PROX-1. Western blot analysis of EC lysates was performed for VEGFR2, Prox-1, podoplanin, VEGFR3. DNA sequencing was performed for PIK3CA mutations. Phosphorylated AKT (Thr308 and Ser473), total AKT, phosphorylated ERK-1/2 and total ERK-1/2 were also assessed and compared to levels in normal lymphatic EC (LEC), human umbilical vein EC (HUVEC), and HUVEC transfected with constitutively active TIE2 mutant (p.L914F). ELISA analysis for angiopoietin-2 (ANG-2) and angiopoietin-1 (ANG-1) was performed using serum from patients (n=15) and controls (n=53).
Results: All EC isolated from CLVM expressed VEGFR2, whereas levels of LEC marker proteins PROX-1, podoplanin and VEGFR3 varied between patients. PIK3CA mutations [p. E454K (n=2), E545A (n=1), H1047R (n=2)] were present in all patients. Phosphorylated AKT (Thr308 and Ser473) levels were higher in the EC from CLVM patients compared to normal LEC and HUVEC. Phosphorylated ERK-1/2 levels were not abnormal. Levels of ANG-2 were higher while ANG-1 lower in the serum of CLVM patients. The ratio of serum ANG-2/ANG-1 was significantly higher in CLVM patients and receiver operating curve analysis showed an area under the curve of 0.90.
Conclusion: AKT is highly activated in EC isolated from the lesions of CLVM patients with PIK3CA mutations. Blood ANG-2/ANG-1 levels may be a useful biomarker for CLVM.

O031
Laser Ablation of Lymphatic Malformation Using Nanoparticle Targeted Therapy

Ravi Sun (University of Arkansas for Medical Sciences); Ekaterina Galanzha (University of Arkansas for Medical Sciences); Dmitry Nedosekin (University of Arkansas for Medical Sciences); Haihong Zhang (University of Arkansas for Medical Sciences); Ting Wei (University of Arkansas for Medical Sciences); Zerina Lokmic (The University of Melbourne); June Wu (Columbia University); Tony Penington (Royal Children's Hospital, Melbourne); Vladimir Zharov (University of Arkansas for Medical Sciences); Gresham Richter (University of Arkansas for Medical Sciences, Arkansas Children's Hospital Inc.)

Purpose: Lymphatic Malformation (LM) lacks a chromophore, rendering clinical laser therapy ineffective. To change this, by using nanoparticles conjugated to markers of lymphatic endothelium, we aim to create a tool that will selectively target lymphatic endothelium of the lesions, and serve as a guide for effective laser ablation of the malformations. This study investigates the labeling of LM lymphatic endothelial cells (LM-LECs) with podoplanin (PDPN)-conjugated gold nanorods (GNR) and ablation with laser treatment.
Methods: LM-LECs were isolated from human LM using CD34- and CD31+ magnetic bead selection. LM-LEC identity was confirmed by detection of lymphatic markers in isolated LM-LECs by real time RT-PCR and immunocytochemistry. Cells were labeled with PDPN-conjugated GNR having high absorption in near infrared range (maximum 1064 nm), a "window" transparency of biotissues. Labeling was assessed by dark-field and photothermal microscopy. Ablation was performed using a 1064 nm pulsed laser and assessed through visual inspection of cell membrane damage.
Results: LM-LECs were positive for lymphatic endothelial cell markers LYVE1, PROX1, VEGFR3, and PDPN by RT-PCR and immunocytochemistry. Analysis of dark-field images demonstrated 36.7% (N=95) of LM-LECs were labeled with an incubation parameter of 10^5 GNR/cell compared to 38.0% labeling (N=117) with 10^6 GNR/cell (p=0.81). Photothermal microscopy on single LM-LECs confirmed GNR labeling. Our pilot in vitro studies provided experimental evidence that GNR-labeled LM-LECs can be completely ablated with a single laser pulse compared with no change to the negative control.
Conclusion: Labeling of LM-LECs with PDPN-conjugated gold nanorods facilitates successful laser ablation and suggests an improved approach to targeted treatment of LM with laser technology. This study is a proof of concept and is the first step in developing a clinical laser treatment for effective ablation of LM.

O032

Excessive PI3K/mTOR signaling causes lymphatic hyperplasia and dysfunction in mice

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Purpose: Somatic activating mutations in PIK3CA have been identified in patients with lymphatic malformation (LM) and patients with generalized lymphatic anomaly (GLA). The objective of this study was to characterize the effect of excessive PI3K signaling in lymphatic endothelial cells on the structure and function of lymphatics.
Methods: We used the Cre-loxP system to express an active form of PIK3CA (PIK3CAH1047R) in lymphatic endothelial cells in mice. LSL-Pik3caH1047R (control) and Prox1-CreERT2;LSL-Pik3caH1047R mice were injected with tamoxifen on postnatal days 31, 33, 35, 39, and 42. Tissues were collected an analyzed from mice 4 weeks and 8 weeks after their last tamoxifen injection. Lymphatic vessel function was assessed in LSL-Pik3caH1047R and Prox1-CreERT2;LSL-Pik3caH1047R mice by Evans blue dye (EBD) lymphangiography. Prevention and intervention studies with rapamycin (4 mg/kg; 5x week) were also performed with Prox1-CreERT2;LSL-Pik3caH1047R mice.
Results: We found that Prox1-CreERT2;LSL-Pik3caH1047R mice had hyperplastic lymphatic vessels in their skin. Surprisingly, Prox1-CreERT2;LSL-Pik3caH1047R mice also had lymphatic vessels in their bones. EBD lymphangiography revealed that lymphatics in Prox1-CreERT2;LSL-Pik3caH1047R mice did not function properly. We found that rapamycin prevented lymphatic hyperplasia and dysfunction in Prox1-CreERT2;LSL-Pik3caH1047R mice. Amazingly, rapamycin also restored lymphatic function in Prox1-CreERT2;LSL-Pik3caH1047R mice with established disease.
Conclusion: Together, our data show that excessive PI3K signaling causes lymphatic hyperplasia and dysfunction by inducing aberrant mTOR signaling. In the future, Prox1-CreERT2;LSL-Pik3caH1047R mice could be used to develop a better understanding of the pathogenesis of LM/GLA and to test new therapies for these devastating diseases.

O033

Gene Expression Detected in Peripheral Blood of Patients with Lymphatic Malformation

Joyce Teng (Stanford University); Kavita Sarin (Stanford); Taehan Kim (Yale University); Ramie Lekwuttikan (Stanford); Elidia Tafoya (Stanford); Malcolm Chelliah (Stanford)

Purpose: Lymphatic malformation (LM) arising from localized abnormal development of the lymphatic system can associate with many systemic manifestations such as disfigurement, organ dysfunction, and recurrent infection. Though excision, pharmacotherapy and sclerotherapy have shown partial success, effective treatment algorithms are still lacking, and recurrence is common following surgical interventions. In addition, the molecular pathways involved in LM pathogenesis are not well characterized. LMs are often associated with risk of edema and cellulitis following upper respiratory viral infection, suggesting a propensity for a systemic inflammatory response. Therefore, we sought to determine if there is a LM-specific gene signature detectable in peripheral blood cells.
Methods: We performed RNA-Seq on blood samples of 19 subjects (ten LM patients and nine healthy individuals) and identified 421 differentially expressed genes associated with the PI3K/AKT, MEK/ERK, Wnt/β-catenin, BMP pathways.
Results: We identified 253 upregulated and 168 down-regulated genes in LM. Unsupervised hierarchical cluster analysis on these 421 serum signature genes accurately differentiated patients with LM from those of healthy individuals. Of note, subjects 9 and 10, who present with severe LMs of the head and neck clustered together. Other than this, however, we noted little correlation between clustering and the clinical characteristics of the patients, suggesting the complexity of LM as molecular heterogeneity may not correlate with clinical heterogeneity. These findings demonstrated that a gene signature associated with LM can be detected in blood, highlighting the systemic impact of LMs. Computational drug repositioning analysis using this LM gene signature predicted sirolimus and vincristine as potential therapeutics, both of which have previously shown efficacy in treating LM, further validating our RNA-Seq results.
Conclusion: Our findings identify novel molecular pathways in LM and demonstrate the ability to detect LM signatures in blood samples, enabling noninvasive diagnosis, pathway analysis, and therapeutic programming.

O034

Superficial Cutaneous Vascular Malformations and Other Skin Manifestations of the PIK3CA-Related Overgrowth Spectrum (PROS)

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Purpose: The PIK3CA-Related Overgrowth Spectrum (PROS) encompasses various clinical mosaic conditions. Cutaneous features are major components of PROS. We sought to define their vascular and non-vascular phenotypic spectrum.
Methods: Retrospective review of photographs and clinical data from patients carrying a postzygotic PIK3CA mutation on affected tissue, either with macrocephaly (MCAP phenotype), or without macrocephaly (Klippel-Trenaunay (KTS), CLOVES or fibroadipose overgrowth (FAO) phenotypes).
Results: Among 91 patients (median age 7.1 years), 30 had macrocephaly and 61 had normal OFC. Superficial capillary malformations (CMs) were the most frequent cutaneous finding (72.5% of all patients). Cephalic CMs were more frequent in patients with MCAP (60.7%), whereas extracephalic CMs were more frequent in patients with normal OFC (56.7%). Extracephalic CMs were frequently located on hypertrophic areas in patients with normal OFC (81.1%). They had a light pink colour in a majority of patients (69.8%), often with a reticulate pattern. This type of CM was more frequent in patients with macrocephaly. Darker CMs with a purple hue, a geographic border and possibly lymphangiectasia were less common and found mainly in patients with normal OFC. CMs with lymphangiectasia were associated with the p.Glu545Lys PIK3CA mutation (p=0.005) and reticulate CMs with mutation p.Cys378Tyr (p=0.004). Lipomas were present in 30 patients (more often with normal OFC), epidermal nevi in 10, and thickened soles reminiscent of connective tissue nevi of Proteus syndrome in 5.
Conclusion: Two types of CMs, light pink reticulate and dark purple geographic CMs with lymphangiectasia allow to discriminate between clinical subtypes of PROS known as MCAP or CLOVES / KTS, and are partly correlated with the underlying PIK3CA mutation.

O035
The full spectrum of post-zygotic PIK3CA mutations in non-syndromic lymphatic malformations

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Purpose: Approximately 80% of isolated lymphatic malformations (LMs) contain post-zygotic activating mutations in the oncogene PIK3CA. Studies of this gene's role in LMs have been limited to sequencing 5 "hotspots", which are the most frequently mutated residues in sporadic human cancers, but cancer-driving mutations outside of these residues have also been reported. Full gene sequencing to determine the complete spectrum of PIK3CA mutations in isolated LM tissue has not been performed or compared with LM clinical data.
Methods: We used single molecule tag based molecular inversion probes (smMIPs) to sequence PIK3CA in 83 individuals with isolated, non-syndromic LMs. This method uses barcodes that permit sensitive detection of very low alternate allele fractions (AAF) genetic variants, a sensitivity not afforded by other laboratory techniques. PIK3CA genotypes and AAFs were also correlated with clinically relevant variables.
Results: Of the 83 individuals included in the study, 70 had reads from at least one affected tissue that was of sufficient quality and depth for analysis. Thirty-nine of these had pathogenic or likely pathogenic variants in affected LM tissue, for an overall diagnostic yield of 56%. The vast majority of pathogenic mutations (34/39) are located in hotspot residues, as expected. However, we identified four non-hotspot mutations in five individuals. Two of these mutations have been previously reported in cancers, but none have been reported in overgrowth or vascular malformations. Two individuals had the same recurrent, non-hotspot mutation. AAFs ranged from 1-28%, with mutations generally only detectable in resected LM tissue. Preliminary analysis suggests a correlation between lower de serre stage and non hotspot mutations.
Conclusion: Full gene sequencing of PIK3CA from resected LM tissue is an effective method for identification of hotspot and non-hotspot mutations. Sequencing depth and access to affected tissue are critical for PIK3CA mutation detection. Genotyping of these mosaic congenital malformations is becoming critically important in management of children with LM as novel PI3K-AKT-mTOR pathway inhibitors are developed.

O036
Activating mutations in PIK3CA are specifically localized in lymphatic malformation-derived lymphatic endothelial cells of young children: therapeutic implications

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Purpose: Activating mutations in PIK3CA in specimens of lymphatic malformations (LM) were described recently. However, as whole tissue had been studied, it remained unclear which cells harbor the mutations, and how kinase inhibitors act at the cellular level. Activating mutations in the PIK3CA gene in specimens of lymphatic malformations (LM) were described recently. However, as whole tissue had been studied, it remained unclear which cells harbor the mutations, and how kinase inhibitors act at the cellular level.
Methods: LM-specimens of patients at the age of 4, 9 and 10 months were put into culture. Cells were sorted according to their CD31 and PROX1 expression. Fibroblasts (CD31-/PROX1-) and lymphatic endothelial cells

(LEC) (CD31+/PROX1+) were isolated and further characterized by marker expression. Three normal LEC-lines were bought from PromoCell. Commonly affected exons 8, 10 and 21 of the PIK3CA gene were sequenced. Proliferation studies of LECs were performed with 7 kinase inhibitors as compared to solvent (DMSO).
Results: We identified activating monoallelic mutations in all 3 LM-derived LECs, including two mutations that have previously only been identified in cancer: 1. in exon 10 (c.1636G>A; p.Gln546Lys), and 2. an in-frame deletion of Glu 109/110. LM-derived fibroblasts did not possess such mutations, showing cell-type specificity of the gene defect. High activity of the PIK3CA/AKT-pathway was demonstrated by hyperphosphorylation of AKT-Ser473 in LM-derived LECs, as compared to normal, foreskin-derived LECs. In vitro, the small molecule kinase inhibitors Buparlisib, Wortmannin, Ly294002, and CAL101 (all inhibitors of PIK3CA), MK2206 (AKT inhibitor), Sorafenib (multiple kinases inhibitor), and Sirolimus (mTOR inhibitor) significantly blocked proliferation of LM-derived LECs. However, proliferation of normal LECs was also blocked. The 9-months-old girl with macrocystic LM at the neck was treated with Sirolimus, after failure of sclerotherapy and complicated surgical debulking due to secondary lymphfistula, with excellent complete remission after 6 months.
Conclusion: Activating mutations of PIK3CA are specifically located in LECs of LM and not in other cells. Therapy with PIK3CA/AKT/mTOR pathway inhibitors has great potential. However, monitoring of such experimental therapy is necessary as normal LECs might also be affected.

O037
Safety and Efficacy of Low Dose Sirolimus in Patients with PIK3CA-Related Overgrowth

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Purpose: The PIK3CA-related overgrowth (PROS) spectrum encompasses a range of conditions with asymmetric overgrowth caused by mosaic activating variants in PIK3CA, which encodes the p110a catalytic subunit of Class 1A phosphatidylinositol-3-kinase (PI3K). As mTOR mediates many of the growth-promoting actions of PI3K, we hypothesized that the mTOR inhibitor sirolimus would slow or even reverse pathological overgrowth. The highly variable anatomy and natural history of overgrowth in PROS pose considerable challenges for trial design, and raises concerns about the likelihood of reporting bias in case reports and small case series. Anecdotal reports of sirolimus therapy in PROS have suggested efficacy while others have reported clinical improvement in patients with vascular overgrowth.
Methods: To address these issues, 39 participants with PROS and progressive overgrowth were enrolled into identical, open label, single arm pilot studies across three centers and results pooled. Tissue volumes at affected and unaffected sites were measured by dual-energy X-ray absorptiometry analyses during 26 weeks of untreated run in and 26 weeks of low dose sirolimus treatment.
Results: To address these issues, 39 participants with PROS and progressive overgrowth were enrolled into identical, open label, single arm pilot studies across three centers and results pooled. Tissue volumes at affected and unaffected sites were measured by dual-energy X-ray absorptiometry analyses during 26 weeks of untreated run in and 26 weeks of low dose sirolimus treatment.
Conclusion: This pilot study suggests that low dose sirolimus can modestly reduce overgrowth, but cautions that the side-effect profile is significant, mandating individualized risk-benefit evaluations prior to sirolimus treatment in patients with PROS.

O038
SEGMENTAL OVERGROWTH IN SYNDROMIC VASCULAR ANOMALIES: TOWARDS A PHARMACOGENETIC THERAPY WITH RAPAMYCIN

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Purpose: Combined capillary-lymphatic-venous malformations (CVM) associated with segmental overgrowth (SO) in a syndromic pattern have been recently related to mosaic somatic mutations of PIK3CA gene, belonging to PI3K/mTOR pathway, and to both somatic and germinal mutations in complementary pathways (TIE2, RASA1, PTEN). These correlations represent the molecular basis of a possible pharmacologic inhibition of mTOR by Rapamycin (Sirolimus) in CVM therapy.
Methods: From January 2015 to December 2017 sixty-nine patients affected by CVM underwent genetic-molecular studies through Next-Generating Sequencing (NGS) on samples of pathologic tissue and peripheral blood. NGS was performed using a MiSeq Illumina instrument optimizing a combination of different approaches. Deep sequencing of multiplex amplicon library generated from custom oligo panel of pre-selected 25 genes involved in vascular anomalies, was performed using an Illumina TSCA kit. Mutations were confirmed with a second different NGS approach. At a first step we performed enrichment of mutated exons with PCR using a new set of primers for amplification. A second round of NGS sequencing was performed with a Nextera XT Illumina kit in order to obtain an ultradeep coverage. Cases were considered mutated when both techniques confirmed the same results. Two patients affected by CVM and SO associated to somatic mutations of PIK3CA were enrolled for Rapamycin therapy.

Results: 29 mutations were identified: nineteen in PIK3CA gene; six in GNAQ gene, four in TEK gene with a 2-30% mosacism rate. In two cases (mother and daughter) familial germinal mutation in TEK gene was detected. The two patients submitted to Rapamycin therapy had a significant favourable response without side effects (follow-up one year).
Conclusion: Genetic-molecular studies through NGS in patients affected by CVM and SO has shown a significant correlation between this phenotype and somatic mutations of PIK3CA gene. NGS could represent a pharmacogenetic screening tool, to select patients possibly responsive to systemic Rapamycin.

O039

"PTEN hamartoma of soft tissue" may also be related to PIK3CA mutations.

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Purpose: Soft tissue angiomatosis (STA) is an intramuscular rare high-flow vascular anomaly characterized by specific histological features consisting of an admixture of venous, arterial and lymphatic vessels with an adipocytic component and lymphoid aggregates. In the context of PTEN hamartoma syndrome (PHTS), it is called PTEN hamartoma of soft tissue (PHOST). Because similar lesions are observed in patients with no medical history of PHTS, we hypothesized that non-syndromic STA arises as a consequence of a somatic mutation.
Methods: All the patients histologically diagnosed with STA in our center were included. Personal and familial medical history and symptoms were retrieved from the patients' records. Histological analysis was reviewed. Genetic analysis of the tissue sample and/or the blood was performed.
Results: 12 patients (7 females, 5 males) were included. Severe pain was consistently observed. The lesion was always tough, painful at palpation, covered by normal skin. Somatic mutations of PIK3CA (p.Glu542Lys;p.Glu545Lys;p.His10471Arg) were identified in the tissue from 7 patients. They all presented a single lesion located in the inferior limb, and had unremarkable medical history. PTEN alterations (deletion n=1, mutations n=3) were identified in the lesion from 4 patients, one of which had a germline PTEN mutation identified in the blood. In 1 further patient, and her sister who presented with similar vascular lesions (not biopsied), a germline PTEN mutation was identified. In the PTEN group (n=6), 3 patients had multifocal lesions. The 3 patients with identified germline PTEN mutations presented with macrocephaly, penile pigmentation in the boy, ovarian tumor in one of the females. The 3 remaining patients whose blood molecular analyses are pending, presented with macrocephaly, but no familial history of PHTS.
Conclusion: STA showing PTEN or PIK3CA mutations present similar histological features. STA may be multifocal in PHTS. Medical history allows suspecting the specific mutation.

O040

How to build a multi-disciplinary vascular anomalies clinic from scratch: Lessons learned from a large, tertiary-care American children's hospital

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Purpose: To describe the process by which physicians at large medical centers can establish a multi-disciplinary, in-person vascular anomalies built for clinical collaboration, prospective data collection, outcomes tracking, and volume growth.
Methods: After identifying a clear need to provide comprehensive clinical care of pediatric patients with vascular anomalies and overgrowth syndromes (an underserved patient population) a multi-disciplinary team of physicians approached hospital administration with a comprehensive proposal detailing the current volume of patients being treated in our community, the inconsistency of care provided (largely driven by which specialty was caring for the patient), and a model for an in-person, multi-disciplinary clinic. The model proposed included 1 half-day of clinic per week with 5 different subspecialists and a full-time nurse practitioner in clinic, as well as a list of 11 different preferred consultants in other subspecialties required to treat these patients (eg. pulmonology, neurology, etc.). Dedicated radiologists and pathologists were also necessary requests. Additional personnel included: a clinical nurse, social worker, case worker, and physical therapist. Data collection tools included: 1) REDCap patient intake form, 2) REDCap clinical database, 3) PedsQL, Functional Disability Inventory (FDI), and the Lymphatic Malformation Function (LMF) data collection tools built into the EMR with data collected at every clinic visit.
Results: The first clinic was held in May 2016. In-clinic specialties include hematology, otolaryngology, pediatric surgery, interventional radiology, and plastic surgery. Since inception, there have been 525 patients seen in clinic and 924 patient visits. 29% of patients have seen multiple providers. There have been over 375 surgeries and minimally invasive procedures performed while 61 patients have been treated with Sirolimus and 67 with oral and/or topical beta-blockers. In 2017 alone, there were >420 referrals to the clinic.
Conclusion: With an organized, collaborative approach, institutions can successfully implement sustainable multi-disciplinary vascular anomalies clinics to serve this largely underserved patient population.

O041

A FAIR compliant registry for the vascular malformation centres within the European Reference Networks. How it was done

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Purpose: The European Commission (EC) launched European Reference Networks (ERNs), connecting specialised health care providers (HCP) to optimise care and research for rare disease (RD) patients. This requires that registries enable data mining between databases within and outside of ERNs. The EU and global organisations (IRDiRC, ELIXIR, NIH, G7) endorse FAIR data principles (Findable, Accessible, Interoperable and Reusable by humans and computers). We present a FAIR registry for vascular malformation centres (VASCA) as a pilot for robust data infrastructure in the context of the RDs GO FAIR implementation network (a means to establish the European Open Science Cloud).
Methods: The registry was developed with the following assumptions: 1. Source registries contain at least a common minimal dataset. 2. Registries are independent of proprietary software. 3. Structure (ontologies) and data elements allow answering questions across registries. 4. The registry conforms to the new privacy directive of the EC and national laws. 5. Data storage and local IT allow compliance with the FAIR principles.
Results: The minimal dataset (16 elements) was determined in a consensus meeting of all ERNs: pseudonym, date of birth, gender, patient's status, date of death, first contact with HCP, age at onset, age at diagnosis, diagnosis, genetic diagnosis, undiagnosed case, agreement to be contacted for research purposes, consent to the reuse of data, biological sample, link to a biodatabank, and classification of functioning/disability. FAIR principles were implemented in close collaboration between FAIR data stewards, software developers, and VASCA experts. The result was tested by queries that required information across multiple databases.
Conclusion: Building a registry based on FAIR principles has huge potential for future collaborative research. It removes the dependency on central solutions that decouple HCP expertise from data, are limited by legal constraints, and difficult to maintain.

O042

The European Reference Network (ERN) criteria for multidisciplinary vascular anomaly clinics (VASCA) in the VASCERN

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Purpose: The European Commission launched a call for networks connecting health care providers (HCP) to improve access to diagnosis, treatment and high-quality healthcare for rare diseases. In the European reference networks (ERN) application, special features had to be fulfilled by HCPs, which were evaluated by an external reviewing company. One of them is the VASC-ERN dealing with Rare Multisystemic Vascular Diseases, representing 31 HCP from 11 member states with five working groups (WG): Hereditary Haemorrhagic Telangiectasia, Heritable Thoracic Aortic Diseases, Medium Sized Arteries, Pediatric and Primary Lymphedema and Vascular Anomalies (VASCA).
Methods: The ERN application criteria included participation in a national or regional assessment program, have expertise in complex rare diseases and highly specialized interventions. More specifically, for full membership in the VASCA WG, a minimum of 150 new patients/year, 300 patients/year for follow-up and a minimum of 250 procedures/year had to be demonstrated. Procedures include: surgery, embolization, sclerotherapy, laser (for rare complex disorders; simple CMs excluded), endoscopy, biopsy and "off label" medication. Moreover, the HCP should have published a minimum 10 peer-reviewed publications dealing with vascular anomalies. In addition, surgery, interventional radiology, dermatology, clinical genetics and a minimum of 4 other specialties had to be present.

Results: Eight HCPs were positively evaluated for the VASCA WG. Smaller centers can be incorporated, but as affiliated centers. Moreover, collaborative centers that do not have full membership can be included, if necessary.
Conclusion: The ERN call criteria helped to identify HCPs that are centers of reference as recognized in their countries. The VASCA WG will develop extensive collaboration and foster and reinforce European cooperation following a common and multidisciplinary approach. The selected HCPs in the VASCA WG will commit to improve diagnosis, treatment, and care for patients.

O043
Patient involvement on vascular anomalies in the European Reference Network VASCERN
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Purpose: European Reference Networks (ERNs) for Rare Diseases were established on the founding principle of patient empowerment, participation and patient-centricity. The object is to improve access, safety and quality of diagnosis, care and treatment for people living with a rare or complex condition. Patient representatives and organisations (POs) are recognized as integral to the strategic and operational delivery of ERNs, and play an active role in network decisions and opinion-making structures.
Methods: EURORDIS, in collaboration with the European rare disease community, established 24 European Patient Advocacy Groups (ePAGs), one for each ERN. These groups aim to optimise the involvement of patients and ensure unity, solidarity and equity of representation in the 24 ERNs. The Multisystemic Vascular Diseases ERN (VASCERN) has 5 disease-oriented working groups. The VASCERN ePAG is represented in all of them. The 5 Patient co chairs + other ePag representatives and members meet virtually once a month. Once a year the VASCERN meets face to face including ePAG. Goals for the Vascular anomaly (VASCA) patient group: 1) improve treatment options and clinical research (biobanks, registries, classification) for patients with vascular anomalies, 2) promote cooperation between HCPs, and 3) find more POs on vascular anomalies.
Results: Four POs are involved in VASCA WG: HEVAS, LGD, VASCAPA and FACVM. Twenty-one more POs were found and contacted to create a larger European community. Data is being gathered to fill a Mobile App with info of HCPs and POs to assist patients in finding help rapidly, when traveling.
Conclusion: The Patient Group of VASCA is in the process of fostering the collaboration and operationalising patient involvement in the network groups and activities, including cooperation on communication between POs and HCPs. POs will also meet and participate at ISSVA 2018, which is a unique step forward for strengthened cooperation.

Difficult Cases 2

O044
Syndromic segmental arterio-venous malformation: a therapeutic challenge
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Purpose: To describe a severe case of segmental arteriovenous malformation associated to epidermal naevus syndrome related to K-RAS somatic mutation, and the ineffectiveness of oral trametinib treatment in this context.
Results: An otherwise healthy male infant presented at birth with a segmental verruco-sebaceous naevus of the left superior limb and adjacent thoracic wall. Cerebral MRI and ophthalmologic examination were normal. Asymptomatic segmental left superior limb AVM was diagnosed, along with aortic coarctation, which was successfully operated. A K-RAS somatic mutation was identified in a biopsy from the epidermal nevus. At 11 y/o, the left elbow became painful. An angiogram was performed to evaluate the embolization possibilities of the "maybe clinically symptomatic" microshunts. During the procedure, catheterism was interrupted as a brachial artery agenesia was seen. Distal ischemia of the ear finger rapidly occurred. The symptoms worsened despite sirolimus treatment (0.1 mg/kg/d). In the hypothesis of vascular stealing syndrome, carotido-brachial bypass was performed. Complete healing was achieved under sirolimus, which was restarted because of venous overload. Occurrence of grade III arthralgia led to sirolimus discontinuation. At 14 y/o, the patient reported back pain and vertebral AVM located to T1 and T2 was identified. Because of

signs of myelopathy (sensory disturbance and urinary retention) and cardiac overload (cardiac index: 7.6L/mn/m^2), medical targeted therapy using Trametinib was decided, before re-considering high-risk interventional procedure. Asthenia and grade III skin side effects led to treatment discontinuation after 3 months of treatment and thalidomide (50 mg/d) was started without clinical worsening until now.
Conclusion: We hypothesized that the clinical manifestations, were related to the K-RAS mutation. Trametinib was expected to be efficient, targeting the causative RAS-MAPkinases pathway. RAS also regulates PIK3CA-AKT-mTOR pathway, explaining the partial therapeutic effect observed with sirolimus. Targeting both pathways may be necessary to reach substantial clinical response.

O045
A difficult case of upper limb venous malformation with intolerance to oral sirolimus

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Purpose: To discuss treatment options for a difficult case of venous malformation of upper limb.
Methods: A 22 year old young man presented to our vascular anomaly clinic with an untreated extensive venous malformation of the entire left upper limb since birth and causing pain for the last few years requiring opiates and adjuvants given by the pain clinic in another hospital.
Results: Imaging showed extensive venous malformation involving the entire left upper limb with the presence of scattered phleboliths. As the channels were thrombosed based on ultrasound Doppler imaging, endovenous interventions such as sclerotherapy, venous coiling and endovascular laser were not deemed appropriate and therefore a trial of oral sirolimus was offered with the goal of pain reduction including reducing his dependence on opiates. He was started on 0.8mg/m2/dose BD of oral sirolimus but within a few days he developed extensive painful oral ulcers, necessitating cessation of the drug. He was restarted on 0.5mg BD a month later which he tolerated but which did not result in a therapeutic drug level.
Conclusion: Issues to address in this difficult case include: 1. Is there any point in continuing oral sirolimus since it is unlikely that a therapeutic level will be reached without significant toxicity? 2. Would newer generation mTOR inhibitors like everolimus be better tolerated? 3. Since there are phleboliths which may contribute to his pain, do anticoagulants have a role in reducing his pain in addition to reducing the risk of embolism? 4. Are there other interventions possible in his case if medical treatment is unable to help?

O046
Management challenges of a complex CLOVES Syndrome patient with severe scoliosis and lipomatous overgrowth

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Purpose: A 3-year-old boy with CLOVES phenotypically with lipomeningocele, tethered cord, spina bifida, intramedullary veno-lymphatic malformation malformation (T1-T4), capillary and lymphatic malformations, and a large posterior truncal lipomatous overgrowth has a complex history beginning with resection of a thoracic spine veno-lymphatic malformation and capillary malformation. This required extensive laminectomies. Post-op complications included paraplegia, neurogenic bladder, and respiratory failure requiring tracheostomy. Clinically, the patient deteriorated secondary to metabolic issues, cachexia, and continued expansion of a large congenital lipomatous growth. MRI revealed a partially-visualized soft tissue overgrowth of the back extending from the low cervical region to the coccyx into the paraspinal muscles that contains a spherical enhancing mass (2.3cm) in the upper aspect; furthermore, there was no evidence of residual veno-lymphatic malformation. Subsequently, he received a wide local excision and debulking of his back lipoma and local tissue rearrangement for definitive wound closure (>45cm x 30cm). Drains and quilting sutures were utilized between the skin flaps and latissimus fascia to decrease dead space and tension from the incision line. Excess skin was resected to achieve a straight-line closure, while the remaining skin flaps were closed primarily in layers. Final pathology revealed a lipomatous mass, without evidence of malignancy, consistent with clinical diagnosis of CLOVES. Postoperative course was complicated by a large area of skin necrosis (9 x 22cm). This was first treated with sharp debridement followed by silvadene dressings then switched to negative pressure wound therapy device after two subsequent debridements down to healthy truncal fat. The patient has an additional right trapezius mixed lymphatic venous malformation that continues to grow. Currently the patient's family desires surgical repair of his severe scoliosis. However, there is significant risk given the mixed lymphatic venous malformation in the proposed operative field and continued refusal of blood product administration for religious purposes.

O047
Case Report: Management of Menorrhagia in a Young Woman with Blue Rubber Bleb Nevus Syndrome: Failures and Successes

Carrie Terrell (University of Minnesota); Sheilagh Maguiness (University of Minnesota); Brenda Weigel (University of Minnesota)

Scientific Session 4: Vascular Malformations 3

O048
Prevalence of Cardiac Failure in Patients with Arteriovenous Malformations

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Purpose: Arteriovenous malformation (AVM) severity has historically been defined by the Schobinger classification system. According to Schobinger, the differentiation between a stage III and IV AVM is evidence of cardiac failure (CF). AVM-related CF is thought to be the result of massive shunting of blood volume towards the malformation, leading to left ventriculomegaly or high-output CF. Few patients with advanced AVM disease have been reported to demonstrate CF. Therefore, this study was undertaken to examine the prevalence of CF in our AVM population.
Methods: A retrospective chart review was performed through a query of the electronic medical record for the international classification of disease (ICD-10) codes which identified patients with AVM's. AVM characteristics of location, focality, and Schobinger classification were recorded. Exclusions were made for intracranial AVM's, and for incomplete documentation of AVM characteristics.
Results: A total of 205 patients with AVM's of various sizes and locations were identified and included in the study. Of these patients, none presented with complaints or physical examination findings concerning for CF. Nonetheless, given signs and symptoms indicative of late-stage AVM, 23 patients were evaluated for possible early, asymptomatic CF using electrocardiography or echocardiography. There were no identified cardiac abnormalities.
Conclusion: Although stage IV AVM disease is characterized in the Shobinger classification system as destructive disease accompanied by cardiac failure, our chart review identified no patients with findings of CF in their history, physical exam, electrocardiography, or echocardiography. Given these findings, we hypothesize that there are other characteristics of advanced-stage AVM that could be analyzed to develop a more specific staging scale. A multi-institutional review is suggested due to the rare nature of AVM.

O049
PET/CT imaging of angiogenesis in arteriovenous malformations

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Purpose: Angiogenesis is key in arterio-venous malformations (AVM); normally quiescent endothelium switches to an activated state, resulting in the breakdown of vessel walls and subsequently causing enlargement of the AVM. Although the exact molecular mechanism has not yet been elucidated, this concept has sparked interest in possible treatments of AVM using angiogenic inhibitors. Molecular imaging allows to non-invasively image angiogenesis. We have developed an RGD peptide targeting the activated αvß3 integrin on endothelial cells of newly formed blood vessels. If labeled with the positron emitting radionuclide gallium-68, this peptide can be used to visualize and measure angiogenesis using PET/CT imaging. The current study aims to assess the feasibility of imaging angiogenesis in AVM patients using [68Ga]Ga-DOTA-(RGD)2 PET/CT.
Methods: Patients with an AVM and who were treated with (endovascular) embolization will undergo [68Ga]Ga-DOTA-(RGD)2 PET/CT scanning 60 minutes after [68Ga]Ga-DOTA-(RGD)2 (70 µg, 200 MBq) injection.
Results: To date, seven patients (4 male, 3 female) with an AVM classified as Yakes AVM type II (5), type IIIa (1), and type IIIb (1), mean age 44 years (28-64 years), are enrolled. Six patients received multiple embolizations before [68Ga]Ga-DOTA-(RGD)2 PET/CT imaging, one patient did not receive any treatment yet. [68Ga]Ga-DOTA-(RGD)2 PET/CT imaging was feasible in all patients, with significantly higher tracer uptake in AVM tissue compared to (surrounding) normal tissue. This study is actively recruiting more patients and further analysis of data will be presented.
Conclusion: These preliminary results suggest that [68Ga]Ga-DOTA-(RGD)2 PET/CT imaging of αvß3 integrin expression in AVM patients is feasible. The tracer uptake is increased in AVM compared to normal tissue, suggesting locally increased αvß3 integrin expression in AVM. Our preliminary findings imply that [68Ga]Ga-DOTA-(RGD)2 PET/CT imaging might be used to stratify patients prior to anti-angiogenic therapies or as response-monitoring tool, but further studies are needed to explore these potential applications.

O050
MELORHEOSTOSIS AND VASCULAR ANOMALIES CAUSED BY SOMATIC MOSAICISM OF KRAS

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Purpose: Melorheostosis is a rare sclerosing bony dysplasia that radiologically resembles dripping candle-wax along bones. Associated extraosseous alterations have been described such as scleroderma-like skin changes and vascular anomalies. We present a case of polyostotic melorheostosis with multiple vascular anomalies.
Methods: A 12-year-old girl presented with cutaneous lesions and multiple extracutaneous findings. History included congenital chylothorax, aortic coarctation and multiple arterial stenoses (superior mesenteric artery, celiac trunk and right renal artery). Soft-tissue lymphatic malformations were present in the posterior cervical and dorsal regions. Melorheostosis involved several bones or her left upper limb, three ribs and five vertebrae. She also had three dural-epidural lipomata. Chronic restrictive lung disease was due to left pulmonary lymphangiomatosis and left chronic pleural effusion. On physical exploration, a large, well-delimited hyperpigmented macule extended forward from the posterior midline. Additionally, an area of atrophic wrinkled skin was present on her left iliac fossa.
Results: Samples for genetic analysis were taken from peripheral blood, dorsal hyperpigmented macule and cervical lymphatic malformation. Next generation sequencing identified a KRAS mutation (Q61H) in the lymphatic malformation and hyperpigmented skin but not in blood. The same mutation has already been identified in another case of melorheostosis without vascular anomalies.
Conclusion: To our knowledge, this is the first report of somatic genetic mosaicism in the vascular anomalies associated with melorheostosis. This would also confirm that both melorheostosis and associated vascular and cutaneous anomalies belong to a spectrum of mosaic rasopathies.

O051
Extracranial Arteriovenous Malformations (AVMs) Are Caused by Activating MAP2K1 Mutations In Endothelial Cells

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Purpose: Arteriovenous malformation (AVM) is a fast-flow, congenital vascular anomaly that may arise anywhere in the body. AVMs typically progress, causing destruction of surrounding tissue and, sometimes, cardiac overload. AVMs are difficult to control; they often re-expand after embolization or resection, and pharmacologic therapy is unavailable. We studied extracranial AVMs in order to identify their biological basis.
Methods: We performed whole-exome sequencing (WES) and whole-genome sequencing (WGS) on AVM tissue from affected individuals. Endothelial cells were separated from non-endothelial cells by immune-affinity purification. We used droplet digital PCR (ddPCR) to confirm mutations found by WES and WGS, to determine if mutant alleles were enriched in endothelial or non-endothelial cells, and to screen additional AVM specimens.
Results: WES and WGS detected in 7 of 10 specimens, and ddPCR confirmed, somatic mutations in mitogen activated protein kinase kinase 1 (MAP2K1; NM_002755), the gene that encodes MAP-extracellular signal-regulated kinase 1 (MEK1; NP_002746.1). Mutant alleles were enriched in endothelial cells and were not present in blood or saliva. Twelve of 18 additional AVM specimens contained mutant MAP2K1 alleles. Mutations were missense or small in-frame deletions that affect amino acid residues within or adjacent to the protein's negative regulatory domain. Several of these mutations have been found in cancers and shown to increase MEK1 activity.
Conclusion: Somatic mutations in MAP2K1 are a common cause of extracranial AVM. The likely mechanism is endothelial cell dysfunction due to increased MEK1 activity. MEK1 inhibitors, which are approved to treat several forms of cancer, are potential therapeutic agents for individuals with extracranial AVM.

O052
Mosaic RAS/MAPK variants cause sporadic vascular malformations which respond to targeted therapy

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Purpose: Sporadic vascular malformations (VMs) are complex congenital anomalies of blood vessels that lead to stroke, life-threatening bleeds, disfigurement, overgrowth, and/or pain. Therapeutic options are severely limited and multi-disciplinary management remains challenging, particularly for high-flow arteriovenous malformations (AVM).
Methods: To investigate the pathogenesis of sporadic intracranial and extracranial VMs in 160 children (high-flow VMs n=25, Low flow VMs n=135) in which known genetic causes had been excluded, we used Next Generation Sequencing of DNA from affected tissue and optimised analysis for detection of low mutant allele frequency. All candidate genetic mutations were confirmed by a second sequencing method. Functional characterisation of novel mutations was performed in vitro using transfected endothelial cell lines to assess MAPK pathway activation and vascular modelling. Novel mutations were further characterised by generation of transgenic zebrafish.
Results: We discovered multiple mosaic activating variants in four genes of the RAS-MAPK pathway, KRAS, NRAS, BRAF and MAP2K1, a pathway commonly activated in cancer and responsible for the germ-line RAS-opathies. These variants were more frequent in high-flow (n=9/25) than low-flow VMs (n=5/135). In vitro characterisation and two transgenic zebrafish AVM models which recapitulated the human phenotype validated the pathogenesis of the mutant alleles. Importantly, treatment of AVM-BRAF mutant zebrafish with the BRAF inihibitor, Vemurafinib, restored blood flow in AVM.
Conclusion: Our findings uncover a major cause of sporadic vascular malformations of different clinical types, and thereby offer the potential of personalised medical treatment by repurposing existing licensed cancer therapies.

O053
The Role of Notch Pathway Components in Extracranial Arteriovenous Malformations

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Purpose: Extracranial arteriovenous malformations (AVMs) are congenital and abnormal direct connections between arteries and veins, bypassing the capillary system. The etiology and pathophysiology of AVMs are not well understood. The Notch pathway represents a group of signaling proteins critical to normal and pathologic vascular development and stability. Notch overexpression has been reported in the development of AVMs in the central nervous system. We hypothesize that disrupted expression of Notch pathway components was related to the progression of extracranial AVMs.
Methods: Fresh human AVMs (n=16) and normal skin and subcutaneous tissue (n=13) were harvested. Messenger RNA levels of Notch receptors (Notch1, Notch2, Notch3 and Notch4) and ligands (DLL1, DLL3, DLL4, Jagged1 and Jagged2) were measured with Real Time RT-PCR assay. Protein expression levels were detected using Western blot assay. Mann-whitney test was utilized to analyze the results.
Results: Messenger RNA levels of Notch3, Notch4 and DLL4 were significantly increased in AVM tissues compared with normal tissues (1.91±0.79 vs. 1.11±0.52, P=0.002; 2.68±1.94 vs. 1.31±1.20, P=0.008; 3.62±3.15 vs. 0.11±0.36, P=0.000 respectively). DLL1 mRNA level was also increased but did not reach the statistical difference (P=0.075). Notch2 mRNA level was decreased in AVMs versus normal groups (0.77±0.34 vs.

1.06±0.42, P=0.05). No statistical difference was noted in mRNA levels of Jagged1, Jagged2 and Notch1 (P=0.215, P=0.11, P=0.812, respectively). Contrarily to the mRNA results and intriguingly, the protein expression levels of Notch3, Notch4 and DLL4 didn't show statistical difference between AVMs and normal controls (0.40±0.18 vs. 0.62±0.41, P=0.315; 0.29±0.15 vs. 0.31±0.19, P=0.80; 0.39±0.15 vs. 0.44±0.20, P=0.66, respectively).
Conclusion: Dysregulation of the Notch pathway disrupts normal vascular specification and maturation. This study suggests that Notch signaling expression may be one of the underlying mechanisms of extracranial AVM progression. The non-concordant expressions of mRNA and proteins in some of the Notch components suggest possible deficits in translation, posttranslational modification or miRNA interruption. Further studies are warranted to explore this pathway in depth.

Scientific Session 5: Hemangiomas and Vascular Tumors

O054
Source of Elevated AFP Levels in Infantile Haemangioma

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Purpose: Infantile haemangioma (IH) is the most common tumour of infancy. Alpha-fetoprotein (AFP) is an oncofoetal protein, produced by the post-partum liver. IH patients exhibit elevated serum AFP levels which decline to normal physiological levels following treatment. We have reported that AFP is not produced within IH. HepG2 cells are a liver-derived tumour cell line that innately produces AFP. In this study, we hypothesised that IH stimulates AFP production by the liver via an intermediary. We co-cultured primary IH-derived cells with HepG2 cells, to investigate the role of IH in promoting AFP production from HepG2 cells.
Methods: Cells derived directly from IH samples from 6 patients were co-cultured with HepG2 cells, with HepG2 cells grown without IH-derived cells as a negative control. HepG2 cells were harvested at days 1, 2, 3 and 4 and analysed for the mRNA expression using RT-PCR, and protein expression using 1DE-Western blotting (WB), of AFP.
Results: RT-PCR results, normalised against GAPDH, demonstrated a significant increase in the levels of AFP mRNA in the HepG2 cells co-cultured with the IH-derived cells. WB showed increased levels of AFP in HepG2 cells co-cultured with IH-derived cells, compared with the control, at days 2 and 4 across all samples.
Conclusion: HepG2 cells co-cultured with IH-derived cells resulted in an increase in the production of AFP at both the transcriptional and translational levels. These findings support our hypothesis that IH secretes an intermediary with a stimulatory effect on AFP production in IH patients, putatively from the liver.

O055
Resistance Index (RI) in Colour Coded Duplex Sonography (CCDS) Easy Use and Reliable Results in the Determination of Activity in Infantile Hemangiomas

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Purpose: Propranolol and laser treatment are helpful tools to solve problems in infantile hemangiomas. The challenge however is to estimate activity i.e. to select those hemangiomas that require treatment. As hemangiomas run through defined stages of development we were looking for an objective criterion to discriminate active from regressive tumours.
Methods: 350 consecutive hemangiomas (243 female, 107 male; age 1 to 95 months; localization capillitium to foot) were classified corresponding to a clinical and CCDS stage from I to V, we had described in a survey some years ago. In each of these hemangiomas we identified the RI as mean value of 3 measurements in different arteries. Then we related our measurements with the corresponding stages. Finally we performed an ANOVA (analysis of variance) procedure to prove significance.
Results: We identified 27 hemangiomas in stage II, 156 in stage III, 155 in stage IV and 12 in stage V. The mean of all RI in stage II was 0,6714 (variance 0,0021), in stage III was 0,6047 (variance 0,0025), in stage IV was 0,5104 (variance 0,0025) and in stage V was 0,4656 (variance 0,0053). ANOVA showed that there was highly significant difference (p value 3,89793E-61) of RI between the stages; this could be ensured by the additional post hoc test according to Bonferroni.
Conclusion: During the natural development of infantile hemangiomas the flow conditions are changing. This can be measured easily by CCDS and expressed as RI. During the physiological ageing progress in infantile hemangiomas the RI constantly decreases, and shows characteristic figures for each stage of development. As these figures differ significantly it is possible to stage hemangiomas by an objective measurement. This could be important for selecting those hemangiomas with need for treatment and vice versa helping to avoid needless therapy.

O056
Non-involuting congenital hemangiomas (nich) with post-natal atypical growth: a case series

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Purpose: Congenital Hemangiomas are fully formed vascular tumours at birth, typically without post-natal growth. Non-Involuting Congenital Hemangiomas (NICH) have a distinctive clinical, radiologic, histopathological and immunohistochemical profile, and lack of expansion or involution over time. We describe a series of NICH cases with atypical post-natal growth.
Methods: A retrospective review of charts and photographic databases from the Vascular Anomalies Clinic of a University Hospital Center was performed. NICH cases diagnosed from 2007 to 2017 by an experienced pediatric dermatologist, and confirmed by imaging and histopathology when available, were analyzed. Cases with evidence of atypical post-natal growth were selected.
Results: From 77 cases of NICH, 7 presented an atypical post-natal growth (6 females; 1 male). All reported post-natal growth of the tumour after a stable period, at ages varying from 1 to 10 years (mean 4.3 years). 5 lesions were located on the trunk, one on the face and one on the upper extremity. 5 patients showed new red papules on the surface of the lesion; 2 reported bleeding from the papules, and 1 developed a pyogenic granuloma. 6/7 patients had doppler-ultrasound and/or MRI compatible with NICH, and confirmatory biopsy was performed in 2 cases. As treatment, 2 patients received an endovascular embolisation, one of them also required surgery; and one patient received topical timolol.
Conclusion: Non-Involuting Congenital Hemangiomas (NICH) are unique vascular tumours, displaying high-flow vessels and, by definition, lack of expansion or involution over time. Proportional growth with age been described, but we found no documented cases of significant post-natal growth. The development of red papules, pyogenic granulomas and bleeding has not been reported either for Congenital Hemangiomas. Since this is a small series, we are not able to establish a profile of NICH with higher risk of post-natal growth or superficial bleeding, but these findings warrant a closer follow-up in these patients.
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O057
Tardive Expansion Congenital Hemangioma: a variation of NICH or a new hemangiomatous entity?

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Purpose: Congenital hemangiomas (CHs) are defined as fully grown at birth and do not exhibit postnatal rapid growth. Two subgroups are designated by acronyms: RICH and NICH. We report a series of unusual CHs that arise prenatally and initially present as NICH, however, a clinical course of tardive expansion of the lesions as proliferative infantile hemangioma (IH) occur before adolescence.
Methods: A total of 9 patients with unusual CHs were reviewed and the lesions were analyzed for history, physical findings, radiologic and histopathologic characteristics.
Results: All lesions arose prenatally and demonstrated neither proliferation nor involuting course after birth. However, a tardive expansion of the lesion occurred before adolescence (mean 37.2±19.4 months, range 11-61 months). The predominant male preponderance was observed (male n=7; female n=2); and the majority of lesions were located on the head (n=8) with only one on the trunk (n=1), and none on the limb. Radiographic studies exhibited heterogeneity in most of the lesions. Fast-flow was documented in all lesions, and calcification was noted in none of the lesions. Six lesions were excised. Overlapping histologic features with NICH, RICH and IH were revealed. However, compared with NICH or RICH, they demonstrated densely cellular areas. The mitotic figures were rare, compared with IH. Immunohistochemical staining was negative for Glut-1 in all specimens.

Conclusion: Distinctive characteristics observed in our series distinguish them from previously identified CHs. Although, expansion of NICH in adolescent years has been reported, in association with pain and the growth of polypoid excrescences, the presented series are not the cases. We proposed the term "tardive expansion congenital hemangioma" to better define these rare hemangiomatous entities. It is yet to be determined whether these lesions are actually variations on a spectrum of NICH in a state of tardive expansion with unknown pathogenesis or a distinct hemangiomatous entity altogether.

O058
Use of the Hemangioma Severity Scale to facilitate treatment decisions for infantile hemangiomas

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Purpose: Propranolol has changed treatment decisions in infantile hemangioma (IH). Referrers should be facilitated and empowered to refer IH-patients on time, in order to prevent or treat complications and avoid long-term consequences. The Hemangioma Severity Scale (HSS) assesses the severity of an IH. Purpose of this study is firstly to compare HSS scores between patients with IH for whom propranolol treatment was indicated at their first visit and those who were not treated. Second target was to assess suitable cutoff values for the need for propranolol treatment.
Methods: All patients with IH who attended one of the lagerst expertcenters in Europe since 2008 and were 0 to 6 months of age at their first visit were included. They were divided into propranolol and no-propranolol groups on the basis of choice of treatment at their first visit. Age, IH-type and HSS scores were assessed, and median scores were compared.
Results: A total of 657 children (342 in the propranolol group) were included. The median HSS score (25th-75th percentile) in the propranolol group was 10 (range, 8-14) compared with 7 (range, 4-9) in the no-propranolol group ($P < .001$). Cutoff values of 6 or lower (no indication for treatment) and 11 or higher (indication for treatment) resulted in 94% sensitivity and 89% specificity, respectively. Younger patients (age of the first consultation) and patients with an IH with a deep component, prone to leaving more residual lesions, also had a greater likelihood of active approach with propranolol.
Conclusion: The HSS with cutoff values of 6 or lower and 11 or higher could be used as a triage tool for propranolol treatment and/or referral of patients from general practitioners or pediatricians to expert centers regarding treatment. Patient age, IH type, and parental preference may also contribute to treatment decisions, especially in HSS-scores in the middle segment.

O059
Multiple cutaneous and visceral GLUT-1 positive congenital vascular tumors: a novel entity or a variant of multifocal infantile hemangiomatosis

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Purpose: Describe a novel vascular condition in an infant born with multiple cutaneous and visceral vascular tumors demonstrating GLUT-1 positive staining without histologic and clinical features of infantile hemangioma (IH).
Results: A female neonate conceived with in-vitro fertilization due to maternal bicornuate uterus, was delivered at term following an uncomplicated pregnancy with >50 cutaneous vascular nodules and tumors on the scalp, face, trunk, extremities and genitalia. A punch biopsy of a skin nodule on day 1 of life demonstrated a vascular tumor with positive immunohistochemical staining for GLUT-1 and negative D2-40 staining, suggestive of an infantile hemangioma. An abdominal ultrasound demonstrated multiple echogenic lesions in liver, pancreas and right kidney with diffusely increased internal vascularity. These lesions were not present on prenatal ultrasound. There were no intracranial lesions on brain MRI. Platelets and Free-T4 levels were normal and stool guaiac negative. Rapid growth and ulceration of forehead lesion prompted propranolol initiation on day 12 of life. Propranolol was increased to 3mg/kg/day and oral and intralesional steroids were added. All treatments were ineffective. Given the lack of diagnosis, an excision of a cutaneous tumor was performed which demonstrated a vascular proliferation with a biphasic pattern with the infiltration of eccrine glands and a diffuse angiomatous component in the dermis and the subcutaneous fat with ectasia of vessels. Despite GLUT-1 positivity, the infiltrative nature of the vascular channels into collagen, fat and muscle, presence of adipose tissue surrounding the vascular channels in a non-involuting lesion and the plump nature of the endothelial cells, suggested a diagnosis other than IH.
Conclusion: The authors present a unique case of >50 congenital cutaneous and visceral GLUT-1 positive lesions, whose histologic features, the tissue infiltration, development in-utero, lack of response to propranolol and corticosteroids suggest a diagnosis different than IH, not previously reported in the literature.

O060
Systemic Timolol Exposures Following Topical Application to Infantile Hemangiomas

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Purpose: Timolol is widely prescribed for off-label treatment of infantile hemangiomas. Little is known about the pharmacokinetics of topical timolol, leaving infants vulnerable to adverse events resulting from systemic exposure. The purpose of this study is to provide data regarding the plasma concentrations of timolol following topical administration for infantile hemangioma.
Methods: In a multi-center, opportunistic pharmacokinetics study, plasma samples were collected from subjects <2 years of age treated with topical timolol per local standard of care. Plasma timolol concentrations were measured at a central laboratory using a validated HPLC/MS/MS assay (analytical range 0.020-150 ng/mL) normalized to timolol dose, and summarized using means (standard deviations) for the entire study cohort with stratification by subject (age, sex, race/ethnicity) and hemangioma characteristics (site, surface area, subtype, thickness, and presence of ulceration). Hemangioma thickness was measured as the elevation of the lesion and categorized into the following categories 1) <0.2cm, 2) >0.2-0.5cm, 3) 0.5-1.0cm, >1.0cm.
Results: In this analysis of 92 plasma samples from 76 subjects, 86 had detectable plasma levels of timolol. Plasma levels were variable with a range of 0.0284-106 ng/mL. 10 subjects had levels ≥10 ng/mL, much higher than expected based on existing literature. Levels did not differ significantly by race, ethnicity, sex, application site, hemangioma surface area, occlusion, or ulceration. Thickness of hemangioma was associated with significant differences in absorption (p-value=0.024), with thicker lesions having higher plasma concentrations. No serious unexpected adverse reactions or serious adverse events were reported.
Conclusion: Systemic absorption resulting in measurable plasma concentration occurs in most subjects receiving topical timolol for infantile hemangioma, especially for thicker highly vascularized hemangiomas. Providers should avoid treating hemangiomas >2mm with topical timolol, as existing data has demonstrated lack of efficacy and we have now shown increased risk of systemic absorption in thicker hemangiomas.

O061
Efficacy and Safety of Topical Timolol Maleate 0.5% Solution for Infantile Hemangioma in Early Proliferative Phase. A Randomized Clinical Trial

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Purpose: Early treatment of Infantile hemangiomas (IH) with topical timolol, in early proliferative phase, may prevent further growing and the need to treat with oral propranolol. Evaluate the efficacy and safety of topical 0.5% timolol maleate for treatment of IH in infants under 8 weeks of life.
Methods: A multicentric, randomized, double-blind, placebo-controlled, phase II clinical trial. Patients with less than 60 days of life with focal or segmental IH, were randomized to treatment with timolol 0.5% 2 drops BID for 24 weeks or placebo. Changes in lesion size, color and thickness were evaluated at 2,4,8,12,24 and 36 weeks. Vital signs and side effects were recorded at each visit. Main outcome was a complete or nearly complete resolution of the IH
Results: Seventy patients were recruited. A total of 52 (75.36%) patients had superficial IHs, (15.9 %) had mixed IHs, and 6 (8.6%) had abortive his equally distributed in both arms. Twenty-two of the 33 infants receiving treatment and 25 of the 37 infants receiving placebo completed the study. Five patients in the placebo arm and 2 in treatment arm were withdrawn because ultimately needed propranolol. We found a 36% complete resolution in the timolol arm vs. 24% placebo arm (P< 0.306). We found a significant color change of the blinded photografic scores at week 12 and week 24 of the study (P < 0.002 and P < 0.01). No severe side effects were found. There was no significant variation in blood pressure and heart rate between groups.
Conclusion: Two drops bid of timolol maleate 0.5% solution for 24 weeks is safe in infants under 2 months of age. Although there was a trend for higher resolution in the timolol group, it was not significant. Twice as many patients in the placebo group ultimately needed propranolol treatment in comparison with the timolol group.

O062
Utility of Prolonged Monitoring During Initiation of Oral Propranolol for Infantile Hemangioma

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Purpose: Guidelines for oral propranolol initiation were published in 2013, based on expert opinion and limited preliminary safety data, and most were not evidenced-based. We aim to update existing monitoring recommendations through a retrospective review.
Methods: A multi-center study was performed, with IRB obtained from 10 institutions. Inclusion criteria included diagnosis of infantile hemangioma requiring propranolol of ≥0.33mg/kg/dose, age <2 years, and prolonged heart rate (HR) monitoring for ≥1 hour. Data entered into a REDCap database included subject demographics, dose, vital signs pre-propranolol and pre-dose escalation, and adverse events. Patients were excluded if taking a concomitant medication with a known cardiovascular effect.
Results: 688 subjects met inclusion criteria, 198 males and 487 females. Median age at propranolol initiation was 110 days. Median initiation dose was 0.38mg/kg/dose. The median change in HR from baseline to 1 hour was -5, and from 1 hour to 2 hours was 0. During the escalation visit, median change in HR from baseline to 1 hour was -4, and from 1 hour to 2 hours was 0. Median dose for dose escalation visit was 0.74mg/kg/dose. Only 60 patients had abnormal vital signs reported during either the initiation or escalation visit, and none warranted immediate intervention. Of these, four patients had alterations in care, and all four were high-risk (preterm). Three had low blood pressure, and one had abnormal vital signs before prolonged monitoring. The only alterations in care were up-titration dose slowing and dose reduction. Abnormal HR at initiation/escalation prolonged monitoring visit did not increase the relative risk of future serious adverse events.
Conclusion: Although four patients had an alteration in care based on abnormal vital signs, none warranted immediate intervention or stopped propranolol therapy. Prolonged monitoring for initiation and escalation of propranolol for infantile hemangioma rarely changed care management.

O063
AQP1 plays a key role in propranolol response in vivo

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Purpose: The non-selective beta-blocker propranolol is currently the first therapeutic option for severe infantile hemangiomas (IH) although its dramatic efficacy remains mechanistically unclear. Neither the molecular target of propranolol nor the mechanism of action of the drug has been identified with sound proof of concept. Aquaporin 1 (AQP1) has been described as a promising therapeutic target in cancer. Our preliminary histopathological studies have shown that IH GLUT1 + vessels have a very specific profile for AQP1 similar to that seen in glioblastoma.
Methods: We have developed a human xenograft tumor model in order to study propranolol antitumor efficacy and to decipher which protein alteration is the most correlated with antitumor effect. Proteomics and shRNA technology have been used to study drug target and downstream effectors of antitumor response to propranolol in vivo.
Results: In a proteomic approach we identified AQP1 as the most significant protein downregulated when mice were treated with propranolol compared to placebo (Anova p=0.008). We also identified a significant positive correlation between AQP1 protein abundance in tumors and tumor burden. In addition propranolol, shADRB2 and shAQP1 greatly improved Avastin antitumor efficacy, a standard of care in glioblastoma. However there was no additive effect between propranolol and shADRB2 or shAQP1, suggesting that a common pathway is involved.
Conclusion: We conclude that Aquaporin 1 downregulation is a possible therapeutic target of propranolol, and is dependent upon ADRB2 signaling. Given that AQP1 upregulation has been documented in numerous tumors, targeting AQP1 with propranolol alone or in combination could be a promising treatment for high AQP1 vascular tumors.

O064
Propranolol treatment does not affect growth and development of children with infantile hemangioma

Andre Moyakine (RadboudUMC)

Purpose: To assess psychomotor development and psychologic (social, emotional, behavioral, and executive) functioning in propranolol treated IH-patients and to compare their growth and development with nontreated healthy controls.
Methods: We performed 3 studies on this topic in our large cohort of propranolol treated IH-patients; all patients were treated for over 6 months. The first study involved 103 IH-patients with a mean age of 35 months analyzing data from the files of the Dutch Well Child Preventive Health Care Clinics using the so called Van Wiechen-scheme (VWS). In a 2nd study data on growth of 82 propranolol treated IH-patients aged 43 to 51 months were collected and parents were asked to complete the 48-months Ages and Stages Questionnaire (ASQ). A matched control group was used to evaluate data. In a 3rd study parents of 27 propranolol treated IH-patients (6.1-7.6 years of age) completed the Behavior Rating Inventory of Executive Function, Social Emotional Questionnaire, Child Behavior Checklist and Strengths and Difficulties Questionnaire. For each questionnaire, the number of patients with abnormal scores, based on established cut-off points, was calculated.
Results: All three studies showed no signs of developmental delay. In the second study comparable height and weight were found in propranolol treated IH patients versus not-treated healthy controls. In the 3rd study on psychological functioning in 7 year olds, no significant abnormalities were seen.
Conclusion: Our 3 studies show no signs for developmental delay, growth abnormalities or psychological dysfunction. Literature on long-term sequel of propranolol is expanding; more and more studies show that propranolol also has no negative consequences in the long term, besides the beneficial effects on IH.

O065
Hemangioma Sequelae In Infantile Hemangiomas Treated With Propranolol

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Purpose: The risk of permanent disfigurement is an indication for propranolol treatment of infantile hemangioma (IH), but sequela or residuum of IHs left to natural involution are difficult to predict. Oral propranolol for 6 months has been shown to achieve complete or near complete resolution in 60% of IHs. The type and degree of sequelae in those with incomplete response have not been studied. This study was designed to describe the sequelae of propranolol-treated IHs and to compare them with the sequelae of untreated IHs.
Methods: A retrospective cohort review of pictures was carried out in 165 patients with IHs treated with oral propranolol (≥ 2 mg/kg/day) for at least 6 months, of whom follow-up pictures between 4 and 5 years of age were available. Eight university hospitals with vascular clinics from 2 different countries participated in the study. The main outcome measurements were: (1) type of sequela; (2) degree of sequela (none, minimal or severe - needing some type of correction);; and (3) age at which no further improvement was seen.
Results: Severe sequelae were observed in 61 (37 %) of 165 treated his, where mean age for propranolol initiation was 5.9 months. Deep IHs had a significantly higher rate of complete resolution without any sequela, than superficial and mixed IHs (X2, p< 0.0001). Mixed IHs significantly led to more severe sequelae than superficial and deep IHs, and 24.6 % of mixed IHs needed excisional or reconstructive surgery. In comparison with a previously published cohort of untreated IHs with matched hemangioma subtypes, treatment with propranolol led to a 33% relative reduction of risk of leaving severe sequelae. The most common types of sequela were telangiectasia (107, 64.8%), fibrofatty tissue (41, 24.8%), and anetodermic skin (35, 21.2%). The average age at which no further improvement was seen was 33.3 months.
Conclusion: In this retrospective study, IHs treated with propranolol regressed at an earlier age and left significantly less permanent sequelae than untreated IHs. These observations provide useful information for treatment decision. Moreover, this study will allow to widen the indication for the treatment of Ihs and to stress the opportunity to start the treatment, when necessary, as soon as possible in order to reduce the sequelae

O066
The positive predictive value of hemangioma location for risk of PHACE syndrome: a retrospective analysis

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Purpose: 1) Assemble a large multicenter retrospective cohort of patients with large facial hemangiomas evaluated for PHACE syndrome since diagnostic criteria were established with data regarding epidemiology, hemangioma characteristics, and comorbid anomalies. 2) Perform sub-group analyses of these categories to determine the positive predictive value (PPV) of clinical features that will provide more data-driven and cost-effective screening of children with large facial hemangiomas.
Methods: Thirteen pediatric dermatology referral centers across the United States and Canada participated in this retrospective study. All patients with a facial, head, and/or neck hemangioma who were evaluated for PHACE syndrome from August 2009 to December 2014 were included. Patients were required to have an MRI/MRA of the head and neck. Data included age at diagnosis; gender; patterns of hemangioma presentation including location, size, and depth; diagnostic procedures and results, and type and number of associated anomalies. An expert reviewed photographs or diagrams to confirm facial segment locations.
Results: 254 patients met inclusion criteria. 33.8% of patients had PHACE syndrome. A multivariate analysis showed multiple hemangiomas on the face (PPV 51.6%), bilateral location (PPV 45.6%), S1 segment (PPV 47.5%), and scalp involvement (PPV 60%) to be independent statistically significant risk factors for PHACE (p values <0.009). Risk of PHACE increased with the number of locations involved, with a sharp increase at 3 or more (PPV 66.7%, p<0.001). Parotid hemangiomas had a negative predictive value (NPV) of 82% (p=.004). Purely deep parotid hemangiomas had an NPV of 93.8%, while S2 segment had an NPV of 68.8%, although neither were statistically significant.
Conclusion: Among children with large facial hemangiomas, those with S1 or scalp involvement, multiple hemangiomas, or bilateral location should be prioritized for PHACE syndrome work-up. Children with S2 facial hemangiomas or parotid hemangiomas (particularly purely deep) may require limited or no work-up for PHACE syndrome. Additional data analysis is ongoing.

O067
Sternal/Midline Anomalies in PHACE Syndrome

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Purpose: The purpose of this study is to describe newly identified histopathologic diagnoses of hamartomas and skin tags in PHACE, especially on the chin, and to analyze the spectrum of sternal/midline defects in patients with PHACE.
Methods: A retrospective chart review was performed to identify and characterize the sternal or midline anomalies in patients with PHACE. Pathology slides/reports were obtained from lesions that had been biopsied or resected.
Results: Eight patients with midline skin tags were identified; one was diagnosed on histopathology as a typical acrochordon, another as rhabdomyomatous mesenchymal hamartoma. Two of four chin hamartomas/papules identified were biopsied, revealing diagnoses of sebaceous hamartoma and hemangioma. Another patient with a surgically resected midline lesion had a histopathologic diagnosis of bronchogenic cyst. Records from 210 patients in a PHACE registry were reviewed. 26% were identified as having a midline or sternal anomaly. Of these, 41% (22) had a sternal cleft, 35% (19) other sternal defect, 20% (11) a sternal pit, 17% (9) a supraumbilical raphe, and 13% (7) a skin tag. Other anomalies reported included bifid sternum, pectus excavatum, midline papule/hamartoma, sternal agenesis/absence, and hypopituitarism/ectopic thyroid. Of the nine patients with supraumbilical raphe, three had a sternal cleft and three had a sternal defect. The two patients with reported hypopituitarism/ectopic thyroid had no associated midline ventral defects.
Conclusion: We report the new histopathologic findings of sebaceous hamartoma and rhabdomyomatous mesenchymal hamartoma in a subset of midline anomalies and tags in patients with PHACE. While skin tags or hamartomatous-like growths are not typically considered to be part of PHACE, this study demonstrates their association with the syndrome. As the etiology of both rhabdomyomatous mesenchymal hamartoma and cutaneous/subcutaneous bronchogenic cyst is thought to be related to aberrations of mesenchymal cells during development, these developmental anomalies may provide clues to the pathogenesis of PHACE.

Difficult Cases 3

O068
Necrotizing Infection of an Infantile Hemangioma: An Uncommon Complication of a Common Disorder

Bridget Shields (University of Wisconsin Department of Dermatology); Lauren Brin Hermans (University of Wisconsin, School of Medicine); Beverly Aagaard-Kienitz (University of Wisconsin - Madison); David Wargowski (University of Wisconsin - Madison); Darya Buehler (University of Wisconsin-Madison); Jason Pinchot (University of Wisconsin); Carrie Kovarik (University of Pennsylvania, Department of Dermatology); Lisa Arkin (University of Wisconsin School of Medicine); Catharine Garland (University of Wisconsin - Madison)

Purpose: Infantile hemangiomas, the most common vascular tumors of childhood, often evolve without complications; however, 10 to 12% require specialty referral for treatment.1We present a rare case of necrotizing infection within a segmental infantile hemangioma leading to sepsis and streptococcal toxic shock syndrome (TSS).
Methods: A 5-week old infant with an enlarging vascular birthmark presented with fever, tachycardia, and respiratory distress. Photos at 4 days and 4 weeks of life (Fig 1a, Fig 1b) demonstrated an enlarging segmental vascular plaque in the S2 distribution. The child appeared ill, with central vesiculation of the tumor (Fig 1c) and associated leukocytosis, hepatitis, and coagulopathy. Broad-spectrum intravenous antibiotics and fluid resuscitation were initiated, and work-up confirmed Group A beta-hemolytic streptococcus (GAS) bacteremia, which subsequently grew from the wound culture. The lesion became rapidly necrotic within 12 hours (Fig 1d). Biopsy demonstrated septic vasculitis within the lobules of an infantile hemangioma (Fig 2a, Fig 2b). After negative imaging evaluation for PHACE syndrome, oral propranolol was initiated with continued antibiotics, with clinical improvement and resolution of septic shock.
Results: The patient has hypertrophic scarring with contracture and lower eyelid ectropion (Fig 1e). Her hemangioma has nearly completely involuted, however she has required reconstructive surgery to release scar burden from her cheek. She is undergoing pulsed dye and fractionated CO2 laser therapy with laser-assisted kenalog delivery for hypertrophic scarring.
Conclusion: This is a rare case of streptococcal TSS due to a necrotizing GAS infection of an infantile hemangioma with significant facial scarring. Leukocytosis, hepatitis, and coagulopathy on admission suggest systemic toxin release which may have accelerated cutaneous necrosis. This case adds to the abundance of literature supporting emergent evaluation and treatment of proliferative vascular tumors. Early referral to specialty care for proliferative vascular tumors is critical to prevent complications including ulceration, scarring and life threatening infection in the newborn period.1
References: *1. Marqueling AL, Oza V, Frieden IJ, Puttgen KB. Propranolol and infantile hemangiomas four years later: a systematic review. Pediatr Dermatol. 2013;30(2):182-91.*

O069
Primary Hepatic Angiosarcoma in a 3 year-old Child Complicated by Consumptive Hypothyroidism: A Case Report

Lara Mrak (University of Wisconsin); Michael Woods (University of Wisconsin-Madison); Carol Diamond (University of Wisconsin-Madison); Jason Pinchot (University of Wisconsin); Beverly Aagaard Kienitz (University of Wisconsin-Madison); Lisa Arkin (University of Wisconsin School of Medicine); Paula North (Medical College of Wisconsin); Darya Buehler (University of Wisconsin-Madison); Kara Gill (University of Wisconsin-Madison)

A previously healthy 3-year-oldfemale presented with abdominal pain. Physical exam revealed firm three quadrant distension. Liver enzymes were mildly elevated; hemoglobin was8.0g/dl. Ultrasound showed a large heterogeneous hepatic mass; contrast-enhanced CT indicated involvement of all hepatic segments and hepatic vascular encasement. On MRI the mass wasT1 hypo intense/T2 hyper intense with progressive centripetal, heterogeneous gadoxetate disodium contrast enhancement and 20 minute washout. The thyroid was enlarged/hyperemic by US; serum testing indicated consumptive hypothyroidism (TSH 49.2 uIU/mL, rT3 >1000 ng/dL). Percutaneous liver needle biopsy showed an atypical vascular lesion within filtration of pleomorphic endothelial cells (ECs) along sinusoids, focally forming epithelioid masses. Lesional ECs were strongly positive for ERG and GLUT1; ECs within uninvolved liver were GLUT1-negative. Pathology interpretation was angiosarcoma, confirmed by expert consultation. No distant metastases were identified via FDG/PET or Technetium 99 mMDP bone scan. The patient was treated with levothyroxine, and forty days post-presentation underwent uncomplicated deceased donor liver transplantation. Four days post-transplant, rT3 was 51.3 ng/dL (compared to >1000 pre-transplant), with continued decline.
Discussion: Primary pediatric hepatic angiosarcoma is rare, but well-documented. More common hepatic vascular lesions, including infantile hemangioma (IH) and congenital hemangioma, were excluded in this case by gross and histologic features of the tumor and consideration of patient age. Although GLUT1 positivity is a universal, diagnostically useful feature of IH, variable GLUT1-positivityhas also been reported in angiosarcoma (North et al, 2000) and is a potential diagnostic pitfall. Consumptive hypothyroidism due to tumoral type 3 iodothyronine deiodinase expression is a well-recognized complication of hepatic IH (Huang et al, 2000), but has not been reported in association with hepatic angiosarcoma.

O070

Controversy RICH or KHE? What constitutes a true Kasabach Merritt syndrome? Necrotizing fasciitis in vascular anomalies: Seeking other centers experience, prevention?

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Purpose: We submit this case for discussion points that will involve multiple specialties including radiology, pathology, hematology, plastic surgery, pediatrics, and dermatology. It is important for pathologists and radiologists to discuss the criteria that aid in differentiating KHE, tufted angioma, and RICH/NICH. Hematologists may help us better understand the range of coagulopathy associated with RICH, vs true Kasabach Merritt syndrome. Plastic surgeons, dermatologists and pediatricians may weigh in on the episodes of thrombophlebitis, finally expressing as necrotizing fasciitis in our patient. We would like to know if any other centers have seen this complication in their vascular anomalies patients and if there would be a means to prevent its occurence.
Methods: A boy was born at term, weighing 3.84 kg, with a huge 10 x 20 cm indurated warm vascular mass of the right forearm. Initial ultrasound doppler and MRI suggested congenital hemangioma but KHE was in the differential. A progessive coagulopathy led to concern for Kasabach Merritt with possible KHE or TA. Biopsy at the time suggested KHE. Skin biopsy revealed a dense lobular proliferating capillary-lymphatic tumor with plump and sometimes spindled endothelial cells. Immunohistochemical analysis with D2-40 revealed a lymphatic differentiation in these endothelial cells, pointing toward a diagnosis of a kaposiform hemangioendothelioma. However, platelets never decreased below 60,000, maximum PTT was 45.3 ($\leq$ 34.8), with a normal prothrombin, normal fibrinogen, however increased D-dimers $\geq$ 2.0 (N $\leq$ 0.25). This coagulopathy rapidly improved in the first month of life. Treatment was initiated with prednisone 2 mg/kg/d for 2 months, compression x 3 mos and Propranolol 3 mg/kg/d max x 14 months. Clinical photos show dramatic improvement with a certain subcutaneous atrophy and dilated veins as seen in RICH.
Results: He subsequently developed episodes of thrombophlebitis mangaged with advil at age 2 yrs, then 3 yrs lasting 2-3 days each time. He presented with pain in his forearm again at age 3 ½, and within hours, developed septic shock. A decompressive fasciotomy was performed urgently revealing multifocal necrotizing fasciitis.
Conclusion: Controversy RICH or KHE? What constitutes a true Kasabach Merritt syndrome? Necrotizing fasciitis in vascular anomalies: Seeking other centers experience, prevention?The ensuing discussion will include multiple specialties including radiology, pathology, hematology, plastic surgery, pediatrics, and dermatology.

O071

Fatal hemorrhage from a rapidly involuting congenital hemangioma in an infant

Aicha Salhi (universite de medecine d'Alger); warda Drali (universite de medecine d'Alger); Nora Cheddani (universite de medecine d'Alger); Toufik Tounsi (universite de medecine d'Alger); Assya Djeridane (universite de medecine d'Alger); Abdelhamid Aitbenamar (universite de medecine d'Alger); zoheir belkaid (universite de medecine d'Alger); Ismail Benkaidali (universite de medecine d'Alger)

Purpose: The term: congenital hemangioma, designates a vascular tumor of intra uterine onset, fully grown at birth, which does not exhibit post natal growth like infantile hemangioma does. The international society for the study of vascular anomalies (ISSVA) distinguishes 3 subgroups: The rapidly involuting congenital hemangioma (RICH), the non involuting congenital hemangioma, and the partially involuting congenital hemangioma (PICH). RICH is characterized by quick regression in 6 to 14 months. This tumor does not have immunoreactivity for GLUT1 and Lewis Y antigen like does infantile hemangiomas. The most frequent topography is scalp, neck and limbs close to a joint. The common morphology is a protuberant round lump, of red color. The natural history is regression, leaving a lipoatrophy area with bluish in surface. Some have central ulceration which can lead to massive life threatening hemorrhage. We report the case of an infant who died after a massive hemorrhage from a RICH.
Methods: A female 7 days old newborn born at term to a 46 years old woman after an uneventful pregnancy, was refered to our department for a congenital vascular tumor. The tumor was violaceous round lump with telangiectasic surface, located on the posterior side of the left arm. It was hot and firm but no thrill was palpated. The tumor was centred by a large ulceration covered by a thick black crust. The lesion was surrounded by a thin whitish halo. Large, blue drainage veins were visible. The retained diagnosis was rapidly involuting congenital hemangioma. Hydrocolloid adhesive dressings were used to aid in the closure of the ulcer. One month later, the tumoral mass was smaller. But the crust has been remover by the dressings, revealing a profound large ulcer, filled with a hematic product. After disappearance of the crust, the hemorrhagic risk was obvious and hospitalization was decided. Unfortunately, during the night before hospitalization, bleeding began. Because of the distance from the hospital, the child arrived at the emergency room only 8 hours later. The rescue was no longer possible despite all the resuscitation efforts. The infant died from a massive hemorrhage.
Results: Rapidly involuting congenital hemangioma is histologically a benign tumor, most lesions are left to shrink spontaneously. But in some cases, it can induce fatal evolution. Two major complications can occur and cause death. Because of significant intra-tumoral arteriovenous shunting, some newborns with RICH, may present with high out-put cardiac failure. The second complication is life threatening hemorrhage.

This risk is mostly present if large vessels are detected close to the ulcer. As the ulcer hollows out, it ends by reaching the underlying vessel. Propranolol is now known to be ineffective in congenital hemangiomas. The treatment of choice when there is a risk of hemorrhage is embolization.
Conclusion: In all cases of RICH with central ulcer or crust, an early Doppler ultrasonography is necessary. If a close vessel can be reached by ulceration, than embolization should be undertaken without delay. In case of impracticable embolization, the achievability of excision, as early as possible must be discussed with pediatric plastic surgeon.

Friday, 1 June 2018

Scientific Session 6: Lymphedema and Lymphatic Malformations

O072
Lymphoscintigraphy for Lymphedema: Establishment of an Evidenced-Based Protocol

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Purpose: Lymphoscintigraphy is used to confirm the diagnosis of lymphedema; pathological findings are abnormal transit time to regional nodes and dermal backflow. A universal protocol for the test does not exist. The purpose of this study was to develop an evidenced-based protocol for patients with lymphedema.
Methods: Individuals treated in our Lymphedema Program between 2009 and 2017 were reviewed. Diagnosis of lymphedema was determined by history, physical examination, and lymphoscintigraphy. Severity was defined by increased volume of the limb: mild (<20%), moderate (20-40%), severe (>40%). Candidate variables included location, age at presentation, duration of symptoms, infection history, and lymphedema type (primary, secondary). An association between lymphedema severity and lymphoscintigraphy findings was determined using the Pearson chi-square test and multivariate logistic regression.
Results: Lymphedema was diagnosed clinically in 169 patients and confirmed by lymphoscintigraphy in 162 (117 primary, 45 secondary; 96% sensitivity). Fifty-eight patients were thought to have a condition other than lymphedema and all had negative lymphoscintigrams (100% specificity). Seven individuals with lymphedema clinically, but normal lymphoscintigrams, all had primary lymphedema and repeat lymphoscintigraphy ≥1 year later showed lymphatic dysfunction consistent with lymphedema. The clinical severity of 181 affected extremities (24 upper, 157 lower) was: 54% mild, 30% moderate, and 16% severe. Delayed tracer transit to the regional nodes was: 45 minutes (34%), 2 hours (18%), and ≥ 4 hours (48%) and 36% demonstrated dermal backflow. Abnormal transit time or dermal backflow was identified in 97% of extremities by 45 minutes and in 3% of limbs by 2 hours.
Conclusion: A lymphoscintigram for lymphedema does not need to exceed 2 hours because abnormal findings are illustrated by this time period. Because only patients with primary lymphedema may exhibit a false-negative study, a patient with a high clinical suspicion for the disease should have the lymphoscintigram repeated one year later.

O073
Proliferative Cells Resembling Mesenchyme Stem Cell-like Pericytes Derived from Kaposiform Hemangendothelioma and Kaposiform Lymphangiomatosis Lesions

Kathryn Glaser (CCHMC); Peter Dickie (CCHMC); Denise Adams (Boston Children's Hospital); Belinda Dickie (Boston Children's Hospital)

Purpose: To isolate and characterize proliferative cells isolated from Kaposiform lymphangiomatosis (KLA) and Kaposiform Hemangendothelioma (KHE) patient lesions.
Methods: Proliferative cells were isolated from three independent KLA patient lesions and one KHE lesion and fractionated based on CD31 surface expression. Cell identification was based on the expression of MSC markers, MSC-like pericyte markers, and endothelial cell markers by flow cytometry, qRT-PCR, and immunoblotting. The in vitro capacity of isolates to support endothelial proliferation and vessel formation was evaluated by co-culture with endothelial cells.
Results: Proliferative KLA/KHE isolates lacked definitive endothelial markers (CD31, CD34) but displayed to varying levels CD73, CD90, CD105, and CD146, as markers of mesenchymal stem cell-like (MSC-like) pericytes. At the gene level, cells expressed a pattern of NG2, alpha-SMA, PDGFBR, and CXCL12 consistent with differentiated MSC-like pericytes. Lesion cells also expressed genes for multiple VEGFs conditioned medium from each promoted the growth of growth-factor starved LECs. VCAM-1 was over-expressed on the surface of patient cells, representing a potential marker of disease. KHE-derived pericytes supported vascular network formation with an efficacy comparable to MSCs when co-cultured with endothelial cells (HUVECs or LECs). KLA-derived cells were functionally inadequate in this respect.
Conclusion: Proliferative cells, isolated from independent KLA/KHE lesions, resembled variably differentiated MSC-like pericytes. Functional attributes of lesion pericytes may be lesion-specific and warrant future investigation.

O074
Kaposiform Lymphangiomatosis Caused by a Somatic NRAS Mutation

Daniel M Balkin (University of California, San Francisco); Carol Nelson-Williams (Yale University School of Medicine); Kristin Shimano (University of California, San Francisco); Tippi MacKenzie (University of California, San Francisco); Jessica L Davis (University of California, San Francisco); William Y Hoffman (University of California, San Francisco); Richard P Lifton (The Rockefeller University); Ilona J Frieden (University of California, San Francisco)

Purpose: Kaposiform Lymphangiomatosis (KLA) is an aggressive diffuse lymphatic disorder characterized by multi-organ involvement and coagulopathy. KLA is considered a severe form of Generalized Lymphatic Anomaly but the molecular pathogenesis is unknown. We sought to capitalize on next-generation whole exome sequencing to decipher the cause of disease.
Methods: Following informed consent, clinical data and blood samples were obtained from a patient with KLA and her unaffected parents, along with the patient's affected splenic tumor tissue. Genomic DNA was extracted and subjected to exome capture followed by next-generation sequencing. Sequence reads were mapped to the human reference genome. Variants with minor allele frequencies in reference databases were assessed for impact on the encoded protein and for conservation of the reference base and amino acid residue among orthologs across phylogeny. Sanger sequencing was employed to verify candidate mutations.
Results: A six-month-old female presented with intracranial hemorrhage, thrombocytopenia and multifocal lymphatic anomaly. The patient's massively enlarged spleen was removed for treatment of refractory Kasabach-Merritt phenomenon. Whole exome sequencing identified a missense mutation in NRAS (1p13.2) present in the patient's affected spleen but absent in patient and parent germline samples, which was confirmed by Sanger sequencing. An adenine-to-guanine nucleotide alteration resulted in conversion of amino acid glutamine 61 to arginine (Q61R) in the conserved switch II region of the NRAS G domain.
Conclusion: Ras proteins play a central role downstream of growth factor receptors to meditate cell survival, proliferation and differentiation. Mutation of Q61, a catalytic residue required for GTP hydrolysis, prevents Ras inactivation resulting in constitutive Ras activation. Somatic NRAS mutations have been implicated in several benign and malignant conditions, including NRAS Q61R in multifocal Giant Congenital Melanocytic Nevus. The observation that KLA is caused by mutations in NRAS signaling offers insight into the basic biology of disease and informs potential therapeutic endeavors.

O075
Generalized Lymphatic Anomaly Is Caused By Somatic Activating PIK3CA Mutations

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Purpose: Generalized lymphatic anomaly (GLA) is a vascular disorder of unknown etiology characterized by diffuse/multifocal lymphatic malformations (LMs). The clinical characteristics and sporadic presentation of GLA suggest that somatic mutations could cause the disease.
Methods: Nine patients with GLA were clinically, radiologically and molecularly evaluated. We performed NGS on paired blood/tissue samples from 9 patients. We also isolated LECs from fresh tissue samples obtained from two patients (GLA-LM-LECs). Isolation was confirmed by flow cytometry and immunofluorescence, and time-course, apoptosis and dose response to Rapamycin was evaluated. Rapamycin treatment in 7/9 patients was also evaluated.
Results: LMs showed mainly a mixed macro/microcystic phenotype. Five patients had bone loss in the medullary cavity, four with both axial and appendicular involvement. Three patients had chylous effusions. Seven patients had visceral involvement, three had associated vascular malformations, and three had skin alterations. We identified four distinct PIK3CA variants (Glu542Lys, Gln546Lys, His1047Arg, and His1047Leu) in LM tissues from 5/9 patients and also in 2/2 GLA-LM-LECs. These same PIK3CA variants occur in cancer and in PIK3CA related overgrowth spectrum (PROS). All mutations were somatic missense single nucleotide variations with a range of mosaicism between 1.1% and 23.0% in LM tissues, and between 28 and 33% in GLA-LM-LECs. All variants detected were confirmed using at least one orthogonal method. None of the mutations detected were present in blood samples. We also found that rapamycin reduced, in part by inducing apoptosis, the proliferation of GLA-LM-LECs. All patients treated with rapamycin reported a reduction in pain. Additionally, three patients showed functional improvement. No improvement of chylothorax or bone regeneration was observed.
Conclusion: We report that somatic activating PIK3CA mutations can cause GLA. We also provide preclinical and clinical evidence to support the use of rapamycin for the treatment of this disorder. We suggest including GLA within the PROS family of diseases.

O076
Lobular Capillary-Lymphatic Malformation of Subcutis: a Newly Recognized Entity with Distinctive Histological and Clincial Features

Paula North (Medical College of Wisconsin); Valerie Salato (Medical College of Wisconsin)

Purpose: Venous malformations, often with combined lymphatic and/or capillary components, occur in distinctive architectural patterns not yet well-described and possibly correlated with successful treatment strategies and as yet undiscovered genetic underpinnings. During institutional prospective histopathological review of all skin, soft tissue, and visceral (~1500, excluding CNS) vascular anomalies submitted for pathological evaluation from 2006-2017, a highly histologically distinctive form of soft tissue capillary-venous malformation, often with combined lymphatic features, was recognized and tracked with immunophenotypic, clinical and radiological correlation.
Methods: All cases of vascular malformations consisting of multiple well-defined (grape-like) lobules of dilated thin-walled vessels were identified by prospective review of routinely submitted H&E-stained sections, then subjected to podoplanin (D240) immunoperoxidase-based staining. Medical and radiological records were reviewed.
Results: A total of 15 cases meeting selection criteria were identified, from 12 female and 3 male patients, age range at resection 4y 2m to 14y 3m. Locations included forearm/elbow (7), lower leg (4), finger (2), neck (1), sub-costal notch (1). 14/15 cases were entirely subcutaneous, with one case extending focally into skin and deep fascia. Skeletal muscle involvement was not seen. 15/15 lesions were reported to be easily separated from adjacent normal tissue, with minimal bleeding from small feeders, slightly more prominent in the case with deep fascial extension. Endothelial mitotic figures were universally absent. There was one incidence of local recurrence 8 years after resection. Age of "noticing lesion" ranged from birth (1), 1-5 years (12), 6-12 years (1), "a long time ago" (1). 12 of 15 cases showed focal endothelial podoplanin positivity ranging from 5 to 20% of lesional vessels.
Conclusion: A highly distinctive capillary-venous malformation with "cookie-cutter" histologic patterning and frequent focal lymphatic differentiation has been identified. Surgical excision is highly successful with rare local recurrence.

O077
Prenatally diagnosed lymphatic malformations: clinical characteristics and outcomes

Nancy Wang (University of California - San Francisco); Isabelle Chumfong (University of California - San Francisco); Lan Vu (University of California - San Francisco); Ilona Frieden (University of California - San Francisco); Kristina Rosbe (UCSF); Josephine Czechowicz (University of California San Francisco - Benioff Children's Hospital)

Purpose: To review presenting features and clinical outcomes of fetuses with prenatally identified lymphatic malformations (LM) in a tertiary prenatal diagnostic and treatment clinic.
Methods: Retrospective review of maternal and infant medical records.
Results: A total of 32 pregnant women carrying fetuses with LM presented to the fetal treatment center between 1/29/1996 and 10/7/2016. The average woman was 30.4 years of age and most frequently gravida 1, para 0. Three of 32 women were carrying multiple fetuses, and in one case both twins had findings consistent with LM. The mean gestational age at presentation was 24.3. Seven of the fetuses were evaluated with MRI. The most common locations of the lymphatic malformations were neck, oral cavity, and oropharynx. 15.6% had polyhydramnios. Of the 33 fetuses with LM in whom outcome data is available (25 fetuses), 10 survived and 15 expired. Of the non-survivors, 10 were electively terminated, 3 had intrauterine fetal demise, and 2 died shortly after delivery. Of the survivors, 3 were born vaginally and 7 were born via C-section, 4 of which were born via Ex-Utero Intrapartum Treatment (EXIT) procedure. Of those in whom EXIT was performed, all survived. All fetuses were intubated. One infant underwent tracheostomy after initial intubation during the EXIT procedure. Management of the LM included a combination of surgical excision, sclerotherapy, and sirolimus. All infants who underwent EXIT had LMs involving the airway though none of the LMs invaded the trachea.
Conclusion: Prenatally diagnosed LM vary in size, location and morbidity. Evaluation by a multidisciplinary care team and the option for delivery via EXIT allows for survival of infants with extensive disease. All-cause mortality was most common in fetuses and infants with LM involving the airway and fetuses who did not undergo EXIT procedure.

O078
ADAMTS3 MUTATIONS CAUSE HENNEKAM LYMPHANGIECTASIA-LYMPHEDEMA SYNDROME 3

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Purpose: Primary lymphedema is due to developmental and/or functional defects in the lymphatic system. It may affect any part of the body, with predominance for the lower extremities. Twenty-seven genes have already been linked to primary lymphedema, either isolated, or as part of a syndrome. The proteins that they encode are involved in VEGFR3 receptor signaling. They account for about one third of all primary lymphedema cases, underscoring the existence of additional genetic factors.
Methods: We used whole-exome sequencing to investigate the underlying cause in a non-consanguineous family with two children affected by lymphedema, lymphangiectasia and distinct facial features.
Results: We discovered bi-allelic missense mutations in ADAMTS3. Both were predicted to be highly damaging. These amino acid substitutions affect well-conserved residues in the prodomain and in the peptidase domain of ADAMTS3. In vitro, the mutant proteins were abnormally processed and sequestered within cells, which abolished proteolytic activation of pro-VEGFC. VEGFC processing is also affected by CCBE1 mutations that cause the Hennekam lymphangiectasia-lymphedema syndrome syndrome type1.
Conclusion: Our data identifies ADAMTS3 as a novel gene that can be mutated in individuals affected by the Hennekam syndrome. These patients have distinctive facial features similar to those with mutations in CCBE1. Our results corroborate the recent in vitro and murine data that suggest a close functional interaction between ADAMTS3 and CCBE1 in triggering VEGFR3 signaling, a cornerstone for the differentiation and function of lymphatic endothelial cells.

O079
Somatic NRAS mutation in patient with Generalized Lymphatic Anomaly

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Purpose: Generalized lymphatic anomaly (GLA, or Lymphangiomatosis) is a rare disease characterized by a diffuse proliferation of lymphatic vessels in skin and internal organs. It often leads to progressive respiratory failure and death but its etiology is unknown. We sought to determine the molecular cause of and the underlying mechanisms in young patient with GLA.
Methods: We isolated lymphangiomatosis endothelial cells (LyECs) from a GLA patient, and characterized them phenotypically and functionally. We employed whole exome sequencing (WES) to survey the exome for disease-causing genes. We also used mouse and zebrafish as model systems to determine the effects of the mutation on the development of the lymphatic system and the effects of drugs on this aggressive disease.
Results: GLA cells were characterized by high proliferation and survival rates, but displayed impaired capacities for migration and tube formation. By WES we identified a somatic mutation in NRAS. In Zebrafish model, endothelial expression of mutant NRAS led to impaired lymphatic development. Systemic treatment with rapamycin led to inhibition of lymphangiogenesis in patient derived xenograft murine model.
Conclusion: In summary, we identify an activating mutation in NRAS as a potential cause for GLA in one young patient. This finding sets the stage for the development of novel therapies for this aggressive anomaly.

O080
Kaposiform hemangioendothelioma: clinical features, complications and risk factors for Kasabach-Merritt phenomenon

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Purpose: Few studies have reported the clinical features, complications, and predictors of Kasabach-Merritt phenomenon (KMP) associated with Kaposiform hemangioendothelioma (KHE). We aimed to determine the clinical characteristics present at diagnosis and to identify features that may aid clinicians in managing KHE.
Methods: We conducted a cohort study of 146 patients diagnosed with KHE.
Results: KHE precursors or lesions were present at birth in 52.1% of patients. In 91.8% of patients, lesions developed within the first year of life. The median age at diagnosis of KHE was 2.3 months (interquartile range, 1.0-6.0 months). The extremities were the dominant location, representing 50.7% of all KHEs. Among KHEs in the cohort, 63.0% were mixed lesions (cutaneous lesions with deep infiltration). Approximately 70% of patients showed KMP. A KHE diagnosis was delayed by ≥1 month in 65.7% of KMP patients. Patients with KMP were more likely to have major complications than patients without KMP (P=0.023). Young age (<6 months), trunk location, large lesion size (>5.0 cm), and mixed lesion type were associated with KMP in a univariate analysis. In the multivariate analysis, only age (95% confidence interval [CI], 4.066-34.753;

P<0.001), a large lesion size (95% CI, 2.239-11.535; P<0.001) and mixed lesion type (95% CI, 1.228-7.132; P=0.016) were associated with KMP.
Conclusion: Most KHEs appeared before 12 months of age. KHEs are associated with various major complications, which can occur in combinations and develop early in the disease process. Young age, a large lesion size and mixed lesion type are important predictors of KMP.

O081
Dynamic contrast enhanced MR lymphangiography in patients with lymphatic anomalies.
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Purpose: Lymphatic Anomalies (LA) are characterized by proliferation of lymphatic tissue often causing deterioration of pulmonary function. Understanding changes in lymphatic anatomy in these patients is hindered by the difficulty of imaging the lymphatic system. The goal of this study is to describe central lymphatic anatomy in this LA patient with pulmonary involvement using Dynamic Contrast Enhanced MR lymphangiography (DCMRL).
Methods: This is a prospective observational study. Tweflth patients (average age 19.5 yo, F/M-6/6) with radiological and or pathological confirmation of lung involvement were included in the study. Six patients presented with Generalized Lymphatic Anomaly (GLA), 5 with Kaposiform lymphangiomatosis (KLA) and one with Gorham-Stout disease. All patients underwent TW2 imaging and DCRML.
Results: On T2 imaging involvement of the bones was in all patients and soft tissues in 11 patients.
On DCMRL, there was abnormal pulmonary lymphatic flow originating from the thoracic duct (TD) or retroperitoneum in 11 patients. In 4/11 patients there was an abnormal pulmonary lymphatic flow from the thoracic duct (TD). In 5/11 patients there was abnormal pulmonary lymphatic flow from retroperitoneum. In 2/11 patients there was a combination of the abnormal pulmonary lymphatic flow from TD and retroperitoneum. In one patient, there was no abnormal pulmonary lymphatic flow on DCMRL.
Conclusion: In majority patients with LA, we demonstrated the abnormal pulmonary lymphatic flow from the TD or retroperitoneum toward lung parenchyma. These findings, can explain the presence of pulmonary symptoms in this patient population. Percutaneous embolization of these pathological lymphatic pathways can potentially improve the symptoms in these patients.

O082
A feasibility study to demonstrate the use of Near Infrared Fluorescent Lymphatic Imaging (NIRFLI) to diagnose and direct treatment in pediatric patients with lymphatic anomalies
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Purpose: NIFRLI allows for real-time assessment of lymphatic anatomy and function in a non-sedated patient without the additional risks inherent with conventional radiological imaging. Early use of this technology has primarily focused on the adult population. This study summarizes our early efforts in utilizing NIFRLI to diagnose lymphatic anomalies in the pediatric population to guide subsequent treatment protocols.
Methods: A prospective cohort utilizing NIFRLI in pediatric patients was conducted from 2014-2017. Patients were enrolled after clinical documentation of lymphedema (LE) or lymphatic malformation (LM). Subjects received multiple intradermal injections of indocyanine green, with NIRFLI illuminating the regions of interest with excitation light and collecting the resultant fluorescent signal using a custom imaging system. Sequences of images were analyzed to assess lymphatic architecture and lymphatic propulsion. Imaging was performed in the clinic without anesthesia. Parents were shown techniques for manual lymphatic drainage (MLD) during the imaging session to provide real-time feed-back for their effort.
Results: Eleven patients underwent 12 sessions of NIRFLI (ave age 7.1yrs (3mos-18yrs)). Patients were diagnosed with LE (6) or mixed LM (5). No complications were seen from the imaging. NIRFLI demonstrated real time flow of lymphatic vessels in all patients, with increased lymphatic flow with topical stimulation. 5 patients with LE had normal anatomy, but low motility. After NIRFLI, one patient with LE from an amniotic band was selected for surgery to remove lymphatic obstruction with follow up imaging demonstrating resolution of LE. One patient with residual LM underwent surgery to resect sites seen in NIRFLI. Based on imaging, 3 patients had sclerotherapy targeting sites of flow seen on NIRFLI.
Conclusion: NIRFLI is a novel technology that shows promise in directing therapeutic interventions for pediatric patients with lymphatic anomalies. Additional work to correlate NIRFLI with conventional radiological imaging is underway to improve its utility.

O083
Differences in clinical findings and plasma cytokine profiles between generalized lymphatic anomaly and kaposiform lymphangiomatosis

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Purpose: Kaposiform lymphangiomatosis (KLA) has recently been distinguished as a novel subtype of generalized lymphatic anomaly (GLA) with foci of spindle endothelial cells amid a background of malformed lymphatic channels. Clinically, patients with KLA have a localized or generalized lymphatic anomaly involving the mediastinum, lungs, retroperitoneum, spleen, bones, soft tissue, or skin. Rapid progression of hemorrhagic lymphatic effusions, hemoptysis, overlying bruising, and variable thrombocytopenia suggest the presence of KLA. The etiology of these diseases remains unknown and diagnosis is confused by their similar clinical findings. This study aimed to clarify differences in clinical findings, coagulation disorders, and plasma cytokine profiles between patients with GLA and those with KLA.
Methods: Data of clinical features of patients with GLA and KLA were obtained from a national survey. Differences in clinical findings, the value of coagulation factors, and the prognosis were analyzed. Plasma was obtained from healthy controls and patients with GLA and KLA. Thirty-six types of angiogenic and lymphangiogenic factors were evaluated for cytokine concentrations using commercially available Luminex multiplex cytokine analysis kits according to the manufacturers' instructions. Correlations between data sets were evaluated using the Mann–Whitney and Kruskal–Wallis tests.
Results: Forty-two patients with GLA and 12 with KLA were registered. A mediastinal mass, hemorrhagic pleural effusion, and coagulation disorder were more frequent in KLA than in GLA. Patients with KLA did not have any ascites. Thrombocytopenia and elevated D-dimer levels were more severe in KLA than in GLA. KLA had a significantly poorer outcome than did GLA (P=0.044). In patients with GLA and KLA, levels of VEGF-A and C were higher than those in controls, whereas there were lower levels of soluble (s) AXL, sHer3, sTie-2, and sneuropillin-1 in patients with GLA and KLA compared with controls. Additionally, angiopoietin-2 levels were 10-fold higher in patients with KLA than in those with GLA and controls.
Conclusion: Patients with KLA have an unfavorable prognosis and serious symptoms (hemorrhagic pleural effusion and coagulation disorder). Our data indicates that some angiogenic cytokines might be potential biomarkers of these lymphatic diseases.

O084
Lymphatic malformations treated by venous anastomosis technique based on flow assessment.

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Purpose: Lymphatic malformations occur in children, and the treatment of microcystic types of such malformations is difficult. This is because conventional treatments, including surgical excision, are inadequate by a high degree of complications and because the efficacy of sclerotherapy is limited. Recent progress in lymphatic surgery has made the following possible: (1) clear visualization of lymph vessels, (2) direct suture approach at the site of lymphatic channels or at the lymphatic malformation itself, allowing the drainage of lymph fluid into the venous system. This technique is called lymphatic venous anastomosis, and it has become the primary option lymphedema treatment. In this study we assessed lymph flow in lymphatic malformations, classified their flow patterns into four types, and assessed the effectiveness of undertaking flow reconstruction with a novel flow oriented anastomosis technique.
Methods: We hypothesized that the flow of lymph would be slow around lymphatic malformation lesions. To assess lymph flow using indocyanine green lymphangiography, we undertook a venous anastomosis technique to reduce pooled lymph in the cysts. Of the patients presenting at our clinic between April 2015 and October 2017, 18 consecutive cases were included in the study. All the patients were diagnosed with lymphatic malformation by magnetic resonance imaging or ultrasound. Patient ages ranged from 1 month to 12 years; 8 patients were boys and 10 were girls. To make a pathological diagnosis, we performed a 3 mm cubic biopsy in the area considered to be unassociated with the lymph flow. At 1-year follow-up visit, the patients' symptoms and the sizes of lymphatic malformations were reassessed.
Results: The venous anastomosis technique, which is based on classification of lymph flow, was successfully performed in all 18 patients. Flow patterns were classified into four types: (1) strong inflow detectable at a typical point where the flow was disrupted just after entry into the lesion, (2) multiple inflows which were weaker than in type 1 flow patterns, (3) flow running above the lesion, and (4) flow running around the lesion which did not connect with the malformation. We performed lymphatic venous anastomosis for type-1 and -2 flow patterns for decreasing inflow which finally lead to the shrinkage of the cysts. For type-3 and -4 flow patterns, we performed direct drainage from the cyst to the venous system as venous anastomosis from the operatively created side hole of the lymphatic cysts. All cases improved following surgery. More than 20% shrinkage of the lesion was achieved in 15 of the 18 cases (83%). Only two sites were associated with complications; these involved the increased presence of vesicles at the wet upper lip in one patient, and a small wound dehiscence in another patient, which closed spontaneously within 1 month.

Conclusion: Lymphatic malformations, especially microcystic types, were difficult to treat because of the high possibility of complications and the limited results that are attainable with scrlotherapy. In this case series, we established a novel approach to surgery with lymph-flow assessment and reconstruction using the venous anastomosis technique. This flow-oriented procedure may be helpful for the treatment of refractable microcystic lesions.

O085
Phase II Study of Sirolimus and Complicated Vascular Anomalies: Long term outcomes in Kaposiform Hemangioendothelioma

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Purpose: Sirolimus treatment for Kaposiform Hemangioendothelioma (KHE) has shown impressive results particularly in hematologic response of KHE patients with Kasabach Merritt phenomenon (KMP). In the year-long Phase II study published in Pediatrics in 2016 (RO1FD003712), 11/12 KHE patients responded. Patients were followed for 5 years after study completion, collecting data on growth and development, complications of therapy, unexpected toxicities, and need for continuing sirolimus.
Methods: Prospective follow-up of patients with a diagnosis of KHE from 2 institutions. Inclusion criteria: follow-up for 4-5 years post-study.
Results: Follow-up included data at 5 year (n=5) and 4-4.5 year (n=4) time points. Average age at the start of treatment was 12 months. 9 of 12 patients were available for follow up. Four patients are no longer on sirolimus: one patient completed study therapy and remains off treatment (OT) (7 years), 1 required 2 years of treatment and is now 2.5 years OT and 2 required an additional treatment course prior to successful discontinuation now 17 and 22 months OT. Of the 5 patients still on sirolimus, all restarted medication for symptoms of pain, swelling and/or edema interfering with quality of life and have made an average of 2.5 attempts to discontinue sirolimus. No patient had reoccurrence of KMP. All patients had improvement in clinical and radiologic appearance of KHE but all have residual lesions noted on imaging and/or clinical exam. No unexpected toxicity, growth delay, developmental issues or other long term toxicity of sirolimus was noted.
Conclusion: This is the first prospective data on long-term follow up of KHE patients treated with sirolimus. Although numbers are small, sirolimus is well tolerated; however, over half the patients were still on medication at 4-5 year follow up. This stresses the need for continued long term follow up in these young patients and investigation of the mechanism of sirolimus effect.

O086
A Multidisciplinary Team Approach to Effectively Treat Abdominal Lymphatic Malformations

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Purpose: Abdominal lymphatic malformations (LM) are a subset of vascular anomalies caused by abnormal development of the lymphatic system. Although these have low risk of mortality, abdominal LMs may lead to significant symptoms including bowel obstruction, vascular compromise and pain. No standardized treatment algorithm has been clearly defined for these complex anomalies. The purpose of this study was to develop a treatment algorithm for patients with abdominal LMs based on current literature and the experience of a multidisciplinary vascular anomalies center.
Methods: We performed a single-institution retrospective review of all patients with LMs in the abdomen, pelvis and retroperitoneum between June 2005 and June 2017. Demographic data, presenting symptoms, imaging, LM subtype (macrocystic, microcystic, combined), treatment course and complications were reviewed. Symptomatic and radiographic response was characterized as excellent (≥95% decrease in lesion size and asymptomatic), satisfactory (≥50% decrease in volume or asymptomatic), or poor (<50% decrease in volume and symptomatic).
Results: 12 patients with abdominal LMs were identified with anomalies located primarily in the abdominal/mesenteric (66.7%), pelvic (16.7%) and retroperitoneal (16.7%) regions. Patients most commonly presented with abdominal pain lasting for an average of 9 months. The majority were pure macrocystic lesions (66.7%). Treatment modalities included sclerotherapy alone (58.3%), surgery alone (8.3%), combination of sclerotherapy and surgery (16.7%), medical treatment with sirolimus (8.3%) and observation (8.3%). 100% of patients who underwent intervention for their LMs had either an excellent or satisfactory response. Complications included one patient with a post-sclerotherapy hematoma requiring no intervention and one patient who developed a post-sclerotherapy bowel stricture requiring bowel resection.

Conclusion: A multidisciplinary approach using percutaneous sclerotherapy, surgery, and medical therapy is essential for effectively treating complex abdominal LMs. Based on our experience with these complex malformations, in addition to review of the current literature, we have developed a treatment algorithm for LMs of the abdomen.

Difficult Cases 4

O087
Generalised Lymphatic Anomaly Treated with Sirolimus and Bevacizumab

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Conclusion: A 20-month old boy presented with a three-week history of cough, lethargy and right sided facial swelling. A CXR showed cardiomegaly; echocardiography confirmed a large pericardial effusion with 500mls of clear fluid drained via pericardiocentesis. Biopsies confirmed a diagnosis of generalised lymphatic anomaly (GLA) affecting the pleura, right parotid gland and lymph nodes, but sparing the pericardium. The patient was managed conservatively post pericardiocentesis as he was asymptomatic. Nine months later, a whole-body MRI showed progression of the GLA with enlarged right lateral cervical complex mass and worsening pulmonary lymphangiomatosis. The selective mTOR inhibitor sirolimus was commenced, titrating to a target trough level of 5-10ng/ml. Following seven months of sirolimus therapy, the patient presented with biphasic stridor with 50% subglottic stenosis and glottic/airway lymphangiomatosis confirmed on biopsy. Subglottic disease failed to respond to balloon dilatation and CO2 laser and the patient had a tracheostomy inserted. Repeat MRI revealed additional areas of involvement in the right subclavian and axillary region, spleen, retroperitoneum and small bowel mesentery. Considering further disease progression, a more individualised therapy was sought. Elevated serum VEGF levels were found on ELISA and therefore bevacizumab, a humanised monoclonal antibody targeting VEGF receptors, was added as a second treatment agent at a dose of 10 mg/kg monthly. Combined sirolimus and bevacizumab therapy has been well tolerated apart from three initial episodes of febrile illness, attributed to an upper respiratory infection in the setting of lymphopaenia associated with both sirolimus and GLA. The patient's facial swelling reduced, and tracheostomy was removed after 7 months of combination treatment. Comparative MRI after 18 months of dual therapy showed generalised improvement in clinical appearance and in particular reduction of GLA volume in the face/neck region and right axilla. In summary, dual inhibition of mTOR and VEGF pathways successfully controlled lymphatic proliferation in our patient.

O088
Difficult case of a lymphedema patient with deteriorating venous outflow of lower limbs

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18 years old girl, suffering from bilateral lymphedema of the lower extremity and of the hip region. Lymphedema appeared first at age 3, at the level of foot, and she had a gradual worsening of the disease, and slowly spread.
3 years ago, her disease worsened significantly. She is suffering from lower extremity motion problems (because of huge lower limbs), time by time she has erysipelas at the groin region. She wears compression stockings, and needs diuretic treatment. She has hypoproteinaemia, hypoalbuminaemia, the serum total protein level is generally lower than 50g/l. No evidence of proteinuria or enteropathy, liver functions are normal. Lymphoscintigraphy did not show any superficial lymphatic transport, the radiotracer leeks slowly into the deep lymphatic vessels. She has polysplenia syndrome with azygos continuation of the inferior vena cava. From the levels of the hepatic veins till the right renal vein, the IVC is missing. The existing, inferior part of the IVC is shunting into dilated, networked paravertebral veins (which drain into the azygos vein). This lesion is congenital, but there is a significant narrowing and decrease in the blood flow of the lower IVC. The whole clotting system seems to be normal, but because of safety, the patient now is on anticoagulant therapy. Patient has deteriorating venous outflow with high venous pressure of the lower limbs, and superficial lymphatic insufficiency too. Lympho-venous shunting at the inguinal region was failed, we found only very tiny fibrotic lymphatic vessels. We did femoro-peritoneal drainage (by implantation of silicone tube) with poor effect. We have thought about venous shunting of the common iliac veins into the upper part of inferior caval vein, but it has potential high complication rates. The other option to reduce the limbs' diameter, is liposuction. Would you do the liposuction or the shunting?

O089
Case of Multifocal Lymphangioendotheliomatosis with Thrombocytopenia (MLT)…without thrombocytopenia and with minimal cutaneous involvement

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Purpose: To discuss a difficult case of an infant with a diffuse, systemic vascular anomaly. Multifocal Lymphangioendotheliomatosis with Thrombocytopenia or Cutaneous Angiomatosis and Thrombocytopenia (MLT/CAT) is a rare vascular malformation described in young children (mostly diagnosed before 2 years old). The classic features include multiple cutaneous brownish-purple plaques, thrombocytopenia, bleeding from the gastrointestinal tract and/or intracerebral. Systemic involvement with lung and bone nodules have been described in a few case reports.
Methods: A four months old baby boy presented to our hospital due to intermittent hematemesis for two months and profound anemia (hemoglobin 4.9g/dL). EGD (esophagogastro-duodenoscopy) revealed three bleeding gastric vascular lesions that were treated with argon therapy.
Results: Physical examination demonstrated two tiny cutaneous brownish-purple plaques (one on the sole of the foot and one on the posterior thorax), everything else was within normal limits. Basic metabolic and hematologic investigation showed only iron deficiency anemia (normal platelets). Screening whole body MRI (magnetic resonance imaging) revealed multiple pulmonary nodules, multiple small intramuscular nodules seen throughout the torso, abdomen, and pelvis, focal nodular bony lesions seen within multiple vertebral bodies, the pelvis, and proximal femurs bilaterally, right choroidal plexus hemorrhage and multiple splenic lesions. Thoracoscopy with wedge resection shows lymphangioendotheliomatosis (LYVE-1+). Oral sirolimus was initiated with progressive improvement in hemoglobin and no recurrences of hematemesis.
Conclusion: While the histologic evaluation was clear for MLT/CAT, the diagnosis is still uncertain as the child is missing an important element: the thrombocytopenia. Also, the cutaneous involvement is minimal. With the multiple organs affected by the vascular lesions, should malignancy still remain on the differential diagnosis? How often should we image the patient? Is monotherapy with sirolimus the best therapeutic option at this moment or biphosphonates should be added due to bony lesions?

O090
Diagnostic and Management Dilemma in a Neonate

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Purpose: We were consulted prenatally for a baby girl diagnosed at 20 weeks gestational age with vascular anomalies on the neck, shoulders, liver and chest wall.
Methods: The vascular tumors continued to grow and were monitored with fetal MRI. Baby was born at 37 weeks gestational age with large high-flow vascular tumors covered with purple plaques in the prenatally described areas. Biopsy performed in the first week of life revealed "congenital hemangioma Glut-1 and D2-40 negative".
Results: Co-morbidities included complete situs inversus with dextrocardia, left sided liver and large omphalocele. The large unifocal liver hemangioma covering multiple hepatic segments was not eligible for surgical resection. Baby developed congestive cardiac failure immediately after birth that became worse over the first 2 months of life. The hepatic artery and left mammary artery were embolized. Initially resulted in mild stabilization, followed by worsening cardiac parameters. After 10 weeks of life, the cardiac failure started to improve. The stabilization overlapped with new development of thrombocytopenia. The platelets were normal for the first 2 months of life, then decreased to a lowest of 45k followed by spontaneous improvement, no transfusion needed. No medical therapy targeting the vascular tumors administered.
Conclusion: The visual diagnosis would indicate Kaposiform Hemangioendothelioma (KHE), but the biopsy rules it out. Also, no growth, no Kasabach-Merritt Phenomenon after birth. Is this a KHE that the biopsy missed? Liver tumor looks more typical of a congenital hemangioma. Can this child have two different vascular anomalies simultaneously? Is thrombocytopenia due to congenital hemangioma involution? Life-threatening congestive cardiac failure slowly improving. Could we have offered any medical therapy to accelerate the process and avoid the cardiac complications? If embolization is/was an option, where to embolize? How to determine which area(s) is causing the most "arterial steal"? Is observation and supportive care in this case still the best option?

O091
Facial reanimation in patients with flaccid facial paralysis after excision of facial vascular anomalies

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Purpose: Facial vascular malformations may involve facial musculature or surround the facial nerve or its branches. Surgery or sclerotherapy may lead to segmental or hemifacial flaccid paralysis, or weakness resulting in an asymmetric smile. Functional (feeding, speech difficulty) and psychosocial consequences are common. Advances in free tissue transfer used alone or in combination with static procedures has made facial reanimation a standard in reconstructive surgery. Patients undergoing excision of vascular malformations or sclerotherapy with resultant facial paralysis may benefit from these procedures.
Methods: A retrospective chart review of patients with a diagnosis of vascular malformation and facial paralysis undergoing 1 or 2 stage free muscle transfer for facial reanimation with at least 1 year follow-up was performed. Medical records included pre-and postoperative photographs/video. Procedure type (1 or 2 stage), time to reanimation, and adjuvant procedures were noted. FACE questionnaires(qualitative) and quantitative evaluations were also employed.
Results: Nine patients ranged in age from 10 to 33 years (average 20). There were 4 males and 5 females. Eight patients underwent a 2-stage procedure, while 1 with bilateral facial paralysis underwent 1-stage simultaneous bilateral gracilis flaps. Two patients undergoing 2-stage had dual innervation (cross-face sural nerve and masseteric branch of V). Timing of the 2nd stage surgery was 11-20 months after the first stage. There were 2 postoperative hematomas requiring drainage. Time to first movement was 2-12 months. All patients had spontaneous movement. Five patients underwent adjuvant procedures: eyebrow lift, external nasal valve suspension, contralateral botox injections. 6 patients had ongoing treatment for residual adjacent disease. All patients had qualitative and quantitative improvement.
Conclusion: Facial reanimation restores a spontaneous smile in pediatric and adult patients with facial paralysis secondary to vascular anomalies surgery and/or sclerotherapy. Adjuvant procedures are also necessary for improved symmetry. Ongoing treatment of adjacent vascular anomaly is also possible.

O092
Three Thousand Sclerotherapy Treatments of Vascular Anomalies with Intralesional Bleomycin Injection

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Purpose: Surgical treatment of venous and lymphatic malformations can be disappointing and prone to recur after resection. 3000 Bleomycin treatments have been performed in our unit in the last 13 years. We present our experience in 703 patients with vascular anomalies treated with intralesional bleomycin sclerotherapy
Methods: Patient demographics, clinical response, treatment and complications details were prospectively recorded. Treatment was administered by ultrasound guided percutaneous IBI. Serial standardised photographs allowed assessment of lesional response. Pulmonary surveillance was performed on all patients.
Results: 376 venous malformations, 138 haemangiomas, 126 lymphatic malformations, 26 capillary-venous malformations, 12 capillary malformations, 5 angiokeratomas and 20 arteriovenous malformations underwent IBI. Complete resolution occurred in 59.3%, significant improvement in 28.3%, and modest improvement in 9%, with a 96.6% overall response rate. Minor complications occurred as follows: swelling (n=6), transient skin hyperpigmentation (n=6), nausea and vomiting (n=3), rash (n=5), pain (n=2), skin ulceration (n=1). Eight malformations recurred
Conclusion: Ultrasound guided non-surgical bleomycin sclerotherapy provides good success and low recurrence rates in treatment of vascular anomalies without the morbidity and limitations of surgery.

O093
Operative treatment of lower extremity venous malformations

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Purpose: Venous malformations (VMs) are most common vascular malformations in clinical practice. In lower extremity, VMs often cause pain and swelling especially during and after exercise. The first treatment option in many centers is sclerotherapy. However, outcome after sclerotherapy varies and surgery may be indicated in case of persisting symptoms. Surgery may be considered as too extensive and leading to functional problems and high recurrence rate. The aim of this study was to analyze complications, reoperations, clinical outcomes, imaging results and identify subgroups which might benefit from primary surgery.

Methods: We included 38 consecutive patients with lower extremity VMs treated operatively (I/2007-I/2017). Their diagnostics and treatment was coordinated by the interdisciplinary vascular anomaly team of our institution. We reviewed patient records and MR images performed postoperatively and graded complications according to Clavien-Dindo classification.
Results: 12 patients had subcutaneus lesions, 22 had intramuscular lesions (19 in single muscle, three in several muscles), four had intra-articular lesions in the knee joint. 25 patients had had previous sclerotherapy without permanent relief of symptoms.Three patients had reoperations of the same lesion, one occurring in the sole of the foot and one in the wide spread intramuscular lesion in the calf. There were no major complications; four Clavien Dindo class I-II. Functional outcome and patient satisfaction was most favorable with intramuscular localized lesions with histological signs of angiomatosis of soft tissue (AST).
Conclusion: Surgery for lower extremity VMs is safe, with low complication rate. The overall outcome is good for localized intramuscular lesions confined to one or two muscles. For such lesions surgery might be considered as primary treatment option. However, with extensive lesions invading several muscles satisfactory results are difficult to achieve. Further prospective studies with functionality and life quality assesments could provide data of the long-term outcomes of different treatment options.

O094
Effectiveness and safety of balloon-assisted sclero-embolotherapy for subcutaneous arteriovenous malformations

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Purpose: We have developed a new sclero-embolotherapy technique, balloon-assisted sclero-embolotherapy (BAST), using a micro balloon catheter to control blood flow. The purpose of this study was to evaluate the effects and safety of BAST.
Methods: 50 patients with subcutaneous AVMs (22men, 20 women) age 13-76y.o. (Av 35.0) total 88sessions location head and neck 21, body 7, upper extremities 10, lower extremities size 5cm> 11, 5-20cm 15, 20cm< 24 angiographic classification (Do Y.S) type IIIa 1, IIIb 2, II+IIIa 1, II+IIIb 1, IIIa+IIIb 30, II+IIIa+IIIb 7, methods ; A micro balloon catheter (2.7 Fr, φ 4.0 mm×10 mm) was used. A sclerotic agent is monoethanolamine oleate foam. We evaluated decreased contrast enhancement on arteriography, 1 month after follow up CTA or MRA, changes in clinical symptoms (using VAS scale) and complications were assessed.
Results: We were able to evaluate the therapeutic outcome by one month follow up CT. Total effective rate (CR 11+PR21) was 62%. The therapeutic outcome of the lesions in Head and neck, of which effective rate was 76.2%, was better than any other areas.The therapeutic outcome was better when the lesions were small (<5cm), of which effective rate was 86.3%. The angiographic classification of the lesions had nothing to do with therapeutic outcomes.
Conclusion: BAST is effective and safer than conventional technique dIn sclero-therapy. The flow control and stagnation of sclerotic agent are important for AVMs, especially high-flow AVMs.Technical success of BAST for AVMs is 100%. BAST might be more effective to flow control and reducing cast migration.

O095
Ethylene vinyl alcohol copolymer in the treatment of high flow arteriovenous vascular malformations: Long- term results and histology

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Purpose: To describe the use, long term results and histologic findings of Ethylene vinyl alcohol copolymer for the treatment of high flow arteriovenous vascular malformations.
Methods: Since 2005, we have used the Ethylene vinyl alcohol copolymers (Onyx 18 and Onyx 34) in the treatment of 38 patients with high flow arteriovenous vascular malformations; 26 females and 12 males with ages ranging from <1 to 67 years (mean = 28.9 years). Twenty-three of the malformations involved the extremities and 15 involved the chest, abdominal wall or pelvis. All patients were evaluated with MRI/MRA pre-treatment and ultrasound if necessary to document lesion visibility. The embolic agent was delivered by subselective transarterial and /or venous micro-catheter techniques with or without ultrasound and fluoroscopic guided direct injection into the lesion under tourniquet control. Tissue from patients whose embolized lesions were subsequently explanted were examined histologically.
Results: Ethylene vinyl alcohol copolymer (Onyx) was found to be durable and effective. Its visibility allowed observation of filling of the malformation vessels during treatment. There was minimal post procedure discomfort with Onyx. Of the 38 patients, two with an extremity lesion developed an area of ischemic skin ulceration, one treated with a skin graft. One patient with a pelvic AVM developed an area of radiation dermatitis and another had worsening of a pre-existing radiation burn. In one neonate a filament of Onyx extended into the right atrium without further migration. In patients who received multiple treatments, multiple imaging obliquities were sometimes needed to allow visualization of untreated portions of the lesion partially obscured by prior Onyx. On histology, the filling of the intraluminal spaces of the malformation with associated foreign body type giant cell reaction was observed.
Conclusion: Ethylene vinyl alcohol copolymer is a safe, durable agent for treatment of high flow arteriovenous malformations.

O096

Ethanol embolization combined or not with surgery and close clinical follow-up can effectively control extracranial arterio-venous malformations (AVMs).

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Purpose: Interventional management of extracranial AVM poses a therapeutic challenge regarding the timing, the approach and the long-term outcomes. We report a long-term longitudinal experience based on a large collaborative database between two pediatric and adult vascular anomaly centers.
Methods: All patients with a diagnosis of extracranial AVMs and a clinical follow-up were included. Clinical presentation, location, type, agent and techniques used, surgical procedures, procedural complications, and clinical and imaging follow-up were included in the analysis. The interventional management was similar across institutions: careful observation of asymptomatic patients and intervention for symptomatic patients with ethanol embolization as a first choice agent and surgical resection if incomplete response following embolization. The primary endpoint was the evolution of the Schobinger stage. The secondary endpoints were complications and clinical recurrence after intervention.
Results: 121 patients were enrolled in the study (mean age at study entry 26.1year (0-77.9y), 48M, 75F). The mean follow up was 6.6 year (0.2-25.2y). The highest Schobinger score during patient follow-up was estimated at 2.12 whereas at last FU it was decreased at 1.41 ($p<0.001$). During follow up, 53.3% of patients were improved on the Schobinger scale, 41.7% remained stable, whereas 5.0% deteriorated. 31 patients (25.8%) with a Schobinger stage 1-2 presented stable lesions (mean FU 5.0y (0.5-13.0y)) and did not require any intervention. Embolization alone was performed in 81 patients and embolization combined with surgery in 7 patients (average of 4.92 (1-24) embolization sessions per patient). Severe complications were observed in 4 patients. 2 patients died, one from procedural complications and one from complications directly related to AVM.
Conclusion: Clinical observation of Stage 1-2 Schobinger AVMs remains a good strategy on long-term. Ethanol embolization with or without surgery can control adequately a large proportion of patients with extracranial AVMs.

O097

Efficacy of flow related color-coded DSA in direct puncture treatment of arteriovenous malformations.

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Purpose: Large arteriovenous malformations(AVMs), typeIIIa and IIIb in modified angiographic typing, are often refractory to treat safely and satisfactory. Although endovascular treatment, especially direct puncture sclerotherapy is good option for these AVMs, we also have difficulty in decision making on using flow control and setting the end point of each session. The purpose of this study is to report our early experience and feasibility of flow related color-coded DSA for typeIIIa and IIIb AVMs.
Methods: Patient selection: Thirty cases of TypeIIIa/IIIb AVM patients treated with direct puncture sclerotherapy under general anesthesia between March 2016 and December 2017. Angiography and image processing: Angiography was performed using commercial angiography systems (Siemens Artis zee, Siemens Healthcare, Forchheim, Germany Siemens /Artis zeego, Siemens Healthcare, Forchheim, Germany). Image processing was performed using also a commercial software (syngo iFlow, Siemens Healthcare, Forchheim, Germany). Sclerosant: Ethanol (70-100%, 0.1-0.25ml/kg) in 21 cases, foamed polidocanol (1~3%) in 15 cases.
Results: All procedures were technically successful. In all cases, no additional angiogram is required to obtain iFlow images. In cases pretreatment iFlow shows slow peak time, direct puncture sclerotherapy was performed without flow control, and in fast peak time cases direct puncture sclerotherapy was performed with flow control. When pretreatment iFlow showed ischemic area around AVM, with adequate treatment of AVM post iFlow image exhibited improvement in the perfusion around AVM. Flow related color-coded DSA provided useful information on flow characteristics of AVM.
Conclusion: Flow related color-coded DSA(iFlow) is helpful on decision making during direct puncture treatment of arteriovenous malformations.

Scientific Session 8: Vascular Malformations Potpourri

O098
Hormone Receptors Expression in Microvascular Proliferation of Arteriovenous Malformation

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Purpose: Previously known as static lesions, composed of mature vessels, a subpopulation of arteriovenous malformation (AVM) was found recently to undergo microvascular proliferation (MVP). Angiogenesis can occur under the influence of several hormonal stimuli. We investigated the in situ expression of 4 different hormones receptors, being follicle-stimulating hormone (FSHR), estrogen (ER), growth hormone (GHR), and progesterone (PR), in resection specimens of AVM and in relation to lesioned occurrence of MVP.
Methods: Paraffin blocks of 15 AVM cases, previously diagnosed histologically with focal MVP, were immunohistochemically stained with antibodies for FSHR, ER, GHR, PR, and double-stained with SMA-1 (smooth-muscle), CD-31 (endothelium), and tryptase (mast cells). Hormones receptor expression was compared in proliferative and mature vessels areas of each lesion and scored semi-quantitatively.
Results: FSHR and ER expression varying in intensity was found in all 15 cases. FSHR expression was strong in 14 (93.33%) in proliferative areas and 5 (33.33%) in mature vessels areas of lesions; ER expression was strong in 7 (46.67%) proliferative and in 4 (26.67) mature areas; all other lesions stained only weakly. GHR expression was only weakly expressed in 5 (33.33%) in proliferative area in 2 (13.33%) of mature vessels areas, and in all other lesions were absent. PR staining was positive in vasoproliferative areas of 8 lesions (strong in 5 (33.33%), and weak in 3(20%), and but also in mature areas (strong in 3 (20%), and weak in 5 (33.33%)). Immuno-double stains showed that FSHR, ER, and GHR expression occurred in vessels walls, whereas PR expression was mostly located in interstitial cells, including mast cells, and only scarcely in vessel walls.
Conclusion: In situ expression of all 4 hormones receptor occur in varying extent and intensity, with a major role of ER and FSHR. More abundant expression in the vasoproliferative areas could indicate their potential participation in angiogenesis of AVM.

O099
Electrosclerotherapy as a novel treatment option for hypertrophic capillary malformations: proof of concept

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Purpose: The current state of the art treatment modality for hypertrophic capillary malformations (CMs), laser therapy, has a considerable rate of non-responders and recurrence. Intralesional bleomycin injections are commonly used to treat other vascular malformations, but the intravascular injections are not feasible in capillary malformations due to the small diameter of the capillaries. Electroporation - an electric field applied to the tissue - could increase the permeability of endothelial cells, which could theoretically facilitate targeted localized bleomycin delivery. We therefore hypothesize that bleomycin injections in combination with electroporation -'electrosclerotherapy' (EST), also known as 'electrochemotherapy'- could potentially be a novel alternative treatment option for CMs.
Methods: In this randomized within-patient controlled pilot trial, 5 patients with hypertrophic CMs were enrolled. Three regions of interest (ROIs) within the CM were randomly allocated for treatment with [A] EST, [B] bleomycin injections without electroporation, and [C] no treatment. Patients and outcome assessors were blinded for the treatment allocation. Treatment outcome was evaluated using patient and physician reported global assessment scores, colorimetry, laser speckle imaging, applied before and 7 weeks after the treatment procedure.
Results: A clear decrease in color, hypertrophy and microvascular blood flow was observed in the ROIs that were treated with electrosclerotherapy, confirmed by the subjective patient- and observer-reported outcome measures and the objective colorimetry and laser speckle imaging measures. The other ROIs (bleomycin without electroporation and no treatment) were measurably unchanged at follow-up.
Conclusion: Electrosclerotherapy may have the potential to become a new valuable addition to the therapeutic armamentarium for capillary malformations. Further research is necessary to determine its effectiveness and safety profile. Additional studies should be designed to investigate the applicability of EST in other types of vascular malformations or vascular tumors.

O100
Bleomycin Electrosclerotherapy (EST); an Exciting Emerging Treatment in the Management of Vascular Malformations

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Purpose: Intralesional bleomycin, a cytotoxic anti-tumour drug, is an established sclerotherapeutic treatment option toward the management of vascular malformations. Electroporation is the temporary application of an electrical field across a tissue with the aim of briefly increasing cellular membrane permeability thus enabling/augmenting drug delivery. Our vascular malformation unit recently published a case report combining the use of electroporation and intralesional bleomycin (electrosclerotherapy) to successfully treat a venous malformation. We now aim to describe our experience with electrosclerotherapy in a case series of twelve patients further establishing the safety and efficacy of this treatment to date.
Methods: We undertook a prospective assessment of twelve patients, not responding to standard sclerotherapy, treated with bleomycin electrosclerotherapy (EST) in our unit.
Results: Overall, eight venous malformations, two capillary venous malformations, one arteriovenous malformation and one lymphatic malformation received electrosclerotherapy over the past 13 months. The majority of these were head/neck malformations. Treatment was conducted either with local anaesthetic, sedation or general anaesthetic based on patient requirements. All patients underwent baseline respiratory assessment and were closely monitored for complications. No patients experienced significant treatment related complications. All patients responded to treatment. Importantly, in this small series, adequate treatment response was achieved in a single treatment session in all but two patients (83%), versus standard bleomycin where an average of at least four sessions are needed.
Conclusion: Electrosclerotherapy is a likely safe and promising method of augmenting the efficacy of intralesional bleomycin when treating vascular malformations with the potential of significantly reducing the administered dose and number of treatment sessions needed. Further follow-on research studies are planned.

O101
Pregnancy in Women with Klippel-Trenaunay Syndrome: Report of a Complicated Case and Proposal for Standardized Care

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Klippel–Trénaunay syndrome (KTS) is a rare congenital disease characterized by two major features: vascular malformations and localized disturbed growth of bone or soft tissue. Both the disturbed growth and the vascular malformations in KTS mostly affect the extremities. The vascular malformations often cover an even larger area of the body, and may extend to the trunk and pelvic region including external and internal genitalia. Literature suggests that women with KTS have a significant risk of venous thromboembolic events, severe postpartum hemorrhage, and aggravation of KTS symptoms during pregnancy and in early postpartum period. There is limited literature available about the management of pregnancy in women with KTS. We report a case of a 19-year old pregnant woman with KTS. As part of this she had extensive venous and capillary malformations located at her lower extremities. Advises was pelvic MRI, but this was refused by the patient because of anxiety. Ultrasound showed no pelvic vascular malformations. The delivery in a second-line hospital was complicated by severe postpartum hemorrhage and two surgeries for manual removal of the placenta. Pelvic MRI after the pregnancy showed extension of the vascular malformations in the pelvic area. Regarding this complicated case and the literature we propose a protocol with the purpose of describing important focuses in preconceptional counseling and obstetric management of patients with KTS, and furthermore, to determine which standard care is needed for these patients.

O102
Chitosan-doxycycline hydrogel: An MMP inhibitor/sclerosing embolizing agent as a new approach to treat AVMs and LM.

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Purpose: Doxycycline possesses non-specific inhibitory effects on various MMPs and is used as a sclerosing agent for lymphatic malformation. MMPs are linked with the progression of intracranial and extracranial AVMs and lymphatic malformations. We developed an injectable occlusive chitosan (CH) hydrogel containing doxycycline (DOX).
Methods: Several CH-DOX hydrogel formulations were characterized for their mechanical properties using a rheometer, their occlusive properties on a bench test and their injectability through microcatheters. DOX cytotoxic dose-response was studied on human umbilical vascular endothelial cells (HUVECs) and assessed on ex-vivo dogs' aorta. The DOX release was tested using an USP Dissolution Apparatus. The ability of the gel to

inhibit MMP-2 secreted from human U-87 glioblastoma cells (U-87MG) was assessed at different time points. The embolization properties of an optimized gel formulation was finally tested in an acute model of renal artery embolization in 6 pigs.
Results: All formulations were injectable through microcatheters and gelled rapidly at body temperature. Only hydrogels prepared with 0.075 M sodium bicarbonate and 0.08 M phosphate buffer as the gelling agent presented sufficient mechanical properties to immediately impede physiological flow. DOX release from this gel was in a two-stage pattern: a burst release followed by a slow continuous release. Endothelial cells showed a substantial decrease in viability when exposed to DOX concentrations above 0.5 mg/mL. Factor VIII staining on ex-vivo embolized aorta demonstrated endothelial ablation for all tested CH-DOX gels (0.1, 0.3 and 1%) while injection of CH gel only slightly affected the endothelial cells layer effectively. Released DOX was bioactive and able to inhibit MMP-2 activity in U-87MG. In vivo testing in pig renal arteries showed immediate and delayed embolization success of 96% and 86%, respectively, good radio-opacity and evidence of endothelial ablation on histology.
Conclusion: CH-DOX hydrogels appear to be promising embolic agents for the treatment of AVMs or LMs.

O103
Pre-operative percutaneous n-BCA glue embolization of truncal and extremity venous malformations: technique, safety, and clinical outcomes

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Purpose: To describe treatment of pediatric extremity and truncal venous malformations (VMs) using percutaneous n-butyl cyanoacrylate (n-BCA) glue embolization immediately prior to surgical excision (glue-excision surgery, GES).
Methods: 63 patients (22 male, 41 female; mean age 12 years (range 1-25)) who underwent 70 GES procedures for extremity and trunk venous malformations were reviewed. Indications for treatment included pain (100%), swelling (22%), and diminished range of motion (ROM) (16%). 37 patients (59%) had undergone prior stand-alone interventional or surgical treatment with incomplete therapeutic benefit. Technical and clinical success of GES were retrospectively assessed.
Results: Embolization was technically successful in 100% of patients. 2 patients (3%) underwent planned, second stage GES for their originally treated lesion. 5 patients (8%) underwent an unplanned, second stage GES procedure for residual disease after the primary operation. No third stage treatments were performed. Mean and median follow-up duration were 18 and 17 months, respectively (range 3 to 35 months). Symptomatic improvement was achieved in 58 patients (92%), of whom 41 (65%) reported complete elimination of pain. There were no instances of non-target embolization or other complications of the interventional procedure. For the surgical procedure, one patient required additional surgery for wound dehiscence and one patient developed an abscess requiring incision and drainage. Minor surgical complications included surgical site skin infections (n = 5) and numbness (n = 1). Mean and median surgical blood loss volumes were 131 mL and 10 mL, respectively. One patient required perioperative blood transfusion.
Conclusion: Pediatric extremity and truncal venous malformations can be safely and effectively treated in a single-stage fashion using percutaneous n-BCA glue embolization immediately preceding surgical excision. Our early experience suggests this technique affords more definitive treatment over stand-alone interventional or surgical techniques.

O104
Intramuscular venous malformations of the calf: surgical treatment outcome of 57 patients

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Purpose: Intramuscular venous malformations (IMVMs) of the lower extremity(LE) are a rare and can be highly symptomatic. Sclerotherapy indications in this location are limited, given the proximity of critical neurovascular bundles. Surgical treatment Indications , need to be discussed in light of the risk of functional impairment. We aimed to report surgical treatment outcomes regarding pain, functional limitation and quality of life=(QOL).
Methods: We retrospectively(2010-2015), reviewed 57 consecutive patients with IMVMs located in the posterior compartment of the leg treated by surgery at a single institution. Data collection was performed by reviewing patient's charts from a prospective database. Imaging by Doppler ultrasound and MRI were reviewed. Outcomes on postoperative morbidity, pain, muscle contracture, residual VMs as seen by MRI and QOL were reported.
Results: 227 patients with IMVMs of the LE were seen at our clinic, 102 had IMVM of posterior compartment. Surgical treatment was performed in 57 patients (37 females, 20males) with a mean age of 26 (range 9-73 y/o). In 82% the lesions were confined to the calf while in 18% the IMVM was diffuse . Pain was seen in 96%, muscle contracture in 10%, pulmonary embolism like initial symptom in 7%. Muscles involvement included soleus muscle in n=28 , gastrocnemius muscle n=25 , deep muscles involvement in n=4. Complete excision was possible in 91%, partial excision in 9%. Associated procedures were: tendinous transposition n=3 , excision

of tibial artery and vein n=3 , muscle lengthening n=3 . No postoperative morbidity was reported. Out of the 44 patients who had an MRI at 6 months, 80 % had no residual VM. Three patients underwent a second procedure. At the last FU(mean 39 months range 6-81), 88% had no residual pain and 92% had normal recreational activities with no functional sequels. QOL was significant better considering the pain relief.
Conclusion: For IMVM of the posterior compartment , we favor surgical resection as first line treatment in symptomatic patients. Our serie suggest improved outcomes with surgery in terms of pain, functional muscular impairment and QOL.

O105
In the Age of B-Blockers Is There A Role For Surgery To Manage Infantile Hemangioma in Sensitive Facial Anatomical Regions?

Jugpal Arneja (University of British Columbia)

Purpose: Facial infantile hemangioma (IH) may cause significant functional impairment and often invoke great parental distress and negatively affect the psychological well being of a child. B-Blockers have become first-line treatment and are often all that is required for management. Outlined herein are results surgical resection of functional or aesthetically concerning facial IH based on the experience with 100 consecutive patients, and from these results an algorithm for their management is presented.
Methods: A retrospective review was performed of all surgically-managed cases of facial (cheek, forehead, nasal tip, periocular, lip subunit) IH presenting to our Multidisciplinary Vascular Anomalies Clinic. Parameters for review included onset age, symptoms, medical therapies utilized, age and status of lesion at time of surgery, outcomes, and complications.
Results: One hundred consecutive patients met inclusion criteria, with a mean IH onset age of 1.43 months. Seventy percent of patients received medical therapy during the proliferative and plateau phases of the tumor's natural history. Sixty-three percent of patients had surgical resection performed in the proliferative phase, while 37% had surgery in the plateau/involutional phase. The complication rate was 6% (hematoma or infection). Recurrences were found in 2% of patients and an acceptable aesthetic result was obtained for all patients.
Conclusion: B-Blockers are clearly first-line treatment for IH. However, non-responding lesions do benefit from early surgical therapy if producing functional complications of amblyopia, airway obstruction, feeding, speech difficulties and psychosocial distress. Our treatment algorithm relies on early medical management, and if non-response or if still producing a functional/aesthetic problem, excision of the residual lesion is performed. An algorithm for the management of specific facial anatomical subunits will be presented.

O106
Comparison of two generation photosensitizers of PsD-007 and HMME photodynamic therapy for treatment of port-wine stain: a retrospective study.

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Purpose: Vascular-targeted photodynamic therapy (PDT) has shown potentially beneficial results in treating port-wine stain (PWS), but the efficacy and safety of different photosensitizers has not been fully investigated.
Methods: To compare the efficacy and safety of two generation photosensitizers- PsD-007 and HMME combined with a 532 nm KTP laser for photodynamic therapy of port-wine stain. Patients and methods: Medical records of 38 patients (age range: 16-44 years old) with port-wine stains were analyzed. Clinical outcomes after one session of PsD-007(n=21) or HMME (n=17) combined with 532 nm KTP laser irradiation (80-90 mW/cm2) PDT were compared.
Results: Both photographic and chromameter optical evaluation showed no significant difference between PsD-007 group and HMME group, respectively (P=0.337, P=0.191). Total response rate was 76.2% (n=16) and 88.2% (n=15) in PsD-007 and HMME group. 42.9% patients were assessed as excellent and good clearance for PsD-007 group and 29.4% for the other. Incidences of swelling, pruritus, scab, and other adverse reactions were similar and there were no blister, scar or hypopigmentation in both groups.
Conclusion: Both PsD-007 and HMME PDT are effective and safe tools to treat port-wine stains. However, in terms of photosensitivity period, HMME is a superior photosensitizer to PsD-007.

O107
Diagnosis and Treatment of Hepatic Venous Malformations
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Purpose: To determine the role of ethanol endovascular therapy in the management of liver "hemangioma" (venous malformation of the liver). Currently, only surgical lobectomy with its attendant severe morbidity is the only other treatment option.
Methods: Ten patients underwent thirty-four treatments by direct puncture into the venous malformation involving single and multiple lobes of the liver. Three males and seven females with age range of 30 years – 50 years, mean age, 40 years. Patients underwent arteriography and direct puncture repair of the malformations in the liver; all patients had follow-up performed by CT and MR imaging. Early in the series one patient developed a fever and was placed on antibiotics. Currently all patients are placed on Flagyl and Levoquin for 7 days.
Results: Reduction in the vein malformation within the liver was noted in all patients. More importantly, their pain symptoms resolved. One patient's intractable hiccups resolved. One patient developed a left foot drop due to pressure on the sciatic nerve because she was thin and laying on a hard angiographic table. This completely resolved. One patient developed a fever and was successfully treated with antibiotic therapy. Patients were followed-up by CT and MR imaging documenting the shrinkage of single and multiple lesions (follow-up range: 13 – 52 months; mean: 37 months). Three of ten patients had minor abdominal and right shoulder pain post-procedure.
Conclusion: Direct puncture ethanol endovascular therapy is efficacious in the management of liver venous malformations just as it is efficacious in venous malformations in other anatomic areas. We recommend covering patients with antibiotics (Flagyl and Levoquin, unless allergic) due to the potential of bacterial seeding of the malformation from the portal system. This procedure is well-tolerated by patients compared to current treatment by liver resections/lobectomy/bile leaks/bile strictures/death that are noted to occur with surgery.

O108
Imaging of Epithelioid Hemangioendothelioma
Yan Epelboym (Boston Children's Hospital); Frederic Thomas-Chausse (Boston Children's Hospital); Ahmad Alomari (Boston Children's Hospital); Cameron Trenor (Boston Children's Hospital); Denise Adams (Boston Children's Hospital); Gulraiz Chaudry (Boston Children's Hospital)

Purpose: Epithelioid Hemangioendothelioma (EHE) is a rare vascular malignancy with variable biologic behavior. The purpose of this study was to identify the imaging findings most characteristic of EHE.
Methods: The clinical and imaging records were reviewed in patients referred to our Vascular Anomalies Center over a 9-year period with a biopsy proven diagnosis of EHE.
Results: There were 27 patients (17 F). The median age at presentation was 16 years (range 2-67 years). The most common presenting symptoms were pain (n=10) and palpable mass (n=4). Nineteen patients (70%) had multiple sites of disease. The most common sites of involvement were lung (n=18), liver (n=13), bone (n=10), lymph nodes (n=2) and soft tissue (n=2). Of patients with a single site of disease, 3 had liver and 3 had lung lesions. The majority of patients with lung disease (16/18) had multiple nodules of varying sizes. Of the patients with hepatic disease, 10/13 had multiple nodules with a predominantly peripheral distribution. Subcapsular retraction was seen in 7/13 and a "lollipop" sign (hepatic or portal vein tapering at the edge of a well-defined hypoenhancing lesion) was also identified in 7/13. The bony lesions were most commonly lytic (8/10). The spine was the most common site of osseous involvement (8/10) and in the majority of cases (9/10) the lesions were limited to the axial skeleton.
Conclusion: EHE has varied clinical and imaging findings. The most common sites of disease are lungs, liver, and bone. Multi-organ involvement is seen in the majority of patients. Lung disease is most commonly characterized by multiple nodules. Hepatic lesions demonstrate the most characteristic findings, with peripheral distribution, subcapsular retraction and "lollipop" sign. Osseous lesions are most commonly lytic and limited to the axial skeleton.

Difficult Cases 5

O109
Management of a massive right lower extremity and buttock venous malformation requiring abdominoperineal resection
Wesley Barry (Children's Hospital Los Angeles); Donna Nowicki (Children's Hospital Los Angeles); Chadi Zeinati (Children's Hospital Los Angeles); Minnelly Luu (Children's Hospital Los Angeles); Lori Howell (Children's Hospital Los Angeles); Dean Anselmo (Children's Hospital Los Angeles)

Purpose: Large venous malformations can cause significant disfigurement, disability, and morbidity due to bleeding, pain, and consumptive coagulopathy. Here we present a difficult case of a massive right gluteal and lower extremity venous malformation. The patient was a previous 33 week premature boy who was diagnosed in utero with a large venous malformation. He subsequently developed thrombocytopenia and coagulopathy due to localized intravascular coagulopathy (LIC) and was treated with steroids, vincristine, sirolimus, and lovenox. Prior to presentation at our institution, he developed acute renal failure and

underwent 10 courses of sclerotherapy with no improvement and required a diverting sigmoid colostomy for persistent perianal bleeding. At three years of age he was unable to ambulate independently and on multiple occasions developed massive hemorrhage following minimal manipulation of the malformation requiring operative hemorrhage control. The patient was then taken to the operating room for surgical debulking of his venous malformation following proximal control of the aortoiliac bifurcation. The patient tolerated the procedure well. His postoperative course was complicated by a left common femoral artery thrombus at a previous arterial line location resulting in significant arterial insufficiency. Given the high bleeding risk, it was decided to start a heparin drip with a goal anti-Xa level of 0.3-0.6 IU/mL. The patient's left lower extremity perfusion improved and the clot resolved however he had several life-threatening perianal hemorrhagic episodes requiring multiple reoperations. Given the persistent hemorrhage risk, the patient was taken for a more extensive debulking operation which included an abdominoperineal resection with fasciocutaneous flaps for closure. Following reoperation the patient improved and was eventually discharged to a rehabilitation unit and subsequently home. This difficult case illustrates some of the pre, intra and postoperative challenges of debulking a large buttock venous malformation near the anus that required an abdominoperineal resection.

O110
Unclear Diagnosis and Management of A Congenital Nasal Vascular Lesion

Nancy Bauman (Children's National Health System, Washington DC); Gina Krakovsky (Children's National Health System, Washington DC); Phillip Guzzetta (Children's National Health System, Washington DC); Bhupender Yadav (Children's National Health System, Washington DC); Albert Oh (Children's National Health System, Washington DC); Yasmine Kirkorian (Children's National Health System, Washington DC); Monica Pearl (Johns Hopkins Medical Institute); Christopher Rossi (Children's National Health Systems); Bernard Cohen (Johns Hopkins University); Amir Dorafshar (Johns Hopkins University Medical Center)

O111
Transvenous and image-guided embolization techniques combined with surgical reconstruction for difficult AVMS of the head and neck.

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19 year old female presents with an expanding left cheek AVM. No significant past medical history. She had been previously treated with pulsed dye laser and proximal embolization at an outside hospital 5 years before the first visit. Combined therapy with preoperative embolization followed by surgical excision was performed. The facial nerve and facial muscles were preserved. Her disease continued to progress. After multiple attempts to control the disease, she underwent attempted combined preoperative embolization, tissue expansion, and radical resection with facial nerve and muscle sacrifice. Eight months later, free muscle transfer was performed for facial reanimation. One year later, she began to experience life-threatening epistaxis and gingival bleeding requiring transfusion. Repeat angiography found residual disease in the pterygopalatine fossa (behind her maxilla). Transvenous catheterization was performed. She was disease-free for 8 months but her life-threatening bleeds resumed. By this stage, the only access was via her internal carotid and ophthalmic arteries. Image guided direct stick embolization was used to avoid the internal carotid and ophthalmic arteries and access the disease directly. Onyx was used to treat the nidus and original vein. The ophthalmic and IMA supplies regressed. Issues to address: 1. Proximal embolization should be avoided. 2. Attemptsatconservativeresectionarefrequentlyunsuccessful.Radicalresectionmaybenecessary. 3. Transvenous catheterization with embolization is a new approach. 4. Percutaneous image-guided nidus catheterization is a novel alternative in high flow AVMS in deep locations in the H&N. 5. Is pharmacotherapy an option?

O112
Complex bilateral cervicofacial lymphatic malformation mandibular deformity in pediatric patient

Tara Rosenberg (Baylor College of Medicine/Texas Children's Hospital); Ionela Iacobas (Baylor College of Medicine, Houston, TX); Priya Mahajan (Baylor College of Medicine, Texas Children's Hospital); Judith Margolin (Baylor College of Medicine/Texas Children's Hospital); Raphael J. Yoo (Baylor College of Medicine/Texas Children's Hospital); Sheena Pimpalwar (Texas Children's Hospital)

Purpose: To discuss multimodality treatment and timing of mandibular reconstruction in pediatric cervicofacial lymphatic malformations
Methods: To review the case of a 6 year old female with bilateral complex cervicofacial lymphatic malformation
Results: This patient was prenatally diagnosed with a large, complex bilateral cervicofacial lymphatic malformation. She was born via an EXIT procedure and tracheostomy tube placement was required. Since birth, she has had multiple surgical interventions for disease resection, sclerotherapy sessions, and sirolimus administration. Her current orofacial deformity is significant, mostly due to the severely deformed mandible that causes large open bite deformity, elongated face and articulation errors.

Conclusion: Pediatric complex cervicofacial lymphatic malformations are challenging lesons to treat. They require multimodality therapy and may result in severe mandibular deformity. Timing of mandibular reconstruction in this patient population is an important aspect of their overall management and age at reconstruction may be considered much younger than traditionally performed.

ABSTRACTS POSTER PRESENTATIONS

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POSTERS

Please note that the poster presenters will be at their posters to answer questions at the following days and times:

Wednesday, 30 May: 12:15 PM - 1:45 PM
Posters P001-P058; P145-P156; & P191-219

Thursday, 31 May: 12:00 PM - 1:30 PM
Posters P059-P144 & P157-P190

P001
Clinical course of extracranial arteriovenous malformations: A retrospective study of 446 cases

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Purpose: This study aimed to describe the clinical course and emphasize the progressive nature of AVMs through a retrospective study of 446 cases.
Methods: Patients with cutaneous and soft-tissue AVMs presenting to our Vascular Anomalies Center between March 2011 and March 2017 were reviewed. Medical records were examined for disease course, age at first presentation at our institution, distributions and locations of lesions, clinical staging, progression, and previous treatments. Progression was defined as advancement to a higher Schobinger stage from a lower stage.
Results: A total of 446 patients (mean age, 25.6±14.0 years) were enrolled in this study, including 232 (52.0%) males (gender ratio, 1.08:1). AVM lesions in 76.7% (342/446) of the patients were located in the head and neck. Children with Stage I AVMs had a 41.9% risk of progression before adolescence and an 80.0% risk of progression before adulthood. Nearly all patients (96.2%) showed progression in adulthood. Diffuse lesions were more likely to progress than localized lesions (P=0.05) in childhood and adolescence. Lesions in the head and neck regions were less likely to progress than those in other regions in childhood (P=0.005). A total of 216 (48.4%) patients had undergone previous treatments. Among these patients, bleomycin showed an unintentional positive effect in the treatment of AVMs.
Conclusion: Extracranial AVMs have a continuously progressive nature. A full understanding regarding the progressive course of AVMs can lead patients and physicians to early and radical treatments. Earlier diagnosis and management may be required to prevent potential destructive progression.

P002
Complications after embolization of peripheral arteriovenous malformations

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Purpose: Embolization therapy plays an important role in treatment of arteriovenous malformations (AVM). Ethanol is a frequently used agent, but it is associated with a high complication risk. We aimed to evaluate the occurrence of complications after embolization therapy of peripheral AVMs in an expertise center.
Methods: All patients with a peripheral AVM, treated with embolization between January 2010 and July 2016, were retrospectively reviewed. Patient characteristics included age at first treatment, AVM location, AVM angioarchitecture according to the Yakes classification system, and number of procedures. Complications were graded as minor or major. Embolization materials and expected side effects as a result of underlying pathology were also reported. Minor complications were transient and without surgical reintervention. Major complications were permanent or required surgical reintervention. Complications were compared between patients and procedures.
Results: During the study period 442 interventions were performed in 93 patients (median 2, range 1-82). In most cases, ethanol was used (n=428; 96.8%). The cohort included 21 children (age <18), in whom 38.5% (n=170) of the interventions were performed. A total of 53 complications were identified (12%),

in 36 patients. Six complications were graded as major (1.4%) and 47 were minor complications (10.6%). Children seem to develop less complications per procedure compared to adults but this was not significant (8.2% versus 14.3%, Figure). Other factors, such as AVM location and type of angioarchitecture, did not significantly affect complication risk (Table).
Conclusion: This study shows few severe complications after use of ethanol in the treatment of arteriovenous malformations in this expertise center. Nevertheless, as a complete treatment course usually consists of multiple embolization procedures, overall complication risk in an individual patient may be substantial and must always be weighed against the treatment indication. Therefore, treatment should take place in centers with experience and a multidisciplinary approach.

P003
LIP ARTERIOVENOUS MALFORMATIONS IN 24 CONSECUTIVE CASES WITH 100% OF PREVALENCE IN FEMALE SEX. STUDY OF HORMONAL RECEPTORS

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Purpose: Arteriovenous malformations (AVM) are high-flow vascular malformations with a complex vascular network that connects the arterial and venous systems without a neural regulation in the capillary bed. Although cutaneous AVMs are present from birth, they rarely show symptoms in the first years of life. Hormonal regulation (puberty, pregnancy) can eventually play an important role in the growth of these malformations. The aim of our study was to study the sex distribution of lip AVMs in a reference tertiary hospital and also to identify hormone receptors within AVM samples.
Methods: We reviewed the medical files of patients with upper or lower lip AVMs treated in the last 25 years in order to analyze age, sex, clinical evolution, treatment and outcome. Surprisingly we found that all patients with lip AVM (24) were female. Double immunostaining for the estrogen receptor (ER) and progesterone receptor (PR) was performed on 24 archival AVM tissue collected from both pediatric and adult patients. Ten breast carcinoma specimens were used as controls, with the carcinoma cells serving as positive controls. AVM samples of 10 men and 10 women, which were removed from another anatomic location other than the lip, were compared with lip AVM in women.
Results: The provisional results of the histological study seem to indicate that there is a higher expression of hormone receptors in lip AVM in women.
Conclusion: Our knowledge about the etiology of AVMs is still very limited despite genetic and molecular advances. The present study demonstrates that there is a higher prevalence of lip AVMs in women. Hormonal factors seem to be associated with this location in the female sex. Investigating the mutations that cause AVMs and the epigenetic factors that can influence its progression will help us to differentiate diverse phenotypes in this group of patients.

P004
Combined soft tissue and intraosseous involvement in arteriovenous malformations, of the hand and foot: outcomes after open surgical cementoplasty in 9 patients

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Purpose: The role of surgery in the management of arteriovenous malformations (AVMs) of the hand and foot remains controversial. None of the different classifications consider bony involvement. Endovascular treatment by arterial or venous route or direct puncture, can rarely be curative. The aim was to evaluate the benefits of treatment of intraosseous AVM nidus by open surgical cementoplasty, selectively in hand and forefoot locations.
Methods: Retrospective, observational, monocentric study. Nine consecutive patients with intraosseous avm nidus underwent open cementoplasty in hand and foot locations between 2014-2017. Data collection was performed using our retrospective database by reviewing patients clinical and imaging records. Reviewed investigations consisted in plain radiographs, Doppler ultrasound, and CT scan with bone and vascular reconstructions. Evaluation of pain, trophic skin lesions, quality of life and residual AVMs as seen by ultrasound and CT scan, were the primary outcomes.
Results: During this time period n= 57 patients with hand (n= 30) or foot (n=27) AVMs were seen at our VAC clinic. Surgical excision was performed in n=25. Nine patients (n=4 females, n= 5 males) with intraosseous avm nidus underwent open cementoplasty in hand and foot locations Patient's mean age was 30y/o (range 10-50 y/o) . In the hand (n=5) : bone involvement was localized in the thumb (n=3), middle finger(n=1) and ring finger(n=1). Lytic bone changes were located in the first metacarpal (n=2), in the proximal and middle phalanx (n=3). In the foot (n= 4), bone involvement was localized in the great toe (n=4), skeletal changes were in the metatarsal (n=3), in proximal and distal phalanx (n=3). Eight patients had a targeted cementoplasty of the involved bone, one had an array of cementoplasty of cortical vessels. Cementoplasty was the only procedure for n=5 ; n=4 needed additional procedure on residual soft tissue AVM (hand= 1, foot= 3). Mean FU was 13 months (range 6-17 m/o). No morbidity, healing delay, or functional sequels were observed. Resolution of pain was the dominant impact in all the patients. Remaining micro shunts were founded in n= 6 in periphery of the surgical resection zone

Conclusion: Open surgical cementoplasty is a new treatment option for intraosseous components of AVMs in hand and forefoot locations . Compared to percutaneous cementoplasty, open surgery creates a larger channel into the bone and allows the cement to fill more homogenously and to occlude small cortical feeders and venous drainage. Major positive impacts on postoperative pain reduction and dominant nidus exclusion were observed. One of the limits of the study is the short follow-up.

P005
Management of arteriovenous malformation of the ear: a protocol for resection and reconstruction

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Purpose: Arteriovenous malformations (AVM) of the ear have singular features. Progressive growth or inadequate management may lead to bleeding, infection, cartilage exposure and ultimately, loss of structure. Total ear amputation is an alternative, but requires a complex reconstructive protocol. The purpose of this study is to present a treatment algorithm based on a clinical classification, including options for resection and immediate and late reconstruction.
Methods: From 2004 to 2017, 10 patients with auricular AVMs were treated from resection to reconstruction. Six were female, and ages ranged from 10 to 34. Parameters considered for resection and reconstruction were compromise in extension (1/3, 2/3 or total), thickness (cutaneous and/or cartilage), symptoms (bleeding, infection, ulceration and cartilage exposure) and extra-auricular involvement . Pre-operative embolization data was collected. Total resection of AVM was always planned as a first step, followed by primary closure. Auricular resection was classified in partial (cutaneous or partial amputation) or total. Definitive treatment was planned according to the resultant defect and cartilage exposure, from primary closure to delayed total ear reconstruction.
Results: Preoperative embolization was performed in all patients but one. The AVMs were totally removed, resulting in 7 total ear amputations. In 5 of these patients, total ear reconstruction was performed after 6 months to certify no recurrence. The remaining 2 patients didn't accept a reconstructive procedure. In the 3 smaller localized AVMs, partial resections were performed and local flaps were used to close the defect. No regrowth was observed in all reconstructed ears.
Conclusion: Treatment of ear AVMs requires a planned approach to achieve clinical control and simultaneously reach a safe and definitive reconstruction.

P006
Auricular arteriovenous malformations: A case series of surgical reconstructive strategies, an evolving approach.

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Purpose: Arteriovenous malformations (AVMs) are uncommon but problematic lesions due to their clinical symptomatology and recurrence rate. Auricular AVMs present a management challenge as surgical intervention requires consideration of the pinna's unique structural anatomy. The purpose of this study is to examine surgical management strategies in our patient population with auricular AVMs.
Methods: Retrospective chart review of patients with auricular AVMs yielded 10 cases, of which 7 involved an identifiable pinna. Interventions undertaken for each patient was entered into a database for subsequent analysis.
Results: There were 6 females and 1 male, ages ranging 13.8-30.2 years at initial presentation to our tertiary care center. The most common presenting symptoms were bleeding, pain, headache and aesthetic deformity. Preoperative photographs documented varying degrees of pinna involvement with typical macrotia and hypertrophy. Majority of patients underwent pre-operative embolization with or without percutaneous sclerotherapy. Subsequent surgical resection occurred within 24-48 hours and consisted of a through-and-through wedge excision of the AVM and macrotic ear followed by subcutaneous elevation and removal of any remaining nidus. Due to the mass effect of the growing AVM on the pinna, reconstruction often required an otoplasty conchal setback. Special consideration was given to maintain symmetry with the contralateral unaffected side. The mean follow-up was 1.33 years, ranging 0.01-5.07 years. During this time, 6 patients had recurrence requiring revision embolization or surgery. One patient required a total auriculectomy and was reconstructed with local soft tissue rearrangement over the remaining cartilaginous framework - similar to techniques used in microtia repair.
Conclusion: This case series demonstrates the largest cohort of patients with auricular AVMs and reveals a high recurrence rate when conservative procedures are performed. Although these procedures preserve the architecture and symmetry as long as possible, more radical procedures may be necessary for long term relief.

P007
Treatment of head and neck arteriovenous malformations (AVMs) involving the facial nerve: a tailored algorithm

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Purpose: Head and neck AVMs involving branches of the facial nerve often cause tremendous cosmetic, functional, and psychological problems which are challenging to treat. We proposed an algorithm to obtain the optimal treatment and aesthetic outcome.
Methods: Medical records of 24 patients were reviewed between 2002 and 2015. The lesions were classified into 4 types. Type 1, involving no more 2 facial nerve branches with max. diameter ≤ 5cm (n=7), Type 2, involving no less than 2 facial nerve branches with max. diameter > 5cm (Type 2a, facial nerve preservation, n=8; Type 2b, facial reanimation, n=5); Type 3, involving the mastoid segments or the trunk of the facial nerve (n=4). Treatment efficacy was assessed and facial function was evaluated using the regional House-Brackmann Facial Nerve Grading System (regional HBFNGS).
Results: Cure was achieved in 11 (45.8%) patients, improvement was achieved in 12 (50.0%) patients ' with a follow-up time of 36.3±32.9 months(range, 12 to 144 months). There was no significant difference of the regional HBFNGS score before and after treatment (Type 1, unchanged; Type 2a, p=0.356; Type 2b, p=0.423; Type 3, unchanged). Treatment outcomes were not significantly related to the type of nerve involvement (p=1.000) and the facial reanimation procedure (p=1.000).
Conclusion: Surgical excision or ethanol embolization alone is efficient for Type 1 AVMs. The optimal approach for Type 2a AVMs was surgery, followed by well-vascularized tissue transfer. In Type 2b AVMs, the satisfied treatment results are achieved by lesion excision and immediately facial reanimation. A two-stage strategy may result in contented treatment outcome in Type 3 AVMs.

P008
Treatment of scalp arteriovenous malformations with therapeutic ethanol embolization and surgical resection: a tailed algorithm

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Purpose: Scalp arteriovenous malformations often cause tremendous cosmetic, functional, and psychological problems which are challenging to treat. We proposed a tailored algorithm based on a comprehensive approach for the treatment of scalp AVMs, with consideration of the clinical characteristics, treatment options, and key factors of defect reconstruction.
Methods: A total of 25 patients with scalp AVMs were enrolled. Based on the location, size, and hairline involvement pattern of the lesion, we were able to identify 5 types. Patients were managed using surgical procedures and ethanol embolization.
Results: Type 1 (Small and Medium lesions) Surgical excision was performed in lesions located on the hair-bearing scalp with no hairline involvement (Type1a). Defects were covered using primary closure and local flap. Patients were managed by ethanol embolization alone when the lesion location involved the hairline (Type1b). Type 2 (large lesions) In the cases of lesions mainly located on the non-hair-bearing scalp or lesions located in the frontal region almost completely on the non-hair-bearing scalp (Type2a), preoperative ethanol embolization was performed to address the lesions on the non-hair-bearing scalp first, followed by total resection of the residual lesion at a later stage. Lesions mainly located on the hair-bearing scalp (Type 2b) were managed by en bloc resection followed by one-stage expander flap reconstruction. Type 3 (Giant lesions) Giant AVMs underwent en bloc resection of the lesion, followed by free ALT flap reconstruction.

Cure was achieved in 23 patients and improvement was achieved in 1 patient; one patient experienced recurrence with clinical (mean, 34.9±19.2) and imaging follow-ups (mean, 17.2±8.8months). One flap necrosis occurred and 4 minor complications were observed in 2 patients during ethanol embolization sessions.
Conclusion: Scalp AVMs should be managed aggressively and approached algorithmically with hierarchically categorized treatment options, including surgery, ethanol embolization or a combination of both, to achieve optimal results.
Key words: arteriovenous malformations, embolization, resection

P009
Pathophysiology of Arteriovenous malformations--Revisited!
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Purpose: To discuss the pathophysiology of AVMs. It is believed by most specialists treating AVMs that they expand primarily by hemodynamic mechanisms and that there is no cellular turnover. our Research indicates that AVMs have many similarities to low grade tumors, which implies cell turnover. If there is cellular proliferation, this will open new methods of treatment.
Methods: At our University Hospital and Children's Hospital we have taken surgical specimens of AVMs for over 20 years and have performed many tests on these tissues. These tests include, testing for stem cells, tumor suppressor genes, DNA repair genes, and Wilms Tumor 1 (WT1) protein.
Results: There were increased levels of both BMI-1 and SALL4 (both oncogenic stem cell markers) in all AVMs tested. Also all AVMs tested showed significantly reduced expression of multiple tumor suppressor genes (mRNA, MGMT gene, hMLH1, p16, and SOCS1 gene). The majority of AVMs (85%) tested revealed overexpression of WT1 proteins, which is seen only in tumors with cell turnover.
Conclusion: For many years, we have used embolizations and surgery as the main methods of treatment for AVMs. We have been unable to cure those patients with extensive AVMs and need to find new treatments. Our research indicates that most AVMs have cellular turnover, as well as hemodynamic mechanisms. this evidence can lead to new treatments using pharmacotherapy to treat these difficult lesions.

P010
Treatment experience of intraosseous arteriovenous malformations in children.
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Purpose: Determine diagnostic and therapeutic measures for arteriovenous malformations (AVM) with intraosseous lesions in children.
Methods: The survey of 13 children between the ages of 4- 12 years with intraosseous AVM was conducted, who were being treated in the surgical dentistry and pediatric maxillofacial department clinic of NMU named after O.Bogomolets (2009-2017). To diagnose were applied: CTA, angiography. Interventional radiology techniques was used with Histoacryl, among them (n = 10) with maxillofacial surgical procedures.
Results: The maxilla lesion with unilateral blood supply (n = 3), the mandibular lesion with unilateral (n = 4) and bilateral (n = 6) blood supply were established. The embolization effectiveness depended on AVM angioarchitectonics, number of involved blood supply parties, presence of multiple wide arteriovenous shunts (n = 6), advanced conductive and drainage vessels (n = 7), whose diameter on the affected side was 1.9 times larger than on a healthy one. Repetitive occlusion was performed in 8 children: four times (n = 2), twice (n = 6). Complications after the embolization were observed in 3 children with bilateral blood supply - soft tissue necrosis. The complete exclusion of AVM vascular vessels from the blood flow by interventional radiology techniques was practically impossible in children, due to contralateral anastomoses of the same arteries presence. The surgical procedure in the mandibular was not carried out in 2 cases. Organo-preserving surgical intervention was performed (n = 10) by bone cavity filling with iodoform gauze and "Surgicel" through removed tooth alveolar socket on 2-3 days after embolization. It was effective in 9 cases, in one child bone destruction was diagnosed after 2 years.
Conclusion: Selective interventional radiology techniques combined with organo-preserving surgery on jaws proved to be most effective for bilateral blood supply intraosseous AVM. If the bone cavity is filled during embolization, you can do without surgery procedures on the jaws.

P011
66 cases of cervico-facial arterio-venous malformations, experience of a single institution.
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Purpose: Treatment of arterio-venous malformations (AVMs) is still a discussed topic in literature. Among the possible therapeutics approaches there are sclerotization, endovascular embolization and surgery, that can be eventually matched together following the different clinico-radiological features of the malformation. The aim of this study is to report the experience reached in the surgical treatment of AVMs, using a radical or palliative approach.

Methods: From January 2012 to November 2017 we treated 66 patient affected by AVM and classified following our SECg staging system. Therefore, we identified the patients eligible for a surgical treatment only (8 patients), endovascular only (2 patients) or combined endovascular and surgical (53 patients). 3 patients were not treated at all because affected by a small and non-growing AVM (2 patients) or by a wide, non-curable AVM with high surgical risk.
Results: All our treated patients showed a significant improvement in terms of aesthetics and function. Patients that performed a curative surgery did not present any relapse of pathology, except for one patient that showed a recurrence of the malformation at three years of follow-up, during pregnancy. Patients that performed a palliative surgery did not show any progression of pathology.
Conclusion: A wide and extensive clinical and radiological study of the malformation in the preoperative phase, joined with the definition of a tailored treatment planning are essential for achieving a stable result with neglectable aesthetic and functional ending. Following our experience, the SECg staging system represents a useful means that allows to identify patients eligible to a curative versus palliative procedures, hence to determine the best therapeutic strategy.

P012
Surgical Management of Arteriovenous Malformations of the Orbit and Eyelids

James Suen (Univ. of Arkansas for Medical Sciences); Gresham Richter (University of Arkansas for Medical Sciences, Arkansas Children's Hospital Inc.)

Purpose: AVMs involving the orbit and/or eyelids are difficult to manage. This paper will address the options for management and present patients treated with surgery.
Methods: We reviewed our AVM patients treated at our University Hospital by a single surgeon. Seven patients with extensive AVMs involving the orbit and/or eyelids were identified. the scans, photos, and medical records were reviewed. Previous treatment was identified and the surgical management was reviewed. Patients' ages ranged from 13 to 60 yo.
Results: All seven patients were treated surgically. Three of those seven patients were also treated with intralesional Bleomycin. Six of the seven patients had had previous embolizations with no improvement. One patient required an orbital exeneration. Two patients required extensive orbital bone resection with the AVM. Four patients were treated with surgical excision of AVM of the orbit and eyelids. Six of the seven patients continue to have persistant AVM and are requiring further surgery or other treatment, such as lasers and intralesional Bleomycin. These 6 patients still have vision and function of their involved eye.
Conclusion: The goal of these extensive AVMs is to control the AVM and to preserve the function if possible. Surgical management should be considered for AVMs involving the eyelids and/or orbit. it can control the AVMs for years while preserving the vision and movement. It should be performed by a surgeon experienced with the eye anatomy and with the treatment of AVMs

P013
Diagnosis and Management of Thoracic and Shoulder Arteriovenous Malformations

Wayne Yakes (Vascular Malformation Center)

Purpose: To determine the efficacy of Endovascular Repair of Thoracic and Shoulder Arteriovenous Malformations (AVMs). Previous reports have documented the futility of nBCA and amputation in treating these lesions in this specific anatomy.
Methods: Twelve patients (8 female, 4 male) presented for repair of shoulder and thoracic AVMs. Three patients had extension of AVM to the supraclavicular and axillary areas. Two patients had multiple AVMs. Seven patients had previous failed therapies (embo: PVA/coils/gelfoam; surgeries: excisions/arterial bypass). All patients underwent ethanol endovascular AVM repair; four patients had additional coil embolizations (132 treatments). Patient age range 18-76 years; mean age 36.
Results: Eleven patients are cured at long-term arteriographic follow-up (follow-up 22 – 192 months; mean follow-up: 42 months). One patient with bilateral shoulder AVM and multiple other AVMs therapy is on-going. Complications include two patients with minor superficial blisters, one patient with transient left radial nerve injury with complete recovery and one patient with clot embolus to hand, Rx with urokinase w/ distal 3rd phalanx removed. Thus, major complications were 2/132 procedures, one being transient.
Conclusion: A report of shoulder AVM repair in JVIR documented failure of nBCA approach even coupled with quadrant amputation whereby recurrence was universal. These authors stated that shoulder AVMs were not possible to treat. This report documents that cure of these difficult lesions is possible with ethanol endovascular approaches and direct puncture approaches. No other publications in world literature documents cure of AVMs in this anatomy. Long-term cures are noted with the use of ethanol, and ethanol and coils to successfully treat these complex, problematic lesions. A low major complication rate is noted. This patient series finally documents a curative procedure for this daunting lesion.

P014
Successful Management Of Complex Arteriovenous Malformations Using Novel Combination Therapeutic Algorithm

Joyce Teng (Stanford University); Huy Do (Stanford University); Zachary Zinn (West Virginia University); Malcolm Chelliah (Stanford University); Rohit Khosla (Stanford University); Mai Thy Troung (Stanford University); Michael Jeng (Stanford); Ann Marqueling (Stanford)

Purpose: Arteriovenous malformations (AVMs) are high-flow vascular malformations that are at risk for life threating hemorrhage and high-output cardiac failure. The natural evolution of AVMs is steady growth with aging, although puberty, pregnancy, trauma, and incomplete surgical excision can trigger rapid progression. Extracranial head and neck arteriovenous malformations (HNAVMs) are rare and challenging to manage. We present a retrospective review of 6 patients with complicated, unresectable HNAVMs who underwent a combined treatment consisting of systemic sirolimus administration and endovascular embolization yielding consistent and lasting beneficial therapeutic results.
Methods: A retrospective chart review was performed on six cases of HNAVMs that were treated with a combination of sirolimus and transarterial embolization from 2013 to 2017. Sirolimus dosing was adjusted to achieve a goal trough level of 10-15 ng/ml throughout the course of the therapy. All patients started sirolimus therapy at least one month prior to transarterial embolization, and were encouraged to continue sirolimus at least a month following embolization. MR imaging were obtained before and post treatments.
Results: A total of four male and two female with HNAVMs are included in this report. The mean age at treatment initiation was 24.5 years (range 9-44 years). All six patients had significant clinical responses to the combined therapies. Five of the patients received follow up imaging studies that confirmed the lasting improvement for more than 6 to 18 months. All patients reported are nearly symptom free following this combined therapeutic algorithm. The average sirolimus treatment duration prior to embolization was 2-3 months. The average duration of sirolimus treatment following last embolization procedure was 13.33 months (range 1-16.5 months).
Conclusion: Our case series has demonstrated promising results using sirolimus as a perioperative adjuvant therapy with endovascular embolization in the management of complex HNAVM. Well-controlled larger scale studies are warranted to validate this approach.

P015
Hereditary Capillary Malformation with RASA-1 Mutation: Capillary Malformation-Arteriovenous Malformation or Lymphatic Malformation?

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Purpose: Capillary malformation-arteriovenous malformation (CM-AVM) is the vascular anomaly which is caused by RASA1 mutation, characterized by atypical, multiple, cutaneous zones of numerous small white pale halos with a central red spot. Fast-flow lesions such as Arteriovenous Malformation(AVMs) have been documented while slow-flow lesions such as Lymphatic malformations (LMs) were rare. Researchers have discovered that RASA-1 regulates the lymphatic vessels and maintains the lymphatic vasculature in a quiescent functional state in mice, not in human.In this case, we report an infant diagnosed with CM-AVM who carries germline and somatic RASA-1 mutation, supporting the "second mutation" pathophysiological mechanism. However, the RASA-1 somatic mutation frequency of superficial erythema lesions was much lower than that for the lymphatic anomaly, which may suggest that lymphatic malformations, rather than CM-AVM, are associated with a RASA-1 mutation in this case.
Methods: We collected the blood from the family and performed a biopsy of the erythema lesions of the patient's left leg. Sample was divided into the superficial dermis and deep connective tissue. All samples went through pathological study and were tested for next generation sequencing (NGS) and sanger sequencing.
Results: Molecular analysis confirmed a familial germline mutation in the RASA-1 gene (c.1015dupG, p.Val339fs) in the peripheral blood of the proband and her mother. A second RASA-1 gene somatic mutation (c.2035C>T, p.Arg679*) was detected at the frequency of 5.02% of the superficial dermis and 15.6% (13938/89224) of deep connective tissue.
Conclusion: In this case, hereditary CM was caused by a germline mutation in RASA1 with a frameshift variant. A somatic RASA-1 stop-gain mutation led to the fast flow lesion as well as the LM. This case not only supports the "second hit" hypothesis of CM-AVM with fast flow lesions but also suggests a causative correlation between RASA1 mutations and lymphatic deficiency.

P017
Evaluation of patients with peripheral arteriovenous malformations in an expertise center

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Purpose: Arteriovenous malformations (AVM) are the most complex lesions in the group of congenital vascular malformations. These lesions go through different clinical stages and have a complicated clinical course, sometimes leading to heart failure if left untreated. However, treatment can also cause serious complications. This study evaluates the population of patients treated for a peripheral AVM in one of the largest expertise centers in Europe.
Methods: All patients with a peripheral AVM, treated with embolization between January 2010 and July 2016, were retrospectively reviewed. Patient characteristics included age, AVM location, AVM angioarchitecture (Yakes classification) and number of procedures. In addition, we evaluated minor and major procedure-related complications.
Results: A total of 442 interventions were performed in 93 patients (median 2, range 1-82). The cohort included 21 children (age <18), in whom 38% (n=170) of the interventions were performed. The median age was 31 (range
2-66) at the moment of the first procedure during the study period. Figure 1 shows the distribution of AVM locations and Figure 2 shows the distribution of angioarchitecture types. Most patients had an AVM type 2 (n=57; 61%) and almost half of all procedures (n=219; 50%) were performed in these patients. AVMs type 4 were present in 13 patients (14%) and accounted for 36% of all procedures (n=157). Overall, the median number of procedures per patient was two with a range of 1-82. The average complication risk per procedure was 12%: 10.6% minor and 1.4% major.
Conclusion: In this expertise center a diverse group of patients has been treated, including a substantial number of patients with complex type 2 and type 4 arteriovenous malformations. Most AVMs were located in the head and neck region and the extremities. The required number of procedures per patient was for a large group very low but varied widely, with a low overall complication rate.

P018
Anatomy of the deep venous system in Vein of Galen Malformation

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Purpose: It is classically thought that the internal cerebral veins (ICV) do not communicate with the venous pouch of Vein of Galen Malformations (VGM). This has important treatment implications as occlusion of a venous pouch which communicates with the ICVs can have devastating consequences. In this study, we report on the anatomy of the deep venous system in VGM with special emphasis on the drainage of the ICV and possible changes after endovascular treatment.
Methods: We retrospectively analyzed DSA and 2D time-of-flight MR venograms of 55 children with VGM treated in our department between 2003 and 2016. All patients were imaged on 1.5T scanners and underwent angiography immediately following MRI. Two experienced reviewers evaluated all pre-and post-operative images for the presence of the ICVs and determined the route of venous drainage of the ICV (i.e. vein of galen, basal vein, falcine sinus, lateral mesencephalic vein, torcula).
Results: Of the 55 children, pre-operative 2D MRV detected the ICVs in 19 cases (35%) compared to 1 case (2%) for pre-embolization DSA (2%) (P<.0001). Of the cases in which the ICVs were seen preoperatively, in 15 cases (78.9%) the ICV drained directly into the VGM while in the other four cases, the ICV used alternative venous drainage routes such as the basal vein of Rosenthal, the falcine sinus, an epsilon-shape type of drainage or directly into the torcular. On post-operative MRV, the ICVs were seen in 17 cases (31%) on MRV and 10 cases (18.2%) on DSA with drainage into an adult-like vein of Galen in 13 cases (76%), respectively (P=0.08). In four cases normal ICV drainage into the vein of galen was seen even when the venous sac was closed. In two cases there was a change in ICV venous drainage from the vein of Galen to the lateral mesencephalic vein.
Conclusion: The communication of the ICV with the VGM is a common phenomenon. Different changes of venous drainage routes do occur after treatment and are best seen on MRV.

P019
The Effect of Shear Stress on Endothelial Cells of Arteriovenous Malformation

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Purpose: Although there are several reports about pathophysiology of arteriovenous malformation (AVM), further investigation is needed. It has been proposed that expansion may result from dormant primal arteriovenous communications, dilation of normal latent arteriovenous shunts by increased pressure and flow, and local ischemia. The mechanical environment of the vessel is of fundamental importance for disease development and progression. We aimed to find the relationship between shear stress stimulation and the arteriovenous malformation phenotype in this sturdy.
Methods: Vascular endothelial cells from 4 normal dermal microvessels and 4 AVM lesions were isolated and cultured on fibronectin (1μg/ml) coated IVF dish. Shear stress (7 dyne/cm2) was applied with orbital shaker device for 12hr. The effects of shear stress were measured by microscopic examination and real-time PCR with several related genes.
Results: Shear stress induced cell alignment in direction of shear flow both normal and AVM endothelial cells. The expression of ephrinB2 and B4 subtype was increased by shear stress. DLL4 and ALK1 expression was also up-regulated by shear stress. Induction of angiogenesis related gene expression by shear stress may correlate in part with AVM.
Conclusion: These results indicate that mechanical shear stress could be an important factor for stimulating downstream angiogenesis and disease progression in AVM. Furthermore, the results of this investigation could provide the basis for future studies of AVM pathophysiology, and ultimately lead to the development of new therapeutic approaches.

P020
Large pediatric arteriovenous malformations with associated cutis aplasia: Case report and systematic literature review

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Purpose: Genetic abnormalities leading to arteriovenous malformations (AVMs) are poorly understood outside of inherited syndromes. Evidence suggests that the etiology may differ between pediatric and adult patients. Implicated genes include PTEN, VEGF and TGF-ß, which can promote the development of these lesions. Here we present two pediatric patients with AVMs and cutis aplasia, and review the literature on pediatric AVMs, with a focus what is known about causal genetic abnormalities.
Methods: We discuss two pediatric patients presenting with a yet-undescribed triad including an AVM. We discuss their clinical presentation, demographics, imaging and multi-disciplinary consensus on management. We subsequently perform a systematic literature review discussing genes implicated in pediatric AVMs.
Results: Two pediatric patients, ages 13 and 5, presented with large, deep AVMs. Both additionally have ipsilateral cutis aplasia, as well as a small path of alopecia on the ipsilateral eyebrow. One presented with worsening dystonia, which was initially attributed to cerebral palsy until imaging showed the AVM. The second underwent imaging due to the cutis aplasia, but was otherwise asymptomatic. These patients do not meet criteria for known craniofacial vascular anomaly syndromes, and genetic testing is ongoing. They are clinically stable with no AVM rupture at last follow up.
Conclusion: There are innumerable factors which lead to vascular pathology in pediatric patients. The genetics underlying cerebrovascular development and pathology is still largely uncharacterized. Here we present two patients with AVMs and unusual associated symptoms, and review the literature on genetic abnormalities in pediatric AVMs.

P021
Single Nucleotide Variations (SNVs) in Blood and Tissue from Children with Extracranial Arteriovenous Malformations (AVMs)

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Purpose: Arteriovenous malformations (AVMs) are rare developmental anomalies that arise from a central "nidus" of anomalous and numerous direct connections of arteries to veins to form an infiltrative and highly vascular mass. The high recurrence rates (even after complete surgical removal) suggest that AVMs act as locally invasive low-grade malignancy likely modulated by somatic mutations. The purpose of this research is to determine whether somatic mutations observed in the literature of extracranial AVMs are also present in

our samples. Secondly, we want to identify other Single Nucleotide Variants (SNVs) or Indels in blood as these may provide surrogate markers for AVMs progression.
Methods: Forty-eight samples from children with AVMs from unaffected tissue, affected tissue and blood underwent Whole Exome Sequencing with an average coverage of 30x. Identification of SNVs and Indels was performed with two variant detection methodologies: GATK and FreeBayes. After the annotation of variants, the genome variation was incorporated into a database using Gemini framework for further interpretation.
Results: Some of the samples showed somatic mutations in mitogen activated protein kinase kinase 1 (MAP2K1) as others have reported. However, it was harder to find those mutations in blood samples. Other important SNVs will also be presented.
Conclusions: Our results showed the utility and limitations of WES in blood as a possible surrogate analysis to monitor the development of AVMs.

P022
Investigation of Sex Hormone Receptors in Extracranial Arteriovenous Malformation

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Purpose: Extracranial arteriovenous malformations (AVM) are rare but devastating lesions arising from inappropriate direct communication between arteries and veins without an intervening capillary system. Unfortunately, the etiology and pathophysiology of AVM are not well understood which limits treatment modalities and leads to high treatment failure. A unique phenomenon has been noticed in clinical practice that most of AVMs are present at birth and remain quiescent for many years. It is triggered to enter into a quick expanding and infiltrating stage during sex hormone fluctuation, such as puberty, pregnancy, menopause and oral contraceptive pills (OCPs) use. We hypothesized that disrupted expression of sex hormone receptors was related to the progression of extracranial AVMs.
Methods: Fresh human AVMs (n=20) and normal skin and subcutaneous tissue (n=17) were harvested. Messenger RNA levels of Estrogen receptor alpha, Estrogen receptor beta, Progesterone receptor and Androgen receptor were measured with Real Time RT-PCR assay.

Results: Progesterone receptor mRNA expression was significantly increased in AVM lesions compared to normal tissues (12.75±12.65 vs. 1.16±0.72, P=0.000). Statistically decreased mRNA levels were detected with Estrogen receptors alpha and beta in AVMs compared with normals (0.67±0.38 vs. 1.12±0.70, P=0.033; 0.57±0.86 vs. 1.26±0.99, P=0.002, respectively). No significant difference was found with Androgen receptor between AVM and normal groups (P=0.517).
Conclusion: Dysregulated expression of sex hormone receptors, especially highly increased Progesterone receptor, maybe is the underlying mechanism of rapid and progressive progression of extracranial AVMs during episodes of sex hormone fluctuation.

P023
Vein of Galen Malformations: Experience in the Modern Endovascular Era

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Purpose: Vein of Galen malformations comprise nearly a third of pediatric vascular anomalies, with potentially devastating neurologic and cardiac complications. While neurosurgeons have always been a critical part of the treatment team, advances in endovascular treatment have improved the clinical outcomes of these high-risk patients. Here we present lessons learned from the 15-year experience at Texas Children's Hospital (TCH) in treating children with modern endovascular techniques.
Methods: Charts from TCH were retrospectively reviewed for the past 15 years. Patients with diagnosis including 'Vein of Galen,' 'Vein of Galen malformation,' 'Vein of Galen aneurysmal malformation,' or any abbreviations (ie VOG, VOGM, VOGAM) were reviewed. Presentation, imaging, treatment specifics, and clinical outcomes were reported.
Results: There were 17 patients with Vein of Galen malformations managed at TCH from 2002-present with a total of 29 embolizations. Of the 29 embolizations, 12 were performed with NBCA only, five with onyx only, and 12 with a combination of NBCA/Onyx/coils. A dual lumen balloon was used as an adjunct in three embolizations for flow arrest during onyx injection. Complications occurred in four embolizations: one intraventricular hemorrhage leading to death, one subarachnoid hemorrhage (asymptomatic), two with emoblisate migration with no sequelae. Two embolizations were terminated due to patient hemodynamic instability. Surviving patients were followed for a mean of 38 months. Seven patients had normal development, while five had developmental delay but continue to make progress.
Conclusion: Vein of Galen malformations can present with a myriad of neurologic and systemic symptoms, potentially in extremis. Neurosurgical involvement in these cases is critical, as urgent treatment can be lifesaving. Modern endovascular interventions have improved outcomes in this high-risk population, and many patients go on to have normal development or only slight deficits. Additional data is needed to determine if type of malformation, presenting symptom, or degree of embolization affects prognosis.

P024
Mid-term and long-term results of ethanol embolization of auricular arteriovenous malformations as first-line therapy

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Purpose: To assess the mid-term and long-term results of patients with auricular AVMs treated by ethanol embolization.
Methods: Medical records of 35 patients (20 male, 15 female; age range, 10-59 years) with auricular AVMs between 2006 and 2016 were reviewed. The short-term results of 4 of the 35 patients were reported in 2009. They were included in the present study with updated follow-up data. The data from the 31 new included patients have not been reported previously. Ethanol embolization were performed with a direct puncture approach. The nidus was eradicated by bolus injection of ethanol with manual compression whenever possible. Treatment outcomes were classified into 4 categories by assessing the resolution of symptoms, as well as the degree of nidus devascularization between the baseline and follow-up angiography.
Results: A total of 86 embolization sessions were performed in 35 patients (mean, 2.5±1.3 sessions). The dosage of ethanol used per single session was 12.0±4.5 mL (range, 6.0 to 24 mL). All patients received post-treatment clinical follow-ups (mean, 40.7±25.8 months), and 28 patients received post-treatment imaging follow-ups (mean, 34.3±25.5months). Ethanol embolotherapy was effective in all patients. Cure was achieved in 16 patients(45.7%), and improvement was achieved in 18 patients(51.4%). One patient experienced recurrence. A total of 13 minor complications and 2 major complications occurred in 12 patients during the 86 treatment sessions (12/35, 34.2%; 15/86, 17.4%). All the complications resolved spontaneously.
Conclusion: The mid-term and long-term results of present study demonstrate that ethanol embolization alone is an effective option for auricular AVMs as first-line therapy with a mild risk of minor and major complications.

P025
The role of accurate ultrasound mapping technique in superficial AVMs prior embolization, surgery or clinical follow-up.

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Purpose: Superficial arteriovenous malformations (AVM) are characterized by abnormally developed vascular networks. Ultrasound mapping allows us to accurately delineate the AVM nidus and afferent arteries, nearly as precisely as on an angiogram. This allows accurate schematic or skin mapping to be a helpful preoperative and follow-up tool.
Methods: Since 2010 we have been using a locally developed hemodynamic ultrasound technique allowing us to localize precisely the AVM nidus. Throughout short videos sequences we will demonstrate Doppler ultrasound features of these lesions. They usually present with increased blood flow velocity. This phenomenon can also be observed next to the afferent and efferent vessels. High flow shunts cause enlargement and enlongation of vessel caliber, leading to increased tortuosity and stenotic kinks. Multilayered compression around the AVM nidus associated to doppler recording of the afferent arteries allows to distinguish between tortuous "" uninvolved arteries and real AV shunts .
Conclusion: This technique allows accurate AVM mapping and delineation of the nidus and distinction between pathological feeding arteries and tortuous ones that are not involved, which may help to limit tissue resection during AVM surgery, especially in locations where large tissue excision might be critical.

P026
Four-dimensional DSA (4D DSA) for direct puncture treatment of arteriovenous malformations in head and neck.

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Purpose: Direct puncture sclerotherapy is one of the important options for treatment of arteriovenous malformation (AVM). We often have difficulty in understanding the angioarchitectural features of AVM,

although it is the key to effective and safe endovascular treatment. With conventional 2D and 3D DSA complex vascular overlaps very often disturb comprehension of the angioarchitecture of an AVM. Four-dimensional DSA(4D DSA) is the unique imaging method to observe the 3D DSA at any moment of 6 or 12 seconds of angiography with voluntary angle. We report our early experience and feasibility of 4D DSA for AVMs in head and neck.
Methods: Patient selection: Twelve cases of head and neck AVM patients treated with direct puncture sclerotherapy under general anesthesia between January 2017 and December 2017. Angiography and image processing: Angiography was performed using a commercial angiography system (Siemens Artis zeego, Siemens Healthcare, Forchheim, Germany). Image processing was performed using also a commercial software (syngo Dyna4D, Siemens Healthcare, Forchheim, Germany). Sclerosant: Ethanol (70-100%, 0.1-0.25ml/kg) in 9 cases, foamed polidocanol (1~3%) in 8 cases. Fusion image: Fusion images of 4D DSA and fluoroscopy were used to make selection of puncture site and to observe distribution of sclerosants.
Results: All procedures were technically successful. In all cases, 4D DSA images provided more details of angioarchitecture than conventional 2D or 3D images. Mapping puncture sites on fusion image of 4D DSA and fluoroscopy allowed more safe and efficient puncture in all cases. Post treatment 4D DSA showed the distribution of sclerosants and residual AVM component.
Conclusion: 4D DSA provides better ability to visualize the angioarchitecture of AVMs than conventional 2D and 3D DSA. By eliminating vascular overlap and providing an ability to see any moment of filling from any angle of 4D DSA enabled us to visually assess AVM.

P027
IS ALCOHOL PERCUTANEOUS TREATMENT EFFECTIVE AND SAFE IN CRANIOFACIAL AVM?

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Purpose: Alcohol percutaneous occlusion of vascular malformation is a well known and effective technique. However, the procedure may have complications, like necrosis. For that reason, a correct technique and a good experience is required for a safe treatment. Recently, alcohol has been reported to have higher incidence of complication in venous defects in craniofacial area. However, very few is reported about treatment with alcohol of AVM. In this study, we analyze 49 cases treated with all techniques available, including percutaneous alcohol.
Methods: A retrospective study of 49 patients affected by craniofacial AVM and treated by percutaneous alcohol, embolization, surgery and laser was performed. Patients were divided in limited and infiltrating AVM. Result of treatment and incidence and type of complications related to alcohol were recorded.
Results: 29 cases had limited AVM while 20 had diffuse, infiltrating forms. Treatments were: percutaneous alcohol 117, embolization 27, surgery 15, interstitial laser 2. Total treatments were 161 and average treatments for each patient were 3,3. Combination of treatments was common but with different incidence in limited and diffuse forms. In limited forms alcohol was more often the only treatment (48%) while in diffuse forms it was mainly combined with the other procedures. In infiltrating forms, alcohol was mainly performed to maintain stable a condition that show a tendency to worsen. In limited forms healing rate with all techniques was 48% while in infiltrating forms 20%. Complications were only noticed in the limited forms and include: two necrosis, one on the scalp and one on the tip of the nose (both corrected by surgery) and one temporarily paresis of the facial nerve that recover completely in two month of physiotherapy. No complications were noticed in the infiltrating forms. Complication incidence in 117 alcohol treatments were 2,5%
Conclusion: Alcohol treatment can be an effective procedure to combine with other methods in craniofacial AVM. However, a precise technique is required to avoid complications which is low in this study

P028
Ethanol Embolotherapy Management of Pelvic Arteriovenous Malformations
Wayne Yakes (Vascular Malformation Center)

Purpose: To determine the curative role of ethanol endovascular and/or ethanol coils in the treatment of large pelvic arteriovenous malformations (AVMs).
Methods: Forty-eight patients (25 females; 23 males; age range: 4 - 86 years; mean age: 37 years) underwent 315 endovascular procedures (6.5 procedure/patient) to treat their pelvic AVMs. Two patients had bilateral pelvic AVMs (1 male; 1 female). Two patients had traumatic lesions (2 males). Patients underwent transarterial, retro-grade transvenous, and direct puncture embolization procedures. Embolic agents included absolute ethanol (Dehydrated alcohol injection, USP; American Regent, Inc.; Shirley, NY); Cook stainless steel and Nester fibered coils (Cook Inc.; Bloomington, IN), and Terumo Azur Hydrocoils (Terumo Europe; Leuven, Belgium).

Results: Thirty-six patients are cured of their pelvic AVM (mean follow-up: 43 months) and 12 patients' treatments are on-going. Pelvic AVMs were cured by using ethanol, coils, or ethanol with coils. The addition of coils was particularly useful in those AVMs with enlarged venous outflows and in those AVMs with giant venous aneurysms. Three patients suffered transient sciatic nerve injuries. One patient suffered an ipsilateral perineal numbness that also completely resolved. Four instances of perineal blistering and tissue injury with one injection, was treated uneventfully. One patient had a rectal wall injury requiring bowel diversion, and after healing, underwent re-anastamosis. One elderly patient died within 30 days of a 4th procedure from pulmonary embolus (PE).

Conclusion: Endovascular approaches to manage pelvic AVM have proven to be curative at long-term follow-up. In our cases, surgery adjunctively to remove the AVM has not been required. Despite previous embolizations with coils, glue, and surgical ligations prior to being referred to our institution, endovascular and direct puncture approaches using ethanol, ethanol and coils, has proven to curatively manage pelvic AVMs involving soft tissue and bone with low complication rates and no recurrences.

P029
Ear Arteriovenous Malformation Management

Wayne Yakes (Vascular Malformation Center)

Purpose: To determine the efficacy of Ethanol Endovascular Repair of Ear Arteriovenous Malformation (AVMs).
Methods: Ten patients (7 female, 3 males; age range 6-39 years; mean age: 22 years) with ear AVMs presented for therapy. Two patients had failed prior embolizations (PVA/coils/nBCA/steroids) and 2 patients had other therapies (laser/excisions/grafting). All presented with a grossly enlarged painful ear, and 5 patients had intermittent bleeding. All patients underwent transcatheter and direct puncture ethanol treatments. (86 procedures).
Results: All 10 patients were cured of their AVM at long-term follow-up (mean follow-up: 52 months). One patient had transient partial VII nerve palsy. Two patients had minor blisters and ear injuries that healed on the outer tragus.
Conclusion: Ethanol endovascular repair of Ear AVMs can achieve cures in this vexing lesion that previously was treated with resection of the ear and with high recurrence rates. This series documents long-term cures of AVMs of the ear and scalp that were not treatable by endovascular approaches as previously documented in the world's literature. Permanent treatment of the auricular AVMs is documented and no recurrence occurred in any patient. Only one article is published (group from Shanghai, China) emulating this technique, that I taught them.

P030
Intralesional Interstitial Injection of Bleomycin in Management of Residual Lesions after treatment in Patient with Extracranial Arteriovenous Malformations

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Purpose: Despite many advances in the treatment of extracranial arteriovenous malformations (AVMs), the treatments are still fraught with tedious dissection and potential unacceptable complications. Previously, we reported prospective results of feasibility and safety of intralesional interstitial bleomycin injection for early-stage AVMs. Here we report the results using bleomycin for the treatment of residual lesions after surgical resection or agent embolization.
Methods: Patients with AVMs underwent DSA screening more than one year following previous treatment. Limited residual disease (≤15cm) within the site of the primary lesion received 6 procedures of intralesional interstitial injection at one month interval between May 2014 and May 2017, with a maximum single dose of 15U and 1U/kg per procedure. The therapeutic effectiveness was evaluated and classified as one of four categories: complete response, partial response, no response and worsening 3 months after the last procedure. Further clinical follow-up outcomes were classified as improved, stable, or worse. Adverse events were recorded according to the Society of Interventional Radiology (SIR) classification.
Results: Twenty-three patients received protocol therapy. Complete response occurred in 7 (30.4%) patients, partial response in 11 (47.8%) patients, no response in 4 (17.4%) patients, and worsening in 1 (4.3%) patient. With a mean follow-up of 22 months, the outcome remained stable in 22 (95.7%) of the 23 patients. A major complication (Class C), anaphylactic shock, was observed in one (4.3%) patient. Minor complications (Class A) were included rash maculopapular, bullate, vomiting, and hyperpigmentation.
Conclusion: Intralesional interstitial injection of bleomycin is a feasible approach for the treatment of residual AVMs following previous treatment, and provides safe and effective outcomes. This method may be alternative to clear residual lesion completely and prevent potential destructive progression.

P031
Endovascular Vein Approach and Direct Puncture Retrograde Vein Approach for Curative AVM Treatment: A New Unreported Technique

Wayne Yakes (Vascular Malformation Center)

Purpose: To evaluate the role of Retrograde Vein and Direct Puncture Retrograde Vein Endovascular Repair of Large Peripheral AVMs.

Methods: Eighty-seven patients (45 males, 42 females; age: 14 - 72, mean age: 27 years) presented for repair of AVMs involving head and neck, shoulder, chest wall, intra-thoracic, abdominal, renal, pelvic, buttock, and extremities. Ethanol and ethanol/coils were the embolic agents used. Retrograde transvenous catheterizations and vein direct puncture retrograde vein approaches were used in all patients.
Results: Eighty-five of 87 patients are cured at long-term follow-up (f/up: 14 months to 138 months; mean: 42 months) and 2 patients' therapy is on-going. Complications include 1 pelvic AVM post-Rx small bleed not requiring transfusion; 1 pelvic AVM coils eroded into bladder wall removed uneventfully via trans-urethra endoscopy; 2 infections treated with antibiotics; 2 patients' coils superficially eroded and uneventfully removed; and 1 patient subcutaneous hematoma removed (7/87 patients; 8% minor complications).
Conclusion: Retrograde vein and direct puncture vein access and embolization of AVMs in many anatomic locations have proven curative at long-term f/up of AVMs in multiple anatomic locations with a low complication rate. Reproducible and consistent results of this technique have been reported by Yakes (1990) et al, Jackson (1996) et al and Cho (2008), et al.

P032
Combination of endovascular embolization and sclerotherapy in the complex treatment of arteriovenous malformations (AVMs)

Igor Altman (Interventional radiologist); Iryna Benzar (Pediatric Surgeon)

Purpose: Arteriovenous malformations (AVMs) are congenital defects of the vessels with pathological high-flow bypass between arterial system and venous system through a variety of reticular structure «nidus» or fistulas. The main currently method of of AVM treatment is endovascular embolization. The main disadvantage of this method is a significant risk of recurrence. The aim of study is to evaluate the outcomes of combination of endovascular embolization and sclerotherapy in the complex treatment of high-flow AVMs for more reliable «nidus» occlusion.
Methods: The study included two groups of patients with face AVMs treated between 2015 and 2017. 15 patients of the first group (8 male and 7 female; mean age 19.4 years; range, 3.6 to 31,7 years) were treated by endovascular embolization of AVMs' afferent arteries using PVA particles or hystacril. The second group of 11 patients (8 male and 3 female; mean age 12.7 years; range, 1.6 to 20,1 years) were treated by the same endovascular embolization with the simultaneous foam sclerotherapy by direct percutaneous injection into the «nidus» 1-3% detergents.
Results: There were no procedural deaths. There was no significant difference in complication rates between patients with malformations treated with embolization only and with combination of endovascular embolization and sclerotherapy. Mean available follow-up was 2.0 ± 1.2 years (range, 0.5 to 3.0 years). During the control period, 11 (73.3%) patients of the first group returned to the clinic with a relapse of AVM symptoms. All 11 patients underwent repeated embolizations. Four patients (26,6 %) required more than three endovascular interventions. In the second group, only two patients (18.8%) returned with a relapse of AVM symptoms during the control period. The number of repeated interventions in the second group did not exceed two per patient.
Conclusion: Combination of endovascular embolization and sclerotherapy in the complex treatment of high-flow AVMs can significantly reduce the number of relapses of AVMs symptoms, and reduce the number of repeated endovascular interventions.

P033
Transvenous Embolization of Large Pelvic Arteriovenous Malformations with Dominant Venous Outflow

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Purpose: To evaluate the efficacy and safety of a transvenous retrograde occlusion technique of the venous outflow of large pelvic arteriovenous malformations (AVMs) using Ethylen Vinyl Alcohol Copolymer (EVOH).
Methods: This retrospective study evaluated the single center experience of using EVOH embolization with retrograde filling of the nidus after building a solid plug in the dominant venous outflow ("retrograde push-through technique"). Clinical signs, technical aspects, clinical and technical success rates, and complications were recorded. Long-term outcome was assessed.
Results: Fourteen interventions in 9 patients (6 males) with a mean age of 38.7 (23-56) years between February 2013 and January 2017 were identified. During a mean follow-up period of 12 months, one patient died eight months after the second intervention caused by cardiac failure. At follow-up eight remaining patients had a complete occlusion and were symptomfree. Only pain as minor complication occurred.
Conclusion: EVOH embolization of large pelvic AVMs with retrograde occlusion of the dominant venous outflow is a safe and effective technique with a low complication rate.

P034
Chronic refractory venous ulcer exacerbated by a pelvic arteriovenous malformation successfully treated by transarterial Onyx embolization.

Naiem Nassiri (Yale School of Medicine; Yale New Haven Hospital); Dustin Crystal (Rutgers RWJ Medical School)

Purpose: Arteriovenous malformations (AVMs) are an important but often neglected cause of lower extremity venous hypertension. A case of a chronic refractory venous stasis ulcer of the lower extremity exacerbated by a pelvic AVM is presented.
Methods: A 67-year-old woman presented with a chronic non-healing left lateral malleolar stasis ulceration with left pelvic and lower abdominal throbbing discomfort exacerbated by activity. Duplex ultrasound showed chronic femoral DVT, deep system reflux exacerbated by a high-flow pelvic vascular malformation detected on MRI. Angiography revealed an enlarged left internal iliac artery with multiple arterial feeders supplying the nidus of a Yakes IIa AVM. Superselective Onyx nidus embolization was performed.
Results: There were no acute or delayed complications. Healing of the ulcer was achieved at 2 months without recurrence at 18 months following embolization.
Conclusion: Chronic venous arterialization should be considered in cases of refractory, nonhealing venous ulcers. Embolotherapy in addition to standard of care therapy can be a therapeutic measure. Modification of relevant societal reporting standards to include AVMs as important contributing pathophysiologic processes is suggested.

P035
Feasibility and safety of arteriovenous malformations surgical resection in functionally important musculoskeletal regions

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Purpose: Successful treatment of high-flow intramuscular arteriovenous malformations (AVMs) in functionally important musculoskeletal regions can be challenging. Shoulder and gluteal lesions may be refractory to endovascular treatment due to diffuse soft tissue involvement and lack of clearly defined nidus. The goal of our study was to describe feasibility and results of wide surgical AVM resection in these challenging regions.
Methods: 11 patients with large gluteal (n=6) and shoulder (n=5) AVMs underwent wide surgical lesion resection. Symptoms included pain, paresthesias, soft tissue disfigurement leading to physical limitations, ulceration and high output cardiac failure. We describe surgical resection techniques depending on involvement of anatomical structures and lesion extent.
Results: Patients aged 10-44 years (mean age 29.5 ±3.6 years), 7 men and 4 women underwent radical resection of intramuscular AVMs. 3 gluteal and 3 shoulder region AVMs were localized to the anatomical region, while the rest were diffuse and involved parts of associated extremity. 4 patients required pre-operative and 1 patient post-operative embolizations to facilitate treatment. 1 patient required multiple surgical procedures to remove affected musculature. Gluteal AVMs were resected by removing gluteus maximus (n=4), gluteus maximus and partially medius (n=1) or gluteus maximus, medius and part of minimus (n=1) muscles. Shoulder lesions required resection of deltoid (n=3) or deltoid and associated supraspinatus, infraspinatus and teres minor muscles (n=1). Cure was achieved in 9 and improvement in 2 cases. During the follow up period of 2.5 years (ranging 3 months to 5 years), none of the patients experienced significant functional impairment, one required short-term rehabilitation, 3 engaged in sports and one continued with physically demanding job.
Conclusion: In our experience, wide surgical excision of intramuscular AVMs in functionally significant musculoskeletal regions is feasible, safe and can be achieved without significant functional musculoskeletal impairment.

P036
Hyperpigmentation Secondary to Bleomycin Sclerotherapy; A Case Series.

Heather Rosengard (Johns Hopkins); Hana Jeon (Johns Hopkins); Margaret Ward (Johns Hopkins); Clifford Weiss (Johns Hopkins); Sally Mitchell (Johns Hopkins); Bernard Cohen (Johns Hopkins University)

Purpose: Flagellate pigmentation is a well-documented adverse effect of systemic bleomycin chemotherapy. However, though bleomycin has been used safely and effectively as a sclerosant in the treatment of congenital vascular malformations since 1977, cutaneous manifestations of bleomycin sclerotherapy have not been reported in the literature.
Methods: We report six cases of patients from the XXXXX Vascular Anomalies Clinic who presented to XXXXXXX with distinctive, geographic, hyper-pigmented skin lesions following bleomycin sclerotherapy.
Results: Our patients range in age from two to 65 and include both African-American and Caucasian males and females. Five of our six patients were treated for venous malformations, while one patient was treated for a lymphatic malformation. The bleomycin treatment dose for our patients varied from 15-45 IU. The locations of the patients' vascular anomalies include the face, neck, and extremities. In all cases, the post-procedural hyperpigmentation was located in close proximity to the patient's vascular anomaly. In four cases, post-procedural cutaneous pressure (e.g., ECG leads or tape) clearly contributed to the development of the

hyperpigmentation in a post-traumatic, Koebner-like phenomenon. For all patients the hyperpigmentation faded over time. However, many patients had increased skin pigmentation nearly one-year post-procedure.
Conclusion: Hyperpigmentation is a complication of bleomycin sclerotherapy that is likely underreported. The risk of hyperpigmentation, which may last indefinitely, should be discussed with patients when choosing a sclerotherapeutic agent. Further, a comprehensive study of this phenomenon may shed light on the mechanism by which bleomycin causes flagellate hyperpigmentation when used systemically.

P037
Bleomycin-Induced Hyperpigmentation Following Sclerotherapy of Vascular Malformations

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Purpose: We describe the development of distant cutaneous hyperpigmentation in 4 patients following sclerotherapy for treatment of vascular malformations using Bleomycin.
Methods: In this case report, we present a unique pattern of distant cutaneous hyperpigmentation in 4 patients following Bleomycin injection during sclerotherapy for vascular anomalies. Contrary to Flagellate Erythema the hyperpigmented lesions in these cases tend to be sharply circumscribed and stable overtime with no cutaneous or systemic manifestations.
Results: 4 cases of hyperpigmentation following sclerotherapy were noted. Three correlate with the shape and location of the adhesive bands used during medical care. One developed color changes in the skin overlying the malformation. The types of malformations treated included lymphatic malformations (n=3) and venous malformations (n=1). The areas treated include cervicofacial (n= 3) and suboccipital (n=1). Bleomycin dosing for each sclerotherapy session ranged between 0.06 u/kg to 0.92 u/kg. The number of procedures that included Bleomycin per patient was 2 (n=2) and 3 (n=2). Total Bleomycin dose for each patient ranged between 5.3 units and 15.5 units. Age of patient at time of the sclerotherapy was between 4 weeks to 9 years.
Conclusion: Hyperpigmentation following intralesional administration of bleomycin can be long-lasting and may occur at low doses. These patchy macular changes correlate with the shape and location of the adhesive devices applied to the skin during the procedure.

P038
Adhesive-related Hyperpigmentation After Direct Puncture Bleomycin for Vascular Malformation Sclerotherapy

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Purpose: In treating vascular malformations (VM), bleomycin sclerotherapy is utilized for its selective cytogenic properties. While it is largely believed that bleomycin stays within or immediately surrounding the VM, we present a case series in which there is evidence of systemic egress of bleomycin following direct puncture sclerotherapy.
Methods: Prior to bleomycin sclerotherapy, all patients are approved by hematology-oncology and followed meticulously with imaging studies and pulmonary function and laboratory tests. After combination surgery of laser treatment, bleomycin sclerotherapy, and subtotal resection of their VM's, three patients were identified with delayed hyperpigmentation at sites distal to treatment location. Patient 1 was a 5 year old (YO) female with a venous malformation of her right cheek and airway, Patient 2 was a 14 YO male with an arteriovenous malformation of his upper lip, and Patient 3 was a 14 YO male with a complex venous malformation of his right parotid, neck, and airway. All patients had been given general anesthesia, with electrocardiogram leads and monopolar cautery pads attached to their skin.
Results: There were no immediate effects, but all patients experienced delayed hyperpigmentation of their skin at the periphery of electrocardiogram lead and cautery pad adhesive as early as 2 weeks postoperatively. The hyperpigmented skin was smooth and devoid of lesions or breaks. There were no reports of pain or irritation. The hyperpigmentation has yet to fade, and has been resistant to laser therapy and bleaching agents. Routine post-therapy laboratory and chest radiographs were normal in all three patients.
Conclusion: This study suggests systemic leakage of bleomycin following direct puncture sclerotherapy of VM's, potentially creating undesired outcomes. Activation of melanocytes may occur consequent to reactions between adhesive and systemic bleomycin when compounded with a monopolar current. Further study is warranted to assess systemic absorption, circulating levels, and effects of bleomycin after sclerotherapy.

P039
Cerebral Vascular Anomalies: Causal and Associated Genetic Mutations

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Purpose: Significant diagnostic and therapeutic advances have been made in management of cerebrovascular disorders related to ischemic stroke or intracranial hemorrhage. Emerging evidence in pediatric patients

supports the importance of multidisciplinary teams, including genetics, to diagnose, screen, and manage children with cerebrovascular disorders. Vascular lesions may be associated with systemic syndromes or alternatively be isolated lesions, and are frequently the presenting symptom of an underlying genetic syndrome. Genetic diagnosis may help target the screening protocol and identify at-risk family members. Here we present the preliminary experience of our newly formed pediatric neurovascular/vascular anomalies program with associated genetic workup.
Methods: We reviewed six months of clinical data from the Vascular Anomalies Center at Texas Children's Hospital. Patients presenting with new intracranial hemorrhage or ischemic stroke undergo full diagnostic workup. Those diagnosed with new vascular pathology are screened for common mutations and hereditary conditions based on the type of malformation.
Results: Twelve patients with newly diagnosed lesions were evaluated. Six patients were diagnosed with cavernous malformations, two with positive CCM testing, one diagnosed with hereditary hemorrhagic telangiectasia (HHT) due to a pathogenic ENG variant and one with negative testing. Four patients presented with cerebral AVMs, of whom one was diagnosed with HHT due to ENG and two had negative HHT panels. Two patients have malformations with known or suspected syndromes, including blue rubber bleb nevus and Sturge Webber . Two patients (17%) were unable to have recommended genetic testing due to limits to insurance coverage, and workup is ongoing for three patients.
Conclusion: Six of twelve pediatric patients with neurovascular symptoms were diagnosed with four different syndromes via clinical evaluation and molecular testing. The expertise of the multidisciplinary team is essential in identifying and treating these patients. With increasing knowledge of the underlying molecular etiology of cerebral vascular anomalies, targeted therapies can be developed and implemented.

P040
Familial Cerebral Cavernous Malformations in New Mexico

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Purpose: Familial Cerebral Cavernous Malformations due to the common Hispanic mutation (FCCM1-CHM) is endemic among the Hispanic population of New Mexico. In this study, we created a database of images characterizing the location and type of cutaneous vascular malformations from 140 persons with confirmed FCCM1-CCM, and attempted to identify a relationship between skin and the potentially fatal brain lesions. With a new database that categorizes and identifies the morphologies of cutaneous vascular malformations (CVMs) in this population, physicians will more readily be able to identify patients with FCCM1-CHM. And if the incidence of CVMs correlate with CCMs, then a new cutaneous screening tool could be used to identify those affected with FCCM1-CHM earlier in the disease course before potentially fatal consequences manifest.
Methods: We performed a cross-sectional study of patients enrolled in a CCM type 1 common Hispanic mutation (CCM1-CHM) database/Registry of individuals with confirmed CCM1-CHM mutation via DNA testing. 140 patients were seen at scheduled clinic follow ups. Cutaneous lesion were photographed, and characterized by morphology and location. Then we took thirty-three members of the original 140 people with MRI proven CCMs and performing various statistical correlational analyses. We created a diagram outlining the location of these CVMs among people with known CCMs. We compared the number of cutaneous lesions and two factors: number of brain lesions present on MRI and patient age. Finally, previously published studies of different patient populations have identified a positive correlation between patient age and number of central lesions. We were interested if this correlation would also be found in our unique patient population.
Conclusion: 32% of 140 individuals had one or more cutaneous lesion. Approximately 85% of cutaneous vascular lesions were located on the extremities. The majority of these lesions were DBNs and PCS, which differs from other large scale studies. We found a statistically significant relationship between patient age and number of brain lesions on MRI, which is consistent with previous studies. However, no significant relationship was found between the age of a patient and number of cutaneous lesions. No significant relationship was identified between the number of cutaneous vascular malformations and number of central lesions. This study reinforces the importance of performing a full review of systems and family history in patients with cutaneous vascular malformations of the types described in Familial CCM. As the Hispanic diaspora continues from the Southwest, the burden of this disease is likely to increase, making clinician education of paramount importance. Physicians are on the front line, and with a new database that categorizes and identifies the morphologies of cutaneous lesions specific to this population, they will more readily be able to identify patients with FCCMCHM before potentially fatal consequences manifest.

P041
Imaging characteristics of cutaneous/subcutaneous venous malformations in the CCM1 population compared to "typical" venous malformation in the general population

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Purpose: Distinguish imaging similarities and differences of venous malformations (VM) in patients with CCM1 compared to venous malformations in the general population.
Methods: Venous malformations are one of the more common vascular lesions to be imaged, however in the current literature there is a lack of information regarding the appearance of the presumed venous malformations seen in the familial CCM1 syndrome, specifically the CCM1 syndrome (KRIT1) that is common in Northern New Mexico. Patients present with multiple cerebral cavernous malformations, along with multiple other manifestations outside the CNS including cutaneous/subcutaneous vascular lesions. One pediatric radiologist and one radiology resident reviewed three CCM1 patients who had MR imaging of their symptomatic cutaneous/subcutaneous vascular lesions; two of these patients are related, grandmother and granddaughter. Imaging characteristics was then compared to known imaging appearance of venous malformations.
Results: VMs in the general population demonstrate avid T2 hyperintensity (fluid signal) and show complete or near complete enhancement depending on degree of thrombosis. However, in our small cohort there were multiple, small flat/plaque-like subcutaneous lesions that did not demonstrate enhancement. Also the MR signal intensity did not demonstrate the expected T2 hyperintensity, but showed a heterogeneous mild-moderate T2 signal. Out of the numerous lesions only the symptomatic lesions within two of three patients enhanced; particularly, the enhancement pattern was stippled and not characteristic of VMs as seen in the general population.
Conclusion: Imaging appearance of the numerous subcutaneous lesions in CCM1 patients is atypical and differs from VMs in the general population. Therefore, these lesions may represent a discrete type of venous malformation compared to the typical VMs in the general population vs a different lesion altogether, given the unique MR characteristics.

P042
MULTIFOCAL CAPILLARY MALFORMATION WITH METAMERIC DISTRIBUTION AND CENTRAL ATROPHY: A NEW ENTITY? A SERIES OF 10 CASES

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Purpose: Although nevus simplex and port wine stains are the most common capillary malformations (CM), there are other types of CM with diverse clinical presentation, other associated findings and therefore different prognoses. The ISSVA classification includes CM within simple vascular malformations and within the combined ones, but does not exhaustively describe their morphological and prognostic characteristics. In 2016, Rozas-Muñoz et al, proposed a clinical classification of CM in Pediatric Dermatology, which classified them into 7 major patterns (nevus simplex, port wine stain, reticulated CM, geographic CM, CM associated with capillary malformation-arteriovenous malformation syndrome, CMTC and telangiectasias). This classification also correlated these 7 major patterns with the CM subtypes of the latest (2014) ISSVA classification. We present the cases of 4 patients with a new phenotype of a characteristic CM, which cannot be classified within any of the 7 described patterns.
Results: The common clinical findings of the CM of our patients are: a) All patients have multiple CM since birth; b) The distribution of the CM is multifocal; c) In all the patients, CM present an area of central anetoderma; d) With regard to the morphology of these CM, they are of bright red color and have well defined margins; e) The histological diagnosis of these CMs was indistinguishable from conventional CM; f) None of the patients presented associated vascular or skeletal malformations
Conclusion: 1. We present a characteristic CM not previously described and provisionally unclassifiable; 2. To differentiate them from the geographical CMs (which are usually associated with other vascular malformations and therefore with greater morbidity), we have named them multifocal capillary malformations with central anetoderma; 3. The analysis of possible mutations in the molecular pathways involved in these vascular malformations will help us to deepen in its pathogenesis. The genetic study of these vascular malformations is in progress.

P043
Diffuse Capillary Malformation with Overgrowth (DCMO): Long-term outcomes by cross-sectional survey

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Purpose: Diffuse capillary malformation with overgrowth (DCMO) is a distinct subtype of vascular anomaly characterized by extensive capillary malformations (CMs) involving more than one anatomic region. Little is currently known about the long-term outcomes in DCMO patients.
Methods: We conducted a Boston Children's Hospital Institutional Review Board-approved anonymous REDCap survey about vascular anomalies, overgrowth, physical and psychological outcomes, and treatment in 70 patients over the age of five years with complete contact information in the Vascular Anomalies Center database.
Results: Thirty-one patients/parents (44%) completed the survey with mean patient age of 14.2 years (range: 6-38 years) with no gender predilection. CMs were most commonly located on the posterior trunk and lower extremities. Nineteen patients (61%) had laser therapy; 95% of these reported response to treatment. Soft-tissue and/or bony overgrowth was reported in 77% of patients and commonly involved extremities. Nineteen patients (61%) reported leg-length discrepancy; and 63% received treatment, including orthotics, surgical interventions, and physical therapy. Eighteen patients (58%) had prominent veins or vein abnormalities; two were treated with compression stockings or partial venectomy. Arm-length discrepancy, macrodactyly, and syndactyly were noted in 19%, 35%, and 6% of patients, respectively. No patients required treatment; daily tasks were largely unaffected. Patients also reported scoliosis (32%), developmental delay (13%), subclavian vein thrombosis (3%), cellulitis (3%), glaucoma (3%), and macrocephaly (3%). Leg-length discrepancy did not correlate with scoliosis (Fisher's exact test, p=0.4472). No patients reported lipomas, hypotonia, seizures, or malignancies. Ten patients (32%) reported psychosocial difficulties, including self-esteem issues, anxiety, and social discomfort.
Conclusion: This study confirms that DCMO portends a favorable prognosis. Nevertheless, long-term clinical follow-up is needed to ensure proper diagnosis and management. DCMO patients may need psychosocial support.

P044
GNAQ related disorders: phenotype spectrum

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Purpose: Port-Wine-Stains (PWS) can present in association with Combined Vascular Malformations (CVM) in different Syndromes. Our purpose was to investigate the molecular bases of patients affected by these complex phenotypes.
Methods: From January 2015 to December 2017 thirty patients affected by PWS-CVM underwent genetic-molecular studies through Next-Generating Sequencing (NGS) on samples of skin biopsy and peripheral blood. Specimen biopsies were taken from the affected arms. NGS was performed using a MiSeq Illumina instrument optimizing a combination of different approaches. Deep sequencing of multiplex amplicon library generated from custom oligo panel of twenty-five genes, choosed from ISSVA classification of mutation involved in vascular anomalies, was performed using an Illumina TSCA kit. Mutations were confirmed with a second different NGS approach. At a first step enrichment of mutated exons with PCR was performed using a new set of primers for amplification. A second round of NGS sequencing was performed with a Nextera XT Illumina kit in order to obtain an ultradeep coverage. Cases were considered mutated when both techniques confirmed the same results.
Results: GNAQ mutations were identified in 6 patients with non homogeneous phenotype. Mosaicism rate was ranging between 2,5% to 9%. All six patient presented capillary malformation with mosaic distribution, associated with segmental overgrowth. In three patients the clinical diagnosis was Sturge-Weber Syndrome overlapping with Klippel-Trenaunay Syndrome. In 3 patients PWS was not affecting the face nor the intracranial district. Femoral vein agenesis in the lower limb affected by PWS was detected in 3 patients. In five patients the mutation was R183Q. In one patient (with no cranio-facial involvement) the mutation was R183G.
Conclusion: This small case series shows heterogeneous GNAQ related phenotypes, including Sturge-Weber Syndrome overlapping with Klippel-Trenaunay syndrome features. Further studies are needed in order to explore the GNAQ related phenotype spectrum.

P045
HISTOPATHOLOGICAL FINDINGS IN CAPILLARY MALFORMATION-ARTERIOVENOUS MALFORMATION SYNDROME

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Purpose: Capillary malformation-arteriovenous malformation syndrome (CM-AVMs) is a recently described disease characterized by the presence of multiple, familiar, atypical and multifocal CM, associated with high-flow vascular malformations in one third of the patients. Scarce publications about the histopathological findings in CM associated with this syndrome have been published.
Methods: We have studied 14 patients with CM-AVM from different hospitals in Spain, in which a histopathological study of CM has been performed. We have carried out immunohistochemical studies in all of them, with VT1, D2-40, GLUT1, Ki67, CD31 markers.
Conclusion: CMs are minimally dilated dermal vessels, lined by a single layer of endotelial cells. Incipient AVMs in stage I can resemble CM, highligting a higher density and vascular tortuosity, with a prominent muscular layer, and without erytrocytes in the lumens. In CMs associated with this syndrome, the findings are very similar to those in incipient AVM.

P046
Characterization of Vascular Stains Associated with High Flow

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Purpose: The purpose of this study is to identify distinguishing features of high flow vascular stains (arteriovenous malformations) from typical port-wine stains (PWS-capillary malformations) in a pediatric population.
Methods: This is a retrospective multicenter cohort study of vascular stains measuring greater than/ equal to 2 cm in diameter and associated with high flow that were seen at two centers between January 1, 2007 and July 31, 2017. Clinical data and photographs were reviewed with a focus on the distribution, color and other clinical features of each stain at different points in time.
Results: Records from 24 patients were reviewed (five additional sites are anticipated to enroll). Preliminary data indicate that the majority of cases were initially diagnosed as PWSs or infantile hemangiomas for an average of over five years prior to correct diagnosis. High flow stains commonly presented in infancy as multifocal red or red-pink patches that were warm to touch with a subtle pale halo. The head and neck were the most common sites followed by the lower extremities. Over time, stains darkened in color and developed more defined, craggy borders. Increased venous prominence and increased prominence of the halo was observed. Other distinguishing features included increased warmth to palpation, rapid capillary refill, swelling or overgrowth of the underlying tissue and bleeding or pain. When multifocal lesions were present, the number of lesions also increased over time. A diagnosis of a high flow stain rested heavily on imaging and genetic testing, with RASA1 mutations identified in 75% of patients with confirmed genetic diagnoses.
Conclusion: Specific clinical features including warmth to touch, multifocality, soft-tissue fullness and a peripheral halo may help physicians distinguish high flow stains from PWSs early on in a patient's course. However, changes in stain appearance and behavior over time remain the most reliable clues to diagnosis.

P047
Macrocephaly – capillary malformation (M-CM) – Clinical and genetic features of the Zurich cohort.

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Purpose: The purpose of this study is to clinically and genetically characterize the Zurich cohort of patients with Macrocephaly – Capillary Malformation (M-CM) in comparison with known cohorts.
Methods: We investigated patients with M-CM referred to our clinic. Next generation sequencing was performed on blood and tissue samples in selected patients.
Results: We identified 12 patients; 8 of them fulfilling the current diagnostic criteria for M-CM and 4 of them with very characteristic features of M-CM but lacking macrocephaly. Mean age at inclusion was 6.44 years (range 0.5 – 15.6 years). All 12 patients had extensive reticular CM. 4 patients (33%) had a prominent, nevus simplex-like midline CM on the face and 5 (42%) a morphologically identical midline stain on the lower back. All patients had segmental overgrowth. In 8 (66%) patients cerebral MRI was abnormal. The majority of patients (8 patients, 66%) had Ehlers Danlos-like connective tissue abnormalities. Of note, two infants

presented with suprasternal retractions and one additionally with inspiratory stridor likely linked to muscle hypotonia. In one patient, we found a somatic PIK3CA-mutation thus far not described in patients with M-CM.
Conclusion: We highlight new clinical features of M-CM. The nevus simplex-like midline stain does not only affect the face but may also appear on the lower spine. The connective tissue abnormality noted in our patients was striking and merits further investigation. We found 4 patients with features clinically indistinguishable from M-CM but lacking macrocephaly. According to Lee et al, these patients should be diagnosed as diffuse CM with overgrowth (DCMO). However, the phenotype of these patients is otherwise strongly consistent with M-CM and should be labelled as such with absent or limited cerebral involvement, in par-ticular as PIK3CA instead of GNA11 mutations were detected. Our genetic data including the so far unknown mutation p.[Asp350=/Asp350Gly] is presented.

P048
How to Improve the Classification of Capillary Malformations: A Dermatotologist's View
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Purpose: Why and how could the ISSVA classification of capillary malformations (CMs) be improved? In principle, the present classification distinguishes CMs by their association with other cutaneous or extracutaneous abnormalities such as arteriovenous malformations, bone or soft tissue overgrowth, CNS defects or ocular anomalies. – However, all of these CMs may occur as an isolated lesion, and how can we distinguish them if we have no specific names? The current ISSVA classification cannot help, whereas dermatological criteria may often be useful.
Methods: The recent reports on CMs were screened with the purpose to give specific names to skin lesions that were described under the ambiguous term "CM". – Within the group of capillary nevi, we can distinguish between nevus flammeus, nevus roseus, Vikkula nevus (rhodoid nevus), cutis marmorata telangiectatica congenita, congenital livedo reticularis or reticulated CM (Happle, 2015; Rozas-Muñoz et al., 2016), segmental angioma serpiginosum, nevus anemicus, nevus vascularis mixtus, and angiokeratoma circumscriptum. – CMs that may or may not represent nevi include the mesotropic port-wine patch as noted in congenital livedo reticularis-megalencephaly syndrome; the Carter-Mirzaa macules as found in "microcephaly-CM"; punctate unilateral nevoid telangiectasia; and patchy unilateral nevoid telangiectasia. CMs that do not represent nevi include X-linked angiokeratoma corporis diffusum (Fabry disease); autosomal dominant angiokeratoma corporis diffusum; hereditary hemorrhagic telangiectasia; hereditary angioma serpiginosum; and the salmon patch.
Results: Several reports contained unidentified cases of nevus roseus, congenital livedo reticularis, or mesotropic port-wine patch. In one report, a mesotropic port-wine patch was mistaken as "nevus simplex". Congenital livedo reticularis was sometimes conflated with cutis marmorata telangiectatica congenita. Moreover, the salmon patch was often decribed as "nevus simplex" although this lesion does not fulfill the criteria of a nevus because it does not reflect mosaicism.
Conclusion: Specific CMs need a specific name. This approach may facilitate further the application of the ISSVA classification in clinical practice.

P049
Capillary malformation of atypical appearance and recurrent ulceration
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Purpose: Title: Capillary malformation of atypical appearance and recurrent ulceration
We introduce a new type of capillary malformation with atypical clinical appearance and recurrent episodes of ulceration.
Results: A three-year-old girl who had congenital cutaneous lesions on the right buttock, thigh and knee. Clinical examination revealed red and polycyclic macules with a paler center and peripheral petechial aspect. She had scab on previous ulcerations. She suffered from episodes of recurrent ulceration of the maculae, followed by spontaneous healing in a few days. Doppler ultrasound examination did not detect any deeper lesional component. We tried propranolol at a dose of two mg / kg / day for four months without any improvement. Currently the girl is six years old and the lesions persist unchanged, with recurrent episodes of ulceration. A skin biopsy was under histopathological analysis compatible with a capillary malformation. It was GLUT 1 negative. Molecular genetic testing showed a GNA11 somatic mutation. This also fits with the diagnosis of a capillary malformation.
Conclusion: We report a case with a peculiar clinical appearance and its evolution with recurrent ulcerations, atypical for classic capillary malformations.

P050
Cutis Marmorata Telangiectasia Congenita in Adams-Oliver Syndrome: Evaluation, Diagnosis, and Management Review

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Purpose: Cutis marmorata telangiectasia congenita (CMTC) is a distinctive skin phenotype with a wide range of severity and associated clinical implications. Adams-Oliver Syndrome (AOS) is a rare inherited condition associated with this phenotype in newborns and may include dramatically enlarged scalp veins. AOS does not currently have well-established recommended screening and diagnostic tools, such as imaging and genetic testing. In this study, we review the literature and present a case series to provide guidance for management of these patients.
Methods: We reviewed our vascular anomaly patient database for patients with CMTC and clinical suspicion for AOS over the past 12 years. Patient data collected included clinical photographs, clinical course, results of diagnostic workup, and patient outcome.
Results: We identified seventeen patients with CMTC; three had clinical findings concerning for AOS. Extremely prominent scalp veins with and without cutis aplasia were seen in these three patients who then underwent further work up with a combination of cranial and abdominal ultrasounds, brain MRI, echocardiogram, and genetic testing. Although these patients had similar clinical phenotypes, there was variability in the extent of systemic disease involvement. One patient only suffered mild skin breakdown, in atrophic areas, managed with local wound care. The second patient had mild developmental delay, white matter abnormalities on MRI, and a variant in PIK3CA (p.P449T) revealed by genetic testing on skin biopsy. The third patient died at 10 months old secondary to pulmonary hypertension after a long hospital course including a period on ECMO.
Conclusion: The literature and our case series support that AOS can manifest as CMTC. In our experience, CMTC patients with severely prominent scalp veins warrant further diagnostic testing to exclude a potentially fatal condition such as AOS. PIK3CA is not an identified causative gene in AOS based on current literature, however our case series suggests it may play a role.

P051
Cutis Marmorata Telangiectatica Congenita: Associated Anomalies.

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Purpose: Cutis marmorata telangiectatica congenita (CMTC) is a capillary malformation characterized by congenital, reticulated, well-defined dark blue or violaceous macules or plaques, with a fixed marble-like pattern that resembles livedo reticularis and may have associated atrophy. The only well recognized association of CMTC, when generalized, is with Adams-Oliver syndrome. The nosologic confusion of the term CMTC and the uncertainty about the real risk of associated abnormalities, hinders the appropriate work-up of patients with CMTC and prognostic information.
Methods: We performed a retrospective review of patients with CMTC seen in our department and a systematic review of the literature to ascertain the risk of associated anomalies.
Results: We included a total of 58 patients. Systematic review of the literature showed all the patients with generalized CMTC had AOS. The associations found in patients with segmental or localized CMTC were mostly epidermal (14 patients) and subcutaneous atrophy (5 patients), skin ulceration in 8, and asymmetry of the extremities in 7 patients. Two patients also presented urological anomalies and 2 congenital heart disease. Of our patients, 1 case had generalized CMTC and had other features of AOS. In the localized CMTC group (21 patients) there only abnormalities found after a follow-up period of 1 to 14 years, were: 6 patients with subcutaneous atrophy, 3 cutaneous atrophy, 1 skin ulceration and 6 patients with hypotrophy of the affected extremity. In all cases the asymmetry improved with age.
Conclusion: Localized CMTC, as shown in the literature and in our cases, is mainly associated with cutaneous, subcutaneous atrophy and skin ulceration, Also, asymmetry of the affected extremity appears as a relevant association. All these features, improve during the first years of life, giving localized or segmental CMTC an excellent prognosis that physicians, patients and their families should be aware to avoid unnecessary studies.

P052
Evaluation of the hemostasis in children with vascular malformations in the head and neck regions.

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Purpose: To evaluate the pre-operative hemostasis in children with vascular malformations (LM, LVM, VM, AVM) in the head and neck regions.
Methods: From 2015 to 2017, the hemostasis system was evaluated in 97 patients aged 1 month to 17 years. The following coagulogram parameters were evaluated: Quick's prothrombin time, activated partial thromboplastin time (APTT), fibrinogen, soluble fibrin-monomer complex (SFMC), D-dimer; thromboelastography parameters: the time of start of clot formation (R), the maximum strength of the platelet-fibrin network (MA), the density of the clot (G); thrombodynamics parameters: the rate of the clot growth (V), the density of the clot (D), the size of the clot (CS). The first group consisted of 47 children with vascular malformations. The control group included children without vascular malformations. This group consisted of 48 patients.
Results: There were no significant differences between the two groups in terms of coagulogram parameters. The thromboelastographic parameter R was met significantly faster in patients with vascular malformations (P = 0.0008); the MA and G parameters did not differ significantly between groups. Based on thrombodynamics parameters, the rate of the clot growth (V) and size of a clot (CS) were significantly higher in patients with vascular malformations (p = 0,0385 and P = 0,0285 respectively), whereas the density of the clot (D) did not differ significantly from the control group.
Conclusion: Children with vascular malformations in the head and neck regions are susceptible to hypercoagulable state. These changes can be suspected by thromboelastographic and thrombodynamics parameters, whereas coagulogram cannot reveal such important information. The main source of hypercoagulation in patients with vascular malformations is activation of the plasma pathway of hemostasis. All the factors mentioned above should be considered during planning of surgical treatment and blood loss correction in order to reduce the risk of complications.

P053
Investigation and Statistical Analysis of Vascular Malformations with Blood Coagulation System in Our Institution: A Review of 116 Cases

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Purpose: Patients with vascular malformations are at risk of significant hemorrhage and large venous malformations (VMs) or severe arteriovenous malformations (AVMs) are especially difficult to manage in the perioperative period. In a retrospective study, a coagulation disorder named localized intravascular coagulopathy (LIC), characterized by elevated D-dimer levels was reported in VMs.
Methods: This study analyzed vascular malformations of 116 patients for 2 years since July 2008, established Center for Vascular Anomalies in our institution. We analyzed VMs, which included the largest number of LIC patients, of the 63 participants, 21(33.3%) showed high D-dimer levels (over 1 μg /ml), as we define LIC.
Results: The results of our analysis showed that large area (over 100 cm2), multiple lesions, syndromic patients were associated with high D-dimer levels, high FDP levels, and low fibrinogen levels in VMs.
Conclusion: These statistical results are the characters of LIC, and large VMs, multiple VMs are at risk of LIC, severe bleeding at wound sites or during surgery. Therefore, our findings suggest that the measurement of D-dimer level, FDP level and fibrinogen level is a useful complementary tool for diagnosing LIC of vascular anomalies in every practice.

P054
Retrospective Study of Hematologic Complications in Vascular Malformation Patients with Localized Intravascular Coagulopathy Undergoing Surgical Intervention

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Purpose: Slow-flow vascular malformations (SFVMs) including multifocal and extensive venous (VM), venous-lymphatic (VLM), capillary-venous (CVM) and capillary-lymphatic-venous malformations (CLVM), are associated with localized intravascular coagulopathy (LIC), which is characterized by elevated D-dimer, low fibrinogen, and/or mild thrombocytopenia. Aggravation of the abnormal endothelium of the malformation may worsen the consumptive coagulopathy causing progression to disseminated intravascular coagulation. Generally, hematological complications occurring with surgical interventions are not well characterized in patients with SFVMs and coagulation abnormalities.
Methods: Retrospectively evaluate hematologic complications in patients with SFVMs and LIC who underwent surgical procedures, excluding sclerotherapy and laser ablation. LIC was defined by D-dimer >/= 5x upper limit of normal, fibrinogen <150mg/dL and/or platelet count <150K/mcL.
Results: One hundred four patients with SFVMs underwent a total of 265 surgical interventions; 29 of which also had LIC and underwent 73 surgical procedures. Although the risk of hematologic complications appears to be similar for adults and children, all significant hematologic complications occurred in patients with extensive combined vascular malformations (table 1). Eight significant bleeding episodes and 3 thrombotic events occurred in SFVMs; six (55%) of which occurred in patients with known LIC. Four of the 6 patients with significant bleeding had LIC and required peri-procedure blood product transfusions. One hundred eight surgeries were performed on or near the malformation; 35 (32%) were performed in the setting of LIC and 23 (21%) lacked coagulation testing. All procedures with significant bleeding and/or thrombotic complications were performed on or near the malformation.
Conclusion: As expected, patients undergoing surgical procedures to or near the malformation appear to be at greatest risk for hematologic complications. Coagulopathy screening including D-dimer and fibrinogen is critical in pre-operative planning for patients with SFVMs, particularly if extensive. Perioperative plans for patients with LIC are imperative and coagulation abnormalities should be corrected pre-operatively if possible.

P055
Blue Rubber Bleb Nevus (BRBN) syndrome: how to treat large venous malformation complicated by chronic consumptive coagulopathy in children.

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Purpose: Patients with large venous malformation (dominant lesion) associated with Blue Rubber Bleb Nevus syndrome (BRBN) may undergo repeated bleeding from ulceration. Preoperative assessment requires clinical, laboratory and radiological investigations as described (Ballieux, et al. 2015). Decompensation of the chronic consumptive coagulopathy remains a problem during resection and reconstructive surgery. We describe the pre- per and post-operative steps important for the surgical treatment of BRBN patients.
Methods: Based on two cases and a review of the literature, we collected the key technical points essential to maintain control over the treatment in a safe manner.
Results: The pre-operative approach required correction of iron deficiency anemia, assessment of pain, psychosocial burden and nutritional status, reduction of chronic consumptive coagulopathy by a systemic low dose of sirolimus (0.1 mg/kg/day), and limitation of the risk of intraoperative bleeding by multiple sclerotherapies and preoperative treatment with low molecular weight heparin (100 IU anti-Xa/kg/day). During the per-operative period, temperature was kept over 36°C. Peroperative blood loss was reduced thanks to preoperative low molecular weight heparin therapy, squeezing with non resorbable sutures of the part of the malformation that could not be easily resected. An experienced surgical team is also mandatory. Covering the large defect required a well planned strategy to manage potential complications and to retain the possibility for additional surgical procedures, such as expanded autografts in a sandwich pattern, protected by allo- or xenograft, negative pressure wound therapy, or local flaps and free-tissue transfer.
Conclusion: These rare and challenging slow-flow vascular malformations allow us to propose a surgical strategy in combination with medical and radiological treatments as a good solution to solve the problem of major bleeding encountered with large BRBN lesions.

P056
How often are vascular anomalies accurately diagnosed prior to referral to a multi-disciplinary vascular anomalies clinic?
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Purpose: Vascular anomalies are poorly understood throughout the medical community. Multi-disciplinary care is often required; however different disciplines have historically treated vascular anomalies very differently. Often times, patients referred to multi-disciplinary vascular anomalies clinics have been treated incorrectly, resulting in unnecessary medical intervention or increased pain/discomfort. We aim to compare the final diagnosis rendered by clinicians in our multi-disciplinary vascular anomalies clinic, as compared to those rendered by referring physicians from the greater medical community and further quantify the percentage of patients who received incorrect treatment based on an incorrect diagnosis.
Methods: A retrospective chart review was performed of all patients seen in the vascular anomalies clinic from May 2016 thru October 2017. Patients where a diagnosis had not been determined were excluded. Pre-referral diagnoses were collected along with final diagnosis after vascular anomalies clinic appointment, how the diagnosis was made and if the patient had any medical or procedural treatment prior to referral.
Results: 405 of 459 patients had a diagnosis rendered by the referring team and were included. 76/405 (18.8%) of patients had an incorrect diagnosis when referred to the multi-disciplinary clinic. Of those with an incorrect diagnosis, 46% (35/76) received incorrect treatment prior to referral. The most common incorrect referring diagnosis was hemangioma that was re-diagnosed as a different vascular anomaly after multi-disciplinary evaluation (44/405; 10.9%). 27 patients incorrectly diagnosed with a hemangioma also received incorrect treatment, including 10 patients receiving unnecessary medical therapy (propranolol and/or steroids), 7 patients receiving unnecessary procedures, and 10 patients being treated with close observation.
Conclusion: Mis-diagnoses of vascular anomalies are common, and can lead to incorrect, sometimes harmful therapy for patients. The findings of this study demonstrate the urgent need for democratization of knowledge about vascular anomalies and the demand for proliferation of multi-disciplinary vascular anomalies clinics.

P057
Clinical spectrum of Fibro-adipose vascular anomaly (FAVA) in a third level pediatric hospital of Argentina
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Purpose: Fibro-Adipose Vascular Anomaly (FAVA) is a distinct vascular malformation characterized by fibro-fatty infiltration of muscles, unusual phlebectasia with pain, and contracture of the affected extremity. Our goal is to describe the clinical and radiological spectrum of FAVA in 6 pediatric patients.
Methods: Our study consists of a case series of 6 patients. We retrospectively reviewed the clinical, radiological, operative, and histopathologic findings of 6 patients with FAVA.
Results: Six patients (1 male and 5 females) met the clinical, radiologic, and histopathologic criteria of FAVA and were included in our study. The age at presentation ranged from 4 to 12 years. The locations of the lesions were: calf (n=4), gluteus (n=1), and thigh (n=1). All patients presented with severe pain. Two patients with calf lesions had limited ankle dorsiflexion. Imaging findings included fat replacement of the affected muscle fibers and of the extra-fascial components with fibro-fatty overgrowth, phlebectasia. The histopathologic features comprised dense fibrous tissue, fat, and lymphoplasmacytic aggregates within atrophied skeletal muscle. Three cases were treated with percutaneous sclerosis without clinical improvement. Surgical resection was performed in two patients and was effective controlling the symptoms. One patient was treated with nerve ablation in order to reduce pain. Three patients were treated with non-steroidal anti-inflammatory drugs with mixed clinical results.
Conclusion: FAVA is a complex vascular malformation that typically presents with pain, discomfort, contracture and other disabling symptoms with unique radiological and histopathological features. Through our small series, we noticed that minimally-invasive treatment is not usually effective to control the symptoms. Surgical options may provide better option to control the symptoms. Further larger studies are required to better characterize this rare, yet important clinical entity.

P058
Chylothorax Following Rib Biopsy in Generalized Lymphatic Anomaly
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Purpose: Core-needle biopsy is a relatively safe procedure. We report the development of chylothorax following core needle biopsy of the ribs in patients with generalized lymphatic anomalies (GLA).
Methods: Three patients with generalized lymphatic anomaly who underwent core-needle biopsy developed chylous pleural effusion. It is important to avoid rib biopsy in generalized lymphatic anomalies (GLA).

Results: Three patients with generalized lymphatic anomaly who underwent core-needle biopsy developed chylous pleural effusion. It is important to avoid rib biopsy in generalized lymphatic anomalies (GLA).
Conclusion: Three patients with generalized lymphatic anomaly (GLA) who underwent core-needle biopsy developed chylous pleural effusion. It is important to avoid rib biopsy in generalized lymphatic anomalies (GLA).

P059
Guidance Document for Hepatic Hemangioma (Infantile and Congenital) Evaluation and Monitoring

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Purpose: Hepatic hemangiomas are benign vascular tumors without a medical home, managed by multiple specialties. There is an acute need of clear definitions and evaluation guidelines using the updated ISSVA classification. This diagnosis has been assigned historically to various vascular lesions with completely different clinical presentations, resulting in difficult standardized management.
Methods: We used a rigorous, transparent consensus protocol, with input from multiple pediatric experts in vascular anomalies from hematology-oncology, surgery, pathology, radiology and gastroenterology.
Results: In the first section, we define the subtypes of hepatic hemangiomas using clinical course, histology and radiologic characteristics. Infantile hemangioma (IH): benign endothelial neoplasm with a natural history of proliferation, followed by stabilization and gradual involution. IH expresses Glut-1 that distinguishes it from other types of vascular anomalies. IH does not express lymphatic markers. Congenital hemangioma (CH): benign endothelial neoplasm proliferating in utero, fully formed at birth and following one of three patterns of natural evolution: rapidly involuting, partially involuting or non-involuting. CH does not express Glut-1 or lymphatic markers. We recommend AGAINST using the term "hemangioma" for any vascular malformations affecting the liver or any hypervascular tumors that are NOT characterized by the above definitions. We recommend AGAINST using the term "hemangioendothelioma" for infantile or congenital hemangioma. The following two sections describe these subtypes in further detail, including complications to be considered during monitoring and respectively recommended screening evaluations.
Conclusion: While institutional variations may exist for specific clinical details, a clear understanding of the diagnosis of hepatic hemangiomas affecting the pediatric population and the possible complications that require screening during the monitoring period should be standard. As patients with hepatic hemangiomas are managed by different medical and surgical specialties, a multidisciplinary consensus based on current literature, on the data extracted from the liver hemangioma registry and on expert opinion was required and was accomplished by this manuscript.

P060
Infantile Hemangioma Ulceration in the Era of Beta-Blockers

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Purpose: To characterize the clinical features and treatment response of ulcerated infantile hemangiomas (IH) in the era of beta-blockers.
Methods: Retrospective cohort study between 2012 and 2016. Clinical characteristics, treatment interventions and course are analyzed. The primary end point is IH ulceration healing.
Results: An interim analysis of 35 patients is presented, composed of 26 females (74%) and a total of 37 individual ulcerated IH. Presentation at ISSVA will include a larger cohort currently being enrolled and analyzed. The average age at presentation was 16.7 weeks (range 1 – 45 weeks). Ulceration occurred most frequently in predominantly superficial hemangiomas (n=22, 59.5%), followed by mixed hemangiomas (n=15, 40.5%), and 70% (n=27) of all ulcerated IH had a thin superficial component. With regards to treatment, timolol was used in 62% (n=23, 12 cases in combination with systemic therapy) and propranolol was used in 70% (n=26) of cases. Ulceration occurred after beta-blockers had been started in 24% of cases (n=6 topical, n=3 systemic). Follow up information to determine time to heal was available in 32 cases. The average time to heal was 44.5 days (range 12 – 90 days), 28% healed in <30 days, 47% healed in 30 to 60 days and 25% healed in 60 to 90 days. Average healing time was 30.8 days in IH treated with propranolol <2 mg/kg/day and 61.5 days with ≥2 mg/kg/day.
Conclusion: While beta-blockers represent an effective treatment for IH ulceration, a subset of patients continues to experience prolonged healing times and this complication can develop during active beta-blocker therapy. Treatment with propranolol at <2 mg/kg/day resulted in faster than average healing time of ulceration in this cohort. A majority of the ulcerations occurred in IH with a thin superficial component. This clinical feature may represent an important risk factor and at the same time could shed light into the pathogenesis of this common complication.

P061
Late and unexpected growth of Infantile Hemangiomas beyond age 3 years: a retrospective study

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Purpose: The growth phase of infantile hemangiomas (IH) is usually complete by 9-12 months of life; late growth of IH beyond 36 months of life is rare. (1,2,3) We describe a cohort of patients with late growth of IH, defined as growth beyond 36 months of life, and determine demographic and clinical characteristics, and specifics of therapy that may be associated.
Methods: Multi-center, retrospective cohort study via investigator recall and use of subjects from propranolol rebound study.
Results: Fifty-nine patients, 85% female, met the inclusion criteria. The first episode of late growth was 4.3 years (range: 3 to 8.5 years). Common characteristics included head and neck location (55/59; 93%), segmental morphology (38/59; 64%), presence of deep hemangioma (52/59; 88%), and size greater than 10cm2 (45/59; 76%). PHACE syndrome was present in 20/38 (53%) with segmental facial IH. Systemic therapy (corticosteroid or beta-blocker) was given during infancy in 58/59 (98%),and 42/50 (84%) receiving ß-blockers experienced rebound growth during taper or after completion of therapy with 36% requiring required a multiple rounds of systemic therapy.
Conclusion: Late IH growth occurring after 3 years of age is an uncommon but documented phenomenon. (3,4,5) Risk factors include female sex, head and neck location, larger size, segmental morphology, presence of PHACE syndrome, and involvement of deep dermal/subcutaneous tissues. We hypothesize that several factors may be contributory. The high prevalence of PHACE in those with segmental facial IH suggests an earlier and more pervasive developmental "hit". The high prevalence of head and neck and deep IH suggest that the cellular milieu within which IH grows may affect growth and involution. Therapy itself may inhibit IH progenitor cells, but not cause cellular senescence, leaving a reservoir of cells capable of regrowth. Further studies are needed to determine specific precipitating factors and better approaches to prevention and management.

P062
LUMBAR/SACRAL/PELVIS spectrum: a multicentric case series

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Purpose: Define the epidemiological and clinical aspects of hemangiomas of infancy (HI) and the congenital regional anomalies associated, in a pediatric population diagnosed within the spectrum described with the acronyms LUMBAR, SACRAL or PELVIS.
Methods: Multicentric and retrospective case study of 10 unpublished LUMBAR cases.
Results: There were 7 females and 3 males, all products of single pregnancies. Nine were born at term and the totality had adequate weight for gestational age. Two cases were referred because of a diaper rash. Four patients presented congenital HI (precursor lesions). The majority of the HI were segmental and with minimal growth (7 of 10), extended over more than 2 of the anatomical areas considered, and underwent spontaneous ulceration (6 of 10). Other cutaneous defects found were 1 skin tag, 1 lumbar tuft of hair and 1 perianal pyramidal protrusion. The extracutaneous anomalies detected were mainly anorectal (8 cases), followed by genital (5), mielopathy (4), bony (4), and urinary alterations (3). Anorectal and urinary findings correlated with a HI affecting the sacral area. Three of the 4 patients with mielopathy had no HI in the lumbar area, but presented lumbosacral lipomas. Eight babies received propranolol with an excellent response and no adverse effects.

Conclusion: HI within the spectrum of LUMBAR predominate in females, born from single and term pregnancies, in a similar way as in PHACEs syndrome and in contrast with non-syndromic HI. Segmental and extensive HI with minimal growth and a high tendency to spontaneous ulceration are characteristics. In this series, we emphasize the misinterpretation of 2 sacral, perineal and genital HI as a diaper dermatitis, the uncommon presence of a perianal pyramidal protrusion as a another cutaneous finding, the anorectal anomalies within the more frequent extracutaneous findings and a case of utero unicorne as a non previously described genital abnormality.

P063
Clinical and Radiological Characteristics of Patients with Retroperitoneal Infantile Hemangiomas

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Purpose: To identify clinical and radiological patterns in patients with retroperitoneal infantile hemangiomas (IHs).
Methods: We reviewed patients from our Vascular Anomalies Center database with IHs and abdominal imaging presenting from 1999-2017 to identify those with retroperitoneal involvement.
Results: Eleven patients (10 females, 1 male) with retroperitoneal IHs were found based on imaging performed for hematochezia (n=3), LUMBAR workup (n=2), >5 cutaneous IHs (n=2), other medical concerns (n=2), or unknown reasons (n=2). Cutaneous IHs were present in 8 patients (5 regional (45%), 3 multifocal (27%)), absent in 1 (9%), and unknown in 2 (18%). Regional hemangiomas involved the face in 2/5 (40%) and lower body in 3/5 (60%), specifically the buttock(s) (n=3), perineum (n=2), lumbosacral area (n=2), and/or lower extremity (n=1). Of the 7 patients with cutaneous findings and available data, 4 (57%) had proliferative IHs while 2 (29%) had arrested IHs. One (14%) had severe ulceration of the perineum, buttocks, and lower extremity with unknown proliferation degree. The most common symptoms were hematochezia (n=4), dyspnea (n=4), and/or ulceration (n=2). Two patients were asymptomatic. Involved retroperitoneal organs included the duodenum (n=4), pancreas (n=3), and adrenal glands (n=1). Non-retroperitoneal organ involvement included the liver (n=5), non-duodenal small intestine (n=4), and large intestine (n=3). Perivascular retroperitoneal hemangiomas were seen in 6/11 patients (54%), most commonly surrounding the aorta (n=5), iliacs (n=2), and/or inferior vena cava (n=2). One patient had dilated abdominal vessels while another had dilated iliac and pelvic vessels. Three of 11 patients (27%) had LUMBAR based on a regional, sacral hemangioma with tethered cord or anorectal malformation. Follow-up information was available in 6/11 patients (55%): 5 symptomatically improved with treatment (propranolol, corticosteroids, and/or vincristine) while one succumbed from extensive liver involvement complications.
Conclusion: Retroperitoneal IHs are rare and tend to involve organs or surround vessels. Associated cutaneous IHs, if present, lack anatomical predilection and may be regional or multifocal.

P064
Minimally Invasive Treatment of Deep Infantile Hemangiomas as an Alternative to Medical Therapy

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Purpose: To present a novel, unique technique for management of deep Infantile Hemangiomas as an alternative to medical therapy or more invasive surgical treatment.
Methods: Review of consensus medical therapy for deep IH. Review of technique of endoscopic and minimal incision use of low-frequency ultrasonic vibrations to fragment and aspirate the deep component of IH. Documentation of technique with video and still photos.
Results: 13 cases of deep IH or compound IH with minimal superficial component managed with novel technique. 8 cases were treated primarily; 5 cases as adjunct to medical therapy to obtain the best result by 3 years of age. Follow up of minimum of 6 months. Complications (1 case needed second procedure to further reduce tumor volume). Results deemed excellent by parents/surgeon in terms of cosmetic outcome and in an appropriate developmental time frame. Compare procedure (one step) vs medical therapy (multiple months) in obtaining result commensurate with developmental milestones
Conclusion: endoscopic or minimal incision ultrasonic fragmentation and aspiration is a viable procedure capable of obtaining excellent results for deep IH. As the goal for obtaining the best results commensurate with development of self-consciousness becomes commonplace, this technique can be useful in appropriately selected patients in lieu or adjunctively to medical therapy.

P065
DERMOSCOPIC FINDINGS IN CONGENITAL HEMANGIOMAS

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Purpose: Congenital hemangiomas (CH) are benign vascular tumors that, unlike infantile hemangiomas (IH), are fully developed at birth. According to its clinical course, 3 subtypes can be distinguished: Rapidly

Involuting Congenital Hemangioma (RICH), Partially Involuting Congenital Hemangioma (PICH), and Non-Involuting Congenital Hemangioma (NICH). These subtypes sharemany histological features, including negativity for the GLUT-1 marker, and are considered a spectrum of the same disease. Apart from IH, the differential diagnosis for CH commonly includes other vascular tumors, such as tufted angioma and kaposiform hemangioendothelioma but also infantile myofibromatosis. Dermoscopy has proven useful in the diagnosis of vascular malformations and diverse vascular tumors including pyogenic granuloma, angiokeratomas and IH. Data about dermoscopy in CH are lacking in the literature.
Methods: We reviewed the dermoscopic findings in a series of CH cases referred to our hospital in the last 8 years. Data about patients (age and sex), as well as the characteristics of the tumor (location, size, morphology, clinical type, and dermoscopic findings) are collected.
Results: Eight patients were included, of whom 6 were female, ranging from 24 h to 7 years of age. In both RICH that has not yet fully regressed, as in PICH, the findings were similar with wide white-yellowish areas with superficial (bright red, well focused) and deep (bluish red and out of focus) vessels. The superficial vessels appeared as clods or linear (straight, curved, or serpentine).
Conclusion: Although this is a small case series, the dermoscopic findings in CH seems to be distinctive and differ from those described in capillary malformations or IH, although some features are reminiscent of abortive hemangiomas. It is still necessary to provide dermoscopic descriptions of other vascular lesions included in the differential diagnosis of CH.

P066
The preliminary attempt to evaluation of treatment effect of superficial infantile hemangioma by digital image analysis

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Purpose: The preliminary attempt to quantify the color of tumor and evaluation of treatment effect of superficial infantile hemangioma with oral propranolol by digital image analysis.
Methods: We included 107 children with superficial infantile hemangiomas treated with propranolol, a digital imaging approach is established, by which data included 4 time points (month 0, 1, 2 and 4) and orderly archived onto a sheet. The RGB value of tumor body were calculated by digital color measuring device. The comprehensive value of tumor RGB and the value of tumor adjacent RGB were defined as cure coefficient. The curative effect of propranolol was evaluated by comparing the cure coefficient of 4 periods.
Results: The cure coefficients of 4 periods were 0.579 + 0.027, 0.722 + 0.028, 0.773 + 0.024 and 0.805 + 0.027. The cure coefficient in 4 month was significantly higher than that before 1 month and 2 month ($P<0.05$). The cure coefficient of 1 month and 2 month increased significantly ($P<0.05$), but the cure rate in 2 month was slightly higher than 1 month ($P>0.05$).
Conclusion: The cure coefficients increased with the prolongation of oral propranolol duration. It increased significantly in 1 month 2 month and 4month, Evaluate the change of cure coefficient of propranolol in the treatment of superficial infantile hemangioma, which provide objective and reliable basis for clinical treatment.

P067
Gastrointestinal hemangiomas presenting as ileocecal intussusception in a patient with a single focal cutaneous infantile hemangioma

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Purpose: Multiple hemangiomas of the skin and solitary segmental hemangioma are recognized as a clue to potential visceral hemangiomas. Gastrointestinal (GI) infantile hemangiomas occur mainly in the small bowel and (IH) usually present as GI bleeding or anemia during the first months of age, correlating with the proliferative phase of IH. Diagnosis can usually be made by ultrasonography, CT or MRI. We report the case of a patient with a single focal cutaneous hemangioma with multifocal IH of the GI that presented with an ileocecal intussusception.
Methods: A Full-term Caucasian old baby was admitted to the hospital at six months of age due to vomits, abdominal pain and bloody stools. Abdominal radiography showed dilated small bowel loops with an absence of distal gas. Lab tests showed no anemia. Abdominal ultrasound confirmed ileocecal intussusception. After unsuccessful water enema reduction, the patient went through immediate surgical intervention, being necessary a 30 cm small bowel resection, with good post-operatory recovery. Assessment of disease extension by abdominal-thoracic-cranial MRI showed diffuse enlargement of the mesentery with multiple nodular images, hyperintense in T2, that surrounded the superior mesenteric vein and artery. Also, two small lesions of similar characteristics in mediastinum and subphrenic perihepatic region, all these findings consistent with multiple IH.

Results: Histopathological study showed a lobular vascular proliferation consistent with IH (positive for GLUT-1 and WT-1 markers). The patient also had a single focal, deep occipital IH of 43x45 mm that had not received any treatment. She was treated with oral propranolol at 3mg/kg/day. At 6 months of treatment was started without any side effects till date. There was an 80% improvement of the cutaneous IH, and follow-up MRI did not show any internal residual lesion.
Conclusion: GI IH should be considered in the differential diagnosis of infants with melena, hematochezia or intussusception even in the absence of segmental or multifocal cutaneous IH. The clinical evolution and response to beta blockers treatment does not differ from cutaneous IH.

P068

Rebound Fatty Overgrowth Mimicking Recurrent Hemangioma

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Purpose: We report two overweight Caucasian female patients who were previously treated successfully for hemangiomas of infancy, then developed fullness at the site of the original hemangiomas, at 8 ½ years of age and at 10 ½ years of age. MRI evaluation demonstrated adipose tissue without recurrent vascular anomaly or mass. Liposuction was a successful intervention for one of the patients.
Results: Patient 1 had a superficial and large subcutaneous bilateral R>L parotid hemangiomas, initially treated with oral Propranolol 2 mg/kg/day, for 15 months at the full dose, then at low dose for ~2 ½ years, and then discontinued. There was a bruit and thrill in the hemangioma during its most active phase; the high flow component resolved with resolution of the hemangioma. At XX years of age, the hemangiomas were barely noticeably. She returned at 8 ½ years of age due to fullness at the site of the hemangiomas, especially on the right. MRI imaging demonstrated complete fatty replacement of the treated hemangiomas within the suprahyoid neck involving the bilateral masticator spaces, parotid spaces, parapharyngeal fat planes, right submandibular space and perhaps pre-epiglottic fat plane. The airway was patent. Patient 2 had a large segmental hemangioma on the left posterior scalp, neck and upper back (>10 cm diameter). She was treated with oral corticosteroids in infancy, with an excellent result. She was seen at 10 ½ years of age due to fullness in the area of the hemangioma, then one year later, with increased bulkiness and pain. MRI imaging demonstrated asymmetric prominence of the subcutaneous fat along the course of the left sternocleidomastoid muscle. She underwent liposuction at 11 ½ years of age, with resolution of the fatty depositions.
Conclusion: Fatty replacement of the therapeutically involuted hemangiomas is an uncommon entity, but is accurately diagnosed with imaging. The triggering mechanisms are yet unknown, but recent weight gain or overweight body habitus likely play a role in the transformation to mature adipose tissue.

P069

Infantile Hemangioma: Evolution in Care

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Purpose: There remains wide variability in initiation protocols for propranolol in patients with infantile hemangiomas including inpatient rapid titrations and slow outpatient protocols as two common models. The aim of this study was to determine the utility of a 2-hour outpatient visit to initiate propranolol.
Methods: The outcome measures to determine utility were complication rates (hypoglycemia, bradycardia and hypotension) and overall cost. All patients were initiated at a goal dose of propranolol 2 mg/kg/d divided twice per day. Three prospective cohorts were compared including: 48hrs inpatient drug titration (0.5 mg/kg/dose x 2 doses then 1 mg/kg/dose x 2 dose); a 24hr observation admission (1 mg/kg/dose x 2 doses) and a 2-hour outpatient initiation visit (1 mg/kg/dose x 1). All three cohorts received a screening EKG and hypoglycemia teaching. Patients were excluded for expedited PHACES evaluation, critical subglottic stenosis, EKG with conduction delay or patients already admitted at the time of diagnosis. Gestational age and weight at initiation were not determining factors.
Results: 168 patients were included in the study over a 5-year period. There were 0 episodes of hypoglycemia, hypotension or bradycardia during the initiation or maintenance phase of treatment with propranolol for all three prospective cohorts. The cost was dramatically impacted as the controllable expenses were reduced by 1000%. The average cost for the 48- hour drug titration cohort was $3521.00 versus $350 for the 2-hour outpatient initiation visit cohort. The total cost saved in the first year of the 2-hour outpatient initiation visit cohort was over $200K.
Conclusion: Initiation of propranolol as an outpatient with a single dose at goal (1 mg/kg/dose twice per day) and a brief 2-hour observation period is safe. Additionally, there is a significant cost savings associated with the expedited treatment protocol.

P070
Pilot project on electronic photo-triage for infantile haemangiomas

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Purpose: The discovery of propranolol as an effective treatment for infantile haemangiomas (IH) has been one of the highlights of paediatric dermatology. IH mainly develop between 4 weeks and 3 months of age. There is evidence now that a period of accelerated growth occurs between 5.5 and 7.5 weeks of life and that those treated earlier have more favourable outcomes. Thus, early IH need to be recognized promptly and infants with high-risk IH should be referred to specialists urgently for either initiation of treatment or close clinical observation. In an era of prolonged waiting lists and unprecedented pressures on general practice, consultant dermatologists need to have mechanisms in place for urgent evaluation of infants with high-risk IH and a triage system to determine what is high-risk in order to optimise timing of consultation and management.
Methods: The aim of this project was to provide a fast-track approach for general practitioners to send a photograph of the haemangioma with the child's date of birth via Healthmail to a paediatric dermatologist. The photographs were reviewed within five working days and the general practitioner was contacted with an outcome.
Results: The project initiated November 2016. To date there have been 88 referrals. Eight of these referrals did not have a photograph attached. At photo-triage 84% (67/80) were infantile haemangioma, 10% (8/80) port-wine stain, 1.3% (1/80) vascular malformation and 5% (4/80) could not have a definitive diagnosis made. Age varied from less than 1 week to 57 weeks, with a mean age of 16.3 weeks. 31% were located on the face, 28% on the trunk, 19% limbs, 11% scalp, 5% ear, 4% genital and 2% on the neck. 46% (31/67) of the IH did not require treatment, 36% (24/67) had a routine review and 18% (12/67) required urgent review.
Conclusion: This novel photo-triage study has shown to be effective at identifying high-risk infantile haemangiomas. This allowed efficient use of resources, with urgent review arranged for infants who would benefit from early intervention. Infants with low-risk IH and port-wine stains were triaged appropriately, allowing appropriate allocation and saving of resources.

P071
Subglottic Hemangioma: A single center's experience in presentation and management of this rare condition

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Purpose: The aim is to characterize presentation, natural history and management of subglottic infantile hemangiomas at a single vascular anomaly center over a 5-year period (2013 – 2017)
Methods: Queried the Vascular Anomaly Database at Children's Hospital of Pittsburgh for all infantile hemangioma(s) and then identified case of subglottic hemangiomas. Characterized key features of presentation, natural history and management for subglottic hemangiomas. A secondary differentiation focused on differences between subglottic hemangiomas associated with Beard Distribution (BD) vs not (NBD).
Results: Analysis of 761 cases of infantile hemangiomas demonstrated only 13 patients with subglottic hemangiomas (1.7%). Of those 13 patients, only 4 patients (30%) had BD while 2 patients (15%) had other cutaneous hemangiomas and 7 patients (55%) had no cutaneous hemangiomas. Secondarily, a total of 31 case of beard distribution cutaneous hemangiomas with only 4 associated subglottic hemangiomas demonstrated an incidence of 13%. A statistically significant difference (<0.01) in age at diagnosis (BD 3 weeks v NBD 12 weeks), time delay from symptom onset to diagnosis (< 1 week BD v NBD 3 weeks) and in percentage of obstruction at diagnosis (BD 22% v ND 76%). Interestingly, 3 of the 4 BD patients had treatment failure on propranolol and required second line treatment with steroids or surgical excision while only 1 of 9 NBD patients failed propranolol treatment.
Conclusion: Subglottic hemangiomas are a rare presentation of infantile hemangiomas but with significant morbidity. While the classic teaching that a segmental beard distribution hemangioma raises concern for a subglottic hemangioma, this cohort indicates subglottic hemangiomas are more common in a NBD presentation, and demonstrated only an approximate 10% incidence rate with a beard distribution. But more importantly, this study raises the question that beard distribution may herald a more recalcitrant and complicated natural history for a subglottic hemangioma.

P072
Immunhistochemical evaluation of cell-cycle and anti-apoptotic markers in infantile hemangioma

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Purpose: To evaluat the immunohistochemical expression of p16 (a cell-cycle inhibitor), BCL-2 (an anti-apoptotic factor), p53 (a cell-cycle regulatory transcription factor), HER2 (a human epidermal growth factor receptor), hormonal receptors (proliferation inductors) ER (estrogen receptor) and PR (progesterone receptor) in GLUT1-positive capillary hemangiomas, associating expression with patient age and cell proliferation index (CPI) determined by Ki-67 staining.
Methods: Information was retrieved from the pathology reports of patients diagnosed with vascular neoplasia/malformation at a pediatric pathology service, covering the period January 2006 to June 2017. Archived specimens were reviewed to exclude cases with lymphatic or cerebrovascular malformations. The remaining specimens were submitted to immunohistochemistry for GLUT-1. Positive cases were then evaluated semiquantitatively for p16, BCL-2, p53, HER2, ER and PR expression in endothelial and stromal cells. Associations and correlations between cell-cycle/apoptotic markers, on one side, and patient age and CPI were calculated and analyzed with the Spearman test, the Mann-Whitney test and Fisher's test at the 5% level of significance ($p<0.05$).
Results: The initial sample consisted of 298 reports. Twenty-seven (15%) of the 181 eligible specimens were positive for GLUT1 and compatible with infantile hemangioma. All GLUT1-positive cases displayed predominantly capillary morphology. No mixed lesion (venous/cavernous, angiokeratoma-like, verrucous) stained positive. All lesions were cutaneous, except two (one hepatic and one in the parotid gland). The mean age was 19 months (1-72), with five patients under 12 months. CPI (median 0.6%; range 0.0-25.2) was significantly higher in patients under 12 months (4.8% vs 0.2%, p=0.019; Rho=-0,53, p=0.01). p16 and p53 were expressed in >1% of cells in 60% and 40% of cases, respectively, with no correlation or association with age or CPI. BCL-2 positivity was rare and observed only in the walls of arteriolar feeding vessels. Two cases of involutional hemangioma stained positive for ER (2-5% of cells). Results for HER2 and PR were negative.
Conclusion: In our sample of infantile hemangioma, p16 and p53 were expressed in over 1% of cells regardless of phase. ER was detected in a few cases of involutional hemangioma. Neoplastic cells tested negative for BCL-2, HER2 and PR.

P073
Atenolol Treatment for Recurrent Infantile Hemangioma after Propranolol Therapy

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Purpose: To evaluate the efficacy and safety of atenolol in the treatment of recurrent infantile hemangiomas (IH) after propranolol therapy.
Methods: Twenty-nine patients with recurrent IH met the inclusion criteria and were treated with atenolol between October 2015 and June 2017. The dosage of atenolol solution (25mg *50) was started at 0.5mg/kg/day (once daily) and increased to 1mg/kg/day after one week. Blood pressure, heart rate and blood glucose were measured at each visit. The therapeutic effect was evaluated by clinical assessment, color Doppler ultrasound and Hemangioma Activity Score (HAS) at weeks 0, 4, 8, 16, 24. Adverse effects were evaluated and managed accordingly. A historical cohort of twenty-five recurrent IH patients treated with propranolol between January 2014 and July 2015 was used as a control.
Results: Clinical improvement was present in 86% (25/29) of the atenolol group and 84% (21/25) of the propranolol group. There was no significant difference between the groups in efficacy (p=0.56). No significant hypoglycemia, hypotension, or bradycardia occurred in either group. Transient diarrhea was the most common adverse effect in both groups. Sleep disturbance occurred in 20% (5/25) of the propranolol group. While sleepiness was observed in one patient treated with atenolol and disappeared after changing the medicine-taken time from 8:00 am to 8:00 pm.
Conclusion: This study shows that atenolol is as effective as propranolol in the treatment of recurrent IH patients and seems to be less frequently associated with sleep disturbance. Atenolol may be used as an alternative to propranolol in the treatment of rebound IH cases, thereby reducing the overall duration of propranolol therapy.

P074
ORAL ATENOLOL FOR INFANTILE HEMANGIOMA

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Purpose: Infantile hemangioma (IH) is the most common benign tumor of infancy. The mainstay treatment for problematic IH is oral propranolol, a non-selective beta blocker. However, a minority of patients undergoing this treatment experience undesirable side effects, which limit its use. We present a single-center experience, in the treatment of IH with oral atenolol, a selective beta-1 blocker.
Methods: Forty infants requiring treatment of their IH were included in the study (30 female and 10 male). Treatment with oral atenolol 1-2mg/kg/daily was indicated in all patients. Controls with photographic documentation at baseline, 2 weeks and monthly were performed. Treatment outcome was assessed as complete involution, partial regression and no response.
Results: The study consisted of 40 infants (30 female and 10 male) presenting with a total of 50 IH. Sixty percent of IH were located in the head and neck area and 14% affected genitals. By type, 68% of IH were superficial, 26% mixed and 6% deep. Of all IH, 12% were ulcerated. The mean age at the start of the treatment with atenolol was 3.4 months (range of age between 1 and 12 months). Treatment duration lasted from 6 to 9 months and treatment response was assessed at 6 months. All patients responded to the treatment with oral atenolol. Complete involution in 71% and partial regression in 29% of patients was observed. Ulcerated IH presented complete wound closure at a mean time of 2,2 weeks. Twenty percent of patients presented mild side effects. The main side effect reported was limited to mild transient diarrhea. No adverse events were reported
Conclusion: In our experience, oral atenolol has proved to be a safe and effective alternative treatment in our case series of IH. We propose atenolol as a possible first line treatment.

P075
Low Dose Atenolol for Infantile Hemangioma

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Purpose: Atenolol (cardioselective beta-blocker) has been used to treat complicated infantile hemangiomas (IH). The recommended dosage atenolol is 1-2 mg/kg per day. The aim of this study was to evaluate the efficacy and safety of oral in low dose of atenolol.
Methods: From 2016-2017 the treatment of 244 children`s with complicated IH used oral atenolol in dose 0,5mg / kg per day. All patients before treatment was carried out a comprehensive survey: photographing hemangiomas, cardiac evaluation (ECG, echocardiography, Holter monitoring, measurement of blood pressure), to determine the level of glucose in the blood, ultrasound with Doppler. It treated 244 patients with IH in age from 1 week to 1,5 years. Of these boys - 67 (27,5%) girls with 177 (72,5%). IH were located: in the face and head in 109 (44,6%); in the body - 51 (20,98%); in the limbs - 41 (16,8%); IH multiple areas in 30 (12,3%), haemangiomatosis - 11 (4,5%), 2 (0.82%) patients had hepatic hemangiomas.
Results: Appointment of oral atenolol was carried out in dosage of 0.5 mg \ kg body weight per day and for a mean treatment duration of 4,4 months. Dose was divided into two equal fractions, every 12 hours. The response rate for patients with IHs treated with atenolol was 98% (range 82%-100%), with response rate defined as any improvement with atenolol. Disturbances of respiration and sleep are not revealed. Reduction of blood glucose in patients not observed. Serious adverse events were rare, with reports of symptomatic hypotension in two patients and symptomatic bradycardia in one.
Conclusion: Appointment of oral atenolol is currently the variant treatment modality for complicated infantile haemangiomas. Our results confirm the significant therapeutic efficacy of low dose Atenolol.

P076
Expression of Col-IV, LN, FN and MMP-9 in different phases of infantile hemangioma

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Purpose: To explore the expression and distribution of extracellular matrix structural proteins and matrix metalloproteinase-9(MMP-9)in different phases of infantile hemangioma(IH).
Methods: Operative specimens of IH were collected and diagnosed by hematoxylin&eosin (HE)staining and Glut-1 immunohistochemistry. And the expression of Col-IV, LN, FN and MMP-9 was detected by immunohistochemical stainingThe average optical density(IOD)of positive staining region on different specimens was measured by Image-Pro Plus 6.0 image analysis software. On the basis of patient age, Patients were divided into<3 months, ≥3-6 months, ≥6-9 months, ≥9-12 months and≥12 months groups. The differences of matrix structural proteins and MMP-9 in different age groups were compared.
Results: Among 34 cases, there were<3 months group(n=8), ≥3-6 months group(n=7), ≥6-9 months group(n=6), ≥9-12 months group(n= 8) and ≥12 months group(n=5). Imrnunohistochemical staining of IH showed that the expressions of Col-1V,LN,FN andMMP-9 varied within each phase of IH. The IOD value showed that COl-IV was more highly expressed in≥12 months group(84·90±12, 48)than<3 months group(55·10±16·06), ≥3-6 months group(56·96±22·66), ≥6-9 months group (51·60 ±20·38). There were statistical differences(P<0·05). The expression of LN was higher in≥9—12 months group(80·04±29·36)than that in<3 months group(38·02±9·88), ≥3-6 months group(68·62±16·19), 6-9 months group(60·67±10·72),

≥12 months group(45·96±5·02). The differences were statistically significant(P<0·05). As compared with<3 months group(32·36±19·79), ≥3-6 months group (43·04±19·78), ≥9-12 months group(36·25±11·19), ≥12 months group(27·57±13·90), the expression of FN was higher in 6—9 months group(62·86±15·41). There were statistical differences (P<0·05). MMP-9 was more highly expressed in<3 months group(73·23±18·19)than 3-6 months group(59·31±12·85), 6-9 months group(35·80±7·50), 9-12 months group(26·89±10·21)and≥12 months group(24·04±10·00). The differences were statistically significant(P<0·05).
Conclusion: The expression of COl-IV, LN, FN and MMP-9 of IH varies in different age groups. These differences may be key influencing factors for the growth and regression of IH.

P077
TREATMENT WITH NATURAL BERRY EXTRACT SENSITIZES ENDOTHELIAL CELL TUMORS TO THE EFFECTS OF LOW DOSE RADIATION

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Purpose: Treatment of tumor forming endothelial (EOMA) cells with natural berry extracts (NBE) has been shown to induce apoptotic cell death through nuclear accumulation of oxidized proteins. Radiation therapy increases oxidation resulting in cellular apoptosis. We hypothesized that NBE treatment synergizes effects of radiation on endothelial cell tumors.
Methods: EOMA cells were treated with NBE (50 µg/ml) or vehicle control (1% DMSO). Murine aortic endothelial (MAE) cells were non-tumor forming endothelial cell (EC) control. In vitro dose response curve (160 kV x-rays) identified the lowest effective radiation dose. Mitochondrial dysfunction, as a precursor to apoptosis, was assessed by measuring oxygen consumption rate (Seahorse) ADP/ATP levels, and mitochondrial membrane potential using JC-1. Mice with EC tumors were given 3 doses (2.5Gy each) radiation and treated daily with NBE (200 mg/kg topical + 20 mg/kg oral). Tumor volume and blood flow were measured by ultrasound.
Results: NBE treatment of EOMA cells resulted in significant increase in cell death in a dose-dependent manner for 0, 0.5 and 1Gy radiation with no evidence of toxicity in MAE cells measured by LDH assay. Oxygen consumption/ basal respiration were 3 times higher in untreated EOMA vs. MAE cells. EOMA treatment with NBE or radiation resulted in a significant decrease in basal respiration, ATP production and mitochondrial membrane potential compared to MAE cells. These effects were synergistic with NBE and radiation combination. EOMA cell injection in 129 P/3 mice generated hemangioendothelioma tumors. Radiation did not decrease tumor size (n=5/group). Treatment with NBE significantly decreased tumor size. The combination resulted in tumors significantly smaller than NBE alone.
Conclusion: Use of NBE as an adjuvant therapy for endothelial cell tumors results in reduction of tumor size after exposure to low dose radiation. The dose of radiation needed to kill EOMA cells had no effect on MAE endothelial cells indicating that the use of NBE may make radiation a potentially safe therapeutic option for life threatening endothelial cell tumors.

P078
Activation of NOTCH Pathway in Infantile Hemangioma

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Purpose: Infantile hemangioma (IH) is one of the most common benign vascular tumors of childhood and is characterized by rapid capillary growth followed by involution phase. The cause of hemangioma remains unclear. NOTCH pathway has been linked with IH pathogenesis due to its prominent role in angiogenesis.
Methods: Total RNA and protein was extracted from tissues of normal and three groups of IH patients in the proliferating stage, involuted stage, and those treated with propranolol. Real-time PCR and western-blot were used to analyze the expression of mRNA and protein of components of NOTCH pathway.
Results: When compared to normal control, the proliferating group showed elevated mRNA levels of NOTCH1, NOTCH3, NOTCH4, DLL1, DLL4, JAG1, and JAG2 as well as increased protein expressions of NOTCH1, NOTCH3, NOTCH4, JAG1, and JAG2; the involuted group displayed higher mRNA of NOTCH1, NOTCH3, NOTCH4, DLL1, DLL4, and JAG1 but only expressed higher protein of NOTCH3 and JAG1; while the propranolol treated group upregulated mRNA levels of NOTCH1, NOTCH3, NOTCH4, DLL4, and JAG1 along with protein levels of NOTCH3, JAG1, and JAG2. The further comparison among IH groups showed that the proliferating group expressed higher mRNA of NOTCH1, NOTCH3, NOTCH4, DLL4, and JAG2 and higher protein of NOTCH1, NOTCH3, NOTCH4, and JAG2 than the involuted and propranolol treated groups.
Conclusion: The significant upregulation of receptors and ligands of NOTCH pathway in different stages of IH suggests that the NOTCH signaling plays a critical role in the pathogenesis of IH. The further investigations of how NOTCH signaling communicates with other angiogenesis-related pathways will shed some light on better understanding of mechanism of etiology of IH.

P079
Characterization of long-term outcomes for pediatric patients with extrahepatic epithelioid hemangioma

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Purpose: Epithelioid hemangiomas (EH) are rare benign vascular tumors that occur in soft tissues and bone and present between the third and sixth decades of life. A subset (29%) of EH harbor FOS rearrangement. EH has been described in children, but little is known about the long-term outcomes of pediatric EH.
Methods: We conducted an Institutional Review Board-approved retrospective review of clinical, pathologic, and radiographic characteristics, and treatment outcomes in 11 patients diagnosed with EH between 1999 and 2017.
Results: Eight patients were male; mean age at diagnosis was 14.8 years (range: 6-23). Lesions involved the lower extremities (n=5), cranium (n=3), pelvis (n=2), and spine (n=1). Multifocal disease was identified in five patients. The most common presentations involved significant localized pain and neurologic symptoms: headache, cranial nerve injury, loss of consciousness. Radiographic studies identified variable features, such as multifocal lytic bony lesions with sclerotic margins, enhancing soft tissue component, and surrounding inflammatory edema. Histologically, all specimens were composed of vascular channels lined by epithelioid endothelial cells without significant cytologic atypia; solid cellular areas (n=2). Endothelial cells were positive for CD31 and EGR, and negative for CAMTA1. FOS rearrangement was assessed in only two specimens and detected in one specimen. Mean follow-up time was 545 days (range: 23-2642). Patients were treated with surgical resection, intravascular embolization, bisphosphonates, propranolol, interferon, and sirolimus. One patient treated with interferon and one with sirolimus exhibited partial response for mean follow-up of 1566.5 days.
Conclusion: Although EH is a benign neoplasm, it is difficult to manage without standard protocols and portends considerable morbidity. Our findings suggest medical management, particularly sirolimus, may benefit these patients; however, long-term follow-up is needed in treated children. Novel FOS inhibitors are in development and may benefit patients with FOS rearrangement.

P080
Epitheliod Hemangioma: Making Sense of an Unusual Vascular Anomaly. A Case Report and Review of the Literature.

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Epithelioid hemangioma (EH) is a rare, benign vascular lesion classically presenting with painless nodules in the head and neck region. Although the etiopathogenesis is uncertain, EH is characterized by an abnormal proliferation of histiocytoid endothelial cells with a lymphocytic and eosinophilic infiltrate. EH lesions are typically small, located within the dermis and subcutaneous tissue, and rarely exceed 10cm in size. Complete surgical excision, with negative margins, is the recommended treatment as local recurrence is common. This study reports an unusual case of a 15 x 15cm EH lesion with deep intramuscular involvement in a 16 year old male. Ultrasound and MRI confirmed a hypervascular mass on the patient's left upper back and biopsy confirmed the diagnosis. Treatment consisted of preoperative embolization followed by excision, including muscle, subcutaneous tissue, and skin. A review of the literature was performed to identify the overall incidence of EH and discuss the potential pathogeneses, differential diagnosis, and management. Over 40 articles were reviewed to gain a full appreciation of the challenging diagnosis and varying clinical features of EH in order to distinguish it from related vascular pathologies. We aim to increase awareness of this condition and obtain more precision in diagnosis, standardizing the approach for those treating individuals with vascular anomalies.

P081
Fractionated CO2 laser treatment to reduce fibro-fatty tissue bulk of involuted hemangiomas: a case series.

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Purpose: The fractionated CO2 laser denatures collagen in the target area effectively creating holes in the collagen matrix which causes subsequent contraction. This treatment may be effective for reducing the unsightly fibro-fatty tissue of involuted infantile hemangiomas. We present the outcome of fractionated CO2 laser treatments to improve skin texture and reduce fibro-fatty tissue of involuted hemangiomas.
Methods: Medical records of 3 patients undergoing fractionated CO2 laser therapy for cosmetically disfiguring involuted hemangiomas were reviewed to collect demographics, size and site of lesion(s), prior therapies, chief complaint(s), indications for addition of CO2 laser therapy, number of treatments, complications, and parental perception of percent of improvement in texture and thickness of fibro-fatty tissue.
Results: All patients were 4 years of age with a 2:1 female ratio. Mean lesion size was 5.9 cm x 5.8 cm (range 2 - 14 cm x 1 - 16.5 cm) and lesions were located on the right cheek (n=1), left upper lip (n=1) and superior and inferior aspects of the right upper arm (n=1), Patients underwent a mean of 3.3 treatments (2-5) over a

course of 2-23 months under a brief general anesthesia. All 10 sessions were combined with pulsed dye laser treatment to address vascular discoloration. Parents reported a 70% reduction (50-80%) in size of residual involuted hemangioma bulk (see photos). The third patient also experienced resolution of impairment in liquid oral intake. Minor adverse events included focal crusting, erythema, mild hyperpigmentation and mild discomfort all of which resolved within 1-2 weeks.
Conclusion: Use of fractionated CO2 laser treatment resulted in improvement in cosmetically disfiguring fibro-fatty tissue bulk of involuted infantile hemangiomas resistant to pulsed dye laser treatment alone. The fractionated CO2 laser shows a promising new role in the treatment of involuted, infantile hemangiomas with residual fibro-fatty tissue scarring and textural change.

P082

Angiosarcoma arising in benign vascular anomalies (cutaneous infantile hemangioma and Parkes-Weber syndrome) without preceding irradiation in two pediatric patients

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Purpose: The great disparity between the rarity of angiosarcomas in children and the relatively high incidence of benign hemangiomas during childhood may present a diagnostic and therapeutic challenge to the clinician. This is especially true when an angiosarcoma arises in the context of a previously benign vascular lesion. We report 2 convincing cases of angiosarcomas arising in benign vascular anomalies (cutaneous infantile hemangioma and Parkes-Weber syndrome) without preceding irradiation in 2 pediatric patients.
Methods: We reviewed and analyzed medical records, radiologic studies, pathology results and treatment outcome of the 2 patients.
Results: Patient 1:A 6-year-old boy presented with a 6-year history of a painless mass on his left temporal scalp that had presented as small red papules on his third day of life. Pathological examination after surgery revealed angiosarcoma. The evidence supporting malignant transformation of a pre-existing IH lesion includes the presence of a history of proliferating phase and involuting phase, which was verified by photos. Additional support for the issue is provided by the presence of an initial histologic diagnosis of hemangioma and a subsequent diagnosis of angiosarcoma. Three months after surgery, local recurrence occurred, and a stable disease was observed after 9 chemotherapy cycles. Patient 2:A 7-year-old boy presented with significant overgrowth of his right lower limb that had been present since birth. A diagnosis of Parkes-Weber syndrome was made. Histopathological examination after amputation revealed an epithelioid angiosarcoma. Both the benign and malignant components were detected pathologically, making the possibility of spontaneous malignant transformation more convincing. No response was observed after 2 cycles of chemotherapy and 2 months of apatinib treatment. The patient died 5 months after disease progression.
Conclusion: The presented 2 cases, presenting diagnosis and treatment challenge, highlight the possibility of malignant transformation of benign vascular anomalies without preceding irradiation and the need for careful differential diagnosis.

P083

Routine liver ultrasound screening does not alter clinical management in cohort study of multiple cutaneous infantile haemangioma

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Purpose: Screening interventions should alter clinical outcome. This study assesses the validity of consensus practice of abdominal ultrasound scan (USS) screening for hepatic infantile haemangiomas (IH) in infants with more than five cutaneous IH.
Methods: Two retrospective cohorts were identified, one of infants with multiple (>1) cutaneous IH seen over a period of 20 years, and one with solitary cutaneous IH. Extra-cutaneous features and adverse clinical outcomes (cardiac failure and hypothyroidism) were modelled using demographic, phenotypic and imaging variables by multiple logistic regression.
Results: 843 infants were studied, 616 (73%) female, and 688 (82%) with multiple IH. Prematurity was associated with multiple IH (OR 2.4, 95% CI 1.6-3.6, p<0.001). 76/388 (20%) of those screened by USS had liver IH (10 with <5 cutaneous IH). Echocardiogram was abnormal in 27/133 (13 with <5 IH). In contrast, only 11/843 (1%) were treated for heart failure (3 with <5 IH) and 6/843 (1%) for hypothyroidism (4 with <5 IH). There were no deaths. All children requiring treatment for heart failure were symptomatic at the time

of presentation (mean age 0.25 years), and 3/5 requiring treatment for hypothyroidism were detected by neonatal screening.
Conclusion: Liver IH are common in infants with multiple cutaneous IH, however adverse clinical outcomes such as cardiac failure and hypothyroidism are rare. Furthermore, these outcomes were not altered by routine USS screening findings in this large tertiary centre cohort. We propose that routine investigation for a defined number of cutaneous IH be abandoned, in favor of a thorough clinical assessment, regardless of cutaneous IH number.

P084
Airway hemangiomas in PHACE syndrome: A multicenter experience

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Purpose: To determine prevalence and clinical characteristics of airway findings in a large multi-institutional cohort of PHACE patients.
Methods: Multicenter retrospective review of patients followed in multidisciplinary vascular anomalies clinics at two institutions. Data collected included clinical presentation, airway findings, treatment and outcomes.
Results: A total of 55 patients met criteria for PHACE syndrome; 22 of 55 (40%) patients had airway hemangiomas. PHACE patients with airway involvement were more commonly female (100% vs. 67%, OR 23, p=0.034) and of Caucasian ethnicity (86% vs. 55%, OR 5.3, p=0.020). Anatomically, patients with airway disease had a lower incidence of facial hemangiomas in the S1 distribution (32% vs 64%, OR 0.26, p=0.024). Stridor was more common in airway patients (68% vs 3.0%, OR 68, p=0.0001). The most common method of airway evaluation was rigid bronchoscopy, performed in 18/22 airway patients. A proportion of these procedures involved intervention: laser resection in 22% and steroid injection in 17%. Of the 55 PHACE patients, 20 were managed prior to the widespread use of propranolol (1989-2007), and 35 in the post-propranolol era (2008-2017). Of 35 post-propranolol patients, 14 had airway involvement; all 14 airway patients (100%) were treated with propranolol while only 13 (62%) of 21 non-airway patients were treated with propranolol (OR 46, p=0.01). The duration of treatment was longer in the airway patients as well (mean of 22.1 months vs. 16.7 months). Three patients (17%) required tracheostomy, all managed pre-propranolol.
Conclusion: Airway hemangiomas in PHACE patients are very common. Risk factors for airway involvement include female gender, Caucasian ethnicity, and stridor, while airway involvement is less common in patients with S1 hemangiomas. Since the emergence of propranolol, fewer patients have required surgical management of their airway disease. Evaluation for an airway lesion in a suspected patient is critical in the PHACE work up and includes flexible and rigid bronchoscopy.

P085
Evaluate the effect of propranolol on learning and memory in P5 rats

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Purpose: Although propranolol has been accepted as a first-line drug for infantile haemangioma (IH), we have found that a few patients of oral propranolol appear a delay in learning. To evaluate the influence of a different dose of propranolol on learning and memory in young rats.
Methods: Pups were weaned at PND 21 and behavioral testing (Morris water maze) began at 1 month and 2 month . Sprague-Dawley rats were randomly divided into 4 groups, namely the saline group (n=8), the low dose of propranolol group (dose=10mg/kg, n=8), the middle dose of propranolol group (dose=20mg/kg, n=8) and the high dose of propranolol group (dose=40mg/kg, n=8). Four groups of rats were injected with propranolol by continuous intraperitoneal injection.
Results: In place navigation, escape latency decreased over the 5 d training period (Fig A,B). Repeated-measures one-way ANOVA identified a significant reduction in escape latency with training (1month and 2month, $P<0.01$). Young rats of also spent a significantly increased escape latency in the middle dose of propranolol group and the high dose of propranolol group (1month and 2month, $P<0.01$). In spatial probe percentage of time spent in the target quadrant decreased over the 3 does (Fig C,D). Repeated-measures one-way ANOVA identified a significant diffience in percentage of time spent in the target quadrant with 3 does (1month and 2month, $P<0.001$). Young rats of also spent a significantly decreased percentage of time spent in the target quadrant in the middle dose of propranolol group and the high dose of propranolol group (1month and 2month, $P<0.001$).
Conclusion: The present results provide convincing evidence that high dose propranolol may reduce the learning and memory ability of young rats. Interestingly, these findings suggesting that low dose propranolol may have no effect the learning and memory ability of young rats.

P086
The value of Holter monitoring in the treatment of infantile hemagiomas with propranolol

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Purpose: to evaluate a value of Holter monitoring in children with infantile hemangiomas treated by propranolol.
Methods: 104 children aged from 1 to 23 months with different location infantile hemangiomas treated with propranolol were Holter monitored before and every 3 months during therapy.
Results: during first 9 months of propranolol treatment with the maintenance dose of 2-2.5 mg/kg/s, all children had a decrease in average daily heart rate by 8% of normal values. In preterm infants with a gestation terms of 33-37 weeks who started treatment at age of 1-2 months, after 6 months of therapy decrease in heart rate became more significant (by 12% of normal). After 6 months of treatment, all children had an increase in heart rate pause compare with age parameters (N is <1100 ms). Maximum pause of the rhythm was observed in children who started treatment at age of 6-8 months (Me - 1100 ms, σ ± 93 ms), as well as in premature infants with a gestation term of 29-32 weeks, regardless of the age of therapy onset (Me – 1367 ms, σ ± 189 ms). In 4% of children, pauses of the rhythm were found so significantly exceeded age norm (deviation from the norm of 47-102%), which required dose correction. Syncope with the followed cessation of therapy was observed in one child. In 12% of children on propranolol therapy, a persistent AV block of the first degree was detected, which was not a contraindication for treatment continuation.
Conclusion: Holter monitoring allowed detecting in children with infantile hemangiomas treated by propranolol such side effects as pauses of the rhythm significantly exceeded the age norm and syncope. Holter monitoring compares to routine ECG considers as more effective in propranolol safety assessing of significant cardiac rhythm and conduction disorders and thus allows timely dose correction.

P087
Improved Outcomes of Periocular Hemangiomas Treated with Propranolol

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Purpose: Periocular infantile hemangiomas (PIH) can cause local complications such as ulceration, disfigurement, and visual deprivation or induced anisometropic astigmatism leading to amblyopia. Oral propranolol is now a primary therapy for PIH. This study sought to compare functional outcomes of PIH before and after the inception of propranolol therapy.
Methods: This was a retrospective study of consecutive PIH treated between 2000 and March 2016. Two groups were compared: PIH treated with propranolol and those not treated with propranolol. Age at presentation, location, visual acuity, cycloplegic refraction, presence of anisometropic astigmatism, and presence of amblyopia were recorded. Chi-squared and t-tests were used to compare groups.
Results: 225 PIH were identified and 200 were included in the study. Median age at presentation was 3.4 months (0.6-111.9 months), and mean ophthalmology follow-up was 13.8 months (2.5-60.1 months). There was no association of PIH location and the presence of amblyopia. Complete clinical resolution was attained in 47/68 (69%) patients treated with propranolol only, 2/16 (12%) receiving only laser therapy, 6/15 (40%) treated with corticosteroids only, and 7/12 (58%) undergoing surgery alone. Amblyopia was present in 1/68 (1%) patients treated with propranolol, 0/16 laser treated, 5/15 (33%) who received steroids, and 1/12 (8%) treated with surgery. Among 35 patients with visual acuity data available at follow-up, visual acuity of 20 patients treated with propranolol alone improved by 0.19 +/- 0.32 logMAR, and worsened by 0.06 +/- 0.32 logMAR in patients who received other therapies (p=0.02).
Conclusion: PIH treated with propranolol had significantly better functional outcomes than patients not treated with propranolol.

P088
Intolerable side effects during propranolol therapy for infantile hemangioma: frequency, risk factors and management

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Purpose: Currently, propranolol is the most preferred systemic therapy for problematic infantile hemangiomas (IHs). However, the side effects such as bronchial hyperreactivity may be intolerable. The aim of this study was to evaluate the frequency, risk factors and management of intolerable side effects (ISEs) during propranolol therapy.
Methods: In total, 1260 children were studied.
Results: The incidence of ISEs was 2.1% (26 patients). Severe sleep disturbance was the most common reason for propranolol cessation, accounting for 65.4% of cases. In total, 23 and 3 patients received atenolol and prednisolone as second-line therapy, respectively. Treatment response was observed in 92.3% (24/26) of cases (showing excellent or good response to therapy). No toxicity-related permanent treatment discontinuation occurred during atenolol or prednisolone therapy. In the univariate analysis, younger age, premature

birth, and lower body weight were associated with ISEs (P<0.05). In the multivariate analysis, only age (95% confidence interval [CI]: 1.201-2.793, P=0.009) and body weight (95% CI: 1.036-1.972, P=0.014) were associated with ISEs.
Conclusion: Our study suggests that ISEs are rare in patients with IHs who are treated with propranolol. Predictive factors for ISEs include younger age and lower body weight. Atenolol and prednisolone are effective and safe alternatives to propranolol in the treatment of refractory IHs.

P089
Social Impact of Involuted Facial Infantile Hemangiomas on Preteen Children

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Purpose: This study assesses the social impact of involuted infantile facial hemangiomas IH in preteen children, a topic of which little is known.
Methods: Observational, cross-sectional study of social anxiety and skills in preteens diagnosed with facial IHs during infancy using following surveys: 1. Social Anxiety Scales for Children-Revised (SASC-R, completed by subjects) with domains of: FNE: Fear of Negative Evaluation & SAD-New: Social Avoidance/Distress in New Situations; 2. Social Competency Inventory (SCI, completed by parents) with domains of: Prosocial Behavior & Social Initiative

Results: 144/236 parents of preteens born between 2000-2005 with a history of facial IH were reachable by telephone and mailed study packets. 30/144 returned completed questionnaires. Subjects' mean age was 10.0 years (5.4–12.9) with a 2:1 female:male ratio. 83% had a single IH and the remaining had multiple with at least one in a cosmetically sensitive area (periocular>cheek>nose >lip/perioral and >ear). 18 subjects had prior IH treatment. SASC-R: Social anxiety of subjects was not increased over normative data however subjects with untreated IH had significantly greater anxiety for new situations compared to those subjects with treated IH (SAD-New mean 15.6 vs. 11.5 p=0.0245). SCI: Prosocial Orientation of subjects was similar to normative data (3.96 vs. 3.89, p=0.501) however Social Initiative tended to be poorer in subjects compared to normative controls (mean 3.81 vs. 4.03 p=0.065). Furthermore Social Initiative was significantly poorer in untreated vs. treated subjects (mean 3.45 vs 4.03 p=0.006).
Conclusion: Preteen children with involuted facial IH showed social scores within normal limits however preteens with untreated facial IH had higher social anxiety scores in new situations and decreased social initiative scores compared to treated children. Although limited by a small sample size, this study raises important considerations for whether early treatment of facial IH in cosmetically sensitive areas has a beneficial impact on social skills in preteens.

P090
Sirolimus as third-line therapy for treatment-resistant hemangiomas

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Purpose: Treatment of infantile hemangioma was dramatically changed by the emergence of propranolol as first-line therapy, with high reported response rates. Steroids may be used in conjunction with propranolol as short-term therapy for function-threatening lesions. Here we describe two cases of infantile hemangioma that were poorly responsive to the combination of propranolol and steroids, and did not stop growing until sirolimus was added.
Methods: Retrospective review of 2 cases of resistant infantile hemangioma treated at our institution in the past 5 years.
Results: Patient 1 presented with multiple hemangiomas including a large parotid hemangioma. She was initially started on propranolol 1mg/kg BID. This was increased to 3mg/kg/day and then prednisolone 2mg/kg/day was added to her therapy as these interventions proved insufficient. The hemangioma continued to grow rapidly despite dual therapy so sirolimus was added, allowing taper of steroids with softening and shrinkage of the hemangioma. Sirolimus was stopped after 8 months, and propranolol at age 2. Patient 2 was diagnosed with PHACE syndrome including severe aortic coarctation. She was started on propranolol 1mg/kg TID for bulky internal disease of her chest preventing coarctation repair and GI bleeding and anemia from intestinal involvement. While on 3mg/kg/day of propranolol, she had rapid new growth of parotid and posterior neck hemangiomas, so prednisolone was added at 2mg/kg/day. There was growth with any attempted wean, so sirolimus was added. This allowed steroids to be tapered off. Sirolimus was weaned off stepwise, initially to half-dose after 5 months, and discontinued 4 months later at age 1. She experienced dramatic regrowth despite still being on 3mg/kg/day propranolol, which resolved with restarting sirolimus. She continues on propranolol and sirolimus at age 2, until she is able to have her coarctation repaired.
Conclusion: Sirolimus is an effective adjunct to current therapies for treatment-resistant infantile hemangiomas

P091
Assessing Current Practices in the Management of Infantile Hemangiomas: A Survey of Pediatric Dermatologists

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Purpose: Since the initial report of propranolol as a therapy for infantile hemangiomas (IHs), there has been a shift in the management of IHs. There are no guidelines addressing which IHs should be treated or first and second line therapies. Our study investigates whether there is a consensus among pediatric dermatologists regarding the treatment of IHs of varying severity. We also sought to understand the current practices of propranolol use.
Methods: An anonymous electronic survey was sent via REDCap to physicians via the Pediatric Dermatology Research Alliance and Society for Pediatric Dermatology list serves. The survey assessed 7 cases of IHs of varying severity based on the Hemangioma Severity Score (HSS). Additional questions were specific to the use of propranolol. Consensus was defined as >70%.
Results: Of the 128 physicians who completed the survey, >71% practice in the USA, are board certified in pediatric dermatology, and have seen >20 infants with IH in the past year. Of the 7 cases, there was consensus to treat 6. Of these 6, there was consensus for treatment indication in 6 and type of treatment in 5. Most (90%) chose topical or oral beta-blockers. Though propranolol is FDA-approved for IH in term infants >5-weeks-of-age, there was consensus to treat younger infants for potential/presence of ulceration or functional impairment. The FDA-approved treatment duration is 6 months; however, 95% of respondents treat patients for 6-18 months when therapy is started at <3-months-of-age. Longer courses are considered for IH that were deep/bulky, those that rebounded upon tapering propranolol, or those involving the parotid. The majority (93%) taper propranolol, rather than discontinue abruptly.
Conclusion: There is consensus to treat IHs on the head with HSS >7 and to initiate therapy early. Topical and oral beta-blockers are considered first line therapies. These findings may provide an updated framework for providers treating IHs.

P092
Surgical Management of Nasal Tip Hemangiomas

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Purpose: Nasal tip hemangiomas commonly result in bulky "Cyrano" deformities consisting of excess fibro-fatty tissue, an expanded skin envelope, and splayed nasal tip cartilages. Propranolol may help to limit or prevent progression and observation for spontaneous regression over many years is often recommended. However, for those with unsightly and psychologically detrimental deformities, debulking surgery prior to complete involution is an attractive option. The ideal timing and technique for resection has yet to be defined and remains a challenge to clinicians.
Methods: 132 patients with nasal hemangiomas were evaluated by the senior author between 1991 – 2017. Sixty-one patients had central nasal tip hemangiomas and 13 patients presented with asymmetric nasal tip hemangiomas. The remaining patients had hemangiomas on other areas of the nose. Early in the series, patients underwent gull wing or transverse elliptical excisions. With more experience, 19 patients underwent a debulking technique involving rim and columella incisions, centralization of the cartilaginous domes, and debulking of the deep surface of the hemangioma while intentionally leaving some hemangioma tissue attached to the overlying tip skin to avoid excessive soft tissue atrophy.
Results: The 19 patients undergoing the senior author's preferred technique were on average 3.25 years old at the time of surgery (range 1.4 to 4.5 years), and the average follow up was 2.56 years (range 1 month to 10.3 years). Compared to results utilizing other techniques, they had improved outcomes with excellent postoperative scars, tip contour, and soft tissue padding. To date, no patients have required secondary revision.
Conclusion: The stigmata of a bulky nasal tip hemangioma can be addressed prior to complete involution of the hemangioma with good results and high parent satisfaction. The technique of rim and columella incisions offers excellent visualization. Centralization of the tip cartilages permits debulking under excellent control and provides a satisfactory aesthetic result.

P093
Procuration recurrence of maternel psoriasis due to timolol application on her infant's hemangioma

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Purpose: Topical use of ophthalmic timolol maleate for infantile hemangioma IH has dramatically increased. The efficacy and safety of timolol in a pediatric population with IH has been confirmed in a large cohort of 731 patients. Otherwise, it is well documented that use of betablockers by oral or transconjonctival route increases the risk of psoriasis eruption. We report the case of a mother presenting typical psoriasis eruption after having applied timolol maleat on her child's IH.
Methods: A girl infant, four months old, born at term after an uneventful pregnancy was referred to our department for 2 large segmental IH. The cephalic one covered the upper part of the left side of her face. The IH was of tuberous type and was occluding the eyelids. Her neck and her torso were free of lesions. The perineal one was of telangiectasic type, covering the buttock, the posterior side of the thigh and labia majora, by the left side. Two small ulcers were seen on the mucosal labia majora. A cerebral CT revealed a cyst of the cerebellum, no other anomalies were found. A PHACE syndrome was retained, but LUMBAR syndrome was excluded. As cardiac examination allowed it, propranolol 3mg/kg/d by oral rout and topical timolol maleate were begun. Two months later, the hemangiomas regressed and the ulcers healed, with no relevant side effects. Propranolol was continued for 4 months and timolol for 9 more months. At the end of this treatment, IH had quite disappeared. At the opposite the mother who applied timolol on her child IHs, with her fingers, developed psoriasis eruption on her arms and legs. Her fingers, nails and hands were spared. She developed large plaques on her elbows and guttate lesions on forearms. Her psoriasis was in remission since at least two years, and it relapsed after timolol application on her child. We advised the mother to wear on medical gloves, when applying timolol
Results: A large cohort study about topical timolol for IH published in September 2016, concluded for effectiveness and good tolerance. Adverse events were listed but psoriasis eruption was not observed. A more recent study focused on adverse events in young and preterm infants receiving topical timolol for IH, such as bradycardia, apnea and hypothermia but no psoriasis eruption was noted. Béta-blockers is one of the most common causative agents for drug induced psoriasis. A case of psoriasiform diaper rash possibly induced by oral propranolol in an infant girl with IH has been reported. A case of reversible psoriatic fingernail changes caused by timolol drops has been reported in a woman treated for glaucoma. But no publication about exacerbated psoriasis eruption after procuration use of timolol maleate has been found. Although the mechanism by which psoriasis may be induced or exacerbated by betablocquers remains unknown. Recent epidemiologic studies seem to accuse timolol more than other betablockers. Timolol is six to ten times more powerful than prorpanolol.
Conclusion: This case underlines the need for caution and close follow up of patients and their families (parents applying the drug product) chiefly when there is a personal or family history of psoriasis. Should we suggest wearing medical gloves by the parent who applies timolol on his child's hemangioma?

P094
Use of Multiplex Laser for treating Non Involuting Congenital Haemangiomas(NICH) in Children.

Samira Syed (Great Ormond Street Hospital for Children NHS Trust); Ben Evans (Great Ormond Street Hospital for Children NHS Trust.)

Purpose: Non-involuting congenital haemangiomas(NICH) are distinguished from other types of haemangiomas by lack of postnatal growth or involution (ref 1). Excision is sometimes indicated for medical or aesthetically troubling lesions (ref 2). The aim of this work, as an audit, was to assess the efficacy of the multiplex laser in the treatment of NICH in the paediatric population.
Methods: Seven patients aged between 5 and 15 years, 2 males,5 females, with NICH, were treated with the Multiplex laser, 595-nm Pulsed Dye Laser(PDL) and the 1064-nm Nd-YAG laser. The probe used was 10mm in 5 cases and 7 mm in 2 cases. Laser parameters used were;group 3 with a pulse duration of 6 ms using PDL and 15 ms using Nd:YAG. Fluences varied between 7.5-11.5(J/cm2) with PDL and 60 Joules with Nd:YAG. Cooling was provided by cryo 6, setting at 4 using continuous flow , ice cooled water and cool USS gel was applied at the time of the procedure. Photos were taken before and after each treatment. Assessment of colour was recorded at the final end point as a percentage change with a colour coded chart and we also assessed clinically. Three of our patients underwent treatment under General Anaesthesia while 4 patients were treated under local anaesthetic gel.
Results: There was marked reduction in the redness in all cases and majority had a significant change in the bulk of the lesion. All families were satisfied with the outcome. The overall average improvement was 75% while 3 patients had more than 90% resolution. Interestingly all three patients showing near complete resolution underwent their procedure with GA and had significantly more total pulses indicating clinicians are more willing to treat while under GA. None of our 7 patients required debulking surgery.
Conclusion: Multiplex laser has a beneficial effect in the management of NICH. None of our patients required surgical interventions. We believe this is an option for treating congenital haemangiomas where we know NICH do not ever regress spontaneously.

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*Conclusion: Conclusions: The mortality was not increased among Danish HHT patients compared to controls. However the HHT-patients do have an increased comorbidity of infections in joints and bones and of bleeding episodes. The patients reported in this study are closely monitored by a highly specialised HHT-Center for relevant diagnostic evaluation, treatment and counsel*ling. This may explain why these patients are less prone to comorbidity as suggested in other studies.

P096
Exome sequencing in Hereditary Hemorrhagic Telangiectasia

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Purpose: Hereditary hemorrhagic telangiectasia (HHT), an inherited vascular disorder, is caused by mutations in three known genes (ENG, ACVRL1, and SMAD4). However, in approximately 10% of individuals with clinical HHT we cannot locate mutations with the current methodology in these genes. Exome sequencing is a powerful tool to identify variants in multiple genes and when applying this technique to several members of large families the following filtering allows substantial reduction of the potential relevant variants.
Methods: This study included family members from four large mutation negative Danish families (n=17) with well characterized clinical HHT, as well as healthy relatives. Genomic DNA was extracted from peripheral blood and whole-exome sequencing was performed. Subsequent filtering using phenotype information and various public mutation databases was performed.
Results: Suspected pathogenic variants were identified in 3 of the 4 families, which segregated with the phenotype in each family and were confirmed by Sanger sequencing. In the last family an intronic variant of unknown significance was identified. These variants were all located in ENG and ACVRL1 loci. Further functional characterization of these variants is on-going.
Conclusion: Our study did not reveal any further HHT causing genes and do not point in the direction that additional genes, besides the three known HHT genes, are causative of HHT. Exome sequencing is useful in variant identification, especially if it is possible to include several patients and healthy relatives from the same family. Future genome sequencing and further knowledge on intronic and regulative variants are expected to be helpful in identifying causative variants in possibly all HHT patients.

P097
Chromosomal translocation as a cause of JP-HHT

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Purpose: Using common molecular genetic screening technics in patients with hereditary hemorrhagic telangiectasia (HHT) will disclose mutations in around 90% of the analyzed patients. In the remaining families the genetic cause despite of adherence to the Curaçao criteria will often remain uncharacterized. Patients with germline mutations in SMAD4 can present symptoms of both juvenile polyposis syndrome (JPS) and hereditary hemorrhagic telangiectasia (HHT) - the JP-HHT syndrome. We here report a translocation event involving the SMAD4 loci to result in HHT and JPS.
Methods: Patients were analyzed for mutations in ENG, ACVRL1 and SMAD4 using standard technics. In brief, DNA was extracted from peripheral blood leukocytes, buccal swaps and urine. The coding region, exon–intron boundaries, and the flanking sequences of the genes were sequenced with targeted NGS using the Agilent targeted sequence capture method followed by sequencing on the Illumina HiSeq1500 NGS platform. Possible pathogenic variants were analyzed by bi-directional sequencing. Cytogenetic analysis was performed using standard procedures. In brief, leucocytes were cultured in A –media in the presence of phytohaemagglutinin and cell divisions stopped by the addition of colcemid. Chromosomes were stained using Leishman´s color. A minimum of 12 metaphases were analyzed.
Results: A patient fulfilling the Curaçao criteria was submitted to molecular genetic analysis. No pathogenic variation was observed. At a later stage the daughter of the patient was submitted for chromosomal analysis due to abortus habitualis and the translocation t(1;18)(p36.1;q21.1) was observed. The family presents with both colorectal cancer and HHT. The translocation segregates with JPS and HHT in the family. Further characterization of the exact breakpoints is on-going.
Conclusion: A translocation between chromosomes 1 and 18 involving a probable breakpoint in the SMAD4 locus co-segregates with colorectal cancer and HHT in an extended family. This observation warrants analysis for chromosomal rearrangements should be considered in individuals with HHT and JP-HHT with no molecular genetic cause idenfied.

P098

Hereditary Hemorrhagic Telangiectasia: A pediatric experience in diagnosis and management

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Purpose: Hereditary Hemorrhagic Telangiectasia (HHT) is an autosomal dominant disorder characterized by the progressive development of AVMs in varied body systems over the course of a lifetime. The aim of this study is to review the clinical experience of a pediatric HHT center of excellence and qualify the pediatric natural history of the disease in the age of genetic testing.
Methods: The Vascular Anomalies Center UPMC database was queried for patients who carried a diagnosis of HHT. 15 patients were identified between 2015 and 2017. A Chart review of the 15 patients focused on genotype and phenotype presentation and progression of the disease.
Results: The genotypic presentation of our patients with HHT were 40% ENG, 27% ACVRL, 2 patients with SMAD 4, 1 patient GDF and 1 patient with normal gene testing (including whole exome). The clinical phenotype at diagnosis demonstrated 2 patients with CNS vascular anomalies (CNS AVM and Spinal AVM), 1 patient with significant anemia and juvenile polyposis, 1 patient with significant epistaxis and CNS cavernoma, 2 patients on screening microarray for intellectual disability and 7 patients secondary to 1st degree relative with known HHT gene defect. The 9 patients diagnosed via gene testing with no overt symptoms at diagnosis were subsequently found to have 1 CNS vascular anomaly and 4 positive bubble TTE but only 1 AVM noted on CTA. None of these screening abnormalities required immediate intervention. In comparison, 3 or the 4 patients with clinical pathology at presentation have required emergent CNS or Pulmonary management of their disease process including one patient found to have extensive GI, Pulmonary and CNS disease on subsequent screening.
Conclusion: The advent of HHT gene testing, has transitioned HHT from a clinical to a genetic diagnosis. Specifically, this has led to making an early diagnosis prior to developing symptomatology or emergent/life threatening condition arises.

P099

Anti-VEGF bevacizumab for the treatment in Hereditary Hemorrhagic Telangiectasia (Osler Weber Rendu Syndrome) patients with severe liver disease

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Purpose: To report preliminary results of bevacizumab treatment in four patients with severe hepatic involvement
Methods: Case series from our Institutional HHT Registry
Results: Three patients were females whose age range was 36-58. All patients presented a high output cardiac failure (HOCF) with pulmonary hypertension; one also presented ischemic biliary necrosis. All four patients suffered from anemia, mainly due to gastrointestinal bleeding. Two patients presented PAVMs and one needed pulmonary embolization. Three patients presented self-limited supraventricular arrhythmia episodes. Two had endocarditis, one in the aortic valve as a young person who needed a prosthetic valve replacement and anticoagulation, and the other patient in the tricuspid valve, developing severe valve regurgitation, progressive right ventricle and biatrial enlargement. All patients exhibited hepatomegaly of which two were severe with ascites and edema. The cardiac index per patient was 6.3, 4.5, 5.1, 6.8 L/min/m2. All reported a low quality of life (QoL). The patients were treated with progressive doses of diuretics, digoxin or propranolol, and iron supplements. They also received tranexamic acid presenting a mild response. The four patients received bevacizumab 5mg/kg every 15 days/six infusions after the intensive medical therapy failed. A patient received two extra bevacizumab cycles to control the anemia. All patients improved the QoL, clinical, hemodynamic and hematologic parameters after the bevacizumab treatment. The follow-up range was 2-36 months. All patients were assessed for liver transplantation. The patient with severe tricuspid regurgitation died the following year due to progressive HOCF. The male patient underwent cadaveric liver transplantation successfully. Two patients developed a slow-healing venous ulcer as an adverse event.
Conclusion: Bevacizumab might represent a useful tool in the management of patients with a severe HHT hepatic disease, especially in those waiting for a liver transplantation or with contraindications for this procedure.

P100

Mutations in Non-coding Regions Cause Hereditary Hemorrhagic Telangiectasia

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Purpose: Hereditary hemorrhagic telangiectasia (HHT) is a genetically heterogeneous disorder caused by mutations in the genes ENG, ACVRL1, and SMAD4. Approximately 15% of HHT patients do not have a mutation in one of these genes, and the genetic cause remains unknown for some families even after exome analysis. The purpose of our study was to determine if mutations in noncoding regions of the known HHT genes that disrupt splicing or modulate gene expression cause HHT in these cases.
Methods: DNA from 35 individuals with HHT and 2 healthy controls from 13 families underwent genome sequencing. Eighty-seven additional unrelated cases with HHT who tested negative were evaluated using a custom designed next generation sequencing (NGS) panel to capture the coding and noncoding regions of ENG, ACVRL1 and SMAD4. Coding regions of GDF2, RASA1, and EPHB4 which have been implicated in the clinical differential for HHT were also included in the NGS panel. All samples were sequenced using 2x100 PE reads on a HiSeq2500 instrument and data were analyzed to identify novel and rare mutations.
Results: Approximately 25% of families had a novel or rare deep intronic noncoding ENG or ACVRL1 variant that could alter splicing. Two families had a variant in ACVRL1 intron 9 that were proven to disrupt splicing, including one family with an ACVRL1 intron 9:chromosome 3 translocation. EPHB4 mutations were identified in 10.3% (9/87) of cases suspected to have HHT indicating that this gene should also be evaluated as part of the clinical differential.
Conclusion: Despite the difficulty of interpreting deep intronic variants, this study highlights the importance of noncoding regions in the disease mechanism of HHT. As the non-coding and regulatory regions of ENG and ACVRL1 are better understood, these regions will be added to HHT molecular diagnostic testing methodologies to increase clinical sensitivity.

P101
High efficacy with Propranolol in patient with hereditary hemorrhagic telangiectasia and refractory epistaxis

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Purpose: To report the epistaxis cessation in a patient with hereditary hemorrhagic telangiectasia after treatment with systemic propranolol
Results: Hereditary hemorrhagic telangiectasia (HHT) or Rendu-Osler-Weber syndrome is an autosomal dominant vascular dysplasia. It affects 1:5000 individuals. Telangiectases can be present in different locations, more frequently in the nasal and digestive mucosa, face, lips, fingertips, ears and conjunctivae. -Spontaneous ruptures usually occur , leading to hemorrhage and anemia in more than 50% of cases.-Epistaxis is the most common symptom and life-threatening episodes may happen. The treatment with propranolol in HHT patients has been recently reported in small case series. We reported a 54 -year-old woman with a severe longtime epistaxis and multiple blood transfusions. We performed an endonasal laser treatment followed by a bilateral nasal closure, the "Young's Procedure" which is a highly effective surgical treatment. The epistaxis stopped completely and she recovers a normal hematocrit. One year after surgery, the hematocrit fell 10% due to a moderate daily bleeding through a new opening in her nostrils. Due to the extreme thinness of the vestibular skin, the surgical closure of the opening was unsuccessful. We prescribed propranolol 1,5 mg/kg. One week after the epistaxis, episodes stop again and she recovers the normal blood parameters. After 18 months of propranolol treatment, she presents a mild and sporadic epistaxis with normal iron and blood parameters.
Conclusion: Propranolol might help to reduce the epistaxis in some HHT patients due to antiangiogenic and vasoconstriction effects. More data are necessary to confirm the role of propranolol in HHT patients.

P102
Volumetric assessment of pediatric vascular malformations using a hand-held three-dimensional imaging system

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Purpose: The effect of percutaneous and medical therapies for vascular malformations (VMs) is often difficult to quantify volumetrically using cross-sectional imaging. Volumetric measurement is often estimated with serial, expensive MRI examinations which may require sedation/anesthesia. We aim to explore whether a portable 3D scanning device is capable of rapid, accurate volumetric analysis of pediatric VMs.
Methods: Using a Structure Sensor, an iPad-mounted infrared scanning device, 3D scans of patient faces, arms, and legs were acquired over an eight-month study period. Proprietary software (LymphaTech) was use to perform subsequent volumetric analysis.
Results: Scans of 29 faces, 5 arm pairs, and 15 legs pairs were analyzed. For patients with unilateral facial VMs (n=10), volume discrepancy between normal and affected sides (Figure1) differed compared with normal controls (n=19). This was true for both absolute (60cc ±55vs 15cc ±8, p=0.03) as well as relative(18.1%±13.1vs 4.0%±2.1,p=0.008) volume discrepancy. Among patients who underwent treatment for facial VMs (n=3), change in volume discrepancy ranged from -0.3% to +2.7%. Arm VMs were correctly localized in 4/5 (80%) patients by detecting increased volume of the affected limb. Relative and absolute volume discrepancy were 7.4% ±21.8 and 167cc ±153, respectively. Leg VMs were correctly localized in15/15 (100%) of patients with relative and absolute volume discrepancy of 19.6% ±29.9 and 603cc ±901, respectively. Following treatment, patients (n=2) experienced change in leg volume discrepancy Ranging from -17.3% to -1.8%.
Conclusion: Using a portable 3D scanning device, we were able to rapidly and noninvasively detect and quantify volume discrepancy resulting from VMs of the face, arms, and legs. Preliminary data suggests this technology will be able to detect volume reduction of VMs in response to standard therapies. Further investigation is needed to fully demonstrate this capability.

P103
Utilization of indocyanine green fluorescence image guidance in an extensive lymphovenous vascular malformation of the airway

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Purpose: Vascular malformations are usually present at birth and may consist of any combination of capillary, lymphatic, venous, and arterial components. The majority of vascular malformations in the younger population have a predilection for the head and neck region. We present the utilization of intra-operative indocyanine green fluorescence (ICG) image guidance for visualization of an extensive lymphovenous malformation of the airway.
Methods: A 35 year old female presented with chronic fatigue, obstructive sleep apnea, dysphagia, and intermittent severe hemoptysis secondary to a lymphovenous malformation. The lymphovenous malformation involves the skull base, retropharyngeal and prevertebral spaces, surrounded the great vessels bilaterally, and had circumferential tracheal mucosal involvement from the subglottis to the mainstem bronchi. A biopsy of the lesion was needed for genetic testing. Given the history of severe hemoptysis, we utilized intravenously injected indocyanine green (ICG) fluorescence using Novadaq Pinpoint Endoscopic Fluorescence Imaging System (Ontario, CA) to perform an airway evaluation and guide biopsies.
Results: The indocyanine green fluorescence using Pinpoint Imaging Systems provides excellent exposure of tissue perfusion of the vascular malformation and anatomical structures of the airway. Figures 1 and 2 demonstrate the lymphovenous malformation of the trachea and carina respectively. Figure 3 demonstrates the trachea and carina after the use of ICG fluorescence. Figure 4 illustrates color segmented fluorescence used to image different levels of ICG uptake and corresponding levels of perfusion. These images were successfully used to guide site selection for biopsy to minimize hemorrhage risk with ensuring that involved tissue was sampled.
Conclusions: The utilization of indocyanine green fluorescence endoscopy provides enhanced visualization of mucosal involvement of vascular malformations of the airway, thus allowing the surgeon to enhance diagnostic and therapeutic interventions.

P104
Beware of venous ectasia, venous lakes associated with arteriovenous shunt - The role of interventional radiology.

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Purpose: Bleeding, ulceration and cardiac failure can occur in the rapidly involuting congenital hemangioma (RICH). Bleeding intensity may range from minor event to life-threatening. The purpose of this study is to determine whether there are sonographic criteria associated with an increased risk of bleeding or cardiac failure in RICH and to identify patients who need close monitoring or embolization treatment.
Methods: Retrospective, single-center study including RICH patients was reviewed with the clinical criteria (bleeding, ulceration and cardiac failure), the sonographic findings (visible vessels, venous ectasia, venous lakes and arteriovenous shunts) and the outcome.
Results: Twenty-four patients (13M, 11F) were included. Ulceration occurred in five cases (20.8%), bleeding in four cases (16.7%), among which one was life-threatening. Cardiac failure (12.5%;3/24) was observed more frequently in RICH with venous lakes ($p = 0.028$). Bleeding and ulceration appeared more frequently in RICH with venous ectasia and venous lakes. Cardiac failure was associated with the presence of venous ectasia. All patients with cardiac failure and/or ulceration had arteriovenous shunts. Four patients were treated with endovascular embolization. Three of them had cardiac failure with the sonographic findings of venous ectasia, venous lakes and arteriovenous shunts. One patient was treated with embolization due to the huge RICH of the face with feeding problem and venous lakes.
Conclusion: Sonography plays an important role in the risk stratification of RICH. Prophylactic treatment with endovascular arterial approach and percutaneous sclerosing therapy should be considered for RICH with arteriovenous shunts associated with venous ectasia or venous lakes.

P105
Sclerotherapy of Orbital Slow Flow Malformations: A 15 year Single Center Experience

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Purpose: Slow flow (Venous and Lymphatic) malformations of the orbit are benign vascular growths. Although uncommon, they pose significant risk to vision and can be challenging to treat. Advances in percutaneous sclerotherapy have made this an effective treatment option. We would like to present our 15-year experience with orbital sclerotherapy.
Methods: This is a retrospective review of patients who underwent percutaneous sclerotherapy for orbital Venous Malformations, Lymphatic Malformations, and combined Venous and Lymphatic Malformations (VM,

LM, VLM) between January 2000 and January 2015. Only patients who underwent more than one treatment were included in the review to maximize pre and post-treatment radiologic and clinical data. The techniques and agents depended upon malformation makeup and the sizes of any cysts. Sodium tetradecyl sulfate 3%, ethanol 98%, doxycycline and bleomycin were used at the discretion of the Interventional Radiologist. Patient demographics, treatment technique, and ophthalmologic and clinical outcomes were evaluated.
Results: Seventy-two patients (32M:40F) with an average age of 13 years (SD ±12) met the inclusion criteria. Twenty-seven patients were classified as having LM, 32 with VLM, and 13 with VM. The mean number of treatments for each malformation type was 2.6 (SD ±0.8) for LM, 3.8 (SD ±1.5) for VLM, and 3.5 (SD ±2.1) for VM. The average follow up time was 52.5 months (SD ±23.6). Four patients experienced a clinical or radiologic recurrence. Twenty-three patients had reliable pre and post-procedural exophthalmometry, 19 of which had baseline proptosis. In no case did the proptosis increase and the average improvement in exopthalmometry was 73.2%. Thirty-seven patients had Snellen visual acuity (VA) readings before and after treatments. No patients experienced a decrease in VA. Eight patients experienced an improvement in VA.
Conclusion: Percutaneous sclerotherapy is an effective and safe treatment option for orbital slow-flow malformations with a low recurrence risk after successful ablation.

P106
Sclerotherapy for the Treatment of Vascular Malformations in the Oral cavity - An Evaluation of 2 Sclerosing Agents

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Purpose: To assess the effectiveness and morbidity of sclerotherapy by intralesional injection of (1) 5% Ethanolamine-Oleate (EO); (2) 3% Sodium-Tetradecyl-Sulfate (STS), for the treatment of vascular malformation (VM) in the oral cavity.
Methods: Twenty-five patients (32 lesions) treated with EO, and 5 patients (6 lesions) treated with STS were retrospectively assessed. A descriptive statistical analysis was performed.
Results: Lesions' maximal diameter ranged from 3-30 mm. Twenty-nine lesions (90%) in the EO-group, and all the lesions in the STS-group (6, 100%) showed total clinical regression with excellent aesthetic results. The average dosage of EO and STS required was 0.05 ml/mm, and 0.04 ml/mm respectively. A single application was sufficient in the majority of cases (EO-group: 23, 72%; STS-group: 6, 100%). In most of the cases (EO-group: 28, 97%; STS-group: 6, 100%) healing was still in process after 3 weeks, and the response for treatment couldn't be determined at that time. Complete resolution achieved usually, no early than 6 weeks. In both groups, a single injection up to 0.5 ml was found to be well tolerable, with minimal side effects. In the EO-group, 1 patient needed further intervention for debridement of necrotic tissue, after which complete healing achieved. Generally, it seems that sclerotherapy by STS resulted with less severe side effects (e.g., pain, swelling, hematoma, and ulceration). No recurrence occurred during the study period.
Conclusion: Sclerotherapy by 5%-EO and 3%-STS is an effective treatment with minimal morbidity when applied in limited dosage. The effective dosage and the number of applications necessary are lower than usually reported. The required interval between treatment sessions and the waiting time necessary for complete healing is longer than previously reported. With the limitation of the present preliminary results, 3%-STS produces less severe side effects than 5%-EO.

P107
Comparison of Percutaneous Polidocanol Injection and Percutaneous Ethanolamine Oleate Injection for the Treatment of Venous Malformations.

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Purpose: In this study, we assessed the efficacy and safety of percutaneous sclerotherapy with polidocanol in comparison to those of percutaneous sclerotherapy with ethanolamine oleate in the treatment of patients with venous malformations in soft tissues.
Methods: In this retrospective study, 68 patients who were treated with percutaneous liquid ethanolamine oleate (group l-EO) injection, 56 who were treated with percutaneous ethanolamine oleate foam (group f-EO) injection, and 63 who were treated with percutaneous polidocanol foam (group f-Po) injection, between May 2000 and July 2015, were enrolled. The patients were evaluated for treatment efficacy and treatment-related side effects.
Results: No significant difference was found in efficacy, but hemoglobinuria was more likely to occur in the l-EO and f-EO groups. Skin necrosis occurred significantly more frequently in the l-EO group than in the f-Po group.
Conclusion: This study shows that percutaneous sclerotherapy with f-Po for venous malformations of soft tissues is equivalent to the treatment with l-EO and f-EO in terms of efficacy but leads to lower complication rates than the l-EO and f-EO treatments.

P108
Radiofrequency Ablation for Management of Lower Limb Phlebectasias and Klippel-Trenaunay Syndrome

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Purpose: Management of lower limb venous malformation (VM) with phlebectasia and Klippel-Trenaunay syndrome (KTS) is challenging. Complications and recurrences can occurr after sclerotherapy or surgical excision. In this study we present our preliminary results of radiofrequency ablation (RFA) for VM with phlebectasia and KTS.
Methods: From 2014 to 2017, patients diagnosed with lower limb VM with phlebectasia and KTS were recruited for RFA. The procedure was performed under general anaesthesia. After mapping by sonography and venogram, the ClosureFast® RFA catheter was inserted into the targeted vein. Tumescent solution was injected under sonographic guidance to achieve vein depth of more than 1cm. Ablation of the dysplastic vein was done with temperature controlled at 120oC treating 3cm segment each time for 20 seconds. After the procedure, 20-30mmHg compression stocking was applied for 6-12 weeks. The patients were followed up clinically and radiologically.
Results: Six patients were recruited with a median age of 27 years old (range 2.7-40), three were males. Three patients had KTS. Indications for treatment were pain (n=3), recurrent bleeding (n=2) and cosmetic concern (n=1). Three patients had received previous sclerotherapy. The median operative time was 146 minutes (range 108-239 minutes) and median length of stay was 1.5 days (range 1-3 days). The median follow up time is 7.5 months (range 2-40 months). No short-term post-operative complications were encountered. Four patients had symptomatic cure and 2 patients (33%) required further sclerotherapy for residual VM.
Conclusion: RFA is a safe treatment of lower limb VM with phlebectasia and KTS with satisfactory short-term results. It may be considered as the first line treatment of this subgroup of VM. Further follow up is require to assess long term results.

P109
Adverse events of different sclerosing agents in the treatment of lymphatic malformations in children

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Purpose: Lymphatic malformations (LMs) often require treatment, because of lesion-related complications. Sclerotherapy is currently considered the primary treatment of choice. Bleomycin has proven to be effective, but a major concern is the risk of interstitial pneumonia and pulmonary fibrosis. This study compares the differences in complications between sclerosing agents in the treatment of LMs in children.
Methods: A retrospective analysis of all sclerotherapy procedures for children with LMs during 2011-2016 at a national referral center was performed. Demographics, short (< 30 days) and long term procedure-related complications were recorded and compared between different sclerosing agents. Patients treated with ethanol were excluded.
Results: A total of 217 procedures in 109 patients were performed using bleomycin (63%), aethoxysclerol (22%), doxycycline (7%) or a combination of bleomycin and aethoxysclerol (9%). The median number of procedures per patient was two (range 1-13). Table 1 shows the short and long term procedure-related complications. There were no significant differences in complications between sclerosing agents. The two cases of functional impairment required an intervention and were thus considered major. Less invasive treatment within 30 days post-intervention, such as analgesics (7%) and antibiotics (3%), was required in 22 cases (10%). In the long term, edema therapy (1%) was the only necessary treatment. One patient developed pneumonia seven days after bleomycin injection, which resolved after antibiotic treatment. No known cases of pulmonary fibrosis occurred during the study period.
Conclusion: Several minor and a few major procedure-related complications occurred. Only one patient developed pneumonia during the study period. This institutional study shows no significant differences in complications between the sclerosing agents, although the design of the study allows patient-specific treatment regimes. The risk of bleomycin on pulmonary toxicity seems to be negligible when used correctly, so it appears to be a safe agent in the treatment of LMs in children.

P110
Cryoablation Only Vs Cryoablation And Bleomycin In Treatment of Fibro-Adipose Vascular Anomaly: Which Is Better?

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Purpose: To compare outcomes in patients with Fibro-adipose Vascular Anomaly (FAVA) who were treated with cryoablation alone versus those treated with combined cryoablation and bleomycin injection.
Methods: The study included a cohort of 40 patients with FAVA. 20 pts underwent percutaneous cryoablation only and 20 pts underwent a combined procedure with cryoablation and bleomycin injection at FAVA sites. Follow up was performed at 1 month, 2 to 5 months, 6 months and 12 months or more. The outcomes were based on the brief pain inventory scoring (BPI), concurrent symptoms, clinical response and patient satisfaction.
Results: Following the procedure there was significant improvement in pain, concurrent symptoms, and quality of life in both groups. However the time for this response was significantly shorter and the response grades better in the pts who underwent cryoablation with additional bleomycin injection. This response was seen earlier at 1 to 3 months in the latter versus 3 to 6 months in the former group.
Conclusion: Image-guided percutaneous cryoablation with bleomycin injection is more effective and provides faster response as compared to cryoablation alone in treatment of FAVA.

P111
Use of ethylene vinyl alcohol(Onyx®) in the treatment of peripheral vascular anomalies: Assessment of clinical efficacy and patient satisfaction outcomes. A single centre experience from Singapore.

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Purpose: To illustrate the use of Onyx®, an ethylene-vinyl alcohol copolymer liquid embolic agent in the treatment of peripheral vascular anomalies. Correlation with technical, clinical success, operator and patient satisfaction.
Methods: 10 patients (8 males and 2 females) were treated for peripheral vascular malformations between January 2015 and October 2017 at our department. All patients were symptomatic and were discussed at dedicated multi disciplinary team meetings. Pre-procedural MRI imaging was performed for all patients. Mean age: 34.2, range (21-59 years). Locations of vascular malformation: thigh (n=2), supraclavicular fossa (n=1), upper limb(n=3), calf (n=2)) and feet (n=2). No of high-flow: 3 ; No of low-flow: 7. Patient satisfaction survey (questionnaire) was carried out at 3, 6, 18 months follow up in 9 patients and 3 month follow up in one patient. Dedicated doppler ultra sound scan (USS) was performed during clinical follow up.
Results: The procedures were technically successful in all the patients (100%). There was one incidence of non target embolization to the left great toe in a patient with plantar high flow AVM. Spontaneous recovery ensued following meticulous wound care and there was no tissue loss. Clinical success was achieved in 9 out of 10 patients. There was no other direct adverse effects as a result of treatment with Onyx®. Follow up showed that flow recurred in one patient with plantar high flow AVM. 9 out of 10 patients were symptom free at 18 months (90%). The median patient satisfaction score was 8 (range7-10). There was significant improvement in quality of life in 9/10 patients.
Conclusion: The ease of handling and control during complex embolization procedures in combination with its established safety profile makes Onyx® the first choice embolic material in suitable morphologies of vascular anomalies. Treatment with onyx in our experience has been effective, safe and resulted in significant improvement in quality of life of the treated patients.

P112
Combined Surgical Technique with Intraoperative Bleomycin Sclerosis to Avoid Postoperative Leakage and Local Recurrence of Lymphatic Malformations

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Purpose: Show our initial experience in the management of extensive lymphatic malformations (LM) treated with sequential sclerosis, surgical resection and intraoperative sclerosis, to avoid postoperative leakage and local recurrence of the lesion.
Methods: We selected from all the patients treated at our VAC with LM, those with large lesions requiring a surgical approach. All the LM were previously treated with percutaneous sclerosis, under ultrasound and fluoroscopic guidance.The macrocystics lesions were treated with doxycycline 20mg/kg/session, for microcystic components, we used bleomycin 15UI/session. MRI was performed at the beginning of treatment, and prior to surgery to assess residual lesion. Surgery was performed always by the same surgical team. After resection of the LM, the surgical bed with remaining unresectable or microscopic disease was directly sclerosed with bleomycin 15UI. Drainages were placed. All data was collected.

Results: We performed 4 combined procedures. Localization: thoracic wall (2), cervical (1) requiring a tracheostomy, forearm and hand (1). Median age at the time of the resection was 4 years (r:3-5). Mean time of surgery 8.8 hours (r:6.5-11). No intraoperative complications were registered. Drainages were placed in all cases, median 7 days (r:2-12) with mean drain output of 2.6 ml/kg/day (r:0.48-4.77). All patients were discharged within 3-8 days. Mean follow up time was 21,5 months (r:6-39). There were no recurrences o persistent leakage of the LMs, with adequate esthetic and functional outcomes.
Conclusion: Our initial experience with this combined approach reduced the postoperative lymph leakage and local recurrence. This is particularly useful when residual skin is infiltrated with microscopic disease or when vital structures are compromised.

P113
Simultaneous Intra-operative Sclerotherapy and Surgical Resection of Cervicofacial Venous Malformations

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Purpose: To review simultaneous intra-operative sclerotherapy (IOS) with immediate surgical resection for the treatment of cervicofacial venous malformations (VMs) at a single institution. While pre-operative sclerotherapy (POS) has been reported in the literature, simultaneous IOS and surgery has not.
Methods: The database from the Hemangioma and Vascular Birthmarks Clinic was reviewed. All patients in both groups had biopsy-proven VMs.
Results: IOS was used in 11 surgical patients with average age 17 years. Sclerotherapy was performed with Sotradecol, absolute alcohol or bleomycin. Immediately after IOS, and under the same anesthetic, all patients had either complete resection or debulking of the VMs. Eight patients had complete resolution of their VM and 3 had improvement. Average duration of the combined procedures done under a single anesthetic was 121 minutes. See Table. POS approach was used for 6 surgical patients with average age 7 years. Sclerotherapy agents used were absolute alcohol or Sotradecol. All patients underwent complete resection of the VM 24-72 hours after sclerotherapy under a separate surgical session. Five patients experienced complete resolution of their VM and one has had further sclerotherapy for recurrent disease. Interventional Radiology suite sclerotherapy times were on average 70 minutes. Surgical times were on average 142 minutes. Total combined anesthesia times for the two procedures added together were 212 min. See Table.
Conclusion: Simultaneous IOS at the time of surgical resection has been successful in our hands. IOS has the advantage of one procedure and decreased cost to the patient. In the era of reducing pediatric exposure to anesthesia, this approach is especially attractive in the pediatric population. As well, at approximately $100/minute cost to the patient to be in either the Interventional Radiology Suite or in the operating room, the reduced length of the procedures seen in the IOS approach results in lower overall cost to the patient.

P114
The Use of Preoperative Embolization with n-Butyl Cyanoacrylate Prior to Surgical Resection of Venous Malformations

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Purpose: Sclerotherapy and surgical resection are used for the treatment of symptomatic venous malformations. Sclerotherapy may require repetitive intervention and surgical resection is often avoided due to excessive operative morbidity. The purpose of this study was to report the use of glue embolization with n-Butyl Cyanoacrylate followed immediately by surgical resection of venous malformations.
Methods: A retrospective review of patients with venous malformations who underwent glue embolization by interventional radiology followed by surgical resection at a single tertiary care vascular malformations center was performed. All embolizations were performed with ultrasound and fluoroscopic guidance under the same anesthetic episode as resection. Patient characteristics and outcomes including surgical blood loss, postoperative complications, and recurrence of malformation are reported.
Results: Ten embolization/resection procedures were performed in 8 patients. Median (range) age was 16 (3,29) years. Malformation locations included scalp (n=2), gluteal (n=2), face, lip, chest (Figure 1), labia, foot, and toe (all n=1). Size of treated malformations ranged from 2 to 10 cm. Median (range) of prior sclerotherapy treatments was 4 (0,13) and 3 patients had previously undergone partial surgical resection. No patients required blood transfusion and 80% had estimated blood loss ≤10 mL. Surgical complications occurred in 3 patients (30%); superficial wound dehiscence in the foot and toe malformations and cellulitis in the facial malformation. No complications required readmission or intervention. At a median follow up of 1.3 (0.5, 4.4) years, no patients have required additional sclerotherapy or resection.
Conclusion: A combined interventional radiology and surgical approach to glue embolization and resection of venous malformations can be used on malformations of all sizes and locations with durable results and low surgical morbidity, often as an outpatient procedure. It may be performed as a primary upfront treatment for symptomatic malformations or can be done if the patient becomes refractory to sclerotherapy.

P115
Ultrasonography and Magnetic Resonance Imaging Features of Kaposiform Hemangioendothelioma and Tufted Angioma

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Purpose: Kaposiform hemangioendothelioma (KHE) is a rare, aggressive vascular tumor, while tufted angioma (TA) is benign and superficial. This study evaluated ultrasonography (US) and magnetic resonance imaging (MRI) features of KHE and TA.
Methods: Pathologically proven TA (n = 12) and KHE (n = 40 [12 KHE + Kasabach-Merritt phenomenon (KMP)]), diagnosed between January 2015 and June 2017 (mean age 7.6 versus 3.9 years, respectively; $p<0.05$), were reviewed. US (n = 52) and MRI (n = 40) findings were retrospectively evaluated.
Results: KHE + KMP lesions were thicker than TA or KHE lesions ($p<0.05$). Most lesions were subcutaneous; 16 KHEs exhibited an infiltrative pattern extending into adjacent muscles. Six (50%) TA lesions were hyperechoic; 38 (96.15%) KHE lesions exhibited mixed echogenicity, with mainly shallow hypoechogenicity and deep hyperechogenicity. The hypoechoic thickness and vascular density of TA, KHE, and KHE+ KMP were significantly increased. The arterial peak systolic blood flow velocity of KHE and KHE + KMP were significantly higher than that in TA. The KHE and KHE with KMP was significantly harder than TA on elastography. For MRI findings, KHE and KHE with KMP was more likely to show diffuse heterogeneous enhancement after contrast than TA.
Conclusion: KHE primarily affected infants, was infiltrative, exhibited ill-defined margins, and was more likely to be thick, hypoechoic, richly vascular, and harder than TA on US. KHE lesions were subcutaneous and reticular, with heterogeneous enhancement on MRI. Awareness of these features should prompt radiologists in the differential diagnosis for pediatric masses.

P116
Metronomic Chemotherapy for Aggressive Vascular Anomalies: Clinical Effect in a Patient with Kaposiform Lymphangiomatosis

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Purpose: Kaposiform lymphangiomatosis (KLA) is a rare, aggressive generalized lymphatic anomaly that typically presents in late childhood and may be triggered by puberty or pregnancy. Clinical presentation is marked by respiratory distress from pleural and pericardial effusions, bleeding with thrombocytopenia and consumptive coagulopathy, and subcutaneous masses with variable involvement of the retroperitoneum, abdominal viscera, bones, and muscles. Biopsy demonstrates characteristic dilated lymphatic channels accompanied by small clusters of spindle-shaped endothelial cells. Prognosis is poor with an overall survival of 30%. Metronomic, or frequent, low dose, administration of traditional chemotherapeutic agents has significant anti-angiogenic effects and has been described in the treatment of other vascular anomalies. We report a patient with refractory KLA who responded to metronomic cyclophosphamide.
Methods: Data collection was performed by a retrospective chart review of clinical records.
Results: A 33 year old female presented at 30 years of age after a miscarriage with pleural effusions necessitating wedge resection. She developed thrombocytopenia with a consumptive coagulopathy, melena, and hemoptysis after her second pregnancy. Imaging revealed a diffuse, infiltrative, multifocal soft tissue density in the mediastinum, mesentery, and retroperitoneum, with hepatomegaly. Biopsy of a rhomboid mass was consistent with KLA. She remained refractory to treatment with octreotide, sirolimus, and steroids. She had profound cachexia and ultimately developed cholestatic liver failure of unclear etiology. Cyclophosphamide was administered at low doses of 300-400 mg/m2 IV approximately every 3 weeks for 6 months. Within 1 month of completing therapy, she exhibited marked clinical improvement with resolution of liver failure. She continues on sirolimus 1 year after receiving cyclophosphamide with no overt signs or symptoms of KLA.
Conclusion: KLA is an aggressive lymphatic anomaly oftentimes refractory to therapeutic interventions. Further investigation is indicated to evaluate the efficacy of metronomic cyclophosphamide and other chemotherapeutic agents in the treatment of KLA.

P117
Chylothorax Following Rib Biopsy in Generalized Lymphatic Anomaly

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P118

A simple method for objective outcome measurement in port-wine stain laser treatment

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Purpose: Port-wine stains, or capillary malformations, are the most common congenital vascular malformation. They often present at birth with disfiguring pink, red or violaceous facial marks that can evolve with time. Pulse-dye lasers are often used for treatment but objective measurement of clinical improvement is challenging. We present a simple method to objectively measure color improvement with laser treatment.
Method: A retrospective review was performed of all patients who were diagnosed with facial port-wine stains at a pediatric institution over 16 years (2002–2017). Demographics, treatment modality and duration, and photographic outcomes were reviewed. Patients were included if they had pre- and post-treatment clinical photographs capturing similar portions of the face and were treated solely with laser therapy. Digital Color Meter, a free utility for Macs (Apple, Cupertino, CA), was used to measure skin color using the RGB color space and maximum aperture. Five points were measured for each lesion (Fig. 1) and on an unaffected area on the corresponding contralateral side or an adjacent area. The lesion measurements were compared against the control using the formula of the square root of (ΔR)2 + (ΔG)2 + (ΔB)2, creating a "color difference" value. This method controlled for differences in lighting and position. Statistical significance was measured by Students t-test.
Result: 47 patients were identified with an average age of 7.4 years. The most common location was the cheek and the mean number of treatments was 6.96 +/- 4.2. Post-treatment lesions were 31% lighter ($p = 0.005$) after pulse-dyed laser therapy.
Conclusion: Port-wine stains are common vascular malformations that may cause significant deformity. We present a simple, readily available technique to objectively measure color improvement after treatment. This modality may help guide clinicians with treatment decisions and offer a standard platform for communication of outcomes.

P119

Less is More: Similar Efficacy in Three Sessions and Seven Sessions of Pulsed-Dye Laser Treatment in Infantile Port-wine Stain Patients

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Purpose: Port-wine stains (PWS) affect 0.3% to 0.5% of newborns and pulsed dye laser (PDL) remains the treatment of choice. However, no reliable study regarding the benefits of more frequent has been conducted. We designed the present study to evaluate whether more frequent PDL treatments in infantile patients would achieve further lightening of erythema.
Methods: We prospectively investigated 20 infants with PWS. Two adjacent sites were both treated for a 12-week duration and randomly allocated to be treated for 7 sessions at 2-week intervals or 3 sessions at 6-week intervals. The efficacy outcome 2 months after the final treatment was determined by visual and chromameter evaluation.
Results: Sixteen patients completed the study with a total of 54 treatment sites. Similar results were observed in the 2 groups. The average blanching rates were 42.93% (SD = 27.92%) and 43.81% (SD = 32.80%) for PDL treatments with 7 and 3 sessions, respectively ($p = 0.374$). Partial recovery from the laser treatment was more frequently observed and side effects were significantly higher at 2-week follow ups ($P < .001$), resulting in a total of 3-13 weeks for skin recovery.
Conclusion: More frequent PDL treatments do not necessarily increase efficacy in infantile PWS patients. Considering the potential risks and added costs, this practice may not be of benefit.

P120
A new approach to the treatment of stubborn/persistent facial port wine stains(PWSs) using triple wavelength laser therapy.

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Purpose: Stubborn, persistent facial port wine stains are difficult to manage, often causing distress to the patient and the family and frustration to the clinician, with limited treatment options. We use multiple passes using three different wavelengths within the same laser procedure. The aim of this case series was to determine the efficacy of triple laser therapy. This was achieved in our preliminary work using standardised photographic evidence and objectively using SIAscopy. All children had previously received 3 to 9 single PDL treatments (mean 6.8).
Methods: Children who had received Triple pass therapy for persistent PWSs, for whom SIAscopy readings had been taken were retrospectively identified for the preminary work(9 patients). Since then 20 more patients have been identified and whose results will be available for presentation at the ISSVA meeting in 2018. All children were treated with combined multiplex laser delivering "first pass" with 585 nm pulsed dye laser and 1064nm Nd:YAG Laser. They were then re-treated with a "second pass" using the V Beam Perfecta laser at 595nm.Probes used were 10 and 7 mms as standard and pulse duration were standardised to group three(PDL 6ms,Nd:YAG 15ms). Multiplex PDL treatment had a median fluency of 10(9-11 J/cm2), Multiplex Nd:YAG had a median fluency of 60 J/cm2(range 50-60)PDL Perfecta laser had a median fluency of 7 (range 6-11). SIAscope readings were taken pre-treatment, after 1st pass and second pass. Cooling was achieved by ice cool water, Cryo 4 continuous air flow and cooled ultrasound gel during multiplex treatment. During the second pass with PDL alone,Dynamic Cooling Device was used.
Results: Early data showed promising results. There was upto 12% further reduction in the absolute number of blood chromophores(siascope data). This was similar with the photographic evidence. One child developed a blister on her lip pws post treatment with post laser treatment scarring. She was type 4 to 5 skin. All patients had 1 to 3 treatments in this cohort.
Conclusion: SIAscopy offers an objective method to assess outcomes and guide treatment during procedure. Triple therapy in our experience is an effective treatment for stubborn/persistent Port Wine Stains.

P121
Intravenous injection of artificial red cells and subsequent dye laser irradiation causes deep vessel impairment in an animal model of port-wine stain

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Purpose: Previously, we proposed the use of artificial blood cells (i.e., hemoglobin vesicles, Hb-Vs) as photosensitizers in the dye laser treatment of port-wine stains (PWSs). A mixture of red blood cells (RBCs) and Hb-Vs could absorb dye laser photons and potentially produce more heat and induce photocoagulation to effectively destroy endothelial cells. We concluded that Hb-Vs combination therapy would therefore improve the clinical outcomes of dye laser treatment for small vessels lack sufficient RBCs in PWSs. In the present study, we analyzed the relationship between the vessel depth from the skin surface and vessel distraction via dye laser irradiation following intravenous Hb-Vs injection in a chicken wattle model.
Methods: Following Hb-Vs injection, the chicken wattles were subjected to irradiation at energy levels higher than those used in previous experiments. The locations of Hb-Vs in the vessel lumen were identified via immunostaining for human Hb to determine the photosensitizing effects.
Results: Dye laser irradiation with Hb-Vs can effectively destroy deep vessels in animal models. The administered Hb-Vs are distributed in blood plasma and can temporarily saturate small vessels without RBCs during irradiation. Hb-Vs tend to flow in the marginal zone of both small and large vessels.
Conclusion: Increasing laser power combined with Hb-Vs injection contributed for deep vessel impairment because of the synergetic effect of both methods. Newly added Hb tended to flow near the target endothelial cells of the laser treatment. Hb-Vs function as photosensitizers to destroy deep vessels within a restricted distance that the laser photon can penetrate.

P122
The role of laser therapy in verrucous vascular malformations: a retrospective analysis

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Purpose: Verrucous Vascular Malformations (VVM's) are a rare type of vascular anomaly that most commonly affect the skin of the lower limbs. VVM's are formed of clustered areas of malformed venules with overlying hyperkeratosis. This presents clinically as single or multiple blue/purplish plaques with verrucous projections. VVM's can have a significant impact on quality of life as development of hyperkeratosis leads to bleeding and infections. Management options currently include laser and surgery. We aimed to assess the efficacy of laser therapy, which, given the low prevalence of VVM's, has not previously been analysed comprehensively.
Methods: Retrospective analysis was undertaken of clinical outcomes of VVM's before and after laser therapy. Patients with a diagnosis of VVM and available clinical photographs that were treated over a 15-

year period were included. Clinical photographs prior to and following laser therapy were graded with a newly devised severity scoring system. This system incorporated lesion elevation, colour, and degree of hyperkeratosis, producing an overall severity score from 0-10. Additionally, clinician assessment and parental comments on outcomes were obtained from review of medical records.
Results: Across the 15-year period analysed, a total of 14 eligible patients were identified (6 females, 8 males). Each patient underwent a mean of 3.92 laser treatment sessions, averaging 31.5 total pulses per session. Patients were a mean of 8.16 years of age at their last laser treatment. Overall, VVM severity scores showed a significant decrease from before (9.07/10) to after (4.26/10) laser therapy (p=0.002).
Conclusion: These results suggest that laser therapy can produce a measurable reduction in VVM severity. Although this provides evidence of benefit, future prospective research would be beneficial in better understanding the role of laser therapy in this relatively rare vascular anomaly.

P123
GENTLE ND:YAG LASER THERAPY IN THE TREATMENT OF CUTANEOUS VENOUS MALFORMATIONS

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Purpose: Venous malformations (VMs) are slow-flow vascular malformations that are present at birth, never involute, and grow progressively. Cutaneous VMs are particularly difficult to treat due to the risk of injury and deformation. Gentle Nd:YAG laser therapy (Gentle YAG) allows for targeted ablation of venous channels with the protection of adjacent soft tissue via selective photothermolysis and dynamic cooling. We hereby examine the safety and efficacy of Gentle YAG in the management of VMs involving the skin.
Methods: A prospective survey of 10 blinded reviewers was conducted on photographs taken before and after Gentle YAG therapy on patients with cutaneous VMs treated between December 2012 and August 2016. The trained and untrained reviewers were independently surveyed on the growth, stability, improvement, or resolution of the VMs. Survey results were tabulated and analyzed. A chart review examined safety and complications.
Results: Forty-five patients, 18 males and 27 females, were identified with a median age of 9 years old at the time of treatment. The areas treated included the lips (9), legs (8), hand (8), neck (7), chest (6), back (2), ear (2), abdomen (2), foot (1), and penis (1). The median interval between before and after photographs was 15 months, with a median of 2 treatments (range 1-5) per patient. Improvement in the appearance of most VMs after Gentle YAG therapy was noted by the reviewers, 2 (1, N = 45) = 25.94, $p < 0.0001$. Reviewer responses were reported as complete resolution in 8.2%, significant improvement in 34.5%, some improvement in 29.3%, no growth or improvement in 20.9%, and growth of the VM in 7.3%. Thirty-nine (86.7%) patients had no reported complications from the treatment. Pain was reported by 4 (8.9%) patients before treatment. Three (75.0%) of these patients had resolution of pain after treatment. Infection, bleeding, blister, and color change at the treated area were each reported in less than 2.5% of the patient population.
Conclusion: Gentle Nd:YAG laser therapy is safe and effective for improving over 70% of superficial VMs of the skin and may have some utility in treating pain as well. Laser treatment should be considered in the multimodal management of venous malformations.

P124
Laser transcutaneous therapy of venous malformations with diode laser 1470nm in children

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Purpose: Analysis of efficacy of diode laser endovascular ablation in selected vascular malformations. Endovascular laser ablation with diode laser is well known method for treatment of varicose veins in adults. This technique was applied by authors for treatment of resistant venous malformations (VM) and used as transcutaneous intraluminal or interstitial application. Diode laser can be used for ablation of hypoplastic patologic veins and glomuvenous malformations.
Methods: In 2016-2017, 21 patients with resistant or complicated venous malformations, aged 10-17 y.o. were treated with diode laser 1470nm. 11 - lover limb (3 Klippel-Trenaunay Syndrome), 3 - upper limb, 7 – face (1 CVLM). All malformations were complex including muscles or joints. Fiber was applied transcutaneously with Seldinger's method or intravenous caniula, under US guidance. Double ring or one ring slim laser fiber was used. Power: 6-8W, total energy: 53-7000J/procedure. To prevent skin burn tumescency with saline and Lidocaine was applied. All patients had Fraxiparine or Enoxaparine for 7 days. In limb VM compressive dressing was used. In all patients Doppler US was done after two days. In December 2017 all patients were contacted to perform survey on results of therapy including movement limitations, pain, deformation, swelling and bleeding (scale 1-5).
Results: In 21 patients 45 laser ablations were performed. Each patient had 1-3 procedures. 19 ablations of embrional veins and 26 ablations of intrastitial VM were done. Patients were reviewed at least two months after the last laser therapy. Improvement was noted nearly in all patients. Total or partial occlusion of ablated vessels in Doppler US was diagnosed. Total survey points before and after treatment was calculated in each patient and improvement of movement range was calculated as 30%, pain relief as 31%, reduction

of deformation as 33%, swelling relief as 32%, deminished bleeding as 26%. Minor complications were noted: wound bleeding in 1 patient with coagulopathy, peripheral sensual neuropathy in the hand in 1 patient. According to extention of VM lesions most patients continued treatment.
Conclusion: Endovascular and interstitial ablation of complex VM with diode laser seems to be alternative for invasive surgery or as part of combined treatment. Method is minimally invasive and safe with adequate knowledge of the specific anatomy of VM.

P125
Bipolar Radiofrequency Ablation (Coblation) of External Auditory Canal Lymphatic Malformation and Other Soft Stenoses.

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Purpose: Soft tissue occlusion of the external auditory canal (EAC) typically causes intense pruritis, recurrent foul smelling otorrhea, recurrent otitis externa and conductive hearing loss. Occlusion of the EAC can be challenging to treat as the area is prone to circumferential scarring. We propose a novel technique of bipolar radiofrequency ablation (Coblation) for occluding EAC vascular malformations. This technology has not been previously reported for treatment of EAC lesions.
Methods: We describe the technique and provide pre and post operative photos demonstrating the novel use of serial bipolar radiofrequency ablation (Coblation) to treat 3 children with complete EAC occlusion from congenital and acquired conditions including lymphedema (1), microcystic lymphatic malformation (1) and venolymphatic malformation (1).
Results: Patients underwent a mean of 3 procedures with post-operative EAC stenting (7 days) and antibiotic and steroid aural preparations (10 days). Problematic otologic symptoms including intense pruritis and conductive hearing loss resolved in all patients and their EACs remain patent 14 months after the final procedure (range:4-32 months). One patient experienced a pinpoint tympanic membrane perforation that healed spontaneously 2 weeks later and should be preventable by careful wand tip placement.
Conclusion: Coblation of soft tissue stenosis of the EAC can be an effective treatment for problematic occluding lesions.

P126
Review and Re-classification of Lymphatic Malformations in an Existing Patient Cohort

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Purpose: Lymphatic malformations which predominantly affect osseous structures can be challenging to accurately diagnose. These disorders typically represent 3 distinct diagnoses: Gorham-Stout disease (GSD), generalized lymphatic anomaly (GLA), and Kaposiform lymphangiomatosis (KLA). Recently, the classification and imaging criteria of these diseases has been updated to provide more distinct diagnostic guidance. A review of our clinic roster and imaging database was performed to identify osseous lymphatic malformations diagnosed prior to the updated classification in order to identify mis-diagnosed patients that may benefit from an altered prognosis.
Methods: A retrospective review of the 542 patients currently registered in our Vascular Anomalies Clinic and a 10 year retrospective imaging database search were performed yielding 12 patients diagnosed with osseous lymphatic malformations. Imaging studies, pathology reports, and electronic medical records were reviewed to ascertain initial diagnosis, imaging findings/reports, disease progression, and final diagnosis using the new classification criteria.
Results: All 12 patients were initially diagnosed with GSD. Using the updated classification criteria, 3 of the diagnoses (25%) were amended to GLA. No patients were identified with KLA. The parameters used to change the diagnosis relied heavily on imaging characteristics of progressive osteolysis versus presence of cortical bone as well as overall disease progression. All biopsy specimens available for review (n=3) were consistent with GSD and were positive for D-240 immunostain. 2 patients presented with appendicular skeletal involvement (met diagnostic criteria for GSD); 10 patients primarily had axial skeletal involvement (met diagnostic criteria for GSD or GLA).
Conclusion: GSD, GLA, and KLA represent osseous lymphatic disease that requires accurate differentiation, yet is commonly mis-diagnosed. Existing vascular anomalies clinics should consider re-evaluating their existing patient cohorts and potentially reclassify these patients. Despite limited treatment options for these conditions, accurate diagnosis helps guide patient expectations with clinical follow up and prognosis.

P127
Evaluation of the population of children with lymphatic malformations treated with sclerotherapy at a national referral center

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Purpose: Lymphatic malformations (LMs) are congenital maldevelopments of the lymphatic vessels and require treatment if symptomatic. This study evaluates the population of children treated for their LMs using sclerotherapy.
Methods: A retrospective study was performed of all pediatric patients with LMs who underwent sclerotherapy during 2011-2016 at a national referral center. The demographics and lesion-related complications were recorded.
Results: A total of 217 sclerotherapy procedures were performed in 109 patients, of whom nine (8%) received a surgical excision prior to the study period. Two patients underwent surgical excision during the study period, however with (almost) no improvement. The median number of procedures per patient was two, with a range of 1-13. The median age at first treatment was 73 months (range 0-211). The majority of the patients (74%) were diagnosed before the age of two years, of whom 13% prenatally and 41% at birth. Three patients required an ex-utero-intrapartum (EXIT) procedure and direct intubation. Figure 1 shows the distribution of the locations of the LMs. Most (46%) were macrocystic, 19% microcystic and 34% were mixed LMs. Comorbidities included Klippel-Trenaunay syndrome (2%), lymphangiomatosis (2%) and PHACE syndrome (1%). The majority of patients presented with multiple lesion-related complications. The most common were pain (43%), increase in size (64%) and functional impairment (33%). Fourteen patients (13%) required treatment for their lesion-related complications, including analgesics (2%), antibiotics (6%) or an intervention (6%).
Conclusion: In our population, most LMs were diagnosed before the age of two years and the median number of procedures per patient was two. Children who underwent surgical excision required additional sclerotherapy interventions, whereas most patients were successfully treated with sclerotherapy alone. Therefore, this evaluation confirms that sclerotherapy is the primary treatment of choice if invasive management is indicated in our population of children.

P128
Angiosarcoma Arising on a Cervical Lymphatic Malformation: Case report

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Purpose: Lymphatic malformations (LM) are low flow lesions, the majority arising in the head and neck. With proper treatment, they have a good outcome. On the other hand, soft tissue sarcomas (STS) are a heterogeneous group of malignant lesions that are classified according to the adult tissue they resemble. Angiosarcoma is an extremely rare STS, even more infrequent in the pediatric population. The little response to chemotherapy determines its poor prognosis leaving surgery as the main treatment for these patients. The aim of this presentation is to report the diagnosis of an angiosarcoma arising within a mixed LM.
Results: Five-year-old female patient with prenatal diagnosis of a cervical mixed LM. Percutaneous sclerosis of the macrocystic component was initiated at 2 months of age due to extent of the lesion. A series of 9 procedures along 5 years were performed. Macrocystic components were treated with doxycycline 20 mg/kg, and bleomycin 15 IU/ session, was used for microcystic disease, achieving a significative reduction of the size. At 5 years old, 14 months after the last procedure, she returned with a new solid palpable mass located in the cervical region compromised by the LM. Ultrasound and MRI were performed showing a large solid heterogeneous lesion with peripheral enhancement after contrast administration, within the remaining microcystic component of the LM. A needle biopsy was taken. Histology and molecular biology analysis confirmed the diagnosis of angiosarcoma. CT and PET Scans showed metastatic lesions in both lungs and sternum bone. Chemotherapy treatment was started.
Conclusion: LM are benning lesion, being percutaneous sclerosis the first line treatment. In rare cases, new lesions can appear within the malformation. In suspicious cases, a correct diagnostic workup is mandatory with new images (US, MRI) and biopsy. Although it is extremely rare, STS can arise in the malformation.

P129
Lymphatic malformation with atypical features on hands and feet presented as soft tissue mass

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Purpose: Lymphatic malformations (LM) are congenital vascular anomalies presenting with fluctuating cystic mass of variable degree. It may appear in all parts of the body, but most commonly in the head and neck, and rarely occurs in the hands and feet. Its clinical and/or radiologic diagnosis may not be so difficult except the lesion of hands & feet in which their clinic-radiologic feature are not typical in these location. So, since clinical manifestation of LM on hands and feet is atypical by repeated local trauma, there were a few reports that mimics other diseases like such as ganglion cysts, epidermal cysts, verruca, and dermatofibroma. The purpose of this study is to investigate the clinicoradiologic feature of LM of hands and feet with unexpected firm soft tissue tumor like mass showing non-LM radiologic findings.
Methods: We conducted retrospective study the clinical characteristics of 22 patients who diagnosed as LM on the hands and feet chosen by immunohistochemistry using D2-40 and Prox-1 of biopsy or surgical samples.
Results: The cases of LMs included in our study were showed as underlying firm soft tissue mass like appearance instead of frog egg-surfaced small papulovesicles and fluctuating cystic mass. Twenty-two patients (12 males (54.5%) and 10 females (45.5%)) were included. The mean age was 17.5±16.0 (yrs) and

duration of disease was 7.1±9.6 yrs. Lesions occurred in the hand (10 cases (45.5%); palmar aspect (9), dorsal aspect (1), followed by the foot (6 cases (27.3%); palmar (3), dorsal (3), lower extremities (4 cases (18.2%); shin (2), knee (1), thigh (1), upper extremities (2 cases (9.1%); wrist (1), elbow (1). Most patients were treated by surgical excision (63.6%) successfully.
Conclusion: It is important to consider small sized atypical LM caused by repeated minor trauma and distinguish LM from soft tissue mass in distal part of extremities such as hands and feet.

P130
Pediatric Head and Neck Lymphatic Malformations: Prenatal Planning and Management Strategies in the Multimodality Era

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Purpose: Lymphatic malformations (LM) frequently occur in the head and neck and can often be disfiguring and even life-threatening. Management options include observation, surgery, sclerotherapy, and sirolimus. The optimal sequence of therapeutic interventions has not been determined due to the lack of comparative clinical trials or established guidelines. Thus, prenatal planning with a multidisciplinary team is beneficial.
Methods: We present a case series of ten children with head and neck LMs evaluated in 2017 at our multidisciplinary vascular anomalies center. A chart review was performed to assess treatment modalities and recent trends.
Results: Seven of 10 patients (70%) with head and neck LMs were diagnosed prenatally. All patients were started on sirolimus at a median age of 12.5 months (range 12 days – 18 years). Four patients most recently started on sirolimus were less than 3 months of age at the time of initiation. Six patients underwent partial excision of LM during the first year of life; none of whom received sirolimus prior to surgery. Sirolimus was discontinued in one patient given chronic Clostridium difficile infections, and non-compliance in another patient. Five patients received sclerotherapy. Tracheostomy was necessary in six patients; one patient was de-cannulated after 7 months on sirolimus. All patients have had radiographic and clinical improvement of LM with various treatment modalities. Current clinical observations show improved response with sirolimus and demonstrate tolerability of sirolimus at a young age.
Conclusion: Treatment of pediatric head and neck LMs is challenging and a multidisciplinary approach is necessary. As the majority of patients are diagnosed prenatally, prenatal planning and discussion of potential use of sirolimus is beneficial. Availability of vascular anomalies experts in the prenatal/neonatal period offers the best management results, and early initiation of sirolimus should be considered for complex lesions. Long-term follow up is warranted to investigate the efficacy and timing of treatment options.

P131
Superficial lymphatic malformation of torso with homolateral breast atrophy: two cases

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Purpose: Lymphatic malformations (LM) most often correspond to cutaneo-mucousl lesions where the development of the lymphatic vessels during embryogenesis has been abnormal. We distinguish on the basis of size, macrocystic, microcystic and mixed LM. There is great variability in clinical expression and the occurrence of complications according to the topography. Hence, limb deformities, painful seizures, and other symptoms related to compression on the neighboring organs, or in relation to a sudden increase in size due to intracystic bleeding, have been reported. ML can be isolated or associated with other malformations or tumors such as limb developmental inequalities or lipomas, or other vascular malformations such as capillary malformation (CM). LM have been reported with Turner syndrome or with trisomy 18. We report 2 cases of cystic LM associated with homolateral breast atrophy. To our knowledge, this association has not been reported previously.
Methods: Case1 A 22-year-old woman had a diffuse vascular malformation affecting the torso and upper limbs (UL). She was operated at the age of 3 years of a macrocystic LM of the left axilla. On examination a hypertrophic operative scar was observed in the left axilla with a post operative microcystic LM. The contralateral UL was covered with a large capillary angioma. There was no inequality of development of the 2 UL. But there was, an atrophy of the left breast, homolateral of the LM. Pulsed dye laser sessions did not improve the capillary angioma on the right UL. A 9-month sildenafil cure combined with 2% polidocanol sclerotherapy sessions resulted in a significant improvement of LM. The ultrasound examination showed a mammary gland in place. A breast lipofilling surgery reduced the asymmetry. Case2 A 15-year-old girl was referred to our department for a microcystic LM of the right axilla. She was born with macrocystic LM of the same seat that had been operated when she was 30 months old. At the age of 4 years, a microcystic LM appeared around the operative scar. On examination, there was a large microcystic LM covering the axilla, the breast and the shoulder to the right. A treatment with sidenafil was instituted for 9 months and brought only a slight improvement. Sclerotherapy sessions with polidocanol 2% improved the lesions. Rapamycin for 1 month proved ineffective, and was interrupted after severe asthenia. Intralesional injections with bleomycin are currently underway. The ultrasound examination found a mammary gland in place. A breast lipofilling surgery is currently being precognized.

Results: The etiopathogenesis of LM is unknown. It is during the 6th week of embryonic development that the first lymph sacs emerge from the large veins of the neck. Macroscopic LM could be the consequence of the rupture of one of these sacs. Another theory considers the possibility of mutation concerning the angiogenic stem cells. These abnormal cells, instead of developing lymphatic spaces that connect to the large lymphatic channels, will develop independent lymphatic spaces that become cysts. In our two patients, mammary atrophy seems primitive and not secondary to surgery that would have carried away the mammary gland.
Conclusion: Different malformations, osseous, genital and cardiac have been reported in association with LM. But to the best of our knowledge, this is the first report of LM associated with primitive homolateral breast atrophy

P132
Expression of Embryonic Stem Cell Markers in Lymphatic Malformation

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Purpose: Lymphatic malformation (LM) affects 1:5000 births. The biology of LM is poorly understood. It is associated with significant morbidity and there is currently no effective treatment for microcystic LM especially those affecting the cervicofacial region. In this study, we investigated the expression of embryonic stem cell (ESC) markers OCT4, NANOG, SOX2, KLF4 and c-MYC in microcystic LM.
Methods: 4μm-thick formalin-fixed paraffin-embedded sections of cervicofacial microcystic LM from 10 patients were analysed for the expression of the ESC markers OCT4, NANOG, SOX2, KLF4 and c-MYC using 3, 3-diaminobenzidine (DAB) immunohistochemical (IHC) staining. In situ hybridization (ISH) and RT-qPCR mRNA analyses were performed on 4 snap-frozen samples of LM from the original cohorts of patients included in DAB IHC staining, to investigate transcriptional activation of these ESC markers. To confirm co-expression of two proteins, immunofluorescence (IF) IHC staining was performed on 4 representative LM samples from the original cohorts of patients included for DAB IHC staining.
Results: All tissue samples were confirmed to be LM by their positive staining for D2-40. DAB IHC staining demonstrated the expression of OCT4, NANOG, SOX2, KLF4 and c-MYC and IF IHC staining showed localized these ESC markers to cells in the endothelium of the LM vessels and cells within the surrounding stroma. ISH and RT-qPCR confirmed mRNA transcriptional activation for all the ESC markers investigated.
Conclusion: This study demonstrates presence of a putative OCT4+/NANOG+/SOX2+/KLF4+/c-MYC+ population within the endothelium of the LM vessels and the surrounding stroma. As to whether this primitive population represent two independent subpopulations or whether one originates from the other, requires further investigation. The novel findings of this study give insights into the biology of LM forms the basis of better targeted therapy for this challenging condition.

P133
Bone abnormalities in patients with head and neck lymphatic malformations: intraosseus lymphatic malformations and skeletal bone deformities

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Purpose: Large lymphatic malformations (LM) of head and neck may be associated with bone abnormalities, which can be divided types: intraosseus lymphatic lesion and bone deformity. The etiology of bony abnormalities related LM is not fully understood. To investigate pathological bone structure associated with LM by use of by histologic anatomy and immunohistochemistry and to prove or disprove the existence of the intraosseus LM.
Methods: evaluation of diagnostics and treatment of the 18 children with head and neck LM with bone lesions. All patients were subject to computer tomography (CT) with three-dimensional reconstruction, morphological examination of gross specimens, which includes immunohistochemistry by Podoplanin (D2-40) – lymphatic-specific marker.
Results: according to the data of CT the18 patients had abnormal anatomy of skeletal bones, such as diffuse thickening of bone, structural damage of bone tissue. According to histopathological examination the 12 patients (76.7%) presented with bone hypertrophy and bone loss. The 6 patients presented with lymphatic channels within cancellous bone (between bone trabeculas) and periosteum, which was proved with use of immunohistochemical methods, such as application of Podoplanin. Thus presense of intraosseus LM was confirmed.
Conclusion: generally bone deformity in patients with large LM are associated with bone hypertrophy and bone loss. However more rarely the intraosseus LM are occur. However more rarely the intraosseus LM are occur. Further investigation date is required. This data requires further investigation.

P134
Operative Management of Congenital Chylous Ascites

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Purpose: We describe our management of an infant with congenital chylous ascites
Methods: This is a case report done via retrospective chart review.
Results: A previously healthy, term female infant developed abdominal swelling and respiratory distress at 2 months of age. She was admitted to the ICU and paracentesis showed chylous ascites; multiple drainage procedures were required. Lymphangiogram demonstrated significantly abnormal lymphatics without visualization of the thoracic duct. No cutaneous, mediastinal, genitourinary, bone or visceral lesions were seen on imaging. Further attempts at control of her ascites included drain placement, octreotide, propranolol and restriction of enteral feeding. Her peritoneal drain output remained approximately 2 liters/day after these interventions. Sirolimus was started. An MR lymphangiogram done 3 months after initial admission was suggestive of a leak in the left lower abdomen; a normal caliber thoracic duct was seen. Intranodal lymphangiogram showed global lymphatic dysfunction. These findings were thought to be most consistent with a central collecting duct lymphatic anomaly (CCLA). Glue embolization was done of an intra-abdominal cystic structure that appeared to communicate with the lymphatic channels. Though initial decrease in drain output was seen, it slowly increased to 1 liter/day. She was then taken for diagnostic laparoscopy with pre- and intra-operative fat loading. A focal lymphatic leak was identified in the colonic mesentery by visualizing the pooling of milky fluid and was ligated with a single figure-of-eight suture; fibrin sealant was placed on this area. An intra-abdominal drain was left. The drain output decreased over the next few weeks to about 200cc per day. This slow drainage persisted for several months. Diagnostic laparoscopy was repeated at 4 months and demonstrated no leak; her drainage stopped 1 week post-operatively.
Conclusion: Operative identification and ligation of leak may be possible in some patients with congenital chylous ascites if pre-operative imaging is suggestive of focal leak.

P135
Treatment of lymphatic malformations with Haemoblock.

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Purpose: The elective treatment of lymphatic malformations in children's has been sclerotherapy with a variety of substances (OK-432, Doxycicline, Bleomicin) is being used in the last years. The aim of this essay is to present our results using sclerotheraphy with Haemoblock (Menora Laboratories, Israel).
Methods: We have reviewed all patients affected by lymphatic malformation that have been treated by sclerosis with Haemoblock (liquid, pH neutral hemostat solution). The Haemobloc forms a clot with proteins of the blood plasma (mainly albumin). When the polymer complex is formed, hemostasis occurs. Nanoparticles of silver have a pronounced bactericidal action against most known microorganisms. Each procedure sclerotherapy was performed under general anesthesia by a radiologist and a pediatric surgeon.
Results: Twenty patients aged from 6 months to 5 years are treated. The average amount of Haemoblock administered was 2 ml/kg in each procedure. After the injection of the Haemoblock into the lymphatic malformation, the drug was evacuated from the cavity. There were two complications; one of them - a large swelling of the tissues, and the other - at an elevated temperature, allowed by antipyretics and antihistamines. Analgesia was used for all patients on the first day after sclerotherapy, no other therapy was required. Sclerotherapy was evaluated after 1, 3 and 6 months. 93% of patients showed a complete response to sclerotherapy for ultrasound and MRI.
Conclusion: Sclerotherapy with Haemoblock is an effective and safe treatment for lymphatic malformation in children's specially the macrocystic ones, therefore it should be considered as first line therapeutic option.

P136
TREATMENT OF LYMPHATIC MALFORMATIONS WITH OK432 AND/OR BLEOMYCIN IN 294 PATIENTS.

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Purpose: Lymphatic malformations are infiltrative lesions and treatment can be challenging. In our institution, treatment with sessions of intralesional injection of OK432 and bleomycin is a reality and has replaced surgery as the first line treatment for microcystic and macrocystic lymphatic malformations. We decided to review this conservative treatment adopted for patients with LM who are referred to the AC Camargo Cancer Center, São Paulo.
Methods: In this study, 294 patients with lymphatic malformation treated at the Hospital AC Camargo Cancer Center, in São Paulo, from 2002 to 2017, were reviewed. All patients were submitted to sessions of intra-lesional injections of OK432, bleomycin or the two drugs, guided by ultrasound and under general anesthesia. Patients were monitored for bleomycin pulmonary toxicity and adverse effects of both drugs.
Results: We reviewed the data of 294 patients, 170 female and 124 male. The predominant anatomic location was head and neck in 182 patients (62%), followed by the trunk in 82 (28%) and limbs in 30 (10%). Two-thirds of the patients had macrocystic or mixed components and one-third only microcysts. The age at

treatment beginning ranged from 1 month to 60 years (mean = 8 years). The number of sessions ranged from 1 to 34 per patient (mean = 4.5). Two hundred ninety-four patients were treated with a total of 1319 sessions of intra-lesional drug injections. A total of 184 patients (63%) were treated with only one drug, 125 with OK432 in 418 sessions and 59 with bleomycin in 138 sessions; 110 patient (37%) were treated with both drugs, in 763 sessions. We observed variable edema and fever in the post-application period. We did not observe pulmonary toxicity or adverse effects.
Conclusion: We did not observe adverse effects or pulmonary toxicity in patients treated with bleomycin or OK432. Although not statistically confirmed, data suggest that patients treated exclusively with OK432 underwent fewer sessions than those treated with bleomycin or with both drugs. Other studies will be required to establish the effectiveness of OK432 and bleomycin in the treatment of lymphatic malformations.

P137
Complications of surgical treatment of children with an extensive mixed form of lymphovenous malformations in the head, neck, and mediastinum regions.

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Purpose: To analyze complications of surgical treatment of children with an extensive mixed form of LVM in the head, neck, and mediastinum regions.
Methods: From 2011 to 2017, 12 patients underwent a surgical treatment. The age of the children was from 1 month to 10 years. In 2 cases abnormal tissues were localized at the orbital, frontal, and infra-orbital regions. In 10 cases LVM were localized at the bottom of the oral cavity, neck, and pa-rotidomasseteric regions. Among them, the unilateral head and neck lesion occurred in 7 children, whereas the bilateral lesion was revealed in 3 patients; in 2 children abnormal tissues were spread to the mediastinum. The examination included USS, MRI, CT, laryngoscopy, as well as hemogram. Abnormal tissues were resected as complete as possible.
Results: The complications occurred in 10 patients (83.3%). These complications were divided into life-threatening, functional, and cosmetic, as well as to reversible and irreversible. The life-threatening reversible complications were in 1 patient (3%): putrefactive-necrotic cellulitis of the bottom of the oral cavity, tongue, osteomyelitis of the mandible on two sides in the settings of hypercoagulation syndrome; septic shock. Functional complications were observed in 10 patients: reversible - lymphorrhoea (5; 16%), transient facial weakness (8; 25%), swallowing difficulties (8; 25%); irreversible - Horner syndrome (2; 6%), secondary decompensated glaucoma resulted in enucleation of the eye (1; 3%). 7 children had reversible cosmetic complications: marginal necrosis of the skin flap with subsequent formation of hypertrophic scar (7; 22%). There were no fatal outcomes.
Conclusion: Reversible complications were observed in 90.6% patients. 9.4% of complications were irreversible. Based on these results, it is possible to conclude that the comprehensive pre-operative evaluation, radical removal of abnormal tissues with sparing the surrounding tissues can reduce the risk of severe irreversible complications.

P138
Verrucous Presentation of a Superficial Lymphatic Malformation

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Purpose: Verrucous hemangiomas are currently unclassified congenital vascular lesions, which grow and become hyperkeratotic over time, frequently causing pruritus, bleeding or ulceration. Historically called "hemangiomas" because of GLUT-1 positivity, recent literature suggests that these lesions are venulocapillary vs venous malformations within the dermal and subcutaneous tissue with reactive epidermal hyperplasia. This report describes a case in which a lymphatic malformation (LM) mimicked the clinical presentation of a verrucous hemangioma.
Methods: Report a case of a verrucous LM to help provide further insight into the understanding and classification of verrucous hemangiomas
Results: Our patient presented at 3 years of age with four hyperkeratotic, red-purple lesions on her right lower leg that occasionally caused pain. At birth, the patient had one flat, pink-purple lesion, which remained stable and asymptomatic until 2.5 years of age. Surgical excision of the largest lesion was

performed and pathology showed verrucoid epidermis overlying dilated malformed PROX-1 positive, GLUT-1 negative vessels within the papillary dermis, sparing of reticular dermis, and fibrotic lobules and abnormal lymphatics in the deep subcutaneous tissue. At age 7, patient returned with regrowth at prior excision site and larger, thicker lesions with pruritus and bleeding. Twice daily 1% topical sirolimus was started and stabilized growth of all but the thickest lesion, which was subsequently excised. Second pathologic specimen demonstrated abnormal lymphatics and numerous scattered capillaries throughout as well as inflammatory cells (multinucleated giant cells, plasma cells, lymphocytes). Next generation sequencing was inconclusive due to low mitotic rate.
Conclusion: This case suggests that venous and LMs within dermal and subcutaneous tissue may cause reactive epidermal hyperplasia and capillary proliferation, likely driven by chronic inflammation. Topical sirolimus appears to control lesion growth, possibly by downstream inhibition of abnormal PIK3CA activation found in some LMs or downstream inhibition of MAPK3/ERK1 as somatic mutations have been reported in venous-type verrucous malformations.

P139
Transient Hypothyroidism Following Lymphangiography Using Oil-Based Contrast (Lipiodol).

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Purpose: We report three children who developed hypothyroidism following intranodal lymphangiography using Lipiodol.
Methods: Following incidental discovery of profound hypothyroidism in an infant following lymphangiography using lipiodol, we subsequently evaluated TSH levels on two other children who had recently undergone a similar procedure and discovered abnormal TSH levels. Children were followed after thyroid hormone replacement was initiated until levels normalized.

Results: Case 1: 3-month-old premature female infant with Trisomy 21, repaired duodenal atresia, SVC syndrome, chylous effusion and respiratory failure. Two weeks following lymphangiography using 4 mL of Lipiodol (Dose 0.625 mL/kg, weight 2.5 kg), the thyroid stimulating hormone (TSH) was elevated at 322 mcunit/mL (normal 1.7-9.1) and free thyroxine (T4) was low at 0.2 ng/ml (normal 0.9-2.3) . Newborn TSH was normal. TSH and T4 normalized in < 1 week of thyroid replacement therapy. Case 2: 43-day-old premature female infant with complex heart disease, s/p arterial switch operation developed chylous effusion. 3.5 weeks following lymphangiography using 1.75 mL Lipiodol (Dose 0.1 mL/kg, weight 1.7 kg), TSH was high (470) and Free T4 was low (0.21). The levels of TSH and Free T4 normalized in < 1 week of thyroid replacement therapy. Case 3: 3 year old boy with heart transplant for progressive cardiomyopathy and persistent chylous effusion underwent lymphangiography using 4 mL of Lipiodol (Dose 0.36 ml/kg, weight 11.2 kg). TSH levels rose from 9.39 on POD 9 to 59.14 at 5 weeks. Both TSH and Free T4 levels were normalized in < 2 weeks of thyroid replacement.
Conclusion: Intranodal Lymphangiography using Lipiodol may alter thyroid function in children, particularly in low birth weight infants and neonates; even if the dose is less than the recommended 0.25 ml/kg of Lipiodol. Periprocedural monitoring of the thyroid function and early initiation of thyroid replacement therapy may be warranted.

P140
Acquired Progressive Lymphangioma (Giant Benign Benign Lymphangioendothelioma) with Deep Tissue Involvement. Case Report.

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Purpose: Lymphatic malformations are a heterogeneous group of conditions characterized by abnormal development of lymphatic vessels in the skin and other tissues. The ISSVA classifies lymphatic malformations as: cystic lymphatic malformations, generalized lymphatic anomaly, Gorham disease, lymphedema, and channel type lymphatic malformation. Acquired progressive lymphangioma (APL) is a superficial lymphatic anomaly, not specifically included in the current ISSVA classification. We present a case with very extensive and deep involvement.
Methods: A 61-year-old woman presented with a slow-growing erythemato-violaceous plaque on the right hemithorax and flank that had been previously treated with radiotherapy without improvement. The lesion measured 50 cm in its greatest diameter and caused induration and hyperhidrosis. Histopathological examination revealed an ill-defined dermal and subcutaneous lesion composed of irregular vascular spaces lined by a single layer of flat endothelial cells with no nuclear atypia or mitotic figures. Intraluminal papillary projections and solid areas of endothelial cells were not observed. Immunohistochemical studies showed positivity for CD31 and D2-40 with focal positivity for WT1. MYC amplification and overexpression, by FISH and IHC analysis, were negative. Computed tomography angiography showed a large vascular lesion involving the right thoracic and abdominal subcutaneous tissue and extending to the mediastinum and pelvis.

Results: After clinicopathological and radiological correlation, APL was diagnosed.
Conclusion: APL is an acquired and progressive superficial anomaly of lymphatic origin also referred as benign lymphangioendotelioma. In our case the involvement of deeper tissues makes differentiation from generalized lymphatic anomaly very difficult, since the latter has been suggested to be the deeper variant of the former and is possible, that our case may represent the missing link between both entities. APL has distinctive clinical entity to be maintained as a different entity although it probably represents the more superficial counterpart of generalized lymphatic anomaly and intermediate forms exist as in our patient.

P141
Experience with treating lymphatic malformations at a reference center.

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Purpose: Lymphatic malformations (LM) are developmental anomalies of lymphatic channels, found in one of every 6000 to 16000 newborns. They are further classified into macro or microcystic, according to the number and size of lymphatic chambers, or they can be mixed. These categories are relevant because treatment options and prognosis differ according to them: macrocystic LM respond better to treatment with surgery or sclerotherapy, and recur less often than microcystic. However, an ideal standard treatment for LM is still not established, several sclerosing agents are currently used. The objective of this study is to describe the results obtained in a cohort of pediatric patients with macrocystic and microcystic LM treated with sclerotherapy with alcohol and bleomycin, respectively.
Methods: This was an observational retrospective study done at a national reference hospital's vascular anomalies clinic. We included pediatric patients with the diagnosis of LM done both clinically and radiologically who were treated by an interventional radiologist with either alcohol or bleomycin sclero therapy from 2014 to 2016. Post-treatment evolution, both clinical and radiological by ultrasound at 60 and 120 days after therapy, was recorded; as well as adverse events occurring in a 3 year follow-up.
Results: We studied 38 patients with equal gender distribution: 24 had macrocystic, 10 microcystic and 4 mixed LM. Nine patients /24%) had LM located in head, 12 (31%) in neck, 10 (26%) in thorax, 3 (7%) in abdomen and 4 (11%) in extremities. All macrocystic and 2 mixed LM (68 %) were treated with alcohol, and the rest (10 microcystic and 2 mixed) with bleomycin. The response to treatment was excellent in 5 patients (90-100% decrease in size), good in 25 (50-89% decrease in size) and poor in 5 (less than 50% decrease in size). Three patients' LM continued to increase in size after treatment. No significant adverse effects were noted. The response to treatment has been sustained during the follow-up period.
Conclusion: We conclude that treatment with sclerosing agents alcohol and bleomycin are safe, effective options for macrocystic and micro cystic LM respectively; and should be considered as first-line options.

P142
Lymphatic Disorders in ISSVA 2016 Abstracts: Critical Analysis of the Terminology and Diagnoses.

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Purpose: The use of erroneous classification and incorrect nomenclature may lead to incorrect treatment and misguided research. The aim of this study is to critically analyze the accepted abstracts for the 21st International Workshop of the International Society for the Study of Vascular Anomalies (ISSVA 2016) and to determine the type and accuracy of the terminology utilized in the abstracts on lymphatic disorders.
Methods: All scientific abstracts, which are either accepted as podium or poster presentations at the ISSVA 2016 meeting, were reviewed.
Results: ISSVA 2016 meeting accepted 234 abstracts including 96 oral presentations and 138 scientific posters. "Lymphatic malformation" (n=40) and lymphedema (or lymphoedema) (n=9) were the most commonly used diagnoses. This was followed by less specific terms such as lymphatic anomalies (n=7), lymphatic disorder (n=2) and lymphatic lesion (n=1). Less commonly used were the inaccurate terms "lymphangioma" (n=3) and lymphangiomatosis (n=5). Generalized lymphatic anomaly (GLA) (n=6), Gorham-Stout Disease (GSD) (n=3), kaposiform lymphangiomatosis (KLA) (n=3) and lymphangioendotheliomatosis (n=2) were more frequently utilized than central conducting lymphatic anomaly (CCLA) (n=1). Combined malformation included "lymphovenous" (or lymphatic-venous or venous lymphatic or mixed venolymphatic malformation) (n=4), lympho-vascular malformation (n=2) and lymphedema-capillary malformation (n=1). In addition, several descriptive terms such lymphangiectasia (n=3), s lymphostasis (n=1) lymphorrhea (n=1) and superficial skin lymphangiectasia (n=1) were occasionally used.
Conclusion: The accepted ISSVA abstracts continue to use inaccurate and abandoned terms and confusing diagnoses in the field of lymphatic disorders. The authors should be encouraged to standardize and refine the use of these terms based on the published ISSVA classification.

P143
Intrinsic Lymphatic Endothelial Cell Defects: A Contributor to Secondary Chylothorax Development in Pediatric Congenital Cardiac Anomaly Patients

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Purpose: Seconday chylothoraces occur in 6.6% of congenital cardiac anomalies after surgical repair resulting in morbidities from lymphatic dysfunction: protein-losing enteropathy, immunodeficiency, and sepsis. Studies using contrast-enhanced MR-lymphangiography demonstrate lymphatic vasculature patterning defects in these patients. Mouse models demonstrate genes such as Prox1 and Podoplanin are essential for both cardiac and lymphatic development. We hypothesize congenital cardiac anomaly patients have intrinsic lymphatic endothelial defects, on a spectrum similar to lymphatic malformations, contributing to postoperative chylothorax development.
Methods: Postoperative chylothorax lymphatic endothelial cells (pcLECs; n=9), isolated from pediatric patients with secondary chylothoraces, were compared to LECs from lymphatic malformations (LMECs;n=5) and human foreskins (HdLECs; n=3). Progenitor and lymphatic endothelial (LEC) transcript and protein expression was assessed by quantitative RT-PCR and fluorescent-activated cell-sorting, respectively. pcLECs (n=2) or LMECs (n=1) were injected subcutaneously into nude mice. At 3 weeks, implants were harvested for histological analysis and immunostaining for PODOPLANIN (LECmarker).
Results: Both pcLECs and LMECs had similar expression of EC progenitor and LEC genes relative to HdLECs. Like LMECs, pcLECs had upregulation of EC progenitor genes (Cd34and Tie2) and the LEC gene (Prox1). Unlike LMECs and Hd LECs, pcLECs had decreased Podoplanin and increased Ve-cadherin expression. Despite upregulation of gene transcription, pcLECs had reduced surface expression of adhesion protein VE-CADHERIN, as well as CD31 (n=9/9). Consistent with loss of adhesion proteins, pcLECs failed to form cellular junctions in culture. Inxenograft model, pcLEC and LMECs formed dilated lymphatic channels lined by poorly associated PODOPLANIN+ pcLECs.
Conclusion: Missexpression of progenitor and LEC genes suggests pcLECs fail to properly differentiate and adhere resulting in a porous lymphatic vasculature. Thus, secondary chylothoraces may lie on a spectrum of lymphatic malformations. The inability of these abnormal lymphatics to uptake post-operative edema may contribute to secondary chylothoraces in congential cardiac patients.

P144
Therapeutic Outcomes of Manual Lymphatic Drainage in Pediatric Patients with Primary Lymphedema

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Purpose: Generalized pediatric lymphedema is primarily due to congenital malformations. Manual lymphatic drainage (MLD) via the Vodder technique incorporates superficial and deep massage to soften tissue, increase lymphatic flow, and improve functional limb performance. However, sparse literature exists discussing MLD outcomes for pediatric lymphedema. Our purpose is to quantitatively measure the effect of MLD on pediatric lymphedema based on differences in girth, weight, and functional performance before and after therapy.
Methods: Retrospective chart review was performed on pediatric patients with primary lymphedema who underwent a 1-month course of MLD between 2015-2017. Data included weight, limb girth, extremity strength, pain scores, and functional performance before and after MLD. Patients with other causes of edema (i.e. heart failure, renal failure) were excluded. Data statistics quantified the effect of MLD.
Results: 10 children with primary lymphedema who completed the MLD course were identified (median age 8 years, range 0.4-18 years). Immediately following MLD, weight reduced by 2-19%, and limb girth reduced by 4-27% in lower extremities, 0-10% in upper extremities, and 5-22% in truncal regions. More pronounced reduction was noted in the distal extremity compared to proximal regions. Validated functional questionnaires showed 50-60% improvement in limb performance. Pain scores improved by 80-100%, soft tissue softened with improved skin quality, and range of motion of affected limbs improved as noted during physical therapy sessions. Two patients had minimal improvement in lymphedema girth and range of motion after MLD and subsequently underwent sclerotherapy and lymphovenous bypass surgery.
Conclusion: Manual lymphatic drainage is not a cure, but does reduce extremity lymphedema with consistent usage. Noticeable improvements include decreased limb girth, softening of skin and tissue, and increased functional limb performance. These findings suggest that MLD can be a reliable noninvasive treatment for pediatric lymphedema until more permanent solutions are available. Large, prospective studies are needed to validate these results.

P145
Further delineation of the clinical history of Maffucci syndrome based on review of the literature and patient survey.

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Purpose: Maffucci syndrome (MS) is characterized by multiple enchondromas in combination with vascular anomalies. Its molecular basis is not completely understood. The risk of developing a chondrosarcoma is up to 57.1%. Other cancers are observed in patients with MS but their prevalence is unknown. The natural history of MS is based on the cases described in the literature and most likely represents the extreme presentation of these disorders. The purpose of this work is to describe the natural history of MS, including its clinical similarities and differences to Ollier disease (OD), the prevalence of chondrosarcomas and other malignancies, and the types of vascular anomalies found in patients with MS.
Methods: We performed review of 199 cases of MS and 162 cases of OD described in the literature and compare to the information collected by a patient survey distributed through private Facebook groups for patients with MS and OD. The survey had 84 questions and collected clinical and family history, molecular test results, and demographic information. Ninety-seven patients with OD and 29 with MS answered it.
Results: In the review and the survey, the prevalence of chondrosarcomas among patients with MS was half of previously described. In the literature, four patients with MS had vascular anomalies in internal organs only. Also, brain tumors were ~3x more common among patients with OD and benign tumors were ~4x more common among patients with MS.
Conclusion: Our findings confirm and strengthen the clinical differences between these two disorders. The survey also showed that dental anomalies and cognitive impairment may be features of OD but not MS. Venous and lymphatic anomalies may be features of MS but not OD. This comparison gave us a better understanding of the natural history, severity and prognosis of these diseases, as well as the prevalence of malignancies in patients with OD and MS.

P146
Malignant Tumors Misdiagnosed As Benign Vascular Anomalies

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Purpose: Malignant soft tissue tumors are rare and difficult to diagnose in children. These can initially be initially misdiagnosed as benign vascular anomalies. Management of these two conditions differs drastically and delay in diagnosis may impact overall survival. The purpose of this study is to predict qualities that may increase the index of suspicion for malignancy in patients presenting with lesions initially considered vascular anomalies.
Methods: A retrospective review at a quaternary Hemangioma and Vascular Malformation Clinic of all patients who presented between 2008 and 2016 with an initial diagnosis of a benign vascular malformation, which on further work up was noted to be a malignancy. Demographics, clinical presentation, laboratory and radiologic studies were analyzed.
Results: 11 patients were identified; the median age at presentation was 2 months (0-24years). The timing of final diagnosis was not associated to patient demographics. 10/11 lesions had rapid growth which prompted biopsy. Pain was an inconsistent finding (36%). Tumor markers were positive in only 1 case. Median follow up was 3 years (± 1.7years), 7 patients have no evidence of disease, 2 patients are under treatment for progression or relapse of disease and 2 patients have died.
Conclusion: Although malignant vascular tumors are rare, a clear index of suspicion needs to be maintained particularly with rapid growth or increasing symptoms. Differentiation of malignant tumor from benign lesions relies on the comprehensive evaluation of clinical manifestations and evolution of the lesion by an experienced multi-disciplinary vascular malformation team. A low threshold for biopsy of unclear vascular lesions should be practiced.

P147
Malignancy mimicking Hemangioma or congenital Vascular Malformation

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Purpose: In most of the imaging studies (ultrasound and MRI) made for hemangiomas and vascular malformations there is no problem to differentiate them from malignant tumors. In a center with good experience in diagnostics and therapy in almost every case there is no doubt about the vascular origin of the tumor. Therefore we present two cases with a fatal misdiagnosis:
Methods: First: A 7-year-old girl with a supposed vascular malformation in the dorsal lower leg. The operative resection revealed a much more solid tumor than suspected. So the resection was extended to the gastrocnemic and soleus muscles. Even though a rhabdomyosarcoma was detected, which extended over the border of the resection. Second: A 2 month-old girl with a suspected hemangioma in the right neck.

Intraoperatively we found a much more solid tumor with contact to the plexus brachialis, which could be resected completely. Histological diagnosis: Neuroblastoma without metastases. In both cases oncologic therapy and follow-up was initiated.
Results: We studied reports and reviews to this aspect and found other singular cases.
Conclusion: Even with precise preoperative workup, there is a risk of missing the diagnosis of malignant tumors mimicking hemangiomas or vascular malformations.

P148
Vascular anomaly mimicking lesions on the radiological imaging: a case-based review

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Purpose: To present a case-based review of vascular anomaly mimicking lesions. The diagnosis of vascular anomaly is based on history, physical examination, and radiologic imaging. Radiological imaging plays an essential role in the management of vascular anomalies, such as diagnosis, evaluation of the lesion's extent and therapeutic planning. Sometimes, a biopsy is necessary to exclude tumorous condition or other non-vascular anomaly lesions.
Methods: We reviewed radiological imaging of lesions, which were misdiagnosed with vascular anomaly and ultimately pathologically diagnosed with soft tissue tumor between July 2015 and November 2017. We also reviewed radiological imaging of lesions, which were misdiagnosed with soft tissue tumor and ultimately pathologically diagnosed with a vascular anomaly.
Results: We discovered 12 cases, which were initially diagnosed with a vascular anomaly based on radiological imaging, and ultimately diagnosed with benign or malignant soft tissue tumor by biopsy. The pathologic diagnoses were neurofibroma, B-cell lymphoma, hemangioma, hematoma, ganglion cyst, tenosynovitis, hibernoma, and unspecified benign tumor. There were 6 cases with equivocal radiological findings and diagnosed with vascular anomalies by biopsy.
Conclusion: Radiological imaging plays an important role in the diagnosis of vascular anomaly. However, vascular anomaly mimicking lesion should be managed by the multi-disciplinary approach, and soft tissue tumor needs to be ruled out by biopsy for the appropriate treatment.

P149
Vascular anomalies as possible skin markers of occult spinal dyrsaphism.

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Purpose: Lumbosacral cutaneous markers may be present in children affected by occult spinal dysraphism (OSD). Guidelines for risk evaluation of skin markers are lacking. The aim of this study is to evaluate the prevalence of the vascular anomalies in a group of children with OSD and propose different class of risk for OSD.
Methods: We enrolled 271 patients (122 male and 149 female), ranging in age at diagnosis from 1 month to 18 years, in the period from January 2006 to April 2016. We analyzed the presence of cutaneous markers and the correlation between skin markers and age of diagnosis. We also divided cutaneous lesions into four categories according to the supposed risk of OSD: absent, low, intermediate or high. A literature review of skin markers in OSD and syndromes with segmental infantile hemangiomas (IHs) and OSD was performed and the vascular lesions were reclassified considering the updated unified nomenclature of vascular anomalies.
Results: Cutaneous markers were found in 152 patients (56%). IHs were observed in 10 cases, as single lesion in 80% of patients, combined with other lesions in 20% of patients. Capillary malformations were found in 25 patients, as single lesion in 84% of cases, combined with other lesions in 16% of cases. A statistically significant correlation was found between time to diagnosis and the presence of skin markers.
Conclusion: Both IHs and capillary malformations on lumbosacral region may be markers of OSD. Focal IHs<2,5 cm may not be considered a marker of OSD, capillary malformations may be considered low-risk lesions, focal IHs>2,5 cm intermediate risk lesions, segmental IHs high-risk lesions. The presence of intermediate or high-risk lesions, low-risk lesions in the presence of symptoms or a combination of two or more skin markers requires magnetic resonance imaging. The multidisciplinary assessment of lumbosacral cutaneous lesions is mandatory to perform a prompt treatment.

P150
ATYPICAL VASCULAR LESIONS AFTER RADIOTHERAPY. REPORT OF 2 CASES.

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Purpose: We report 2 patients with previous medical history of breast cancer, having receiving combined treatment, including radiotherapy. Both of them developed atypical vascular lesions (AVLs) within the radiated field.
Methods: We reviewed their clinical histories and histological studies.
Results: Case 1: 41-year-old woman with previous medical history of left breast carcinoma (mastectomy, lymphadenectomy and radiotherapy 7 years ago, followed by hormonal treatment). A 1cm brown-yellowish rubbery lesion was incidentally observed on the left breast. A punch biopsy showed, within the dermis, dilated irregular vessels lined by a single layer of endothelial cells with slight atypia and hyperchromatism, leading to the diagnosis of atypical vascular lesion. Case 2: an 80-year-old woman with bilateral breast carcinoma (left breast: 14 years ago: mastectomy, lymphadenectomy, radiotherapy, chemotherapy, and hormonal treatment; right breast: 8 years ago: tumorectomy, lymphadenectomy, radiotherapy and hormonal treatment), was referred for consultation due to erythema and slight tenderness on the left breast. Physical examination showed a sclerotic plaque with overlying telangiectasias. Histologically, irregular and dilated vascular spaces, lined by minimally atypical endothelial cells were evidenced within the dermis. Atypical vascular lesion diagnosis was made.
Conclusion: Atypical vascular lesions may occur on the field of previous radiotherapy. Although, in general, AVLs have a benign behaviour, it has been suggested that they are part of a continuum and precursors of angiosarcoma (AS). In fact, correct differentiation between AVL and AS may be a challenge due to several degrees of histologic overlapping. Therefore, recognition of the AVL and its differentiating features from AS are of paramount importance. There are no standard guidelines for the management of AVLs. Complete excision with negative margins is a prudent approach. Moreover, close follow-up and re-biopsy any new suspicious lesions within the radiated area are necessary.

P151
Evaluating Vascular Malformations using the ISSVA-classification

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Purpose: Our objective was to analyse the frequency of consensus between medical doctors and radiologists in diagnosing a presumed vascular malformation. We furthermore analysed the frequency in using the ISSVA classification by both physicians.
Methods: As a golden standard we obtained a diagnosis based on clinical presentation and follow-up made in retrospect by expert team X of a university medical center, following the lat-est ISSVA classification of 2014. This diagnosis was re-evaluated for paediatric patients with presumed vascular malformations referred to expert team X between January 1991 and June 2015. Patient data were analyzed using medical records and imaging studies. Only imaging data of the first radiological requests to evaluate diagnosis and with a final concluded diagnosis by the radiologist, were analyzed.
Results: In total 355 vascular malformations were diagnosed by expert team X following ISSVA 2014 (table1). Radiology was performed in 309 (87.0%) lesions, of which 212 for a first diagnostic pur-pose (59.7%). Radiological imaging techniques used for evaluation are represented in table 2. In 175 (83.0%) evaluated first imaging requests, the radiologist was also able to suggest a diagnosis . In 109 lesions (62.3%) clinical diagnosis before imaging was corresponding with the diagnosis after imaging. The ISSVA 2014 classification terminology was used in 124 (70.9%) first radiology requests and in 143 (81.7%) imaging diagnoses.
Conclusion: Despite the historical perspective of 25 years, the evolution of the ISSVA classification during these years and evaluating the first imaging request, this study shows that in 62.3% of the evaluated vascular malformations clinical and radiological diagnosis were corresponding. Also in this expert team of medical doctors and radiologists there are still opportunities for improvement in using the ISSVA classification in the diagnostic process of vascular malformations.

P152
Comparison of ICD-11, Orphanet and ISSVA Classification systems for vascular anomalies: call for standardization and unification of nomenclature

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Purpose: To compare the three current classification systems for vascular anomalies: The ICD-classification (1948; WHO) is the most common international standard for reporting diseases and health conditions. ICD-11 is in the Beta Phase for comments and change proposals. The ISSVA classification (1996;last updated in 2014) is specific for vascular anomalies and based on the classification of Mulliken and Glowacki in 1982. Orphanet codes (1997; French Ministry of Health and National Institute of Health and Medical Research INSERM) will be used by the European Reference Networks (ERNs) for Rare diseases, including VASCERN, for rare multisystemic vascular diseases. The VASCERN Working Group has begun revision of the vascular anomaly Orphanet codes with INSERM.
Methods: "Hemangioma" was chosen as an index diagnosis for the comparative evaluation, because it is commonly applied to describe any type of vascular anomaly. "Hemangioma and Haemangioma" was used as a search term in these databases to measure the number of diagnostic codes available.
Results: The diagnostic codes or synonyms for "hemangioma or haemangioma" are shown in Table 1

	Hemangioma	Hemangiomatosis	Hemangioma+syndrome	Total
ICD-11	27	1	1	29
Orphanet	12	2	6	20
ISSVA	9	0	3	12

Use of the term "hemangioma" to describe vascular anomalies with a different pathologic basis was present in both Orphanet and ICD-10 under multiple codes.
Conclusion: A total of 29 diagnostic codes in ICD-11, 20 in Orphanet and 12 in the ISSVA classification systems are currently available for the diagnosis of "hemangioma or haemangioma." Disparities between terminology and pathologic basis are also highlighted. In order to secure high quality of diagnoses, clinical care and epidemiological figures international collaboration between ISSVA and the VASCERN Working Group is necessary to update, clarify and standardize the current nomenclature of vascular anomalies.

P153
Pain in Head and Neck Extracranial Vascular Malformations

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Purpose: There are patients with extracranial vascular malformations who have significant pain. We reviewed our patients with lymphatic, venous and AV malformations to determine what the incidence was.
Methods: We reviewed the medical records of the senior author's patients which included, 71 Lymphatic malformations, 205 Venous Malformations, and 158 AVMs. Most of these patients have been followed for more than 5 years. We looked at the extent and location of the malformations and other factors which appeared to be associated with their pain, such as infection or treatment.
Results: Of the 71 Lymphatic malformation patients, only 2 patients complained of significant pain and it was always associated with some type of infection and swelling of their malformation. Treatment with steroids and antibiotics usually resolved the pain. Of the 205 Venous malformations, there were 9 patients who had significant pain and 7 of those patients had Venous malformations involving the temple and/or periorbital areas. Three of these patients had severe pain requiring large doses of narcotics daily to control their pain. Surgical resection of the malformation and Trigeminal nerve branches to those areas was performed and their pain was controlled. Two of the Venous malformations had involvement of their brachial plexus. Pain was resolved after resection. Of the 158 AVM patients, only 6 patients had significant pain and they all had extensive facial disease or tongue involvement with ulcerations.
Conclusion: Facial pain is not common in vascular malformations. Patients with Venous malformations, expecially when involving the temple or periorbital areas, are the most likely to have problems with pain. When pain is present, it can be severe, requiring significant narcotics to control the pain. The senior author has found that excising the branches of the Trigeminal nerve innervating the area of pain can help control the pain.

P154
A Patient-Friendly Internet Resource about Vascular Anomalies: Meeting Patients at Their Reading Level

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Purpose: The purpose of this study was to evaluate current online patient education resources about vascular anomalies, and to create an improved resource with comprehensive diagnosis and treatment information written at the 7th grade reading level, with patient-friendly illustrations depicting vascular anomalies.
Methods: A 2016 study of 30 online resources about vascular anomalies, including those from several leading medical institutions, revealed none of these resources adequate for patient use, being written well above the recommended reading level for patient education of 6th to 8th grade, measured using Flesch-Kincaid Grade Level (FKGL). Diagnostic and treatment information about vascular anomalies was gathered from texts published by several experts in the field. The text was rewritten using simple words, shorter sentences, and well-defined and consistently-used abbreviations; it was then evaluated using FKGL. Medically accurate and patient-friendly illustrations were created to accompany the text.
Results: According to the 2016 study, the average reading level of online resources about vascular anomalies estimated by FKGL was 12; only one website was scored at less than 9th grade level. Only one resource featured illustrations, two images. This new web resource, which includes a comprehensive page for each of the major vascular anomalies, has a combined word count of 7217, with an FKGL of 7.5 (7th grade level), and thirteen illustrations, including patient-friendly diagrammatic explanations of problematic vasculature; these illustrations are the first of their kind.
Conclusion: Comprehensive information about vascular anomalies maintains some inherent complexity; oversimplification of diagnostic and treatment information may sacrifice the quality of the information. However, improving the readability of health resources is possible, broadening the spread of health information, and should be the aim of health providers.

P155
The HEVAS-Signal bank; information about infantile hemangioma from the perspective and experience of patients and parents; A pilot study.

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Purpose: In vascular anomalies, patient-registries are an important means to collect data. Data are generally gathered from physicians' perspective. The question is, whether this information is complete; is the professional view all-encompassing and without omissions? Purpose of the study is to analyze data collected by patients who have (had) an infantile hemangioma (IH) themselves or by their parents. Can adequate, new data on IH, (natural) course of IH, impact and long term (treatment) effects of IH be acquired? As propranolol changed making treatment-decisions significantly, we will gather data concerning IH severity, impact/quality of life, (long-term) safety and efficacy of propranolol and relate them to treatment-decisions.
Methods: The national patient organization on vascular anomalies (HEVAS) has taken the initiative to launch 'a SIGNAL BANK' on IH, in cooperation with an IH-specialist from one of the largest expert centers in Europe. Questionnaires on patient signals were compiled and content was discussed and completed in several focus groups of (parents of) IH patients. These questionnaires were subsequently transposed into an online registry (Castor, meeting GCP-standard) in which a patient/parent can upload his or her data. Different lists have been created: for children in the active phase of the IH; follow-up lists (every six months until the age of four years) and for adult IH patients or patients who are no longer treated. By means of pilot, part of the data will be collected by using the FAIR-principle: Findable, Accessible Interoperable, Reusable. The questionnaires have been put online via the website of HEVAS; being announced through social media and flyers at the Preventive Child Health Care clinics.
Results: Data are being collected.
Conclusion: We hope to conclude that patient-supported data will give valuable information beyond the scope of the physician, especially on impact of IH with which better direction can be given to treatment-decisions.

P156
An International Evaluation of Internet Based Patient Resources for Benign Vascular Tumours

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Purpose: Patient information has proven to improve health outcomes and provide patients with better control of their disease(s). Health literacy is recognized as a significant predictor of health status. Current resources on vascular tumours disseminated to patients continue to lack essential information and remain above the general population's reading level (eighth grade). The purpose of the study is to review Internet-based patient resources to understand areas requiring improvement, and to assess their readability level.
Methods: The search strategy included Ovid MEDLINE, EMBASE (1966-2017), and World Wide Web resources on benign vascular tumours. Any material that contained information on vascular tumours intended for

patients, accessible by patients, or pertaining to patient education was included and analyzed using the validated DISCERN tool. An overall DISCERN score of four or higher indicated a good quality resource. The Flesch Reading Ease formula was used to evaluate readability.
Results: A preliminary total of 35 resources were analyzed. Three studies and eleven websites (32 unique website links) were included. Eight websites originated from major children hospitals in the United States, United Kingdom, and Canada. The overall DISCERN rating for the patient resources was 1.7±1.1, with only four good quality resources. The clinical course, signs and symptoms, diagnostic modalities, and treatment options were almost consistently included. The majority of resources lacked additional sources of support, treatment mechanisms, treatment benefits and risks, support for shared decision-making, and information beyond the basics. The mean Flesch score was 28±20 and correlated to a college-level readability.
Conclusion: A review of patient resources for vascular tumours demonstrated that the majority of resources were not comprehensive and written to a college level readability. Combined efforts should be placed on standardizing the quality and quantity of information provided to patients. Future efforts should concentrate on assessing patient information for uncommon vascular malformations, which have even less available information.

P157
Congenital disseminated pyogenic granuloma treatment with sirolimus and propranolol

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Purpose: We introduce a new case of a rare entity known as Congenital Disseminated Pyogenic Granuloma (CDPG).
Results: Male, six days old, showing multiple skin lesions with vascular appearance and generalized distribution. Some lesions were reddish simil hemangiomas, other violaceous, and other violaceous - blackish and crusted on its surface. On the first day of life, he also presented pulmonary hemorrhage and respiratory difficulty. On his third day of life, he suffered from an episode of seizures. A nuclear magnetic resonance image of the brain showed multiple subcortical and deep bilateral and asymmetric lesions. Abdominal ultrasound and abdominal CT revealed three vascular liver lesions. Pathology examination was compatible with congenital GLUT 1 negative hemangioma. During the first week of hospitalization, some lesions decreased in size while others clearly increased. Some new lesions appeared and we started treatment with propranolol and corticosteroids. After fifteen days of life, we started treatment with sirolimus, we continued with propranolol and slowly decreased corticosteroids. After 6 months of treatment, the disappearance of almost all the skin lesions, cerebral involvement, and the evidence of a frank decrease in hepatic lesions led us to interrupt the administration of sirolimus and to continue with propranolol.
Conclusion: Currently there is reference of only five cases with CDPG. Our case is the only one treated with sirolimus and propanolol. After six months of treatment, we obtained an excellent response with almost total resolution of skin, brain and liver lesions. We cannot assure that propranolol and / or sirolimus were the cause of the involution of the lesions, versus the evolution of the disease itself. It is important to recognize CDPG as a differential diagnosis from other entities such Multifocal Hemangiomatosis, or Multifocal Lymphangioendotheliomatosis with Thrombocytopenia. Further publications will be necessary to clarify these doubts and to learn more about this infrequent entity.

P158
Expression of Components of the Renin-Angiotensin System in Pyogenic Granuloma

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Purpose: Pyogenic granuloma (PG) is a relatively common benign vascular tumour, compromised of hyperplastic vessels and a fibromyxoid stroma. Stem cells has recently been reported in PG, with a subpopulation localised to the endothelium and another localized to the stroma. Components of the renin-angiotensin system (RAS): pro-renin receptor (PRR), angiotensin converting enzyme (ACE), angiotensin receptors 1 (ATIIR1) and 2 (ATIIR2), have been proposed to be crucial for the proliferation of stem cells within infantile haemangioma. In this study, we investigate the expression of these aforementioned components of RAS in PG.
Methods: 4μm-thick formalin-fixed paraffin-embedded sections of PG from 10 patients were analysed for the expression of PRR, ACE, ATIIR1 and ATIIR2, using 3, 3-diaminobenzidine (DAB) immunohistochemical (IHC) staining. NanoString mRNA analyses was performed on 4 snap-frozen samples of PG from the respective original cohorts of patients included in DAB IHC staining. To confirm co-expression of two proteins, immunofluorescence (IF) IHC staining was performed on 4 representative samples of PG from the original cohorts of patients included for DAB IHC staining. Cells derived from 4 PG samples were analysed using RT-qPCR for the expression of the same components of the RAS.

Results: All PG samples demonstrated the presence of ACE, ATIIR1 and ATIIR2 on the endothelium of the microvessels. PRR was expressed by the ACE+ endothelium as well as cells within the stroma. Nanostring and RT-qPCR confirmed the presence of mRNA for all the components of the RAS investigated in both the PG tissues and PG-derived cells.
Conclusion: This study demonstrates the expression of components of RAS: PRR, ACE, ATIIR1 and ATIIR2 by the endothelium of PG. PRR was also expressed by cells within the stroma. This study offers novel insights into the biology of PG, and potentially novel targeted therapy for PG by modulating the RAS.

P159
Clinical Observation on 52 Cases of Phakomatosis Pigmentovascularis

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Purpose: Phakomatosis pigmentovascularis (PPV) is a rare disorder characterized by the association of widespread capillary malformation and pigmented nevus. This study aims to determine the clinical characteristics of PPV and evaluate treatment outcomes.
Methods: We conducted a retrospective chart review of 52 PPV cases from 2003 to 2017.
Results: The patients' female-to-male ratio was 1.7 : 1, and the patients' age at the first visit ranged from 0 to 47 years (mean 4.2 years). The most common classification was type IIa (76.9%). Blue sclera (28.8%) was the most common extracutaneous finding followed by glaucoma (25.0%). There were no extracutaneous findings in 44.2%. Sturge-Weber syndrome was diagnosed in 9.6%. Capillary malformation was most commonly present in head and neck (84.6%) and pigmented nevus was in trunk (80.8%). The patch pattern without midline separation was the most common mosaicism pattern in both of capillary malformation (65.4%) and pigmented nevus (82.7%). The extent of capillary malformation and pigmented nevus were 25 ± 3 % and 21 ± 3% of total body surface area, respectively. There was not a significant relation between skin lesion extent and the internal organ involvement. Capillary malformation was nearly cleared in 28.6% by pulsed dye laser. Pigmented nevus was nearly cleared in 23.7% and completely cleared in 42.1% by Q-switched Nd:YAG laser. Large capillary malformation and pigmented nevus tended to reduce the treatment efficacy respectively ($P < 0.05$).
Conclusion: This study which is the largest PPV case series confirms that clinical features of PPV. Capillary malformation is more resistant to treatment than pigmented nevus. The extent of skin lesion has a negative correlation with the treatment efficacy.

P160
Low Risk of Embryonic Cancer in PIK3CA-Related Overgrowth Spectrum: Impact on Screening Recommendations.

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Purpose: The PIK3CA-Related Overgrowth Spectrum (PROS) encompasses various conditions caused by mosaic activating mutations in the PIK3CA gene (Klippel-Trénaunay, CLOVES, MCAP syndromes). PIK3CA somatic mutations are frequently involved in various cancer types. Some overgrowth syndromes are associated with an increased risk of Wilms' tumour warranting screening and surveillance. In PROS, even though the risk of cancer is unknown, abdominal ultrasound monitoring every 3 months has been recommended. We aimed to determine the risk of cancer in patients with PROS in order to evaluate the relevance of surveillance recommendations.
Methods: Data from 130 patients with a post-zygotic PIK3CA mutation in affected tissue were analysed using a retrospective questionnaire focusing on surveillance modalities and occurrence of cancers.
Results: Clinical data were available in 110 patients (84.6%). Among them, 101 (92%) underwent iterative clinical examination. Median age at last visit was 7 years and 9 months (range: 5 months-52 years). Initial routine screening at diagnosis was performed for 44 patients (40.0%). Among them, 37 patients had abdominal ultrasonography alone or in conjunction with MRI or CT-scan. Iterative abdominal imaging was performed in 35 patients (31.8%). No routine imaging for cancer screening was done in 54 patients (53.5%). Only two patients developed a cancer (1.8%): one gastric adenocarcinoma at 52 years old as a consequence of atrophic gastritis due to Helicobacter Pylori and one nephroblastoma of left kidney diagnosed on annual abdominal ultrasonography.
Conclusion: Only six cases of Wilms' tumour on 431 patients with PIK3CA mutation have been reported so far (including our cohort). A systematic review of the literature showed no increased risk of nephroblastoma in Klippel-Trénaunay and MCAP syndromes. The risk of cancer in PROS appears therefore lower than that of other hypertrophic syndromes. It may depend on the extent of tissue mosaicism. There is insufficient evidence to recommend routine abdominal imaging in PROS

P161
Immunohistochemical profiling in PROS (PK3CA related overgrowth spectrum)

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Purpose: The aim of this study is to evaluate immunohistochemical profile in PROS.
Methods: We studied blood samples and affected tissue sections of 20 patients with clinical diagnosis of PROS undergoing fenotypic profile (macrodactyly to Cloves syndrome). Genetic diagnosis was performed with Next Generation Sequencing (NGS) with a panel of genes from ISSVA classification of mutations involved in vascular anomalies. Histologic and immunohistochemical study was performed on tissue looking for common markers of vascular characterization and PIK3/AKT/mTORC1 pathway related.
Results: In our cases we confirmed the maintenance of the typical immunohistochemical profile of the vascular malformation in endothelial cells (CD31 + and WT-1 - in all vascular anomalies and D2-40 expression in lymphatic malformation) except for a loss, partial or complete, of CD34. On the other side we were not able to find immunohistochemical expression of markers at the end of the pathway PIK3/AKT/mTORC1, such as MDM-2, p16, p21, p53 and ciclin D in the stromal and vascular compartments.
Conclusion: In histological examination the decrease of CD 34 expression in the endothelial cells of pathological tissues could suggest a PROS diagnosis to be confirmed by genetic analysis. On the other hand absence of MDM-2, p16, p21, p53 and ciclin D could support the hypothesis that low percentage of PK3CA alone could induce overgrowth, while high percentage of PK3CA or association with other mutations could induce neoplastic development.

P162
Spine deformities in patients with CLOVES syndrome

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Purpose: The acronym CLOVES was given on a heuristic basis to stand for congenital lipomatous overgrowth (CLO), vascular malformation (V), epidermal nevi (E), and scoliosis and spinal deformities (S). It is a sporadic malformational syndrome that has been first described in 2007, and in 2009 the letter S added since all patients have skeletal deformities.
Methods: We report 7 cases of CLOVES syndrome in children aged 3 month 12 years. All patients were examined for scoliosis, looking for spinal asymmetry, shoulder, and waist imbalance. Imaging studies include plain x-rays (radiography) of the spine, magnetic resonance imaging (MRI) of the chest, abdomen, pelvis, spine and limbs and ultrasound for vascular anomalies and kidneys.
Results: In our patients CLOVES syndrome initially diagnosed as Proteus syndrome (n=3), chest infantile hemangiomas (n=1), Klippel-Trenaunay syndrome (n=2), multiple chest lipomas (n=1). Chest asymmetry due to lipomatous mass, slow flow vascular malformations, and scoliosis revealed in all patients. On x-ray wedge-shaped vertebrae was found in 3 patients. On MRI visualized paraspinal disorders, that is fatty masses (n=3), venous malformations (n=2), microcystic lymphatic malformations (n=2), macrocystic lymphatic malformations (n=1). Fatty infiltration of the erector spine muscles causes the muscular imbalance and worsens the course of scoliosis. Secondary extrinsic pulmonary restriction (caused by scoliosis) appeared in a 12 year old girl. Before special treatment of scoliosis we performed soft tissue debulking (n=3) and percutaneous treatment of vascular malformations (n=2). Bracing is less effective than for idiopathic scoliosis; however, it can be useful for curves between 20 and 40 degrees. In two patients with chest venous malformations bracing was combined with compression garments. Dilated anomalous conducting trunk veins can be a source of lethal pulmonary emboli. Chest compression reduces abnormal veins space and prevents blood clots.
Conclusion: Spine deformities in patients with CLOVES syndrome is also multifactorial and can be difficult to manage. Using a combination of back brace and compression garments is promising for these patients.

P163
Proteus Syndrome: Study of 20 Cases and Protocol for Ultrasound Doppler Diagnosis

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Purpose: Proteus Syndrome (PS) is an extremely rare disorder characterized by overgrowth of various body tissues. It is caused by a mosaic mutation in the AKT1 gene. PS may affect bone, connective tissue, fatty tissue, skin, central nervous system, and internal organs. The main characteristic is disproportionate asymmetric limb overgrowth with partial gigantism. Vascular malformations are common, impairing capillaries, veins, and lymph vessels. A skin lesion known as cerebriform connective tissue nevus is often found on the sole of the foot. The spine may be affected, resulting in scoliosis. PS complications include deep vein thrombosis and pulmonary embolism. Affected individuals also have a predisposition to develop tumors, most of which are benign. The purpose of this study is to report clinical and sonographic findings encountered in PS.

Methods: Between September 2009 and July 2017, 20 patients with a clinical diagnosis of PS (ages ranging from 8 months to 56 years old; 65% women) were examined. An Ultrasound Doppler protocol using high-frequency linear transducers (5-12Mhz) was developed to optimize the study of the vascular anomalies.
Results: Clinical findings: Increase in limb length and volume (100%); Port-wine skin patches (90%); Lower limb lesions (45%), Upper limb lesions (5%), Lower and upper limb lesions (50%); Number of affected limbs: two (40%), three (35%), one (15%), four (10%); Main deformity: foot (55%), hand (30%), foot and hand (25%); Thickening of the sole of the foot (90%), Scoliosis (40%); Partial gigantism (10%); and isolated macrodactilia (10%). Sonographic findings: Femoral vein hypoplasia (72%); Lateral marginal vein (72%); Venous aneurysm (37%); Persistent sciatic vein (28%); Thrombosis (25%); Saphenous vein hypoplasia (24%); Lymphatic cysts (20%); Arteriovenous fistula (20%); Popliteal vein hypoplasia (10%); and pulmonary thromboembolism (10%).
Conclusion: The appropriate US-Doppler protocol enables the morphologic and hemodynamic evaluation of complex vascular malformations, which is indispensable in the therapeutic planning and treatment of PS.

P164
The role of immunohistochemistry of PROX-1 in differential diagnosis of venous malformation and lymphatic malformation with no diagnostic superficial stigma

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Purpose: Venous malformation (VM) and lymphatic malformation (LM) or lymphovenous malformation (LVM) are types of vascular malformation that often tend to be confused unless they have a diagnostic feature on the surface like so-called frog eggs. The purpose of this study is to investigate the usefulness of lymphatic endothelial cell markers such as D2-40 and PROX-1 for the differential diagnosis of VM and LM/LVM.
Methods: A retrospective study has been conducted based on the medical records of VM, LM/LVM patients of subcutaneous or muscular lesions who underwent biopsy specimen with IHC D2-40 and PROX-1 from November 2013 to December 2017. We compared the initial clinical and/or radiologic diagnosis with the final pathological diagnosis, and identified cases of changes in diagnosis. Patients who had definite surface diagnostic features or image findings for accurate diagnosis such as arteriovenous malformation, verrucous hemangioma, port-wine stain, targetoid hemosiderotic hemangioma, hemolymphangioma, Klippel-Trenaunay syndrome and etc. were excluded.
Results: Of the total 248 patients with VM or LM/LVM, 96 patients remained after excluding patients who had definite surface diagnostic features. As a result of expression of lymphatic endothelial cell markers, 31 of 96 (32.3%) patients' final diagnosis were changed from VM to LM/LVM in 28 cases or from LM/LVM to VM in 3 cases. Among these 31 cases, diagnosis was not changed by D2-40 positivity alone, but diagnosis was changed in 16 cases by PROX-1 positivity alone (51.6%) and in 15 cases by both (48.4%). The diagnostic changes were more frequent in intramuscular type (39.0%) than subcutaneous & dermis type (27.3%).
Conclusion: It is important to identify the expression of lymphatic endothelial cell markers like D2-40 and especially PROX-1 in the differential diagnosis of VM and LM/LVM. And it may provide important guidance in determining the treatment regimens for vascular malformation.

P165
Temporal Evolution, Management and Outcomes of Fast Flow Vascular Anomalies in PTEN hamartoma syndrome.

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Purpose: To review the temporal evolution, management and outcomes of fast flow vascular anomalies (FFVA) in patients with PTEN hamartoma tumor syndrome (PHTS).
Methods: A retrospective review of 26 patients (10 males) in the age range of 1 to 18 (median 9) years diagnosed with PHTS (on the basis of heterozygous germline mutation or clinical criteria) at a tertiary care pediatric hospital between October 2002 and August 2017 revealed 5 patients with FFVA. Imaging (ultrasound, MRI, angiography), management (medical, surgical, interventional radiology), treatment complications and outcomes were reviewed.
Results: Five patients presented with FFVA within PTEN hamartoma of soft tissue tumor (PHOST). During a median follow-up of 7 (range: 3-13) years, ultrasound and MRI performed for recurrent pain, showed progressive increase in size of PHOST and development of new FFVA within existing PHOST in 3/5 patients. Medical management included pain medications, oral sirolumus, physical and psychiatric therapy. Surgical excision of PHOST in one patient resulted in recurrence within 3 months. Between 4-24 (average 1.5/year) embolization procedures were performed per patient. An average of 3 procedures/ FFVA were performed for initial staged occlusion and 3 procedures/ FFVA for recurrence. Pain related to tissue ischemia secondary to FFVA responded well to embolization. Pain secondary to PTEN hamartoma responded poorly to both trans-arterial embolization and percutaneous sclerosant injection but demonstrated improvement with sirolimus. There was no correlation between serum levels of sirolimus and the frequency and timing of recurrence of FFVA or PHOST. Complications included migration of sclerosant into digital arteries (n=1), subclavian vein occlusion due to glue migration (n=1) and intra-procedural premature ventricular contractions (n=1).

Conclusion: FFVA in PHTS are part of PHOST and present with recurrent pain requiring life-long management with a multi-disciplinary team. Pain due to FFVA responds to embolization and pain due to hamartoma responds to sirolimus.

P166
Quality of life in patients with vascular malformations; comparison with the background population.

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Purpose: There is limited knowledge about health-related quality of life (HRQoL) in patients with vascular malformations outside the central nervous system. The aim of our study was to assess HRQoL in this patient group, and to compare the results with data from a national reference population.
Methods: 112 consecutive patients referred to the national vascular malformation center from September 2010 to December 2011 were included. Patients' HRQoL was assessed using the Short-Form 36-item questionnaire (SF-36), which is a validated questionnaire with eight multi-item scales. The results were compared with national reference values published in august 2017 (n=2107). Differences in SF-36 score between the two groups were analyzed with independent samples t-test. The results were adjusted for age and gender by linear regression.
Results: The cohort consisted of 47 males (42%) and 65 women (58%). The median age was 27 years (range 12-63). 93 patients (83%) were diagnosed with venous malformations and 9 patients (8%) with arteriovenous malformations. 10 patients had other types of malformations (9%). The patients scored significantly lower on the SF-36 scores for all multi-item scales, except for General health (GH), compared to the reference population (physical functioning (PF) 79,9 vs. 86,3; social functioning (SF) 79,5 vs. 87,2; role-functioning physical (RP) 58,0 vs. 75,5; role-functioning emotional (RE) 76,5 vs. 88,3; mental health (MH) 75,4 vs. 80,8; vitality (VT) 52,6 vs. 59,3; bodily pain (BP) 56,4 vs. 64,9 (all $p<0.01$); GH 68,5 vs. 71,5 $p=0.154$). When adjusted for age and gender, the differences remained statistically significant in all item scales, except for MH and VT. For GH, the difference was significant when adjusted for age and gender.
Conclusion: Our data revealed that patients with vascular malformations outside the central nervous system have impaired quality of life, compared to the background population. The study adds knowledge that may be important when making treatment decisions.

P167
The Development of a Decision Aid for Vascular Malformations: Improving the Shared Decision Making Process

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Purpose: Shared decision making (SDM) is an approach in which the patient and the clinician have an equal role in deciding which treatment option is most suitable for the patient, considering the best available evidence, the physician's experience and the patient's values and preferences. In clinical practice, digital decision aids can be applied to improve SDM as they increase patients' knowledge regarding the potential risks and benefits of the available treatment options prior to the outpatient clinic visit. Particularly in the management of vascular malformations (VMs) implementation of decision aids may be valuable, as a broad variety of treatment options exist and patients commonly face treatment dilemmas.
Methods: A concept decision aid for VMs was designed according to the IPDAS-guidelines. A literature search was performed in MEDLINE, Embase, and Cochrane Central Register of Controlled Trials for studies describing the 4 main types of VMs and safety and effectiveness of the most common treatment modalities. A data summary was made for each treatment option and VM type separately. A focus group for patients with VMs revealed patients' personal experiences regarding the decisional process and their opinions on the contents of a future decision aid. Physicians specialized in VMs designed the content. A literacy check improved readability.
Results: Compression stockings, laser therapy, embolization, sclerotherapy and surgical excision were the most commonly utilized treatment modalities according to the literature. The focusgroup revealed that patients felt they received incomplete information about available treatment options and desire clear information including the effectiveness and potential complications.
Conclusion: As the current SDM-process regarding patients with VMs is not yet in its ideal form we aim to enhance the patients' knowledge and decrease decisional conflict by implementing a decision aid. Further research is necessary to test if the concept decision aid is an effective tool to reach these goals.

P168
Interventional treatment of peripheral vascular malformations – Long-term results with special emphasis on Quality of Life aspects

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Purpose: We present our long-term results of patients with peripheral venous malformations (PVM) and peripheral arteriovenous malformations (PAVM) after interventional treatment.
Methods: We retrospectively analyzed the medical files of 100 patients with PVM (41) and PAVM (59) that were treated between 2002 and 2014 at our department (Department of Radiology and Neuroradiology, Sana Kliniken Duisburg GmbH, Duisburg, Germany). The interventional procedure of choice for PAVM was primarily a transarterial superselective embolization using liquid embolic agents, and percutaneous sclerotherapy with Polidocanol for PVM. Patients answered a symptoms based Quality of Life (QoL) questionnaire before and after treatment.
Results: 30 patients with PVM and 44 patients with PAVM answered the questionnaire. In 407 therapeutic sessions (PVM: 112, PAVM: 295) 16 minor complications directly related to the treatment were encountered. 70% in PVM-group reported an improvement in motion pain, 54% in PAVM-group. 70% in PVM-group reported an improvement in rest pain, 50% in PAVM-group. 50% in PVM-group reported an improvement in functional impairment, 52% in PAVM-group. 40% in PVM-group reported an improvement in skin deformity, 27% in PAVM-group. 56% in PVM-group reported an improvement in swelling, 50% in PAVM-group. 34% in PVM-group reported an improvement in sensibility disorders, 13% in PAVM-group. 53% in PVM-group reported an improvement in impairment in daily life, 50% in PAVM-group. More than 95% of patients with PAVM and PVM were very satisfied with their treatment in general.
Conclusion: Interventional treatment is a well-tolerated therapy for PAVM an PVM with a low complication rate. Positive subjective results and improvement in different aspects of QoL can be achieved.

P169
Pediatric Emergency Physician-Administered Sedation Protocol for Vascular Anomalies Interventions in Children

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Purpose: Interventional radiology management of pediatric vascular anomalies has traditionally required general anesthesia in order to maintain adequate analgesia, patient comfort and immobility, especially for head and neck lesions. Anesthesia specialist availability, interventional radiology suite capability to accommodate anesthesia equipment, prolonged room time, and extended post-anesthesia recovery are factors that limit the feasibility and attractiveness of this service to the interventional radiology practice. Pediatric sedation administered by non-anesthesiologist providers, is widely used in the emergency room setting for invasive procedures in children. We propose extending this sedation protocol to the pediatric vascular anomalies practice in the interventional radiology suite.
Methods: We retrospectively reviewed 50 invasive pediatric vascular anomalies procedures under pediatric emergency physician-administered sedation, between March, 2016 and December 2017. All patients were treated in the interventional radiology suite by a single interventional radiologist and a single pediatric sedation provider.
Results: 50 procedures were performed on 35 patients (average 1.4 procedures per patient) over the included time period. All patients received combination of intravenous Ketamine and Propofol +/- addition of Fentanyl. Average age was 8.5 years (range 5 months to 17 years, median age 8 years) Average procedural sedation time was 45 minutes (range 30-75). There were 34 procedures performed for venous malformations, and 16 for lymphatic malformations. Procedures per anatomic locations were as follows: head/neck 14, extremities 26, trunk 10. Sclerosant agents used in number of procedures: sodium tetradecyl sulfate (STS) 27, doxycycline 10, bleomycin 6, ethanol 3, and combination therapy in 4 (ethanol/doxycycline 1, ethanol/STS 2, STS/doxycycline 1). Planned technical endpoint was reached in all procedures. There were no procedures that required anesthesiologist back-up or re-scheduling due to adverse events, or inadequate sedation/analgesia. Adverse events were recorded in 7 procedures (14%). These included need for intervention (bag-valve mask use) due to low oxygen saturation in 4, and minor hypoxic events not requiring intervention in an additional 3 patients. None of the events required additonal treatment or prolonged observation/admission following standard sedation recovery.

Conclusion: Pediatric emergency physician-administered procedural sedation for vascular anomalies interventions in children is safe and effective. It may be considered a feasible alternative to anesthesiologist-administered general anesthesia or sedation for interventional treatment of low-flow vascular malformations, including head and neck lesions.

P170
Sirolimus in superficial arteriovenous malformations: a retrospective study of 10 children and adults

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Purpose: Superficial arteriovenous malformations (AVMs) are rare, potentially aggressive, congenital fast-flow vascular malformations; guidelines on management are lacking, as are satisfactory treatments for advanced forms. Sirolimus (rapamycin), the oldest inhibitor of mammalian target of rapamycin (mTOR), has anti-proliferative and anti-angiogenic properties. It has provided promising results in venous and lymphatic malformations. The aim of the study was to determine the efficacy and tolerance of sirolimus for superficial AVMs in children and adults.
Methods: This retrospective study included all patients with a superficial AVM treated with sirolimus between January 2010 and April 2017 who were followed up in 2 French tertiary centers for vascular anomalies (university hospitals of Paris-Necker and Tours). The outcomes were efficacy (complete response, partial response, no response) based on the volume of the AVM and on necrosis/hemorrhage as well as side effects.
Results: We included 10 patients (7 children, including 6 males). The starting dose of sirolimus ranged from 0.6 to 3.5 mg/m2. Five patients showed partial response at a median of 3 months (interquartile range [IQR] [1; 5]), with no response in the 5 remaining patients. Median treatment time was 24.5 months (IQR [4.5; 35]). Among the 5 responders, 2 showed an initial partial response followed by therapeutic resistance, with progressive disease after 9 and 24 months of treatment, respectively. We found no high-grade toxicity. The most frequent side effect was mouth ulcers, in 6 patients.
Conclusion: Contrary to previous descriptions of lymphatic and venous malformations, sirolimus was only slightly efficient in half of our 10 patients with AVMs. New therapy drugs targeting other pathways need to be developed for this rare and aggressive condition.

P171
A CASE OF MULTIFOCAL LYMPHANGIOENDOTHELIOMATOSIS WITH THROMBOCYTOPENIA WITH PULMONARY INVOLVEMENT SUCCESSFULLY TREATED WITH RAPAMYCIN.

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Purpose: Multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT) is a congenital vascular disorder characterized by multifocal cutaneous vascular lesions, and it features thrombocytopenia and extracutaneous disease but mostly severe gastrointestinal involvement. There is great variability in the spectrum of clinical manifestations among the patients that have been diagnosed to date. Data are lacking on the clinical spectrum, long-term prognosis and treatment of this disease.
Methods: We reviewed the clinical histories of all patients diagnosed with MLT in a reference tertiary hospital during the last 15 years.
Results: Four patients, diagnosed with MLT were included. All of them had clinical and histopathological criteria for this disease although clinical manifestations were highly different from one patient to the other. One of the patients, in addition to multifocal skin and digestive lesions, presented multiple, aggressive and diffuse lung lesions that were successfully treated with oral rapamycin. After the treatment, the patient presented dramatically complete remission of the pulmonary lesions but surprisingly the skin lesions did not involute.
Conclusion: Given the clinical variability of this disease, it seems necessary to establish major and minor criteria for the accurate diagnosis of this entity. The fact that our patient's skin lesions did not respond to oral rapamycin raises the question about what digestive, lung and skin lesions have in common. The discussion remains open about what differentiates skin and lung lesions taking into account a different response to the mammalian target of rapamycin inhibitor.

P172
Complications leading to admission in the 3 months following the start of oral sirolimus for vascular anomalies

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Purpose: Oral sirolimus is increasingly used for treating vascular anomalies. Response to sirolimus on these anomalies is usually expected within the first 3 months of treatment but to our knowledge, the adverse effects leading to admission within the same time frame have not been reported.
Methods: Describe clinical presentation, radiological findings and complications of all episodes of new admission occurring in the first 3 months after the start of oral sirolimus (targeted levels: 5-15ng/ml). Two physicians independently rated the likelihood of the admission being a potential adverse effect to sirolimus on a seven point Likert scale (1=most likely, 7=most unlikely) taking patient's clinical characteristics and previous medical history into account. Scores ≥6 were not considered associated to sirolimus.
Results: 16 patients were treated with oral sirolimus for a vascular anomaly (5 LM, 2 LVM, 2 AVM, 1 VM, 1 RICH, 1 primary lymphedema, 4 Kaposiform hemangioendothelioma). The median age at start was 3.9 years (Q1-Q3: 1.1-11.1). 5 admissions in 4 patients (25%) occurred. Likert scale was 7 in one patient with AVM who presented a recurrence of bleeding while on sirolimus. 3 out of 4 admissions potentially associated to oral sirolimus (75%) were for abdominal complications consisting of fever, acute abdominal pain and significant biological inflammation that occurred between 4 days and 4 weeks after the start of oral sirolimus. All 3 patients had abdominal lymphatic malformations: 2 truncular and 1 extratruncular and all were treated with broad spectrum antibiotics. Moreover, 1 patient was admitted with abdominal pain and suspicion of mild pancreatitis that quickly resolved.
Conclusion: Acute abdominal pain with fever and inflammation suggestive of infection is a possible adverse effect associated to oral sirolimus occuring early after treatment start. Patients with intraabdominal lymphatic malformations may be at risk for this complication.

P173
Expression of TOR receptors (Target of Rapamycin) in vascular anomalies

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Purpose: To date, there has been limited research on the molecular mechanisms involved in the treatment of vascular anomalies(VA). The mammalian target of rapamycin complex 1 (mTORC1) has been implicated in the biology of some vascular anomalies. Inhibitors of mTORC1 signalling (Rapamycin/Sirolimus) have been recently used selectively worldwide with some recorded success. The aim was to determine the level of expression of mTORC1 signaling proteins in formalin fixed paraffin embedded (FFPE) biopsies of VA as a first step in predicting VA response to Rapamycin.
Methods: An IRB approved retrospective review of pathology archives was carried out and 34 cases of VA were retrieved. Immunohistochemistry (IHC) was carried out with primary antibodies against various protein components of the mTORC1 pathway. Staining intensity was graded by a pathologist on a semi-quantitative scale that ranged from 0 to 4. The percent of positive cells were estimated in the following bins: 0, 1-33%, 34%-66% and >67%.
Results: The intensity and percent positivity of the IHC were as follows (intensity, %): 7 infantile hemangioma (1, 1-33%); 1 epithelioid hemangioendothelioma (2, 34%-66%); 2 tufted angioblastomas (1, 1-33%), 3 lymphatic malformations (1, 1-33%); 2 venous malformations (1, 1 -33%); 2 capillary malformations(0, 0%); 6 pyogenic granulomas(3, >76%).
Conclusion: There was no obvious correlation between high mTORC1 activity and lesions with architectural or cytological atypia. The expression was found to be strongest in lesions with high levels of inflammation, damage and repair. IHC expression for mTOR pathway markers does not appear to cluster with classes of VA known to be responsive to mTOR inhibition. Clinical response may be mediated through indirect pathways such as immunomodulation or through mTORC1 independent signaling pathways.

P174
The use of Sirolimus to treat Vascular Tumors and Malformations: A Canadian Experience

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Purpose: Vascular tumors (VT) and malformations (VM) are a heterogenous group of disorders that can cause significant morbidity. Recently, inhibition of the mTOR pathway using sirolimus has led to promising results in patients that have previously had limited therapeutic options. Over the past 6 years our institution has increasingly been using sirolimus to treat VT and VM. We performed a retrospective chart review to assess the efficacy and safety of using sirolimus to treat VT and VM.
Methods: Patients with VT and VM referred to Haematology and treated with sirolimus were evaluated. Sirolimus was initiated at a dose of approx. 1.6-2 mg/m2 given as one morning dose or split into 2 daily doses. The dose was titrated to maintain a sirolimus trough level of 5-15 ng/L.

Results: Both VT and VM were included (see table). 27/31 patients were diagnosed in the first year of life. Sirolimus was initiated at a median age of 7.5 years. Most patients had previously undergone procedures (11 surgical resections, 9 sclerotherapy) pre-sirolimus. Of the 26 children treated for a minimum of 4 months, 21 (81%) exhibited a clinical response as evaluated by a significant decrease in mass size, pain, blood loss, or improvement of laboratory parameters (ex. fibrinogen). Mean time to response was 2.5 months (range: 1.75-3 months). 9/10 children <5 years of age, and all 5 children < 1 year of age showed clinical response. 7/26 patients had mouth sores. No patient discontinued Sirolimus due to toxicity. The median duration of treatment was 10 months and 21/26 patients remain on Sirolimus.
Conclusion: Sirolimus is safe and efficacious in most children with VT and VM. Young children appear to respond better than older children, suggesting that early initiation of sirolimus should be considered in children with VT or VM.

P175
Sirolimus for the treatment of progressive kaposiform hemangioendothelioma: a multicenter retrospective study

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Purpose: Kaposiform hemangioendothelioma (KHE) is an aggressive disease with high morbidity and mortality. The aim of this study was to retrospectively evaluate the efficacy and safety of sirolimus for the treatment of progressive KHE.
Methods: A multicenter, retrospective cohort study was conducted in patients with progressive KHE treated with sirolimus.
Results: A total of 52 patients were analyzed. Thirty-seven (71%) patients exhibited Kasabach-Merritt phenomenon (KMP) and were significantly younger than the patients without KMP (95% confidence interval [CI], 14.39-41.61; P<0.001). Patients without KMP were all treated with sirolimus alone, whereas 21 KMP patients with severe symptoms received short-term combination therapy with prednisolone. Overall, 96% and 98% of patients showed improved relief of notable symptoms and/or improved complications at 6 and 12 months after treatment, respectively. After sirolimus treatment, significant decreases in mean severity scores occurred at 6 (95% CI, 2.23-2.54, P<0.001) and 12 (95% CI, 1.53-1.90, P<0.001) months. Compared with KMP patients, patients without KMP showed a response that was similar to but less pronounced during the 12 months of treatment (95% CI, 40.87-53.80; P<0.001). For subgroup analysis of KMP patients, there were no significant differences in tumor shrinkage between those treated with combination therapy and those receiving sirolimus alone (95% CI, 18.11-25.02; P>0.05). No patients permanently discontinued treatment due to toxicity-related events, and no drug-related deaths occurred.
Conclusion: Sirolimus was effective and safe for the treatment of progressive KHE. Sirolimus may be considered as a first-line therapy or as part of a multidisciplinary approach for the treatment of KHE.

P176
Effectiveness of rapamycin in the treatment of CLAPO syndrome

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Purpose: The CLAPO syndrome, described in 2008 by JC Lopez in 6 unrelated patients, associates a lower lip capillary malformation (C), a facial and neck (L) lymphatic malformation, an asymmetric development of face and limbs (A) with localized or generalized excess growth (O for overgrowth). The capillary malformation is constant. Excess growth was observed at birth in 3 patients and was generalized in one case; in other patients it was partial and involved only one or more segments of the body. The mode of transmission of this syndrome is unknown. We report a case of CLAPO syndrome favorably progressing after rapamycin treatment.

Methods: A male infant was followed since the age of 40 days for a complex vascular malformation of the face and neck. His parents were consanguineous. He was 3rd of siblings of 3. He presented a capillary malformation in the aspect of a purple red spot of the lower lip sparing the outer 1/3 of the left lip. There was a marked asymmetry of the face and neck, the cheek and the neck were more hypertrophic by the left side. A macrocystic lymphatic malformation occupied the 2 cheeks and the two sides of the neck but always larger by the left. The tong was completely covered with a microcystic lymphatic malformation. There were also large veins of drainage on the neck and face. Ultrasound confirmed multiple cystic structures with intracystic organized hematomas and cervical adenopathies. MRI of head and neck showed hypertrophy of the left maxillary bone. Successive inflammatory flares were hardly controlled by long-course antibiotics (azithromycin) and betamethasone drops. At the age of 30 months, Sildenafil 3mg/kg/d was tried without real improvement. At the age of 4.5 years, rapmycin 2mg/m2/d was started. By the end of the second month of treatment, we noticed a clear response with involution of the lymphatic malformations of the face and healing of the tongue. Rapamycin was continued for one year with real improvement of the aspect of the face.

Results: The pathogenesis of this syndrome is unknown. The regional disposition of the lesions following the dermatomes led to suspect a somatic mosaicism and an anomaly of the innervation of the vessels. The capillary malformations would result from an inability to vasoconstriction by inadequate sympathetic innervation. A mutation of PI3K (known in syndromic hypertrophies and in some cancers) and hyperphosphorylation of AKT (belonging to the signaling pathway of mTOR) have been recently found in endothelial cells taken from a microcystic lymphatic malformation. In our case, Rapamycin wich is mTOR inhibitor, has improved the lymphatic malformation but did not modify the labial capillary malformation.
Conclusion: This syndrome reflects a close relation between angiogenesis/vasculogenesis and somatic growth. Rapamycin has already been reported as a good treatment for vascular malformations. But to the best of our knowledge, this is the first case of CLAPO syndrome responding to rapamycin.

P177
Treatment of congenital vascular malformations using Sirolimus: first results of a multicenter open-label study with Sirolimus

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Purpose: Treatment options for patients with congenital vascular malformations are limited. Recently, promising results have been published regarding treatment with Sirolimus in patients with lymphatic and venous or combined vascular malformations. To substantiate these initial reports, we performed a pilot study followed by a just recently started nationwide study. The primary purpose of this nationwide study on the effect of Sirolimus on pain reduction and quality of life of patients with so far untreatable vascular malformations.
Methods: A pilot study including 14 patients was performed between June 2015 and August 2016. Subsequently, this pilot study was extended to a nationwide study according the same treatment protocol. All patients are being treated for a period of six months with Sirolimus. Pain is assessed using the VAS score system. Quality of life questionnaires and MRIs are performed prior to study and after 6 months of treatment to investigate the efficacy of Sirolimus. After stopping Sirolimus and returning complaints, patients will be treated with Sirolimus for a second time period of one year.
Results: In total 23 patients started Sirolimus therapy (n=14 pilot study and 9 patients in nationwide study. 19 patients responded well (pain free), 1 patient partially responded. Two patients did not respond: one patient had stable disease and in one patient the disease progressed (with respect to pain/subjective symptoms or also objectivated by imaging)
Conclusion: These data demonstrate that Sirolimus has a positive effect in patients with vascular malformations. Uncertain is the duration of treatment with Sirolimus needed to keep the patients in a clinical good condition. Based on the present nationwide study we hope to gain more insight in this.

P178
Improvement of refractory pain with sirolimus in a patient with glomovenous malformation

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Purpose: Glomovenous malformation (GVM) is a subtype of venous malformation with a distinct, nodular, cobblestone-like appearance, typically involving skin and subcutaneous tissues. GVM is associated with autosomal dominant glomulin mutations. GVM is often painful to palpation. Treatment of symptomatic lesions includes surgical excision, laser, sclerotherapy, and pain management. No known medical therapies target GVM.
Methods: Retrospective review of one case of genetically-confirmed GVM of the right lower extremity involving subcutaneous and intramuscular tissues treated with sirolimus for refractory pain.
Results: 12 year old male presents with extensive GVM with refractory pain, contracture, disuse atrophy and anxiety after sclerotherapy. Pain began at 13 months old and three sclerotherapy procedures occurred at ages 4, 6 and 7. Pain significantly worsened at age 10. When sirolimus was initiated, his pain medications included gabapentin, meloxicam, MSContin, morphine, lorazepam, topical diclofenac and lidocaine patches. He was minimally tolerant of physical exam due to pain and anxiety. Biofeedback, cognitive behavioral therapy and an intensive outpatient pain management partial program were utilized. Sirolimus was started 1mg BID, target level 7-13 ng/ml. Time to response of appearance and color of GVM was one month and pain was improving by 3 months. Pain was only occasional by one year on therapy, including while walking and playing. Narcotics were weaned off by 6 months and all pain medications were stopped by 21 months on therapy. His pain remained controlled through weaning to daily sirolimus dosing, with 12 hour levels of 2-3 ng/ml, though pain worsened with doses below 1.5mg daily. He has been treated for a total of 30 months. Side effects have been mucositis, gastroesophageal reflux and mild elevation of cholesterol.
Conclusion: Sirolimus appears effective in treating refractory pain in the first reported case of glomovenous malformation. Prolonged therapy may be needed and is well-tolerated. Further study is warranted.

P179
Clinical effectiveness of Sirolimus treatment in pediatric patients with complex vascular malformations. Search for the minimum clinically effective dose.

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Purpose: To evaluate the effectiveness and safety of the use of Sirolimus in the treatment of complex vascular malformations in pediatric patients. To report the minimum clinically effective doses used.
Methods: We performed a retrospective analysis of the medical records of 8 pediatric patients with complex vascular malformations treated with Sirolimus orally from January 2015 to May 2017. The initial dose was 0.8 mg/m2 per dose every 12 hours, with follow-up based on blood dosages, looking for the minimum clinically effective dose in each case. The clinical conditions that led to enrolling patients in the treatment protocol with Sirolimus were: venolymphatic malformations in extremities with severe pain (n = 2), microcystic lymphatic malformations of the neck and lower jaw with severe aesthetic compromise (n = 2), coagulation disorders associated with extensive venous malformation (n = 1), scrotal microcystic lymphatic malformation prior to reduction surgery (n = 1), airway compromise due to presence of intrathoracic lymphatic malformation in patients who could not undergo tracheostomy because of the location of the lesion (n = 2). The lack of clinical response to other treatments was used as an inclusion criterion. Patients with abnormal laboratory parameters (hepatogram, renal function, lipidogram) were excluded.
Results: The clinical response was favorable in 100% of the cases. Good clinical response was defined as reduction of the lesion on imaging studies and/or clinical improvement of the symptoms. The mean onset of improvement was 60 days [12-102]. No patient presented clinical worsening during treatment. One patient presented complete resolution of the disease with resolution of the symptoms and disappearance of the radiological findings. Sirolimus was well tolerated in all cases. One patient presented an increase in alkaline phosphatase serum levels and another patient presented severe sepsis in the context of a gastrointestinal infection that led to multiorgan failure and death. The mean of the minimum clinically effective dose (the level of drug in blood in which the patients presented clinical and radiological improvements) was 6.6 ng/ml. This corresponded to an average dose of 0.5 mg/m2 per dose.
Conclusion: Sirolimus has become a new safe and effective therapeutic option, for treatment of complex vascular malformations that do not respond adequately to other treatments. The clinical response was favorable in all the cases of our analysis, confirming the results published in the few series found in the literature. The minimum clinically effective dose in our series was below those reported in other publications. Signs of early infections should be monitored to avoid severe complications.

P180
Sirolimus treatment improves clinical symptoms and quality of life of patients with intractable lymphatic malformations

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Purpose: Intractable lymphatic malformations (LMs) include several disorders in which abnormal lymphatic tissue invades the neck, chest, and bone. These disorders may cause a lethal outcome and are difficult to treat. The mammalian target of rapamycin inhibitor sirolimus shows promising results for managing vascular anomalies. We examined the efficacy and safety of sirolimus treatment for patients with intractable LM.
Methods: All patients with LM who were treated with sirolimus from May 2015 to November 2017 were included. They received oral sirolimus once a day and the dose was adjusted for the nadir concentration to remain within 5–15 ng/mL. We retrospectively reviewed the response to drugs (the response rate of radiological volumetric change of the target lesion), severity scores, reported quality of life (QOL) and adverse effects at 6 months after administration.
Results: Thirteen patients (3 cystic LM, 3 kaposiform lymphangiomatosis, 1 generalized lymphatic anomaly, 5 Gorham-Stout disease, and 1 Central conducting lymphatic anomaly; mean: 13.7 months, 3–30 months) were treated with sirolimus at our institution. Administration in one patient was interrupted because of an operation before sirolimus was going to finish. A total of 58.3% (7/12) of patients demonstrated a partial response by a radiological examination and significant improvement of the QOL and severity scores ($p=0.0469$ and $p=0.0014$). Five patients who did not obtain a reduction of the lesion (stable disease group) showed no significant improvement of the QOL and severity scores. Nine patients remained on uninterrupted sirolimus. A total of 76.9% (10/13) patients had side effects, such as stomatitis, infection, and hyperlipidemia, but did not discontinue sirolimus.
Conclusion: Sirolimus reduces the lymphatic tissue volume of LM, and leads to improvement of clinical symptoms and QOL.

P181
A Multi-Institutional Retrospective Analysis of Sirolimus and Bisphosphonates for the Treatment of Generalized Lymphatic Anomaly (GLA) and Gorham-Stout Disease (GSD)

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Purpose: GLA and GSD can aggressively destroy bone, with significant impact on morbidity and mortality. Sirolimus is effective in the treatment of these diseases. Based on the addition of mTOR inhibition to bisphosphonate therapy in metastatic cancer therapy, regimens have been used for refractory or high risk GLA and GSD but there is heterogeneity of diagnosis, and variability of drug regimens and assessment of effectiveness.
Methods: We conducted a retrospective review from 5 institutions of 19 cases of GLA and GSD treated with sirolimus and bisphosphonate with assessment of clinical features, treatment, response and side effects.
Results: Patients included GLA (n=8) and GSD (n=11). The average age at diagnosis was 10 years. Clinical features included effusions: GLA (n=4), soft tissue lymphatic malformations: GLA (n=3), GSD (n=1), multiple splenic lesions: GLA (n=3), and soft tissue swelling at the site of bony lesion: GSD (n=3). The presenting symptom in 17 patients was pain with 2 patients (GLA) with shortness of breath. Fracture was noted in 5 patients: GLA (n=1), GSD (n=4). Diagnostic and/or response imaging included MRI, CT, bone scan, skeletal survey and Dexa scan. Treatment consisted of: initial sirolimus use with the addition of bisphosphonate secondary to worsening disease (n=4), initial therapy with other agents (interferon, chemotherapeutic agents, radiation) and change to sirolimus and bisphosphonate secondary to toxicity (n=6), sirolimus and bisphosphonates (n=7) and sirolimus, bisphosphonates and interferon (n=2). Seventeen patients had stable disease and 8 patients had disease response. Sirolimus protocol was standard; however, bisphosphonate protocol varied in dosing and frequency. Side effects were tolerable and expected with no Grade III or IV toxicity.
Conclusion: Sirolimus and bisphosphonates are a safe and effective therapy for GSD and GLA. A consistent medication regimen, redefined response criteria and improved radiologic classification will be important for the development of a prospective clinical trial.

P182
Evaluating quality of life after initiation of Sirolimus in pediatric patients with vascular anomalies : A new paradigm for official approval

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Purpose: The concept of quality of life appears in the 1946 World Health Organization constitution. It took several decades to develop tools to measure specific (e.g. pain) or general aspects of quality of life in the pediatric population (PedsQL Questionnaires, Varni, 1998). Government health authorities which approve new therapeutic agents now require not only proof of medical effectiveness but also improvement in functional, emotional and social well-being. Sirolimus, an immunomodulator used in oncology and transplantation, has been introduced to treat refractory vascular anomalies (Adams, 2011). We assessed the change in quality of life of patients with vascular anomalies treated with Sirolimus, and their families.
Methods: In this pilot study, parents of 6 out of 10 children currently being treated in our multidisciplinary clinic with Sirolimus answered PedsQL questionnaires. These patients' conditions included thoracic and lower limb lymphatico-vascular malformations, a pelvic vascular malformation, disseminated lymphangiomatosis and pulmonary lymphangioendotheliomatosis. Responses were tracked on a numerical scale from 0 to 100, positive results generating higher scores. Topics included general functioning (physical, emotional, social, school), family functioning and specific issues such as pain, worries and treatments. Comparison was made with quality of life prior to initiating Sirolimus, using paired t-tests.
Results: Patients had a median age of 5.8 years (range 9 months - 12 years). Statistically significant improvement following initiation of Sirolimus was observed especially with respect to pain (mean, 45 -> 83), the grouped sub-category of pain, worries and treatment (mean, 62 -> 80) and family functioning (mean, 46 -> 65).
Conclusion: This pilot study demonstrates the feasibility of generating quantitative data about quality of life in pediatric patients and their families. Improvement in several aspects was noted following initiation of Sirolimus for treatment of complex vascular anomalies, both in individual patients (e.g. pain control) and in family functioning. Expansion of use of Sirolimus in this population should be accompanied by assessment of quality of life as well as biologic and radiologic parameters.

P183
Safety and Patient-Reported Efficacy of Sirolimus in 120 Patients with Vascular Anomalies: a Report from the Lymphatic Anomalies Registry

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Purpose: Sirolimus is increasingly utilized for a variety of vascular anomalies complications. Available data about safety and efficacy are drawn from case series and one phase 2 study of 57 patients. Off label use is increasing and additional safety and efficacy data are urgently needed.
Methods: Patients in an IRB-approved, international registry who received systemic sirolimus therapy for at least 6 months were retrospectively reviewed for adverse events, goals and outcomes of sirolimus therapy.
Results: 120 patients received sirolimus for at least six months. Sirolimus therapy was utilized for several different vascular anomalies, mostly with lymphatic complications. Median age at initiation of therapy is 7.5 years (range=0.1-52.6) and 45% were female. Median total duration of sirolimus therapy was 24 months (range=6-90). Similar to prior reports, the more common adverse events occurring at least once and attributed to sirolimus were mucositis (31%), headache (8%), diarrhea (4%) and nausea (4%). The following goals of therapy were predetermined: improved swelling (40%), improved quality of life (38%), improved pain (31%), improved functionality (26%), fewer infections (23%), improved bleeding (23%), other (21%), improved effusion (19%), stable effusion (13%), improved bone mineralization (13%), stable bone mineralization (13%), decreased transfusions (9%), improved imaging (3%), and stable imaging (3%). Using patient/parent reported outcomes, 99% (112/113) reported any one or more positive responses to sirolimus. Analyzing response based on goals of therapy, highest responses to sirolimus were reported for bleeding (78.6%), pain (62.2%), stable bone involvement (60%), fewer transfusions (54.6%), fewer infections (50%), improved swelling (50%), improved effusion (39.1%) and improved quality of life (35.6%).
Conclusion: Oral sirolimus is a well-tolerated and effective therapy for complications of vascular anomalies, especially bleeding, pain, infections and swelling. Sirolimus therapy needs further multidisciplinary, prospective study for patients with vascular anomalies.

P184
Sirolimus for Refractory Fibroadipose Vascular Anomaly

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Purpose: Fibroadipose vascular anomaly (FAVA) is a rare, challenging disorder associated with PIK3CA mutations. FAVA often causes painful replacement of muscle and soft tissues with fibrotic and adipose tissue and is associated with ectatic draining veins. Treatments for focal lesions are surgical excision, cryoablation or sclerotherapy and the role of medical therapy is unclear. Some FAVA lesions are too extensive or directly involve neurovascular structure, resulting in refractory pain.
Methods: Retrospective review of individual 7 cases from 6 institutions of FAVA refractory to other therapies treated with sirolimus for at least 3 months.
Results: All seven patients report improvement on sirolimus therapy. All patients had received prior procedures, including sclerotherapy (6 patients), cryoablation (2 patients) and/or resection (3 patients). Mean age at sirolimus initiation was 16y (range 6-29y). Mean length of therapy is 18.4 months (range 3-29 months). Six patients were treated with BID dosing and one adult received daily dosing. Goals of sirolimus were improvement in pain or musculoskeletal dysfunction. Pain and function improved in all patients, including discontinuation of narcotic use and resumption of participation in sports. Time to symptom improvement ranged from 1-4 weeks. In four patients for whom dose was lowered, pain recurred in all four and responded to restarting or increasing sirolimus dose. While all patients do not have pre- and post-sirolimus imaging, decrease in FAVA lesion size is seen in cases with available imaging. Sirolimus side effects are similar to prior reports, most commonly mouth sores, elevated lipids and acne.
Conclusion: We report the first known data supporting a role of sirolimus in refractory FAVA cases. Sirolimus is well-tolerated and initial improvement is rapid, within 4 weeks of initiation. Whether sirolimus has a role in upfront therapy to reduce lesion size prior to procedures deserves further study.

P185
Sirolimus Therapy in a Pediatric Patient with Blue Rubber Bleb Nevus Syndrome

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Purpose: To describe the treatment for a case of recurrent occult gastrointestinal bleeding in a child with Blue Rubber Bleb Nevus Syndrome. Background: Blue rubber bleb nevus syndrome (BRBNS) is a rare disorder characterized by widespread, protuberant venous anomalies, with the potential for significant hemorrhage. The skin and GI tract are most commonly affected. BRBNS is caused by somatic mutations in TIE2/TEK. Recent studies suggest that mTOR inhibitors, such as sirolimus are effective in treating this condition (1).

Results: We report a case of a 12-year-old boy who presented at 2 years of age with blue lesions in the plantar aspects of the feet. Over time, he developed anemia which required multiple red cell transfusions. Over time, he was found to have vascular lesions in multiple locations, including the scalp, paraspinal muscles, chest wall, liver, colon, penis, right hand and bilateral thighs. He underwent surgical resection and laser therapy of the painful malformations in his feet, but continued to struggle with chronic gastrointestinal bleeding, which resulted in multiple hospital admissions. He was treated with sirolimus between November 2014 and September 2017, at which point a wean was initiated. His hemoglobin normalized and remained stable throughout treatment (Figure 2). His hemoglobin has remained stable, despite the Sirolimus wean. D-dimer levels decreased, yet remain elevated (Figure 3). An abdominal MRI repeated in September 2017 demonstrated two new lesions in the abdomen, despite long-term sirolimus therapy. There has been improvement in many of the painful vascular lesions however, he continues to experience pain with the lesions in his feet.
Conclusion: As previously reported in the literature, sirolimus was successful in controlling gastrointestinal blood loss in our patient with BRBNS (1). However, our patient developed new lesions on sirolimus therapy, and did not have complete resolution of the pain that was caused by the lesions in his feet. Important questions arise from this case, including: What is the ideal treatment duration for patients with BRBNS who are started in Sirolimus? What is the clinical significance of the D-dimer in monitoring the disease course in BRBNS and what counselling should be provided in terms of long-term use of this medication in pediatric patients? Longitudinal case series may be beneficial in answering these questions.

P186
Is it safe to use Sirolimus among infants with Kaposiform Hemangioendotheliomas? -A Case Report of Two Sirolimus-related Deaths

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Purpose: Kaposiform hemangioendothelioma (KHE) is a rare infiltrative vascular tumor which is potentially life-threatening when presenting with Kasabach-Merritt phenomenon (KMP). There is no standard of cure for KHE currently. Potential medications including corticosteroids, propranolol and chemotherapy drugs, such as sirolimus are often used for alleviating KHE symptoms. Although some case reports of sirolimus treatment have shown promising results with recovered coagulant parameters, the off-target effects may cause severe problems.
Methods: Here, we described 2 cases of KHE+KMP infant patients who planned to receive sirolimus on a long-term basis. However, both patients developed paroxysmal cough and tachypnea when they received treatments at other hospitals, shortly after the onset of sirolimus treatment and succumbed to infection thereafter.
Results: The fatal complication highlights the importance of antibiotic prophylaxis and serum sirolimus level monitoring in order to ensure the safe use of sirolimus in the treatment of infant KHE patients. In addition, we recommend pharmacodynamics monitoring during sirolimus treatment to avoid liver toxicity and other complications in KHE infant patients with antibiotic prophylaxis.
Conclusion: This report reveals a potential risk of infection in sirolimus-treated infant patients. Considering the long-term application of sirolimus therapy, further studies should focus on the optimal time window of antibiotic prophylaxis in infant KHE patients.

P187
Rapamycin for vascular malformations. Three therapeutics approaches. Communication of six patients.

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Purpose: Here in we report six patients with vascular anomalies that were treated with rapamycin with different therapeutic approaches, preserve the functionality or resolve a life threatening medical condition, as a complementary therapy prior to another therapeutic strategy, such as surgery and in other cases improve the quality of life given by the aesthetic improvement.
Methods: we reviewed the records of 6 patients between 2014 and 2017. 1 with Blue Rubber Bleb Syndrome (BRBS); 1 with combined venous-capillary malformation (VCM); 1 with combined venous lymphatic malformation (VLM); 3 with lymphatic malformation (LM).
Results: We evaluated the treatment response of the different malformations in correlation with blood levels of rapamycin. The blood levels were between 5-10ng / ml. In our experience, the coagulopathy was controlled with blood levels in the range of 5-8 ng / ml. However, the patient with BRBS after an initial stabilization period, had to increase blood levels to a range between 10- 15 to limit the appearance of skin lesions and control the recurrence of bleeding. In the case of LM, in our series, patients improved with blood levels around 7 ng / ml. As it was previously reported in the literature, the best results were seen in the

mucous component, the macroglosia and in the disappearance of the superficial vesicles, while it was not so radical, in the dimensions of the malformation mass. The average time to observe clinical changes in terms of bleeding improvement was within the first week, while the improvement in clinical appearance or volume was appreciated after one month of treatment. In our experience, the medication was well tolerated.
Conclusion: There is no consensus on the most appropriate doses, ideal age to start therapy and length of treatment, so it seems important to share our observations that could be useful for future investigations.

P188
The anatomic distribution of venous malformations of the head and neck

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Purpose: To investigate patterns in anatomic distribution of head and neck venous malformations (VMs) and the possible relationship between locations in the cervicofacial soft tissue and upper aerodigestive tract (UADT).
Methods: A thorough examination of anatomical locations of VMs in the head and neck region of all patients presenting to a tertiary vascular anomalies referral center between 2004 and 2012 was performed. Data was collected from medical charts, clinical photographs, laryngoscopy images and Magnetic Resonance Imaging.
Results: The average age of patients at presentation was 26 years. Male to female ratio was 1:1.8. Distribution within the UADT is as follows: lip 60%, oral mucosa 48%, tongue 40%, palate 23%, floor of mouth 13%, pharynx 23%, and larynx 11%. Laryngeal involvement was highly associated with multiple sites of involvement within the aerodigestive tract as well as the premandible, masseter, parotid and buccal space. 45% of patients received multidisciplinary treatment (>2 modalities).
Conclusion: Although many cervicofacial and UADT VMs have diffuse infiltrative involvement, there are certain patterns which may guide treatment protocols. In our series, it is obvious that a diffuse distribution pattern is more likely to receive multimodal treatment. Airway VMs affect all levels of the upper airway and may be transglottic. Multiple cutaneous sites will be associated with a higher likelihood of laryngeal disease.

P189
Monotherapy with Topical Sirolimus for Treatment of Vascular Tumors and Malformations

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Purpose: Vascular anomalies encompass a heterogeneous group of lesions that are classified based on their biology into tumors or malformations. For many of these vascular anomalies, the genetic basis has been linked to somatic mutations in the PIK3CA/AKT/mTOR signaling pathway. Sirolimus, an mTOR inhibitor, is an evolving new therapy for vascular anomalies. Topical sirolimus has recently been reported in the management of several vascular lesions including facial angiofibromas in tuberous sclerosis, capillary malformations, and recently lymphatic malformations. We sought to evaluate the efficacy and tolerability of topical sirolimus as monotherapy in a variety of vascular anomalies.
Methods: Eighteen patients with any type of vascular malformation or tumor treated with topical sirolimus were retrospectively reviewed. Seven patients were omitted from final analysis due to concurrent laser therapy or inadequate follow up. Eleven patients met inclusion criteria and were included in the study.
Results: Nine children/adolescents and 2 young adults were treated exclusively with topical sirolimus. 8/11 had CLVM, 2 had tufted angiomas, and 1 had a simple LM. The most common indication for treatment was blebs/leakage in 70% of patients followed by bleeding in 45% of patients. All patients reported some degree of improvement. 4/11 and 3/5 patients experienced greater than 50% reduction in blebs/leakage and bleeding respectively. Sirolimus levels were obtained in 7/11 patients, one of whom was applying it to an area of >100cm2, with none having detectable systemic absorption. Sirolimus was well tolerated. Main side effects were discomfort with application and xerosis, but neither lead to discontinuation.
Conclusion: Topical sirolimus appears to be a safe and useful non-invasive therapy that is well tolerated. Specifically, it was effective in reducing blebs/leakage and bleeding. The study is limited by small sample size, heterogeneity of skin lesions, and lack of standardized topical preparations due to insurance coverage. Topical application of sirolimus may function as a first line therapy for patients with predominant concerns of blebs/leakage and bleeding who wish to undergo conservative treatment. Larger studies are needed to confirm this effect.

P190
Efficacy and absorption of Topical Sirolimus for the treatment of vascular anomalies in children: A Case Series

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Purpose: Efficacy of topical sirolimus has recently been described in lymphatic anomalies but not in other types of vascular anomalies. To our knowledge, systemic absorption of topical sirolimus in these lesions has not yet been reported. To evaluate topical 0.1% sirolimus efficacy, tolerance and absorption in different types of vascular anomalies in paediatric patients.
Methods: 0.1% sirolimus was applied on cutaneous vascular anomalies in 6 patients aged 2 to 17 years. These anomalies included extratruncular micro and macrocystic lymphatic malformations (n=3), verrucous hemangiomas (n=1), truncular lymphatic malformation with angiokeratomas (n=1) and infantile hemangioma (n=1). Sirolimus blood levels were measured after 1 week, 1 month and 3 months.
Results: A rapid decrease in the size of superficial lymphatic malformations in 3 out of 46 patients and a significant decrease in discharge from oozing lesions were observed. Response occurred in less than 3 months. The truncular lymphatic malformation, verrucous and infantile hemangiomas did not respond to topical sirolimus. Sirolimus levels were undetectable. Adverse effects were limited to local irritation.
Conclusion: Topical 0.1% sirolimus is a useful treatment for the cutaneous manifestations of extratruncular lymphatic malformations. The only adverse effect is local irritation. No systemic effects are expected, as blood levels are clinically insignificant.

P191
Hybrid Operation: A contemporary approach for treatment of vascular malformations

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Purpose: Treatment of vascular malformation by surgical excision alone has risk of massive bleeding which can be life-threatening. In our institute, we have been using hybrid approach, combining embolization and immediate surgical excision, to treat various high flow and low flow vascular malformations since 2011.
Methods: All hybrid operations performed between October 2011 and December 2017 were reviewed retrospectively. They were done under GA in the endovascular operating theatre (EVOR). Low flow lesions were managed by converting a blood-filled space to a bloodless glue cast by injecting histoacryl glue directly into the lesion, followed by immediate surgical excision; for high flow lesions, the arteriovenous shunts were embolized with histoacryl glue either transarterially or by direct puncturing of the nidus, followed by surgical removal of glue cast. Univariate analysis of factors associated with recurrence and residual disease was done by Chi-Square test.
Results: There were 60 hybrid operations in total, comprises 11 high flow lesions (AVF or AVM) and 47 low flow lesions (VM, LM or haemangioma). Sites of vascular malformation included 48 in head and neck regions and 10 over trunk and limbs. The mean age at the time of operation was 33.1 years (range 2-71 years). The mean operative time was 176 mins (range 45-364 mins). The mean post op length of stay was 2 days (range 1-8 days). We achieved a success rate of 92% without recurrence. Only 7 cases (12%) have reported minor complications that could be managed conservatively. Orbital vascular lesions were associated with more residual disease ($p = 0.001$). High flow lesions, on the other hand, were associated with more complete removal of vascular lesions ($p = 0.04$).
Conclusion: Hybrid operation is a safe treatment for both high flow and low flow vascular malformations. It can attain a low recurrence and low complication rate with careful case selection.

P192
Surgical approaches to vascular malformations of the midface

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Purpose: Vascular anomalies of the midface present a therapeutic challenge given their sensitive location and intimate relationship with the facial nerve and muscles of facial expression. In this study, we describe the optimal surgical approach to a vascular lesion based on its anatomical location.
Methods: Operative records and charts of all patients with vascular malformations involving the midface that were treated surgically with facial nerve monitoring at a tertiary referral center from April, 2004 through May, 2013. We documented the type of lesion, its anatomic location and the surgical approach. Extensive lesions required more than one approach and the mean number of operations were grouped based on type of vascular anomaly, and compared using ANOVA method.
Results: We report on 139 unique patients; 35% (48/139) had lymphatic malformations, 30% (42/139) venous malformations, 21% (29/139) hemangiomas, 12% (17/139) arteriovenous malformations, 2 port wine stains and 1 kaposiform hemangioendothelioma. The median age was 7.7 years (range 3 months – 56 years). The female:

male ratio was 2.1:1. These 139 patients required 243 operations, utilizing 275 separate surgical incisions/ approaches. On average there were 1.75 surgeries and 1.98 surgical approaches per patient. The most common anatomical sites were the parotid, masseter and buccal fat space (29.6%).. The surgical approach that provided the best and safest access was an extended parotidectomy incision. This was followed by lesions of the pre-maxilla, pre-mandible and anterior placed lesions (28.6%). An intraoral approach or a modified Weber-Ferguson (14.7%) was used. Other less common approaches included elliptical excision for small superficial lesions, a cervical crease incision for cervical lesions, and a lateral brow incision for temporal lesions. Arteriovenous malformations required the greatest number of operations, followed by lymphatic malformations, and then venous malformations, and lastly hemangiomas (mean number of operations 2.3 vs 1.9 vs 1.7 vs 1.2, respectively) (p-value = 0.016).
Conclusion: Our approach to vascular anomalies of the midface is based on its anatomic location. Extensive lesions required multiple approaches. Surgeons must be prepared and comfortable with a multitude of surgical approaches to treat these lesions adequately.

P193
Muscle patch graft technique for uncontrolled bleeding in the resection of extended vascular malformations

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Purpose: Ablative surgery of extended vascular malformation sometimes results in a massive bleeding which can be rarely controlled by ligation or electrocoagulation. This is because vascular malformation is often composed of huge cavities with large stump. To overcome such life-threatening bleeding, we used muscle patch graft covering the stump of bleeding cavity. In this paper, technique and the result of this method are described.
Methods: Between 2014 and 2017, twenty seven vascular malformations larger than 10cm in diameter were resected. Among these, 6 cases (2 males, 4 females; mean age, 32 years) which required muscle patch graft to control life-threating bleeding from the large stump of the lesion were employed for this study. Three out of 6 cases are composed of venous malformations and the remaining 3 cases are composed of arteriovenous malformations. As soon as uncontrollable bleeding is encountered, the stump of the vascular cavity is compressed using gauze with 1:500000 diluted epinephrine. During compression, optimal size of muscle segment which can cover the whole stump of the bleeding portion is harvested within the operative field. Then, the muscle belly is patched over the stump and compressed for around 15 minutes. After the bleeding from the vascular malformation is lessened, wound is closed with compressive dressing.
Results: All cases obtained thoroughly good control of life-threating bleeding by using this method, and recovered from anemia by means of transfusion without any severe damage. Surgical blood loss ranged from 1589ml to 16000ml (average amount was 4570ml).
Conclusion: In the resection of extended vascular malformations, embolization of feeder arteries in arteriovenous malformations and heparinization for LIC (localized intravascular coagulopathy) in venous malformations are standard pre-treatment to avoid massive bleeding during operation. However, these pre-treatment are not enough for all cases. This technique is preferable especially when the pre-treatment cannot be effective.

P194
The PEPSI (Periorbital Elevation and Positioning with Secret Incisions) Technique for the Reconstruction of Large-sized Periorbital Cutaneous birthmarks

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Purpose: To repair large-sized periorbital cutaneous defects after resection of vascular birthmarks or nevi by an innovative technique called PEPSI (periorbital elevation and positioning with secret incisions) technique with functional and aesthetic outcomes.
Methods: A retrospective study was performed in 15 patients who had unilateral periorbital cutaneous defects in a single institution from 2014 to 2016. The ages of patients ranged 3 to 46 years (average, 19 years). The defects were repaired by the PEPSI technique. The outcome evaluations included scars (VSS and VAS score), function and aesthetic appearance of eyelids and patient satisfaction (no improvement, partial satisfaction and completed satisfaction). The repair size was measured by the maximum advancement distance of skin flap during operation.
Results: All (100%) patients achieved an effective repair with a mean follow-up of 30.3 months (range 22-38 months). Of those, 14 (93.3%) patients achieved excellent outcomes. The mean maximum advancement distance of skin flap was 20.2 mm (range 8-50mm). The mean scores of VSS and VAS score were 2.1±1.7 and 8.5±1.2, respectively. The outcomes of cosmetic and functional evaluations were ideal in 14 patients (93.3%). A 10-year-old boy developed a small (ca. 0.3 cm2) necrosis in the distal end of advancement flap. There was no new-onset epiphora, serious ectropion, keloid formation, dyskinesia during the follow-up period.

All patients achieved complete satisfaction except one patient with partial satisfaction
Conclusion: This study demonstrated that the PEPSI technique is an effective method to repair large periorbital cutaneous defects with acceptable functional and aesthetic outcomes.

P195
Defining the Complexity and Morbidity of Vascular Malformation Resection Using a National Sample of Surgical Patients in the United States

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Purpose: Surgical excision of symptomatic vascular malformations is often the last resort after multiple rounds of medical or radiologic treatment to avoid potential operative morbidity. The purpose of this study was to determine surgical extent and outcomes using a multi-institutional cohort so that potential risk can be weighed against the benefits of surgical resection.
Methods: Patients <18 years of age who underwent excision of skin and subcutaneous tissue hemangiomas or lymphatic malformations were identified from the 2012-2015 National Surgical Quality Improvement Program-Pediatric, a national sample of surgical patients treated at participating hospitals in the United States. Standardized data are clinically abstracted from medical records prior to undergoing centralized audit. Resource utilization and complications were determined based on type of malformation, magnitude of resection, and complexity of wound closure using univariate and modified Poisson regression analyses.
Results: Of 1078 patients identified, 1011 (94%) had hemangiomas and 67 (6%) lymphatic malformations. Most excisions were <4 cm (75%). Complex wound closure or tissue transfer occurred in 15%. Outpatient procedures were performed in 1038 (96%). Of the inpatient procedures, median (IQR) stay was 1 (1-2) day. Complications occurred in 48 patients (5%); unplanned reoperation was most common (n=15) followed by readmission (n=13) and surgical site infection (n=9). Complication rate did not vary based on diagnosis, size of excision, wound class, or complexity of closure however younger age, impaired cognitive status, ASA class, and operative time were associated with complications on univariate analysis (Table). Only ASA class ≥3 remained predictive after adjustment (risk ratio=5.6, 95%CI 2.4-13.2).
Conclusion: Surgical excision of vascular malformations is a low-morbidity procedure often performed as an outpatient based on this large multicenter cohort. It should receive consideration as treatment for symptomatic malformations along with medical and radiologic options. Patient comorbidity rather than type of malformation or operative extent confers increased risk of complications.

P196
Endoscopic Surgical Approaches to Manage Skull Base Vascular Anomalies

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Purpose: To describe technique, efficacy, and safety of novel endoscopic approaches to sinonasal and skull base vascular malformations. Vascular malformations of the skull base are particularly challenging to treat due to risk of bleeding and close proximity to critical structures. Advances in multiportal endoscopic skull base surgery have enabled major surgical interventions to be performed using an endoscope through narrow portals in the craniofacial skeleton. This is the gold standard for pituitary surgery, but there are very few reports of these techniques for skull base vascular malformations.
Methods: Index patients (n=3) were selected that illustrate endoscopic surgical techniques for excision of skull base vascular malformations. Data on pathology, preoperative planning and embolization, operative details including management of bleeding, post operative course, and complications were collected.
Results: Pathologies treated were two Juvenile Nasopharyngeal Angiofibromas (JNA) with extension into middle cranial fossa and orbital apex (UPMC Stage IV) and an arteriovenous malformation (AVM) of the maxilla with intracranial extension at the infratemporal fossa. Surgical approaches utilized were transnasal, transorbital, transmaxillary, and a lateral sublabial approach to the infratemporal fossa. Preoperative embolization with polyvinyl alcohol foam was done for the two JNA cases, and select preoperative embolization with N-butyl cyanoacrylate for the AVM. Intraoperatively, endoscopic harmonic shears were used to obtain hemostasis. One patient required a blood transfusion on POD 1. Complete excision without recurrence at 2 years post operatively was obtained in the JNA patients. The AVM patient has relief of her symptoms of bleeding and pain, and the small persistent AVM adjacent to the internal carotid artery has been stable for 10 months.
Conclusion: Vascular malformations of the skull base can be treated with endoscopic surgical approaches that minimize skin incisions and collateral tissue damage. Multidisciplinary surgical planning including interventional radiology is required both for the surgical approach and preoperative embolization technique.

P197
Financial Feasibility of a Multidisciplinary Vascular Anomaly Clinic

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Purpose: Multidisciplinary vascular anomaly clinics (VACs) offer important value to pediatric patients with complex vascular anomalies whose care overlaps specialties. These clinics are labor-intensive and costly to operate since providers see fewer patients compared to in their individual specialty clinic. Our tertiary care institution's VAC specialists include a pediatric otolaryngologist, a pediatric surgeon, a pediatric plastic surgeon, a pediatric dermatologist and an interventional radiologist. To assess financial feasibility, we conducted a cost analysis of our VACs comprised of two ½ day multidisciplinary physician attended clinics (5 specialists at our main campus and 2 specialists at a satellite clinic) and a ½ day nurse practitioner clinic.
Methods: Net revenue was based on net collections for clinic, professional, operative, hospital-setting and facility charges generated during 12 consecutive monthly VACs beginning July 1st 2015. Expense calculations included provider and staff salaries, benefits, supply costs and clinic leasing costs.
Results: There were 469 clinic visits of which 202 were new patient evaluations. 68 patients underwent 96 surgical procedures under general anesthesia, including sclerotherapy/embolization by the interventional radiologist (n=34), surgical excision (n=20) or laser procedure (n=19). 3 patients were admitted. Gross revenue was $1,313,144 and net revenue was 42.7%, or $561,721. Expenses totaled $331,314 for a net positive revenue of $230,415.
Conclusion: When including direct downstream revenue, our VAC program operates on a net positive margin making the program financially feasible.

P198
Developing a Canadian Vascular Anomalies (VA) Network: Initial Steps Toward a First National Clinical Trial

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Purpose: To highlight the unique opportunities the Canadian health care system presents in fostering a network of health care providers involved in the care of patients with vascular anomalies.
Methods: To describe the accomplishments of two, one-day national meetings (2015/2016) hosting seven centres from across Canada. Descriptive statistics were used to summarize the centres' characteristics.
Results: An interdisciplinary approach has been recognized as the ideal model of care for children afflicted with vascular anomalies. In the USA, where a fee-for-service-based healthcare cost recovery system exists, pediatric hematologist-oncologists have played a pivotal role in this model of care. In Canada, seven formal VA Clinics exist. All are affiliated with academic pediatric hospitals. Each clinic sees between 50-500 patients/year, depending on geographic location (total in Canada 1,700-2,000 patients /year). Each VA clinic consists of an interdisciplinary team. At the national meetings there was interdisciplinary representation. Several initiatives specific to: a) education (E); b) clinical care/advocacy (CCA); and c) research (R) were proposed/started. These included: 1) Website creation (E, CCA), hosting information from all centres, and educational material for patients/families; 2) Bi-annual Webinars (E), with a rotational responsibility amongst centres to present challenging cases for interdisciplinary discussion; 3) National VA REDCap Database development (CCA, R), lending data elements from an already established VA-specific dataset, to serve as a platform for initial descriptive research projects. Projects include a retrospective review of patients in Canada treated with Sirolimus, and the use of acetyl salicylic acid vs. low molecular weight heparin in patients with slow flow vascular malformations with symptomatic phleboliths.
Conclusion: While there are only 7 VA centres formally recognized across Canada, a relatively large number of patients with VA are seen. Despite a paucity of resources, interdisciplinary care delivered to this patient population has flourished throughout the country. A "low budget" collaborative and interdisciplinary approach may overcome some of the local limitations, furthering national efforts in this field.

P199
Canadian Vascular Anomaly Care and Treatment- A cross country glance

Pam Cox (Registered Nurse, IWK Health Center); Lori Vollmerhaus (Registered Nurse, Alberta Health Services); Wendy Moss (Registered Nurse, BC Children's Hospital); Julie Miller (Registered Nurse, Alberta Health Services)

Purpose: The purpose of this poster presentation is to highlight the varied approaches to managing and treating vascular anomalies across Canada. Statistics gathered on all known Canadian vascular anomaly clinics with a focus on clinic structure, medical specialists and clinicians, patient population, treatments offered, patient mix and nursing support are presented. Through this research, a diversity in approaches has been identified among the country's varied clinic formats. Identification of clinical resources for vascular anomalies across Canada is essential to the advancement of patient care through collaboration and knowledge sharing. A network of Canadian experts in the study of vascular anomalies has been created and continues to develop with the goal of continuously advancing knowledge and care for patients with vascular anomalies. Sharing this information globally will provide other clinicians with information on Canadian resources as well as potentially lead to further advancements with national participation in future research and global developments within the field.

P200
Essentials for a Vascular Anomaly Center - steps and procedures for efficient and effective patient care

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Purpose: Vascular anomalies are a diagnostic and therapeutic challenge for medical and paramedical disciplines and require dedicated interdisciplinary management. Effectice and efficient patient care is based on integral medical evaluation with a dedicated set up for diagnosis and treatment. Involved disciplines managing vascular anomaiies have to dedicate their expertise. Optimal patient care adresses multifactorial logistic and medical subject related issues.
Methods: A dedicated classification system modified is presented. The vast spectrum of diagnostic modalities, ranging from ultrasound with color Doppler, conventional X-ray, CT with 4D imaging and MRI as well catheter angiography for appropriate assessment of the existent vascular anomalies is being discussed. Logistic requirements for a functioning vascular anomaly center are discussed as well as minimalinvasive interventional radiology skills for treatment.
Results: Establishing knowledge and diagnostic and therapeutic expertise for vascular anomalies requires a multidisciplinary effort. According to their appearance, venous malformations are the most common representative of vascular anomalies (70%), followed by lymphatic malformations (12%), arterio-venous malformations (8%), combined malformation syndromes (6%) and capillary malformations (4%).
Conclusion: The aim of this overview is to provide information that is required to establish a vascular anomaly center with multidisciplinary interaction of interacting clinical fields. This should facilitate interdisciplinary approach to vascular anomalies. Effective and efficient patient management in a vascular anomaly center requires: 1. Provision of optimal patient management consisting of diagnosis, therapy and patient care on the basis of interdisciplinary exchange and collection of clinical experience in all areas of specialization for vascular anomalies; 2. Application of individualized, dedicated diagnostic tools that address patient-specific symptoms and the severity of disease manifestation; 3. Treatment decisions based on interdisciplinary agreement and under consideration of the available minimal invasive therapeutic spectrum; 4. Performance of dedicated interventional radiological procedures; 5. Establishment of diagnostic and therapeutic quality standards; 6. Assurance of a high level of patient satisfaction with regional and national perception and recognition of the center; 7. Interdisciplinary application of all available technical and scientific resources; 8. Establishment of interdisciplinary research collaborations (including scientific applications for research funding); project funding by industry and medical sciences and technology; strategic positioning of the center; 9. Collaboration with foundations and patient self-help groups

P201
Verrucous venous malformation of the hand

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Purpose: Verrucous venous malformation (VVM), sometimes called verrucous hemangioma, is a rare vascular anomaly that is most commonly seen in the extremities. The lesion typically presents as a deep purple skin stain in early infancy and evolves into a larger scaly, keratotic (verrucous) lesion later in life. Early recognition of this lesion is important because minimally-invasive techniques such as sclerotherapy or cryotherapy are ineffective; surgical intervention is the best method of treatment. We provide our unique clinical experience of treating patients with VVM of the hand.
Methods: We identified patients with VVM of the upper extremity from 1990-2017. The disorder was diagnosed based on history, physical examination, histopathology, and imaging. Patients with clinical data, photographs and imaging studies were included in this study. The database consisted of 10 patients with VVM of the hand and 8 of these patients met the inclusion criteria. The findings were categorized by location, size, appearance, histopathology, imaging, and surgical outcome.
Results: Upper extremity lesions were single or grouped (range 0.3-20 cm). In seven patients the lesion presented at birth, in one patient at the age of four months. Four patients underwent one operation; two patients underwent multiple (n=6). Excision was performed at 3-14 years of age. Immunostaining showed focal GLUT1 positivity in five patients. Patients with small lesions isolated to one area (n = 4) remained disease free but those with grouped or larger lesions experienced recurrence or continued growth.
Conclusion: VVM is an unusual and rare lesion. Although similar in appearance to venous malformation, its clinical characteristics and natural history differentiate it from this other entity. Early recognition of this entity can help the patient avoid unnecessary procedures such as sclerotherapy, cryotherapy, or laser that are likely to be ineffective. Although recurrence or persistent growth can occur with surgery, it is the most effective option for treatment.

P202
Idiopathic Colonic Varices: A Rare Vascular Anomaly
Eileen Duggan (Boston Children's Hospital); Steven Fishman (Boston Children's Hospital); Victor Fox (Boston Children's Hospital)

Purpose: Colonic varices are rare and typically thought to be secondary to portal hypertension. Several cases with a hereditary pattern have been reported. We describe the presentation, evaluation, and treatment of a patient series with non-hypertensive congenital colonic varices.
Methods: We performed a retrospective review of patients evaluated at our institution who were diagnosed by colonoscopy with colonic varices without portal hypertension. IRB approval was obtained. Patients were identified by review of our institutional vascular anomalies database. Chart review was conducted to determine history, presentation, evaluation, management and outcomes.
Results: Twenty patients were included with bleeding presenting at an average age of 8.8 (range 2-21) years. Sixty percent were male. Average follow-up time for these patients was 5.4 years. Three patients were siblings whose mother had the same condition. Acute, overt hemorrhage was reported in 95% of patients, typically occurring 1-3 times per year. All patients experienced anemia; hematochezia occurred in 70% and melena in 65%. Eighty percent of patients were transfused with a median of 2 units of blood; 75% received iron therapy. On endoscopy, additional involvement was seen in the terminal ileum in 70%, jejunum in 10% and stomach in 10%. Six subjects underwent limited bowel resection before their presentation to us but had recurrent bleeding. We performed endoscopic therapy in 12 patients. Sclerotherapy and argon plasma coagulation (APC) were used in the elective treatment of 11 patients Four of these patients needed repeated endoscopic therapy. Endoscopic clipping was used in 4 patients for acute hemorrhage. One patient underwent right hemicolectomy due to persistent hematochezia.
Conclusion: Idiopathic non-hypertensive colonic varices are a rare cause of acute lower GI bleeding in the pediatric population. Despite diffuse anatomic distribution, endoscopic therapy can successfully manage bleeding in the majority of patients.

P203
The use of Kinesio tape in children with vascular malformations.
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Purpose: The most frequent complication in the early postoperative period after sclerosing is the occurrence of edema and pain syndrome. To reduce these complications in the early postoperative period, we used kinesiotherapy technology in the area of sclerotherapy.
Methods: 50 children who were on treatment in the St.Vladimir Children's Municipal Clinical Hospital from 2016 to 2017. 32 children (64%) were treated with a diagnosis of venous malformation, 11 (22%) with venous lymphatic malformation and 7 (14%) with lymphatic malformation. The overwhelming majority of malformations were located in the head region - 24 (48%), 11 (22%) in the lower limbs, 10 (20%), upper extremities - 3 (6%), trunks - 2 (4%). All children underwent surgery - sclerotherapy of the pathological cavity. On the operating table, immediately after the operation was completed, 1-2 Kinesio tape (Rock Tape) were placed on the sclerosing area in the form of a "fan", with at least five "fingers" in the position of lymphatic correction (crosswise with 10% tension). The tape was re-glued after 2 days (the 3rd day after the operation), new Kinesio tape were placed in the position of lymphatic correction ("fan-shaped" form with at least 5 "fingers" crosswise, with 10% tension). On the 5th day after surgery, a cross tape was applied to the sclerosing area. During the treatment, photographic registration and ultrasound were performed to assess the dynamics of edema resolution in the field of surgery.
Results: With the introduction of Kinesio tape into the protocol of treatment of children with vascular malformations, we noted that in the early postoperative period, the edema in the area of the operation was less pronounced (when compared of a "classical" pressure bandage). The elimination of edema, on average 1-3 days. There was a decrease in the pain syndrome both in intensity and duration (on average, the duration was 5-8 hours). After sclerotherapy with Kinesio tape, children did not require analgesia and additional therapy.
Conclusion: Using Kinesio tape ("fan-shaped" form with a tension of no more than 10%) allows to reduce edema soft tissues in the sclerosing area, to accelerate its regression, and also reduces the intensity and duration of the pain syndrome, which improves the quality of life of patients and shortens the period of stay in the hospital.

P204
Skin-Related Complications of Klippel-Trenaunay Syndrome
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Purpose: Klippel-Trenaunay syndrome (KTS) is a rare, complex vascular anomaly defined by capillary malformation (CM), venous malformation (VM) +/- lymphatic malformation (LM), and limb overgrowth, and has been linked to mutations in the PIK3CA gene. Reported skin-related complications of KTS include eczema, ulceration, verrucous changes, vascular ectasias (blebs), bleeding, and infection. The prevalence of these complications and their determinants are unknown. We aimed to determine the spectrum, prevalence, and predictors of skin-related complications occurring in patients with KTS.

Methods: A retrospective review of 410 patients evaluated between 1976 and 2012 and fulfilling strict KTS criteria was performed. Skin-related complications were identified including eczema, ulceration, cellulitis, skin cancer, and CM complications (thickening, bleeding, blebs).
Results: Skin-related complications were present in 45% (184/410) of patients. Patients with LM were over 17 times more likely to experience a skin-related complication compared with patients without LM (odds ratio 17.17; p<0.001). Additional features associated with skin-related complications were male sex (odds ratio 1.63; p=0.034), location of VM on the buttocks/perineum/genitalia (odds ratio 1.92; p=0.009), and presence of CM on the feet (odds ratio 1.77; p=0.039). The prevalence of skin-related complications was as follows: 103/410 (25%) with a CM complication, 89/410 (22%) cellulitis, 85/410 (21%) ulceration, 6/410 (1%) eczema, and 2/410 (<1%) skin cancer. Of those with CM complication, the most common findings included bleb formation (83/103; 81%), bleeding (71/103; 69%), and thickening (21/103; 20%). Of those with cellulitis, 79% (70/89) had recurrent cellulitis with 34 patients requiring hospitalization.
Conclusion: Skin-related complications affect nearly half of patients with KTS with cellulitis, ulceration, and bleb formation being most common. Awareness of these complications and their predictors is vital to early diagnosis and appropriate management.

P205
Venous Malformations of the Skeletal Muscle: histologic variation, atypical clinical presentations and unique imaging features that help in the diagnosis

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Purpose: Venous malformations of the skeletal muscle (intramuscular venous malformations, IMVM), sometimes incorrectly termed intramuscular hemangiomas, are those largely contained within a muscle or a muscle group. Their diagnosis is frequently challenging. These lesions are not infrequently referred to our Vascular Anomaly Clinic for unnecessary and potentially risky biopsies. The purpose of this poster is to emphasize the histologic variability, atypical clinical presentation including the associated coagulation abnormalities and unique imaging features as well as the differential diagnosis of venous malformations of the skeletal muscle to avoid unnecessary biopsies and guide to the correct treatment.
Methods: On this poster we will show a series of patients with venous malformations of the skeletal muscle seen at our Vascular Anomaly Clinic that include clinical photographs, histologic photographs and series of radiographs, ultrasound and MR images. We also discuss the laboratory abnormalities related to the associated coagulation anomalies and the risks factors inherent to these malformations. The differential diagnosis and pitfalls of these lesions will be discussed as well. Finally we will discuss the multidisciplinary approach and specific therapeutic options for this type of lesions.
Results: Clinically, because they are deeply seated lacking skin discoloration and the tendency to rapid growth during adolescence due to hormonal stimulation, IMVM are frequently confused with neoplasms and frequently referred to our Vascular Anomaly clinic for biopsy. By imaging (largely US and MRI) this subset of venous malformations has its own features despite sharing several characteristics with other venous malformations that would be discussed. Their propensity to thrombose and produce coagulation abnormalities (i.e. localized intravascular coagulopathy) can add confusion to the clinical and imaging presentation.
Conclusion: On this poster we emphasize the histologic variability, atypical clinical presentation including the associated coagulation abnormalities and unique imaging features as well as the differential diagnosis of venous malformations of the skeletal muscle that can help making the correct diagnosis in order to to avoid unnecessary biopsies and guide to the proper treatment.

P206
Compartmentalization using barbed sutures in the treatment of infiltrative venous malformations.

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Purpose: To investigate the usability of barbed sutures for compartmentalization of infiltrative or extensive venous malformations (VMs) in soft tissues.
Methods: Between March 2015 and March 2017, a total of four patients with venous malformations were treated with compartmentalization using barbed sutures. In this technique, large barbed sutures are continuously placed from the skin to the periosteum or muscle within the lesion to compartmentalize each lesion. Subsequently, three patients with VMs in the buccal and lip region, orbital region, and lower extremity, respectively, received sclerotherapy while one patient with VM in the orbital region underwent partial resection. The sclerosant used was 3% foam polidocanol, absolute alcohol, or a combination of the two. The sutures were removed immediately after the injection of sclerosant or surgical resection.
Results: In all patients, a small amount of bleeding was seen, and the lesions were successfully reduced in size. Post-operative serious complications were not encountered.

Conclusion: Using continuous suturing with barbed sutures, it was easy to compartmentalize infiltrative or extensive VMs. With this technique, the sclerosant spread effectively in each lesion and controlled serious bleeding.

P207
Microsurgical Resection of Vascular Malformations of the Upper Extremity

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Purpose: Vascular anomalies of the upper extremity, particularly those with a venous component, occasionally arise from venae comitantes of a major artery. These malformations are intimately associated with the artery, usually circumferentially enwrapping it. In these instances, resection of the lesion is desired without sacrifice of a patent artery, especially in an end organ such as the upper extremity where distal perfusion relies mainly on end-vessels.
Methods: We reviewed the records of 7 patients who presented with vascular malformations (predominantly venous in nature) that were circumferentially wrapped around a major blood vessel in the upper extremity. Surgical resection was undertaken due to symptoms of pain or persistent growth. A microscope and microsurgical instruments were used to dissect the lesion free from the involved artery(ies).
Results: The common and/or proper digital arteries were involved in 6 cases and the radial artery was involved in one case. In all instances, the malformation was meticulously removed from the artery with preservation of arterial continuity and blood flow. The pathology was venous malformation in 6 patients and fibroadipose vascular anomaly (a variant of venous malformation with more fibrous/fatty characteristics and smaller venous channels) in one patient. Two patients experienced delayed skin wound healing. No patient experienced distal ischemia, bleeding, functional compromise, or recurrence of the excised lesion.
Conclusion: Microsurgical dissection using a microscope and microinstruments is a viable technique for removal of difficult vascular malformations that are circumferentially wrapped around major arterial channels in the upper extremity. Use of this technique allows preservation of maximum blood supply while excising symptomatic vascular lesions.

P208
Clinical Characteristics of Venous Malformations in Head and Neck: A Retrospective Review of 82 Cases

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Purpose: A number of studies have been conducted on venous malformations (VMs) as they are one of the most common types of vascular malformation. However, there are disagreements over causes and management of the disorder, and studies specific to VMs of the head and neck are limited. Thus, this study aims to share our experience with the diagnosis and treatment of VMs of the head and neck.
Methods: A retrospective study was conducted involving 82 patients who had received treatment for head and neck VMs among 222 VM patients who had visited our vascular anomalies center for 10 years. Based on their medical records, commonalities in the results of their diagnosis and treatment were investigated. The diagnosis of head and neck VMs was confirmed based on the results of imaging studies or biopsies, and the patients were classified based on the evaluation of magnetic resonance images, computed tomography, and Doppler sonography.
Results: Women had slightly higher incidence rates at 59.8%, and 45.1% of the patients developed the first symptom of VMs at the age of ten or below. The incidence of lesions was slightly higher on the right side at 47.3%. The main sites involved were cheeks (27.7%) and lip area (25.5%). The muscle layer was most commonly involved at 98.7%. Small lesions less than 5 cm in diameter formed a majority at 60.8%, and well-defined types were slightly more prevalent at 55.4% than ill-defined types. Regardless of grades, 77.1% of the tracked patients showed improvement and 22.9% exhibited recurrence.
Conclusion: For the successful treatment of VMs, an early and accurate diagnosis and appropriate choice of treatment method according to each patient's symptoms are important. Therefore, for an early and accurate diagnosis, VMs require a multidisciplinary approach more than any other disorders, and an appropriate treatment option should be determined for each case.

P209
Vascular Anomalies of the lips: Anatomic Distribution and Deformity Patterns in 150 consecutive patients.

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Purpose: Vascular anomalies (VA) of the lips are markedly visible and require frequent and challenging approaches. Two key problems are recurrent for both tumors and malformations: worsening of the deformity with patient growth and involvement beyond the anatomical limits of the lip. This study aims to analyze lip deformities caused by the presence of VAs, searching for correlations between specific diagnosis, anatomic mapping and pattern of the deformity.
Methods: Between 1999 and 2017, 150 patients with deformities caused by lip VAs were consecutively evaluated. Diagnosis was based on ISSVA 2014 Classification and clinical and photographic analysis were performed to match the pattern to a lip chart. The following parameters were considered: lip involved (upper/lower/both), location (central, lateral, both and comissure), extension, skin affected beyond vermillion and volume distortion.
Results: VAs were diagnosed as infantile hemangiomas (IH) in 76, venous malformations (VM) in 35, arteriovenous (AVM) in 20, capillary (CM) in 16 and lymphatic (LM) in 3. Female predominance was due the higher prevalence of IHs. The patterns for IH was up to 50% single lip compromise, more centrally located, extending beyond vermillion. VMs were predominant in the upper lip, more laterally located, with up to 75% compromise, causing marked deformation. AVMs presented similar pattern, except for compromising the vermillion limits. CMs caused predominant total lower lip compromise with rare volume deformation (Table).
Conclusion: Specific patterns could be identified for different lip vascular anomalies. It might help as an addictive tool in diagnosis and management of lip vascular anomalies.

P210
Usefulness of vessel sealing system (LigaSure® small jaw) for debulking of massive venous malformations

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Purpose: The therapeutic options of the venous malformation (VM) are generally resection and sclerotherapy to control the amount of bleeding. However, massive VM which involve muscles requires segmental and multi-phase resection to reduce the volume of VM, resulting in the possibility of uncontrollable bleeding. Conventional ligation and electrocoagulation cannot control bleeding from the stump of VM. To overcome this concern, we adopted vessel sealing system (LigaSure® small jaw, Tokyo). In this paper, technique to handle this device and the results are described.
Methods: Between 2015-2017, 6 patients underwent resection of massive VM with LigaSure®. 2 males and 4 females were included, and their average age was 26.1 years old. There were 3 VM of the trunk, 2 of the face and 1 of the forearm.
Results: LigaSure® small jaw was very useful especially when the VM involved face and intercostal muscle in back region and segmental resection was obligatory. Furthermore, damage to the nerves in the forearm which were involved in the VM were prevented, because LigaSure® small jaw was able to resect severe VM parallel to the nerves. Average amount of bleeding was 1371ml (135ml-3745ml) and average operation time was 421mins. No significant complications such as motor dysfunction or loss of sensation was detected.
Conclusion: LigaSure® small jaw instrument may enable reduction of blood loss and division of the VM to preserve functional tissue.

P211
Isolation of primary endothelial cells from human venous malformations

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Purpose: Venous malformations (VMs) are the most common vascular malformations, with an overall incidence of 1/5000. VMs are usually congenital lesions that consist of dilated venous channels with scarce mural cell coverage. These VMs can be of different sizes and be present in any tissue, such as subcutaneous tissue or internal organs. VMs are painful and disfiguring, many lead to bleeding and obstruction of organs, and in some cases to localized intravascular coagulopathy. Recently, it has been found that most venous malformations are caused by either somatic mutations in the TEK or PIK3CA genes; however, the molecular and cellular mechanisms behind the pathogenesis of VMs remain unclear. Here, we describe a novel technique to successfully isolate and culture primary endothelial cells derived from human VMs.
Methods: We have been able to isolate endothelial cells from surgical resections and biopsies of VMs from different body sites, either in skin or mucosa. Briefly, fresh human VMs are subjected to tissue digestion until reaching a single-cell suspension; then endothelial cells are isolated through positive selection using

antibody-coated magnetic beads. Primary endothelial cells are cultured with a specific culture medium enriched with endothelial growth factors.
Results: Unlike non-pathologic primary endothelial cells, VM-derived endothelial cells grow perpetually, similar to tumour-derived cells. Microscopically, these cells show the typical cobblestone appearance of the endothelial cell culture. Further characterization by immunoblotting and immunofluorescence shows that these cells express endothelial-specific markers such as VE-Cadherin, CD31, and VEGFR2.
Conclusion: Our newly developed protocol has a strong impact on the research field of vascular malformations since this will allow 1) genetic analysis of patient-derived lesions without the need of ultra-deep sequencing techniques, 2) molecular and cellular understanding of the pathogenesis of vascular malformations, 3) setting up pre-clinical systems towards precision and personalised medicine. Importantly, this protocol may be translated to other types of vascular malformations.

P212
Discrepancy between the clinical and histopathologic diagnosis of soft tissue vascular malformations

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Purpose: Soft tissue vascular malformations are generally diagnosed clinically, according to the 'ISSVA classification'. Diagnostic histopathologic examination is rarely performed. We sought to evaluate the validity of the current diagnostic workup without routinely performed diagnostic histopathology.
Methods: We retrospectively determined whether there were discrepancies between clinical and histopathologic diagnoses of patients with clinically diagnosed vascular malformations undergoing therapeutic surgical resections in our center (2000-2015). Beforehand, a pathologist revised the histopathologic diagnoses according to the ISSVA classification.
Results: Clinical and histopathologic diagnoses were discrepant in 57% of 142 cases. In these cases, the pathologist made a different diagnosis than the clinician: this was not at all a vascular malformation (n=24; 17%), a completely different type of vascular malformation (n=26; 18%), or a partially different type with regard to the combination of vessel-types involved (n=31; 22%). Possible factors associated with discrepancy were both clinician-related (e.g. diagnostic uncertainty) and pathology-related (e.g. lack of immunostaining).
Conclusion: The large discrepancy between clinical and histopathologic diagnoses raises doubt about the validity of the current diagnostic workup for vascular malformations. Clear clinical and histopathologic diagnostic criteria seem the essential first step toward a uniform diagnosis.

P213
Orthopedic Complications of Klippel-Trenaunay Syndrome

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Purpose: Klippel-Trenaunay syndrome (KTS) is a rare combined vascular malformation composed of capillary malformation, lymphatic and/or venous malformation, and limb overgrowth, which commonly affects the extremities. Due to limb involvement, it is not uncommon for these patients to require referral to an orthopedic surgeon. While small case series and case reports exist regarding orthopedic management of KTS, large cohort studies are lacking.
Methods: Between 1976 and 2012, 410 patients fulfilling strict KTS criteria were reviewed retrospectively. Orthopedic complications and surgical interventions were identified.
Results: 264 of 410 patients (64%) with confirmed KTS required orthopedic evaluation. Of these 264 patients, 84% had documented limb length discrepancy. Other common diagnoses included: angular deformities (10%), scoliosis (9%), osteopenia/osteoporosis (7%), pathologic fractures (6%), joint contracture (5%), degenerative joint disease (4%), and limb/joint pain (4%). Of the 264 patients evaluated by orthopedic surgery, 133 patients (50.4%) underwent 169 surgeries. Surgery was most commonly performed for limb length discrepancy (62%). Forty-three patients (32% of those who required surgery) underwent amputation of all or part of an affected limb. Other common procedures included arthroscopic debridement (10%), debulking of venous or lymphatic malformation (7%), total joint arthroplasty (5%), and pathologic fracture fixation (4%). A subgroup analysis of KTS patients based on the type of vascular malformation was also performed. The presence of a lymphatic vascular malformation was associated with an increased need for orthopedic evaluation (OR 2.5, p=0.004). A multivariable model confirmed an orthopedic complication was more likely in patients with lymphatic malformation (OR 3.78, p<0.001), as well as those with bone and/or soft tissue hypertrophy of the lower extremity (OR 7.51, p<0.001).

Conclusion: Klippel-Trenaunay Syndrome remains a complex problem with clinical ramifications that bridge multiple medical subspecialties. Orthopedic manifestations of KTS are ubiquitous, with over half of patients requiring surgical intervention, particularly KTS patients with lymphatic components.

P214
Arthropathy in patients with vascular malformations – long term follow-up results of a rare condition

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Purpose: Vascular malformations (VM) represent a challenge in diagnosis and treatment of orphan diseases. If these VM cause decreased joint mobility and/or pain, this may be accompanied by destructive joint changes. This entity is called Hauert`s Disease (HD) or angiodysplastic destructive arthropathy and is classified into 3 stages – from only synovial thickening in MRI (grade 1) to decreased cartilage in grade 2 and destructed bone in grade 3. With this long-term follow-up we describe the outcome of this condition.
Methods: The files of patients treated for HD in our institution from 1983-2017 were collected in retrospective study. Medical data was entered in an MS Excel file. For evaluation of the joint damage, native x-ray, MRI and arthroscopy was conducted. Follow-Up was taken out by examination of the patient. The patients were classified according to the extent of the VM, localization of the arthropathy and orthopaedic procedures performed.
Results: 50 patients (34 female; 16 male) with HD were diagnosed. The Disease was isolated to one joint in 48 cases (2 shoulder; 3 hip; 41 knee; 2 ankle) and found in multiple joints in 2 cases (both knee + ankle). Out of the 48 single-joint-cases 14 were grade 1, 13 grade 2 and 21 grade 3. One of the poly-joint-case showed grade 3 in both, the other grade 3 in one and grade 1 in the other joint. Besides numerous vascular interventions, the patients were treated with arthroscopic debridement (n=29) or by joint replacement (n=10; all of which were grade 3). The other patients either did not require debridement (n=7) or due to excessive VM orthopaedic treatment was not possible (n=4).
Conclusion: Angiodysplastic destructive arthritis is a rare disease. Orthopedic treatment is a good option to improve the patients mobility with excellent long time results. The classification suggested by Hauert seems reasonable to compare cases.

P215
Using three-dimensional volumetric analysis of venous malformations to assess the effectiveness of percutaneous sclerotherapy

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Purpose: To explore the feasibility of 3D software (MIMICS) in the evaluation of sclerotherapy, there is no more accurate statistical way to measure the efficacy of VMs after sclerotherapy. In this study,MIMICS was evaluated to calculate the performance of the lesion after treatment.Therefore, we can pre-evaluate the effect of the clinical treatment dose on the lesion in advance.
Methods: Head and neck (n = 14), trunk (n = 2), and 16 patients with venous malformation were treated with ethanol sclerotherapy or foam sclerotherapy every 8 weeks. The VMs volume before and after treatment were measured using MMICS. Each treatment of the patient will be recorded.We analysis the relationship between the number of treatment and the reduced volume of VMs.
Results: In MIMICS,we use superposition method: lesion images each plane thickness of 0.7 mm. According to the MRI image on the difference between the different gray values ofthe region of interest will be divided into two categories of pixels, that is, the skin andgland bright signal and Fat black signal and then determine the threshold of VMs internal organization and VMs are separated from the external background, which can be obtained lesions volume with high accuracy and practical. This operating statistics for the MRI before and after treatment twice, the relationship can be derived therapeutic efficacy and dose.
Conclusion: After the MIMICS software calculates the region of interest, we can conclude that using 1ml of ethanol sclerotherapy can reduce the lesion by 478 mm^3 and using one dosage of foam sclerotherapy which has 4.8ml polidocanol can reduce the lesion by 2388 mm^3. Using the MIMICS 3D volume reconstruction method it can effectively and safely evaluate the efficacy of sclerotherapy, and give preoperative evaluation. This method is simple, accurate and feasible.

P216
Cyanoacrylate embolization as adjunct to sclerotherapy of intramuscular venous malformations.

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Purpose: To assess the safety and efficacy of cyanoacrylate embolization as adjunct to sclerotherapy in the treatment of intramuscular venous malformations.
Methods: Retrospective review of patients with intramuscular venous malformations treated with cyanoacrylate embolotherapy as adjunct to other sclerotherapy agents. Clinical features, procedural details, and clinical and imaging outcomes were assessed.
Results: Twenty-three patients underwent a total of 49 cyanoacrylate embolization procedures. Mean age at the time of initial treatment was 9 years (range 6 months – 8 years). Fifteen lesions were located in the lower extremity, 6 in the upper extremity, 1 in the sternocleidomastoid and 1 in the paraspinal muscles. All lesions were treated with an image-guided percutaneous approach. Sclerosants injected during the procedures included STS, ethanol and bleomycin. The cyanoacrylate was diluted with lipiodol to 20-25% ratios. There was clinical follow-up after 39 of the 49 procedures; symptoms improved in 37 and were unchanged in 2. None of the patients experienced worsening of symptoms. Follow up imaging demonstrated no or minimal (<10%) residual patent venous channels in 14, moderate residual component in 3 (<25%) and large (25-75%) residual component in 6. There were no major complications. There was 1 minor complication. A small glue cast migrated to the proximal femoral vein in 1, which was flushed and patency of the vein maintained.
Conclusion: Cyanoacrylate embolization is safe and effective as adjunct treatment for intramuscular venous malformations. This technique has the potential to reduce the amount of sclerosant used and the number of total procedures performed.

P217
Sclerotherapy-based treatment in slow flow vascular malformation: our experience of 1493 cases

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Purpose: Slow flow vascular malformation are common vascular anomalies, and account for 40% of all vascular malformations. They are caused by malformed and dilated venous channels, and progressed with age. Functional disability, bleeding, and disfiguration are the most complications for medical consultancy. These diseases are complex because they cannot easily separate from normal tissue by traditional surgery, and complicated with bleeding. We developed several sclerotherapy-based treatment strategies to treat this disease by anatomic location and anesthetic consideration.
Methods: Although our senior author has been major in these complex diseases for more than 4 decades, complete data collection have only begun from 2000. Total 1493 cases are included in this study with equal gender distribution. We use Magnetic Resonance Imaging study (MRI) as guideline for treatment. The mainstay of our treatment is sclerotherapy. If the lesion is diffuse or in critical area, we perform only sclerotherapy every two months, following with local compression in between. Otherwise, if the disease is localized or surgical removable, we do sclerotherapy to establish solidification, then follow with immediate excision to avoid massive bleeding. Other possible combination therapies include echo-assisted injection, and laser therapy.
Results: Most cases were proved to be effective to our treatment, which means more than 20% reductions in size by MRI studies. Some of them got complete remission with sclerotherapy only, while others were free from disease under combination sclerotherapy with surgery. Overall complication rate in our series is low. Minor complications, defined as mild skin necrosis without need for surgical repair, skin hyperpigmentation, and local paresthesia, are presented as low as 1.5%. Major complications including large area skin/soft tissue loss need surgery, limb amputation, cerebrovascular accident, and organ dysfunction, happened in 7 of all 1493 patients. No mortality occurred in our series.
Conclusion: We use sclerotherapy-based multidisciplinary treatment to deal with slow flow vascular malformations. We report our result with statistical methods and review literatures.

P218
Bleomycin Polidocanol Foam Sclerotherapy of Venous Malformations: Interim Results of a Novel Sclerotherapy Technique

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Purpose: To prospective evaluate the clinical and radiographic outcomes of patients with venous malformations (VMs) treated with bleomycin polidocanol foam sclerotherapy.
Methods: The institutional review board waived ethical approval for this retrospective review in which 55 patients (31 female and 24 male patients; mean age 18.8y, 2–60 y) with symptoms of swelling, pain, and deformities, were treated with bleomycin polidocanol foam sclerotherapy. Lesions were located in the head and neck in 38 patients (69.1%), e xtremities in 15 patients (27.3%), and trunk in 2 patients (3.6%). 111 sclerotherapy sessions were performed, with a mean of 2.0 treatments per patient (range, 1–6). An average of 10 mL bleomycin polidocanol foam (15 mg bleomycin, 2 mL 3% polidocanol, and 8 mL air) was used per procedure, with total amount range of 2.5 mL to 60 mL. Technical and clinical success of the treatment was evaluated. Informed consent, as well as pain, swelling, infection, risks of anesthesia, skin injury, nonresolution or worsening of symptoms, and possible need for further or multiple procedures, was obtained for all patients. Standard sclerotherapy techniques were used. Technical details of all procedures were recorded prospectively. Follow-up included immediate postprocedural assessment and outpatient clinic review.
Results: All procedures were technically successful with no intraprocedural complications. Mean follow-up was 7 months, with a range of 1-12 months. Postprocedure complications were minor in 15 of 111 procedures (13.5%) and no major complications occurred. All 55 patients (100%) reported improvement in their symptoms after treatment sessions. Postprocedural magnetic resonance (MR) imaging demonstrated volume reduction of treated lesions in 55 of 55 patients (100%), with a mean lesion volume reduction of 84.6%.
Conclusion: The use of bleomycin polidocanol foam for the percutaneous sclerotherapy of VMs is safe and effective. Bleomycin polidocanol foam may be a promising first line agent for venous malformation.

P219
Bleomycin Recruits fibroblasts and increases the deposition of ECM to facilitate the regression of Early-Stage Extracranial Arteriovenous Malformation

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Purpose: We previously reported that interstitial injection of bleomycin (BLM) reduces the size of early-stage extracranial AVM. Here we seek to investigate the role of fibroblast recruitment and the deposition of extracellular matrix (ECM) in the BLM-treated AVM.
Methods: Samples of human extracranial AVM (n=8) treated with bleomycin were harvested and underwent immunostaining. The transcript as well as protein level of collagen, laminin, matrix metallopeptidases (MMP) and metallopeptidase inhibitor (TIMP) were examined. Specimens from human extracranial AVM (n=8) with no treatment were used for control.
Results: A large body of fibroblasts were found around the malformed vessels in bleomycin-treated AVM samples but not in those of control group. Expression of MMP1, MMP10, MMP14 collagen IV were found significantly increased whereas collagen I and TIMP3 were downregulated in BLM-treated group.
Conclusion: Bleomycin Recruits fibroblasts and increases the deposition of ECM to facilitate the regression of Early-Stage Extracranial Arteriovenous Malformation. Inflammation-induced fibroblast recruitment is the key to the mechanistic action of bleomycin in treating AVMs.

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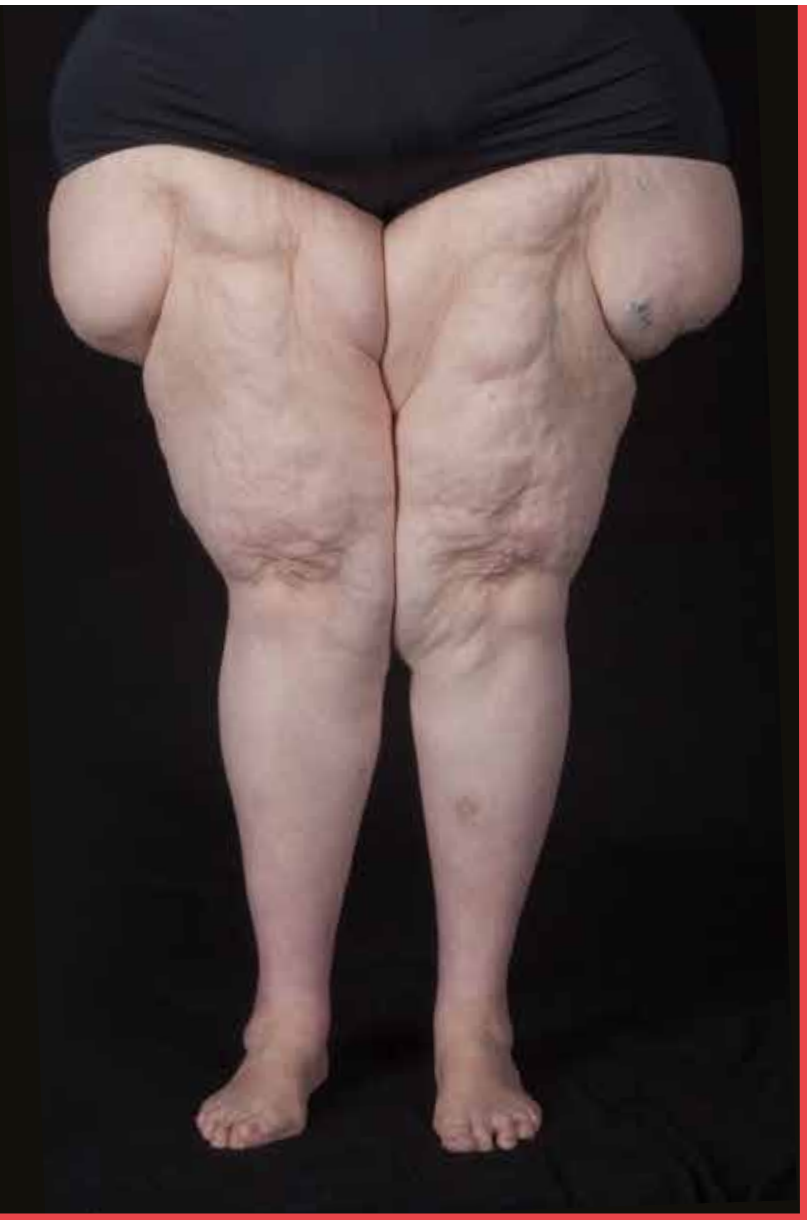

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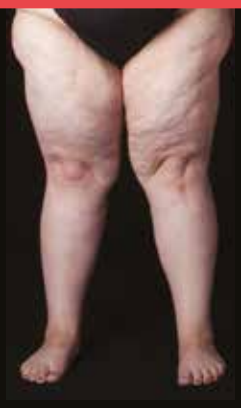

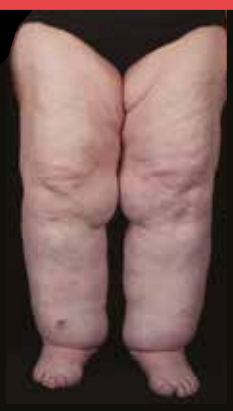

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