Ablation Procedures for Peripheral Neuromas

Policy Number: 7.01.147  Last Review: 08/2017
Origination: 08/2015  Next Review: 08/2018

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for Ablation Procedures for Peripheral Neuromas. This is considered investigational.

When Policy Topic is covered
Not Applicable

When Policy Topic is not covered
Minimally invasive ablation procedures, RFA, and cryoablation, are considered investigational for treatment of peripheral neuromas.

Description of Procedure or Service

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
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</table>
| 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  
* Treatment-related morbidity |
| Individuals:  
* With peripheral neuroma(s) other than Morton neuroma | Interventions of interest are:  
* Ablation | Comparators of interest are:  
* Conservative therapy  
* Surgical therapy | Relevant outcomes include:  
* Symptoms  
* Functional outcomes  
* Treatment-related morbidity |

Morton neuroma is a common and painful compression neuropathy of the dorsal foot. Historically, Morton neuroma has been treated with conservative measures (pads, orthotics, drugs) or surgical approaches. Minimally invasive procedures that include radiofrequency ablation (RFA) or cryoablation have been investigated as an alternative to open surgery. RFA uses heat delivered by a probe to denature proteins and destroy cells within a lesion. Cryoablation uses a coolant to chill a
cryoprobe, which freezes and ablates a lesion on direct contact. These ablation methods have been used to treat other peripheral neuromas.

For individuals who have Morton neuroma who receive RFA, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Three case series have reported outcomes of RFA to treat Morton neuroma. The body of evidence is highly heterogeneous in terms of RFA protocols, prior conservative management, patient characteristics, follow-up durations, outcome measures, and reporting of outcomes. The available evidence is also limited by variable proportions of patients requiring surgery after RFA. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have Morton neuroma who receive cryoablation, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Only retrospective case series on the use of cryoablation to treat peripheral nerve pain were identified in the literature review. The case series were heterogeneous regarding cryoablation protocols and length of follow-up. Outcome measures did not provide functional information. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peripheral neuroma(s) other than Morton neuroma who receive ablation, the evidence is very limited (no published literature was identified). Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes.

**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.1 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 Neuroma
Morton 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 metatarsalgia. 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 that occurs secondary to compression of the common digital nerve under the overlying transverse metatarsal ligament. The incidence and prevalence of Morton 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.

Although a host of imaging methods may be used to aid diagnosis of 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. 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 Neuroma
Management of patients with a diagnosis of Morton 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 foot. 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 a case series, investigators 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), 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, 24 patients (21%) eventually required surgical excision of the nerve, and 23 of those (96%) had satisfactory results.

Surgical Techniques
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 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.
A Cochrane systematic review that was originally published in 2004 showed insufficient evidence to assess the effectiveness of surgical and nonsurgical interventions for Morton 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, 2-10 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 vs 23 days, respectively) and return to work (mean, 22 days vs 37 days, respectively) compared with 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 with 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 more than 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%-82%), scar tenderness or hypersensitivity (6%-32%), and wound infection (1.4%-9.7%).

Long-term outcomes of surgical resection have been reported in 2 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, 0.8-8.1 years). With a dorsal approach, a total of 82% of patients with long-standing 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 with persistent hypersensitive scars, and 4 developing 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, 10-20 years), the longest available in the literature. With a mostly dorsal approach (97% of cases), outcomes were reported excellent in 45%, good 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 neuroma involves several minimally invasive procedures aimed at in situ destruction of the pathology: RFA and cryoablation (also known as cryoneurolysis, cryolysis, cryoanalgesia). 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. Cryoablation uses a coolant to chill a cryoprobe to temperatures below \(-75\)\(^\circ\)C, which when inserted into a lesion, freezes and kills the tissue that is treated. It has been used to treat Morton neuroma and other chronic nerve pain syndromes, as well as many other conditions in which RFA has been used.

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

Rationale
This evidence review was originally created in December 2014 and has been updated with searches of the MEDLINE database. The most recent literature review was performed through April 25, 2017.

Assessment of the efficacy of therapeutic interventions involves a determination whether an intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial 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 NEUROMA
The literature review identified 3 case series that reported outcomes with radiofrequency ablation (RFA) treatment of Morton neuroma.

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. Thirty-seven patients who had failed conservative management (not described) and had symptoms of at least 12 months in duration were treated with RFA using a NeuroTherm® NT1000 (NeuroTherm, Wilmington, MA) radiofrequency generator. At an average follow-up of 11 months (range, 3-21 months), among the 37 patients (38 neuromas) treated, 7 (19%) reported complete relief of symptoms, 21 (58%) reported partial relief, and 10 (27%) reported no relief. Among those with no relief, 8 (22% of cohort) had open surgical revision, with 6 of 8 reporting complete relief, 3 reporting partial relief, and 1 was unchanged. No complications due to RFA were reported.

Moore et al (2012) reported a second retrospective series of RFA management of Morton neuroma. This series included 29 patients (22 women; age range, 23-73 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, Durham, NC) under monitored anesthesia using an electrode inserted dorsally with fluoroscopic guidance. 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 them, 1 patient had 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 a 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.(34) This series included 25 patients (21 women) with a mean age of 55 years (range, 33-73 years) who had 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, 3.0-9.0) on a 10-point visual analog scale (VAS). Four weeks after RFA, the average VAS pain score was 1.7 (range, 0-8.0; p<0.001), 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 (10%) patients proceeded to open surgical excision within 6 months of RFA due to incomplete pain relief or recurrence.

**Section Summary: Radiofrequency Ablation for Morton Neuroma**

Three case series 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 (eg, using denominators of “feet,” “neuromas,” or “patients,” which required conversion to “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 3 series, a variable proportion of patients required further surgical excision, making the value of prior RFA uncertain.

**CRYOABLATION FOR MORTON NEUROMA**

Two 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 an on a series of patients who had undergone sonographically-guided cryoneurolysis.(35) Among a total cohort of 20 patients, 5 had Morton neuroma (all women; mean age, 55 years). Cryotherapy was administered using a Frigitronics CE 2000 (Cooper Surgical, Trumbull, CT) device using nitrous oxide coolant. A cryoprobe was inserted into the Morton neuroma under ultrasound guidance and proximal nerve block. 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,” 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), describes 20 patients (24 lesions) with Morton neuroma who underwent magnetic resonance-guided cryoablation.(36) 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, St. Paul, MN) was inserted into the center of the lesion. A single freezing cycle of 150 seconds was performed. Mean procedural time was 41 minutes (range, 35-60 minutes). Patients were followed up 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. Fourteen (78%) of the 18 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 due to the retrospective nature of the study.

**Section Summary: Cryoablation for Morton Neuroma**

Two 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 both studies, daily functioning did not clearly improve after the procedure. The weakness of the body of evidence precludes conclusions on the efficacy of cryoablation for Morton neuroma.

**OTHER PAINFUL NEUROMAS**

The literature review for this update did not identify any controlled studies on the use of ablative procedures to treat painful peripheral neuromas other than Morton neuroma. Two recent review articles reported little evidence for any other sites.(1,35)

**SUMMARY OF EVIDENCE**

For individuals who have Morton neuroma who receive RFA, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Three case series were identified that reported outcomes for RFA to treat Morton neuroma. The body of evidence is highly heterogeneous regarding RFA protocols, prior conservative management, patient characteristics, follow-up durations, outcome measures, and reporting of outcomes. Variable proportions of patients require surgery after RFA, making the benefit of RFA for avoiding more invasive treatment uncertain. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have Morton neuroma who receive cryoablation, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Only two retrospective case series on the use of cryoablation to treat peripheral nerve pain were identified in the literature review. The case series were heterogeneous regarding cryoablation protocols and length of follow-up. Outcome measures did not provide functional information. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals who have peripheral neuroma(s) other than Morton neuroma who receive RFA or cryoablation, the evidence is very limited (no published literature was identified). Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS
The Association of Extremity Nerve Surgeons published clinical practice guidelines in 2014.(37) The guidelines stated that “We do not recommend ablation in the primary treatment of Intermetatarsal Entrapment (Morton’s Neuroma).” The guidelines warned that cryoablation should be used with extreme caution, and if used, should be performed in an open technique, not percutaneously. The guidelines also warned that radiofrequency ablation may cause thermal necrosis of adjacent tissues.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
Not applicable.

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.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

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<td>NCT02838758</td>
<td>A 3-Arm Randomized Controlled Study Comparing Ultrasound-Guided Cryoablation, Ultrasound-Guided Perineural Lidocaine, and Ultrasound-Guided Perineural Saline to Treat Intrametatarsal Neuroma</td>
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<td>Dec 2020</td>
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References:


### Billing Coding/Physician Documentation Information

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<th>Code</th>
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<tr>
<td>64632</td>
<td>Destruction by neurolytic agent; plantar common digital nerve</td>
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<td>Destruction by neurolytic agent; other peripheral nerve or branch</td>
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### ICD-10 Codes

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### Additional Policy Key Words

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### Policy Implementation/Update Information

- **8/1/15**: New Policy, considered investigational.
- **8/1/16**: No policy statement changes.
- **8/1/17**: No policy statement changes.