Radiofrequency ablation of peripheral nerves to treat pain associated with knee osteoarthritis or plantar fasciitis is considered investigational.

Cryoneurolysis of peripheral nerves to treat pain associated with knee osteoarthritis or total knee arthroplasty is considered investigational.

Radiofrequency ablation of peripheral nerves to treat pain associated with occipital neuralgia or cervicogenic headache is considered investigational.

Ablation of peripheral nerves to treat pain is considered investigational in all other conditions, with the exception of facet joint pain (see evidence review 7.01.116).

Radiofrequency treatment is considered a neurolytic agent by CPT so codes in the Codes table would be reported for radiofrequency ablation of a peripheral nerve.

CPT instructs that pulsed radiofrequency treatment is reported with an unlisted code.
these devices may be assessed only by their medical necessity.

BACKGROUND

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**

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 and 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 water-cooled probe that applies more energy at the desired location without excessive heat diffusing beyond the area, causing less tissue damage away from the nerve (see Table 1). The goal of ablating the nerve is the same.

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 but is thought to cause less damage than standard RFA. Some studies refer to pulsed RF treatment as ablation.

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.

**Table 1. Types of Radiofrequency Ablation**

<table>
<thead>
<tr>
<th>Type</th>
<th>Procedure</th>
<th>Tissue Temperature</th>
<th>Key Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard RFA</td>
<td>Electrode tip provides thermal energy for 90 – 130 seconds</td>
<td>70 – 90 °C</td>
<td>Longer lasting but with more adjacent thermal tissue injury and limitation in size and shape of lesion.</td>
</tr>
<tr>
<td>Pulsed RFA</td>
<td>Non-ablative - provides 20 ms pulses every 30 seconds</td>
<td>42 °C</td>
<td>Limits tissue damage but results in incomplete and transient pain relief</td>
</tr>
<tr>
<td>Cooled RFA</td>
<td>Water circulates through RF electrode to cool the tip</td>
<td>60 °C</td>
<td>Larger lesion with limited thermal injury to tissue. Less complete and shorter durability than standard RFA</td>
</tr>
</tbody>
</table>

RF: radiofrequency; RFA: radiofrequency ablation

Adapted from Oladeji et al (2019)

**Cryoneurolysis**

Cryoneurolysis is being investigated to alleviate pain in knee OA 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 the maintenance of the perineural and epineural elements of the nerve bundle. Wallerian degeneration allows complete regeneration and recovery of nerve function in about three to five months. The iovera® cryoablation system is a portable
handheld device that applies percutaneous and targeted delivery of cold to superficial peripheral nerves.

**Regulatory Status**

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 Snnergy® (Kimberly-Clark/Baylis), a water-cooled single-use probe, was cleared by the 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 the FDA through the 510(k) process. The 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 the FDA through the 510(k) process (K123516). Predicate devices were the Cryo-Touch II (K102021) and Cryo-Touch III (K120415).

In 2017, the COOLIEF Cooled Radiofrequency Probe (Avanos, previously known as Halyard Health) was cleared for marketing by the FDA through the 510(k) process to be used in conjunction with a radiofrequency generator to create lesions in nervous tissue (K163461). "The device is also indicated for creating radiofrequency lesions of the genicular nerves for the management of moderate to severe knee pain of more than 6 months with conservative therapy, including medication, in patients with radiologically-confirmed osteoarthritis (grade 2-4) and a positive response (≥ 50% reduction in pain) to a diagnostic genicular nerve block." FDA Product Code: GXI

**RATIONALE**

This evidence review was created in January 2016 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through July 9, 2019.

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 technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and 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, two domains are examined: the relevance, and 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 with knee OA who have severe refractory pain is to provide a treatment option that is an alternative to intra-articular injections or total joint replacement. Pain in OA can be transmitted via the genicular sensory nerves, which are branches of the femoral, tibial, peroneal, saphenous, and obturator nerves around the knee. The genicular nerve branches can be divided into a four-quadrant system—superomedial, superolateral, inferomedial, and inferolateral. Nerves in the superomedial, superolateral, and inferomedial quadrants are located near the periosteum, but the inferolateral branch is close to the peroneal nerve and is usually avoided. The exact neuroanatomy around the knee is variable and can also be affected by chronic OA. Although the location of the target nerves is aided by palpating the bony landmarks and fluoroscopy, variability may prevent the exact localization. Diagnostic nerve blocks have been evaluated to confirm the location of the genicular nerves and predict efficacy. In addition to the genicular nerves, studies have reported RFA of the saphenous nerve, the sciatic nerve, the femoral, tibial, saphenous nerves, and peripatellar plexus in combination, and the intra-articular joint space. (Jamison ref)

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

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

Patients

The relevant population of interest are patients with knee OA.

Interventions

The therapy being considered is RFA of the superomedial, inferomedial, and superolateral genicular nerves. Due to the variable location of the genicular nerves, it is thought that the increased area of denervation associated with cooled-RFA may be more effective than standard or pulsed RFA

Comparators

The following therapy is currently being used to make decisions treating OA: conservative management, which may include analgesics, physical therapy, or intra-articular injections.

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 the 12-Item and 36-Item Short-Form Health Survey. The Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) is also frequently used to evaluate pain and function due to OA. The WOMAC includes three subscales: pain, stiffness, and physical functioning. Scores range from 0 to 96, with higher scores indicating greater disability.

Because of the variable natural history of OA and the subjective nature of the outcome measures, RCTs are needed to determine whether outcomes are improved with interventions for pain. Trials should
Radiofrequency Ablation of Peripheral Nerves to Treat Pain

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.

The effect of RFA is likely to be transient, so the period for follow-up is within a month to determine procedural success and at least one year to evaluate durability. Longer follow-up is needed to evaluate whether denervation of sensory nerves of the knee could have adverse long-term effects on knee anatomy in patients with OA.

**Study Selection Criteria**

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of six months outcomes, and systematic reviews of RCTs.
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

**Systematic Reviews**

Jamison and Cohen (2018) identified 8 RCTs on RFA techniques to treat chronic knee pain for their qualitative systematic review. The number of participants ranged from 38 to 151, and techniques included RFA, cooled (C-RFA), and RFA combined with a variety of intra-articular treatments. The most common targets were the superomedial, superolateral, and inferomedial genicular nerves (six trials). One trial reported intra-articular treatment, and one trial did not specify the location. One trial evaluated the use of prognostic blocks. Thus, out of the eight RCTs, there were four trials that evaluated RFA or C-RFA of the genicular nerves compared to sham or other treatments in patients with OA (Tables 2 and 3). Trial size ranged from 38 to 151, and follow-up ranged from 3 to 6 months. Limitations of the studies included lack of blinding and insufficient follow-up. The trials by Davis et al (2018) and El-Hakeim et al (2018), both of which had 6 months follow-up, are described in greater detail below.

### Table 2. Systematic Review Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N (Range)</th>
<th>Design</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jamison and Cohen</td>
<td>to February 2018</td>
<td>4</td>
<td>Patients with OA of the knee who were treated with</td>
<td>322 (38 to 151)</td>
<td>RCT</td>
<td>3-6 mo</td>
</tr>
<tr>
<td>(2018)</td>
<td></td>
<td></td>
<td>RFA or C-RFA</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OA: osteoarthritis; RFA: radiofrequency ablation; C-RFA: cooled radiofrequency ablation; RCT: randomized controlled trial.

### Table 3. Comparison of RCTs Included in the Systematic Review by Jamison and Cohen

<table>
<thead>
<tr>
<th>Study</th>
<th>Trial Size</th>
<th>Prognostic Block</th>
<th>RF Method</th>
<th>Comparator</th>
<th>Follow-up</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choi et al</td>
<td>38</td>
<td>Yes</td>
<td>RFA</td>
<td>Sham</td>
<td>3 months</td>
<td>Short follow-up</td>
</tr>
<tr>
<td>Sari et al</td>
<td>73</td>
<td>No</td>
<td>RFA</td>
<td>IA Steroid</td>
<td>3 months</td>
<td>Short follow-up</td>
</tr>
<tr>
<td>Davis et al</td>
<td>151</td>
<td>Yes</td>
<td>C-RFA</td>
<td>IA Steroid</td>
<td>6 months</td>
<td>Patients not</td>
</tr>
</tbody>
</table>
Radiofrequency Ablation of Peripheral Nerves to Treat Pain

El-Hakeim et al (2018)\(^6\)

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al (2018)(^6)</td>
<td>U.S.</td>
<td>11</td>
<td>151 patients with chronic (&gt;6 mo) knee pain unresponsive to conservative therapy(^a); pain score ≥6; OA grades 2-4; Oxford Knee Score of ≤35; a positive diagnostic genicular nerve block(^b)</td>
<td>Cooled RFA of the genicular nerves under fluoroscopic guidance (n=76)</td>
</tr>
<tr>
<td>El-Hakeim et al (2018)(^2)</td>
<td>Egypt</td>
<td>1</td>
<td>60 patient with stage III or IV knee osteoarthritis</td>
<td>RFA of the genicular nerves under fluoroscopic guidance (n=30)</td>
</tr>
</tbody>
</table>

OA: osteoarthritis; RCT: randomized controlled trial; RFA: radiofrequency ablation.
Radiofrequency Ablation of Peripheral Nerves to Treat Pain

a. Conservative treatment included physical therapy, oral analgesics: ≤60 mg morphine equivalence, stable for 2 months; intra-articular injections with steroids and/or viscosupplementation, body mass index (BMI) <40, and reporting ≥50% response to blocks as

b. 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 5. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean Pain Scores (SD)</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At 1 Month</td>
<td>At 3 Months</td>
</tr>
<tr>
<td>Davis et al (2018)</td>
<td>NRS</td>
<td>136</td>
</tr>
<tr>
<td>RFA</td>
<td>3.0 (2.3)</td>
<td>2.8 (2.2)</td>
</tr>
<tr>
<td>Steroid injection</td>
<td>3.9 (2.2)</td>
<td>5.2 (2.0)</td>
</tr>
<tr>
<td>p-Value</td>
<td>0.025</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2 Weeks</td>
<td>3 Mo</td>
</tr>
<tr>
<td>N</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>RFA</td>
<td>2.47 (0.3)</td>
<td>2.83 (0.5)</td>
</tr>
<tr>
<td>Analgesics</td>
<td>3.63 (0.27)</td>
<td>4.93 (0.2)</td>
</tr>
<tr>
<td>p-Value</td>
<td>0.004</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SD: standard deviation; NRS: numeric rating scale; RCT: randomized controlled trial; RFA: radiofrequency ablation; VAS: visual analog score; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

a Greater than 50% reduction in the NRS.

Table 6. Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Populationa</th>
<th>Interventionb</th>
<th>Comparatorc</th>
<th>Outcomesd</th>
<th>Follow-Upe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al (2018)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1. Follow-up &gt;6 mo is needed to evaluate durability of the procedure</td>
</tr>
<tr>
<td>El-Hakeim et al (2018)</td>
<td>4. Patients were not selected by a positive response to a nerve block</td>
<td>2. Controls received only analgesics and physical therapy if needed</td>
<td></td>
<td>1. Follow-up &gt;6 mo is needed to evaluate durability of the procedure</td>
<td></td>
</tr>
</tbody>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
Radiofrequency Ablation of Peripheral Nerves to Treat Pain

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 7. Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation</th>
<th>Blinding</th>
<th>Selective Reporting</th>
<th>Data Completeness</th>
<th>Power</th>
<th>Statistical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al (2018)</td>
<td></td>
<td>1. Patients were not blinded to treatment assignment, which might have affected subjective scores</td>
<td>1. Unequal loss to follow-up</td>
<td>2. The study used Wilcoxon signed-rank sum test rather than a repeated-measures test</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>El-Hakeem et al (2018)</td>
<td>2. Allocation concealment not described</td>
<td>1. Patients were not blinded to treatment assignment, which might have affected subjective scores</td>
<td></td>
<td>2. The study did not use a repeated-measures test for the different time points</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

RFA: radiofrequency ablation.


Radiofrequency Ablation of Peripheral Nerves to Treat Pain

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).

Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

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. The follow-up to 12 months was reported by Santana Pineda et al (2017) in a prospective study of 25 patients (see Tables 8 and 9).\textsuperscript{d} The response rate was 88\% at 1 month after treatment, decreasing to 64\% at 6 months and 32\% at 12 months. Davis et al (2018) reported 12-month follow-up from the Davis et al (2018) RCT described above.\textsuperscript{e} Out of the 76 patients randomized to C-RFA, 52 (68\%) patients were available for follow-up at 12 months. Out of those 52, 34 (65\%) reported at least a 50\% decrease in pain on an NRS. Limitations of this observational portion of the study include the 32\% loss to follow-up and the lack of blinding for this subjective measure. All but 4 of the patients in the intra-articular steroid arm had crossed over to C-RFA by the 12-month follow-up.

Kapural et al (2019) reported a retrospective assessment of pain relief in 183 out of 205 (86\%) patients who had been treated with RFA of the genicular nerves and returned for evaluation.\textsuperscript{f} At follow-up (time not reported), 65\% of patients reported greater than 50\% pain relief and 77\% had a decrease in VAS of at least 2 points. The average duration of reported pain relief was 12.5 months (range 0 to 35). Opioid use was not reduced, but this result is confounded because 80\% of patients reported at least 1 additional source of chronic pain (eg, back, shoulder). The publication notes that pain scores were assessed at three and six months and at the latest visit, but is unclear about the range of follow-up and the time of the reported results.

These observational studies suggest that between one-third and two-thirds of patients will continue to report at least a 50\% reduction in pain at 12 months following RFA of the genicular nerves. No prospective studies have been identified that reported on the durability of the procedure after 12 months. One retrospective study was identified that had major flaws in reporting but concluded that 65\% of patients had continued treatment success at 12 months.

Table 8. Summary of Key Case Series Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Participants</th>
<th>Treatment Delivery</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Santana Pineda</td>
<td>E.U.</td>
<td>25 patients with grade III-IV knee OA (n=24) or after total knee arthroplasty</td>
<td>RFA of superior medial, superior lateral, and inferior medial genicular nerves with</td>
<td>12 mo</td>
</tr>
<tr>
<td>et al (2017)\textsuperscript{a}</td>
<td></td>
<td>(n=1) and intractable pain with VAS \geq 5 for \geq 6 mo.</td>
<td>electrode tips placed on periosteal areas and guided by ultrasound and neurostimulation</td>
<td></td>
</tr>
<tr>
<td>Davis et al</td>
<td>U.S.</td>
<td>52 out of 67 (78%) patients with knee OA treated with C-RFA in the RCT by</td>
<td>C-RFA of the geniculate nerves under fluoroscopic guidance as described in Davis et</td>
<td>12 mo</td>
</tr>
<tr>
<td>et al (2018)\textsuperscript{a}</td>
<td></td>
<td>Davis et al (2018; described above)\textsuperscript{b}</td>
<td>et al (2018)</td>
<td></td>
</tr>
<tr>
<td>Kapural et al</td>
<td>U.S.</td>
<td>205 patients with knee pain (21 had pain after TKA) who</td>
<td>C-RFA of the geniculate nerves under fluoroscopic guidance as described in</td>
<td>NR</td>
</tr>
</tbody>
</table>
had a positive response to a geniculate block and underwent C-RFA. Mean VAS pain prior to treatment was 8.5 and 2.2 after the nerve block.

C-RFA: cooled radiofrequency ablation; NR: not reported; OA: osteoarthritis; RFA: radiofrequency ablation; TKA: total knee arthroplasty; VAS: visual analog scale.

Table 9. Summary of Key Case Series Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Proportion With ≥50% Improvement in pain, n/N (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At 1 Month</td>
<td>At 6 Months</td>
</tr>
<tr>
<td>Santana Pineda et al (2017)13</td>
<td>RFA of genicular nerves</td>
<td>22/25 (88)</td>
</tr>
<tr>
<td>Davis et al (2018)10</td>
<td>C-RFA of genicular nerves</td>
<td>47/67 (70) (95% CI: 59.2 to 81.1)</td>
</tr>
<tr>
<td>Kapural et al (2019)11</td>
<td>C-RFA of genicular nerves</td>
<td>NR</td>
</tr>
</tbody>
</table>

CI: confidence interval; C-RFA: cooled radiofrequency ablation; NR: not reported; RFA: radiofrequency ablation; VAS: visual analog scale.

Section Summary: RFA for Knee OA

Knee OA is a common disorder in older adults. RFA of the genicular nerves has the potential to alleviate pain and improve function in this population, and might also delay or eliminate the need for TKA. To date, the evidence on RFA for knee pain includes 2 RCTs with a total of 211 patients with 6-month follow-up and prospective observational studies with 12 months of follow-up. The larger of the RCTs compared C-RFA to active control of steroid injection and utilized genicular nerve blocks to select patients for the study. At 1 month after treatment, pain scores on an 11-point NRS differed by less than 1 point, a finding that was statistically significant but of marginal clinical significance. By three months after treatment, pain scores had increased in the steroid group, consistent with the known durability of the treatment. Pain scores in the RFA group remained low in patients who remained in the study. The durability of this treatment approach to 1 year has been evaluated in a follow-up to the RCT, a retrospective study, and a small (n=25) independent prospective study. In both of the industry-sponsored publications, 65% of the patients treated with C-RFA reported a greater than 50% reduction in pain scores at 12 months. In an independent and prospective observational study, about one-third continued to show a response at one year after RFA of the genicular nerves. The second RCT used stimulation to identify the genicular nerves, rather than genicular nerve blocks with an anesthetic. None of the studies were blinded, which may have biased the subjective outcome measures. It should be noted that the anatomy of the genicular nerves is variable, and the best method for their identification has not been determined. Study in a larger number of patients, preferably in blinded studies with active
control and follow-up longer than 12 months, is needed to determine the benefits and potential harms of this treatment.

**Cryoneurolysis for Knee Osteoarthritis or Total Knee Arthroplasty**

**Clinical Context and Therapy Purpose**

The purpose of cryoneurolysis in patients who have OA or TKA is to provide a treatment option that is an alternative to standard therapies. Pain control in patients with knee OA 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 OA or following TKA?

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

**Patients**

The relevant population of interest are patients with OA 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 OA or TKA: conservative management, which may include corticosteroid injection or oral medications, for OA, and opioid 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 the 12-Item and 36-Item Short-Form Health Survey. The WOMAC score is also frequently used to evaluate function due to OA.

**Timing**

The time for follow-up is within days to determine procedural success and at least six 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 OA.

**Randomized Controlled Trials**

Radnovich et al (2017) reported a double-blind multicenter RCT of cryoneurolysis for patients with mild-to-moderate OA (see Table 10). 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 11). 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 10. Summary of Key RCT Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radnovich et al (2017)</td>
<td>U.S.</td>
<td>17</td>
<td>2013-16</td>
<td>180 patients with mild-to-moderate (grade II-III) knee OA with knee pain ≥40 mm/100-mm VAS and ≥50% reduction in pain on diagnostic block</td>
<td>n=121 percutaneous cryoneurolysis targeting the IBSN with anatomic landmarks (visual and palpation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n=59 sham cryoneurolysis with a sham tip and local anesthetic</td>
<td></td>
</tr>
</tbody>
</table>

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

Table 11. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Change in WOMAC Score (SEM)</th>
<th>VAS Score (SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pain at 30 Days</td>
<td>Total at 30 Days</td>
</tr>
<tr>
<td>Radnovich et al (2017)</td>
<td>-16.65 (1.26)</td>
<td>-78.78 (5.81)</td>
</tr>
<tr>
<td>Cryoneurolysis</td>
<td>-9.54 (1.63)</td>
<td>-48.26 (7.51)</td>
</tr>
<tr>
<td>Sham</td>
<td>-7.12 (1.32)</td>
<td>-30.52 (12.53)</td>
</tr>
<tr>
<td>Diff (95% CI)</td>
<td>-11.01 to 3.22</td>
<td>-48.52 to -12.53</td>
</tr>
<tr>
<td>p</td>
<td>0.004</td>
<td>0.001</td>
</tr>
</tbody>
</table>

CI: confidence interval; Diff: difference; RCT: randomized controlled trial; SEM: standard error of mean; VAS: visual analog score; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

* Statistical significance was set at a 1-sided level of 0.025.

Tables 12 and 13 display notable limitations identified in the studies evaluated.

Table 12. Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Populationa</th>
<th>Interventionb</th>
<th>Comparatore</th>
<th>Outcomesd</th>
<th>Follow-Up*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radnovich et al (2017)</td>
<td>4. A more relevant population would be patients with moderate- to-severe knee osteoarthritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
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.

Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.


### Table 13. Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation</th>
<th>Blinding</th>
<th>Selective Reporting</th>
<th>Data Completeness</th>
<th>Power</th>
<th>Statistical</th>
</tr>
</thead>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.


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).

Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

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 OA**

An RCT with 180 patients has compared cryoneurolysis with sham treatment in patients who had knee OA. 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 are 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 six 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 14). 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 14. 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 alternate treatment was allowed at four 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 15). In a graphic presentation of results, patient pain levels for all three 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 14. Summary of Key RCT Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wu et al (2017)</td>
<td>Taiwan</td>
<td>1</td>
<td>2014-2016</td>
<td>36 patients (40 feet) with recalcitrant plantar fasciitis</td>
<td>Ultrasound-guided pulsed RF stimulation of the posterior tibial nerve</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sham with ultrasound-guided lidocaine injection</td>
</tr>
<tr>
<td>Landsman et al (2013)</td>
<td>U.S.</td>
<td>Multicenter</td>
<td>NR</td>
<td>17 patients failed at least 3 prior types of treatments, pain for &gt;3 mo,</td>
<td>RFA procedure, including stimulation of sensory nerves in an awake patient</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sham with all aspects of the RFA procedure, except delivery of RF energy at the final step</td>
</tr>
</tbody>
</table>
Radiofrequency Ablation of Peripheral Nerves to Treat Pain

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

Table 15. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study</th>
<th>First Step Pain on VAS Score</th>
<th>Average VAS Pain Score</th>
<th>AOFAS Ankle-Hindfoot Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At 12 Weeks</td>
<td>At 12 Weeks</td>
<td>N</td>
</tr>
<tr>
<td>Wu et al (2017)</td>
<td></td>
<td></td>
<td>RFA (SD)</td>
</tr>
<tr>
<td>Sham (SD)</td>
<td>6.13 (1.75)</td>
<td>6.09 (1.70)</td>
<td>60.05 (11.38)</td>
</tr>
<tr>
<td>Change At 4 Weeks</td>
<td>Change Score</td>
<td>Change in Peak Pain</td>
<td></td>
</tr>
<tr>
<td>Landsman et al (2013)</td>
<td>17</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Sham</td>
<td>1.33</td>
<td>0.8</td>
<td>1.80</td>
</tr>
<tr>
<td>p</td>
<td>0.30</td>
<td>0.047</td>
<td>0.048</td>
</tr>
</tbody>
</table>
| AOFAS: American Orthopedic Foot and Ankle Society; RCT: randomized controlled trial; RFA: radiofrequency ablation; SD: standard deviation; VAS: 10-cm visual analog score.

Tables 16 and 17 display notable limitations identified in each study.

Table 16. Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcomes</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. Targeted nerve not clearly defined</td>
<td>1. Targeted nerve not clearly defined</td>
<td>1. Targeted nerve not clearly defined</td>
<td>1. Targeted nerve not clearly defined</td>
<td></td>
</tr>
</tbody>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations 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.
Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.


Table 17. Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocationa</th>
<th>Blindingb</th>
<th>Selective Reportingc</th>
<th>Follow-Upd</th>
<th>Powere</th>
<th>Statisticalf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wu et al (2017)</td>
<td></td>
<td></td>
<td>3.</td>
<td>1. Power calculations not reported</td>
<td>3. Confidence intervals not reported</td>
<td></td>
</tr>
<tr>
<td>Landsman et al (2013)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.


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).

Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

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 two randomized trials enrolled a few subjects. Due to crossover at four weeks in one of the trials, the randomized comparison only evaluated outcomes to four 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 are 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 the 12-Item and 36-Item Short-Form Health Survey.

**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. They included ten studies that met their criteria, with three RCTs, three prospective studies, and four retrospective studies. There were no high-quality RCTs. Two of the RCTs evaluated RFA of the genicular nerves 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 three 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 three to ten 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 three 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 a 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 OA who receive RFA of peripheral nerves, the evidence includes 2 RCTs with a total of 211 patients with a 6-month follow-up and observational studies with 12 months of follow-up. The relevant outcomes include symptoms, functional outcomes, and QOL. Knee OA is a common disorder in older adults. RFA of the genicular nerves has the potential to alleviate pain and improve function in this population, and might also delay or eliminate the need for TKA. To date, the evidence on RFA for knee pain includes 2 RCTs with a total of 211 patients with a 6-month follow-up and prospective observational studies with 12 months of follow-up. The larger of the RCTs compared C-RFA to active control of steroid injection and utilized genicular nerve blocks to select patients for the study. At 1 month after treatment, pain scores on an 11-point NRS differed by less than 1 point, a finding that was statistically significant but of marginal clinical significance. By three months after treatment pain scores had increased in the steroid group, consistent with the known durability of the treatment. Pain scores in the RFA group remained low in patients who remained in the study. Durability of this treatment approach to 1 year has been evaluated in a follow-up to the RCT, a retrospective study, and a small (n=25) independent prospective study. In both of the industry-sponsored publications, 65% of the patients treated with C-RFA reported a greater than 50% reduction in pain scores at 12 months. In an independent and prospective observational study, about one-third continued to show a response at one year after RFA of the genicular nerves. The second RCT used stimulation to identify the genicular nerves, rather than genicular nerve blocks with an anesthetic. None of the studies were blinded, which may have biased the subjective outcome measures. It should be noted that the anatomy of the genicular nerves is variable, and the best method for their identification has not been determined. Study in a larger number of patients, preferably in blinded studies with active control and follow-up longer than 12 months, is needed to determine the benefits and potential harms of this treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have knee OA or TKA who receive cryoneurolysis of peripheral nerves, the evidence includes an RCT with 180 patients and a retrospective comparative study. The relevant outcomes include symptoms, functional outcomes, and QOL. Cryoneurolysis in patients with knee OA resulted in a greater decrease in WOMAC pain score, WOMAC total score, and VAS 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 VAS 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 TKA. 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 two RCTs. The relevant outcomes include symptoms, functional outcomes, and QOL. 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. The relevant outcomes are symptoms, functional outcomes, and QOL 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 a 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.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS

The American College of Foot and Ankle Surgeons (2018) issued consensus guidelines on the diagnosis and treatment of acquired infracalcaneal heel pain. The safety and efficacy of bipolar radiofrequency was listed as uncertain (neither appropriate nor inappropriate).

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable.

MEDICARE NATIONAL COVERAGE

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.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently ongoing and unpublished trials that might influence this review are listed in Table 18.

Table 18. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>A Randomized Controlled Study to Compare Efficacy of Continuous Versus Pulsed Radiofrequency Treatment of Genicular Nerves to Alleviate Pain and Improve Functional Impairment in Patients With Advanced</td>
<td>188</td>
<td>Aug 2019</td>
</tr>
</tbody>
</table>

*Ongoing*
### Osteoarthritis of the Knee

<table>
<thead>
<tr>
<th>Study Identifier</th>
<th>Description</th>
<th>Participants</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT03381248</td>
<td>A Prospective, Multi-center, Randomized, Clinical Trial Evaluating the Safety and Effectiveness of Using COOLIEF™ Cooled Radiofrequency Probe to Create Lesions of the Genicular Nerves and Comparing a Single Injection of Hyaluronic Acid in the Management of Knee Pain</td>
<td>168</td>
<td>Oct 2019</td>
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<tr>
<td>NCT02925442</td>
<td>Comparison Between Cooled (C-RFA) and Standard (t-RFA) Radiofrequency Ablation, and Control for Pain Management Following Unilateral Knee Arthroplasty: A Double-Blinded, Parallel-Grouped, Placebo-Controlled Randomized Clinical Trial</td>
<td>150</td>
<td>Feb 2020</td>
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<tr>
<td>NCT02915120</td>
<td>Ultrasound-Guided Pulsed Radiofrequency Of The Genicular Nerves In The Treatment Of Patients With Osteoarthritis Knee Pain: Randomized, Double-Blind, Placebo-Controlled Trial</td>
<td>142</td>
<td>Dec 2020</td>
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<tr>
<td><strong>Unpublished</strong></td>
<td><strong>A Controlled Comparison of Pulsed Radiofrequency Vs Physical Therapy on Treating Chronic Knee Osteoarthritis</strong></td>
<td>50</td>
<td>Apr 2017 (unknown)</td>
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<tr>
<td>NCT02260869</td>
<td>Efficacy of Cooled and Monopolar Radiofrequency Ablation of the Geniculate Nerves for the Treatment of Chronic Osteoarthritic Knee Pain</td>
<td>78</td>
<td>Jun 2019 (completed)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

*a Industry sponsored or partially sponsored.

### ESSENTIAL HEALTH BENEFITS

The Affordable Care Act (ACA) requires fully insured non-grandfathered individual and small group benefit plans to provide coverage for ten categories of Essential Health Benefits (“EHBs”), whether the benefit plans are offered through an Exchange or not. States can define EHBs for their respective state.

States vary on how they define the term small group. In Idaho, a small group employer is defined as an employer with at least two but no more than fifty eligible employees on the first day of the plan or contract year, the majority of whom are employed in Idaho. Large group employers, whether they are self-funded or fully insured, are not required to offer EHBs, but may voluntary offer them.

The Affordable Care Act requires any benefit plan offering EHBs to remove all dollar limits for EHBs.

### REFERENCES


**CODES**

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>64640</td>
<td>Destruction by neurolytic agent; other peripheral nerve or branch</td>
</tr>
<tr>
<td>ICD-10-CM</td>
<td>M17.0-M17.9</td>
<td>Investigational for plantar fasciitis and knee osteoarthritis</td>
</tr>
<tr>
<td></td>
<td>M72.2</td>
<td>Knee osteoarthritis code range</td>
</tr>
<tr>
<td></td>
<td>M72.2</td>
<td>Plantar fascial fibromatosis (includes plantar fasciitis)</td>
</tr>
<tr>
<td>ICD-10-PCS</td>
<td>015D3ZZ, 015F3ZZ, 015G3ZZ, 015H3ZZ</td>
<td>ICD-10-PCS codes are only used for inpatient services. There is no specific ICD-10-PCS code for this procedure.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peripheral nervous system, destruction, percutaneous. Codes for various nerves of the lower extremity.</td>
</tr>
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</table>

**POLICY HISTORY**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/14/16</td>
<td>New Policy – Add to Surgery Section</td>
<td>Policy created with literature review through December 10, 2015. RFA of peripheral nerves to treat pain associated with plantar fasciitis or knee osteoarthritis is considered investigational.</td>
</tr>
<tr>
<td>02/24/17</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho annual review; no change to policy.</td>
</tr>
<tr>
<td>09/28/17</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes as noted. Policy updated with literature review through July 20, 2017; no references added. Policy statement unchanged.</td>
</tr>
<tr>
<td>09/19/18</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes as noted, effective 12/15/2018. Policy updated with literature review through July 9, 2018; references 2-6, 8, and 11-13 added. Investigational policy statements added on cryoneurolysis for knee osteoarthritis or total knee arthroplasty and on radiofrequency ablation for occipital neuralgia and cervicogenic headache.</td>
</tr>
<tr>
<td>09/19/19</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes as noted, effective 09/19/2019. Policy updated with literature review through July 9, 2019; references added. Policy statements unchanged.</td>
</tr>
</tbody>
</table>