Article

HAND
1–7
© American Association for Hand Surgery 2016
DOI: 10.1177/1558944716643277
hand.sagepub.com

Clinical Evaluation After Peripheral Nerve Repair With Caprolactone Neurotube

Gabriel Costa Serrão de Araújo[1,2], Bernardo Couto Neto[1,3], Renato Harley Santos Botelho[2,3], and Marcio Carpi Malta[1]

Abstract

Background: Peripheral nerve injuries with substance loss are challenges to surgeons because direct suture repair may result in malfunction due to nerve suture tension. Autologous nerve grafts are alternatives for treating those lesions; however, harvesting grafts adds morbidity at donor sites. Synthetic substitutes are options to bridge the gaps in these situations. The caprolactone neurotubes are used to assist nerve regeneration, but the literature lacks studies that evaluate their results. **Methods:** This research was designed to clinically evaluate patients undergoing repair of peripheral nerves with that conduit. We described results of 12 case series consisting of operations with Neurolac®. All nerves severed were sensory and had small gaps (ie, less than 25 mm). Subjective and objective clinical evaluations were performed and registered. **Results:** Physical examination by monofilament testing and 2-point discrimination showed results rated as good or excellent. However, the patients had complaints regarding sensory changes. **Conclusions:** Synthetic bioabsorbable guides for nerve repair are promising. The caprolactone conduits were demonstrated to be a safe option treatment and with a simple technique. Although in our study there were some operative complications, they were in line with previous descriptions in the literature. This case series added information about the treatment prognosis, but a higher evidence level study is necessary for decision making.

Keywords: peripheral nerve injury, caprolactone, nerve conduit, materials testing, clinical evaluation, postoperative period

Introduction

Traumatic injuries to the peripheral nerves are clinically presented with changes of sensation and mobility as well as pain. Anatomically, the most serious type of injury is the severance of the nerve, known as neurotmesis, involving the total loss of function. In this situation, surgical repair is necessary to guide the regeneration.[12]

Nowadays, conventional alternatives for the treatment of neurotmesis are the direct suture of the stumps and nerve grafting.[1,18] In small gaps, one may flex a joint to be able to mobilize the stumps and perform a direct repair. However, this technique may lead to scar contracture and joint stiffness.[4] The interposition of autogenous graft has been developed to bridge the defect, making a connection between the stumps possible and allowing axonal growth in an environment that is adequate for biological regeneration. This technique is recommended when there is loss of a nerve segment and the direct suture without tension is impossible. Nevertheless, harvesting a nerve for grafting may lead to scarring, the formation of neuroma, and loss of function of the donor area as well as an increase in surgery and anesthesia time.[6]

The search for techniques that could guarantee the peripheral nerve growth through hollow tubes has existed since the 19th century.[10] Since that time, many different types of materials have been used, such as fragmented tubes of decalcified bone, veins, arteries, and different types of tubes made of silicon, polyglycolic acid, collagen, and caprolactone.[19]

The neurotube of caprolactone is a hollow tube, and its walls are made of a synthetic polymer, which is semipermeable, flexible, transparent, and bioabsorbable. All these features together are of great interest for manufacturing a substitute for nerve grafts.[9,13,23] It has been preferably used for the repair of sensitive nerves of small diameter in gaps that are less than 3 cm in length.[6,24]

[1]Universidade Federal Fluminense, Niterói, Brazil
[2]Instituto Nacional de Traumatologia e Ortopedia, Rio de Janeiro, Brazil
[3]Universidade do Estado do Rio de Janeiro, Brazil

Corresponding Author:
Gabriel Costa Serrão de Araújo, Hospital Universitário Antônio Pedro, Rua Marques de Paraná, 303-Centro, Niterói, Rio de Janeiro, CEP 24033-900, Brazil.
Email: gabrieldearaujo@gmail.com

Our goal was to clinically evaluate the results of the surgical treatment of the peripheral nerve injuries in which neurotubes composed of caprolactone were used instead of nerve grafts.

Materials and Methods

Between 2010 and 2014, 14 patients were operated on with the use of the neurotube of caprolactone. The product used was the Neurolac®, which is manufactured by the Dutch company Polyganics Innovations.

All volunteers were informed of the research and gave their written consent to participate in the study. The research project was submitted to and approved by an independent ethical committee, respecting the institutions guidelines and the international agreements for scientific experiments with human tissues, including the Declaration of Helsinki (1964) and their following recommendations until Fortaleza/Brazil (2013).

All patients underwent brachial plexus block and had a tourniquet wrapped around their arm. After identifying the injuries, the neuromas and the gliomas of all stumps were excised under the microscope. The distance between the gaps was measured after the preparation of the nerve ends. Only gaps less than 2 cm were eligible for the repair with the neurotube. The only exception was patient 9, who presented a 2.5-cm gap of the radial sensory nerve at the level of the left wrist.

The neurotubes of caprolactone selected were 1.5 mm in diameter for the digital nerves and 2 mm for the sensory nerves at the wrist. The tubes were soaked in a warm saline solution to make them more flexible and facilitate manipulation and suture. The stumps were inserted in the tubes and advanced 1 to 3 mm on each side with the use of 7-0 polypropylene U-shaped stitches. The skin was closed with Nylon stitches, and the limbs were immobilized with a cast. The stitches and the cast were removed after 15 days.

We registered data from the history of each patient and the evolution of each case. The pain was measured using the visual analog scale. The physical examination started with the inspection of the hands and the evaluation of the scars, skin hydration and sweating, allergic and inflammatory reactions, hypersensitivity in the innervated area, and mobility. Then, we carried out the monofilament test, the Semmes-Weinstein test, and the static 2-point discrimination test. Both hands were examined to compare the operated side with the opposite side.

All data were organized in tables to compare with previous studies. Because of the small number of cases, no statistical tool was used; instead, we only describe the findings of the research.

Results

Three men and 11 women comprised the 14 patients who underwent surgery with the use of the neurotube of caprolactone. All presented injuries to the digital nerves or the sensory branches of the radial or the ulnar nerve. One man did not want to participate and was excluded. One woman was contacted, but she did not show up for the evaluation and was excluded as well. Three patients including 1 man and 2 women presented with worsening pain during the postoperative period and were submitted to revision surgery. As the goal of this article is to evaluate the clinical results of the repair using the neurotube, we included these 3 cases, considering them as treatment failures.

Table 1 contains information regarding the identification of the participants. In this table, we highlight the following: The average age was 44 years, with a standard deviation of 12 years; there existed a female and Caucasian predominance; and only 1 patient was left-handed. Associated diseases, medications, and the occupations of all patients are also listed in Table 1, but we did not observe any relation of these characteristics with the prognosis.

Table 2 shows the data related to the injury and the observations of the patients concerning the treatment. The average time between the injury and the surgery was 8 months, and the standard deviation was 9 months. The average follow-up time was 2 years, with a standard deviation of 9 months. Severance of the nerve with a knife was the most common type of injury. The digital nerves were the most frequently affected. There were 2 cases of injuries to the sensory branch of the radial nerve: 1 case of injury to the dorsal branch of the ulnar nerve and 1 case of injury to the radial dorsal digital nerve for the thumb. The injuries occurred at the proximal third of the fingers in 4 cases, at the middle third in 5 cases, and at the wrist level in 3 cases. Two patients presented associated injuries to the flexor tendons, and another one had a fracture of the phalanx.

Table 2 also shows that 10 patients had complaints related to the treatment. Among them, 1 patient showed loosening of the stitches of the surgical wound, which was treated with a longer period before the removal of the stitches and dressings for 25 days. Another patient complained about the stiffness of the operated finger and claimed the necessity for physical therapy to handle the problem. The majority of patients complained about changes in the sensation in the operated region. These complaints varied from a discomfort related to pain from contact, shock sensation, and numbness. Both patients who presented injuries to the sensory branches of the radial and the ulnar nerve stated the incapacity of wearing wristwatches due to the local discomfort. The dominant side was affected in 5 cases. All patients were referred to a specialized hand therapy service for rehabilitation. However, the patients identified by the numbers 4, 6, 7, 8, and 9 did not attend the therapy. They all stated the lack of need for physical therapy and carried out some exercises at home by themselves.

The physical examination is presented in Table 3. Data from the patients identified by the numbers 10, 11, and 12

Table 1. Demographic Information.

Patient No.	Gender	Age, y	Profession	Ethnicity	Associated diseases	Medicine usage	Dominant hand
1	F	44	Teacher	Brown	—	—	R
2	F	56	Machine operator	White	—	—	R
3	F	25	Administrative assistant	White	—	—	L
4	F	33	Environmental management	Brown	Ankylosing spondylitis	Methotrexate	R
5	M	57	Ironmaster	Black	Hypertension	Hydrochlorothiazide, losartan	R
6	F	61	Retired caseworker	White	Hypertension	Enalapril	R
7	F	27	Dentist	White	—	—	R
8	F	37	Businesswoman	White	—	—	R
9	F	46	Merchant	White	Hypothyroidism	Thyroxine	R
10	F	43	Student	White	Bronchitis	Cortisone	R
11	M	54	Merchant	Brown	—	—	R
12	F	45	Sales consultant	White	Rheumatoid arthritis, hypothyroidism, hypertension, nephrolithiasis, endometriosis	Hydroxychloroquine, methotrexate, levothyroxine	R

were not included because these patients were submitted to other surgeries after the implantation of the neurotube. The analogical visual scale showed an average level 2 of pain, with a standard deviation of 1.7. Only patient 6 presented cold intolerance; variations in the temperature did not cause discomfort to the others. Patient 3 showed a small degree of extension loss of the proximal interphalangeal (PIP) joint of the finger. Patient 5 showed full range of motion of the PIP joint, but the distal interphalangeal (DIP) joint was stiff and there was a "shock" sensation when the region was tapped. Patient 4 presented with a hypertrophic scar and subcutaneous adherence as well as flexion contracture of the PIP joint and discomfort when touching the innervated area. Patient 6 complained of touch discomfort in the innervated area. Patient 7 exhibited inflammatory reaction of the operated area, with redness, swelling, and increase of temperature 1 year after surgery. She was treated with nonsteroidal anti-inflammatory drugs (NSAIDs), and the signs of inflammatory reaction disappeared. Besides, she complained of hypersensitivity when touching the innervated area. Patient 9 had the same complaint, but in the dorsal area of the wrist proximal to the neurotube. None of the patients showed any disturbance regarding skin hydration or sweating or any allergic reaction.

Concerning the functional tests, Table 3 shows that on the normal side, 5 patients identified a pressure of 0.07 g (green monofilament) and 4 patients identified the pressure of 0.4 g (blue monofilament). On the operated side, only 2 patients identified the green monofilament, whereas the others identified the blue one. Among them, 6 patients were able to identify the same pressure on both sides, except patients 1, 8, and 9, who showed a decrease in the perception of pressure.

Still concerning the functional test, the static 2-point discrimination test exhibited an average 4-mm value on the normal side and an average 6-mm value on the operated side. Except for patient 3, all of the patients had a decrease in the capacity of discriminating 2 points on the operated side compared with the contralateral side.

Discussion

In 1990, Mackinnon and Dellon[17] were the first authors to study the regeneration of nerves in monkeys using bioabsorbable tubes. They suggested that the use of polyglycolic acid tubes was an alternative for the repair of gaps up to 3 cm. Since 1993, several authors have published experimental studies that compare the reconstruction with autologous graft with neurotubes composed of caprolactone for the repair of sciatic nerve gaps in rats.[7,8,15,16,22] The nerve regeneration with the use of the synthetic tube provides more and wider nerve fibers with functional results similar to the use of grafts. The direct repair provides better anatomic, sensory, and motor results.

Weber et al[26] presented a random, prospective study in humans that compared the clinical results of the nerve repair in 3 groups: direct repair, autologous graft, and neurotube of polyglycolic acid. They concluded that the best sensory results were found in the neurotube group. Besides, in gaps less than 3 cm, the results of the neurotube group were better than the nerve graft group because of the lack of morbidity in the donor area.

Table 2. Trauma Data.

Patient No.	Time to surgery, days	Follow-up, days	Mechanism	Nerve	Level	Other injury	Postoperative notes	Complains
1	78	1215	Blade cut	Radial digital left ring	Proximal third of finger	Superficial and deep flexor tendons	—	Forearm pain
2	287	650	Press machine	Ulnar digital left middle	Middle third of finger	Phalanx fracture	—	—
3	113	605	Traffic crash	Ulnar digital left index	Middle third of finger	—	—	—
4	191	682	Knife cut	Radial digital middle left	Middle third of finger	—	Suture maintained for 25 days by dehiscence	Scar retraction
5	447	943	Cut on a screw	Radial digital middle right	Middle third of finger	Deep flexor tendon	Maintained physiotherapy, stiffness	Decreased strength in the right hand
6	33	674	Knife cut	Ulnar digital left thumb	Proximal third of finger	—	—	She feels like something is stuck in the finger, discomfort to the local touch
7	61	940	Glass cut	Right ulnar dorsal cutaneous nerve	Wrist	—	—	Altered sensation, discomfort to the touch, cannot wear bracelets or watches
8	136	611	Glass cut	Right radial sensory	Wrist	—	—	Decreased strength, altered sensation, discomfort to the touch, cannot wear bracelets or watches
9	147	155	Scissor cut	Left radial sensory	Wrist	—	—	Shock and numbness
10	1012	603	Knife cut	Dorsal radial left thumb	Proximal third of finger	—	Local pain, submitted to nerve graft	Pain and movement limitation
11	392	857	Drilling machine	Radial digital left middle	Proximal third of finger	—	No improvement of symptoms, submitted to neurolysis	Shock and altered sensation
12	88	859	Glass cut	Radial digital left little	Middle third of finger	—	Allodynia, submitted to neurolysis and thereafter to nerve graft	Numbness, pain, shock, temperature changes

Table 3. Examination.

Patient No.	Pain scale	Observed alterations	Monofilament test (normal side)	Monofilament test (operated side)	Two-point discrimination (normal side)	Two-point discrimination (operated side)
1	4	—	Green	Blue	3	4
2	0	—	Green	Green	4	5
3	0	Mobility	Green	Green	4	4
4	1	Scar, hypersensitivity, mobility	Blue	Blue	2	3
5	3	Hypersensitivity, mobility	Blue	Blue	4	7
6	4	Hypersensitivity	Blue	Blue	4	9
7	2	Hypersensitivity, inflammatory reaction	Blue	Blue	5	8
8	0	Hypersensitivity	Green	Blue	6	9
9	0	Hypersensitivity	Green	Blue	6	8

Bushnell et al[3] presented a series of 9 cases evaluated after the repair with the use of a neurotube of collagen. They showed sensory results and complications very similar to our study. They considered that 8 patients had good or excellent results in the 2-point discrimination test and also observed that only 3 patients showed a decrease of sensation in the monofilament test. Lohmeyer et al[14] used collagen tubes in 12 patients with small gaps of the digital nerves. They classified the results as follows: 4 excellent, 5 good, 1 bad, and 2 without sensation. In 2010, Wangensteen and Kalliainen[25] published a retrospective series of 126 nerves operated with the use of collagen tubes. Among them, 64 were followed up and described. The study demonstrated that 45% of them showed an improvement of the nerve function after the surgeries, but 11 underwent revision procedures.

In our series, only 3 patients had a decrease of pressure in the Semmes-Weinstein test, yet they were able to identify the blue monofilament. We have to consider that the blue monofilament is referred to the pressure identified on the normal side of the exam of 4 patients.

The 2-point discrimination tests showed that the results in our series were considered good and excellent by the American Society for Surgery of the Hand (ASSH) criterion. All patients showed the return of protective sensation, except for the 3 patients who presented complete treatment failure.

In our series, there were 3 patients who needed revision surgery a few months after the implantation of the neurotube due to local pain. In 2 of these cases, the neuroma and glioma were excised, and an autologous graft was interposed. In patient 11, we only performed a neurolysis because the nerve was adequately connected to the stumps within the neurotube. The other 2 patients persisted with initial complaints and bad sensory results. The possibility of this type of failure must be addressed with the patient before the operation because besides being theoretically plausible, it has been experienced and described by other surgeons.[11]

In a Chiriac et al series,[5] 28 nerves were operated with caprolactone tubes. The authors did not consider the results favorable regarding the use of this neurotube and did not recommend it. They considered the results to be satisfactory only in 6 cases and the rate of complications to be high. We highlight the fact that they operated patients with injuries to the ulnar, median, musculocutaneous, and digital nerves. Some nerve gaps were up to 25 mm with associated injuries to tendons, arteries, and bone in smokers. Such associations may have had an influence on the results that were different than the ones that we had. As described in our results, few patients showed associated injuries, the injuries affected small-diameter sensory nerves, and the gaps were less than 20 mm in length. Probably the selection of less serious injuries may have contributed to a lower incidence of complications in this series.

The randomized prospective study described by Bertleff et al[2] compared the results of 21 nerve injuries repaired with caprolactone tubes with a control group of 13 patients who underwent direct repair or nerve graft. The results were considered satisfactory for the tube group in injuries shorter than 20 mm. It is important to consider that the studies that compared the direct repair with the neurotube may be mistaken due to fact that the suture may have been done under tension or after bending the joint. Such factors may be relevant concerns to the sensitivity of the results because it is known that those strategies provide worse results.[4] Hence, we believe that in prospective studies, the neurotubes must be compared with the grafts instead of the direct repair.

Regarding the physical features of the caprolactone tube, we can highlight the fact that the transparency clearly facilitates the operative procedure because it allows us to inspect the stump of the nerve inside the tube to verify the distance between the stump and the extremity of the tube. However, the caprolactone neurotube is harder than the tubes of polyglycolic acid and collagen. Such feature makes the manipulation of the tube during the surgery more difficult. Immersing the tube in a warm saline solution improves the flexibility

and therefore facilitates the suture. It seems that more flexible tubes have a better accommodation in the finger and allow an earlier mobilization. The patients noticed some sort of discomfort in the operated area with the tube because the tube is clearly palpable in the subcutaneous tissue. The discomfort seems to be more important when it is placed across a finger joint. Hernandez-Cortes et al[11] and Chiriac et al[5] reported cases of tube extrusion after being placed across the joint in the proximal area of the thumb. Likely, the greater mobility of this area, which was associated with the hardness of the tube, favored the bad results. In their report, the authors suggested that the inflammatory process created by the degeneration of the tube might have influenced the failure of the surgery. Only patient 7 had an exacerbated inflammatory process. The fact occurred 1 year after the surgery and was resolved with NSAIDs, which was followed with a good result after the treatment. The tube of caprolactone is different from the tube of polyglycolic acid in that it does not suffer a degradation process that is as quick as the latter; also, the degradation product is not so acidic, and therefore, it is less harmful to the surrounding tissues.[19,21]

Often, the decrease in the time of surgery is used as an argument to favor the use of neurotubes as it reduces the time necessary to harvest the nerve graft. We did not measure this time, but our experience with the surgeries does not prove it to be a relevant vantage because the manipulation of the tube for suture also takes some operative time.[5] Bertleff et al[2] also made this observation and verified a difference of a few minutes between the operative times.

The postoperative follow-up time of our patients varied between 5 and 40 months, with an average time of 2 years. We considered this time to be adequate for evaluation because all cases involved only sensory nerve injuries in the distal end of the upper limb. After this period, most likely, the nerve was already healed, the tube degraded, and the scar stable.

The time elapsed between the injury and the surgery was too long. In some cases, it was longer than a year, such as in patients 5, 10, and 11. The delay in repairing an injury is considered critical for the motor nerves due to the effects of the prolonged denervation in the muscle. Concerning the sensory nerves, good results have been reported even after several years have elapsed since injury. We could perform the surgeries 8 months after the injuries on average, and it did not seem to influence either the onset of complications or the bad results.

The repair of a nerve with the use of the caprolactone neurotube has been proven to be beneficial. Nevertheless, a residual loss may be verified in experimental studies[20] as well as in humans, according to the reported series. In our experience, hypersensitivity in the operated region associated with a discomfort related to touching was a very prevalent complaint, even for the patients who presented good results regarding protective and touch sensation.

During the nerve repair postoperative follow-up period, we observed that there is a difference between the way doctors and patients perceive the quality of the results. This series clearly showed that in spite of the fact that the objective tests classified the results as good or excellent, the patients complained of an uncomfortable sensation in the operated region, pain, restriction of daily activities, and sensory alterations. Furthermore, some patients whose cases were classified as a complete failure in terms of their results had similar complaints to patients whose tests were classified as good. This type of evaluation, owing to its subjectivity, is difficult to compare with others. Future studies could develop a questionnaire that is focused on the perception of the patient to facilitate comparison with medical guide classifications.

Ethical Approval

This study was approved by our institutional review board.

Statement of Human and Animal Rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Statement of Informed Consent

Informed consent was obtained from all individual participants included in the study.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

References

1. Batista KT, Araújo HJ. Microcirurgia das lesões traumáticas de nervo periférico do membro superior. *Rev Bras Cir Plást*. 2010;25:708-714.
2. Bertleff MJ, Meek MF, Nicolai JP. A prospective clinical evaluation of biodegradable neurolac nerve guides for sensory nerve repair in the hand. *J Hand Surg*. 2005;30(3):513-518. doi:10.1016/j.jhsa.2004.12.009.
3. Bushnell BD, McWilliams AD, Whitener GB, Messer TM. Early clinical experience with collagen nerve tubes in digital nerve repair. *J Hand Surg*. 2008;33(7):1081-1087. doi:10.1016/j.jhsa.2008.03.015.
4. Bustamante J, Socolovsky M, Martins RS, et al. Effects of eliminating tension by means of epineural stitches: a comparative electrophysiological and histomorphometrical study using different suture techniques in an animal model. *Arq Neuropsiquiatr*. 2011;69:365-370.

5. Chiriac S, Facca S, Diaconu M, Gouzou S, Liverneaux P. Experience of using the bioresorbable copolyester poly(DL-lactide-ε-caprolactone) nerve conduit guide Neurolac™ for nerve repair in peripheral nerve defects: report on a series of 28 lesions. *J Hand Surg Eur Vol*. 2012;37(4):342-349. doi:10.1177/1753193411422685.
6. Deal DN, Griffin JW, Hogan MV. Nerve conduits for nerve repair or reconstruction. *J Am Acad Orthop Surg*. 2012;20(2):63-68. doi:10.5435/JAAOS-20-02-063.
7. Den Dunnen WF, Van der Lei B, Schakenraad JM, et al. Long-term evaluation of nerve regeneration in a biodegradable nerve guide. *Microsurgery*. 1993;14(8):508-515.
8. Den Dunnen WF, van der Lei B, Schakenraad JM, et al. Poly(DL-lactide-ε-caprolactone) nerve guides perform better than autologous nerve grafts. *Microsurgery*. 1996;17(7):348-357. doi:10.1002/(SICI)1098-2752(1996)17:7<348::AID-MICR2>3.0.CO;2-C.
9. de Ruiter GC, Malessy MJ, Yaszemski MJ, Windebank AJ, Spinner RJ. Designing ideal conduits for peripheral nerve repair. *Neurosurg Focus*. 2009;26(2):E5. doi:10.3171/FOC.2009.26.2.E5.
10. Freitas TS, Flores LP. Uso da técnica de tubulização para o reparo de lesões do sistema nervoso periférico. *Arq Bras Neurocir*. 2007;26(1):16-23.
11. Hernandez-Cortes P, Garrido J, Camara M, Ravassa FO. Failed digital nerve reconstruction by foreign body reaction to Neurolac nerve conduit. *Microsurgery*. 2010;30(5):414-416. doi:10.1002/micr.20730.
12. Isaacs J. Treatment of acute peripheral nerve injuries: current concepts. *J Hand Surg*. 2010;35(3):491-497; quiz 8. doi:10.1016/j.jhsa.2009.12.009.
13. Ivirico JL, Cruz DM, Monros MC, Martinez-Ramos C, Pradas MM. Synthesis and properties of caprolactone and ethylene glycol copolymers for neural regeneration. *J Mater Sci Mater Med*. 2012;23(7):1605-1617. doi:10.1007/s10856-012-4649-8.
14. Lohmeyer JA, Siemers F, Machens HG, Mailander P. The clinical use of artificial nerve conduits for digital nerve repair: a prospective cohort study and literature review. *J Reconstr Microsurg*. 2009;25(1):55-61. doi:10.1055/s-0028-1103505.
15. Luis AL, Rodrigues JM, Amado S, et al. PLGA 90/10 and caprolactone biodegradable nerve guides for the reconstruction of the rat sciatic nerve. *Microsurgery*. 2007;27(2):125-137. doi:10.1002/micr.20317.
16. Luis AL, Rodrigues JM, Lobato JV, et al. Evaluation of two biodegradable nerve guides for the reconstruction of the rat sciatic nerve. *Biomed Mater Eng*. 2007;17(1):39-52.
17. Mackinnon SE, Dellon AL. A study of nerve regeneration across synthetic (Maxon) and biologic (collagen) nerve conduits for nerve gaps up to 5 cm in the primate. *J Reconstr Microsurg*. 1990;6(2):117-121. doi:10.1055/s-2007-1006810.
18. Martins RS, Bastos D, Siqueira MG, Heise CO, Teixeira MJ. Traumatic injuries of peripheral nerves: a review with emphasis on surgical indication. *Arq Neuropsiquiatr*. 2013;71:811-814.
19. Meek MF, Coert JH. US food and drug administration/conformit Europe-approved absorbable nerve conduits for clinical repair of peripheral and cranial nerves. *Ann Plast Surg*. 2008;60(1):110-116. doi:10.1097/SAP.0b013e31804d441c.
20. Meek MF, van der Werff JF, Klok F, Robinson PH, Nicolai JP, Gramsbergen A. Functional nerve recovery after bridging a 15 mm gap in rat sciatic nerve with a biodegradable nerve guide. *Scand J Plast Reconstr Surg Hand Surg*. 2003;37(5):258-265.
21. Schlosshauer B, Dreesmann L, Schaller HE, Sinis N. Synthetic nerve guide implants in humans: a comprehensive survey. *Neurosurgery*. 2006;59(4):740-747; discussion 7-8. doi:10.1227/01.NEU.0000235197.36789.42.
22. Shin RH, Friedrich PF, Crum BA, Bishop AT, Shin AY. Treatment of a segmental nerve defect in the rat with use of bioabsorbable synthetic nerve conduits: a comparison of commercially available conduits. *J Bone Joint Surg Am*. 2009;91(9):2194-2204. doi:10.2106/JBJS.H.01301.
23. Sivak WN, Bliley JM, Marra KG. Polymeric biomaterials for nerve regeneration: fabrication and implantation of a biodegradable nerve guide. *Methods Mol Biol*. 2014;1162:139-148. doi:10.1007/978-1-4939-0777-9_11.
24. Strauch RJ, Strauch B. Nerve conduits: an update on tubular nerve repair and reconstruction. *J Hand Surg*. 2013;38:1252-1255. doi:10.1016/j.jhsa.2013.02.034.
25. Wangensteen KJ, Kalliainen LK. Collagen tube conduits in peripheral nerve repair: a retrospective analysis. *Hand*. 2010;5(3):273-277. doi:10.1007/s11552-009-9245-0.
26. Weber RA, Breidenbach WC, Brown RE, Jabaley ME, Mass DP. A randomized prospective study of polyglycolic acid conduits for digital nerve reconstruction in humans. *Plast Reconstr Surg*. 2000;106(5):1036-1045; discussion 46-8.