Ablation of Peripheral Nerves to Treat Pain

Policy # 00503
Original Effective Date: 05/18/2016
Current Effective Date: 02/01/2019

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Facet Radiofrequency Denervation is addressed separately in medical policy 00199.

Note: Spinal Cord Stimulation is addressed separately in medical policy 00260.

Note: Sacroiliac Joint Fusion is addressed separately in medical policy 00558.

Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers radiofrequency ablation (RFA) of peripheral nerves to treat pain associated with plantar fasciitis or knee osteoarthritis (OA) to be **investigational.***

Based on review of available data, the Company considers cryoneurolysis of peripheral nerves to treat pain associated with knee osteoarthritis (OA) or total knee arthroplasty to be **investigational.***

Based on review of available data, the Company considers radiofrequency ablation (RFA) of peripheral nerves to treat pain associated with occipital neuralgia or cervicogenic headache to be **investigational.***

Based on review of available data, the Company considers diagnostic block performed before radiofrequency ablation (RFA) to be **investigational.***

Based on review of available data, the Company considers ablation of peripheral nerves to treat pain in all other conditions, with the exception of facet joint pain (see medical policy 00199) to be **investigational.*** .

Background/Overview

KNEE OSTEOARTHRITIS
Knee osteoarthritis is common, costly, and often the cause of substantial disability. Among U.S. adults, the most common causes of disability are arthritis and rheumatic disorders.

Treatment
Treatment for osteoarthritis of the knee aims to alleviate pain and improve function. However, most treatments do not modify the natural history or progression of osteoarthritis and are not considered curative. Nonsurgical modalities used include exercise; weight loss; various supportive devices; acetaminophen or nonsteroidal anti-inflammatory drugs (eg, ibuprofen); nutritional supplements (glucosamine, chondroitin); and intra-articular viscosupplements. Corticosteroid injection may be considered when relief from nonsteroidal anti-inflammatory drugs is insufficient, or the patient is at risk of gastrointestinal adverse

events. If symptom relief is inadequate with conservative measures, invasive treatments may be considered. Total knee arthroplasty is an operative treatment for symptomatic osteoarthritis of the knee.

PLANTAR FASCIITIS
Plantar fasciitis is a common cause of foot pain in adults, characterized by deep pain in the plantar aspect of the heel, particularly on arising from bed. While the pain may subside with activity, in some patients the pain persists and can impede activities of daily living. On physical examination, firm pressure will elicit a tender spot over the medial tubercle of the calcaneus. The exact etiology of plantar fasciitis is unclear, although the repetitive injury is suspected. Heel spurs are a common associated finding, although it has never been proven that heel spurs cause the pain. Asymptomatic heel spurs can be found in up to 10% of the population.

Treatment
Most cases of plantar fasciitis are treated with conservative therapy, including rest or minimization of running and jumping, heel cups, and nonsteroidal anti-inflammatory drugs. Local steroid injection may also be used. Improvement may take up to 1 year in some cases.

OCCIPITAL NEURALGIA
Occipital neuralgia is a specific type of headache that is located on one side of the upper neck, back of the head, and behind the ears, and sometimes extending to the scalp, forehead, and behind the eyes. The pain, which may be piercing, throbbing, or electric-shock-like, follows the course of the greater and lesser occipital nerves. Occipital neuralgia is believed to occur due to pressure or irritation to the occipital nerves, which may result from injury, entrapment by tight muscles, or inflammation.

Treatment
Treatment may include massage and rest, muscle relaxants, nerve blocks, and injection of steroids directly into the affected area.

CERVICOGENIC HEADACHE
Cervicogenic headache is a headache that is secondary to a disorder of the cervical spine. The pain may be referred from facet joints, intervertebral discs, or soft tissue. The pain is constant rather than throbbing, and may be aggravated by movements of the neck or pressure to certain areas on the neck. The first 3 cervical spinal nerves can refer pain to the head. The C1 suboccipital nerve innervates the atlanto-occipital joint; the C2 spinal nerve and the C3 dorsal ramus have close proximity to and innervate the C2-C3 facet joint. The C2-3 facet joint is the most frequent source of a cervicogenic headache. A diagnosis of a cervicogenic headache may be confirmed by an anesthetic block of the lateral atlanto-axial joint, the C2-3 facet joint, or the C3-4 facet joint.

Treatment
Treatment may include nerve blocks, physical therapy, and exercise.

NERVE RADIOFREQUENCY ABLATION
Nerve radiofrequency ablation (RFA) is a minimally invasive method that involves the use of heat and coagulation necrosis to destroy tissue. A needle electrode is inserted through the skin and into the tissue to be ablated. A high-frequency electrical current is applied to the target tissue. A small sphere of tissue is coagulated around the needle by the heat generated. It is theorized that the thermal lesioning of the nerve destroys peripheral sensory nerve endings, resulting in the alleviation of pain. Cooled radiofrequency (RF) treatment is a variation of nerve RFA using a special device that applies more energy at the desired location without excessive heat diffusing beyond the area, causing less tissue damage away from the nerve. The goal of ablating the nerve is the same.

For the indications assessed in this evidence review, nerve RFA should be distinguished from RF energy applied to areas other than the nerve to cause tissue damage. Some patients have been treated for plantar fasciitis with a fasciotomy procedure using an RF device. This procedure does not ablate a specific nerve.

Nerve RFA is also distinguished from pulsed RF treatment, which has been investigated for different types of pain. The mechanism of action of pulsed RF treatment is uncertain, but it is thought not to destroy the nerve. If it does produce some degree of nerve destruction, it is thought to cause less damage than standard RFA. Some studies refer to pulsed RF treatment as ablation.

CRYONEUROLYSIS
Cryoneurolysis is being investigated to alleviate pain in knee osteoarthritis and to manage pain following total knee arthroplasty. Temperatures of -20° to -100°C applied to a nerve cause Wallerian (anterograde axonal) degeneration, with disruption of nerve structure and conduction but maintenance of the perineural and epineural elements of the nerve bundle. Wallerian degeneration allows complete regeneration and recovery of nerve function in about 3 to 5 months. The iovera cryoablation system is a portable handheld device that applies percutaneous and targeted delivery of cold to superficial peripheral nerves.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
A number of RF generators and probes have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. In 2005, the SInergy®‡ (Kimberly-Clark/Baylis), a water-cooled single-use probe, was cleared by FDA, listing the Baylis Pain Management Probe as a predicate device. The intended use is with an RF generator to create RF lesions in nervous tissue. FDA product code: GXD.

In 2011, NeuroTherm®‡ NT 2000 (NeuroTherm) was cleared for marketing by FDA through the 510(k) process. FDA determined that this device was substantially equivalent to existing devices for use in lesioning neural tissue. Existing predicate devices included the NeuroTherm NT 1000, Stryker Multi-Gen, and Cosman G4 RF Generator.

In 2013, the Cryo-Touch IV (iovera; Myoscience) was cleared for marketing by FDA through the 510(k) process (K123516). Predicate devices were the Cryo-Touch II (K102021) and Cryo-Touch III (K120415).

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Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source

This review includes indications for heel pain due to plantar fasciitis and knee pain due to osteoarthritis. This review also evaluates the evidence for radiofrequency ablation (RFA) of a cervicogenic headache. RFA and cryoablation of other peripheral nerves are not addressed herein.

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 a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one 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. RCTs 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.

RADIOFREQUENCY ABLATION FOR KNEE OSTEOARTHRITIS

Clinical Context and Therapy Purpose
The purpose of RFA in patients who have knee osteoarthritis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in patients with knee osteoarthritis?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is patients with knee osteoarthritis.

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Interventions
The therapy being considered is RFA.

Comparators
The following therapy is currently being used to make decisions treating osteoarthritis: conservative management, which may include analgesics, physical therapy, or corticosteroid injection.

Outcomes
The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most commonly measured with a visual analog scale (VAS) or numeric rating scale (NRS). The Oxford Knee Score is scaled between 12 and 60, with 12 representing the best outcome. Quantifiable pre- and posttreatment measures of functional status are also used, such as 12-Item Short-Form Health Survey (SF-12) and SF-36. The Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) is also frequently used to evaluate function due to osteoarthritis.

Because of the variable natural history of osteoarthritis and the subjective nature of the outcome measures, RCTs are needed to determine whether outcomes are improved with interventions for pain. Trials should include a homogenous population of patients with a defined clinical condition, use standardized outcome measures when possible, and define a priori the clinically significant magnitude of response.

Timing
The time for follow-up is within days to determine procedural success and at least 6 months to 1 year to evaluate durability.

Setting
RFA would be administered in an outpatient setting, typically pain clinics.

Randomized Controlled Trials
Davis et al (2018) reported on a multicenter randomized trial comparing RFA with corticosteroid injection in 151 patients who had chronic (>6 months) knee pain unresponsive to conservative therapy (see Table 1). At 1 month after treatment, both groups showed a reduction in pain, with a 0.9-point difference on an 11-point NRS (see Table 2). By 3 months after treatment, pain scores had increased in the steroid group, while pain scores in the RFA group remained low throughout the 6-month follow-up. At the 6-month follow-up, 74.1% of patients in the RFA group were considered responders (≥50% decrease in the NRS), compared with 16.2% of patients treated with steroid injections ($p<0.001$). Follow-up is continuing to assess the durability of this more resource-intensive treatment approach.

Table 1. Summary of Key RCT Characteristics

Study	Countries	Sites	Participants	Interventions	
				Active	Comparator
Davis et al (2018)	U.S.	11	151 patients with chronic (>6 mo) knee pain unresponsive to conservative therapy; pain score ≥6; OA grades 2-4; Oxford Knee Score of ≤35; a positive diagnostic genicular nerve block[a]	76 patients treated with cooled RFA under fluoroscopic guidance	75 patients treated with intra-articular steroid

OA: osteoarthritis; RCT: randomized controlled trial; RFA: radiofrequency ablation.
[a] At least 50% reduction in numeric rating scale for pain with anesthetic injection to the superomedial and inferomedial branches of the saphenous nerve and the superolateral branch of the femoral nerve.

Table 2. Summary of Key RCT Results

Study	Mean NRS Pain Scores (SD)			Responders at 6 Months, %[a]	Mean Oxford Knee Score at 6 Months (SD)	Global Perceived Effect at 6 Months, %
	At 1 Month	At 3 Months	At 6 Months			
Davis et al (2018)						
N	136	132	126	126	125	126
RFA	3.0 (2.3)	2.8 (2.2)	2.5 (2.3)	74.1	35.7 (8.8)	91.4
Steroid	3.9 (2.2)	5.2 (2.0)	5.9 (2.2)	16.2	22.4 (8.5)	23.9
p	0.025	<0.001	<0.001	<0.001	<0.001	<0.001

SD: standard deviation; NRS: numeric rating scale; RCT: randomized controlled trial.
[a] Greater than 50% reduction in the NRS.

The purpose of the gaps tables (see Tables 3 and 4) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 3. Relevance Gaps

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Davis et al (2018)					1. Follow-up >6 mo is needed to evaluate durability of the procedure

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
RFA: radiofrequency ablation.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 4. Study Design and Conduct Gaps

Study	Allocation[a]	Blinding[b]	Selective Reporting[d]	Data Completeness[e]	Power[d]	Statistical[f]
Davis et al (2018)		1. Patients not blinded to treatment assignment, which might have affected subjective scores		1. Unequal loss to follow-up in both groups 3. Crossovers to RFA were allowed at 6 mo		2. The study used Wilcoxon signed-rank sum test rather than a repeated-measures test

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
RFA: radiofrequency ablation.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Observational Studies

Observational studies can provide information on durability that is not available from RCTs. Follow-up to 12 months was reported in a prospective study of 25 patients (see Tables 5 and 6). The response rate was 88% at 1 month after treatment, decreasing to 64% at 6 months and 32% at 12 months.

Table 5. Summary of Key Case Series Characteristics

Study	Country	Participants	Treatment Delivery	Follow-Up
Santana Pineda et al (2017)	E.U.	25 patients with grade III-IV knee osteoarthritis (n=24) or after total knee arthroplasty (n=1) and intractable pain with VAS ≥5 for >6 mo	RFA of superior medial, superior lateral, and inferior medical genicular nerves with electrode tips placed on periosteal areas and guided by ultrasound and neurostimulation	12 mo

RFA: radiofrequency ablation; VAS: visual analog scale.

Table 6. Summary of Key Case Series Results

Study	Treatment	Proportion With ≥50% Improvement in VAS, n/N (%)		
		At 1 Month	At 6 Months	At 12 Months
Santana Pineda et al (2017)	RFA of genicular nerves	22/25 (88)	16/25 (64)	8/25 (32)

VAS: visual analog scale.

Section Summary: Radiofrequency Ablation for Knee Osteoarthritis
The evidence on RFA for knee pain includes an RCT with over 100 patients that compared RFA with steroid injection. At 1 month after treatment, pain scores on an 11-point NRS differed by 0.9 points, a variance that was statistically significant but of marginal clinical significance. The subjective outcome measures might also have been influenced by the novelty of the treatment in this unblinded study. By 3 months after treatment, pain scores had increased in the steroid group, consistent with the known durability of treatment. Pain scores in the RFA group remained low throughout the 6-month follow-up. Follow-up is continuing to assess the durability of this treatment approach. In an observational study of 25 patients, about one-third continued to show a response at 1 year after RFA of the genicular nerves.

CRYONEUROLYSIS FOR KNEE OSTEOARTHRITIS OR TOTAL KNEE ARTHROPLASTY

Clinical Context and Therapy Purpose
The purpose of cryoneurolysis in patients who have osteoarthritis or total knee arthroplasty (TKA) is to provide a treatment option that is an alternative to or an improvement on existing therapies. Pain control in patients with knee osteoarthritis can delay TKA, while pain control following TKA is essential for patients to participate in physical therapy and promote recovery.

The question addressed in this evidence review is: Does the use of cryoneurolysis improve the net health outcome in patients with osteoarthritis or following TKA?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is patients with osteoarthritis or who are undergoing TKA.

Interventions
The therapy being considered is percutaneous cryoneurolysis of the anterior femoral cutaneous nerve and/or the infrapatellar branch of the saphenous nerve.

Comparators
The following therapies are currently being used to make decisions about treating osteoarthritis or TKA: conservative management, which may include corticosteroid injection or oral medications, for osteoarthritis, and opioids or peripheral nerve blocks with anesthetics, for TKA.

Outcomes
The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is most commonly measured with a VAS or NRS. The Oxford Knee Score is scaled between 12 and 60, with 12 representing the best outcome. Quantifiable pre- and posttreatment measures of functional status are also used, such as SF-12 and SF-36. The WOMAC score is also frequently used to evaluate function due to osteoarthritis.

Timing
The time for follow-up is within days to determine procedural success and at least 6 months to a year to evaluate durability.

Setting
Cryoneurolysis would be administered in an inpatient surgical setting for TKA, and in an outpatient setting, typically pain clinics, for osteoarthritis.

Randomized Controlled Trials
Radnovich et al (2017) reported a double-blind multicenter RCT of cryoneurolysis for patients with mild-to-moderate osteoarthritis (see Table 7). Compared with sham-treated patients, cryoneurolysis resulted in a greater decrease in WOMAC pain score, WOMAC total score, and VAS score at 30 days (see Table 8). The cryoneurolysis group also had better WOMAC total scores at 90 days, but not at 60 days. Improvements in VAS scores did not differ significantly between active and sham treatment groups at 60 and 90 days.

Table 7. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Radnovich et al (2017)	U.S.	17	2013-2016	180 patients with mild-to-moderate (grade II-III) knee osteoarthritis with knee pain ≥40 mm/100-mm VAS and ≥50% reduction in pain on diagnostic block	n=121 percutaneous cryoneurolysis targeting the IBSN with anatomic landmarks (visual and palpation)	n=59 sham cryoneurolysis with a sham tip and local anesthetic

IBSN: infrapatellar branch of the saphenous nerve; RCT: randomized controlled trial; VAS: visual analog score.

Table 8. Summary of Key RCT Results

Study	Change in WOMAC Score (SEM)				VAS Score (SEM)		
	Pain at 30 Days	Total at 30 Days	At 60 Days	At 90 Days	At 30 Days	At 60 Days	At 90 Days
Radnovich et al (2017)							
N	180	180	180	180	180	180	180
Cryoneurolysis	-16.65 (1.26)	-78.78 (5.81)	-75.75 (5.87)	-80.31 (5.89)	-40.09 (2.87)	-38.53 (2.91)	-37.90 (3.01)
Sham	-9.54 (1.63)	-48.26 (7.51)	-56.28 (7.58)	-56.51 (7.60)	-27.83 (3.68)	-32.44 (3.73)	-31.58 (3.86)
Diff (95% CI)	-7.12 (-11.01 to -3.22)	-30.52 (-48.52 to -12.53)	-19.47 (-37.64 to -1.30)	-23.80 (-42.02 to -5.57)	-12.25 (-21.16 to -3.35)	-6.09 (-15.11 to 2.94)	-6.32 (-15.66 to 3.01)
p	0.004	0.001	0.036[a]	0.011	0.007	0.185	0.183

CI: confidence interval; Diff: difference; VAS: visual analog score; WOMAC: Western Ontario and McMaster Osteoarthritis Index.
[a] Statistical significance was set at a 1-sided level of 0.025.

Tables 9 and 10 display notable gaps identified in the studies evaluated.

Table 9. Relevance Gaps

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Radnovich et al (2017)	4. A more relevant population would be patients with moderate-to-severe knee osteoarthritis				

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 10. Study Design and Conduct Gaps

Study	Allocation[a]	Blinding[b]	Selective Reporting[d]	Data Completeness[e]	Power[d]	Statistical[f]
Radnovich et al (2017)						2. Unclear whether data were modeled for each time point independently or longitudinally

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Retrospective Studies

Dasa et al (2016) conducted a chart review of patients who underwent TKA with or without cryoneurolysis. Pain control for the first 50 patients who had received perioperative cryoneurolysis was compared with that of 50 patients who were treated before cryoneurolysis was introduced at their institution. The nerves targeted were the infrapatellar branch of the saphenous nerve and the anterior femoral cutaneous nerve. Aside from cryoneurolysis, both groups received the same multimodal pain control. The length of stay was 2 days or more in 6% of the cryoneurolysis group compared with 67% of the control group p<0.001). The mean length of stay was 0.8 days (SD=1.14) for the treatment group compared with 1.7 days (SD=1.01) for the control group. The cryoneurolysis group also required 45% fewer opioids in the first 12 weeks after

surgery and had significantly reduced symptoms at the 6- and 12-week follow-up compared with the control group. Prospective RCTs are needed to confirm the results of this retrospective study.

Technical Issues
As noted in a review by Gabriel and Ilfeld (2018), several technical issues have yet to be resolved, including the optimal number of applications for each nerve, the duration of treatment, and the duration of thawing before moving the cannula. The most effective method for determining the location of the probe (eg, ultrasound or using anatomic landmarks) also needs to be established.

Section Summary: Cryoneurolysis for Knee Osteoarthritis
An RCT with 180 patients has compared cryoneurolysis with sham treatment in patients who had knee osteoarthritis. Cryoneurolysis resulted in a greater decrease in WOMAC pain, WOMAC total, and VAS score at 30 days compared with sham-treated controls. Subsequent measurements showed no significant benefit of cryoneurolysis on WOMAC score at 60 days or in VAS scores at 60 or 90 days. Several technical issues including the optimal number of applications for each nerve, the duration of treatment, and the duration of thawing before moving the cannula, have yet to be resolved. Perioperative cryoneurolysis has been shown to reduce the length of stay and opioid consumption in patients undergoing TKA. These results need to be confirmed in an RCT.

RFA FOR PLANTAR FASCIITIS

Clinical Context and Therapy Purpose
The purpose of RFA in patients who have plantar fasciitis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in patients with plantar fasciitis?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is patients with plantar fasciitis.

Interventions
The therapy being considered is RFA.

Comparators
The following therapy is currently being used to make decisions about treating plantar fasciitis: conservative management, which may include corticosteroid injection.

Outcomes
The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most commonly measured using a VAS. Quantifiable pre- and posttreatment measures of functional status are also used, such as the American Orthopedic Foot and Ankle Society (AOFAS) ankle-hindfoot score. The AOFAS ankle-hindfoot scores range from 0 to 100, with up to 40 points for pain, 50 points for functional aspects, and 10 points for alignment. A high score indicates a better outcome.

Because of the variable natural history of plantar fasciitis and the subjective nature of the outcome measures, RCTs are needed to determine whether outcomes are improved with interventions for pain. Trials should include a homogenous population of patients with a defined clinical condition, use standardized outcome measures when possible, and define a priori the clinically significant magnitude of response.

Timing
The time for follow-up is within days to determine procedural success and at least 6 months to a year to evaluated durability.

Setting
RFA would be administered in an outpatient setting, typically pain clinics.

Randomized Controlled Trials
Two double-blind sham-controlled randomized trials have assessed RFA for the treatment of chronic heel pain (see Table 11). Wu et al (2017) randomized 36 patients to ultrasound-guided pulsed radiofrequency of the posterior tibial nerve. First step pain, average pain, and the AOFAS ankle-hindfoot score were assessed at baseline and at 1, 4, 8, and 12 weeks. Scores at 12 weeks are shown in Table 12. Changes in VAS score in the sham group were modest (<1 on a 10-point VAS) and of short duration (statistically significant at weeks 1 and 4, but not weeks 8 and 12). The AOFAS ankle-hindfoot score was 60.55 at baseline and 60.05 at 12 weeks in the sham group. In the RFA group, VAS scores at weeks 1, 4, 8, and 12 were all significantly lower than baseline ($p<0.001$), and the AOFAS ankle-hindfoot score increased from 55.5 to 87.6 ($p<0.001$). The improvements in pain and function were greater in the RFA group than in the control group ($p<0.001$ for all measures).

Landsman et al (2013) reported on a double-blind randomized crossover trial of RFA applied along the medial aspect of the heel. Crossover to the alternative treatment was allowed at 4 weeks. Outcomes assessed weekly were a pain VAS score reported at the first step in the morning, average pain level, and peak pain level (see Table 12). In a graphic presentation of results, patient pain levels for all 3 outcomes decreased after RFA but showed minimal change after sham. After patients crossed over from sham to RFA, there was a steep drop in all pain outcomes. The maximum follow-up assessment was at 16 weeks and appeared to show similar pain levels throughout the follow-up period.

Table 11. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Wu et al (2017)	Taiwan	1	2014-2016	36 patients (40 feet) with recalcitrant plantar fasciitis	Ultrasound-guided pulsed RF stimulation of the posterior tibial nerve	Sham with ultrasound-guided lidocaine injection
Landsman et al (2013)	U.S.	Multicenter	NR	17 patients failed at least 3 prior types of treatments, pain for >3 mo, and VAS score ≥5	RFA procedure, including stimulation of sensory nerves in an awake patient	Sham with all aspects of the RFA procedure, except delivery of RF energy at the final step

NR: not reported; RCT: randomized controlled trial; RF: radiofrequency; RFA: radiofrequency ablation; VAS: visual analog scale.

Table 12. Summary of Key RCT Results

Study	First Step Pain on VAS Score	Average VAS Pain Score		AOFAS Ankle-Hindfoot Score
	At 12 Weeks	At 12 Weeks		
Wu et al (2017)				
N	36	36		36
RFA (SD)	1.79 (1.62)	1.54 (1.26)		87.60 (9.12)
Sham (SD)	6.13 (1.75)	6.09 (1.70)		60.05 (11.38)
	Change At 4 Weeks	Change Score	Change in Peak Pain	
Landsman et al (2013)				
N	17	17	17	
RFA	5.0	4.06	5.33	
Sham	1.33	0.8	1.80	
p	0.30	0.047	0.048	

AOFAS: American Orthopedic Foot and Ankle Society; RCT: randomized controlled trial; RFA: radiofrequency ablation; VAS: 10-cm visual analog score.

Tables 13 and 14 display notable gaps identified in each study.

Table 13. Relevance Gaps

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Wu et al (2017)	3. Study did not report a minimum VAS for inclusion criteria				
Landsman et al (2013)		1. Targeted nerve not clearly defined			1. Crossover allowed at 4 wk

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
VAS: visual analog score.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 14. Study Design and Conduct Gaps

Study	Allocation[a]	Blinding[b]	Selective Reporting[d]	Follow-Up[e]	Power[d]	Statistical[f]
Wu et al (2017)						
Landsman et al (2013)				3. Crossovers at 4 wk prevented longer term assessments	1. Power calculations not reported	3. Confidence intervals not reported

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Case Series

The largest case series with the longest follow-up is by Cozzarelli et al (2010). This study reported on a 12-year follow-up of 82 patients who had undergone RFA for heel pain. Patients had undergone RFA between 1994 and 1995 and had been interviewed at 5, 10, and 12 years postprocedure. Baseline pain levels before the procedure were recalled retrospectively at the follow-up interviews. Of 99 patients potentially eligible to be interviewed, the study evaluated 82 patients. The results were presented without statistical testing. It appears that 73 of 82 patients reported being pain-free at 12 years. On a 0-to-10 pain VAS, the pain-free patients rated their preprocedure pain at a mean of 7.1 and at 0 postprocedure.

Cione et al (2009) reported on a retrospective case series of 75 patients treated with RFA. Patients who underwent RFA between 2000 and 2003 were surveyed in 2004 to assess preprocedure and current pain status. In this series, the actual number of treated patients is unknown, and preprocedure pain status was assessed only at the follow-up survey. Median preprocedure pain VAS was 9 (range, 2-10) and the postprocedure pain VAS was 1 (range, 0-8; $p<0.001$).

Section Summary: Plantar Fasciitis

Two randomized, double-blind trials and several case series have shown consistent sensory nerve reductions in pain after RFA for patients with heel pain due to plantar fasciitis. However, several case series had methodologic weaknesses. In two of them, all pain assessments were performed retrospectively, including pretreatment pain assessment. The 2 randomized trials enrolled a few subjects. Due to crossover at 4 weeks in one of the trials, the randomized comparison only evaluated outcomes to 4 weeks. To be

more confident in the efficacy of this treatment, studies with larger samples and longer follow-up would be necessary. The safety of the procedure cannot be fully evaluated in the small samples studied so far.

RFA FOR OCCIPITAL NEURALGIA AND CERVICOGENIC HEADACHE

Clinical Context and Therapy Purpose

The purpose of RFA in patients who have occipital neuralgia or a cervicogenic headache is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in patients with occipital neuralgia or a cervicogenic headache?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is patients with occipital neuralgia or a cervicogenic headache.

Interventions

The therapy being considered is RFA. RFA involves the percutaneous insertion of a catheter that is directed toward the nerve of interest. RFA can be used to ablate the nerve by thermal lesioning.

Comparators

The following therapy is currently being used to make decisions about treating occipital neuralgia or a cervicogenic headache: conservative management.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is most commonly measured with a VAS or RNS. Quantifiable pre- and posttreatment measures of functional status are also used, such as SF-12 and SF-36.

Timing

The time for follow-up is within days to determine the procedural success and months to years to evaluate durability.

Setting

RFA would be administered in an outpatient setting, typically pain clinics.

Systematic Reviews

Grandhi et al (2018) conducted a systematic review of RFA for the treatment of a cervicogenic headache. Ten studies met selection criteria, including 3 RCTs, 3 prospective studies, and 4 retrospective studies. There were no high-quality RCTs. Two of the RCTs evaluated RFA of the facet joints and failed to find a benefit of RFA. The third RCT compared RFA with steroid injection of the greater occipital nerve, finding no difference between the groups in the short term, but a longer duration of pain control in the RFA group.

A systematic review by Ducic et al (2014) did not identify any RCTs assessing RFA for chronic occipital neuralgia. Reviewers identified 3 case series (total N=131 patients) on pulsed RF treatment. Success rates in these series ranged from 51% to 100%, with an overall success rate of 55%. Follow-up ranged from 3 to 10 months.

Section Summary: RFA for Occipital Neuralgia and Cervicogenic Headache
No RCTs of RFA for chronic occipital neuralgia have been identified. A systematic review identified 3 RCTs of RFA for a cervicogenic headache, none of which were high quality. Pain is a subjective, patient-reported measure that is particularly susceptible to placebo effect. Trials with sham or active controls are needed to evaluate the efficacy of this treatment.

SUMMARY OF EVIDENCE
For individuals who have knee osteoarthritis who receive RFA of peripheral nerves, the evidence includes an RCT with over 100 patients. Relevant outcomes include symptoms, functional outcomes, and quality of life. The RCT compared RFA with steroid injection. At 1 month after treatment, pain scores on an 11-point numeric rating scale differed by 0.9 points, a variance that was statistically significant but of marginal clinical significance. The subjective outcome measures may also have been influenced by the novelty of the treatment in this unblinded study. By 3 months after treatment, pain scores had increased in the steroid group, while pain scores in the RFA group remained low throughout the 6-month follow-up. In an observational study of 25 patients, about one-third continued to show a response 1 year after RFA of the genicular nerves. Longer follow-up in controlled trials is needed to establish the durability of this treatment approach. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have knee osteoarthritis or total knee arthroplasty who receive cryoneurolysis of peripheral nerves, the evidence includes an RCT with 180 patients and a retrospective comparative study. Relevant outcomes include symptoms, functional outcomes, and quality of life. Cryoneurolysis in patients with knee osteoarthritis resulted in a greater decrease in WOMAC pain score, WOMAC total score, and visual analog scale score at 30 days compared with sham-treated controls. However, subsequent measurements showed no significant benefit of cryoneurolysis on WOMAC score at 60 days or visual analog scale scores at 60 or 90 days. Perioperative cryoneurolysis was shown in a retrospective comparison to reduce the length of stay and opioid use in patients undergoing total knee arthroplasty. These results need to be confirmed in an RCT. Several technical issues including the optimal number of applications for each nerve, the duration of treatment, and the duration of thawing before moving the cannula have not been resolved. The most effective method for determining probe insertion location (eg, ultrasound-guided or based on anatomic landmarks) also need to be established. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have plantar fasciitis who receive RFA of peripheral nerves, the evidence includes 2 RCTs. Relevant outcomes include symptoms, functional outcomes, and quality of life. One of the randomized trials only evaluated 17 patients, and assessment of randomized outcomes was limited to 4 weeks posttreatment. A second RCT evaluated 36 patients out to 12 weeks. The case series generally had small sample sizes, and many had methodologic deficiencies such as retrospective assessment of pain. To

be more confident in the efficacy of this treatment, controlled trials with larger samples and longer follow-up would be necessary. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have occipital neuralgia or cervicogenic headache who receive RFA of peripheral nerves, the evidence includes systematic reviews. Relevant outcomes are symptoms, functional outcomes, and quality of life. No RCTs of RFA for chronic occipital neuralgia have been identified. Three RCTs of RFA for a cervicogenic headache have been published, none of which were high quality. Pain is a subjective, patient-reported measure that is particularly susceptible to placebo effect. Randomized trials with sham or active-controls are needed to evaluate the efficacy of this treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

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Ablation of Peripheral Nerves to Treat Pain

Policy # 00503
Original Effective Date: 05/18/2016
Current Effective Date: 02/01/2019

Policy History

Original Effective Date: 05/18/2016
Current Effective Date: 02/01/2019

05/05/2016	Medical Policy Committee review
05/18/2016	Medical Policy Implementation Committee approval. New policy.
11/01/2016	Coding update
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
05/04/2017	Medical Policy Committee review
05/17/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/03/2018	Medical Policy Committee review
05/16/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Title changed from "Radiofrequency Ablation of Peripheral Nerves to Treat Pain" to "Ablation of Peripheral Nerves to Treat Pain". Added four investigational statements as follows: cryoneurolysis of peripheral nerves to treat pain associated with knee osteoarthritis (OA) or total knee arthroplasty is considered to be investigational; radiofrequency ablation (RFA) of peripheral nerves to treat pain associated with occipital neuralgia or cervicogenic headache is considered to be investigational; diagnostic block performed before radiofrequency ablation (RFA) is considered to be investigational; and ablation of peripheral nerves to treat pain in all other conditions, with the exception of facet joint pain is considered to be investigational.

Next Scheduled Review Date: 11/2019

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Ablation of Peripheral Nerves to Treat Pain

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	64450, 64640
HCPCS	No codes
ICD-10 Diagnosis	M17.0-M17.9, M72.2

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B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
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