Recurrent Intermetatarsal Neuroma
A Follow-up Study

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Sixteen patients were evaluated following excision of recurrent intermetatarsal neuroma. Each underwent removal of a segment of nerve through an incision on the plantar aspect. The nerve stump was buried in the flexor digitorum brevis muscle. At the time of follow-up examinations, six patients were asymptomatic, seven experienced mild pain after extended activity, one suffered mild consistent pain with activity, and two suffered pain that limited activities.

Excision of an intermetatarsal neuroma that has failed to respond to conservative care has been an accepted technique commonly used for years. In most instances, the removal of the offending portion of nerve has resulted in satisfactory improvement of symptoms. However, the failure rate of this type of procedure is higher than initially suspected, ranging from 3% to 24% with most studies citing failure rates at the higher end of these values.[1-10]

One of the complications that may be experienced following removal of an intermetatarsal neuroma is that of the recurrent or "stump" neuroma. Bradley et al[1] found five recurrent neuromas in 85 patients (6%) , while Mann and Reynolds[3] found 11 recurrent lesions in 76 sites where previous surgery had been performed (14%).

Historically, it has been the anecdotal experience of surgeons at the authors' institution that the simple excision of the recurrent neuroma often did not suitably alleviate symptoms. This led to the search for a better way to approach the problem.

For the past several years, the authors have used a technique for the surgical treatment of recurrent intermetatarsal neuroma similar to that previously described by Dellon[11] and DiNapoli[12]. A follow-up study has been undertaken to evaluate the results of this procedure in patients treated at the authors' institution.

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Normal Response to Axotomy

A brief review of the physiologic response that follows nerve transection will justify the approach selected by the authors. By understanding this process, the surgeon may have a greater appreciation of the difficulty that may be encountered in attempting to alleviate the painful stump or recurrent neuroma.

Following transection of the axons, the nerve cell body within the dorsal root ganglion, or anterior horn, will respond by metabolizing the products required to reconstruct the cytoskeleton of the damaged nerve. These substances are delivered to the injury site by axoplasmic transport.[13-15]

Wallerian degeneration occurs in both the proximal and distal nerve segments. In the proximal portion of the nerve, the length of degeneration is variable and corresponds with the severity of injury. The proximal nerve segment will then develop regenerating fibers that contain numerous axon sprouts. These budding axons will attempt to bridge the gap between the nerve ends. Distally, the nerve undergoes wallerian degeneration to a greater extent.[14] The Schwann's cell will phagocytose the inner myelin and axon debris, leaving columns of collapsed Schwann's cells or empty endoneurial tubes.

The axon fibers that regenerate from the proximal nerve segment will seek these empty endoneurial tubes. If these proximal nerve fibers make

the appropriate sensory or motor connection distally, then function of the nerve may be maintained. Loss of function will occur if these regenerating axons do not connect with similar fibers distally or if the axons become lost in the peripheral environment. In the latter instance, a neuroma will form. This represents the inevitable consequence of complete nerve division and failed repair.[14-17]

There are two theories as to how the proximal axon sprouts find the more distal endoneurial tubes. One concept, termed neurotropism, proposes that chemical agents from the distal segment attract the regenerating axons and encourage growth across small gaps.[14, 16] After axotomy, and during wallerian degeneration, the distal Schwann's cells show an increased expression of nerve growth factor. The distal nerve receptors decrease when axonal contact is restored to the distal nerve segment.[15, 18, 19] Furthermore, there is a high degree of specificity associated with neurotropism. Nerve tissues that are regenerating can discriminate between nerve and tendon (tissue specificity), sensory and motor nerves (end-organ specificity), and posterior and peroneal nerve distally (fascicular specificity).[14, 16]

Contact guidance is another theory used to explain nerve regeneration across a gap. Regeneration is said to be influenced by the surrounding substrate of the sprouting axon as opposed to chemical substances released distally. Contact guidance is important as axons have been found to elongate and orient themselves along a linear fibrin matrix more effectively than in a random fibrin matrix. Therefore, both neurotropism and contact guidance influence the overall regenerative and repair process.[14, 16]

As mentioned earlier, stump neuroma formation is the predictable outcome of nerve transection and failed repair. Therefore, a stump neuroma cannot be prevented without destroying the nerve cell itself.[14, 16, 17] However, simply because a stump neuroma forms does not imply that it is a painful condition. Histologically, there is no difference between a painful and an asymptomatic stump neuroma.[16, 17]

The classic histologic appearance of a stump neuroma is a "massive swirling of disorganized axonal sprouts, regenerating neural units, embedded in dense collagen scar."[16, 17, 20] When the endoneurium is disrupted, regenerating axons grow into the surrounding connective tissue in a disorganized fashion forming "whorls" in an attempt to reach the distal segment.[21] Collagen-producing fibroblasts form scar tissue that blocks penetration of the axons toward the distal target. Myofibroblasts have been found in this reactive tissue.[16, 21] Myofibroblasts may cause the scar component of the neuroma to contract, thereby creating pain.[21] It has also been proposed that the neurons within the stump possess the potential to independently produce painful impulses.[16, 17]

Treatment of Painful Stump Neuromas

Several techniques have been described to treat painful stump neuromas. Obviously, preventing this condition would be preferred. Studies in primates have shown that following resection of a segment of nerve, the axons subsequently regenerated into the overlying skin. When the nerve end was located proximally and away from the incision, the nerve stump still formed but failed to adhere to the skin.[17, 20]

In most instances, surgeons place gentle traction on the nerve prior to transection, anticipating that the proximal severed portion of the nerve will retract into a more protected area away from scar tissue and painful stimuli. However, two studies have shown that this may not occur as anticipated following the resection of an interdigital neuroma. Anatomical dissections have shown that the intermetatarsal nerves may be tethered by multiple small branches that actually prevent this proximal retraction once the nerve is severed.[22, 23]

Other methods have been used in the attempt to control stump neuroma formation. From a conservative standpoint, this may consist of desensitization procedures or repeated nerve stimulation in the form of local percussion, massage, ultrasound, and electrical stimulation.[21, 24] The treatment time is usually protracted and the results inconsistent.[21] Local infiltration of steroids may also be used.[21, 24-26] The potential success of steroids may be related to softening of the scar around the neuroma or stabilizing the cell membrane and reducing action potentials, thus suppressing neural discharge.[21, 25] However, in most situations, these measures are not typically used until there appears to be a problem postoperatively.

Surgical treatment may be categorized into two major areas: attempts to inhibit axonal growth or translocation of the nerve away from noxious stimuli. Physical measures that have been used to help contain nerve growth include crushing, freezing, cauterization, and electrocoagulation of the proximal nerve segment.[17, 21, 27] In dog models, these methods have been successful in reducing the size of the neuroma formation, but not in prevention of this process.[21, 28]

Chemical agents have been used to sclerose the end of the nerve including alcohol, tannic acid, formaldehyde, chromic acid, uranium nitrate, gentian violet, phenol, iodine, mercuric chloride, picric acid, hydrochloride, and nitrogen mustard.[14, 17, 21, 29, 30] None of these measures has shown any significant value in preventing neuroma formation because of the inability of these agents to completely seal the end to the nerve. Furthermore, these methods may stimulate scar formation in the surrounding tissues.[21, 27]

Pulling the epineurium over the end of the nerve and suturing it closed (funiculectomy or epineuriplasty) has also been described.[14, 16, 21, 24, 30-33] The purpose of this technique is to attempt to prevent axonal escape. One study showed an 81% excellent or satisfactory result.[32] However, the results were no better that simple excisional neurectomy alone.[21, 33] Fibrin glue has also been used in conjunction with epineuriplasty to enhance the seal at the nerve end.[30] Synthetic materials have also been used to "cap" the nerve end and include methyl methacrylate in acetate, collodium, glass, tin, tantalum, silver, gold, foils, and cellophane.[16, 21, 24, 27] Fascia, placental tissue, bone, and arterial walls are examples of nonsynthetic materials that have been used in the same manner.[21]

Although translocating the nerve end to a relatively undisturbed area may prevent adherence to local skin, it will not alter the formation of the nerve stump.[17, 20] From a histologic standpoint, the only method that has been shown to make a distinct difference in the formation of the neuroma has been the implantation of the nerve end into muscle. Nerve ends implanted into muscle were found to have less connective tissue and to show no evidence of invasion or regeneration into surrounding structures. A distinct interface developed between the nerve and the surrounding muscle. The nerve fibers were all oriented in the same direction, as opposed to a disorganized mass of tissue typically seen in stump neuromas. Furthermore, there were no myofibroblasts seen in these stumps and the perineurium appeared to be reconstituted over the end of the nerve.[17, 20, 34] Clinical reports using this technique have been favorable.[35]

It has been the anecdotal experience of surgeons at the authors' institution that simple nerve excision in the treatment of recurrent intermetatarsal or stump neuromas has failed to a large degree. This would include attempts to resect additional nerve from both a dorsal and plantar incisional approach. Furthermore, attempts to seal the nerve end with fibrin glue or epineuriplasty as individual procedures, or in conjunction, have provided inconsistent relief of pain.

Based on the research previously discussed, it would appear from a scientific standpoint that implantation of the nerve end into muscle would be a reasonable option. Therefore, some surgeons for the past several years have used a technique whereby the newly resected proximal nerve stump is embedded in the muscle belly of the flexor digitorum brevis. The methods used and the results achieved are described herein.

Surgical Technique

A plantar incisional approach is required to gain complete visualization of the nerve stump and to provide access for the repair techniques. The authors prefer a slight S- or Z-shaped incision to reduce the tendency for hypertrophic scar formation.[36, 37] As the incision is directed proximally, it is also angled slightly medialward, paralleling the course of the medial plantar nerve branches. An ankle tourniquet is typically used for hemostasis.

When evaluating the patient prior to surgery, the trigger point is invariably located just proximal to the third and fourth metatarsal heads. Extensive visualization of tissues distal to this level is not required. Therefore, there is no reason to routinely extend the incision directly beneath the metatarsal heads. This will preserve the fat padding at this primary weightbearing portion of the forefoot and tend to reduce the risk of postoperative metatarsalgia.

Dissection may be facilitated by beginning at the proximal end of the incision. At this level, there is a thin, subcutaneous layer immediately overlying the plantar fascia. Further distal, the plantar fascia begins to split into multiple digitations making identification of the tissue layers more difficult in the initial phase of dissection. Once the plantar fascia is identified proximally, this layer may be followed distally and maintain the integrity of the tissue planes.

When dissecting through the superficial fascia, occasionally the nerve stump will be lying as an easily identifiable mass adjacent to the metatarsophalangeal capsule or flexor plate. In other cases, the nerve stump will be difficult to distinguish from the surrounding tissues. In the latter instance, the easiest way to find the nerve stump is to linearly incise the plantar fascia and then gently separate the fascia from the underlying flexor digitorum brevis muscle. The branches of the medial plantar nerve are then easily visualized. The nerve may then be traced distally until the stump is evi-

dent. At this stage, further dissection is performed with the use of loupe magnification.

Once identified, the stump and the proximal trunk of the nerve are gently separated from the surrounding tissue. Occasionally, a separate branch may be found leading to the second intermetatarsal space. Dissection is continued proximally until past the primary weightbearing area of the forefoot. In most instances, this is still distal to any adjacent large branches of the medial plantar nerve.

Using loupe or microscopic magnification, the epineurium is incised circumferentially about the nerve. This tissue is then gently peeled proximally for several millimeters until there is enough tissue to cover the nerve end once it is transected. The epineurium is then tagged at two or three points with 8-0 nylon or polypropylene suture. A needle will need to be left attached to one of the suture ends. Tension is then placed on the distal portion of the nerve end and the nerve trunk is sharply transected where the epineurium has been reflected. The suture tags are then tied together to provide an epineural covering over the end of the nerve.

The flexor digitorum brevis muscle belly is readily accessible as the nerve branches lie on the more plantar aspect of this structure. A blunt separation is made into the deeper fibers of the muscle through which the suture, needle, and nerve are guided. The suture is then tied into the muscle fibers to secure the nerve end so that it remains embedded in the flexor muscle. The nerve should not be placed under any tension when the foot and digits are dorsiflexed.

The plantar fascia is then reapproximated with 3-0 absorbable suture, the subcutaneous tissue with 4-0 absorbable suture, and the skin with 4-0 nylon or polypropylene suture. A compression dressing is applied and the patient does not walk for 4 weeks. Sutures are then removed and weightbearing is initiated.

Modifications

Modifications have been used for some patients. One of the authors has used a buried angiocatheter in the plantar aspect of foot for the first 1 or 2 days postoperatively. This allows the local anesthetic to infiltrate into the area and enhances postoperative analgesia. This has been used primarily in patients with chronic pain syndromes to reduce the need for narcotic medications. However, this is not a routine measure as most individuals have experienced little postoperative pain.

The use of a suture to anchor the nerve end into the muscle was not used consistently in the first few patients in this series. However, it is part of the standard procedure at this time. It was believed that anchoring the nerve into muscle provided a more reliable repair with less tendency for the stump to be dislodged. In fact, studies by Dellon et al[34] have shown that nerve implanted into muscle does not develop a strong adhesion, and therefore, may be pulled free fairly easily.

In several patients, a tissue glue was introduced into the epineural cuff prior to suturing the epineurium over the tip of the nerve. This tissue glue was compounded from a mixture of calcium chloride, thrombin, and cryoprecipitate.[30] It was believed that this would provide a mechanical barrier to the any potential sprouting axons that might regenerate. Although no specifics can be derived from this study, in a limited number of cases using this technique for nerve surgery in other anatomical areas, subsequent reexploration of the wound revealed that the axons had been able to penetrate through the tissue and glue barrier and the epineural cuff.

Results

Sixteen patients who had undergone resection of recurrent intermetatarsal neuroma using the described technique were available for follow-up clinical or telephone evaluation. The time elapsed since surgery ranged from 6 to 27 months, with an average of 12.6 months. The patients were asked to rate their pain preoperatively and postoperatively using the scale provided in Table 1. Prior to revisional surgery, all patients possessed symptoms that limited activities (average pain rating, 3.7). Following surgery, the pain rating was significantly reduced for most individuals (average pain rating, 0.9; standard deviation, 1.0). However, two patients continued to experience symptoms that limited their activities.

One patient who rated her preoperative and postoperative pain level at 3 (pain that limits some ac-

Table 1. Patients' Assessment of Pain

Scale	Pain	
	Pre-operative	Post-operative
0 = No pain	0	6
1 = Mild pain after extended activity	0	7
2 = Tolerable pain, yet present with most activity	0	1
3 = Pain that limits some activities	5	2
4 = Pain that limits most activities	11	0
Average rating	3.7	0.9

tivity) was available for clinical evaluation. Distinct pain was noted with palpation at the surgical site close to where the nerve stump was located. The findings were identical to those seen prior to the revisional surgery with the exception of the location of the trigger point. In this individual, the nerve stump was implanted into muscle but was not anchored with the suture into the flexor digitorum brevis. Therefore, it is postulated that the nerve end may have retracted into the subcutaneous tissue.

The other patient who rated both preoperative and postoperative pain levels at 3 possessed a thick, deep hyperkeratosis underneath the third and fourth metatarsal heads. This lesion had been previously excised and treated using different modalities without resolution. At some point in her treatment process, a neuroma was excised from the third interspace. Therefore, there was some question as to the degree of symptoms attributable to potential nerve entrapment *versus* the extremely thick hyperkeratotic scar. After revisional surgery, she related that her symptoms were basically unchanged. Local debridement of the hyperkeratosis provided brief, partial relief.

Two patients showed a transient metatarsalgia postoperatively once they were allowed to begin weightbearing. Symptoms appeared to be derived from the third or fourth metatarsophalangeal joints. In one instance, this complaint resolved using a combination of conservative modalities. In another, mild symptoms at the third metatarsophalangeal joint persisted. However, this patient also had a dorsal nerve entrapment in the original dorsal surgical incision. This dorsal entrapment was not a primary complaint prior to the revisional surgery, but may help to account for some degree of the persistent symptoms.

Two patients developed wound dehiscence that later healed uneventfully. In both instances, during the initial postoperative phase, dexamethasone and a local anesthetic had been infiltrated through an angiocatheter inserted at the time of the surgery. This postoperative use of dexamethasone has since been discontinued.

Discussion

Achieving successful resolution of symptoms following recurrent interdigital neuroma has at times been difficult (Table 2). Bradley et al[1] noted that of the five patients who underwent revisional surgery, only one sustained a satisfactory result. Using a dorsal incision, Mann and Reynolds[3] noted significant improvement in nine of 11 patients.

Nelms et al[38] reported on 27 patients undergoing surgery for recurrent Morton's neuroma. The surgical approach consisted of a longitudinal incision on the plantar aspect to identify the nerve and an incision on the dorsal aspect to achieve access to the third metatarsal. A hole was then created in the metatarsal through which the nerve stump was anchored with 4-0 nylon suture from plantar to dorsal. The investigators reported 11 excellent results, 13 good results, and three poor results. The three patients who sustained poor results had undergone previous metatarsal osteotomies and explorations of the adjacent interspace prior to the nerve transposition.

Beskin and Baxter[39] described their results with 39 recurrent intermetatarsal neuromas. Although a dorsal longitudinal incision was used for several patients, these authors preferred a plantar transverse approach just proximal to the metatarsal heads. They believed that the plantar incision provided easier and more consistent identification of the nerve and reduced the traumatic dissection and retraction of muscle. Significant improvement was noted in approximately 80% of the cases. The remaining patients noted moderate limitations of activity because of their pain. Furthermore, 58% of the patients noted residual symptoms of a lesser degree in certain shoes.

Johnson et al[40] described using a longitudinal plantar incision for 33 of the 37 recurrent lesions in their series. A dorsal longitudinal incision was used in the other four cases. These authors described findings that were believed to be representative of residual or incomplete excision of the original neuroma in 67% of the feet. Twenty-two patients noted complete or marked improvement (67%), three patients were improved but noted persistent pain (9%), and eight patients noted no improvement or exacerbation of symptoms (24%).

Dellon[11] reported on a case where a young runner underwent revisional surgery using a plantar surgical approach whereby the nerve end was implanted into the flexor digitorum brevis muscle. The epineurium was anchored into the muscle with 6-0 nylon. Complete relief and return to function were noted.[11]

DiNapoli[12] described his experience with the surgical treatment of recurrent intermetatarsal neuroma in 13 patients. Each was evaluated from 7 to 26 months postoperatively. The repair in one of these patients consisted of a plantar Z- or S-type of incision. In the remaining patients, a dorsal longitudinal incision was used. In two patients, the nerve was simply transected and allowed to re-

Table 2. Previous Surgical Treatments of Intermetatarsal Neuroma

Author	Patients	Incision Choice	Nerve Technique	Satisfactory Results
Bradley et al[1]	5	Dorsal longitudinal	Transection	1
Mann and Reynolds[3]	11	Dorsal longitudinal	Transection	9
Nelms et al[38]	27	Longitudinal on the plantar aspect	Osseous implantation	24
Beskin and Baxter[39]	14	Dorsal longitudinal	Transection	8
	24	Transverse on the plantar aspect	Transection	17
Johnson et al[40]	4	Dorsal longitudinal	Transection	4
	32	Longitudinal on the plantar aspect	Transection	21
Dellon[11]	1	Longitudinal on the plantar aspect	Muscle implantation	1
DiNapoli[12]	2	Dorsal longitudinal	Transection	2
	9	Z- or S-type on the plantar aspect	Epineuriplasty or muscle implantation	8

tract. Both patients had resolution of symptoms. In nine patients, the neuroma was excised and the epineurium was sutured over the nerve end and embedded into the musculature on the plantar aspect. Eight of these nine patients had resolution of symptoms with the other patient suffering not only a recurrence, but the development of reflex sympathetic dystrophy. One patient developed a recurrence of a painful plantar hyperkeratosis that was present previously. Another patient developed several small punctate lesions along the scar, but was asymptomatic.[12]

Prior to using the technique described, the authors and several colleagues treated a number of patients with this condition. In these initial cases, nerve resection was performed without implantation of the stump into muscle tissue. Although no formal follow-up study was performed, the experience seemed to indicate that the results were poor.

It would appear that the technique used in this series of patients is fairly reliable, but poor results were still encountered with some patients. Although it would appear that performing the epineuriplasty would not be required, if the suture is maintained after the epineurium is closed, then the nerve may be easily anchored into the flexor muscle. However, this is certainly not the only means of accomplishing the task.

The use of an incision on the plantar aspect did not create any painful or hypertrophic scars in this patient series. This has also been the experience of other surgeons who have used different incisional approaches on the plantar aspect for this problem.[12, 38-40]

As noted earlier, the success of interdigital neuroma excision is typically reported to be approximately 80%. However, it should be noted that this does not mean that all of the patients rated as sustaining successful results were completely free of symptoms. For many patients, the symptoms may be improved as opposed to resolved. In three studies that used the same criteria for rating success of the procedure, a subjective improvement of only 50% or better was sufficient criterion for a successful result (Table 3).[3, 6, 7]

Is it possible that the incidence of stump neuroma, or at least stump sensitivity, is understated, or could it be that other pathologies may have been present concomitantly, yet not addressed with removal of the nerve? In any event, the surgeon may need to reconsider the significance of what many may believe to be a rather benign procedure.

The authors must also mention the inaccurate nomenclature used to describe the intermetatarsal, or Morton's neuroma. This condition is not actually a neuroma, but a painful neuropathy most likely caused by local entrapment as a result of compressive forces.[41] The painful stump developing after the removal of the symptomatic intermetatarsal

Table 3. Comparative Studies of Intermetatarsal Neuroma Surgery

	Gaynor et al[7] 1989 35 patients (%)	Gudas and Mattana[6] 1986 206 patients (%)	Mann and Reynolds[3] 1983 65 patients (%)
Successful (75% to 100% improved)	80	42	71
Good (50% to 75% improved)	2.8	37	9
Fair (25% to 50% improved)	8.6	13	6
Poor (< 25% improved)	8.6	8	14

nerve is a true neuroma. However, it is customary for authors and surgeons to refer to the former entrapment neuropathy as Morton's neuroma, or intermetatarsal neuroma. The authors have retained this terminology simply to remain consistent with the language used by most individuals treating foot and ankle conditions.

Conclusion

Although the authors believe that the technique described for the surgical management of recurrent intermetatarsal neuroma is an improvement over simple nerve excision, it is not fail-safe. The additional experiences of other authors in treating this complication show the frustrations of both the patient and surgeon. However, muscle implantation of the nerve stump appears to be based on sound scientific principles and would merit consideration in the treatment of this and other types of recurrent nerve problems.

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ERRATUM

The name of Patricia M. Schultz, DPM, was omitted from the list of authors in "Magnetic Resonance Imaging of the Foot: Rheumatologic Disorders Mimicking Osteomyelitis," p 228, May 1996 JAPMA. The authors regret the error.