Neurophysiology, Vol. 52, No. 1, January, 2020

Restoration of the Integrity of a Transected Peripheral Nerve with the Use of an Electric Welding Technology

**V. Yu. Molotkovets,[1] V. V. Medvediev,[1] A. V. Korsak,[1]
Yu. B. Chaikovsky,[1] G. S. Marynsky,[2] and V. I. Tsymbaliuk[1]**

Received April 28, 2019

Mechanical damage to the peripheral nerves, especially their transection, is a serious disabling injury, treatment of which and rehabilitation related to the consequences of such traumas are an urgent and important medical/social problem. In experiments on animals, we evaluated the effectiveness and safety of multiple-point epineural connection of segments of the transected sciatic nerve using an electric welding technology. Left-side transection of the above nerve at a middle third of the thigh was performed in adult albino mongrel male rats. The experimental groups were the following: intact animals (I, $n = 5$), those subjected to sham surgery (Sh, $n = 6$), rats with neurotomy and no additional interventions (NT, $n = 21$), neurotomy + epineural neurorrhaphy (NT+NR, $n = 18$), and neurotomy + electric welding of the nerve segments (NT+EW, $n = 21$). It was found that the EW connection provided fast and reliable fixation of the nerve segments with subsequent significant recovery of transmission via the injured nerve and progressing partial normalization of morphological characteristics of the fibers within a regenerative neuroma at the site of nerve transection; indices characterizing the density of nerve fibers and mean angle of their deviation from the longitudinal nerve axis were the best in the NT+EW group. Most intense positive changes in the sciatic functional index (SFI), an integrative index characterizing the level of functional disorders of locomotion-related movements performed by the hindlimb at the NT side, were observed in the NT+NR and NT+EW groups. Our data clearly showed that the efficiency of the welding connection of an injured nerve is at least not lower than that provided by neurorrhaphy; the dynamics of recovery after both operations are quite comparable. The EW connection is much simpler and does not require an exclusively high qualification of the surgeon; in the case of operations on nerves in humans, the respective surgery will require less time and will be less expensive.

Keywords: peripheral nerve, transection, neurorrhaphy, electric welding connection of biological tissues, electroneuromyography, morphometry, sciatic functional index, regenerative process.

INTRODUCTION

At present, mechanical damages of trunks of the peripheral nerves amount 1 to 3% of the total number of traumatic cases treated in clinics. If one takes into account special cases of injuries of the nerve plexuses and spinal nerve roots, this proportion increases to 5% [1]; during active military conflicts, this index reaches 12% [2]. This type of damage is characterized by significant age and sex specificities [3, 4]. Such injuries are accompanied by a complex of long-term sensorimotor, trophic, and pain-related disorders [5–12], and their treatment requires considerable direct and indirect financial costs [8–11, 13–16]. Reparative surgical interventions on the peripheral nerves are technically highly difficult.

The most common types of the respective traumas are lesions of distal portions of the nerves of the upper extremities, in particular the radial nerve branch of the index finger and the small ulnar nerve branch of the little finger [4, 17]. Only about 11% of all respective cases are injuries of the lower limb nerves [12, 18].

Despite remarkable recent achievements, improvement of approaches to the treatment of peripheral nerve injuries remains an unresolved and urgent biomedical/social problem [17, 19–25]. The primary technical approach to repair the injured nerve integrity is the neurorrhaphy operation [26, 27, 30], i.e., linking of the epineurium and perineurium of proximal and distal nerve segments

---

[1] Bogomolets National Medical University, Ministry of Public Health of Ukraine, Kyiv, Ukraine

[2] Paton Electric Welding Institute, National Academy of Sciences of Ukraine, Kyiv, Ukraine

Correspondence should be addressed to V. Yu. Molotkovets
(e-mail molotkovets@gmail.com)

0090-2977/20/5201-0038

with biocompatible miniature sewing materials (monofilaments). This approach has significant disadvantages; among them there are extremely high requirements on the surgeon's qualification and an inevitably long duration of the operation, its high cost, as well as the incomplete spatial isolation of the injury area and persistence of a xenogenic suture material [19, 20, 28]. All these factors require the development of new methods of seamless tight connection of the nerve fragments, namely adhesion with a glue, laser, photochemical [19, 20, 28–36], and nanocomposite [37] technologies. The least studied among the respective technologies is the use of electric welding (EW) connection [38, 39]. The latter method is currently being improved to ensure the strength of joining and to limit side effects related to the action of high temperatures [40, 41].

In experiments on animals, we compared the effectiveness of the EW and suturing of the epineural junction of parts of the transected sciatic nerve. This was done on adult rats; electroneuromyographic, morphological/anatomical, and functional approaches were used for the analysis.

METHODS

Experimental groups. The study was performed on albino mongrel male rats ($n = 71$, body mass 350–450 g, age 7 months). The animals were obtained from the vivarium of the Romodanov Neurosurgery Institute (National Academy of Medical Sciences of Ukraine) and kept at a normal room temperature under natural light conditions and regular feeding with *ad libitum* access to water.

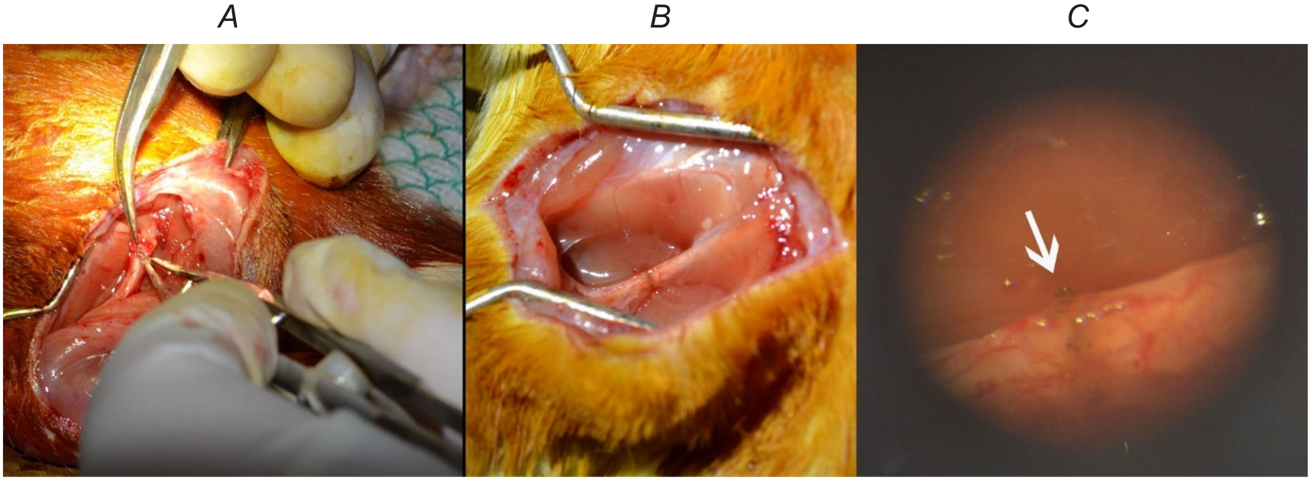
Five experimental groups of animals were formed, intact (I) rats (group 1, $n = 5$), sham-operated (Sh) animals (group 2, $n = 6$), rats with left sciatic nerve transection (NT) at the level of the middle third of the thigh with no additional interventions (group 3, $n = 21$), rats with nerve transection and immediate subsequent epineural neurorrhaphy of the segments (NT+NR, group 4, $n = 18$), and rats with nerve transection and immediate electric welding of the nerve parts (NT+EW, group 5, $n = 21$).

In experimental groups 2–5, surgery was performed under general anesthesia by i.p. injections of a mixture of xylazine (Sedazin, Biowet, Poland, 15 mg/kg) and ketamine (Calypsol, Gedeon Richter, Hungary, 70 mg/kg). In animals of the above groups, the skin on the left thigh was cut, femoral muscles were separated, and the sciatic nerve was mobilized from its output from the pelvis to ramification in main branches. In group 2 (Sh) animals, the nerve trunk was left intact. In animals of groups 3–5, the nerve was transected with ophthalmic scissors. In animals of group 3 (NT), the nerve segments were brought close to each other but not connected. In animals of group 4 (NT+NR), the standard epineural neurorrhaphy using an operational microscope, microneedles, and a monofilament was performed. In rats of group 5 (NT+EW), electric welding connection of the nerve segments was performed (Fig. 1). Edges of the epineurium of the proximal and distal nerve parts were simultaneously fixed and brought closer to each other with the help of special coagulation tweezers; then, the epineurium edges were welded by compressing the tweezer branches in an automatic mode with alternating high-frequency (440 kHz) modulated current (0.3 A, 34 V, rectangular pulse duration 0.8 sec) using the dA2 mode of an EKVZ-300 device (Patonmed, Ukraine). Five to six identical point connections were formed around the transection zone with a complete matching of the nerve segment ends [38].

In groups 2–5, the skin and muscles in the zone of surgery were sewed, and the wound was treated with an antiseptic. In order to prevent the development of inflammation and edema, the animals were subcutaneously injected with bicillin-5 (10^6 IU per 1 kg, approx. 150–200 thousand IU per animal) and a solution of dexamethasone (6 mg/kg, i.p.). After these manipulations, the animals of the above groups were kept for 2–4 h in a room with an air temperature of 30°C until the resumption of behavioral activity and then in standard cages (4 rats per cage) under familiar conditions.

In animals of groups 3–5, the hindlimbs on the surgery side were gently immobilized by applying suture ligatures between the *m. psoas major* and a proximal part of *m. tibialis cranialis* using an atraumatic needle and a vicryl thread. The knee joint was fixed in a 30 deg flexion position. Animals of all groups were subjected to observation during 5 months after transection of the sciatic nerve performed in rats of groups 3–5.

Electroneuromyography. Single animals randomly selected from groups 2–5 were subjected to electroneuromyographic examination 1, 3, and 5 months after surgery. For this purpose, the sciatic nerve in a deeply anesthetized animal (see above) was opened, prepared, and dissected from the pelvis



F i g. 1. Connection of the epineurium of segments of the transected sciatic nerve using the multiple-point electric welding technique. A, B) Two stages of operation; C) zone of connection at a ×6 magnification.

level to the level of sciatic nerve ramification. A proximal portion of the nerve (proximally with respect to the site of nerve transection and surgical connection) was placed on hook platinum stimulating electrodes fixed in a Teflon cannula (diameter 0.22 mm, interelectrode distance 2.5 mm). The nerve was stimulated with rectangular electric pulses (duration 1 msec, frequency 0.2 sec^{-1}, i.e., one stimulation per 5 sec) with automatically introduced increments of the amplitude of each subsequent pulse. Bipolar needle electrodes insulated except for the tip were inserted in the *m. soleus*. This allowed us to record the M response from this muscle induced by electrical stimulation of the proximal part of the sciatic nerve. Stimulation was stopped when the M response reached its maximum amplitude. The mean distance between the levels of stimulation and recording was 30 ± ± 1 mm; a precise value was measured for each animal separately. Based on this distance and latency of the M response, the conduction velocity along the nerve was evaluated.

Morphometry. After the mentioned three post-surgery terms, some (from two to five) animals of the experimental groups were euthanized by cervical dislocation, and samples of the sciatic nerve were collected for morphological examination; in groups 1 and 2, the respective samples were taken in a parallel manner. A part of the sciatic nerve between its output from the pelvis and a lower third of the thigh was cut off, fixed in 10% neutral formalin for at least 48 h, and then divided into three segments corresponding to the zone of the regenerative neuroma and proximal and distal parts with respect to the latter. Longitudinal sections of each segment were obtained using a cryostat microtome and stained according to a rapid technique of impregnation with silver nitrate [45]. The obtained slices were examined using an Olympus BX51 microscope and an Olympus Zoom 4040 digital camera (Olympus, Japan). Morphometric studies were performed using ImageJ ver. 1.50 software for the analysis of biomedical images (NIH, USA). The mean density of nerve fibers within three examined zones and average values of the angles of deviation of axonal segments from the longitudinal axis of the nerve within the area of the regenerative neuroma were estimated.

The **sciatic functional index** (SFI) was calculated in rats of groups 2–5 on the first, third, and fifth months after surgery. This index is a generalized indirect characteristic of the function of the above large nerve trunk; it characterizes the normality of locomotion-related hindlimb movements calculated according to the parameters of hindlimb footprints during walking along the test distance. A detailed description of the method was published earlier [42–44]. Each tested animal was pre-trained, and several training trajectory passes were recorded before the main test. During these tests, the feet of the walking animal were covered with a dye (in our case, fucorcin), and footprints on a paper stripe covering the floor of the horizontal tunnel path were collected. The following parameters were measured: distances between the heel point and the 3rd toe footprint (PL), between the 1st and 5th toe fingerprints (NT), and between the 2nd and 4th toe fingerprints (IT; Fig. 2). The empirically determined SFI formula is the following [42–44]:

$$SFI = -38.3 \cdot \frac{EPL - NPL}{NPL} + 109.5 \cdot \frac{ETS - NTS}{NTS} + 13.3 \cdot \frac{EIT - NIT}{NIT} - 8.8 \ ,$$

where E and N correspond to the injured and intact limbs, respectively.

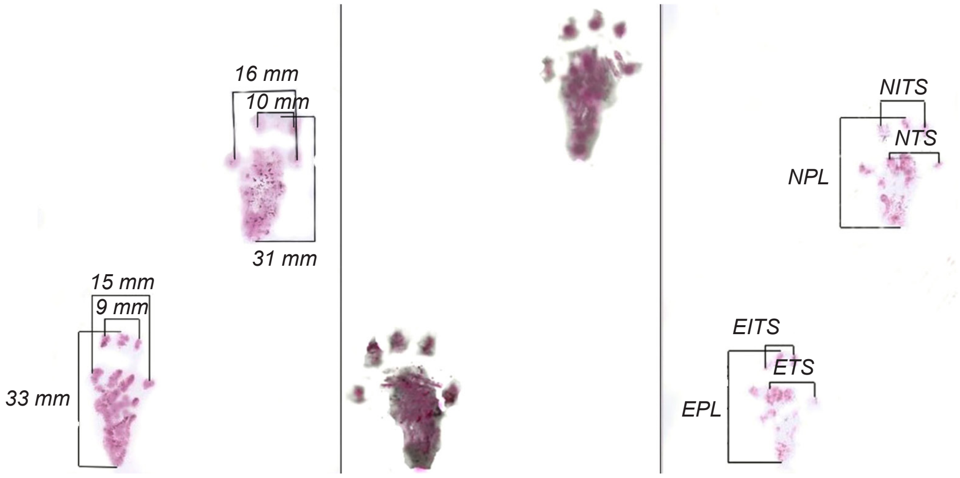
The SFI values are negative; they characterize functionally the level of the nerve injury; the greater the negative SFI value, the stronger the functional disorders. The SFI for intact animals is conventionally considered equal to zero.

Statistical analysis of numerical data was performed using STATISTICA 10.0 software; the values were represented as means ± s.e.m or means ± s.d. The Mann–Whitney *U*-test was used for unpaired comparisons, and the Wilcoxon test was used for paired ones. Morphometric data were analyzed using SPSS Statistics Base v.22 software (IBM, USA). The Kolmogorov–Smirnov test was used to assess the normality of distributions. Multiple comparisons within groups were performed by one-way ANOVA with the Scheffé *post-hoc* test; intergroup differences for the morphometric data were assessed with the Mann–Whitney *U*-test. The null hypothesis was rejected at $P < 0.05$.

RESULTS

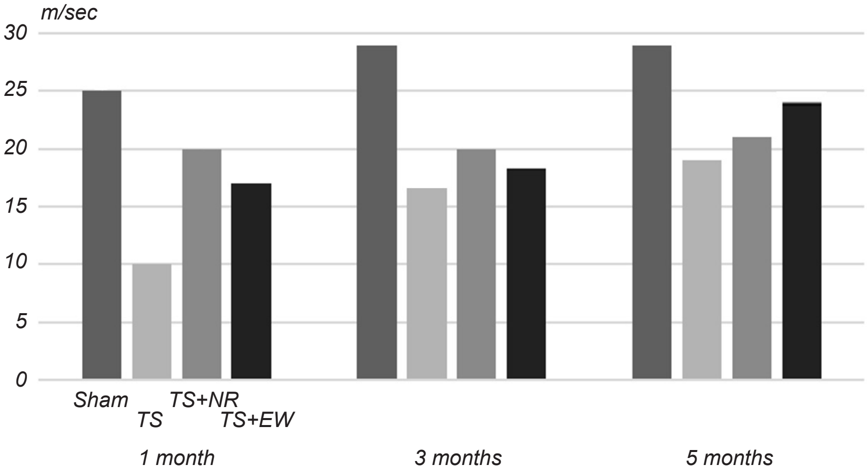
Conduction along the injured or intact sciatic nerve. In the Sh group, stimulation of a proximal portion of the intact sciatic nerve evoked high-amplitude and well-synchronized M responses in the *m. soleus*. Calculation of the conduction velocity according to the distance between points of nerve stimulation and recording of the above M response gave values from about 25 to 28 m/sec (Fig. 3). It should be mentioned that a small-amplitude, poorly synchronized, but readily visible M response could be recorded from the *m. soleus* even at the earliest time of observation (one month post-surgery; Fig. 3, 1). Within later terms of observation (3 or 5 months), the amplitude of the M response noticeably increased, and this reaction became better synchronized. After five months postsurgery, the value characterizing the conduction velocity via the earlier transected sciatic nerve in an animal of group NT reached 62% of the respective value in the Sh group.

In groups NT+NR and NT+EW, values characterizing the conduction velocity along the sciatic nerve were considerably higher within the entire period of observation (1–5 months) than those in the NT group. The M responses of *m. soleus* in rats of the former two groups had higher amplitudes and showed better synchronization than those in animals of the latter group. The value characterizing the conduction velocity in animals of the NT+NR group showed mild changes within the



F i g. 2. Representative footprints of the hindlimbs of experimental rats and the principle of measurements of the parameters for SFI calculation.

period of observation (1 to 5 months). At the same time, analogous values obtained for animals of the NT+EW group demonstrated a progressive increase within the above period. This value in the NT+EW group was the highest in comparison with values typical of all other groups and corresponded to 78% of the respective value in the animal of the Sh group, i.e., in that with the intact sciatic nerve (Fig. 3).



F i g. 3. Dynamics of changes in the conduction velocity (m/sec) via the regenerating sciatic nerve (1, 3, and 5 months after transection of the latter). For designations of the experimental groups, see Methods.

Morphometric indices. Representative photomicrographs of slices of the regenerating nerve at different post-surgery terms are shown in Figs. 4 and 5. In rats of group Sh, the mean density of the nerve fibers within a region corresponding to that of the regeneration neuroma in groups 3–5, calculated at the end of the 5th month after surgery, slightly exceeded ten thousand units per one square millimeter, namely (10137 ± 214)/mm^2 (mean ± ± s.d.). This value can probably be considered a normative for further comparisons (Fig. 6 A).

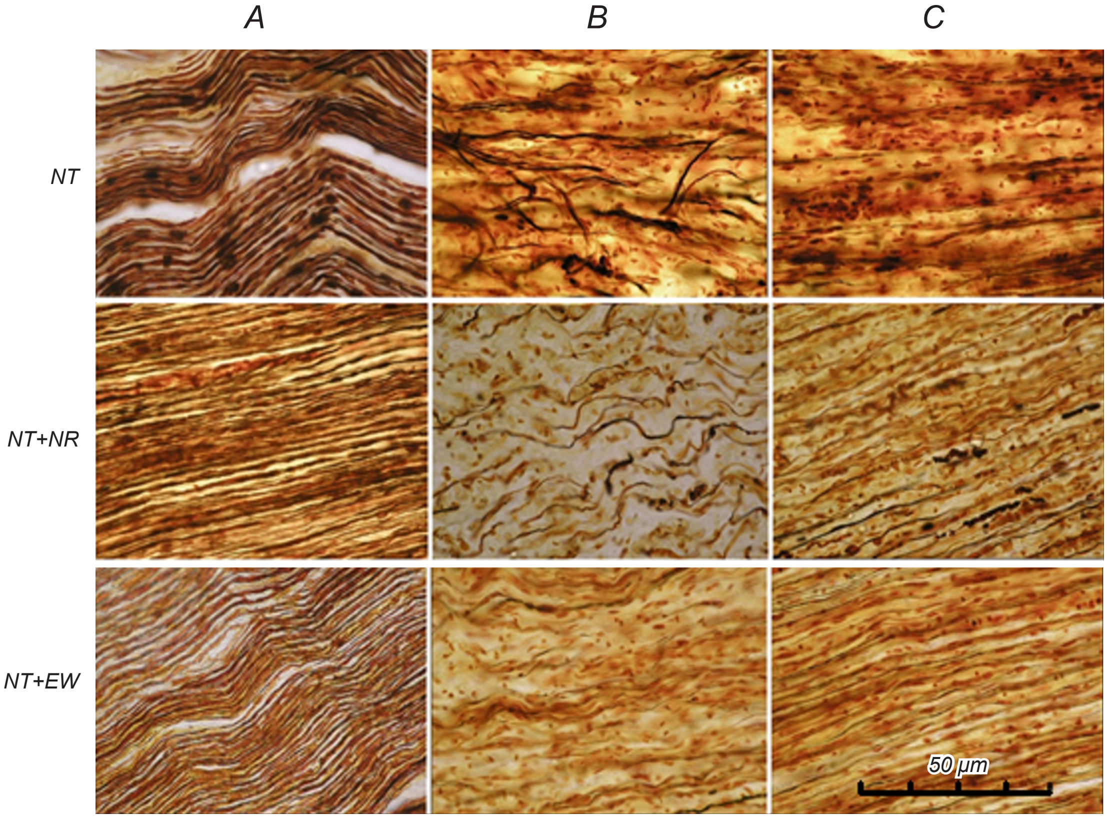
In the NT group, this index on the first month (4493 ± 271) was more than two times smaller than the above-mentioned one. After three months, the fiber density in animals of this group became considerably greater (on average, 6964 ± 220; $P < 0.05$ in comparison with the former value). After five months, however, no increment of this index was observed (5608 ± 278).

In group NT+NR, the fiber density within the neuroma region (5809 ± 208) was significantly greater ($P < 0.05$) than that in the NT group. After three postsurgery months, this index in the NT+NR group demonstrated a significant increase ($P< 0.05$), reaching a 8642 ± 206 value, and this index was significantly greater than the respective value in the NT group ($P < 0.05$). Within the later period (5 months), there was, however, no increase in the above index in the NT+NR group.

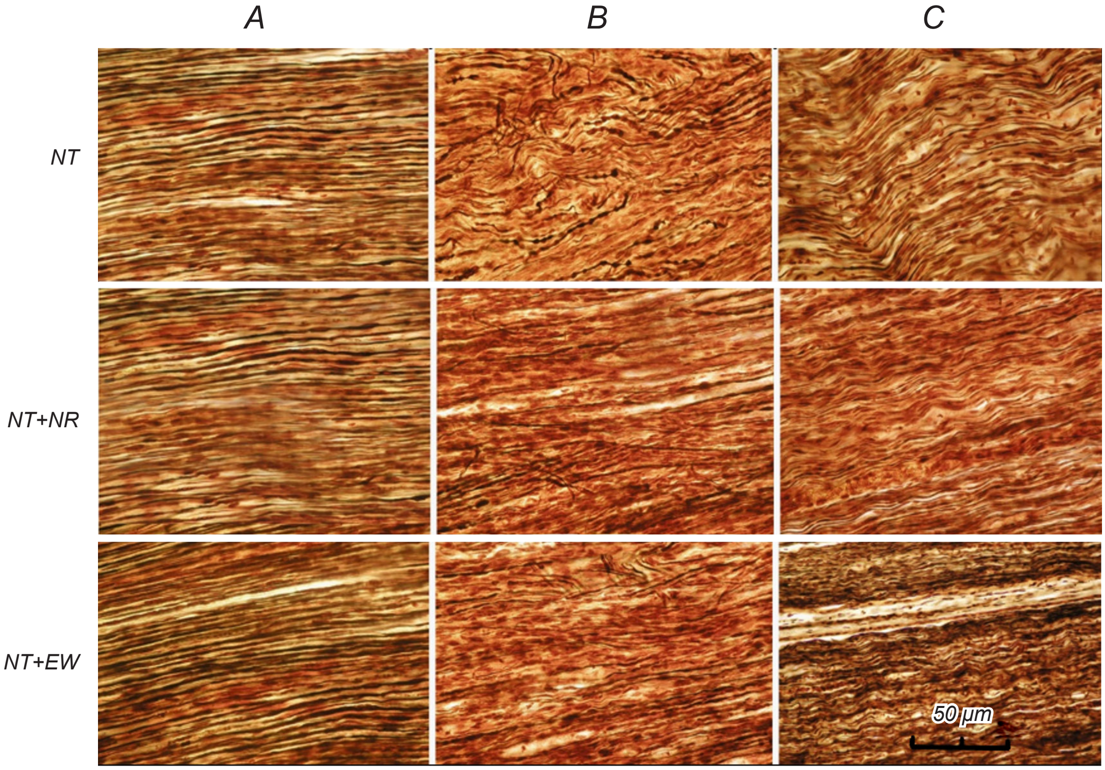
In the NT+EW group, the fiber density within the regenerative neuroma on the first month of observation (6139 ± 229) was significantly greater ($P < 0.05$) than the respective value in the NT group; it differed insignificantly from the analogous value in the NT+NR group. After three months, the analyzed index in the NT+EW group (9156 ± 249) demonstrated a significant increase in comparison with the one-month value in this group ($P < 0.05$) and slightly (insignificantly) increased on the 5th month (9448 ± 282). The latter value insignificantly differed from that in the Sh group taken as a normative.

Thus, the fiber density within the regeneration neuroma region, which may be considered an index reflecting the regeneration dynamics in the transected sciatic nerve, was significantly greater in the NT+NR and NT+EW groups than in the NT group. This dynamics in the NT+EW group was somewhat better in comparison with that in the NT+NR group (the progressive increase in the fiber density was more evident; Fig. 6 A).

Deviations of the segments of nerve fibers from the longitudinal axis of the sciatic nerve, observed in the regeneration neuroma region of animals of group NT, were rather significant (mean values reached 44–47 deg); these values did not show significant changes within the 5-month-long observation period (Fig. 6 B). In the NT+NR group, these values



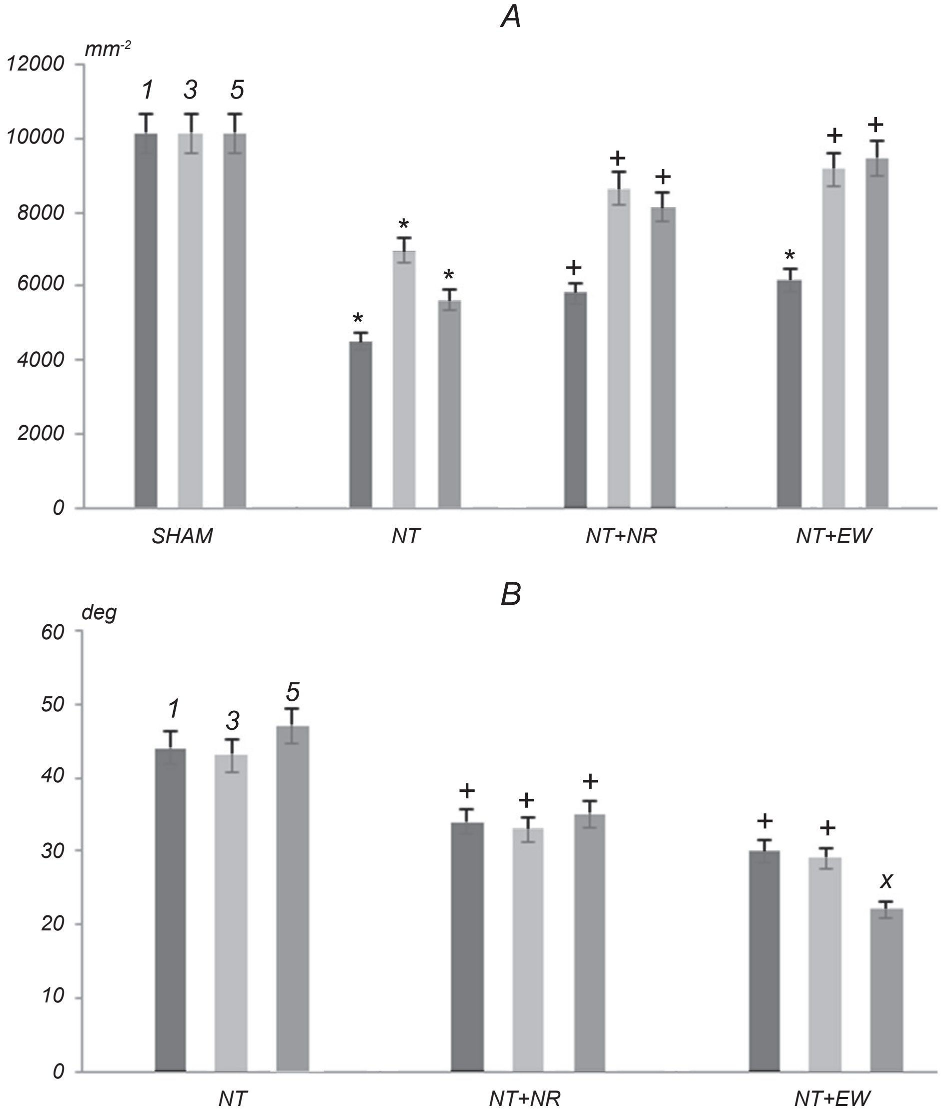
F i g. 4. Longitudinal slices of the distal and proximal segments of the sciatic nerve (A, C) and of the regenerative neuroma (B) one month after transection of the nerve. Impregnation with silver nitrate. For designations of the experimental groups, see Methods.



F i g. 5. The same as in Fig. 4, but for three months after transection of the nerve.

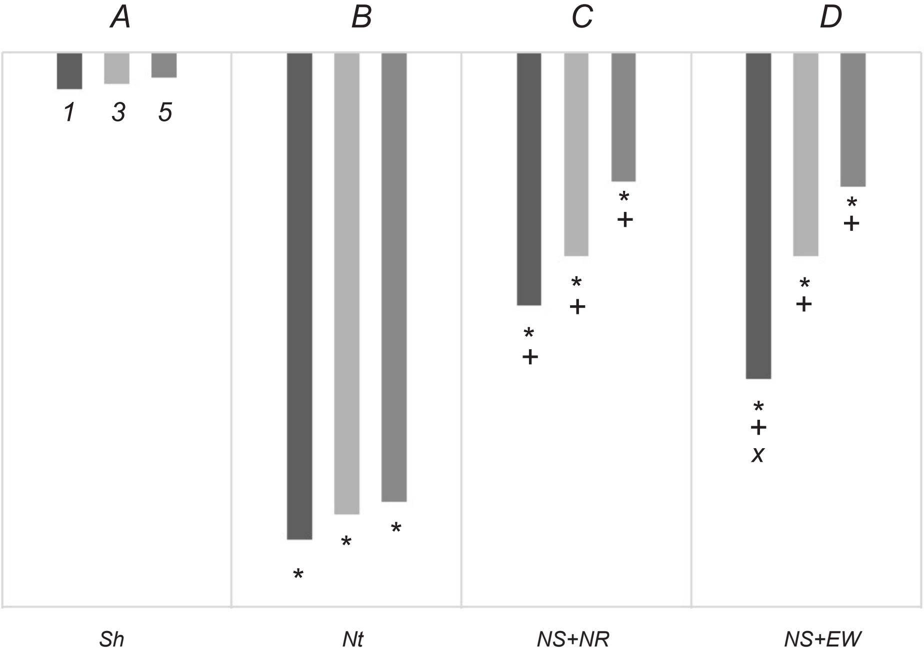
(34–36 deg) were significantly smaller than the respective values in the NT group but also demonstrated no clear dynamics within the observation period (Fig. 6 B). In contrast to this, the mean angle of deviation of regenerating fibers from the longitudinal nerve axis in the NT+EW group showed clear positive dynamics, decreasing, on average, from 30.1 ± ± 1.6 deg after one month to 22.6 ± 3.6 deg after five months (Fig. 6 B).

Functional examination. Negative SFI values in rats of the NT group were rather high (greater than –70) within the entire period of observation (up to five months). There was a slight trend toward decrease in the above SFI values from the first to the fifth months, but this decrease was statistically insignificant ($P > 0.05$; Fig. 7 B). In both NT+NR and NT+EW groups, negative values of this index were considerably smaller than in the NT group ($P < 0.05$ for all comparisons within similar post-surgery periods). On the first month, the mean SFI value in the group NT+NR was noticeably smaller than that in the NT+EW group ($P < 0.05$). Within the later period (3rd and 5th months), negative SFIs in both above groups progressively decreased



F i g. 6. Dynamics of the morphometric indices for the zone of the regenerative neuroma after transection of the sciatic nerve. A) Density of nerve fibers (number of fibers per 1 mm^2); B) angle of deviation (deg) of segments of the nerve fibers from the longitudinal axis of the nerve at different time intervals post-surgery (1, 3, and 5 months). Means ± s.e.m. are shown. Designation of the groups, see Methods. Asterisks, crosses, and diagonal crosses show cases of significant differences ($P < 0.05$) in comparisons with the corresponding values in animals of group Sh, in comparisons with group NT, and in comparisons between groups NT+NR and NT+EW, respectively.

to values of –22 to –24, and the dynamics of such decrease were nearly similar (Fig. 7 C, D). In the Sh group, negative SFI values were small during the entire observation period (Fig. 7 A). Thus, both neurorrhaphy and electric welding of the segments of the transected sciatic nerve provided rather effective (while partial) progressive recovery of the locomotor function of the injured limb.



F i g. 7. Dynamics of values of the sciatic functional index (SFI) in experimental groups at different post-surgery times (1, 3, and 5 months). For designation of the experimental groups, see Methods. Means ± s.e.m. are shown. Designations of the significance of differences in intergroup comparisons are similar to those in Fig. 6.

DISCUSSION

Injuries of large peripheral nerves is a type of pathology that, despite low mortality, has a dramatic impact on the quality of life of patients and is characterized by a vast cumulative effect [1–12]. There is substantial progress in the techniques of treatment of such injuries, but the state of the respective problem regretfully still cannot be characterized as satisfactory. The main approach in the corresponding surgical interventions is restoration, with the use of one or another technique, of the integrity of the injured (frequently, transected) nerve. The successive development of techniques of microsurgical operations on the nerves is undoubtedly obvious, but such surgical interventions are technically highly complicated, require extremely high qualification of the surgeon, very expensive, and need permanent development of better equipment and materials. This is why the development of simpler, cheaper, and, simultaneously, successful techniques for the respective surgical operations is extremely desirable. The technique of electric welding connection of segments of the transected nerve is one of such approaches.

Our model experiments on rats demonstrated that multiple-point electric welding of the epineurium of the disconnected segments of the sciatic nerve using the respective original instruments provides structural and functional recovery, which is at least quite comparable with that observed at standard suturing connection of such segments (neurorrhaphy). At the same time, the EW technique is much simpler, needs much less time for the operation *per se*, and does not require exceptionally high qualification of the surgeon. Naturally, in the case of the analogous interventions on humans, restoration of nerve integrity using the EW technique will require much less financial resources.

Our model experiments on rats with comparison of the success of operations with the use of the standard methods of neuroplasty (neurorrhaphy) and that of multipoint electric welding of the epineurium convincingly demonstrated that the latter technology provides at least quite comparable postsurgery results.

Transmission via the regenerating transected sciatic nerve was recovered with rather similar dynamics in rats of both NT+NR and NT+EW groups. In the latter group, even a somewhat higher value of the conduction velocity was observed within the latest phase of the observation period (5 months post-surgery). From this aspect, the EW technology could be qualified as a better one, but the mentioned difference was rather moderate.

When analyzing the dynamics of post-transection recovery of conduction via the injured regenerating nerve, we should mention that such recovery was also observed in animals of the NT group, in which segments of the transected nerve were not sutured or welded but were only positioned in close proximity to each other. Probably, even in this case some regenerating fibers of the proximal segment penetrate the distal segment of the nerve and restore the conduction via its trunk. Nonetheless, the recovery of transmission in the NT group was obviously worse than that in the NT+NR and NT+EW groups. In any case, it seems that regenerative capabilities of the peripheral nerves in rats are higher than those in humans. Clinical observations demonstrate that regeneration of an injured peripheral nerve in humans in most cases meets significant difficulties, and early surgical connection of segments of the transected nerve is an undoubtedly expedient intervention that considerably accelerates the course of the rehabilitation process.

It should be taken into account that the parameter calculated in our study according to the measurements of the distance between the points of stimulation of the sciatic nerve and recording of the M response from the *m.soleus* and of the time interval between the moment of stimulation and beginning of the latter response should be qualified as the conduction velocity only with certain reservations. The latter time interval includes not only time of conduction of the excitation value along the nerve but also the value of synaptic delay in the neuromuscular junctions. Nonetheless, the obtained values of velocity characterize well the state of conduction via the sciatic nerve under our experimental conditions.

Results of morphometric examination of the regenerative neuroma in our experiments showed that, after one month post-surgery, the density of fibers within this region in group NT was more than two times smaller than the respective index in the control (group Sh). In groups NT+NR and NT+EW, this index within the mentioned time interval was significantly greater than that in the NT group. During later time intervals, progressive increases in the density of fibers were obvious in the NT+NR and NT+EW groups, and the dynamics of such changes was the best precisely in the latter group. In five months after transection of the sciatic nerve, the density of fibers within the regenerative neuroma reached more than 90% of the control value (in group Sh), and this index was the greatest among all three experimental groups.

It seems that one other morphometric index observed in the regenerative neuroma deserves mentioning. It is obvious that orientation of segments of regenerating fibers in this region in rats of group NT is dramatically disordered, and there are significant deviations of many fibers with respect to the longitudinal axis of sciatic nerve, and this index did not show noticeable dynamics within the observation period. In group NT+NR, the mean angles of deviation of fibers were significantly smaller than the respective values in rats of group NT, but this index also showed practically no positive dynamics until month 5. At the same time, the above-mentioned mean angle of deviation in group NT+EW at one month post-surgery decreased significantly ($P < 0.05$) until the fifth month.

The dynamics of the SFI index in rats after transection of the sciatic nerve deserve special attention. In rats of group NT, values of this index were indicative of dramatic disorders in the locomotion-related function of the hindlimb on the side of nerve transection, and the trend toward decrease of negative SFI values within the observation period was in this group rather weak. At the same time, negative SFI values in rats of groups NT+NR and NT+EW were significantly smaller than the corresponding values in the NT group and, at the same time, demonstrated clear positive dynamics until the fifth month. On the latter time interval, the SFI values in the NT+NR and NT+EW groups insignificantly differed from each other and were about three times smaller than the respective value in the NT group. This fact confirms the statement that NR and EW technologies used for connection of segments of the transected nerve provide quite comparable results with respect to the dynamics of the recovery period.

Highly negative SFI values in the group NT and their rather weak positive dynamics within the 5-month-long observation period look somewhat strange, if we take into consideration the significant recovery of transmission via the injured sciatic nerve in this group. The conduction velocity in the group NT on the fifth month reached more than 60% of the respective value in the Sh group, and differences of this value from those in groups NT+NR and NT+EW did not look dramatic. Thus, strong functional disorders of the injured hindlimb could not be fully related to deficiencies of conduction via the regenerated nerve. We can speculate that neuromuscular transmission in rats of group NT underwent some significant negative modifications that are stronger than those in the NT+NR and NT+EW groups. This question should probably be answered based on the results of a special investigation.

Thus, results of our experiments convincingly demonstrated that connecting the segments of the transected sciatic nerve using the electric welding technique provides the recovery of structural and functional characteristics disturbed after the above trauma, which is quite comparable with the recovery observed after neurorrhaphy using the standard microsurgical technique and even possesses certain advantages. The operation using the EW technology is much simpler, takes much lesser time, and does not require extremely high requirements on the qualification of the surgeon. The EW technology deserves widespread adoption in the treatment of severe traumas of the peripheral nerves.

The research has been conducted following the principles of bioethics in accordance with the “European Convention for the Protection of Vertebrate Animals Used for Experimental and other Scientific Purposes” (86/609/EEC, 1986 Strasbourg), and the Law of Ukraine №3447- IV “On the Protection of Animals against Cruelty” (2006). The design of experiment has been approved by the Commission on Bioethical Expertise and Ethics of Scientific Research of the Bogomolets National Medical University (No. 126 of 13.11.19).

The authors of this paper, V. Yu. Molotkovets, V. V. Medvedev, A. V. Korsak, Yu. B. Chaikovsky, G. S. Marynskyy, and V. I. Tsymbaliuk, declare the absence of any conflicts regarding commercial or financial relationships with organizations or individuals who may be involved in the study, as well as conflicts between the co-authors.

REFERENCES

1. K. Bekelis, S. Missios, and R. J. Spinner, “Falls and peripheral nerve injuries: an age-dependent relationship,” *J. Neurosurg.*, **123**, No. 5, 1223–1229 (2015).
2. V. I. Tsymbaliuk, V. V. Medvediev, V. M. Semenova, et al., “A model of transverse hemisection of the spinal cord. Part I. Technical, pathomorphological, and clinical/experimental peculiarities,” *Ukr.Neirokhirurg. Zh.*, **2**, 18–27 (2016).
3. C. H. Foster, M. Karsy, M. R. Jensen, et al., “Trends and cost-analysis of lower extremity nerve injury using the national inpatient sample,” *Neurosurgery*, **85**, No. 2, 250–256 (2019); doi: 10.1093/neuros/nyy265.
4. R. M. McAllister, S. E. Gilbert, J. S. Calder, and P. J. Smith, “The epidemiology and management of upper limb peripheral nerve injuries in modern practice,” *J. Hand Surg. Br.*, **21**, No. 1, 4–13 (1996).
5. J. A. Kouyoumdjian, “Peripheral nerve injuries: a retrospective survey of 456 cases,” *Muscle Nerve*, **34**, No. 6, 785–788 (2006).
6. C. A. Taylor, D. Braza, J. B. Rice, and T. Dillingham, “The incidence of peripheral nerve injury in extremity trauma,” *Am. J. Phys. Med. Rehabil.*, **87**, No. 5, 381–385 (2008).
7. T. Scholz, A. Krichevsky, A. Sumarto, et al., “Peripheral nerve injuries: an international survey of current treatments and future perspectives,” *J. Reconstr. Microsurg.*, **25**, No. 6, 339–344 (2009).
8. S. Saadat, V. Eslami, and V. Rahimi-Movaghar, “The incidence of peripheral nerve injury in trauma patients in Iran,” *Ulus Travma Acil. Cerrahi. Derg.*, **17**, No. 6, 539–544 (2011).
9. G. Antoniadis, T. Kretschmer, M. T. Pedro, et al., “Iatrogenic nerve injuries—prevalence, diagnosis and treatment,” *Dtsch. Arztebl. Int.*, **111**, No. 16, 273–279 (2014).
10. M. L. Castillo-Galván, F. M. Martínez-Ruiz, O. de la Garza-Castro, et al., “Study of peripheral nerve injury in trauma patients,” *Gac. Med. Mex.*, **150**, No. 6, 527–532 (2014).
11. S. Missios, K. Bekelis, and R. J. Spinner, “Traumatic peripheral nerve injuries in children: epidemiology and socioeconomics,” *J. Neurosurg. Pediatr.*, **14**, No. 6, 688–694 (2014).
12. K. Dalamagkas, M. Tsintou, and A. Seifalian, “Advances in peripheral nervous system regenerative therapeutic strategies: A biomaterials approach,” *Mater. Sci. Eng. C: Mater. Biol. Appl.*, **65**, 425–432 (2016); doi: 10.1016/j.msec.2016.04.048.
13. H. E. Rosberg, K. S. Carlsson, S. Höjgård, et al., “Injury to the human median and ulnar nerves in the forearm – analysis of costs for treatment and rehabilitation of 69 patients in southern Sweden,” *J Hand Surg.*, **30**, No. 1. 3 5–39 (2005).
14. I. Immerman, A.E. Price, I. Alfonso, and J. A. Grossman, “Lower extremity nerve trauma,” *Bull. Hosp. Jt. Dis.*, **72**, No. 1, 43–52 (2013).

15. A. R. Wali, C. C. Park, J. M. Brown, and R. Mandeville, “Analyzing cost-effectiveness of ulnar and median nerve transfers to regain forearm flexion,” *Neurosurg. Focus*, **42** No. 3, E11 (2017); doi: 10.3171/2016.12.FOCUS16469.
16. J. M. Khalifeh, C. F. Dibble, C. J. Dy, and W. Z. Ray, “Cost-effectiveness analysis of combined dual motor nerve transfers versus alternative surgical and non-surgical management strategies to restore shoulder function following upper brachial plexus injury,” *Neurosurgery*, **84**, No. 2, 362–377 (2019); doi: 10.1093/neuros/nyy015.
17. S. K. Trehan, Z. Model and S. K. Lee, “Nerve repair and nerve grafting,” *Hand Clin.*, **32**, No. 2, 119–125 (2016); doi: 10.1016/j.hcl.2015.12.002.
18. L. Rasulic, I. Cinara, M. Samardzic, et al., “Nerve injuries of the upper extremity associated with vascular trauma-surgical treatment and outcome,” *Neurosurg. Rev.*, **40**, No. 2, 241–249 (2017); doi: 10.1007/s10143-016-0755-2.
19. M. J. Barton, J. W. Morley, M. A. Stoodley, et al., “Nerve repair: toward a sutureless approach,” *Neurosurg. Rev.*, **37**, No. 4, 585–595 (2014); doi: 10.1007/s10143-014-0559-1.
20. R. Li, Z. Liu, Y. Pan, et al., “Peripheral nerve injuries treatment: a systematic review,” *Cell Biochem. Biophys.*, **68**, No. 3, 449–454 (2014); doi: 10.1007/s12013-013-9742-1.
21. G. N. Panagopoulos, P. D. Megaloikonomos, and A. F. Mavrogenis, “The present and future for peripheral nerve regeneration,” *Orthopedics*, **40**, No. 1, e141–e156 (2017); doi: 10.3928/01477447-20161019-01.
22. C. A. Kubiak, T. A. Kung, D. L. Brown, et al., “State-of-the-art techniques in treating peripheral nerve injury,” *Plast. Reconstr. Surg.*, **141**, No. 3, 702–710 (2018).
23. S. Chaudhry, K. R. Ipaktchi and A. Ignatiuk, “Updates on and controversies related to management of radial nerve injuries,” *J. Am. Acad. Orthop. Surg.*, **27**, No. 6, 280–284 (2019); doi: 10.5435/JAAOS-D-17-00325.
24. S. K. Narayan, M. Arumugam, and R. Chittoria, “Outcome of human peripheral nerve repair interventions using conduits: a systematic review,” *J. Neurol. Sci.*, **396**, 18–24 (2019); doi: 10.1016/j.jns.2018.10.012.
25. R. Midha and J. Grochmal, “Surgery for nerve injury: current and future perspectives,” *J. Neurosurg.*, **130**, No. 3, 675–685 (2019); doi: 10.3171/2018.11.JNS181520.
26. G. Y. Liu, Y. Jin, Q. Zhang, and R. Li, “Peripheral nerve repair: a hot spot analysis on treatment methods from 2010 to 2014,” *Neural Regen. Res.*, **10**, No. 6, 996–1002 (2015); doi: 10.4103/1673-5374.158368.
27. A. Forli, M. Bouyer, M. Aribert, et al., “Upper limb nerve transfers: A review,” *Hand Surg. Rehabil.*, **36**, No. 3, 151–172 (2017); doi: 10.1016/j.hansur. 2016. 11. 007.
28. A. Eren, H. Atalar, C. M. Seymen, et al., “Sutureless approach with vein grafts and mesenchymal stem cells in primary nerve repair: Functional and immunohistological results,” *Microsurgery*, **38**, No. 7, 780–789 (2018); doi: 10.1002/micr.30315.
29. J. D. Bloom, B. S. Bleier, S. A. Goldstein, et al., “Laser facial nerve welding in a rabbit model,” *Arch. Facial Plast. Surg.*, **14**, No. 1, 52–58 (2012); doi: 10.1001/archfacial.2011.61.
30. N. G. Fairbairn, J. Ng-Glazier, A. M. Meppelink, et al., “Light-activated sealing of nerve graft coaptation sites improves outcome following large gap peripheral nerve injury,” *Plast. Reconstr. Surg.*, **136**, No. 4, 739–750 (2015); doi: 10.1097/PRS.0000000000001617.
31. N. G. Fairbairn, J. Ng-Glazier, A. M. Meppelink, et al., “Light-activated sealing of acellular nerve allografts following nerve gap injury,” *J. Reconstr. Microsurg.*, **32**, No. 6, 421–430 (2016); doi: 10.1055/s-0035-1571247.
32. C. Wang, S. Oh, H. A. Lee, et al., “*In vivo* feasibility test using transparent carbon nanotube-coated polydimethylsiloxane sheet at brain tissue and sciatic nerve,” *J. Biomed. Mater. Res. A*, **105**, No. 6, 1736–1745 (2017); doi: 10.1002/jbm.a.36001.
33. P. W. Henderson, “Immediate and complete restoration of peripheral nerve function after injury is attainable by a combination of surgical and chemical interventions,” *Med. Hypotheses*, **113**, 65–67 (2018); doi: 10.1016/j.mehy.2017.10.032.
34. N. J. Turner, S. A. Johnson, L. J. R. Foster, and S. F. Badylak, “Sutureless nerve repair with ECM bioscaffolds and laser-activated chitosan adhesive,” *J. Biomed. Mater. Res. B Appl. Biomater.*, **106**, No. 5, 1698–1711 (2018); doi: 10.1002/jbm.b.33975.
35. W. Wang, L. Degrugillier, M. Tremp, et al., “Nerve Repair with fibrin nerve conduit and modified suture placement,” *Anat. Rec. (Hoboken)*, **301**, No. 10, 1690–1696 (2018); doi: 10.1002/ar.23921.
36. J. R. Soucy, E. S. Shirzaei, L. R. Portillo, et al., “Photocrosslinkable gelatin/tropoelastin hydrogel adhesives for peripheral nerve repair,” *Tissue Eng. Part A*, **24**, Nos. 17–18, 1393–1405 (2018); doi: 10.1089/ten.TEA.2017.0502.
37. S. Frost, D. Mawad, J. Hook, et al., Micro- and nanostructured biomaterials for sutureless tissue repair,” *Adv. Healthcare Mater.*, **5**, No 4, 401–414 (2016).
38. Patent of Ukraine for a utility model No. 101487, MPK (2015.01), Method of restoring the spatial integrity of the injured peripheral nerve of adult male rats, V. I. TsymbalyukI, V. Yu. Molotkovets, V. V. Medvedev, et al., Published 09/10/2015 Bull. № 17.
39. N. N. Massarweh, N. Cosgriff, and D. P. Slakey, “Electrosurgery: history, principles, and current and future uses,” *J. Am. Coll. Surg.*, **202**, No. 3, 520–530 (2006).
40. Z. Okhunov, R. Yoon, A. Lusch, et al., “Evaluation and comparison of contemporary energy-based surgical vessel sealing devices,” *J. Endourol.*, **32**, No. 4, 329–337 (2018); doi: 10.1089/end.2017.0596.
41. E. A. Kramer and M. E. Rentschler, “Energy-based tissue fusion for sutureless closure: applications, mechanisms, and potential for functional recovery,” *Annu. Rev. Biomed. Eng.*, **20**, 1–20 (2018); doi: 10.1146/annurev-bioeng-071516-044702.
42. A. S. Varejão, M. F. Meek, A. J. Ferreira, et al., “Functional evaluation of peripheral nerve regeneration in the rat: walking track analysis,” *J. Neurosci Methods*, **108**, No. 1, 1–9 (2001).

43. Patent of Ukraine for a utility model No. 118157 MPK: G09B 23/28, Device for conducting the “walk on a track” test. V. Yu. Molotkovets, V. I. Tsumbalyuk, and V. V. Medvedev, publ. 25.07.2017, Bull. No. 14.
44. Patent of Ukraine for a utility model No. 111515 MPK: G09B 23/28, A method of calculation of the sciatic nerve functional index in rats, V. I. Tsumbalyuk, V. Yu. Molotkovets, and V. V. Medvedev, publ. 25.07.2017, Bull. No. 14.
45. A. K. Kolomiytsev, “A rapid technique of impregnation of the peripheral nerve elements by silver nitrate, which is applicable for celloidin and paraffin slices,” *Arkh. Anat. Gistol. Embriol.*, No. 8, 93 – 96 (1981).