

## Medical Policy



### Title: Minimally Invasive Ablation Procedures for Morton and Other Peripheral Neuromas

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Populations	Interventions	Comparators	Outcomes
Individuals: • With Morton neuroma	Interventions of interest are: • Intralesional alcohol injection(s)	Comparators of interest are: • Conservative therapy • Surgical excision	Relevant outcomes include: • Symptoms • Functional outcomes • Treatment-related morbidity
Individuals: • With Morton neuroma	Interventions of interest are: • Radiofrequency ablation	Comparators of interest are: • Conservative therapy • Surgical therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Treatment-related morbidity
Individuals: • With Morton neuroma	Interventions of interest are: • Cryoablation	Comparators of interest are: • Conservative therapy • Surgical therapy	Relevant outcomes include: • Symptoms • Functional outcomes

Populations	Interventions	Comparators	Outcomes
			<ul style="list-style-type: none"> <li>• Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>• Peripheral neuroma(s) other than Morton neuroma</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Conservative therapy</li> <li>• Surgical therapy</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Symptoms</li> <li>• Functional outcomes</li> <li>• Treatment-related morbidity</li> </ul>

## DESCRIPTION

Morton neuroma is a common and painful compression neuropathy of the dorsal foot that is also referred to as intermetatarsal neuroma, interdigital neuroma, interdigital neuritis, and Morton metatarsalgia. Morton neuroma has been treated with conservative measures (pads, orthotics, drugs) or surgery. Minimally invasive procedures, including intralesional alcohol injection, radiofrequency ablation (RFA) and cryoablation, have been investigated as alternatives to open surgery. These methods have also been used to treat other peripheral neuromas.

## OBJECTIVE

The objective of this evidence review is to determine whether the use of minimally invasive ablation procedures improves the net health outcome in individuals with peripheral neuromas.

## BACKGROUND

### Neuroma

A neuroma is a pathology of a peripheral nerve that develops as part of a normal reparative process. Neuromas may develop after nerve injury or result from chronic irritation, pressure, stretch, poor repair of nerve lesions or previous neuromas, laceration, crush injury, or blunt trauma.<sup>1</sup> Neuromas typically appear 6 to 10 weeks after trauma, with most presenting within 1 to 12 months after injury or surgery. They may gradually enlarge over 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 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. Neuromas may coexist with phantom pain or can predispose to it.

### Morton Neuroma

Morton neuroma is a common and painful compression neuropathy of the common digital nerve of the foot that may also be referred to as interdigital neuroma, interdigital neuritis, and interdigital or Morton metatarsalgia.<sup>1,2,3</sup> It is histologically characterized by perineural fibrosis, endoneurial edema, axonal degeneration, and local vascular proliferation. Thus, some investigators do not consider Morton neuroma to be a true neuroma; instead, they consider it to be an entrapment neuropathy occurring secondary to compression of the common digital nerve

under the overlying transverse metatarsal ligament. Morton neuroma appears 10-fold more often in women than in men, with an average age at presentation of around 50 years.<sup>4</sup>

The pain associated with Morton neuroma is usually throbbing, burning, or shooting, and 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 proximal locations.<sup>1,2</sup> 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 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.

### **Diagnosis**

Although a host of imaging methods are used to diagnosis Morton 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.<sup>1</sup> 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).<sup>5</sup>

### **Treatment**

Management of patients diagnosed with Morton neuroma typically starts with conservative approaches, such as the use of metatarsal pads in shoes and orthotic devices that alter supination and pronation of the affected foot.<sup>3</sup> These approaches try to reduce pressure and irritation of the affected nerve. They may provide relief, but do not alter the underlying pathology. There is scant evidence to support the effectiveness or comparative effectiveness of these practices.<sup>2,6,7</sup> In a case series, Bennett et al (1995) evaluated a 3-stage protocol of "stepped care" through which private practice patients (N=115) advanced from stage I (education plus footwear modifications, and a metatarsal pad) to stage II (steroid injections with local anesthetic or local anesthetic alone), and into stage III (surgical resection) if stages I and II were not relieved within 3 months.<sup>8</sup> Overall, 97 (85%) of 115 patients believed that pain had been reduced with the treatment program. However, 24 (21%) patients eventually required surgical excision of the nerve, and 23 (96%) of them had satisfactory results.

### **Minimally Invasive Ablation Procedures**

Several minimally invasive procedures to treat refractory Morton and other peripheral neuromas are aimed at in situ destruction of the pathology, including intralesional alcohol injection, radiofrequency ablation (RFA) and cryoablation (also known as cryoneurolysis, cryolysis, and cryoanalgesia).<sup>2</sup>

Dehydrated ethanol has been shown to inhibit nerve function in vitro, has high affinity for nerve tissue, and causes direct damage to nerve cells via dehydration, cell necrosis, and precipitation of protoplasm, leading to neuritis and a pattern of Wallerian degeneration.<sup>2</sup> Technically, ethanol is a sclerosant that causes chemical neurolysis of the nerve pathology but is considered an ablative procedure for this evidence review. The use of ultrasound guidance during this procedure has been shown to increase surgical accuracy, improve outcomes, and shorten procedure duration. RFA uses heat generated by an electrode that conducts electromagnetic energy into a tissue or

lesion to denature proteins and destroy cells. RFA is used to ablate a wide range of tissues or lesions, including osteoid osteoma; cardiovascular system pathologies; cervical pain syndromes; liver, lung, and other cancers; and varicosities.<sup>9,10,11,12,13,14,15,16,17,18,19,20</sup> Cryoablation uses coolant to chill a cryoprobe to temperatures below -75°C, which when inserted into a lesion, freezes and kills the tissue. It has been used to treat Morton neuroma, other chronic nerve pain syndromes, and conditions for which RFA has been used.<sup>21,22,23,24,25,26,27,28</sup>

This review primarily focuses on evidence for the use of intralesional alcohol injection, RFA, and cryoablation on painful neuromas, with emphasis on Morton neuroma and the comparative effectiveness of these less invasive therapies with open surgical resection of the nerve pathology.

## **REGULATORY STATUS**

Alcohol injection for Morton neuroma is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration (FDA).

Although RFA probes and generators and cryoablation equipment have been cleared for marketing by the FDA through the 510(k) process, none appear to be specifically indicated for the treatment of Morton neuroma or any other specific peripheral neuroma.

**POLICY**

Minimally invasive ablation procedures, including intralesional alcohol injection, radiofrequency ablation, and cryoablation, are considered **experimental / investigational** for the treatment of Morton and other peripheral neuromas.

**Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

**RATIONALE**

This evidence review was created using searches of the PubMed database. The most recent literature update was performed through April 22, 2025.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**MINIMALLY INVASIVE ABLATION PROCEDURES FOR MORTON AND OTHER PERIPHERAL NEUROMAS****Clinical Context and Therapy Purpose**

The purpose of minimally invasive ablation procedures in individuals who have Morton or other peripheral neuromas is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

***Populations***

The relevant population of interest is individuals with peripheral neuromas, with emphasis on Morton neuroma.

**Interventions**

The therapies being considered are: intralesional alcohol injection, radiofrequency ablation (RFA), and cryoablation for painful neuromas.

**Comparators**

The following practices are currently being used to make decisions about the treatment of peripheral neuromas: conservative therapy and open surgical resection of the nerve pathology.

**Outcomes**

The general outcomes of interest are pain, typically measured with a visual analog score (VAS), ability to walk, and adverse events related to ablation procedures. The timing ranges from hours for the immediate effect of treatment, to months to assess recurrence of pain.

**Study Selection Criteria**

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

**INTRALESIONAL ALCOHOL INJECTION FOR MORTON NEUROMA****REVIEW OF EVIDENCE****Case Series**

No RCTs or nonrandomized interventional trials were identified. Several published case series have used alcohol injections to treat Morton neuroma. Summaries of these series appear in Table 1.

Treatment in all the case series consisted of injections of alcohol combined with an anesthetic (eg, lidocaine or bupivacaine). Injections were repeated at 2-week intervals, if symptoms persisted. On average, across studies, each patient received approximately 4 injections. Ultrasound guidance was used in all of the series described in Table 1. Outcomes were patient-reported and consisted of various measures of pain and satisfaction.

The largest series identified was reported by Pasquali et al (2015), who described a retrospective 2-center case series of 508 patients who received ultrasound-guided alcohol injection from 2001 to 2012 for Morton neuroma.<sup>29</sup> Eligible patients presented with 2nd or 3rd web space symptoms and had failed 3 months of conservative treatment with insoles and nonsteroidal anti-inflammatory drugs. Patients were injected with a 50% alcohol plus mepivacaine solution, with a mean of 3 injections (range, 1 to 4 injections) per neuroma. Pain at the Morton neuroma site was assessed on a VAS ranging from 0 to 10, by local adverse reactions at 1 week post-procedure (0 = no reaction; 1 = minimal swelling, pain, redness; 2 = significant swelling, pain, redness), and patient-reported satisfaction. Pain scores improved from a mean preinjection VAS score of 8.7 to a mean postinjection score of 3.6 at 1 year (change in VAS score,  $p < .001$ ). At 1 year

postinjection, 74.5% of patients were completely satisfied with the procedure. Fifty (9.3%) feet eventually required operative excision.

**Table 1. Case Series of Intralesional Alcohol Injection for Morton Neuroma**

Study	N	Treatment	Mean follow-up, mo	Results	Surgical follow-up, n (%)
Perini et al (2016) <sup>30</sup> ,	220	Alcohol, lidocaine	19	<ul style="list-style-type: none"> <li>Median NRS pain score improved from 9 to 3</li> <li>88.6% reported reductions in limitations of everyday activities</li> <li>Reduction in neuropathic pain (100% to 45%)</li> <li>No change in nociceptive pain (47% to 53%)</li> </ul>	14 (6)
Pasquali et al (2015) <sup>29</sup> ,	508	Alcohol, mepivacaine	12	<ul style="list-style-type: none"> <li>Mean VAS pain score improved from 8.7 to 3.6</li> <li>74.5% completely satisfied</li> </ul>	50 (9)
Musson et al (2012) <sup>31</sup> ,	75	Alcohol, bupivacaine	14	<ul style="list-style-type: none"> <li>Mean VAS pain score improved from 8.5 to 4.2</li> <li>32% complete symptom relief; 33% partial relief; 35% no relief</li> </ul>	17 (20)
Hughes et al (2007) <sup>32</sup> ,	101	Alcohol, bupivacaine	12	<ul style="list-style-type: none"> <li>Mean VAS pain score improved from 8 to 0</li> <li>84% "essentially pain free"; 8% "mild/moderate pain"; 8% "no difference"</li> </ul>	3 (3)
Fanucci et al (2004) <sup>33</sup> ,	40	Alcohol, carbocaine	10	<ul style="list-style-type: none"> <li>21 completely satisfied; 9 satisfied with minor complications; 6 satisfied with major complications; 4 dissatisfied</li> </ul>	4 (10)

NRS: numeric rating scale; VAS: visual analog scale.

Morgan et al (2014)<sup>34</sup>, reported on a systematic review that included the studies above published through February 2012 plus another by Dockery (1999)<sup>35</sup>, and compared the need for subsequent surgery after alcohol injections for Morton neuroma with or without ultrasound guidance. Reviewers concluded that use of ultrasound guidance for alcohol injections to treat Morton neuroma could reduce the need for subsequent surgery better than unguided treatments.

### **Section Summary: Intralesional Alcohol Injection for Morton Neuroma**

Case series of intralesional alcohol injection for Morton neuroma have generally found that many patients experience pain relief and express satisfaction with the procedure. Some evidence has suggested that surgery after failed cases of alcohol injections is more complex and challenging than in untreated patients due to the presence of fibrosis. There is a lack of controlled trials comparing alcohol injections with alternative therapies, and there are no controlled studies comparing outcomes for alcohol injections with those for surgery in surgical candidates.

## RADIOFREQUENCY ABLATION FOR MORTON NEUROMA

### REVIEW OF EVIDENCE

#### Systematic Reviews

Llombart et al (2024) published results of a systematic review and meta-analysis of 8 studies (N=237) evaluating the safety and efficacy of RFA for Morton's neuroma.<sup>36</sup> Studies included were retrospective cohort studies, retrospective case series, and prospective case series (Table 2). Some case series included in the review are further detailed below. The comparison was pre-RFA and post-RFA, within the same cohort. Meta-analysis characteristics and results are detailed in Tables 3 and 4. At the final follow-up ( $\geq 12$  months), significant reductions in pain were observed post-RFA and 47.57% of patients experienced complete pain relief, while 16.40% reported no benefit. Complications were minimal (2.1%) and most resolved without significant interventions. These results are limited by the low quality of included studies, no identified RCTs, high heterogeneity, significant publication bias, relatively short duration of follow-up, and lack of a control group, making it difficult to draw conclusions from these results.

**Table 2. Comparison of Studies Included in SR & M-A of RFA**

Study	Llombart et al (2024) <sup>36</sup>
Brooks et al (2017)	●
Chuter et al (2013)	●
Connors et al (2020)	●
Deniz et al (2015)	●
Masala et al (2017)	●
Moore et al (2012)	●
Paolo et al (2013)	●
Shah et al (2019)	●

M-A: meta-analyses; RFA: radiofrequency ablation; SR: systematic reviews.

**Table 3. RFA SR & M-A Characteristics**

Study	Dates	Trials	Participants	N (Range)	Design	Duration, months
Llombart et al (2024) <sup>36</sup>	Date of search not specified, dates of included articles: 2012-2020	8	Adults diagnosed with Morton's neuroma receiving RFA (81.4% female; mean age, 46.3 to 57 years)	237 (22 to 52)	Retrospective cohort studies, case series	6 to 35

M-A: meta-analyses; RFA: radiofrequency ablation; SR: systematic reviews.



**Table 4. RFA SR & M-A Results**

Study	Change in VAS pain score at 2 months	Change in VAS pain score at 6 to 8 months	Change in VAS pain score at ≥12 months
Llombart et al (2024) <sup>36</sup> ,			
Total N	73 (2 studies)	117 (4 studies)	111 (4 studies)
MD (95% CI)	6.85 (6.51 to 7.19)	5.20 (5.0 to 5.41)	6.45 (6.01 to 6.90)
p-value	<.00001	p<.00001	p<.00001
$I^2$ (p)	67% (.08)	99% (<.00001)	79% (.002)

CI: confidence interval; M-A: meta-analyses; MD: mean difference; RFA: radiofrequency ablation; SR: systematic reviews; VAS: visual analog scale.

### Case Series

Four case series reporting outcomes of RFA for treating Morton neuroma are summarized in Table 5 and Table 6.

Genon et al (2010) reported on a retrospective review of a single center's experience with RFA to treat Morton neuroma according to a clinical algorithm that proceeds from nonoperative interventions to RFA and to open neurectomy if initial approaches failed.<sup>37</sup> Thirty-seven patients who had failed conservative management (not described) and had symptoms for at least 12 months in duration were treated with RFA using a NeuroTherm NT1000 (NeuroTherm) radiofrequency generator. At an average follow-up of 11 months (range, 3 to 21 months), among the 37 patients (38 neuromas) treated, 7 (18%) reported complete relief of symptoms, 21 (55%) reported partial relief, and 10 (26%) reported no relief. Mean numeric rating scale (NRS) decreased from 9.0 (interquartile range [IQR], 8.0 to 9.0) pre-intervention to 5.0 (IQR 3.0 to 8.0) post-intervention. Of 38 neuromas, 11 (28.9%) required open surgical revision following RFA.

Moore et al (2012) reported on a second retrospective series of RFA management of Morton neuroma.<sup>38</sup> This series included 29 patients (22 women; age range, 23 to 73 years) who had not responded to conservative management (primarily steroid and alcohol injections) over 1 to 2 months. Patients were treated with RFA (Smith & Nephew) under monitored anesthesia using an electrode inserted dorsally with fluoroscopic guidance. Among the 29 patients, 24 (83%) expressed complete relief of symptoms 1 month after RFA; none reported more pain. The remaining 5 (17%) had minimal to no relief. Of them, one had an open revision, and the others had no additional treatment or were lost to follow-up. One patient reported recurrence 9 months following RFA, and another had superficial cellulitis that responded to antibiotic therapy. All patients returned to normal shoe gear and activities within 2 days of RFA.

Chuter et al (2013) reported on a third retrospective series of RFA to treat Morton neuroma.<sup>39</sup> This series included 25 patients (21 women) 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 failed conservative management. Before RFA, patients had an average pain score of 6.0 (range, 3.0 to 9.0) on a 10-point VAS. Four weeks after RFA, the average VAS pain score was 1.7 (range, 0 to 8.0;  $p<.001$ ), an average symptom improvement of 76%. The only complication reported involved a patient who experienced irritation of the posterior tibial nerve following the procedure. Three (9%) patients proceeded to open surgical excision within 6 months of RFA due to incomplete pain relief or recurrence.

The most recent case series retrospectively reviewed the records of 32 (25 women; mean age 46 years) patients who underwent RFA for treatment of Morton neuroma following failure of conservative management that included orthotic treatments, alcohol injection, and corticosteroid injection.<sup>40</sup> Compared with pre-intervention, significant reductions in pain scores ( $p=.001$ ) were found after a single treatment in 21 patients (65%). The remaining 11 patients (35%) underwent a second ablation procedure, of whom 10 reported significant pain reduction following the second procedure. No patients were reported to have undergone open surgical revision, although 6 patients (19%) required a corticosteroid injection within 6 weeks of RFA due to the return of pain. No harms of treatment were reported.

**Table 5. Summary of Case Series Characteristics of Radiofrequency Ablation for Morton Neuroma**

Study	Country	Participants	Follow-Up
Genon et al (2010) <sup>37</sup> ,	Australia	n=37 (38 neuromas) with previously failed conservative management	11 months
Moore et al (2012) <sup>38</sup> ,	United States	n=29 (32 neuromas) with previously failed conservative management	13 months
Chuter et al (2013) <sup>39</sup> ,	United Kingdom	n=25 (30 neuromas) with previously failed conservative management	6 months
Connors et al (2020) <sup>40</sup> ,	United States	n=32 (33 neuromas) with previously failed conservative management	34 to 35 months

**Table 6. Summary of Case Series Results of Radiofrequency Ablation for Morton Neuroma**

Study	Treatment	Symptom Relief	Pain	Need for Surgical Revision
Genon et al (2010) <sup>37</sup> ,	RFA	Proportion with: Complete symptom resolution: 18% (7/38 neuromas) Partial symptom resolution: 55% (21/38 neuromas) No symptom resolution: 26% (10/38 neuromas)	Mean pain pre-intervention: NRS 9.0 (IQR, 8.0 to 9.0) Mean pain post-intervention: NRS 5.0 (IQR, 3.0 to 8.0)	28.9% (11/38 neuromas)
Moore et al (2012) <sup>38</sup> ,	Fluoroscopically-guided RFA	Proportion with: Complete symptom resolution: 83% (24/29 patients) No or minimal resolution: 17% (5/29 patients)	Pain scores not reported	3.4% (1/29 patients)
Chuter et al (2013) <sup>39</sup> ,	Ultrasound-guided RFA	Proportion with a "satisfactory outcome": 86.7% (26/30 neuromas)	Mean pain pre-intervention: VAS 6.0 (range, 3.0 to 9.0)	9.4% (3/32 patients)

Study	Treatment	Symptom Relief	Pain	Need for Surgical Revision
			Mean pain post-intervention: VAS 1.7 (range, 0 to 8.0); p<.001	
Connors et al (2020) <sup>40</sup> ,	RFA	Median success score (scale 0 to 100; higher score=greater subjective success): 92.5 (IQR, 50 to 100)	Mean pain pre-intervention: VAS 7.0 (IQR, 4.75 to 8.0); Mean pain post-intervention: VAS 1.0 (IQR, 0 to 5.0); p=.001	None reported

IQR: interquartile range; NRS: numeric rating scale; RFA: radiofrequency ablation; VAS: visual analog scale.

### Section Summary: Radiofrequency Ablation for Morton Neuroma

Case series and a systematic review including case series and cohort studies have reported outcomes of RFA to treat Morton neuroma. The body of evidence is highly heterogeneous regarding RFA protocols used, prior conservative management, patient characteristics, follow-up durations, outcome measures, and the reporting of outcomes (e.g., using denominators of "feet," "neuromas," or "patients"). Although favorable outcomes were achieved in substantial proportions in each study, the outcome measures were unclear as to their clinical meaning, except the VAS used in the Chuter report. Furthermore, in all case series, a highly variable proportion of patients required further surgical excision, making the value of prior RFA uncertain.

## CRYOABLATION FOR MORTON NEUROMA

### REVIEW OF EVIDENCE

#### Case Series

Multiple retrospective case series on the use of cryoablation to treat peripheral nerve pain have been identified.

One case series by Friedman et al (2012) reported on a series of patients who had undergone sonographically guided cryoneurolysis.<sup>41</sup> Among a cohort of 20 patients, 5 had Morton neuroma (all women; mean age, 55 years). Cryotherapy was administered with a Frigitrionics CE 2000 (Cooper Surgical) device using nitrous oxide coolant. A cryoprobe was inserted into the Morton neuroma; the probe temperature was decreased to -75°C and left in place until a continuous series of ice balls was created (one or two 3-minute cycles of cooling). Patients were scheduled for follow-up at 4 to 6 weeks. However, actual follow-up varied due to patient discretion. Among the 5 Morton neuroma patients, 3 had "marked relief," 1 had "moderate relief," and 1 had no relief, at a mean follow-up of 14 weeks (range, 6 weeks to 14 months). Complications of cryoablation were not reported.

The second case series, by Cazzato et al (2016), retrospectively described 20 patients (24 lesions) with Morton neuroma who underwent magnetic resonance-guided cryoablation.<sup>42</sup> All patients were previously treated with ultrasound-guided corticosteroid injections and had not reported relief. While positioned in the magnetic resonance unit, a cryoprobe (Ice-Seed; Galil

Medical) was inserted into the center of the lesion. A single freezing cycle of 150 seconds was performed. Mean procedural time was 41 minutes (range, 35 to 60 minutes). Patients were followed with a telephone survey. The number of months between procedure and last follow-up ranged from 1 to 50 months. Results were reported by lesion, with data available for 18 of the 24 lesions treated. Patients with 14 (78%) of the 18 lesions were "completely satisfied," 17% were "satisfied with minor reservations," and 6% were "satisfied with major reservations." Mean local pain score was 3.0 on a 0-to-10 VAS. Post-VAS scores were not available.

Another case series by Moulin et al (2024) retrospectively described 53 patients (59 lesions) with Morton neuroma who underwent ultrasound-guided cryoneurolysis after failure of conservative therapy.<sup>43</sup> Previously failed conservative therapy included footwear modification, orthotic devices, or steroid injections. Cryotherapy was administered with an Icesphere cryoprobe (Boston Scientific) via an interdigital approach. Time of freezing and the number of cycles depended on the size of the neuroma and the extension of the ice ball. Mean procedural time was  $47 \pm 22$  minutes. Follow-up occurred via telephone interview at 4 weeks and 6 months. At 6 months post-procedure, pain NRS scores were significantly decreased ( $2.7 \pm 2.2$  vs  $7.1 \pm 1.1$ ; mean decrease, 4.1 points;  $p < .0001$ ). Thirty-two patients (60.4%) reported complete pain relief, 15 (28.3%) reported partial pain relief, and 6 (11.3%) reported no pain relief or increased pain. No major adverse events were observed.

### **Section Summary: Cryoablation for Morton Neuroma**

Multiple retrospective case series have investigated cryoablation to treat Morton neuroma. The body of evidence is heterogeneous regarding cryoablation protocols used, prior conservative management, and length of follow-up. Although large proportions of patients reported satisfaction with the procedure in all studies, daily functioning did not clearly improve after the procedure. The weaknesses in the body of evidence preclude conclusions on the efficacy of cryoablation for Morton neuroma.

## **OTHER PAINFUL NEUROMAS**

### **Review of Evidence**

The literature review for this update did not identify any controlled studies on the use of ablative techniques to treat painful peripheral neuromas other than Morton neuroma. Two recent review articles reported little evidence for any other sites.<sup>1,41</sup>

### **Section Summary: Other Painful Neuromas**

The current literature base on the use of ablative techniques for peripheral neuromas other than Morton neuroma provides insufficient data on which to form conclusions about treatment efficacy.

## **SUPPLEMENTAL INFORMATION**

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

### **Clinical Input From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate

reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

### **2015 Input**

In response to requests, input was received from 2 specialty societies and 5 academic medical centers while this policy was under review in 2015. Input was consistent that the use of alcohol injections to treat Morton neuroma is investigational.

### **Practice Guidelines and Position Statements**

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

### **Association of Extremity Nerve Surgeons**

The Association of Extremity Nerve Surgeons issued practice guidelines (2020)<sup>44</sup>, which drew the following conclusions:

- "We do not recommend ablation in the primary treatment of Intermetatarsal Nerve Entrapment ("Morton's Neuroma").
  - Alcohol injections: The literature regarding alcohol injections is equivocal. There may be some short-term positive effect, but long-term effect is poor for this therapy. Some of the literature recommends using 30% alcohol solution to get effective results. However, new research has shown the use of 30% alcohol does not create any measurable change in the histology of nerve tissue. There is also a moderate risk of necrosis of surrounding tissues. As a general rule, we do not advocate the use of alcohol injections.
  - Radiofrequency ablation: Radiofrequency ablation has use in the lower extremity, but must be done with caution as this procedure has the potential for thermal necrosis of the adjacent tissues. Judicious use of fluoroscopy and other visualization techniques is advised while utilizing radiofrequency ablation...further research in this technique is needed.
  - Cryoablation: Cryoablation (cryotherapy) should be used with extreme caution, as the amount of literature in the lower extremity is limited. If cryotherapy is used, it should ideally be performed with an open technique rather than percutaneously for optimal results."

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

Not applicable.

### **Ongoing and Unpublished Clinical Trials**

Some currently ongoing and unpublished trials that might influence this review are listed in Table 7.

**Table 7. Summary of Key Trials**

<b>NCT No.</b>	<b>Trial Name</b>	<b>Planned Enrollment</b>	<b>Completion Date</b>
<b><i>Ongoing</i></b>			
NCT05501262	Comparative Effectiveness of Cryoablation Using the ICE-Seed Cryoablation Needle With Steroid and Lidocaine Versus Steroid and Lidocaine Alone for Treatment of Morton's Neuroma	32	Dec 2023 (unknown status)
<b><i>Unpublished</i></b>			
NCT02838758	A 3-Arm Randomized Controlled Study Comparing Ultrasound-Guided Cryoablation, Ultrasound-Guided Perineural Lidocaine, and Ultrasound-Guided Perineural Saline to Treat Intrametatarsal Neuroma	66 (actual enrollment: 10)	Jun 2018*

NCT: national clinical trial.

\*As of April 2025 , no results posted.

**CODING**

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.**

**Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

**The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.**

<b>CPT/HCPCS</b>	
64632	Destruction by neurolytic agent; plantar common digital nerve
64640	Destruction by neurolytic agent; other peripheral nerve or branch
0441T	Ablation, percutaneous, cryoablation, includes imaging guidance; lower extremity distal/peripheral nerve

<b>REVISIONS</b>	
Posted 08-22-2023 Effective 09-21-2023	Policy added to the bcbsks.com web site.
08-27-2024	Updated Description Section
	Updated Rationale Section
	Updated References Section
08-12-2025	Updated Description Section
	Updated Rationale Section
	Updated References Section

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