

What is new in peripheral nerve repair?

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Abstract: In the last few years, several new techniques have been added in the repair of peripheral nerves. Some of them are convincing and are gaining popularity amongst peripheral nerve surgeons. Magnification has certainly improved the results of nerve repair. Although autografts are the gold standard for repair of peripheral nerves, allografts have been practiced as an alternative, by incorporation of new immunosuppressive agents such as FK - 506. In select patients with a paucity of autografts, allograft nerve transplantation may be of some utility. For small defects (< 3 cm), nerve conduits made of biological materials or autologous vein, have produced promising results. As an alternative to simple suture repair, fibrin glue is being used for nerve coaptation. Narakas found a 30% decrease in operation time with slightly superior functional outcome relative to traditional suture based coaptation. End - to - side neurorrhaphy may be helpful when the proximal nerve stump is not available.

Keywords: nerve repair, autografts, allografts, nerve conduits, fibrin glue, end - to - side neurorrhaphy

INTRODUCTION

In recent past there have been significant developments in the management of peripheral nerve injuries. The advent of microsurgical techniques with use of magnification, micro-sutures and micro instruments has considerably improved the results in nerve repairs. Many advances have been made in the area of neurobiology of nerve injury and regeneration, and increasing attempts are being made in the use of nerve allografts and nerve conduits for bridging the gaps.

NERVE AUTOGRAFTS AND ALLOGRAFTS

Nerve autografts are considered the gold standard technique for the peripheral nerve lesions. The nerve grafting technique was first reported between the years 1870 and 1900, but it was Millessi¹ who worked extensively on the nerve grafting techniques. He made it clear that nerve grafting without tension was superior to epineural suture under tension. Tension across a direct suture repair decreases blood flow and excessive tension will cause the repair to break down. The sural nerve is by far the most commonly used donor nerve, others being

the cutaneous nerves of arm and forearm, dorsal sensory branch of radial nerve and distal portion of anterior interosseous nerve. One current practice that accounts for the success of nerve grafts is the use of small, thin grafts which get vascularized faster than the large and thick grafts. For bridging the long gaps (greater than 20 cm) with associated soft tissue loss over the repaired area, current recommendation is to use free vascularized nerve grafts^{2,3}. In global brachial plexus palsy with C8 and T1 root avulsions, pedicled vascularized ulnar nerve^{4,5} has been used for a contralateral C7 root transfer to the median nerve.

The endoscopic technique for harvesting the sural nerve^{6,7,8,9,10} has been devised to overcome the potential drawbacks of the open technique, e.g.; long, unaesthetic scar, wound infection and wound pain. However the cost of the equipment and learning curve can be a barrier to switching to the endoscopic approach.

The use of allografts has been experimented in nonhuman primates¹¹ and later practiced by Mackinnon et al in the humans¹² and the groups involved in hand transplantation¹³. Nerve allografts act as a temporary scaffold across which host axons regenerate. Ultimately, the allograft tissue is completely replaced with host material¹⁴. Once regeneration has occurred through the graft, immunosuppression may be discontinued. A new immunosuppressant FK 506, also known as tacrolimus, has greater potential and fewer side effects than other

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immunosuppressants^{15,16}. It has been established that FK 506 has neuroregenerative and neuroprotective effects regardless of its immunosuppressive activity¹⁷.

NERVE CONDUITS

Although autologous nerve graft transplantation has been considered the “gold standard” for the treatment of patients with peripheral nerve gap injuries, their major disadvantage is the limited number of donor nerves available. This problem has led to the development of new techniques for bridging the nerve gap. Natural or synthetic guidance channels are being developed as alternatives to autografts. These nerve conduits help direct axonal sprouts from the proximal stump to the distal nerve stump. They also provide a channel for diffusion of neurotropic and neurotrophic factors secreted by the Schwann cells of the injured distal nerve stump and minimize infiltration of fibrous tissue¹⁸. Synthetic tubes constructed from materials such as polyglycolic acid, polylactide-co-caprolactone, and silicone have been used as alternatives to autologous graft placement, but in general, they have yielded poor results^{19,20}. Tubes made of biological materials such as laminin and collagen have been used with more success for distances of less than 3 cm²¹.

USE OF FIBRIN GLUE IN NERVE REPAIR

Synthetic nerve suture may induce considerable fibrotic and inflammatory reactions at the coaptation site which could seriously hamper regeneration of nerve fibres. Young and Medawar²² devised a method by which the nerve stumps were held together with concentrated coagulated blood plasma. In 1988 Narakas²³ revived the use of fibrin in nerve repair. Since then, its use has steadily gained popularity amongst the peripheral nerve surgeons. A recent study²⁴ has compared the use of fibrin glue and microsutures in the repair of rat median nerve and found that nerve repairs performed with fibrin sealants produced less inflammatory response and fibrosis, better axonal regeneration, and better fiber alignment than the nerve repairs performed with microsuture alone. In addition, the fibrin sealant techniques were quicker and easier to use. Bozorg et al²⁵ have reported promising results with fibrin glue in the repair of facial nerve in human beings.

END TO SIDE NEURORRHAPHY

In last two decades, there has been a volume of research evaluating end-to-end versus end-to-side repairs²⁶ but it

is generally accepted that end-to-side will provide only limited sensory recovery²⁷. The technique seems most successful when the epineurium is opened and there has been a small amount of damage to the enclosed fascicles during the placement of a distal nerve stump to the whole nerve. An end-to-side repair will allow motor reinnervation through collateral sprouting only when there has been a direct nerve injury at the repair site, such as a partial neurectomy.

End – to – side neurorrhaphy has been used in some clinical situations such as in dealing with long segmental nerve defects and nerve defects in which the proximal part of the nerve is unavailable. Although some workers have accepted end – to – side neurorrhaphy as an alternative for nerve repair, others have reported limited sensory and motor recovery when using this technique^{27,28,29}. It has also been reported that motor axons have better regeneration capacity than sensory axons³⁰.

CONCLUSIONS

Autograft remains the gold standard for bridging a nerve gap. Endoscopic harvesting of sural nerve graft is less traumatic, safer and a more aesthetic technique. An understanding of nerve regeneration and immunosuppression has generated considerable interest in the use of allografts in peripheral nerve surgery. Recent advances in the field of neurobiology of nerve growth and genetic engineering has led to the development of guiding channels or nerve conduits. Fibrin glue is being increasingly used as an alternative to synthetic nerve sutures. New techniques of nerve repair (end-to-side repair) are being practiced especially where nerve transfers are deemed impossible.

REFERENCES

1. Millesi H. Techniques for nerve grafting. *Hand Clinics* 2000;16: 73-91.
2. Doi K, Kuwata N, Kawakami F, et al. The free vascularized sural nerve graft. *Microsurgery* 1984; 5: 175-84.
3. Hasegawa T, Nakamura S, Manabe T. et al. Vascularized nerve grafts for the treatment of large nerve gap after trauma to an upper extremity. *Arch Orthop Trauma Surg* 2004; 124: 209-13.
4. Gu YD, Chan DS, Zhang GM et al. Long term functional results of contralateral C7 transfer. *J Reconstr Microsurg* 1998; 14: 57-9.
5. Waikakul S, Orapin S, Vanadurongwan V. Clinical results of contralateral C7 root neurotization to the medial nerve in

- brachial plexus injuries with total root avulsions.
J Hand Surg [Br] 1999; 24: 556-60.
6. Kobayashi S, Akizuki T, Sakai Y, Ohmori K. Harvest of sural nerve grafts using the endoscope.
Ann Plast Surg 1995; 35: 249-53.
 7. Capek L, Clarke HM, Zuker R.M. Endoscopic sural nerve harvest in the pediatric patient.
Plast Reconstr Surg 1996; 98: 884-8.
 8. Clarke HM. An update on endoscopic sural nerve harvest.
Plast Reconstr Surg 1998; 102: 1304.
 9. Hallock GG. Endoscopic retrieval of the sural nerve.
J Reconstr Microsurg 1995; 11: 347 – 50.
 10. Eich BS, Second, Fix RJ. New techniques for endoscopic sural nerve harvest.
J Reconstr Microsurg 2000; 16: 329-31.
 11. Bain JR, Mackinnon SE, Hudson AR, Wade J, Evans P et al. The peripheral nerve allograft in the primate immunosuppressed with cyclosporine A.I. Histologic and electrophysiologic assessment.
Plast Reconstr Surg 1992; 90: 1036-46.
 12. Mackinnon SE, Doolabh VB, Novak CB, Trulock EP. Clinical outcome following nerve allograft transplantation.
Plast Reconstr Surg 2001; 107: 1419-29.
 13. Jones JW, Gruber SA, Baker JH, Breidenbach WC. Successful hand transplantation. One year follow up. Louisville Hand transplant team.
N Engl J Med 2000; 343: 468-73.
 14. Atchabahian A, Doolabh VB, Mackinnon SE et al. Indefinite survival of peripheral nerve allografts after temporary cyclosporin A immunosuppression.
Restor Neurol Neurosci 1998; 13: 129-39.
 15. Ohara K, Billington R, James RW, Dean GA, Nishiyama M, Naguchi H. Toxicologic evaluation of FK-506.
Transplant Proc 1990; 22: 83-6.
 16. Starzl TE, Todo S, Fung J, Demetris AJ, Venkataraman R, Jain A : FK 506 for liver, kidney and pancreas transplantation.
Lancet 1989; 2: 1000-4.
 17. Gold BG, Katoch K, Storm-Dickerson T: The immunosuppressant FK 506 increases the rate of axonal regeneration in rat sciatic nerve.
J Neurosci 1995; 15: 7505-16.
 18. Hudson TW, Evans GR, Schmidt CE: Engineering strategies for peripheral nerve repair.
Orthop Clin North Am 2000; 31: 485-97.
 19. Francel PC, Francel TJ, Mackinnon SE, Hertl C. Enhancing nerve regeneration across a silicone tube conduit by using interposed short segment nerve grafts.
J Neurosurg 1997; 87: 887-92.
 20. Midha R, Munro CA, Dalton PD, Tator CH, Shoicher MS: Growth factor enhancement of peripheral nerve regeneration through a novel synthetic hydrogel tube.
J Neurosurg 2003; 99: 555-65.
 21. Ashley WW, Weatherly T, Park TS. Collagen nerve guides for surgical repair of brachial plexus birth injury.
J Neurosurg 2006; 106: 452-6.
 22. Young IZ, Medawar PB. Fibrin suture of peripheral nerves.
Lancet 1940; 2:126.
 23. Narakas A. The use of fibrin glue in repair of peripheral nerves.
Orthop Clin North Am 1988; 19: 187-98.
 24. Ornelas L, Padilla L, Di Silvio M, Schalch P, Esperantes, Infante RL, Bustamante JC, Avalos P, Varela D, Lopez M: Fibrin glue: an alternative technique for nerve coaptation – Part-II. Nerve regeneration and histomorphometric assessment.
J Reconstr Microsurg 2006; 22: 123-8.
 25. Bozorg GA, Mosnier I, Julien N, El Gareem H, Bouccara D, Sterkers O. Long term functional outcome in facial nerve graft by fibrin glue in the temporal bone and cerebellopontine angle.
Eur Arch Otorhinolaryngol 2005; 262: 404-7.
 26. Viterbo F, Trindale JC, Hoshino K, Mazzori Neto A. End to side neurorrhaphy with removal of the epineural sheath: An experimental study in rats.
Plast Reconstr Surg 1994; 94: 1038-47.
 27. Tarasidis G, Watanabe O, Mackinnon SE, et al. End-to-side neurorrhaphy: a long term study of neural regeneration in a rat model.
Otolaryngol Head Neck Surg 1998; 119: 337-41.
 28. Noah EM, Williams A, Jorgensen C, Skoulis TG, Terzis JK. End – to – side neurorrhaphy – a histologic and morphometric study of axonal sprouting into an end – to – side nerve graft.
J Reconstr Microsurg 1997; 13: 99 – 106.
 29. Shah MH, Kasabian AK, Karp NS, Kolker AR, Dublin BA, Zhang I, et al. Axonal regeneration through an autogenous nerve bypass: An experimental study in the rat.
Ann Plast Surg 1997; 38: 408 – 15.
 30. Tham SKJ, Morrison WA. Motor collateral sprouting through an end – to – side nerve repair.
J Hand Surg (Am) 1998; 23: 844 – 85.