Foot & Ankle Specialist

Abstract: Compression and irritation at the plantar aspect of the transverse intermetatarsal ligament may lead to a compressive neuropathy called Morton’s neuroma. There are many treatment options for Morton’s neuroma, with the most common surgical option being traction neurectomy. While there has been success in many surgical procedures, up to 35% of patients treated with traction neurectomy have recurrent pain and up to one-third of these patients have a recurrent stump neuroma. These neuromas are caused by abnormal axonal growth during regeneration, leading to an unorganized mass of fibrotic collagenous tissues, Schwann cells, and axons. More recent surgical treatments of neuromas have included nerve capping, which has been proposed to prevent painful neuroma formation by isolating the nerve end from external chemosignaling and reducing disorganized axonal outgrowth. An off-the-shelf, biocompatible porcine small intestine submucosa (pSIS) derived nerve cap with internal chambering has been investigated in a rodent study, which showed less pain sensitivity and less axonal swirling indicative of reduced likelihood of neuroma formation. Furthermore, a recent clinical study indicated that patients experienced a significant reduction in pain 3 months after Morton’s neuroma excision followed by repair using a nerve cap. This article describes the surgical technique of the aforementioned clinical study to mitigate neuroma formation, where a Morton’s neuroma is excised, and the remaining proximal nerve stump is inserted within a nerve cap and buried in the surrounding muscle.

Level of Evidence: Level V: Expert opinion

Keywords: Morton’s neuroma; compressive neuropathy; neurectomy; neuroma; nerve cap

Introduction

Morton’s neuroma is a compressive neuropathy related to a perineural fibroma of the common plantar interdigital nerve, which results from compression and constant irritation at

A Method for Entubulating Exposed Nerve Ends Following Neurectomy Using a Porcine Extracellular Matrix Nerve Cap

Craig H. Thomajan, DPM

Techniques

DOI: 10.1177/19386400221106642. From Austin Foot and Ankle Specialists, Austin, Texas (CHT). Address correspondence to: Craig H. Thomajan, DPM, Austin Foot and Ankle Specialists, 5000 Bee Caves Road, Suite 202, Austin, TX 78746; e-mail: thomajan@austinfootandankle.com.

For reprints and permissions queries, please visit SAGE’s Web site at http://www.sagepub.com/journalsPermissions.nav.
the plantar aspect of the transverse intermetatarsal ligament, primarily in the third intermetatarsal space. This compression or irritation may lead to a disruption or injury to the peripheral nerve's continuity, which microscopically results in Renaut's bodies, axonal demyelination, axonal loss, and fibrosis. Morton's neuroma is the second most common compressive neuropathy and is present in females at a rate of 4 to 15 times that observed in males.

The treatment algorithm for management of Morton's neuroma typically involves nonoperative intervention, which may be followed by surgical intervention if necessary. Nonoperative treatment commonly includes footwear modifications and injections to manage pain. When these nonoperative treatments do not meet the goals and expectations of patients, surgical options are considered. Although there is no consensus for the optimal treatment of Morton's neuroma, the most common surgical treatment is a dorsal approach with traction neurectomy, where the affected segment of the nerve is excised and removed under tension to ensure that the remaining nerve stump retracts proximal to the weight-bearing zone of the metatarsals. This procedure can achieve good results for 70% to 85% of subjects. However, postneurectomy residual pain has been reported in 14% to 35% of patients with worsening pain in as many as 8% of patients. While the precise etiology is unknown, such recurrent pain may be due to incorrect initial diagnosis, treatment of the wrong interdigital space, inadequate resection, or the formation of a stump neuroma at the terminal end of the nerve stump. It has been found that as many as one-third of patients with recurrent pain after neurectomy may develop a recurrent neuroma on the nerve stump.

These nerve stump neuromas develop due to an abortive attempt of the nerve to repair an injury. During the regeneration process, the nerve end develops into an unorganized bulbous mass of fibrotic collagenous tissues, Schwann cells, and axons. Neurona pain may be due to a higher ratio of unmyelinated axons in the neuroma, which increases the sensitivity of the nerve fibers to mechanical stimulation such as scar contracture or transdermal compression or tapping. Several treatments have been proposed as an alternative to traction neurectomy, which may inhibit the formation of a painful nerve stump neuroma including targeted muscle reinnervation (TMR), burying of the nerve end into muscle or bone, and capping the nerve stump. Results from these procedures are promising; however, the limited space between the metatarsal heads restricts the surgical options after Morton's neuroma resection with the nerve stump entubulated within a nerve cap. This article presents a dorsal approach for surgical removal of a Morton's neuroma with insertion of the proximal nerve stump within a pSIS chambered nerve cap device (Axoguard Nerve Cap, Axogen Inc., Alachua, FL, USA) and burying within the local muscle tissue.

Methods

Surgical Procedure

Dorsal exposure of the intermetatarsal nerve. A linear incision is placed equidistant between the metatarsal heads from a dorsal approach (Figure 1). The incision should be made in the metatarsal space with an identified Morton's neuroma. This incision is deepened down through superficial and subcutaneous tissue being careful to isolate and protect all vital structures with utilization of microsurgical
Microsurgical instruments and loupe magnification are used to deepen the incision between the metatarsal heads (indicated by black asterisk) through the superficial and subcutaneous tissues to ensure that all vital structures are isolated. A Freer elevator may be used to separate and identify the deep transverse metatarsal ligament (indicated by green asterisk) and the intermetatarsal nerve. The Freer elevator insert is at the distal aspect of the incision (indicated by black arrow).

The distal aspect of the hypertrophic perineural fibroma may be freed through the interspace of the metatarsals (metatarsal heads indicated by black asterisks). The fibroma (green asterisk) is elevated through the intermetatarsal space by palpation through the plantar surface of the foot (black arrow).

Using a modified sterile ruler, measure the diameter of the unaffected, healthy nerve (indicated by green arrow) proximal to the fibroma (indicated by green asterisk) to approximate the proper sizing for the nerve cap. This nerve stump should be measured proximal to the fibroma (in healthy nerve tissue), to ensure that an appropriately sized nerve cap is selected for implant. The nerve can be secured by the digital nerve (indicated by blue asterisk) distal to the fibroma.

Placement of nerve cap. Axoguard Nerve Cap (Axogen Inc., Alachua, FL) is soaked for approximately 2 minutes immediately before application. This soak time can range between 30 seconds and 20 minutes, according to the nerve cap instructions for use. As the nerve cap soaks, the material softens. It is recommended to use the nerve cap when the nerve cap is

Figure 2. Microsurgical instruments and loupe magnification are used to deepen the incision between the metatarsal heads (indicated by black asterisk) through the superficial and subcutaneous tissues to ensure that all vital structures are isolated. A Freer elevator may be used to separate and identify the deep transverse metatarsal ligament (indicated by green asterisk) and the intermetatarsal nerve. The Freer elevator insert is at the distal aspect of the incision (indicated by black arrow).

Figure 3. The distal aspect of the hypertrophic perineural fibroma may be freed through the interspace of the metatarsals (metatarsal heads indicated by black asterisks). The fibroma (green asterisk) is elevated through the intermetatarsal space by palpation through the plantar surface of the foot (black arrow).

Figure 4. Using a modified sterile ruler, measure the diameter of the unaffected, healthy nerve (indicated by green arrow) proximal to the fibroma (indicated by green asterisk) to approximate the proper sizing for the nerve cap. This nerve stump should be measured proximal to the fibroma (in healthy nerve tissue), to ensure that an appropriately sized nerve cap is selected for implant. The nerve can be secured by the digital nerve (indicated by blue asterisk) distal to the fibroma.
surgeon’s preferred method.

The skin tissue should be closed with intradermal, or subcuticular the muscle. The subcutaneous, with burying the nerve cap within

be placed through the distal end mattress suture. (C) A suture may

be added 180° from the first suture. A second suture should

upon completing the mattress anchor suture can be removed

cap and secured. The epineurial anchor suture is then

passed back through the nerve cap to allow for visualization of the nerve stump. A mattress stitch is placed approximately 2 to 3 mm from the open end of the nerve cap, suturing from outside to inside using an 8-0 or 9-0 monofilament nylon suture (see Figures 5B and 8). A mattress suture allows for entubulation of the nerve within the cap and secures the nerve to the cap. The suture is then placed transversely through the epineurium of the native nerve matching the distance of the provisional mattress stitch (ie, 2-3 mm from the end of the proximal nerve stump), which is then returned through the lumen of the nerve cap. This completes the mattress stitch. To guide the nerve into the cap, an assistant may hold the previously placed epineural anchor suture above the plane of the surgical field as the native nerve is placed within the nerve cap, ensuring that the nerve stump does not encroach on the partition. The epineurial anchor suture is then removed and the mattress stitch is tied to the dorsal surface of the cap. A second suture should be placed 180° from the first suture, which secures the edge of the cap to the epineurium of the nerve stump. At the surgeon’s discretion, a 5-0 monofilament absorbable suture may be placed to act as an anchoring suture through the distal tab of the nerve cap to allow for burying in the muscle, where the cap is inserted within the interosseous muscle belly within the intermetatarsal space (Figure 5C). Subsequent closure of the subcutaneous, intradermal, or subcuticular tissues should be performed with monofilament absorbable suture. Skin closure should be performed using the surgeon’s preferred method (Figure 9). If multiple Morton’s neuromas have been identified, multiple neuromas may be excised simultaneously; however, adequate space between the incisions should be left to ensure that there is adequate blood supply to prevent tissue necrosis.

Discussion

Following disruption of a nerve end, whether due to traumatic injury, iatrogenic injury, or planned surgical excision, a symptomatic neuroma often forms. In particular, following Morton’s neuroma surgery, recurrent pain in the foot has been reported between 14% and 35% of patients. This article describes a dorsal approach to secure a chambered nerve cap to the proximal nerve stump after Morton’s neuroma excision with subsequent burying of the nerve stump and cap intermetatarsal space. The plantar approach to Morton’s neuroma excision is not described in this article, as there are notable comorbidities associated with the plantar surgical approach including wound complications and scar sensitivity. Therefore, the preferred surgical approach is dorsal; however, visualization of the surgical field in this procedure is challenging for several reasons. First, the incision is small, and the nerve is located deep to the metatarsal heads. Furthermore, the procedure must be performed in a hole, with limited ability to retract the surrounding tissues.

This surgical technique offers 2 main benefits. First, dorsal incisions provide the patient an opportunity for a faster return to normal activities. Second, entubulating the terminated nerve end within the chambered nerve cap helps to prevent disorganized axonal sprouting and may help to limit residual neuroma pain after surgery. The pSIS material used for the nerve cap has been used clinically for over 20 years in various indications. The pSIS material serves
as a biologic scaffold that revascularizes and remolds into a new permanent soft tissue layer, which may reduce neurotrophic signaling from the surrounding environment while also providing permanent protection of the nerve end from mechanical stimulation.

This nerve cap has been successfully used in both preclinical and clinical studies. In a preclinical study, the nerve cap exhibited less sensitivity to mechanical stimulation and reduced likelihood of a neuroma compared to an untreated nerve stump in a rat tibial nerve model up to 16 weeks postoperative. Furthermore, results of a recent clinical study that utilized the procedure described in this article showed that patients reported a significant reduction in pain as soon as 3 months postoperative, with a sustained reduction in pain throughout the 12-month follow-up. These studies indicated that with correct use, the nerve cap can be successfully used to reduce the likelihood of neuroma recurrence after excision and repair with a nerve cap.

Successful use of the nerve cap can be dependent on several factors including, proper hydration, using appropriate tools for microsurgery, care when suturing the nerve and the nerve cap, and ensuring the nerve and nerve cap are not under tension prior to closure. The handling of any extracellular matrix requires proper saturation to improve tissue handling with microsurgical instrumentation and microsurgical suture. The use of a suture as an epineurial anchor provides guidance for the entubulation of the nerve while in the intermetatarsal space. Furthermore, experience in microsurgical technique and microsurgical instrumentation is a prerequisite to doing these procedures. As the surgeon becomes more comfortable with the surgical technique and materials, the surgical exposure can be reduced to approximately 5 cm. The size of the surgical incision is highly dependent on ability to access the nerve. It is important to suture the nerve to the muscle belly without tension; therefore, additional neurolysis may be needed to free the nerve from surrounding soft tissue before securing the nerve in the muscle belly. This will allow the nerve to glide within the intermetatarsal space after wound closure. The foot can be flexed and extended to evaluate the tension on the nerve and nerve cap prior to closure.

**Conclusions**

In patients with painful Morton’s neuroma recalcitrant to conservative
treatment, surgery is an effective method for relieving pain. Isolating and protecting the distal nerve end after removal of the perineural fibroma in these patients may help prevent recurrent neuroma formation and the return of pain. In this example, the incisions were shifted medial or lateral to increase the dermal flap surface area between the incisions while ensuring the incisions could be used to access the deep tissues between the metatarsal heads (indicated by black asterisks).
6. Bhatia M, Thomson L. Morton’s neuroma—current concepts review. *J Clin Orthop Trauma*. 2020;11(5):406-409. doi:10.1016/j.jcot.2020.03.024.

7. Gougoulias N, Lampidis V, Sakellariou A. Morton’s interdigital neuroma: instructional review. *EFORT Open Rev*. 2019;4(1):14-24. doi:10.1080/2058-5241.2018.180025.

8. Valisena S, Petri GJ, Ferrero A. Treatment of Morton’s neuroma: a systematic review. *Foot Ankle Surg*. 2018;24(4):271-281. doi:10.1016/j.fas.2017.03.010.

9. Coughlin MJ, Pinsonneault T. Operative treatment of interdigital neuroma. A long-term follow-up study. *J Bone Joint Surg Am*. 2001;83(9):1321-1328.

10. Kasparek M, Schneider W. Surgical treatment of Morton’s neuroma: clinical results after open excision. *Int Orthop*. 2013;37(9):1857-1861. doi:10.1007/s00264-013-0302-6.

11. Bucknall V, Rutherford D, MacDonald D, Shalaby H, McKinley J, Breusch SJ. Outcomes following excision of Morton’s interdigital neuroma. *Bone Joint J*. 2016;98-B(10):1376-1381. doi:10.1302/0301-0302.98-B(10).20160301.0000000000000337.

12. Pace A, Scammell B, Dhar S. The outcome of Morton’s neuromectomies in the treatment of metatarsalgia. *Int Orthop*. 2010;34(4):511-515. doi:10.1007/s00264-009-0812-3.

13. Pet MA, Ko JH, Friedly JL, Smith DG. Traction neurectomy for treatment of painful residual limb neuroma in lower extremity amputees. *J Orthop Trauma*. 2015;29(9):e321. doi:10.1097/BOT.0000000000000357.

14. Lu C, Sun X, Wang C, Wang Y, Peng J. Mechanisms and treatment of painful neuromas. *Rev Neurosci*. 2018;29(5):557-566. doi:10.1515/reneuro-2017-0077.

15. Souza JM, Cheesborough JE, Ko JH, Cho MS, Kuiken TA, Dumanian GA. Targeted muscle reinnervation: a novel approach to postamputation neuroma pain. *Clin Orthop*. 2014;472(10):2984-2990. doi:10.1007/s11999-014-3528-7.

16. Pet MA, Ko JH, Friedly JL, Mourad PD, Smith DG. Does targeted nerve implantation reduce neuroma pain in amputees? *Clin Orthop*. 2014;472(10):2991-3001.

17. Mass DP, Ciano MC, Tortosa R, Newmeyer WL, Kögore ES. Treatment of painful hand neuromas by their transfer into bone. *Plast Reconstr Surg*. 1984;74(2):182-185. doi:10.1097/00006534-198408000-00002.

18. Delmol AL, Mackinnon SE. Treatment of the painful neuroma by neuroma resection and muscle implantation. *Plast Reconstr Surg*. 1986;77(3):427-438. doi:10.1097/00006534-198605000-00016.

19. Koch H, Haas F, Hubmer M, Rapp T, Schraml E. Treatment of painful neuroma by resection and nerve stump transplantation into a vein. *Ann Plast Surg*. 2003;51(1):45-50. doi:10.1097/01. SAP.0000054187.72439.57.

20. Galcano M, Manasesti B, Risitano G, et al. A free vein graft cap influences neuroma formation after nerve transection. *Microsurgery*. 2009;29(7):568-572. doi:10.1002/micr.20652.

21. Rungprai C, Cychosz CC, Phruetthiphat O, Femino JE, Amendola A, Phisitkul P. Simple neurectomy versus neuromectomy with intramuscular implantation for interdigital neuroma: a comparative study. *Foot Ankle Int*. 2015;36(12):1412-1424. doi:10.1177/1071100715596741.

22. Stokvis A, van der Avoort DJJC, van Neck JW, Hovius SER, Goet HJ. Surgical management of neuroma pain: a prospective follow-up study. *Pain*. 2010;151(3):862-869. doi:10.1016/j.pain.2010.09.032.

23. Tupper JW, Booth DM. Treatment of painful neuromas of sensory nerves in the hand: a comparison of traditional and newer methods. *J Hand Surg*. 1976;1(2):144-151.

24. Wu J, Chiu DT. Painful neuromas: a review of treatment modalities. *Ann Plast Surg*. 1999;43(6):661-667.

25. Tork S, Faleris J, Engernann A, Deister C, DeVinney E, Valerio IL. Application of a porcine small intestinal submucosa nerve cap for prevention of neuromas and associated pain. *Tissue Eng Part A*. 2020;269-10(5):503-511. doi:10.1089/ten.TEA.2019.0273.

26. Pereira R, Dauphinée D, Frania S, et al. Clinical evaluation of an innovative nerve termination cap for treatment and prevention of stump neuroma pain: results from a prospective pilot clinical study. *Foot Ankle Tech Rep Cases*. 2022;2(2):100179. doi:10.1016/j.fastc.2022.100179.

27. Cook WA, Hiles MC, Kozma TG, Patel UH. Cook Biotech, Inc. (West Lafayette, IN), MED Institute Inc. (West Lafayette, IN). https://www.cookbiotech.com/. Published online 2001. Accessed February 6, 2021.

28. D’Eredita R. Porcine small intestinal submucosa (SIS) myringoplasty in children: a randomized controlled study. *Int J Pediatr Otorhinolaryngol*. 2015;79(7):1085-1089. doi:10.1016/j.ijporl.2015.04.037.

29. Guest JF, Weidlich D, Singh H, et al. Cost-effectiveness of using adjunctive porcine small intestine submucosa tri-layer matrix compared with standard care in managing diabetic foot ulcers in the US. *J Wound Care*. 2017;26(suppl 1):S12-S24. doi:10.12968/jowc.2017.26.Sup1.S12.

30. Mosala Nezhad Z, Poncelet A, de Kerchove L, Gianello P, Fervaille C, El Khoury G. Small intestinal submucosa extracellular matrix (CorMatrix®) in cardiovascular surgery: a systematic review. *Interact Cardiovasc Thorac Surg*. 2016;22(6):839-850. doi:10.1093/icvts/ivw020.

31. Iannotti JP, Codsi MJ, Kwon YW, Derwin K, Ciccone J, Brems JJ. Porcine small intestine submucosa augmentation of surgical repair of chronic two-tendon rotator cuff tears. A randomized, controlled trial. *J Bone Joint Surg Am*. 2006;88(6):1238-1244. doi:10.2106/JBJS.E.00524.

32. Neumayer L, Giobbe-Hurder A, Jonasson O, et al. Open mesh versus laparoscopic mesh repair of inguinal hernia. *N Engl J Med*. 2004;350(18):1819-1827. doi:10.1056/NEJMoa040093.

33. Kokkalis ZT, Pu C, Small GA, Weiser RW, Venouziou AI, Sotereanos DG. Assessment of processed porcine extracellular matrix as a protective barrier in a rabbit nerve wrap model. *J Reconstr Microsurg*. 2011;27(1):19-28. doi:10.1055/s-0030-1267379.