Nerve Conduits for Nerve Reconstruction

Huan Wang, MD, PhD, and William C. Lineaweaver, MD, FACS

When a nerve is cut, the proximal segment is able to regenerate and re-establish nerve function under favorable conditions. The two ends must be reapproximated for the growth cone of regenerating axon to navigate and enter endoneurial tubes (bands of Bungner) at the distal stump and proceed toward its target. Small gaps can be sutured end-to-end directly. However, tension at the suture site is a very unfavorable factor.[65,98] If tension at the sites of coaptation is completely avoided, the axon sprouts are able to cross two sites of repair more easily than one site under the scarring associated with tension at the repair site.[64,66] Therefore inserting a graft between the proximal and distal stumps has been widely accepted for repair of nerve defects.

Based on their extensive search of the literature, Lee Dellon and Evan Dellon[22] cited two papers by Philipeaux and Vulpian[75,76] as being the first nerve allografts and autografts performed. In 1870, Philipeaux and Vulpian reported using autologous lingual nerve grafts to bridge hypoglossal nerve defects in seven dogs. They had some evidence of success in two of seven animals.

More than a century has passed, and autologous nerve grafting remains the method of choice for bridging nerve defects.[44,99] Its disadvantages, such as limited availability of donor tissue, need of a second surgical step, morbidity at the donor site (painful neuroma formation, anesthesia or irritating hypaesthesia), mismatch between nerve and grafts, increased operating room time and anesthesia time, have provoked extensive research to seek alternative grafts.

Simple Tube Conduits

Tube repair provides physical guidance to the regenerating axons, prevents axonal escape into the surrounding tissues and ingrowth of fibrous tissue into the nerve gap, and creates a microenvironment whereby trophic and tropic factors from the injured nerve can accumulate and facilitate axonal survival and growth. Because tubes provide a space for regenerating axons to align themselves as the result of chemotactic attraction, another advantage of it is that it allows incorrect surgical alignment to correct itself and produces functional recovery similar to correct repair.[24]

From the Department of Hand Surgery, Hua Shan Hospital, Fudan University, Shanghai, P.R. China, and Department of Surgery, Division of Plastic Surgery, University of Mississippi Medical Center, Jackson, MS.

Address reprint requests to Dr William C. Lineaweaver, Department of Surgery, Division of Plastic Surgery, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216.

1071-0949/03/0902-0104$35.00/0

doi:10.1053/otpr.2003.125479

Biological Conduits

Vein. The use of vein grafts to bridge small nerve gaps is currently the most popularized technique. The tissue composition of vein is similar to that of nerve tissue, providing vein grafts with properties inherently beneficial to regrowing nerves, including the ability to furnish important neurotrophic and neurotropic factors. The laminin-rich basal lamina constitutes the endothelium of the vein, the media also contains a significant degree of laminin, and the adventitia is composed primarily of collagen. Successful regeneration across the vein conduit and reinnervation has been proven in rodent[83,103,104] and rabbit[80,92] models.

A good axonal regeneration has been demonstrated through autologous vein grafts of up to 3 cm.[92] Failure of regeneration was evident with increasing gap length. Lack of viable Schwann cells in the graft and fibrosis and collapse of the vein grafts are factors in these failures. Vein conduits longer than 3 cm are not recommended for clinical use.[16,94,102]

A notable shortcoming of vein grafts involves midgraft patency. In conduits longer than 1.5 cm, collapse of the lumen of the conduit may result in obstruction of axon outgrowth and decreased axon diameter within the tube. Various strategies to maintain conduit patency include use of built-in metal spiral supports, sleeve insertion and collagen coating of the vein lumen,[103] insertion of nerve segments at mid-vein graft.[86]

Another disadvantage of vein graft is the valves. Even reversed valves in vein conduits may contribute to obstruction of regrowing axons and result in neuroma formation.[104] Valveless sections of donor veins should be chosen. The vein graft should be interposed in a reversed fashion.

Denatured muscle. In peripheral nerve regeneration, the basal lamina represents a component of the extracellular matrix to which regenerating axons attach preferentially, and the basal lamina tubes provide spaces for the regenerating axons to grow through. Thus, basal lamina tubes as in acellular muscles represent apparently favorable scaffolds for regenerating axons. Each muscle tube is large enough for the passage of one or more regenerating axons. Muscle tubes also provide open passage for the migration of Schwann cells and other neurotropic factors from the proximal and distal nerve stumps. Denatured muscle grafts have been shown to be effective in bridging gaps up to 4 cm in rats, rabbits, cats, dogs, sheep, monkeys, and man.[27,30,31,39,71,87] Most investigators reported that nerves repaired by muscle basal lamina grafts regenerated as well as those in which live nerve autografts were used. Denatured skeletal muscle interposition is also found to favor sensory recovery.[91]

Soleus muscles and adductor magnus muscles,[27] masseter muscle,[87] extensor caudae internus muscle,[15] gracilis muscle,[26] gluteus maximus muscle,[20] pectoralis major muscles, and sar-

torius muscles[82] have been used. The method for denaturing the muscle is a sequential freezing and thawing procedure. This method allows autografting of the muscle. Treating the muscle in different chemical solutions has also been used.[27,28] Graft material is taken from a donor animal in this procedure. However, basal lamina grafts do not seem to undergo immune rejection by their hosts. Grafts derived from one species have also been successful in another.[27] Evacuation of the myoplasm from the muscle before it is grafted into a nerve influenced the number of regenerated axons.[27] The anatomical prerequisites of the muscle used, such as fiber diameter and configuration, seem to influence the morphologic appearance of the regenerated graft.

Epineurial sheath. Three fashions of using epineurial sheath tubes were reported: sliding,[4] turnover,[5] and resection-tube re-formation.[41] Rat sciatic nerve defects 7 mm to 10 mm in length were repaired. Walking track analysis and histologic and quantitative histomorphometric evaluation revealed regeneration comparable to nerve grafts. Harvesting the epineurium only caused minimal adhesions at the donor site without harming the nerve trunk or interfering with conduction. An epineurial-like layer re-covered the donor site. This technique possesses such advantages as neural tissue origin, ready-for-harvest availability at the nerve repair site, and matching size of the conduit and the nerve end. However, technical difficulties were reported when dissecting and sliding the epineurium onto polyfascicular nerves in fresh cadaver studies.[5]

Intestine sleeve. Small intestines of rats were turned inside-out so the serosa, which is rich in collagen and laminin, lined the lumen. The segments were frozen and thawed to lyze the sacrolemma. Membrane antigens were denatured by 70% ETOH. 10 mm gap of rat sciatic nerve was repaired by the inside-out intestine sleeve. Saline was injected into the lumen to help the conduit remain patent. The intestine sleeve exhibited faster conduction velocity and greater axon counts when compared with autologous nerve graft.[105]

Another application of intestine as a nerve guide is small intestine submucosa (SIS).[34] The intralumenal mucosa and the serosa were rubbed away to obtain intact SIS. The SIS patch was then trimmed and rolled to form cylinder graft that bridged a 7-mm gap in rat sciatic nerve. Some regeneration was observed in the acellular SIS rolled grafts. When plated with Schwann cells, the rolled SIS demonstrated an improved regeneration and functional recovery which approached that achieved through autologous nerve grafts. The rolled architecture provided an order of magnitude greater surface area than simple hallow conduits, which contained more extracellular matrix known to be permissive to axonal migration. However, the rolled conduit had no spacer to keep the area between lamellae from collapsing onto one another.

Amnion tube. Human amniotic membrane is rich in collagen, laminin, fibronectin, and other basement membrane components. It is a natural material readily available with a very weak antigenicity. The amnion sheet is rolled with the fetal side facing inward to form an amnionic tube. This tube was used to repair a 10 mm sciatic nerve defect in rats.[68] A uniform nerve tissue with normal diameter was found crossing the gap with neovascularity. Morphologic and functional assessment of nerve regeneration was comparable with that seen in autograft. Incorporation of NGF/hyaluronic acid in the amnionic tube enhanced additional axonal regeneration in a rabbit 25-mm sciatic nerve defect model.[69]

Mesothelial chamber. To create a mesothelial chamber, a silicone rod or tube (outer diameter of 2.0 mm) surrounded by a thin metal spiral was implanted subcutaneously in the back of rats. After 3 to 4 weeks a mesothelial lining was generated around the silicone form. When the latter was removed, a mesothelial chamber remained, held open by the metal spiral in its wall. The preformed mesothelial tubes were used to bridge 10 mm gap in rat sciatic nerve.[46] A well-defined regenerated nerve was found to grow across the gap. Nerve morphology and conduction velocity was comparable to those of autologous nerve graft. The merit of this tube might be the neuronotrophic effect of the mesothelial chamber fluid, which was found, in in vitro study, to have similar neuron survival and neuritic development effect as NGF. The preformed mesothelial sheath was also used in a primate model.[54] The ulnar nerves of adult cynomolgus monkeys were divided 3 cm apart and repaired with the pseudosheath. Histological evaluation confirmed regeneration across the 3-cm gap, with fibers organized into regeneration units randomly arranged within the sheath with a considerable amount of connective tissue between the 'mini fascicles'. Although its morphology was different from a nerve graft, the quality of regeneration was similar. Evidence of reinnervation of sensory receptors was demonstrated.

Pseudo-nerve. The pseudo-nerve, created by inserting the proximal and distal stumps of a cut sciatic nerve into a silicone tube, contains longitudinal Schwann cell columns without axons and surrounded by perineurium-like tissue. It was used to repair a 10-mm rat sciatic nerve defect, which induced nerve regeneration to a similar extend as a real nerve graft.[114] The pseudonerve hosted neurobiological composition similar to a nerve graft: longitudinally organized Schwann cell columns surrounded by basal laminae and ensheathed by a layer of vascularized perineurium-like structure. Macrophages and their products, interleukin -1β and transforming growth factor-β1, were constantly present.

Fibronectin mat. Another natural conduit material is orientated mats of fibronectin produced from plasma fibronectin. The fibronectin sheet was tubed across 10-mm gap of rat sciatic nerve to form a cylinder that expanded to form a solid conduit without a hollow center because of its hydroscopic nature. This conduit supported a significantly faster rate of growth and greater amount of axons than muscle graft, which was comparable to nerve graft.[109]

Collagen tube. Collagen tube fabricated from Type I collagen has been used to repair 10-mm sciatic nerve defects in rats,[100] 5 mm facial nerve defect in cats,[42,43] 5 mm and 15 mm median and ulnar nerve defects in monkeys.[3] Excellent regeneration comparable to nerve graft repair was demonstrated. The fibrillar structure of the collagen can be maintained throughout the processing permitting construction of a tubular matrix with adequate mechanical strength and defined permeability. The collagen tube can be totally absorbed, the degradation speed of which can be controlled by manipulating the thickness of the tube and the temperature for thermal dehydration.

Vein grafts, muscle grafts, and perineurium sheath can be harvested and used at the time of the nerve repair procedures, whereas other biological conduits have to be pre-prepared.

Synthetic Conduits

Nonresorbable conduits. Silicone tube is one of the first and most frequently used nonresorbable material because of its

good biocompatibility and elasticity.[47,110] Other nonresorbable materials such as polytetrafluoroethylene have also been used.[67,101] Regeneration occurs across these conduits, showing good sensory and motor recovery over the short term. These conduits, however, have long term complications including fibrosis and chronic nerve compression that require surgical removal. Therefore, nonresorbable conduits are mainly used for the study of spatiotemporal phases of regeneration, the influence of target tissue on the proximal axon stump, and the role of numerous growth factors in the regrowth of peripheral neurons. Because no biodegradable conduits are clinically available in a diameter large enough to repair major nerves, use of silicone and Goretex tubes in man has been reported.[48,90]

Biodegradable conduits. To achieve successful long term results, a conduit made of biodegradable materials is a promising alternative. The rate of biodegradation of nerve guides should be in accordance with axonal growth rates. Tube dimensions and swelling of degrading biomaterials are important factors influencing the final outcome of nerve regeneration and should be taken into account. A variety of resorbable materials have been used. Polyglactin conduits resulted in an inflammatory response and poor nerve regeneration.[70] Better results have been obtained with poly(L-lactide-ϵ-caprolactone),[13,25,60,61] poly-β-hydroxybutyrate,[36,45] and polyglycolic acid[8,21] conduits. These conduits are used to entubulize nerve gaps ranging from 5 to 30 mm in rats, rabbits, cats, and monkeys with nerve regeneration comparable to nerve grafting.

Conditioning of Conduits

Nerve regeneration is regarded as a biological, in addition to a mechanical, problem. Restoration of the proper microenvironment at the lesion is essential for optimal regeneration. The success of simple tubulization, however, is dependent on the length of the gap between the two nerve stumps. The distal nerve stump exerts a chemotactic attraction guiding the regrowing axons. This tropism is inversely proportional to the length of the gap and is not able to attract regenerating axons at a distance greater than 0.8 to 1.0 cm. In nerve guides, Schwann cells appear to migrate from the proximal and distal nerve stumps into the conduits. However, in longer nerve gaps, the migration of Schwann cells and resulting myelinization may reach a limit. Another concern of conduit length is collapse of the chamber in nerve guides such as vein grafts that lack elasticity. Failure is usually found when the gaps are longer than 6 mm in mise,[12,32] 15 mm in rats,[47,84,110] 30 mm in rabbits,[92] or 50 mm in human.[14] To overcome these unfavorable conditions and achieve better recovery over an extended gap, nerve conduits have been conditioned in various ways.

Implantation of Schwann Cells

Schwann cells are crucial components in the microenvironment through which regenerating axons grow to reach their peripheral targets. Therefore, it is likely that measures which increase the rate of Schwann cell mitosis and migration, or speed the population of the graft with Schwann cells, will increase the rate of axon regeneration through the grafts and probably also increase their maximum useful length. Conduits without viable Schwann cells show an inferior axonal regeneration.[1,28,33,35,37]

Nerve conduits containing Schwann cells are used to overcome the 10-mm gap barrier. Schwann cells forming a monolayer on the inner wall of a polyethylene tube and Schwann cells injected into muscle grafts allowed axon regeneration across a 20-mm gap in rats.[11,26] Schwann cells suspended in gelatin within polyglycolic acid conduits and autogenous Schwann cell suspension in venous grafts have supported nerve regeneration over a 30 mm gap in rabbits.[17,113] Isolation of autologous Schwann cells and addition of the propagated cells to autogenous venous nerve conduits in a two-stage fashion showed excellent nerve growth through a 60-mm gap in rabbit peroneal nerves.[93] However, no functional evaluation was provided.

The trick for application of Schwann cells is to adjust Schwann cell seeding densities that balance the effects of NGF production with competition for available nutrients. Another pitfall is Schwann cell survival and propagation. While heterogenous cells may induce an immune response that might hinder regeneration, it is now possible to isolate and propagate Schwann cells from adult human tissue retrieved at the injured site.

Filling of Growth Factors

Supplementing conduit chamber with growth factors and exogenous matrix precursors has also been shown to promote regeneration across larger gaps (15–20 mm) than would be repaired by empty tubes. Adding fibronectin, laminin and collagen into the chambers has been shown to advance the regeneration progress and increase the critical gap length.[6,56,59,111] Among the growth factors that have been shown to enhance nerve regeneration in conduits are nerve growth factor (NGF),[23,81,88] acid and basic fibroblast growth factors (FGF).[18] Brain-derived neurotrophic factor (BDNF), insulin-like growth factor (IGF), ciliary neurotrophic factor (CNTF), and transforming growth factor (TGF) also play a role in axon survival and repair, their effects on regeneration within a conduit have yet to be established.[97]

Introduction of Vascularity

Enhancement of vascularity, either by application of vascular endothelial growth factor[38] or by insertion of blood vessels into the conduit chamber,[40] resulted in better functional recovery and achieved nerve regeneration across longer gaps.

Combination of Grafting Materials

Because each conduit has advantages and disadvantages, combination of different grafting constructs to overcome the disadvantages and benefit from the advantages is a logical design. Vein conduits filled with muscle fibers lead to promising results in that the muscle inside the vein (1) prevents collapse of the vein, (2) supplies a good substratum for the regrowing axons, and that (3) the vein around the muscle avoids dispersion of fibers at two ends, (4) scar invasion is prevented, and (5) a good blood supply of the regenerating nerve is allowed.[10] Combination of conduits with nerve segment have been shown to be effective in bridging a longer gap, either in an interposed fashion[29] or a "stepping-stone" fashion,[57] because of the supplement of Schwann cells in the form of a short segment of nerve graft. Other combinations have also achieved to various extends either by providing Schwann cells as in nerve-muscle sandwich grafts,[108] or by providing collagen and longitudinal

basement membrane as in poly (DLLA-ϵ-CL) tubes inserted with autologous denatured muscle tissue.[60]

Construction of Inner-structure

Most of the conduits are tubes which merely encase the regenerating axons whilst offering them no internal structural support. Fibrin matrix that forms inside the tube and that represents regenerating substrate may be absorbed before durable link between nerve ends is established. Therefore, it is reasonable to introduce filaments within the tube to provide a stable intrinsic framework which would stabilize the fibrin matrix and support axon growth.[50] This type of construction has been tested to bridge extended nerve gap and has been shown to be successful.[51] Different types of filaments have been tested, achieving functional recovery regardless of the material.[2] The idea of coating these filaments with neurotrophins, neurotropic factors, adhesion molecules, and other matrix components is attractive.

Various manipulations of the conduits playing with bioartificial framework, living cells, and various factors lay the foundation of tissue engineering nerves. These are the future substitutes for autologous nerve grafts.[85]

Clinical Application

The following characteristics would define an ideal nerve conduit in clinical use: (1) biocompatibility with the surrounding tissues, (2) low antigenicity, (3) minimal inflammatory stimulus, (4) sustenance of axon regeneration throughout the length of the conduit, (5) biodegradability, (6) no potential for entrapment or compression, (7) easy manufacturing, (8) economic availability, (9) easy technical handling characteristics.

Although conduits of different materials have various success rates in experimental studies, only vein grafts, muscle grafts, polyglycolic acid tubes, polytetrafluoroethylene tubes, and silicone tubes have been adopted in clinical practice. An overview of the literature is provided in a recent article.[62]

Vein

Early attempts using vein grafts in humans showed some sensory and motor recovery.[112] Satisfactory functional sensation was uniformly obtained in cases of digital nerve repair with vein conduits when the gap was less than 3 cm.[16,58,94,95,102] No sensory recovery was found in digital nerve defects longer than 5 cm even though fresh nerve slices were inserted in the vein lumen.[94,96] Superficial branch of radial nerve (1.5–4.5 cm),[7,16,95] dorsal cutaneous branch of ulnar nerve (2–3.5 cm),[16,58] median nerve (2.5–4 cm),[7,95] ulnar nerve (2–4.5 cm),[7,95] radial nerve (3.5–4 cm),[7] musculocutaneous nerve (6 cm),[7] and posterior cord of brachial plexus (4 cm)[7] have also been reported to be successfully repaired by nerve conduits. Interposition of nerve segments[95] and filling of muscle graft[7] expended the use of vein conduits for nerve defects up to 4.5 cm and 6 cm, respectively. The first and only report[79] of using vein conduits to repair terminal branches of human trigeminal nerve demonstrated some return of sensation in lingual nerve defects smaller than 5 mm and no return of sensation in defects between 5 and 14 mm. The inferior alveolar nerve showed good sensory recovery in half of the cases. The spontaneous recovery of the inferior alveolar nerve, however, should be taken into account.

Vein conduits have been successfully used both in primary and secondary reconstruction. Although there are data indicating a trend toward more favorable results with vein grafts in acute nerve repair,[94,102] the unsuccessful repair is mostly found in cases that are delayed for 6 months or more when greater difficulty in reinnervation of end organs is to be expected.

Veins from the leg, dorsal foot, forearm, and finger are used as grafts. The type of vein graft utilized remains questionable regarding its influence on nerve regeneration. Theoretically, grafts with more rigid walls would be less likely to collapse, which is one of the biggest obstacles for vein conduits bridging long gaps. On the other hand, the advantage of a thick-walled vein graft is negated by its less permeability to oxygen and nutrients. Practically, the donor site of vein grafts is determined by the size of conduits needed, the tubulization technique used, and the surgical vicinity (eg, cephalic vein for superficial branch of radial nerve, basilic vein for dorsal cutaneous branch of ulnar nerve,[16] facial vein for inferior alveolar nerve[79]).

There are basically three fashions of using vein conduits. In some instances, the proximal and distal nerve stumps are telescoped into the vein graft lumen and secured by fine sutures.[16,102] In this fashion, the vein selected should be larger and longer (twice the diameter and 50% longer[16]). In some instances, simple end-to-end coaptation is performed.[7,102] Vein grafts slightly larger are selected. The third option is a combination of telescoping and simple end-to-end coaptation.[79,94,95] A rim of epineurium is cut back, and the protruding nerve ends are entirely tucked into a slightly overlength vein graft so the epineurium and the vein are approximated and sutured. Big nerve trunks are bridged either by a single vein conduit,[7] or by 2 to 3 bundles of vein conduits.[95] Most authors also advocate reversion of the vein grafts because of existence of intralumen valves. It is also important to leave vein conduits on favorable soft tissue bed. Vein conduits are not recommended when there is possibility of extensive scar formation.[96]

There is consensus for using vein grafts as nerve conduits to repair distal sensory nerve defects 3 cm or less based on the fact that although direct repair is superior, the vein grafts are at least adequate.[16,58] The efficacy of vein conduits for larger, more proximal, and mixed nerves needs to be justified by randomized, prospective clinical studies of larger series.

Muscle

The first clinical application of muscle graft was for repair of 8 digital nerve defects 15 to 25 mm in length,[71] either primarily or secondarily. All but one of the eight patients attained S3+ at 3 to 11 months follow-up, a result comparable to conventional repair method. The authors later on reported long-term results of a series of 12 digital nerves of 15 to 28 mm gaps, with comparison to a group of digital nerve end-to-end sutures.[72] Again, good sensory recovery was observed in muscle grafting group, which was superior to that of end-to-end coaptation. This is not a well-controlled comparison since tension at the suture site could not be excluded, which otherwise can be avoided by autogenous nerve grafts. The same group of authors reported muscle graft repair of 6 median nerve and 7 ulnar nerve defects, ranging from 1.5 to 10 cm[14]. Sensory recovery to S3+ was only obtained in 2 median nerves of 4.0 to 5.0 cm gaps and 3 ulnar nerves of 2.0 to 3.0 cm gaps. Motor recovery was generally poor, one of the reasons being delayed secondary repair with an average postinjury interval of 17 months. Radial

nerve with missile neurotmesis was repaired with denatured muscle grafts, with results comparable to sural nerve grafting 9 months after the operation.[82]

Another group of reports concern leprosy patients.[73,74] In one prospective study, defects between 25 and 60 mm in 3 median nerves and 9 posterior tibial nerves were repaired using denatured muscle grafts. Another retrospective study reviewed 48 nerves (11 median and 37 posterior tibial nerves) with gap lengths from 2 to 14 cm. Restoration of protective sensation of the hands and feet were encouraging.

Any skeletal muscle may be used to provide graft material as long as its fibers are arranged in parallel and its long axis can be aligned with nerve gap. A rectangular block of muscle of at least double the size of the gap is harvested. It is then freeze-thawed and trimmed to a rectangular graft as long as the nerve gap and about 2-mm wider in each plane than the diameter of the nerve. The graft is then sutured to the epineurium of the nerve endings, surrounding the nerve ends with a 1 to 2 mm cuff of muscle. Technically, problems of muscle fracturing on freezing in liquid nitrogen may occur. This may be solved by spray freeze. Large muscle blocks need to be freeze-thawed several times.

Although there are sporadic reports of using muscle grafts as nerve conduits clinically, their use is limited by the slow rate of regeneration, the inability of axons to regenerate effectively over distances greater than 5 cm, and difficulty in ensuring that all the muscle protein is completely denatured while retaining the correct orientation of the basal lamina tubes.

Polyglycolic Acid (PGA) Tube

PGA tube is a resorbable tube with some degree of mechanical strength. The standard tube is preformed crimped with a corrugated external surface and smooth inner surface that prevents kinking. PGA tube slightly larger than the nerve diameter and 1 cm longer than the measured nerve gap is selected so the nerve can be telescoped 5 mm into either end of the tube and compression of the nerve can be avoided. The tube is filled either with heparinized saline or autologous serum to preclude blood clot inside the lumen.

First series of clinical application involved 16 digital nerve defects in 15 patients.[55] The gaps ranged from 0.5 to 3 cm. The results showed that excellent functional sensation was present in 33% and good functional sensation in 53%. Failure was judged in 14%, one being tube extrusion. The outcome was comparable to digital nerve grafts. A multi-center randomized prospective study[106] recruited 98 patients of 136 digital nerves. PGA conduits were used to repair 62 nerves of gaps up to 3 cm. The conduit repair showed better results than conventional repair methods in defects of 4 mm or less and in defects over 8 mm. Extrusion of PGA tubes was found in 3 cases. Besides digital nerves, there is a case report of inferior alveolar nerve reconstruction.[19] A PGA tube used for 2.5 cm gap of the right inferior alveolar nerve completely relieved preoperative pain and restored excellent sensation judged both subjectively and with specific tests of sensibility. Spontaneous recovery could be excluded because of the long postinjury interval of 16 months.

Both vein grafts and PGA tubes appear to be reliable nerve conduits with less complications. PGA tubes are readily available while vein grafts require surgical harvest. Besides, PGA tubes are more resistant to compression, and therefore, collapse less than the soft veins. PGA conduits can be considered a first choice technique for short nerve gaps of 3 cm or less.

Polytetrafluoroethylene (PTFE) Tube

There is also an important role for nonabsorbable conduits since no biodegradable conduits are clinically available in a diameter large enough for repair of major nerves.

PTFE tubes with a corrugated external surface which are slightly larger and 1 cm longer are selected. The nerve stumps are telescoped 5 mm into the tube at each end. The lumen is filled with heparinized saline.

PTFE tubes have been used to treat median nerve and ulnar nerve injury at forearm, elbow or upper arm levels.[89,90,107] Nerve gaps ranged from 1.5 to 6 cm. When gaps were longer than 5 cm, nerve slices were interposed into the lumen. 79% of patients with gaps 4 cm or less and 13% patients with gaps of 4 to 6 cm regained functional sensory and motor recovery. The maximal gap length that was successfully reconstructed by PTFE conduit was 5 cm. In only one of 44 patients, a secondary surgery was required to remove the tube because of slight discomfort at the site of injury. Reconstruction of inferior alveolar nerve and lingual nerve failed to either reduce pain or restore function in the majority of the cases reported.[77,78] The nonresorbable property that leads to late compression of the nerve accounted for the failure. PTFE tube is not recommended for repair of trigeminal nerves.

Silicone Tube

Clinical application of silicone tubes involves exclusively median nerve, ulnar nerve and radial nerve.[9,48,49,52,53,63] The series reported by Lundborg[48,49,52] are rather wrapping and creating a regeneration chamber than bridging the defect. A silicone tube with an inner diameter slightly larger (30%) than the nerve was spliced to house the two nerve ends, leaving a gap of 3 to 5 mm. The tube was then closed by suture. Motor and sensory recovery was satisfactory, showing no difference between tubular and conventional techniques with the exception of perception of touch that favored tubulation. One of 11 cases required tube removal because of irritation at repair site. It should be noted, however, the follow-up period of this series was only up to 12 months. Another series included 26 median and/or ulnar nerves with gaps ranged from 2 to 5 cm.[9] Silicone conduit was found to be effective in the repair of nerve injuries with gaps up to 3 cm, with better results in ulnar nerves than in median nerves. The average follow-up was 30 months. Seven of the 26 patients required removal of the tube because of irritation (mostly patients with longer nerve gaps with larger tubes). Silicone tube has also been used to bridge 7 median nerves, 5 ulnar nerves, and 3 radial nerves with gap lengths up to 5 cm.[53] Long-term follow-up revealed M4S4 in 8 nerves, M3S3 in 3 and M1S1 in 2 nerves.

Silicone tube will inevitably cause fibrosis and develop nerve compression over a period of 6 to 12 months.[63] Therefore, it should be removed after placement when regeneration across the gap is achieved.

Summary

Although autogenous nerve grafting remains the gold standard for repair of peripheral nerve defects, the use of various conduits can be a substitute provided these conduits meet the

above-mentioned prerequisites. For the moment, autogenous vein grafts or denatured muscle grafts can be used to bridge short defects, especially in distal sensory nerves. Incorporation of muscle into a vein graft expands its application to longer defects in bigger nerves. PGA conduits have also been clinically proven to be reliable in reconstruction of digital nerve defects. Although nonabsorbable conduits cause irritation and nerve compression that necessitates secondary surgery removal, silicone tubes or Goretex tubes can be used in selected cases until absorbable conduits large enough for major peripheral nerves are available. To date, 3 cm seems to be the barrier for conduits. Incorporation of trophic factors and Schwann cells into the conduits will make their way into the clinic if problems like controlled release of trophic factors, obtaining and sustenance of an appropriate number of viable Schwann cells, are solved.

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