Ablation Procedures for Peripheral Neuromas

Summary

Morton’s neuroma is a common and painful compression neuropathy of the dorsal foot that may be referred to by other names, including intermetatarsal neuroma, interdigital neuroma, interdigital neuritis, and interdigital/Morton’s metatarsalgia.

Historically, Morton’s neuroma has been treated with conservative measures (pads, orthotics, drugs) or surgical approaches. However, new minimally-invasive procedures that include radiofrequency ablation (RFA) or cryoablation have been investigated to treat Morton’s neuroma as an alternative to open surgery. RFA uses heat delivered by a probe to denature proteins and destroy cells within a lesion. Cryoablation (also known as cryoneurolysis, cryolysis, cryoanalgesia) uses a coolant to chill a cryoprobe, which freezes and ablates a lesion on direct contact.

Three case series reported outcomes of RFA to treat Morton’s neuroma. The body of evidence is highly heterogeneous in terms of RFA protocols, prior conservative management, patient characteristics, follow-up duration, outcome measures, and the reporting of outcomes (e.g., using denominators of “feet,” “neuromas,” or “patients,” which required conversion to “patients”).

Only one retrospective case series on the use of cryoablation to treat peripheral nerve pain was identified in the literature review. This evidence is insufficient to draw conclusions on the use of cryoablation to treat Morton’s neuroma, such that it is investigational for this condition. No published literature was identified on treatment of peripheral neuromas other than Morton’s neuroma.

Due to the lack of controlled trials comparing ablative techniques with alternatives, the evidence on the use of ablative techniques for painful peripheral neuromas is insufficient to form conclusions; as a result, these techniques are considered investigational for treatment of peripheral neuromas.

Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Minimally invasive ablation procedures, including RFA and cryoablation are considered investigational for treatment of peripheral neuromas.
Background

A neuroma is pathology of peripheral nerve that develops as part of a normal reparative process. Neuromas may develop after injury to a nerve or as a result of chronic irritation, pressure, stretch, poor repair of nerve lesions or previous neuromas, laceration, crush injury, or blunt trauma. Neuromas typically appear about 6 to 10 weeks after trauma with most presenting within 1 to 12 months after injury or surgery. They may gradually enlarge over a period of 2 to 3 years and may or may not be painful. Pain from a neuroma may be secondary to traction on the nerve by scar tissue, compression of the sensitive nerve endings by adjacent soft tissues, ischemia of the nervous tissue or ectopic foci of ion channels that elicit neuropathic pain. Patients may describe the pain as a low-intensity dull pain or intense paroxysmal burning pain, often triggered by external stimuli such as touch or temperature. Neuroma formation has been implicated as a contributor of neuropathic pain in residual limb pain, postthoracotomy, postmastectomy, and postherniorrhaphy pain syndromes. They may coexist with phantom pain or can predispose to it.

Morton’s Neuroma

Morton’s intermetatarsal neuroma is a common and painful compression neuropathy of the common digital nerve of the foot that may be referred to by other names, including interdigital neuroma, interdigital neuritis, and interdigital or Morton’s metatarsalgia. It is histologically characterized by perineural fibrosis, endoneurial edema, axonal degeneration and local vascular proliferation. Thus, some investigators do not consider Morton’s neuroma to be a true neuroma; instead they consider it to be an entrapment neuropathy that occurs secondary to compression of the common digital nerve under the overlying transverse metatarsal ligament. The incidence and prevalence of Morton’s neuroma are not clear, but it appears 10-fold more often in women than in men with an average age at presentation of around 50 years.

The pain associated with Morton’s neuroma is usually a throbbing, burning or shooting pain that is localized to the plantar aspect of the foot. It is typically located between the 3rd and 4th metatarsal heads although it may appear in other close-by locations. The pain may radiate to the toes and can be associated with paresthesia. The pain can be severe, and the condition may become debilitating to the extent that patients are apprehensive and anxious about walking or touching their foot to the ground. It is aggravated by walking in shoes with a narrow toe box or high heels that cause excessive pronation and excessive forefoot pressure; removal of tight shoes typically relieves the pain.

Although a host of imaging methods may be used to aid diagnosis of Morton’s neuroma, including plain radiographs, magnetic resonance imaging, and ultrasonography, objective findings are unique to this condition and are primarily used to establish a clinical diagnosis. Thus, a patient’s toes often show splaying or divergence. Patients may describe the feeling of a “lump” on the foot bottom or a feeling of walking on a rolled-up or wrinkled sock. Clinical examination with medial and lateral compression may reproduce the painful symptoms with a palpable “click” on interspace compression (Mulder sign).

Treatment of Morton’s Neuroma. Management of patients with a diagnosis of Morton’s neuroma typically proceeds through a pathway that starts with conservative approaches, such as the use of metatarsal pads in shoes, and orthotic devices that alter supination and pronation of the affected
These approaches are aimed at reducing pressure and irritation of the affected nerve. They may provide some relief, but do not alter the underlying pathology. There is scant evidence to support the effectiveness or comparative effectiveness of these practices. In one case series, investigators evaluated a 3-stage protocol of “stepped care” through which private practice patients advanced from stage I (education plus footwear modifications, and a metatarsal pad) to stage II (steroid injections with local anesthetic or local anesthetic alone), into stage III (surgical resection) if stages I and II did not bring relief within 3 months. Overall, 97 of 115 patients (85%) believed that they had improved with the treatment program. However, twenty-four patients (21%) eventually required surgical excision of the nerve and 23 of those (96%) had satisfactory results.

Historically, surgical intervention is considered the definitive therapy. The most common procedure is open excision of the interdigital nerve pathology through a dorsal or plantar approach. A second procedure referred to as nerve decompression with neurolysis or translocation of the affected part of the interdigital nerve has been used to treat Morton’s neuroma. Although this approach uses smaller incisions and seems to have more rapid recovery than open excision of the neuroma, it is reported to be a more demanding procedure that requires specialist training and equipment and is less common in practice. No randomized clinical trials have been reported which compared the effectiveness of different management approaches for Morton’s neuroma.

A Cochrane systematic review (SR) that was originally published in 2004 showed insufficient evidence to assess the effectiveness of surgical and non-surgical interventions for Morton’s neuroma. A more recent review published in 2013 summarized the results of surgical excision studies that included a total of 250 patients. In general, these series were poorly reported and highly heterogeneous, used disparate outcome measures, had short follow-up periods (average 2 to 10 years) and could not be directly compared. In the only prospective comparative study of surgical methods, the dorsal approach resulted in earlier weight-bearing (mean 16 days versus 23 days, respectively) and return to work (mean 22 days versus 37 days, respectively) compared to a plantar approach in 52 total cases at average follow-up of 3 years. Painful scars were more common with the plantar approach (n = 5) compared to the dorsal approach (n = 2), with only 1 patient in each group experiencing a recurrence of symptoms. Other case series of primary neurectomy showed reduction of pain in > 50% to 100% of patients, with self-reported satisfaction rates from 52% to 86%, at mean follow-up periods that ranged from 24 to 126 months. Common complications included paresthesia (51% to 82% reported), scar tenderness or hypersensitivity (6% to 32%), and wound infection (1.4% to 9.7%).

Long-term outcomes of surgical resection have been reported in two additional series that involved a total of 159 cases that were refractory to conservative management. One series (n = 78) reported mean follow-up of 4.6 years (range 0.8 to 8.1 years]. With a dorsal approach, a total of 82% of patients with longstanding symptoms (mean duration 33 months) reported excellent or good results, 10% had a fair result with restriction of activities or pain, while 8% had no improvement at all after surgery. Complications included wound infections in 8 cases that resolved with antibiotics, 5 had persistent hypersensitive scars and 4 developed local keloid formations. Eight cases (10%) required revision due to neuroma recurrence at a mean of about 2 years after index surgery. The second long-term series (n = 81) reported mean follow-up of 15.3 years (range 10 to 20 years), the longest available in the literature. With a mostly dorsal approach (97% of cases), outcomes were reported excellent in 45%, good in in 32% and fair in 15%; 8% reported poor results after surgery and were referred for revision. Paresthesia in the supplying area of the resected nerve was reported in 72% of
cases, while normal sensation was reported in 26%. Other surgical complications were not reported in this series.

**Ablation techniques.** A third middle approach that has been investigated to treat refractory Morton’s neuroma involves several minimally invasive procedures aimed at *in situ* destruction of the pathology: RFA and cryoablation (also known as cryoneurolysis, cryolysis, cryoanalgesia).[2] RFA uses heat generated by an electrode that conducts electromagnetic energy into a tissue or lesion to denature proteins and destroy cells. RFA has been used to ablate a wide range of disparate tissues or lesions that include osteoid osteoma, cardiovascular system pathologies, cervical pain syndromes, liver, lung and other cancers, and varicosities.[12-23] Cryoablation uses a coolant to chill a cryoprobe to temperatures below -75 degrees Celsius, which when inserted into a lesion, freezes and kills the tissue that is treated. It has been used to treat Morton’s neuroma and other chronic nerve pain syndromes, as well as many other conditions in which RFA has been used.[24-31]

This policy will primarily focus on evidence available on the use of RFA and cryoablation of painful neuromas, with emphasis on Morton’s neuroma and the comparative effectiveness of these less-invasive therapies and open surgical resection of the nerve pathology.

**Regulatory Status**

Although RFA probes and generators and cryoablation equipment have received U.S. Food and Drug Administration (FDA) 510(k) marketing clearance, none appear to be specifically indicated for treatment for Morton’s neuroma or any other specific peripheral neuroma.

**Rationale**

This policy is based on a literature review of MEDLINE performed on October 22, 2014 with no date restrictions. Specific evidence was sought on the use of radiofrequency ablation (RFA) or cryoablation to treat Morton’s neuroma or other painful neuromas.

Assessment of efficacy for therapeutic intervention involves a determination of whether the intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Intermediate outcome measures may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition.

**Radiofrequency Ablation for Morton’s Neuroma**

The literature review identified 3 series that reported outcomes with radiofrequency ablation (RFA) treatment of Morton’s neuroma. Genon and colleagues report their experience with RFA to treat Morton’s neuroma according to a clinical algorithm that proceeds from non-operative interventions to RFA, or ultimately to open neurectomy upon failure of the initial approaches. [32] Thirty-seven patients who had failed conservative management (not described) and had symptoms of at least 12 months duration were treated with RFA using a Neurotherm® NT1000 (Neurotherm, Wilmington, MA) radiofrequency generator and 22 gauge electrode inserted through the dorsum into the Morton’s
neuroma. Patients were treated under propofol sedation. The intensity of the current was increased until the electrode tip reached a temperature of 90 degrees C and left in place for 3 minutes to ablate the lesion. At average follow-up of about 11 months (range 3 to 21 months), among 37 patients (38 neuromas) treated, 7 (19%) reported complete relief of symptoms, 21 (58%) reported partial relief and 10 (27%) reported no relief. Among the 10 who had no relief, 8 (22% of cohort) went on to open surgical revision, with 6 of the latter 8 reporting complete relief, 3 reporting partial relief and 1 was unchanged. No complications due to RFA were reported.

A second retrospective series of RFA management of Morton’s neuroma was reported by Moore and colleagues. [33] This series included 29 patients (22 female, age range 23 to 73 years) who had not responded to conservative management (primarily steroid and alcohol injections) over a period of 1 to 2 months. Patients were treated with RFA (Smith & Nephew, Durham, NC) under monitored anesthesia using an electrode inserted dorsally with fluoroscopic guidance. The electrode was heated to 85 degrees C and left in place for a total of 90 seconds. Among the 29 cases, 24 (83%) expressed complete relief of symptoms 1 month following RFA, none reported more pain. The remaining 5 (17%) had minimal to no relief. Of these 5, 1 went to open revision; the other 4 had no additional treatment or were lost to follow-up. One patient reported recurrence 9 months following RFA, and another had a superficial cellulitis that responded to antibiotic therapy. All patients returned to normal shoe gear and activities within 2 days of RFA.

A third retrospective series by Chuter and colleagues examined RFA to treat Morton’s neuroma.[34] It included 25 patients (21 female) with a mean age of 55 years (range 33 to 73 years) who had a mean symptom duration of 3.8 years (range 6 months to 15 years). All had failed conservative management that included orthotics (n = 20) or cortisone injections (n = 15). Thirteen patients described their symptoms as “nuisance”, 12 described them as “disabling”, representing the need to significantly modify activities of daily living. Ultrasound guidance was used to insert a 22 gauge RFA electrode (Neurotherm NT 500 generator) dorsally, with the probe tip maintained at a temperature of 81 degrees C for 5 cycles of 2 minutes each using a local anesthetic to control pain. Before RFA, patients had an average pain score of 6.0 (range 3.0-9.0) on a 10-point visual analogue scale. Four weeks after RFA, the average VAS pain score was 1.7 (range 0-8.0) (p < 0.001), resulting in an average overall symptom improvement of 76% (range 0-100). Eight patients (32%) described RFA as “unpleasant”, 1 experienced irritation of the posterior tibial nerve following the procedure; otherwise no other complications were reported. Three patients (10%) proceeded to open surgical excision within 6 months of RFA due to incomplete relief or recurrence.

**Section Summary.** Three case series reported outcomes of RFA to treat Morton’s neuroma. The body of evidence is highly heterogeneous in term of RFA protocols used, prior conservative management, patient characteristics, follow-up duration, outcome measures, and the reporting of outcomes (e.g., using denominators of “feet”, “neuromas” or “patients”, which required conversion to “patients”). Although favorable outcomes were achieved in general in substantial proportions in each study, the measures are unclear as to their clinical meaning with the exception of the VAS scale used in the Chuter report. Furthermore, in all 3 studies a variable proportion of patients required further surgical excision, thus negating the value of prior RFA. The weakness of the body of evidence precludes conclusions on the efficacy of RFA for Morton’s neuroma.
Cryoablation for Morton’s Neuroma

Only one retrospective case series on the use of cryoablation to treat peripheral nerve pain was identified in the literature review. [35] Among a total cohort of 20 patients, 5 had Morton’s neuroma (all female, mean age 55 years). Cryotherapy was administered using a Frigitronics® CE 2000 (Cooper Surgical Inc., Trumbull, CT) device using nitrous oxide coolant. A cryoprobe was inserted into the Morton's neuroma under ultrasound guidance and proximal nerve block. The probe temperature was decreased to -75 degrees C and left in place until a continuous series of ice balls was created (1 or 2 3-minute cycles of cooling). Among the 5 Morton’s neuroma patients, 3 had “marked relief”, 1 had “moderate relief”, 1 had no relief, at mean follow-up time of 14 weeks (range 6 weeks to 14 months). Complications of cryoablation were not reported.

Other Painful Neuromas

The literature review for this Policy did not identify any controlled studies on the use of ablative procedures to treat painful peripheral neuromas other than Morton’s neuroma. Two recent review articles report little evidence for any other sites.[1, 35] Therefore, the use of any ablative technique for any other painful peripheral neuroma is considered investigational.

Ongoing and Unpublished Clinical Trials

A search of the online site ClinicalTrials.gov in November 2014 found no ongoing trial(s).

Summary of Evidence

The overall body of evidence evaluating the efficacy of minimally invasive ablation techniques is weak, consisting of case series reporting on outcomes following ablative treatment. There are no controlled studies to compare outcomes with those of surgery in patients who all are surgical candidates.

Three case series reported outcomes of RFA to treat Morton’s neuroma. The body of evidence is highly heterogeneous in term of radiofrequency ablation protocols, prior conservative management, patient characteristics, follow-up duration, outcome measures, and the reporting of outcomes (e.g., using denominators of “feet,” “neuromas,” or “patients,” which required conversion to “patients”).

Only one retrospective case series on the use of cryoablation to treat peripheral nerve pain was identified in the literature review. This evidence is insufficient to draw conclusions on the use of cryoablation to treat Morton’s neuroma, such that it is investigational for this condition. No published literature was identified on treatment of peripheral neuromas, or peripheral nerve lesions, other than studies treating Morton’s neuroma.

Due to the lack of high-quality, controlled trials comparing ablative techniques with alternatives, the evidence on the use of ablative techniques for painful peripheral neuromas is insufficient to form conclusions, as a result these techniques are considered investigational for all indications.
### Supplemental Information

#### Practice Guidelines and Position Statements

No guidelines or statements were identified that recommend ablative procedures to treat Morton’s neuroma.

#### U.S. Preventive Services Task Force Recommendations

The U.S. Preventive Services Task Force has not addressed peripheral nerve ablation procedures for Morton’s neuroma.

#### Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

#### References


### Policy History

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<tr>
<td>March 2015</td>
<td>New Policy</td>
<td>Policy created with literature review through October 22, 2014. Radiofrequency ablation and cryoablation procedures of any type are considered investigational for treatment of all peripheral neuromas.</td>
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 20, 2015 and is effective April 15, 2015.

Signature on file

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