гострий період розвитку АА на тлі АГ. За комбінованого застосування лефлуноміду, целекоксибу та амлодипіну лише у гострий період запалення, що розвивається на тлі артеріальної гіпертензії, реєструється протинабряковий ефект на рівні  $12\,\%$ , що суттєво знижується в інші періоди спостереження.

**Ключові слова:** лефлуномід, протинабрякова дія, ревматоїдний артрит, артеріальна гіпертензія, коморбідна патологія.

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значимым этот эффект был в острый период развития AA на фоне AГ. При комбинированном применении лефлуномида, целекоксиба и амлодипина только в острый период воспаления, развивается на фоне артериальной гипертензии, регистрируется противоотечный эффект на уровне 12%, что существенно снижается в другие периоды наблюдения.

**Ключевые слова:** лефлуномид, противоотечное действие, ревматоидный артрит, артериальная гипертензия, коморбидной патологии.

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### CORRECTION OF BREAST ASYMMETRY: STRUCTURAL CHANGES OF ADIPOSE TISSUE IN AUTOLOGOUS FAT GRAFTING

The purpose of the work was to determine the structural features of adipose tissue during auto transplantation of a fat transplant. It was found that changes in aspirated adipose tissue indicate partial trauma and violation of the integrity of individual adipocytes in preparation for transplantation. However, an analysis of the structural organization of adapted adipose tissue found that the decrease in adipocyte volume was 19,4 % - 23,1%. Thickening of the layers of connective tissue in adapted adipose tissue is due to compensatory-reparative processes and the maturation of the fibrous component and the amorphous substance of the connective tissue during transplant engraftment. These phenomena are accompanied by an increase in the number of migrant cells in perivascular tissue. On the part of the blood vessels of the hemomicrocirculatory bed, changes were found to have a stereotypic nature on the action of exogenous factors.

Key words: adipose tissue, fat transplant, breast volum asymmetry.

Autologous fat grafting (AFG) technique, used for augmentation of the breast or correction of breast asymmetry is becoming more popular for several reasons. First, fat is autologous and, in most cases, abundant. Second, it is malleable material with the ability to naturally integrate into tissue at the site of injection and is widely used in correction of breast asymmetry. Another advantage of AFG is the possibility of removing excess fat from the areas of the inner surface of the knees, the inner surface of the thigh, the anterior abdominal wall, thus, reducing fat in these areas. Owing to these positive properties autologous fat grafting is increasingly being used as an alternative to commercial fillers, if necessary, for soft tissue expansion and correction of aesthetic defects [4]. According to the report of International Society of Aesthetic Plastic Surgery (ISAPS), in 2009, the frequency of use of autologous fat grafting technique accounted for 5.9% in the structure of aesthetic procedures [6]. The effectiveness of the autologous fat transplantation has improved significantly after the development and standardization of lipoaspiration techniques. The refined techniques have led to reduction of injury to adipose tissue during liposuction and preservation of the graft survival [7]. The basic standards for increasing the autologous fat graft survival are the safe lopoaspiration and non-traumatic processing of the fat graft. Lipofilling should be made by tunnel method, without the formation of bulk cavities [9]. I.V. Kraiinik reports that the use of autoplasma proteins with centrifugation, and the formation of a single protein-fat conglomerate and injection of the material through cannulas with a diameter of 2 mm provides high survival rate, and the rate of graft resorption is not more than 15% [2]. According to the publications, autologous graft retention varies from 40 to 90% [5]. Such variability of results suggests that there is no objective method for evaluation the viability of a fat autograft. Moreover, estimation of lipofilling results is subjective, often made "by eye" or by photos before and after surgery, which is not objective. There is no method that determines how much volume is added to donor sites. That is, the volume in the donor site was augmented due to the quantitative increase in adipocytes due to transplantation or due to the qualitative increase in the volume of old adipocytes through weight, gained by a patient. Therefore, determination of the major changes that occur in lipoaspirate and integrated fat, compared to the intact one, is crucial in the state-of-the-art reconstructive surgery.

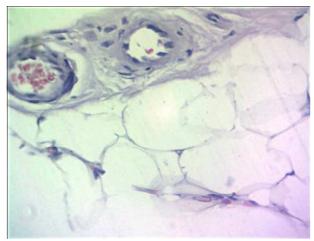
**The purpose** of the study was aimed at determination of the structural features of the adipose tissue during autologous fat grafting.

**Methods and Material.** Flaps of the adipose tissue were used in the primary correction of breast asymmetry (intact group), lipoaspirate (fat from the anterior abdominal wall) and fragments of oleomas were taken during re-correction. Flaps of adipose tissue and lipoaspirate were placed in 10% buffered

formalin for 24 hours. The material was embedded into paraffin, using conventional technique and sections of 5 µm were made, which were stained with hematoxylin and eosin [1].

Migroimaging and morphometric study was performed using the Biorex-3 BM-500T microscope with digital DCM 900 microphotohead with software, adapted to these studies. The average number of adipocytes in the field of view, area, perimeter and radius of the cells, measured in  $\mu$ m, was determined. Statistical processing of the morphometric data and quantitative analysis were performed by conventional statistical methods using the Exel program [3].

**Results and Discussion.** Histological study of the specimens of the intact adipose tissue, stained with hematoxylin-eosin, revealed the particles formed by adipocytes, surrounded by the layers of connective tissue, where vessels of the microvasculature and nerve fibers were visualized. The layers of loose connective tissue inside the particles were thin and formed by basophilic collagen fibers. Between the adjacent 3-4 adipocytes, capillary-type vessels, free from red blood cells in the lumens were detected; consequently, trophic processes in the tissue were provided by the flow of blood plasma in the capillaries. Arteries and veins, containing blood corpuscles were determined in the interparticle layers (Fig. 1).



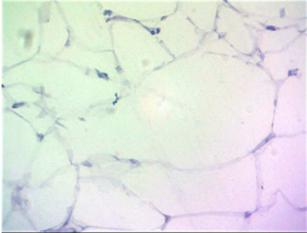


Fig. 1. Adipocytes and vessels of the microvasculature in the particles of the intact adipose tissue. Microimage. H&E stain. 400×magnification.

Fig. 2. Adipocytes in the lipoaspirate. Microimage. H&E stain.  $400\times magnification.$ 

The analysis of the structural features of the lipoaspirate has shown disintegration of the plasmalemma in the majority of adipocytes. This phenomenon is caused by injury and partial destruction of individual adipocytes during lipoaspiration.

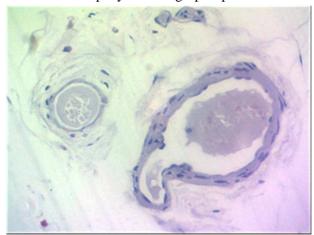


Fig. 3. Vessels of the microvasculature and leukocyte-type cells in the integrated adipose tissue. Microimage. H&E stain. 400×magnification

Histological study of the integrated fat has established that the layers of connective tissue between the particles were thickened, similarly to the loose connective tissue between the individual adipocytes. Perivascularly, young oxyphilic collagen fibers and the leukocyte-type cells, namely, macrophages, lymphocytes, and plasmocytes were detected in the interparticle septa (Fig. 3).

Adipocytes were predominant in the particles of intact adipose tissue and their average number accounted for  $28.4 \pm 0.19$  FOV. The analysis of the features of the lipoaspirate has shown that the average number of cells was 22.8 + 0.03 FOV that was significantly lower than the value in the intact group. The findings of the

morphometric study of specimens of integrated adipose tissue has established that the number of cells in the field of view was significantly less by 10.74% compared to intact adipose tissue (25.35 + 0.15).

The analysis of the qualitative indices of adipocytes in the samples has found that the largest and smallest average area was occupied by the cells of the lipoaspirate and adipocytes of integrated adipose tissue, respectively. The values were significantly smaller at p<0.05 (see the Table). In determining the mean perimeter of the cells it was found that adipocytes of intact adipose tissue and integrated adipose tissue had significantly lower values compared to the lipoaspirate, but did not differ significantly. We obtained similar results for the values of cell radius (Table).

The comparison of the metric data of the intact adipose tissue and integrated adipose tissue has found that the values of the latter were by 10.48% lower compared to intact adipose tissue values.

Table

#### Metric data of adipocytes (µm)

|           | Lipoaspirate     | Intact adipose tissue | Integrated adipose tissue |
|-----------|------------------|-----------------------|---------------------------|
| Area      | 17459,08±2562,37 | 11536,19±236,12 *     | 10071,09±150,98 *, **     |
| Perimeter | 139,56±9,27      | 113,38±6,74 *         | 98,98±10,43 *             |
| Radius    | 22,21±1,48       | 18,29±1,42 *          | 16,33±1,25 *              |

Note \* - the difference is reliable at p<0,05, compared to the lipoaspirate, \*\* - the difference is reliable at p<0,05, between the values on the intact and integrated adipose tissues.

Thus, the established changes in the lipoaspirate indicate its partial injury and disintegration of the individual adipocytes during preparation for transplantation. However, the analysis of the structural organization of the integrated adipose tissue has found that the resorption was less than 15% that was consistent with the data of other researchers [2].

The thickening of the layers of connective tissue in the integrated adipose tissue is caused by compensatory-reparative processes and maturation of the amorphous substance and the fibrous component of the connective tissue during autologous graft retention. These phenomena are accompanied by an increase in the number of migrant cells in perivascular tissue. Regarding the vessels of the microvasculature, the established changes have stereotyped character due to the effect of exogenous factors [8].

#### Conclusion

It was found that in auto-transplantation of adipose tissue for the purpose of breast asymmetry correction adipocyte volume loss does not exceed 19.4% - 23.1% and depends on the peculiarities of the microcirculatory bed of the donor region of each individual patient. This phenomenon is due to the processes of restructuring of the adipose tissue and vessels of the hemomicrocirculatory bed and is a manifestation of compensatory-restorative processes and processes of aseptic inflammation. The adaptive ability of the fat graft in invasive methods of fat preparation (centrifugation) is somewhat diminished, because the centrifugal force during rotation partially emulsifies the fat aspirate, which, when introduced, is replaced by unformed connective tissue. Methods of non-invasive fat preparation (applique - upholding) increase the ability to adapt fat, because tissue fragments with their microcirculatory bed in the aspirate - are not injured.

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#### Реферати

# СТРУКТУРНІ ОСОБЛИВОСТІ ЗМІН ЖИРОВОЇ ТКАНИНИ ПРИ АУТО ПЕРЕСАДЦІ ЖИРОВОГО ТРАНСПЛАНТАТА З МЕТОЮ КОРЕКЦІЇ ОБ'ЄМНОЇ АСИМЕТРІЇ МОЛОЧНИХ ЗАЛОЗ

Слюсарев М.И., Єрошенко Г.А., Сусак Я.М. Маркулан Л.Ю., Крижановський О.А.

Метою роботи було визначити структурні особливості зміни жирової тканини при аутопересадці жирового трансплантата. Встановлено, що зміни в аспірованій жировій тканині свідчать про її часткову

## СТРУКТУРНЫЕ ОСОБЕННОСТИ ИЗМЕНЕНИЙ ЖИРОВОЙ ТКАНИ ПРИ АУТО ПЕРЕСАДКЕ ЖИРОВОГО ТРАНСПЛАНТАТА С ЦЕЛЬЮ КОРРЕКЦИИ ОБЪЕМНЫХ АСИММЕТРИИ МОЛОЧНЫХ ЖЕЛЕЗ

Слюсарев М.И., Ерошенко Г.А., Сусак Я.М. Маркулан Л.Ю., Крижановський О.А.

Целью работы было определить структурные особенности изменения жировой ткани при аутопересадке жирового трансплантата. Установлено, что изменения в аспирированной жировой ткани свидетельствуют о ее

травматизацію і порушення цілісності окремих адипоцитів при підготовці до трансплантації. Однак, аналіз структурної організації адаптованої жирової тканини встановив, що зменшення об'єму адипоцитів при цьому склало 19,4 % - 23,1%. Потовщення прошарків сполучної тканини в адаптованій жировій тканині обумовлено компенсаторно-репаративними процесами і дозріванням волокнистого компоненту і аморфної речовини сполучної тканини при приживлені трансплантата, асептичним запаленням . Означені явища супроводжуються збільшенням кількості клітинмігрантів в периваскулярній тканині. З боку судин гемомікроциркуляторного русла встановлені зміни мають стереотипний характер на дію екзогенних чинників.

**Ключові слова**: жирова тканина, ауто пересадка, асиметрія молочних залоз.

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частичной травматизации и нарушении целостности отдельных адипоцитов при подготовке к трансплантации. Однако, анализ структурной организации адаптированной жировой ткани установил, что уменьшение объема адипоцитов при этом составило 19,4 % - 23,1%. Утолщение слоев соединительной ткани в адаптированной жировой ткани обусловлено компенсаторно-репаративными процессами и созреванием волокнистого компонента и аморфного вещества соединительной ткани приживлении трансплантата. Указанные сопровождаются увеличением количества клеток-мигрантов периваскулярной ткани. Со стороны гемомикроциркуляторного русла установлены изменения имели стереотипный характер на действие экзогенных факторов.

**Ключевые слова:** жировая ткань, аутопересадка, асимметрия молочных желез.

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### MORPHOFUNCTIONAL FEATURES OF RAT TESTES INTERSTITIAL ENDOCRINOCYTES AND SUSTENTOCYTES AFTER 90 DAYS OF CENTRAL TESTOSTERONE SYNTHESIS DEPRIVATION

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With the social system development, there is a tendency to change attitudes towards family and family values. In developed European countries, there is a trend towards high sexual activity in elderly men and late creation of a family with children, which undergoes certain difficulties in connection with a decreased testosterone production in later years. The purpose of the study was to establish the microscopic organization of rat interstitial endocrinocytes and sustentocytes, to determine the sources of nitric oxide production and the intensity of oxidative stress in the testes with experimental central deprivation of testosterone synthesis with diphereline on the 90th day of the experiment. The experiments were carried out on 20 sexually mature male white rats of the Wistar line. Rats were divided into 2 groups: the control group (10) and the experimental group (10), which were injected subcutaneously with diphereline (Triptorelin embonate) at a dose of 0.3 mg / kg of the active substance for 90 days. Prolonged central deprivation of testosterone synthesis in animals leads to emergence of functional stress structural signs in population of sustentocytes and interstitial endocrinocytes, which are aimed to support testicular secretion. Central deprivation of testosterone synthesis within 90 days causes oxidative stress development owing to reactive oxygen species hyperproduction and nitrite accumulation in testicular tissue due to increased inducible NO-synthase activity.

**Key words:** testes, interstitial endocrinocytes, sustentocytes, NO-synthase, iNOS, cNOS, L-arginine, superoxide dismutase, rats.

The study is a fragment of the research project "Experimental morphological study of cryopreserved placenta transplants action diphereline, ethanol and 1% methacrylic acid on the morphofunctional status in a number of internal organs", state registration No. 0119U102925.

With the development of the social system, there is a tendency to change attitudes towards family and family values. In developed European countries, there is a trend towards high sexual activity in elderly men and late creation of a family with children, which causes certain difficulties in connection with a decreased testosterone production in older age [2]. Testosterone deficiency leads to infertility and redox imbalance, which further downgrades sperm quality and even causes inflammation in different organs [3, 4]. Besides inflammation and redox imbalance testosterone deficiency may lead to apoptosis in testicular tissues [5].

At the same time, the use of testosterone drugs in uncontrolled quantitative doses may worsen spermatogenesis by suppressing the components of the hypothalamic-pituitary system according to the feedback principle [11].

In our previous article, we showed that 30-days central deprivation of testosterone synthesis had led to the development of compensatory reactions in sustentocytes and interstitial endocrinocytes, which had been accompanied by morphological signs of functional overstrain. Development of oxidative stress and a change in the source of nitric oxide production from constitutive forms of NO synthase (cNOS) to an inducible form (iNOS) were also reported [12].