The Turnover Distal Epineurial Sheath Tube for Repair of Peripheral Nerve Gaps

Chalermpong Chatdokmaiprai MD*,
Watin Suwansingh MD*, Surapon Worapongpaiboon MD**

** Division of Plastic and Maxillofacial Surgery, Department of Surgery, Ramathibodi Hospital, Mahidol University*
*** Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University*

Background and objective: *Autologous nerve grafting is the conventional technique for bridging nerve gaps. However, the drawback of this technique is the morbidity associated with the left over donor site. The purpose of the present study was to investigate the effects of the turnover distal epineurial sheath tube as an alternative to nerve grafting for the repair of nerve gaps.*
Material and Method: *The experimental model included 14 male Wistar rats. The left and right sciatic nerves were resected and the 14 left sciatic nerve gaps were reconstructed using conventional autologous nerve grafts while the other 14 right sciatic nerve gaps were reconstructed with turnover distal epineurial sheath tubes. All the repaired sciatic nerves were harvested for histologic and quantitative histomorphometric evaluation at the 11th week after the operations.*
Results: *There were no statistical differences in quantitative evaluation of Schwann cells between the conventional nerve grafting group and the distal epineurial sheath tube group ($p > 0.05$).*
Conclusion: *The turnover distal epineurial sheath tube provides a suitable conduit between two stumps, eliminates donor-site morbidity, reduces the operating time, and might be an alternative modality to nerve grafting for nerve gap repair.*

Keywords: *Turnover distal epineurial sheath tube, Nerve gap repair*

J Med Assoc Thai 2006; 89 (5): 663-9
Full text. e-Journal: *http://www.medassocthai.org/journal*

The main purpose of peripheral nerve repair is functional recovery by regaining nerve conduction. In nerve repair, a clinical situation often arises in which there is not a sufficient portion of a nerve present to allow an end-to-end repair when needed, as in the case of trauma or neuroma resection. It has been shown experimentally and clinically that tension at the nerve anastomosis will inhibit nerve regeneration(1). Management of short gaps by flexing joints to facilitate a tension-free repair will consequently produce scar formation when the limb is mobilized(2). Currently, autologous nerve grafting is the most reliable and conventionally used technique for bridging nerve gaps, despite its various disadvantages which are scarring, neuroma formation, loss of donor-site function, and size discrepancies between the nerve ends as well as increased operating room and anesthesia time. There exists, then, an impetus to develop another method of managing short nerve gaps. Nerve regeneration across a nerve gap through various tubes and conduits has been demonstrated in a number of recent studies. These conduits include natural materials such as collagen(3), silicone(4), muscle basal lamina(5), human amniotic membrane(6) and vein graft(7). The synthetic conduits made from polymer materials include polyglycolic acid(8), polyglactin(9), polycaprolactone(10), polyurethane(11), and polyphosphazene(12).

The turnover epineurial sheath tube, formed by proximal epineurial sheath, was previously described by Ayhan et al(13-,14). The advantages of this technique are its tissue properties that provide a suitable conduit between two stumps, eliminate the use of a donor nerve and donor site morbidity, and reduce the number of

Correspondence to : Chatdokmaiprai C, Division of Plastic and Maxillofacial Surgery, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand. Phone: 0-2201-2281, Fax: 0-2201-2281, E-mail: raccd@mahidol.ac.th

suture sites, thus reducing the amount of fibrosis and operating time. Although comparable results with nerve grafting were obtained, the disadvantage of using proximal epineurial sheath is the possibility of disturbance to blood supply and viable axons in proximal stump. From this point of view, the authors were convinced to use epineurium from the distal stump, which will undergo Wallerian degeneration, as a conduit for the repair of nerve gaps.

The purpose of the present study was to compare two methods of nerve repair in the rat model in terms of nerve healing: the turnover distal epineurial sheath tube versus nerve grafts for the repair of significant-sized nerve gaps.

Material and Method

Fourteen male Wistar rats, weighing in the range of 250 and 300 grams, were used in the present study. Surgical procedures were carried out under intraperitoneal pentothal (50mg/kg) by using standard microsurgical techniques under an operating microscope. The surgical procedures were performed on the rats in a prone position by the same surgeon.

Surgical procedure

Bilateral gluteal incisions and muscle splitting were used to expose the sciatic nerve from the sciatic notch to the point of bifurcation. Bilateral segmental nerve resections were done in these fourteen rats, producing 7mm nerve gaps, at the point of 5 mm distal to ipsilateral sciatic notch.

On the left limb of the rats, the segmental nerve was resected and the gap was grafted with the resected segment of right sciatic nerve. Each nerve graft endings was anastomosed to both stumps by epineurial repair with eight interrupted stitches of 10/0 nylon suture.

On the right limb of the rats, the segmental nerve was resected and the gap was connected with turnover epineurial sheath tube from the distal nerve stump. After segmental nerve resection, the epineurium was incised circumferentially about 10 mm distal to the distal stump by using microscissors. The epineurial sheath was held by jeweller's forceps and turnover in a proximal direction, forming a tube flap. The proximal free margin of the turnover epineurial tube was sutured to the epineurium of the proximal stump with four to six interrupted stitches of 10/0 nylon suture (Fig. 1a & 1b).

After these surgical steps, the muscular layer and skin were sutured in layers and the rat was placed back and fed in the cage. At the 11th week after the operation, the rat was sacrificed by pentothal overdose, and both sciatic nerves were harvested for histo-morphometric evaluation.

Histomorphometric evaluation of the nerves

Nerve segments were harvested in both sides. One was at the point of 2 mm proximal to proximal anastomosis, the other was at the point of 2 mm distal to distal anastomosis. Their length was 2 mm. These four specimens in each rat were labeled as Left Proximal segment (LP), Left Distal segment (LD), Right Proximal segment (RP), Right Distal segment (RD) (Fig. 2). These specimens were fixed with 10% buffered formalin overnight, sent to conventional tissue processing, cut into 6 mm slides and stained with H&E.

Quantitative histomorphometric evaluations were made by counting the nuclei of Schwann cells in a 0.152 mm^2 area. Two areas were used to calculate the mean number of cells in each specimen. Calculations were determined by using a light microscope, a connected video camera, and a computer analysis system. The cell counts were calculated by count/size measurement program (Imagepro-Plus).

Statistical analysis

Paired t-test was used to test the difference between the two groups. Statistical significance was set at the level of 0.05 or less.

Results

At the 11^{th} week after operation, no gross difference was observed between the sciatic nerves on the left and the right side (Fig. 3).

On histologic evaluation, the quantities of axonal regenerations and Schwann cells in each microscopic view (Fig. 4) had good quantitative correlation. Results of the quantitative histomorphometric evaluation of Schwann cells are shown in Table 1.

There were no statistically significant differences in the mean number of Schwann cells per square millimeter between the turnover distal epineurial sheath tube group and the nerve graft group at both the proximal and distal sites of the sciatic nerves (p-values of 0.452 and 0.869 respectively).

Discussion

Several techniques have been described for repair of peripheral nerve gaps, but currently, reconstruction by using autologous nerve grafts is the most popular option. Although negligible sequelae are

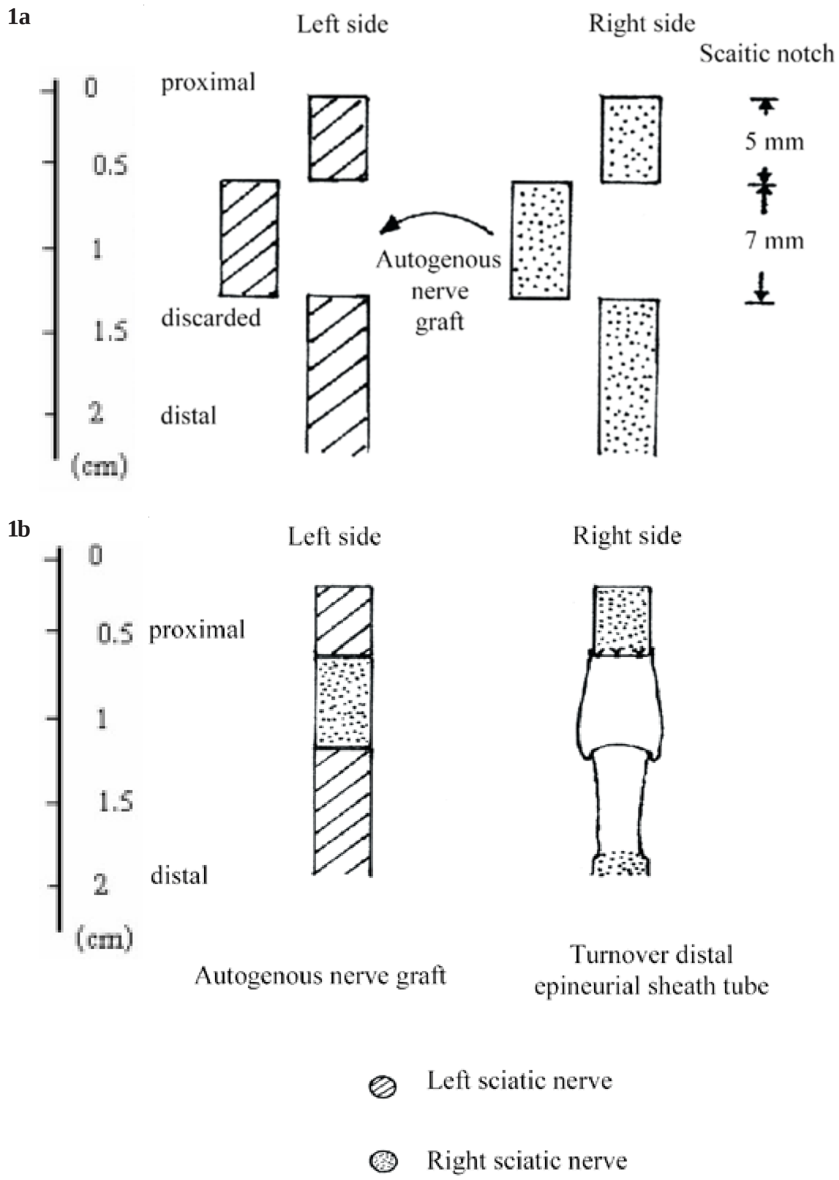

Fig. 1 Schematic illustration of the surgical technique. 1a: resection of sciatic nerves. 1b: autogenous graft, from right sciatic nerve, at left sciatic nerve defect; turnover distal epineurial sheath tube for right sciatic nerve defect

expected from harvesting the nerve grafts from less functionally important areas, the nerve grafts are still associated with disadvantages including paresthesia or anesthesia, formation of neuroma, pain, and additional scars at the donor site. Furthermore, size discrepancies between the nerve ends, enhanced foreign body reaction due to the stitches at two coaptation sites, compromise in the revascularization of the graft, and longer operating time are also negative aspects of this technique.

Because of these factors, there is still an ongoing search for alternative options to nerve grafts. Tubulization techniques, using either natural or synthetic conduits, have been developed in recent years. These materials have various experimental success rates, but only vein grafts have gained routine clinical use as tubular conduits.

Bridging a nerve gap with native tissue offers several advantages. Firstly, the epineurium that will constitute the conduit between the stumps is always

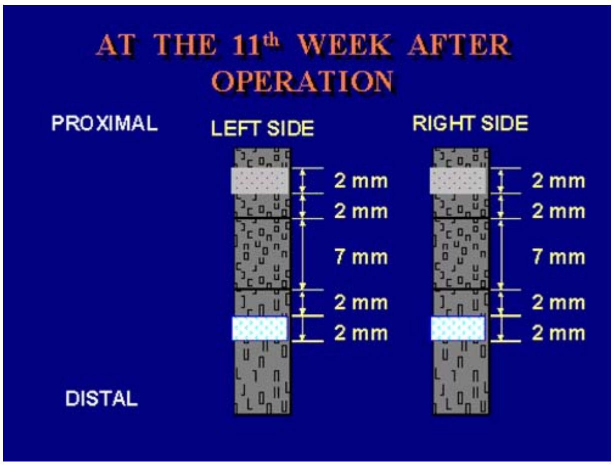

Fig. 2 Schematic illustration of the location of resected specimens for histomorphometric analysis on the sciatic nerves

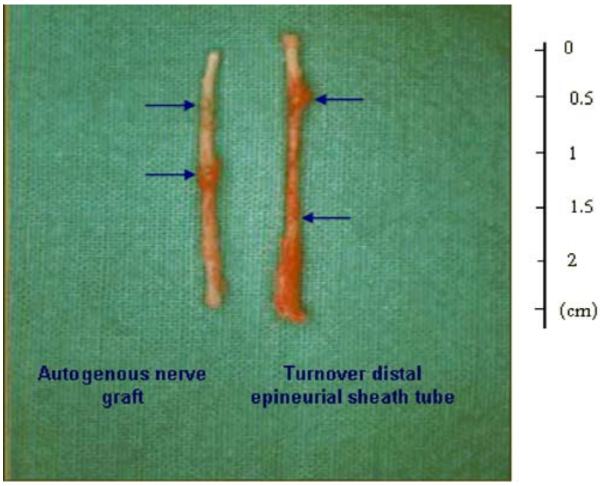

Fig. 3 Gross appearance of both sciatic nerves and anatomosis area (arrow) Both operated nerves had smooth configuration, well-structured bridge across the gap

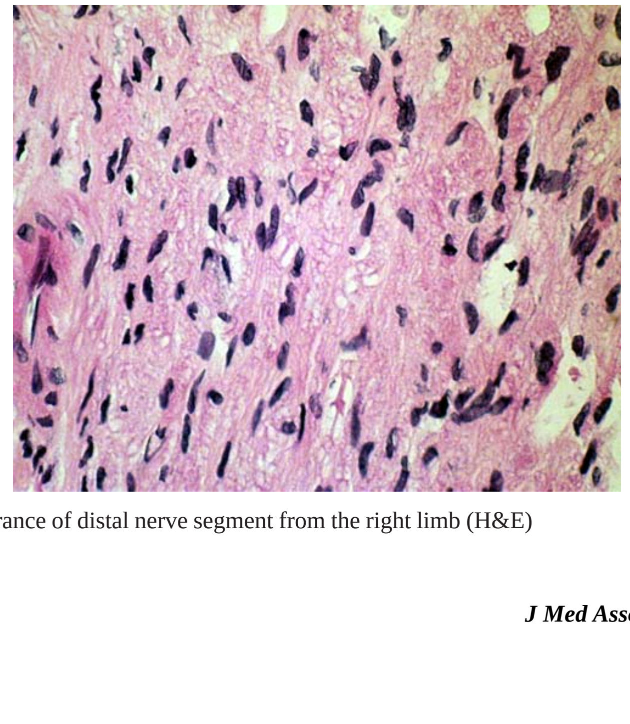

Fig. 4 Microscopic appearance of distal nerve segment from the right limb (H&E)

Table 1. Number of Schwann cells per square millimeter in each nerve specimen

Rat number	LP	LD	RP	RD
1	1434	395	1908	1204
2	3257	678	2329	1171
3	4546	2882	1730	1901
4	1579	1651	1461	1263
5	2434	605	1329	1204
6	1605	395	2066	1336
7	2224	1145	2553	2809
8	3934	3020	2467	5178
9	1711	921	1645	1855
10	1382	993	2296	1125
11	3026	3895	2349	1961
12	1868	3013	3783	2434
13	2237	678	2257	2329
14	1987	5651	1737	1230
means $\pm$ SD	2373.1 $\pm$ 974.2	1851.6 $\pm$ 1595.2	2136.4 $\pm$ 610.7	1928.6 $\pm$ 1085.2

LP: left proximal segment of sciatic nerve; LD: left distal segment of sciatic nerve; RP: right proximal segment of sciatic nerve; RD: right distal segment of sciatic nerve ($p = 0.452$, $p = 0.869$)

available at the surgical site and precludes the use of a conduit harvested from another area. Secondly, the poor matching in the diameter of the conduit and the nerve stump ends may be a problem when using other autologous conduits. Thirdly, regarding the origin of native tissue with neurotrophic potential, the chamber within the epineurial tube probably provides a very suitable milieu for axonal regeneration.

The use of the sliding epineurial sheath tube for nerve gaps has been described by Atabay et al(15). It was demonstrated that epineurium, as a tube originating from the native tissue of the nerve itself, could slide into the gap without harming the nerve trunk or interfering with conduction. Evidence of axonal regeneration shown in the present study suggested that this technique might be an alternative option to nerve grafts.

The use of epineurium in another way, described by Ayhan et al, was the turnover epineurial sheath tube from proximal nerve stump as a tube flap. It regained normal nerve configuration and minimal adhesions at the donor site. Late postoperative functional, histologic, and histomorphometric evaluations revealed similar results between this technique and the nerve grafts. In the turnover epineurial sheath tube technique, there is only one coaptation site between the free margin of the epineurial tube and the nerve end, reducing the number of stitches, and therefore foreign body reaction at the surgical site. One coaptation site also offers an advantage in reducing operating time, compared to other conduits that require coaptation both at proximal and distal ends.

The present study, using turnover distal epineurial sheath tube for repair of peripheral nerve gaps, avoids such disadvantages of turnover proximal epineurial sheath tube as possibility of disturbance to blood supply and viable axons in the proximal stump. In quantitative evaluation of Schwann cells count, the difference between conventional nerve graft group and distal epineurial sheath tube group was not significant.

Conclusion

The turnover distal epineurial sheath tube provides a suitable conduit between two stumps, eliminates donor-site morbidity and reduces the operating time. Consequently, it might be an alternative to nerve grafting for nerve gap repair.

Acknowledgements

The authors wish to thank Miss Umaporn Udomsubpayakul, MSc (Biostatistics) for help in statistical analysis. We also wish to thanks Associate Professor Arthi Kruavit, the chief of Division of Plastic and Maxillofacial Surgery, for his encouragement and support of the research fund.

References

1. Terzis J, Faibisoff B, Williams B. The nerve gap: suture under tension vs. graft. Plast Reconstr Surg 1975; 56: 166-70.
2. Millesi H. The nerve gap. Theory and clinical practice. Hand Clinics 1986; 2: 651-63.
3. Colin W, Donoff RB. Nerve regeneration through collagen tubes. J Dent Res 1984; 63: 987-93.
4. Zhao Q, Lundborg G, Danielsen N, Bjursten LM, Dahlin LB. Nerve regeneration in a 'pseudo-nerve' graft created in a silicone tube. Brain Res 1997; 769: 125-34.
5. Fawcett JW, Keynes RJ. Muscle basal lamina: a new graft material for peripheral nerve repair. J Neurosurg 1986; 65: 354-63.
6. Mohammad J, Shenaq J, Rabinovsky E, Shenaq S. Modulation of peripheral nerve regeneration: a tissue-engineering approach. The role of amnion tube nerve conduit across a 1-centimeter nerve gap. Plast Reconstr Surg 2000; 105: 660-6.
7. Chiu DT, Strauch B. A prospective clinical evaluation of autogenous vein grafts used as a nerve conduit for distal sensory nerve defects of 3 cm or less. Plast Reconstr Surg 1990; 86: 928-34.
8. 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: 1036-45.
9. Molander H, Olsson Y, Engkvist O, Bowald S, Eriksson I. Peripheral nerve regeneration through polyglactin tube. Muscle Nerve 1982; 5: 54-7.
10. Nicoli Aldini N, Perego G, Cella GD, Malterello MC, Fini M, Rocca M, et al. Effectiveness of a bioabsorbable conduit in the repair of peripheral nerves. Biomaterials 1996; 17: 959-62.
11. Robinson PH, van der Lei B, Hoppen HJ, Leenslag JW, Pennings AJ, Nieuwenhuis P. Nerve regeneration through a two-poly biodegradable nerve guide in the rat and the influence of ACTH4-9 nerve growth factor. Microsurgery 1991; 12: 412-9.
12. Langone F, Lora S, Veronese FM, Caliceti P, Parnigotto PP, Valenti F, et al. Peripheral nerve repair using a poly(organo)phosphazene tubular prosthesis. Biomaterials 1995; 16: 347-53.
13. Ayhan S, Yavuzer R, Latifoglu O, Atabay K. Use of the turnover epineurial sheath tube for repair of peripheral nerve gaps. J Reconstr Microsurg 2000; 16: 371-8.
14. Yavuzer R, Ayhan S, Latifoglu O, Atabay K. Turnover epineurial sheath tube in primary repair of peripheral nerves. Ann Plast Surg 2002; 48: 392-400.
15. Atabay K, Hong C, Heil BV. The use of "sliding epineurial sheath tube" for repair of peripheral nerve defects. Plast Surg Forum 1995; 18: 121-3.

การใช้เยื่อบุเส้นประสาทส่วนนอกด้านปลายแบบกลับหัวในการซ่อมช่องว่างของเส้นประสาท

เฉลิมพงษ์ ฉัตรดอกไม้ไพร, เวทิน สุวรรณสิงห์, สุรพล วรพงศ์ไพบูลย์

ที่มาและวัตถุประสงค์*: ในปัจจุบัน การซ่อมเส้นประสาทที่ขาดหายไปบางส่วนและมีช่องว่างเกิดขึ้น ยังคงใช้การตัดเส้นประสาทส่วนอื่นของร่างกายมาเชื่อมต่อ แม้ว่าวิธีดังกล่าวจะมีข้อเสียคือต้องทำลายเส้นประสาทปกติ การศึกษานี้มีวัตถุประสงค์เพื่อ ศึกษาการใช้เยื่อบุเส้นประสาทส่วนนอกด้านปลายแบบกลับหัว มาเชื่อมช่องว่างเส้นประสาทเพื่อเป็นทางเลือกแทนการตัดเส้นประสาทที่ยังดีอยู่มาใช้เชื่อมต่อเส้นประสาท*

วัสดุและวิธีการ*: หนูพันธุ์ วิสตาร์เพศผู้ 14 ตัว ถูกนำมาตัดเส้นประสาท sciatic ทั้ง 2 ข้างให้เกิดช่องว่าง และซ่อมช่องว่างดังกล่าวด้วย nerve graft สำหรับเส้นประสาทข้างซ้าย แต่ซ่อมด้วย เยื่อบุเส้นประสาทส่วนนอกแบบกลับหัวสำหรับเส้นประสาทข้างขวา หลังจากนั้นรอจนครบ 11 สัปดาห์ จึงทำการตัดเส้นประสาทที่รับการซ่อมแซมทั้ง 2 วิธี มาตรวจวิเคราะห์ทางพยาธิวิทยา*

ผลการศึกษา*: การตรวจทางพยาธิวิทยาในเชิงวัดปริมาณ ของ Schwann cells ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของการซ่อมเส้นประสาท sciatic โดยวิธีการใช้ nerve graft และ การใช้เยื่อบุเส้นประสาทส่วนนอกด้านปลายแบบกลับหัว ($p > 0.05$)*

สรุป*: การใช้เยื่อบุเส้นประสาทส่วนนอกด้านปลายแบบกลับหัวสามารถเชื่อมช่องว่างจากการสูญเสียเส้นประสาท โดยเมื่อเปรียบเทียบกับวิธีการใช้เส้นประสาทแบบเดิม จะลดความพิการที่เกิดจากการตัดเส้นประสาทที่ดีมาใช้ และลดระยะเวลาผ่าตัด จึงน่าจะเป็นทางเลือกอีกวิธีหนึ่งที่มาทดแทนการซ่อมเส้นประสาทแบบเดิมได้*