Treatment of Morton's Neuroma with Alcohol Injection Under Sonographic Guidance: Follow-Up of 101 Cases

Richard J. Hughes[1]
Kaline Ali[1]
Hugh Jones[2]
Sue Kendall[3]
David A. Connell[1]

OBJECTIVE. Morton's neuroma is a common cause of forefoot pain. For this study, we assessed the efficacy of a series of sonographically guided alcohol injections into the lesion.

SUBJECTS AND METHODS. One hundred one consecutive patients with Morton's neuroma were included in this prospective series. An average of 4.1 treatments per person were administered, and follow-up images were obtained at a mean of 21.1 months after the last treatment (range, 13–34 months).

RESULTS. Technical success was 100%. Partial or total symptom improvement was reported by 94% of the patients, with 84% becoming totally pain-free. The median visual assessed pain score decreased from 8 before treatment to 0 after treatment ($p < 0.001$). Transitory increased local pain occurred in 17 cases (16.8%). There were no major complications. Thirty patients underwent sonography at 6 months after the last injection and showed a 30% decrease in the size of the neuroma.

CONCLUSION. We conclude that alcohol injection of Morton's neuroma has a high success rate and is well tolerated. The results are at least comparable to surgery, but alcohol injection is associated with less morbidity and surgical management may be reserved for nonresponders.

Keywords: ablation, alcohol injection, foot, Morton's neuroma, musculoskeletal imaging, sonographic guidance

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[1]Department of Radiology, Royal National Orthopaedic Hospital and Kingston Hospital NHS Trust, Brockley Hill, Stanmore, Middlesex HA7 4LP, United Kingdom. Address correspondence to D. Connell.

[2]Department of Rheumatology, Royal National Orthopaedic Hospital and Kingston Hospital NHS Trust, Middlesex, United Kingdom.

[3]Department of Orthopaedic Surgery, Royal National Orthopaedic Hospital and Kingston Hospital NHS Trust, Middlesex, United Kingdom.

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Plantar interdigital neuroma of the foot, or "Morton's neuroma," has been described since the mid-19th century and is a common cause of forefoot pain and paraesthesia [1, 2]. The condition is believed to be an entrapment neuropathy secondary to compression of the common interdigital nerve under the overlying transverse metatarsal ligament. Histologically, the condition is not a true neuroma and is characterized by perineural fibrosis, endoneurial edema, axonal degeneration, and local vascular proliferation [3–6]. The most common affected site is between the third and fourth interspace.

The diagnosis of Morton's neuroma is suggested clinically by pain and paraesthesia radiating from the midfoot to the toes. Clinical examination with medial and lateral compression may reproduce symptoms and a palpable "click" on interspace compression (Mulder sign) [7]. Sonography is sensitive and specific in confirming the diagnosis of Morton's neuroma, with a 95–98% accuracy having been reported in many studies [8, 9]. Neuromas are usually readily identifiable as a hypoechoic mass in the interspace. Also, contrast-enhanced MRI has been shown to be highly accurate [10] in confirming the diagnosis. Of interest, MRI features diagnostic of Morton's neuroma have been described incidentally in 33% of asymptomatic individuals [11].

At our institution, sonography is the mainstay of diagnosis because it is readily available, quick, and noninvasive. Injection therapy can also be considered at the same visit if indicated when sonography is used as the first-line diagnostic technique. Sonography guidance is important to accurately inject the lesion and prevent extravasation of alcohol into the soft tissues to minimize local pain and soft-tissue reaction.

We assessed a prospective series of patients with Morton's neuroma undergoing alcohol injection for safety, tolerance, and outcome.

Subjects and Methods

One hundred forty-one consecutive patients with a clinical and sonographic diagnosis of Morton's neuroma were enrolled in the study between August 2004 and August 2005 after undergoing clinical assessment by a foot and ankle surgeon, rheumatologist, or general practitioner with a special interest in foot disorders. Forty patients were excluded because they had two lesions in the same foot ($n = 32$), metatarsophalangeal joint synovitis ($n = 6$), a stress fracture ($n = 1$), or rheumatoid arthritis ($n = 1$). Multiple

Fig. 1—Photograph shows scanning position for percutaneous access to neuroma with ultrasound probe directed perpendicular to long axis of metatarsals.

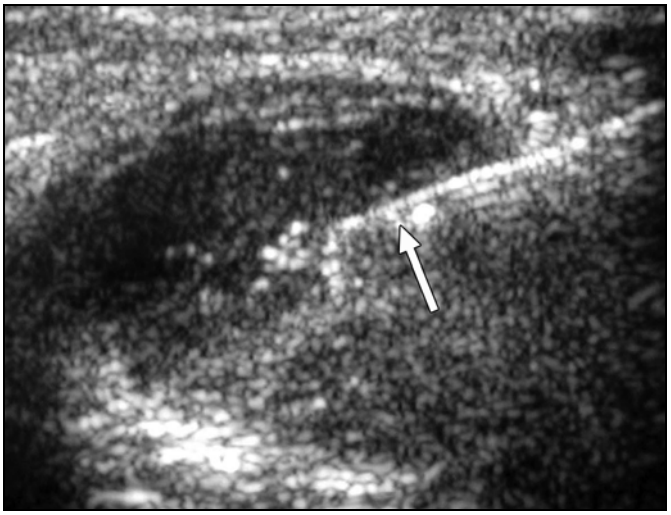

Fig. 2—46-year-old woman with Morton's neuroma. Sonogram shows that needle tip is within hypoechoic mass of neuroma (*arrow*).

lesions in the same foot were initially treated surgically in our local practice at the time of the study, hence their exclusion from this series. This left 101 patients in the study group. These 101 cases comprised 84 women and 17 men whose mean age was 53.8 years, with an age range of 30–74 years.

All patients were assessed for the clinical symptoms of a neuroma and also for other causes of forefoot pain, such as mechanical metatarsalgia. The mean duration of symptoms was 20.8 months with a range of 4–48 months. The diagnosis of Morton's neuroma had been made clinically and had been confirmed on sonography in all cases. No patients had undergone MRI because only patients with a firm sonographic diagnosis of Morton's neuroma were included and we reserve MRI for equivocal cases in our practice. Only symptomatic neuromas were treated.

At sonography, the size of the lesion was measured. The lesions ranged in size from 7 to 20 mm, with a mean of 11 mm. Of the 101 lesions, 59 were at the third–fourth interspace, 39 at the second–third interspace, and two at the fourth–fifth interspace. A comprehensive sonography examination was performed to exclude bursitis, synovitis, and tendon sheath abnormalities.

Local review board approval was obtained for this study before commencement. Informed consent was obtained from all patients before they were treated, and all were warned of the risk of some transient increased pain. Sonography was used to guide injection placement. With the patient supine and knee flexed at 45°, a high-frequency linear array ultrasound transducer was orientated longitudinally to the long axis of the metatarsals on the dorsum of the foot and the hypoechoic mass of the Morton's neuroma was identified (Fig. 1).

Under direct sonographic control, the tip of a 23-gauge needle was positioned in the center of the mass (Fig. 2). A solution of 0.1 mL of 100% ethyl alcohol diluted in 0.4 mL of 0.25% bupivacaine (total = 0.5 mL of 20% ethyl alcohol) was slowly injected while scanning in real time with stable needle position to assess for leak of injectate outside the Morton's neuroma. Fluid was observed spreading within the lesion on sonography, and no leaks were directly visualized. Each patient was observed in the department for 15 minutes before gentle mobilization and was allowed to return to full activity the next day.

The injections were repeated at 14-day intervals on four occasions, and additional injections were performed if there was partial but incomplete response based on patient-assessed level of pain at further 14-day intervals.

Patients were sent a questionnaire and followed up by telephone in March 2006. One hundred patients were contacted, but one patient could not be contacted. Follow-up ranged from 7 to 19 months (mean, 10.5 months) after the last injection.

Patients were asked to grade their pain on an outcome scale and a visual analogue scale (VAS) and on a modified scale from Johnson et al. [12] (Table 1). Pain associated with treatment was also scored on a VAS. Comparison was made between the preprocedure VAS score, taken before the first injection, and the postprocedure VAS score, taken at follow-up after the final injection. The normality of the difference between the pre- and postprocedural VAS scores was assessed using the Kolmogorov-Smirnov test. Because the data did not follow a normal distribution, the Wilcoxon's signed rank test was used to analyze the data. All statistical analysis was performed using SPSS software (version 14.0, SPSS) for Microsoft Windows, and p values of less than 0.05 were considered statistically significant.

TABLE 1: Questionnaire That 100 Patients[a] Received 7–19 Months After the Final Alcohol Injection for Treatment of Morton's Neuroma

Questions	No. of Patients
Which of the following best describes your outcome:	
I am essentially pain free; I can wear almost any shoes and do any activities I like.	84
I have mild/moderate pain with moderate restrictions to my footwear and activities.	8
The injections have made no difference to my pain or made it worse; I have major restrictions with my footwear and activities.	8
Which of the following best describes your outcome:[b]	
Completely satisfied	62
Satisfied with a few reservations	24
Satisfied with some major reservations	5
Dissatisfied	3
I wish I had never had injections	6

[a]One patient could not be contacted.
[b]Modified from Johnson et al. [12].

A subset of 41 patients were invited to undergo follow-up sonography and clinical assessment. Thirty responded and this follow-up was performed at 6 months after the last injection.

Results

One hundred one patients were treated in the study with a total of 408 injections. A mean of 4.1 injections per patient were performed (range, 3–6). Technical success was achieved in all cases (100%). Seventeen patients (16.8%) reported a plantar pain that settled after 2 days–3 weeks (mean, 4.5 days). In one such case, postprocedural MRI showed intense mid- and forefoot marrow edema that clinically and radiologically was presumed secondary to complex regional pain syndrome. This spontaneously settled after 3 weeks. Most cases of plantar pain were presumed to be due to an inflammatory reaction secondary to perilesional leakage of sclerosant. There were no other procedural complications or reactions.

The median (interquartile range) VAS score preprocedure was 8 (7, 8) with a range of 6–10 and had decreased to zero (0–1) after the procedure at follow-up with a range of 0–10. Statistical analysis found the difference to be significant ($z = 8.483$, $p < 0.001$).

Pain related to treatment was rated on a VAS as 3.9 on average with a range of 1–10.

At follow-up, 100 patients were given a questionnaire composed of two scales on which to rate their response to the injection treatments. The results are shown in Table 1.

Three patients who still had forefoot pain proceeded to surgery; we assumed that injection treatment had failed in these cases. All neuromas were surgically excised through a dorsal approach with division of the intermetatarsal ligament. In all cases, surgery was technically demanding because of the degree of fibrosis present. Macroscopically, the neuromas and proximal extensions appeared fibrotic as did the neurovascular bundles in one case.

During the treatment course, an alteration in the echotexture of the lesions was observed: progressive central hyperechogenicity. We thought that this change represented evolving intraneural fibrosis. At the sonography follow-up of 30 patients, the mean decrease in lesion size compared with pretreatment lesion size was 30% and the mean lesion diameter in these patients was 10 mm (range, 7–15 mm) before intervention and was 7 mm (range, 5–11 mm) at follow-up.

Discussion

The natural history of Morton's neuroma has not been well described. To our knowledge, there are no randomized controlled trials regarding treatment, and historically treatment has tended to be surgical with excision of the neuroma and perineural fibrosis. Gradated treatment regimes have been proposed with conservative management, corticosteroid injections, and surgical resection [13].

Conservative measures to treat Morton's neuroma include the use of metatarsal pads and orthotic devices. Bennett et al. [13] reported that 41% of the cases treated in their study improved with these measures alone.

Injection of local anesthetic and steroid into symptomatic Morton's neuroma has been used for many years. Greenfield et al. [14] reported total symptom relief from a series of corticosteroid injections (mean, 3.07 injections) in 30% of cases and partial response in 50% in their study. At a 2-year follow-up examination, 80% of their patients indicated complete relief of pain or had only slight pain. Bennett et al. [13] reported a response to a single injection of corticosteroid in 47% of patients for whom conservative measures had failed. Rasmussen et al. [15] reported good early response but disappointing long-term outcome with corticosteroid therapy, but again these results were for only a single injection. Repeated injections seem more efficacious but do have associated complications, with plantar fat pad atrophy [16], dermal thinning, and hyperpigmentation reported in previous studies [17].

Surgery for Morton's neuroma is a well-established treatment with various techniques described. Successful outcome is seen in 80–85% with surgical management [13, 18]. Complications of surgery include dense sensory deficit [19], and as with any open procedure, there are wound-related morbidities to consider.

The use of alcohol ablation is a promising treatment option in Morton's neuroma. Ethanol injected around a nerve produces chemical neurolysis through dehydration, necrosis, and precipitation of protoplasm [20]. The maximum effect appears to be in large myelinated fibers [20]. Dockery [21] in a series of 100 patients described an 82% complete response rate and 89% complete or partial response rate after a series of 4% ethyl alcohol injections. Fanucci et al. [22] reported a 90% partial or complete response at 10-month follow-up in a cohort of 40 patients after a series of four injections of 30% alcohol. Hyer et al. [23] in 2005 also reported good results with good response in six of eight neuromas in their small study.

In our series, a solution of 20% alcohol in local anesthetic was used. This concentration was chosen on the rationale that 20% is the minimum concentration producing nervous signal inhibition in in vitro studies [20]. We elected not to inject higher concentrations to attempt to minimize local complications. Most of the patients in our series did experience 5–10 seconds of moderate transient discomfort during the injection with 16.8% having increased plantar pain that lasted from 2 days to 3 weeks and there was one case of complex regional pain syndrome. We think that these cases were likely the result of a local inflammatory reaction. All were treated symptomatically with oral nonsteroidal antiinflammatory drugs or paracetamol, and all resolved without adverse sequelae.

We have found that a minimum of four injections is necessary to totally alleviate symptoms and reduce the risk of recurrence.

We believe real-time sonographic reviewer control is essential in delivering alcohol to the neuromas because the chance of sclerosant leak and the resultant complication must be minimized. With the use of sonography guidance, we were able to observe changes in the neuromas on sonography during the treatment regime. During the injection series (over several weeks), the lesions developed internal high echotexture areas that we believe represent areas of intraneural fibrosis (Fig. 3). We were able to obtain histologic correlation in a patient who had persistent forefoot pain after the alcohol injection regime at the second–third interspace neuroma who developed a new neuroma in the third–fourth interspace. Both neuromas were removed surgically. The injected neuroma showed reduced cellularity and intraneural fibrosis compared with the noninjected neuroma; the gross surgical specimens are shown in Figure 4.

As we stated in the Results section, in our series in the three patients who had surgery, we found the procedure was technically more demanding because of the degree of fibrosis present. Macroscopically the neuromas and proximal extension appeared fibrotic as did the neurovascular bundles in one case. The latter raises a potential problem with toe vascularity when injecting consecutive web space neuromas, but this was not borne out in practice.

A potential discrepancy in our findings was that 84 of 100 patients classified themselves as pain-free, whereas only 62 classed themselves as "completely satisfied," with another 24 "satisfied with a few reservations." We presume that these reservations may have related to procedure-related pain or the multiple visits to clinic, but we did not further inquire regarding this.

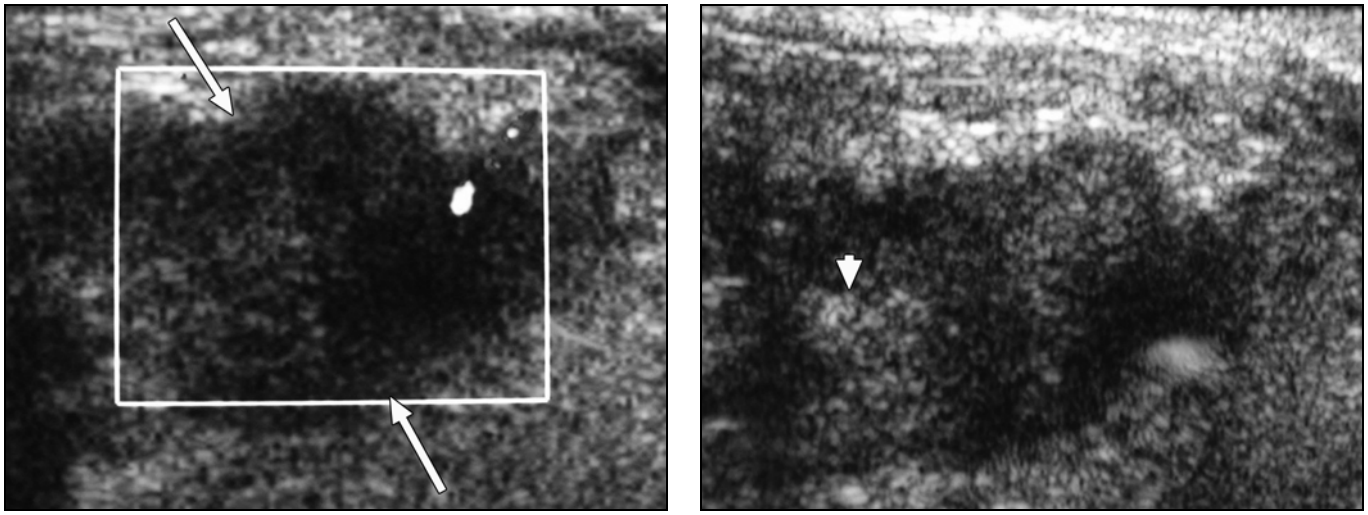

Fig. 3—58-year-old woman with Morton's neuroma.
A, Sonogram shows classical appearance of hypoechoic mass within second–third interspace (*arrows*) before treatment.
B, At follow-up imaging 6 months after treatment, sonogram shows there is developing high echotexture within center of neuroma (*arrow*).

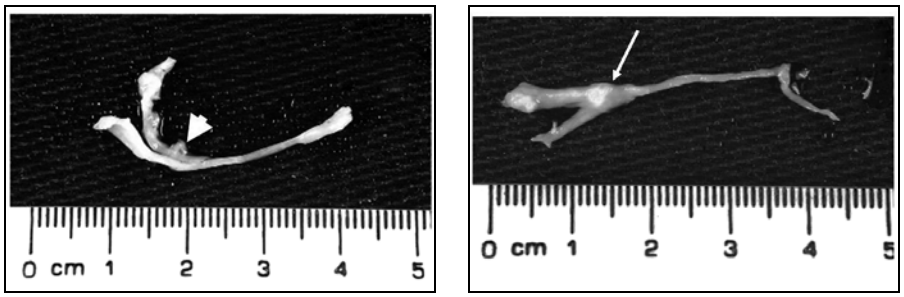

Fig. 4—Photographs show gross specimens of one neuroma treated with alcohol injections and another neuroma not treated with injections in 51-year-old woman.
A, Surgically resected specimen that was treated with alcohol injection. Mass was within second–third metatarsal interspace; arrow outlines neuroma. There was histologic evidence of fibrosis and reduced cellularity in microscopic sections of posttreatment specimen (not shown).
B, Surgically resected specimen that was not treated with alcohol injection. Mass was within third–fourth interspace. Arrow points to neuroma.

Two of the three patients with failed injections had cavovarus feet. Symptomatic relief of forefoot pain after surgery was poor suggesting either that mechanical metatarsalgia played a role in the cause of the pain or that these patients had a subtle motor-sensory neuropathy known to be present in some patients with cavovarus feet. Interestingly, these patients also had neuromas in the third–fourth interspace and this location may relate to injection failure.

One patient with failed injections had a neuroma of 20 mm; once the neuroma was removed, the patient experienced pain relief. It may be that there is a size above which injection therapy has limited benefit, and we are undertaking further work to assess this possibility. Injecting the nerve proximal to a large neural tumor may be one method to address this problem.

In conclusion, the results of our study show that a series of sonographically guided 20% alcohol injections for symptomatic Morton's neuroma is well tolerated, safe, and efficacious with results comparable to surgical resection. The treatment avoids surgery and allows early mobility with the patients being able to bear weight and perform their usual activities of daily living the day after treatment. If treatment fails, surgical excision remains an option.

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