The Role of Nerve Graft Substitutes in Motor and Mixed Motor/Sensory Peripheral Nerve Injuries

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Continuing Medical Education

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Disclosures for this Article

Editors

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Learning Objectives

Upon completion of this CME activity, the learner should achieve an understanding of:

- The currently available conduits for repairing a nerve gap
- The indications for using conduits in small sensory nerves and for large mixed nerves
- The reasons for the limitations in available best evidence to guide the practitioner in treating patients with a traumatic nerve gap
- How best to assess functional nerve outcome after peripheral nerve repair

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Alternatives to nerve autograft have been invented and approved for clinical use. The reported outcomes of these alternatives in mixed motor nerve repair in humans are scarce and marked by wide variabilities. The purpose of our Current Concepts review is to provide an evidence-based overview of the effectiveness of nerve conduits and allografts in motor and mixed sensory/motor nerve reconstruction. Nerve graft substitutes have good outcomes in mixed/motor nerves

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in gaps less than 6 mm and internal diameters between 3 and 7 mm. There is insufficient evidence for their use in larger-gap and -diameter nerves; the evidence remains that major segmental motor or mixed nerve injury is optimally treated with a cabled nerve autograft.

Key words Conduit, allograft, peripheral nerve injury, motor nerve.

THE GOLD STANDARD TREATMENT for reconstruction of a motor or mixed sensory/motor peripheral segmental nerve defect is autologous sensory cable nerve grafting.[1] Apart from the well-known drawbacks of this technique, such as donor site morbidity and a limited availability of donor nerves, the functional outcome has not been consistently successful, especially in terms of mixed sensorimotor nerve function.[2]

The repair of motor and mixed nerves presents additional challenges secondary to the need for precise identification of the fascicles. As Brushart's experiments[3–5] have demonstrated, motor pathways differ from sensory pathways and there is fundamental evidence that a pure sensory nerve graft is more effective in promoting sensory rather than motor axon regeneration.

Occasionally, a patient objects to autologous nerve grafting or there are no available donor nerves to be used; in these instances, nerve conduits could provide a readily available and relatively unlimited supply, offering an alternative to the nerve autograft. Nerve conduits made from various materials have been used since the late 1980s. They provide a protective environment that serves as a physical barrier to isolate the injured nerve from the surrounding tissues and also provide an enclosed chamber for the diffusion of neurotrophic factors released by the nerve ends.[6]

The first type 1 collagen nerve conduit approved by the U.S. Federal Drug Administration (FDA) in 2001 was NeuraGen (Integra Life Sciences, Plainsboro, NJ).[7] Two additional FDA-approved synthetic conduits: polyglycolic acid (PGA) and polylactide-caprolactone, subsequently became commercially available for nerve repair.[8] The first human nerve allograft transplantation was reported in 1878. However, rejection has been one of the major adverse effects in these early reports and immunosuppressive medications were required.[9] To overcome the disadvantage of immunosuppression, several authors have evaluated processing techniques including radiation, freeze-drying, and chemical techniques. Hudson et al[10] and Sondell et al[11] improved a chemical decellularization treatment in the late 1990s that removes myelin and Schwann cells while leaving the basal lamina tubes intact. Their research resulted in the development of the only commercially available decellularized human nerve allograft (Avance Nerve Graft; Axogen, Inc., Alachua, FL), which was approved for clinical use in 2007.

Bioabsorbable nerve conduits and decellularized allografts have been extensively studied for sensory nerve repairs and have demonstrated improved sensory recovery compared with direct nerve repair or nerve graft in several studies.[12–17] The data on the use of conduits/allografts for mixed sensory/motor or pure motor nerve repair in humans, however, are scarce, consisting mainly of case reports and are marked by wide discrepancies and bias. Nerve conduits have been shown to be effective for mixed motor-sensory nerves in rat and monkey models of nerve repair,[18–20] but the translation from rat to human has been under debate because of the strong regenerative potential of the rat, which is in sharp contrast to the human patients, who often have major comorbidities or concomitant injuries.[21] In recent years, clinical reports have described both successful and failed motor reinnervation with bioabsorbable nerve conduits in the upper limb[22–24]; These inconsistent results have limited the current application to noncritical small-diameter sensory nerve defects of less than 3 cm.[25]

DATA COLLECTION

At present, there are no evidence-based guidelines that are applicable regarding the use of conduits/allografts versus cabled autograft for the reconstruction of major motor or mixed peripheral nerve gaps. The question surgeons have is should an autologous nerve graft be harvested or should a nerve conduit or decellularized allograft nerve be used in these cases? We provide an evidence-based overview of the effectiveness of nerve conduits and allografts in motor or mixed sensorimotor nerve reconstruction and define their role in current practice to assemble this Current Concepts article.