Ablative Procedures of the Peripheral Nerves to Treat Pain*

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DESCRIPTION

Ablative procedures such as radiofrequency ablation, cryoneurolysis (cryoablation) and chemical neurolysis of the nerves has been proposed as a treatment for several different types of pain. It has been used to treat several pain syndromes such as trigeminal neuralgia, cervical and lumbar facet joint pain and headache syndromes. This medical policy evaluates the evidence for ablative procedures to include radiofrequency ablation, cryoneurolysis (cyroablation) and chemical neurolysis in peripheral sites distant from the cranium or spine. See also medical policies: 07.01.66 Ablative Treatments of Occipital Neuralgia, Chronic Headaches and Atypical Facial Pain; 07.01.41 Pulsed Radiofrequency; 07.01.58 Radiofrequency Ablation and Alternative Ablative/Denervation Methods for Chronic Facet Joint Mediated Neck, Back and Sacroiliac Joint Pain*.

Ablative procedures including radiofrequency ablation (RFA), cooled radiofrequency, pulsed radiofrequency, cryoneurolysis (cryoablation, cryotherapy, cryoanalgesia) and

chemical neurolysis (chemodenervation) have been proposed as a treatment of the peripheral nerves to treat pain related to conditions including but not limited to the following: osteoarthritis, neuralgias/neuritis (intercostal neuralgia, inguinal neuralgia), chronic orchialgia, postherpetic neuralgia, peripheral neuromas and plantar fasciitis, for individuals that have not been effectively managed by pharmacologic (anti-inflammatories [NSAIDs], opioids, corticosteroids, injections of biologics) or other alternative therapies (physical therapy/exercise).

Ablative Procedures

- 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 then 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 (80 to 85°C). It is theorized that the thermal lesioning of the nerve destroys peripheral sensory nerve endings, resulting in the alleviation of pain. However, the results are typically not permanent as the nerves may regenerate which can cause the pain to return and may require the repetition of the RFA procedure to alleviate the pain.
- Cooled radiofrequency is a newer technology that is a variation of conventional (standard) radiofrequency using a special device that uses a water-cooled radiofrequency probe to ablate a larger lesion size and treat a larger area than standard RFA technology. Cooled radiofrequency applies more energy at the desired location without excessive heat diffusing beyond the area, causing less tissue injury away from the nerve. The goal for ablating the nerve is the same.
    - COOLIEF Cooled RF (radiofrequency) treatment (Haylard Health, Inc.) is a minimally invasive outpatient procedure that uses cooled radiofrequency energy to target the sensory nerves causing pain. COOLIEF circulates water through the device while heating nervous tissue to create a treatment area that is larger than conventional RF treatments. This combination targets the pain causing nerves without excessive heating, leading to pain relief. The procedure time varies depending on the treatment needed, the actual radiofrequency treatment time typically is less than 20 minutes. COOLIEF RF treatment is used in the treatment of hip and knee pain associated with osteoarthritis.
- Pulsed radiofrequency treatment uses short bursts of radiofrequency current (temperature will not exceed 42°C), rather than continuous current (RFA). The mechanism for action of pulsed radiofrequency treatment is uncertain, but it is thought the heat is not enough to cause tissue coagulation or permanent damage to the nerve. If it does produce some degree of nerve destruction, it is thought to cause less damage than conventional (standard) RFA. Pulsed radiofrequency has been proposed as a possibly safer alternative to non-pulsed or continuous RFA in the treatment of variety pain syndromes.

Type	Procedure	Tissue Temperature	Key Differences
Standard RFA	Electrode tip provides thermal energy for 90 – 130 seconds	70 – 90° C	Longer term pain relief but with more adjacent thermal tissue injury and limitation in size and shape of lesion.
Pulsed RFA	Non-ablative - provides 20 ms pulses every 30 seconds	42° C	Limits tissue damage but results in shorter duration of pain relief
Cooled RFA	Water circulates through RF electrode to cool the tip	60° C	Larger lesion with limited thermal injury to tissue. Longer term pain relief.

- Cryoneurolysis, also called cryoablation, cryotherapy or cryoanalgesia uses freezing temperatures to treat chronic pain of either sensory or motor nerves and uses a wide range of temperatures with treatment often occurring at temperature as cold as -196°C (liquid nitrogen coolant) or -20 to -100°C or colder (nitrous oxide coolant). Because peripheral nerve function is disrupted due to the destruction of the axon and myelin sheath, the desired result provides pain relief until the nerve(s) regenerate. Cryodenervation has been used for patients with various types of pain including but not limited to post-herpatic neuralgia, intercostal pain, neuroma, and osteoarthritis (OA).
    - The iovera system (Myoscience, Inc) is a handheld device that delivers a controlled dosage of liquid nitrous oxide to the closed-end probes of the smart tip, which is then applied to specific targeted nerves. As this highly pressurized liquid travels from the handheld piece to the smart tip, it undergoes a phase change becoming very cold, drawing in heat energy from the surrounding tissue and forming a precise zone of cold at the targeted nerve. The gaseous nitrous oxide returns into the hand piece, leaving nothing behind in the body. This precise cold treatment causes a reversible nerve block based on a process called Wallerian degeneration. Pain is relieved as the signal is not able to conduct along the sensory nerves until the axon is regenerated. The nerve axon regenerates at the rate of about 1 mm per day, which provides a predictable indicator for restoration of nerve function.
- Chemical Neurolysis (chemodenervation) is the use of a chemical using phenol, alcohol, glycerol or a hypertonic saline to cause destruction of nerve(s) by

causing a temporary degeneration of the nerve(s) fibers to interrupt the transmission of nerve(s) signals for pain relief.

In 2014, Zhou et. al completed a systematic review regarding neurolysis therapy with radiofrequency, phenol/alcohol and cryotherapy in pain management. Each of these modalities were reviewed to include history, mechanism, clinical indication, contraindication, side effects and efficacy. They provided an overview of each technique and summarizes the comparison literature. Chronic pain is a serious public health problem both in the United States and globally. The nuisance of chronic pain results in serous negative economic consequences due to disability and the cost of therapies. The treatment of chronic pain is complex and includes physical therapy, biofeedback, pharmacotherapy, peripheral nerve injection therapy and neuroablation therapy also, known as neurolysis. Neuroablative intervention, however, can be a double edge sword in that the mode of ablation chosen may result in relief that is not permanent and may have serious complications. We have extensive clinical experience in the most used modes of neuroablative therapy: radiofrequency (heat), chemoneurolysis (chemical) and cryoablation (cold). However, it has not been determined which therapy is determined as superior in achieving the goal of abolishing symptoms of pain while preserving function to the affected location of chronic pain.

Clinical effectiveness

- **Radiofrequency**: results of the literature review on radiofrequency produced a wide range of outcomes. From the data review currently there is very limited evidence towards the effectiveness of radiofrequency therapy. Most studies are of a limited patient size and of a limited long-term follow-up. The authors concluded, there is a need for further double blinded, randomized trials to further elicit the efficacy of radiofrequency neurolysis therapy in the treatment of pain.
- **Chemoneurolysis**: the clinical literature on chemical neurolysis is very deficient of well-constructed studies. Most evidence is of anecdotal observations.
- **Cryoanalgesia**: cryoablation has mixed results in the literature. The mostly widely studied area has been the application of cryoanalgesia with post-thoracotomy pain. Studies on cryotherapy for pain syndromes other than post-thoracotomy pain have also yielded mixed results. Clinically outcomes to cryotherapy appear to be dependent on the temperature of the probe and there continues to be no literature comparing clinical outcomes of cryoanalgesia with different probe temperatures.

The authors performed an extensive literature search looking for comparison articles of the three neurolytic techniques discussed above. In a Cochrane Database review of radiofrequency ablation versus chemical ablation in the treatment of sympathetically mediated pain four studies were found which met the inclusion criteria of which was only a randomized study. There wasn't enough evidence to show if either technique was superior or even effective individually for sympathectomy. The only difference they alluded to, was the increased incidence of post-sympathectomy neuralgia with the chemolytic therapies. The other study of interest was a randomized trial comparing

peripheral blocks of cryoablation versus phenol in the management of chronic pain. Significantly more patients in the phenol group received 20% or greater pain relief at 1, 12 and 24 weeks after the procedure. However, only 27% of patients in the study received significant pain relief demonstrating poor effectiveness overall. Wang performed a randomized double-blind trial to compare the outcome of cryotherapy, chemoneurolysis, and lidocaine injection to spinal dorsal rami for low back pain. In this study, 60 patients were randomized into three groups for cryotherapy, alcohol neurolysis and lidocaine injection respectively. In the 7 days after the procedure, there was no difference in these three groups. However, in 1, 3, and 6 months, there were significant differences of pain relief between the cryotherapy group, alcohol neurolysis group and lidocaine injection group. In direct comparison of the cryotherapy and alcohol groups, 65% (13/20) of the cryotherapy group compared to only 45% (9/20) of the alcohol group achieved complete pain relief.

The authors concluded, despite the above studies, we conclude that there is no literature that currently demonstrates which neurolytic modality can provide better and longer pain relief. Although there is some evidence that cryoanalgesia may cause less complications of neuritis, no head-to-head comparisons of adverse effects have been studied. We see a need for continued randomized, double-blinded studies to establish the overall effectiveness of these treatments and to compare their outcomes against one another.

Osteoarthritis of the Knee

Osteoarthritis of the knee is a common cause of joint pain and disability. The treatment of osteoarthritis (OA) is directed towards reduction of symptoms and improve function. However, most treatments do not modify the natural history or progression of OA and are not considered curative. Nonsurgical modalities used include exercise; weight loss; various supportive devices; acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs), nutritional supplements (glucosamine, chondroitin); corticosteroid injections; and intra-articular viscosupplements. Operative treatments for symptomatic OA of the knee include arthroscopic lavage and cartilage debridement, osteotomy, and ultimately a total joint arthroplasty.

When an individual exhibits knee pain, the pain signals can be generated from the peripheral nerves innervating the knee including several branches of the genicular nerve, an ablative procedure to include radiofrequency ablation, cryoneurolysis and chemical neurolysis of the genicular nerves may be performed to restore function and alleviate knee pain as an alternative therapy. Surgical treatment may not be an option for patients with multiple comorbidities, these ablative procedures have been proposed as an alternative for the treatment of chronic pain.

Radiofrequency Ablation

Clinical Context and Therapy Purpose
The purpose of radiofrequency ablation (RFA) in patients with knee osteoarthritis (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.

Patients
The relevant population of interest are patients with knee osteoarthritis (OA).

Interventions
The therapy being considered is radiofrequency ablation (RFA) of the 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 treat OA: conservative management which may include analgesics, physical therapy (PT) 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 the12-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, randomized controlled trials (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.

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.

Systematic Reviews

Gupta, et. al. (2017) completed a systematic review aimed to analyze published studies on radiofrequency ablation (conventional, pulsed or cooled radiofrequency) for patients suffering from osteoarthritis of the knee and patients post total knee arthroplasty who have developed refractory disabling chronic knee pain. The systematic review aimed to provide an overview of the current knowledge regarding variations in procedures, nerve targets, adverse events and temporal extent of clinical benefit. The results showed seventeen publications were identified in the search, including articles investigating conventional, pulsed, or cooled radiofrequency ablation. These studies primarily targeted either the genicular nerves or used an intraarticular approach. Of the studies, 5 were small-sized randomized controlled trials, although one involved diathermy radiofrequency ablation. There were 8 retrospective or prospective case series and 4 case reports. Utilizing the strength of evidence grading, there is a low level of certainty to suggest a superior benefit between targeting the genicular nerve, an intraarticular approach, or targeting the larger nerves such as femoral and tibial nerves. Utilizing the strength of evidence grading, there is a low level of certainty in supporting the superiority of any specific RFA procedure modality. The majority of the studies report positive patient outcomes, but the inconsistent procedural methodology, inconsistent patient assessment measures, and small study sizes limit the applicability of any specific study to clinical practice. The authors concluded overall the studies showed promising results for the treatment of severe chronic knee pain by radiofrequency ablation at up to one year with minimal complications. Numerous studies, however, yielded concerns about procedural protocols, study quality, and patient follow-up. Radiofrequency ablation can offer substantial clinical and functional benefit to patients with chronic knee pain due to osteoarthritis or post total knee arthroplasty.

In 2018, Jamison et. al. completed a comprehensive literature review regarding radiofrequency techniques to treat chronic knee pain to include anatomy, effectiveness, treatment parameters and patient selection. They identified nine relevant clinical trials, which included 592 patients, evaluating knee RFA for osteoarthritis and persistent postsurgical pain. These included one randomized, placebo-controlled trial, one randomized controlled trial evaluating RFA as add-on therapy, four comparative-effectiveness studies, two randomized trials comparing different techniques and treatment

paradigms, and one non-randomized, controlled trial. The results of these studies demonstrate significant benefit for both reduction and functional improvement lasting between 3 and 12 months, with questionable utility for prognostic blocks. There was considerable variation in the described neuroanatomy, neural targets, radiofrequency technique, and selection criteria. The authors concluded, RFA of the knee appears to be a viable and effective treatment option, providing significant benefit to well-selected patients lasting at least 3 months. More research is needed to better identify neural targets, refine selection criteria to include the use of prognostic blocks, optimize treatment parameters, and better elucidate relative effectiveness compared to other treatments.

In 2021, Chen et. al. conducted a systematic literature review regarding thermal nerve radiofrequency ablation of the nonsurgical treatment of knee osteoarthritis. Five high-quality and two moderate-quality randomized controlled trials (RCTs) met the inclusion criteria for this review. The results showed consistent agreement across all RCTs in favor of geniculate nerve thermal RFA use for nonsurgical treatment of knee OA. One high-quality RCT and one moderate-quality RCT found geniculate nerve RFA to provide statistically significant outcome improvement compared with control or sham procedures regarding pain, function, quality of life, and composite scores. When compared with IA corticosteroids and hyaluronic acid, geniculate nerve RFA also provided notable improvement in pain, function, and composite scores (visual analog scale, Western Ontario, and McMaster Universities Arthritis Index, and Oxford Knee Score). RFA was markedly favored for all pain and composite outcomes (Western Ontario and McMaster Universities Arthritis Index and visual analog scale). The included RCTs did not report any serious AEs related to geniculate nerve RFA. The authors concluded thermal RFA of geniculate nerves is more effective at treating knee OA pain and function than current treatments including NSAIDs or IA corticosteroids, and the pain relief is clinically notable to 24 months. No serious AEs were noted with the application of geniculate nerve thermal RFA in this systematic review. Future studies are needed to determine whether patients receiving geniculate nerve thermal RFA benefit from more than a single treatment to compare geniculate nerve thermal RFA to other NSAIDs and to determine whether geniculate nerve thermal RFA is associated with AEs or poorer outcomes if patients progress to TKA.

Randomized Controlled Trails

Bellini et. al. (2015) treated 9 patients using cooled RFA of the genicular nerve and the follow-up was extended to one, three, six- and twelve-months using Pain Visual Analogue Scale (VAS), patient global assessment and the Western Ontario McMaster Universities OA index (WOMAC). The study subjects comprised elderly patients with chronic knee pain (knee pain of at least moderate intensity on most days for > 3 months), radiologic tibio-femoral osteoarthritis and did not respond to conservative treatments including physiotherapy, oral analgesics, and intra-articular injections or steroids. They were not candidates for invasive treatments due to comorbidities. VAS scores improved from a baseline mean of 8 to 2, 2.3, 2.1, 2.2 at 1, 3, 6 and 12 months after treatment respectively. WOMAC scores improved from a baseline mean of 88 to 20, 22, 21 and 20

at the same assessment intervals. No adverse events of treatment were mentioned. The authors concluded; our research has some limits. One is the small number of patients and secondly, the follow-up was limited to 12 months. Even given these limitations, our results suggest cooled RF neurotomy of genicular nerves has the potential to significantly improve pain, function, and satisfaction, with the possibility of probing a larger tissue lesion than classical RF neurotomy. Moreover, cooled RF can be used in patients in whom an invasive procedure is not recommended. The decreases of chronic pain and medication usage, along with improvement in quality of life and high degree of satisfaction, may justify the use of cooled RF in a broader population.

Bhatia et. al. (2016) completed an evidence-based narrative review regarding radiofrequency procedures to relieve chronic knee pain. Chronic knee pain from osteoarthritis or following arthroplasty is a common problem. A number of publications have reported analgesic success of radiofrequency (RF) procedures on nerves innervating the knee, but interpretation is hampered by lack of clarity regarding indications, clinical protocols, targets and longevity of benefit from radiofrequency (RF) procedures. The following medical literature databases were reviewed for publications on RF procedures on the knee joint for chronic pain: MEDLINE, EMBASE, Cochrane Central Register for Controlled Trials, Cochrane Database of Systematic Reviews, and Google Scholar up to August 9, 2015. Data on scores for pain, validated scores for measuring physical disability, and adverse effects measured at any time point after 1 month following the interventions were collected, analyzed, and reported in this narrative review. Thirteen publications on ablative or pulsed radiofrequency treatments of innervation of the knee joint were identified. A high success rate of these procedures in relieving chronic pain of the knee joint was reported at 1 to 12 months after the procedures, but only 2 of the publications were randomized controlled trials. There was evidence for improvement in function and a lack of serious adverse events of RF treatments. The authors concluded that radiofrequency treatments on the knee joint (major or periarticular nerve supply or intra-articular branches) have the potential to reduce pain from osteoarthritis or persistent post-arthroplasty pain. Ongoing concerns regarding the quality, procedural aspects, and monitoring of outcomes in publications on this topic remain. Randomized controlled trials of high methodological quality are required to further elaborate the role of these interventions in this population.

In 2017 the COOLIEF Cooled RF FDA approval for the treatment of osteoarthritis of the knee was based on Halyard Health Inc. sponsored study, which was a prospective, multi-center randomized clinical trial that included 151 patients over 12 months with primary effectiveness at six months and 12 months. The study found: in 74.1% of the cooled RF patient group, pain was reduced by at least 50 percent at six months and maintained in over 65.4% of those patients for a full 12 months post procedure; at baseline 67.1% of the cooled RF group and 62.7% of the steroid injection group reported symptoms of severe arthritis; Six months post-procedure only 5.2% of the cooled RF group reported the same severity level versus 37.3% of patients treated with steroid injections as measured by the Oxford Knee Score. The Oxford Knee Score is a validated outcomes instrument designed to assess function and pain associated with the knee; in addition, the cooled RF patient

group's Oxford Knee Score remained low for 12 months with only 11.5 percent reporting severe symptoms at that point. The author concluded that COOLIEF Cooled RF provides more lasting relief than steroid injections for patients suffering from chronic osteoarthritis knee pain.

In 2017, McCormick et. al. completed a cross sectional survey to determine six-month outcomes of cooled radiofrequency ablation (C-RFA) of the genicular nerves for treatment of chronic knee pain due to osteoarthritis (OA) at an academic medical pain center. Consecutive patients with knee OA and 50% or greater pain relief following genicular nerve blocks who underwent genicular nerve C-RFA were included. Survey administration six or more months after C-RFA. Pain numeric rating scale (NRS), Medication Quantification Scale III (MQSIII), Patient Global Impression of Change (PGIC), and total knee arthroplasty (TKA) data were collected. Logistic regression was used to identify factors that predicted treatment success. Thirty-three patients (52 discrete knees) met inclusion criteria. Thirty-five percent (95% confidence interval [CI] = 22-48) of procedures resulted in the combined outcome of 50% or greater reduction in NRS score, reduction of 3.4 or more points in MQSIII score, and PGIC score consistent with "very much improved/improved." Nineteen percent (95% CI = 10-33) of procedures resulted in complete pain relief. Greater duration of pain and greater than 80% pain relief from diagnostic blocks were identified as predictors of treatment success. The accuracy of the model was 0.88 (95% CI = 0.78-0.97, P < 0.001). The authors concluded, Genicular C-RFA demonstrated a success rate of 35% based on a robust combination of outcome measures, and 19% of procedures resulted in complete relief of pain at a minimum of six months of follow-up. Report of 80% or greater relief from diagnostic blocks and duration of pain of less than five years are associated with high accuracy in predicting treatment success. Further prospective study is needed to optimize the patient selection protocol and success rate of this procedure.

Santana et. al. (2017) completed a single-center, prospective, observational non-controlled, longitudinal study on the analgesic effect and functional improvement caused by radiofrequency treatment of genicular nerves in patients with advanced osteoarthritis of the knee until one year following treatment. Long term efficacy of such treatment remains to be assessed. The study included 25 patients with grade 3 to 4 gonarthrosis (n=24) or after total knee arthroplasty (n=1) suffering from intractable knee pain, scoring 5 or more on the visual analog scale (VAS) for >6 months. Therapy was based on ultrasound guided radiofrequency neurotomy of the superior medial, superior lateral and inferior medial genicular nerves. Visual analog scale and Western Ontario and McMaster Universities Osteoarthritis scores were assessed before therapy and at 1-, 6-, and 12-months following treatment. Radiofrequency neurotomy of genicular nerves significantly reduced perceived pain (VAS) and disability (Western Ontario and McMaster Universities Osteoarthritis) in the majority of participants, without untoward events. The proportion of participants with improvement of 50% or greater in pretreatment VAS scores at 1-, 6-, and 12-months following intervention were 22/25 (88%), 16/25 (64%) and 8/25 (32%), respectively. The authors concluded, ultrasound-guided radiofrequency neurotomy of genicular nerves alleviates intractable pain and disability in the majority of

patients with advanced osteoarthritis of the knee. Such a treatment is safe and minimally invasive and can be performed in an outpatient setting. The beneficial effect of treatment started to decline after 6 months, but even 1 year after the intervention, 32% of patients reported 50% improvement or greater in pretreatment VAS scores.

In 2018, Davis et. al. completed a prospective, multicenter, randomized, crossover clinical trial comparing the safety and effectiveness of cooled radiofrequency ablation (CRFA) with corticosteroid injection in the management of knee pain from osteoarthritis of 151 subjects with chronic (≥6 months) knee pain that was unresponsive to conservative modalities. Knee pain (Numeric Rating Scale [NRS]), Oxford Knee Score, overall treatment effect (Global Perceived Effect), analgesic drug use, and adverse events were compared between CRFA and IAS (intra-articular steroid) cohorts at 1, 3, and 6 months after intervention. There were no differences in demographics between study groups. At 6 months, the CRFA group had more favorable outcomes in NRS: pain reduction 50% or greater: 74.1% versus 16.2%, $P < 0.0001$ (25.9% and 83.8% of these study cohorts, respectively, were non-responders). Mean NRS score reduction was 4.9 ± 2.4 versus 1.3 ± 2.2, $P < 0.0001$; mean Oxford Knee Score was 35.7 ± 8.8 vs 22.4 ± 8.5, $P < 0.0001$; mean improved Global Perceived Effect was 91.4% vs 23.9%, $P < 0.0001$; and mean change in nonopioid medication use was CRFA > IAS ($P = 0.02$). There were no procedure-related serious adverse events. While the authors concluded the findings of this study indicated that cooled radiofrequency ablation (Coolief) for genicular nerve ablation is superior to a single corticosteroid injection in osteoarthritic subjects for managing knee pain, the limitations of this study included the following: the comparison group (IAS subjects underwent a singular injection rather than multiple injections, and the 6 month time point at which the primary outcome was assessed is not consistent with the expected duration of effectiveness of a steroid injection; the IAS injections are not truly a "control" intervention, given that corticosteroids are analgesics; this was an open label trial and so not all study site observers were blinded to procedures; medication diaries were not used to record medication usage in this study which introduced potential for error and/or inability to identify acute changes in medication dosage during the study; and the effect of each treatment on opioid use for OA related knee pain could be specifically measured because patients in both study groups used opioids for medical indications other than OA related knee pain.

In 2018, Sari et. al. compared the efficacy of intra-articular injection and radiofrequency (RF) neurotomy of genicular nerves in patients with chronic knee osteoarthritis (OA). Seventy-three patients with knee OA were included in the study. Patients were randomly assigned to Group IA (intra-articular 2.5 mL of bupivacaine, 2.5 mg of morphine and 1 mL of betamethasone, 6 mL of fluid injection) or Group RF (RF neurotomy of the genicular nerves). The outcome measures included a pain scale (visual analog scale, VAS) and Western Ontario and McMaster Universities (WOMAC) Index of Osteoarthritis. No statistically significant difference was found between the two groups in baseline VAS-pain. In Group RF, a significant reduction was observed in VAS-pain at the first month ($P < 0.001$) and the third month ($P < 0.001$) in comparison to Group IA.

Also, in Group RF, a significant reduction was observed in WOMAC total scores in the first month ($P < 0.001$) in comparison to Group IA.

In 2018, El-Hakeim et. al. evaluated the efficacy of fluoroscopic guided neurotomy of the genicular nerves for alleviation of chronic pain and improvement of function in patients with knee osteoarthritis (OA) in a single-blind randomized controlled trial. This study involved 60 patients with chronic knee osteoarthritis (OA). Radiofrequency neurotomy of the genicular nerves was done for 30 patients (Group A) while the other 30 patients (Group C) received conventional analgesics only. The outcome measures included visual analog scale (VAS), Western Ontario and McMaster Universities Index (WOMAC), and Likert scale for patient satisfaction in the 2nd week,3rd, and 6th months. There were significant differences regarding the VAS in the 2nd week, 3rd, and 6th months between the 2 groups, and a significant difference in total WOMAC index in the 6th month only. There were significant changes when comparing pretreatment values with the values during the whole follow-up period with regard to the VAS and total WOMAC index in both groups. No diagnostic block was done prior to radiofrequency. The authors recommended the use of such a technique on a larger number of OA patients, with a longer follow-up period.

In 2019, Kapural et. al. completed a retrospective electronic chart review of an outpatient private practice that evaluated the long-term effectiveness of cooled radiofrequency ablation (CRFA) in the general chronic knee pain population. After institutional review board approval, we reviewed data of 275 consecutive patients who had undergone a geniculate nerve block at a single-site pain practice between July 1, 2014 and July 1, 2017. A total of 44 patients had a negative response to the geniculate block, and 11 patients had long-term pain relief from the block and declined CRFA. Eight patients underwent knee surgery after the block, and 7 never followed up for further treatment. Finally, 205 patients had undergone CRFA, and 183 (89%) of them returned to provide data. The average age of the 183 patients was 61 (28-95) years, body mass index 34 (18.5-57), and there were 105 women and 78 men. A total of 137 patients had unilateral knee pain, whereas 46 patients had bilateral knee pain. Eighty percent (146/183) reported at least one or more additional sources of chronic pain (back, shoulder, and others). The average opioid use at baseline was 50 mg morphine sulfate equivalents (median 30 mg). The average baseline pain scores were 8.5, which decreased to 2.2 after the geniculate local anesthetic block, and to 4.2 after CRFA. A total of 65% of the patients claimed > 50% pain relief, whereas 77% had 2 or more Visual Analog Scale points decrease, and 26 (14%) patients reported no pain at all after CRFA. The mean duration of > 50% pain relief after CRFA was 12.5 months (range 0-35 months). There was no significant decrease of opioid use. Patients who underwent a repeated procedure ($n = 43$) achieved a similar pain relief ($P = 0.402$). We could not find a statistical difference in geniculate CRFA outcomes between the group who had total knee arthroplasty (TKA; $n = 21$) and maintained chronic knee pain and patients who had no prior surgery ($P = 0.542$). Limitation of this study is the retrospective nature. The authors concluded, this study demonstrates the clinical effectiveness of CRFA in the treatment of chronic knee pain from osteoarthritis, and even in those patients who maintained chronic knee pain after

TKA. Our real-life data seems to agree with data previously published in a randomized controlled trial, even though this was quite a heterogenous patient population with various sources of chronic pain.

In 2019, Oladeji et. al. the objective of this review article was to provide the rationale, available evidence, indications, and outcomes associated with cooled radiofrequency ablation (C-RFA) for the treatment of chronic knee osteoarthritis (OA). Knee osteoarthritis (OA) is a common condition associated with pain and physical impairment in a large segment of the population. The traditional treatment algorithm progresses from conservative modalities to nonsurgical options to surgical intervention. Surgical intervention often provides reliable pain relief but not all patients are surgical candidates and there are some patients who prefer not to have surgery. Cooled radiofrequency ablation (C-RFA) is a treatment with the potential to provide pain relief for patients who no longer benefit from noninvasive modalities and who desire an alternative to surgery. A total of eight reports that use C-RFA in the treatment of chronic knee pain were identified and analyzed. There were two prospective trials, one retrospective cohort study, and five case reports or case series. C-RFA is an emerging procedure with encouraging early results; however, additional long-term prospective clinical trials are necessary to further characterize how C-RFA can best be used to treat chronic knee pain.

A manufacturer-sponsored trial on cooled radiofrequency ablation (CRFA) was reported by Chen et.al. 2020. In a prospective 1:1 randomized study the investigators randomized 177 patients to CRFA or a single injection of hyaluronic acid (Synvisc ONE). Although widely used, the efficacy of hyaluronic acid has not been supported by evidence. Therefore, it might be considered a placebo treatment. Crossovers to CRFA (n=68, 82.9%) were allowed at 6 months. A major limitation of this publication is that results were reported only for the 83% of control patients who crossed over; the authors noted that the remainder of the patients reported long-term pain relief from hyaluronic acid. An additional report of this trial is currently in press and may provide further detail to compare RFA and hyaluronic acid for patients with OA.

Limitations of these studies, which include potential for bias due to lack of patient blinding and insufficient number of patients in follow-up. Overall, the available studies have methodological limitations and the number of patients studied for this common condition is low.

Joint denervation has been shown to lead to progression of knee OA in animal models. It may be that thermally denaturing the sensory nerves around the knee in order to block the afferent transmission of pain from the knee joint allows the patient to become more active for a time but subsequently leads to more rapid progression of OA. This may also be true for other modalities of treatment such as knee injections. Loss of sensation in a joint in other settings can lead to a Charcot joint. At this time current studies have been unable to determine the long-term outcomes of loss of knee sensation or whether the nerves regenerate and over what time frame.

In 2020, Hunter et. al. performed an observational, prospective, multicenter study evaluating the long-term outcomes, including pain, function, and perceived effect of treatment, in subjects undergoing cooled radiofrequency ablation (CRFA) who have pain due to osteoarthritis (OA) of the knee. This analysis included a subset of subjects previously enrolled in a prospective, multicenter randomized study comparing the safety and effectiveness of CRFA and intra-articular steroid injection in patients with knee OA through 12 months who were contacted to participate in this extension study. Subjects were enrolled if they agreed to participate in up to 2 additional follow-ups, at 18 and 24 months. Eighty-three subjects from the 5 participating sites underwent CRFA during the original study and were contacted for this extension study. Of the 33 subjects enrolled, 25 were evaluated at 18 months after CRFA treatment, and their mean numeric rating scale (NRS) score was 3.1 ± 2.7, with 12 subjects reporting ≥50% pain relief compared to baseline. At 24 months, 18 subjects reported a mean NRS score of 3.6 ± 2.8, with 11 demonstrating ≥50% pain relief. Functional improvement as measured by the Oxford Knee Score continued to be present, with an overall mean change from baseline of 26.0 ± 9.6 points at 18 months and 29.9 ± 10.4 points at 24 months. A limitation of this study was its small sample size, with only a subset of patients enrolled in the trial being included in this analysis. There are several reasons driving this outcome, including the loss of 2 investigators, participation at only 5 of the original 11 trial sites, the inability to contact 35 of the patients, and patient exclusion due to use of alternate methods for treating their OA knee pain post-CRFA. Consequently, data from the 2 different CRFA-treated study populations were combined to facilitate an "N" for each outcome at the 18-month time point from which statistical analyses could be performed. Moreover, because this study was initiated 6 months after the conclusion of the original study, the timing of this latest data analysis contributed to patient attrition. In an attempt to compensate for this timing, wide follow-up windows of 3 months were allowed; however, 3 patients reported data beyond the windows for the study. There may also have been a bias towards unwillingness to return for follow-up, as CRFA does not involve a permanent implant and all patients had been referred to pain physicians for their symptom management. Additionally, the unblinded nature of the trial presents potential for bias.

Elawamy et. al. in 2021 performed a single-blind randomized interventional clinical trial on the efficacy of genicular nerve radiofrequency ablation versus intra-articular platelet rich plasma in chronic keen osteoarthritis. Two hundred patients with chronic knee osteoarthritis were equally and randomly distributed into 2 groups. Group PRF received pulsed radiofrequency, whereas the group PRP received intraarticular platelet-rich plasma. The visual analog scale and index of severity of osteoarthritis were evaluated before intervention, after one week (for visual analog scale only), then after 3, 6, and 12 months. Visual analog scale was significantly lower in the PRF group compared to the PRP group at 6 and 12 months with P-values of 0.01 and 0.04, respectively. Regarding to the postinterventional index of severity of osteoarthritis, it was significantly lower in the PRF group than the PRP group with P-values of 0.001 at 3-, 6-, and 12-months follow-up. Limitations of this study included physical and analgesic therapy were not included in data collection, and there was no control group.

Summary of Evidence
Knee osteoarthritis (OA) is a common disorder in older adults. Radiofrequency ablation (RFA) of the genicular nerves has the potential to alleviate pain and improve function in this population and might delay or eliminate the need for total knee arthroplasty (TKA). To date, the evidence on RFA for knee pain includes systematic reviews, randomized controlled trials (RCTs), prospective and retrospective trials and case series. Majority of trials reveal a high likelihood of biases to include lack of blinding, insufficient number of patients in follow-up, and methodological limitations to include heterogenous patient population with various sources of chronic pain. While Chen et. al. (2021) reported in systematic review that thermal RFA showed promise that pain relief was clinically notable at 24 months, it should be noted that the anatomy of the genicular nerves is variable, and the best method for their identification has not been determined and RCTs comparing conventional RFA, pulsed RFA and cooled RFA and their outcomes against one another are needed. Additional studies should also include how the use of radiofrequency ablation delays or eliminates the need for total knee arthroplasty. Also, while some studies may demonstrate that RFA allows some patients to reduce or eliminate opioid use, the overall dosing before and after RFA showed patients increased their opioid use post RFA likely due to opioid initiation for acute procedure related pain, or the need for additional management options after failure of the RFA procedure and a percentage of patients maintained their opioid dosing which may relate to failure of the procedure or the use of opioids for unrelated pain conditions. In addition, tapering opioids can be challenging and opioid use may not decrease despite RFA success. This possibility is supported by the finding that those who had a second RFA procedure and were therefore suspected of having some degree of benefit from initial RFA, had similar mean opioid doses pre-post RFA as the entire opioid cohort. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Cryoneurolysis (Cryoanalgesia, Cryotherapy, Cryoablation)
Knee osteoarthritis (OA) patients spend 50% of post diagnosis time receiving conservative, nonsurgical treatments, as total knee arthroplasty (TKA) is typically reserved for patients with end stage disease due to the limited lifespan of implants and associated risks. The use of low-risk minimally invasive therapies to treat chronic knee pain associated with osteoarthritis have been recommended to include cryoneurolysis.

Cryoneurolysis involves the technique of blocking peripheral nerve ending through freezing. Percutaneous application of low temperatures (-20°C to -100 °C) to peripheral nerves cause Wallerian degeneration, in which the nerve structure and conduction are disrupted while the structural elements of the nerve bundle remain intact, allowing for complete regeneration and functional recovery of the nerve. The nerve axon is able to regenerate along the previously established path to eventually reinnervate the sensory receptor. It is proposed that cryoneurolysis of sensory peripheral nerves can provide pain relief for a variety of chronic pain conditions, however, most studies have not been randomized controlled trials (RCTs).

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

Patients
The relevant population of interest are patients with osteoarthritis (OA) or who have undergone total knee arthroplasty (TKA).

Interventions
The therapy being considered is percutaneous cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) of the anterior femoral cutaneous nerve and/or the infrapatellar branch of the saphenous nerve.

Comparators
The following therapies are currently being used to treat OA or pain with TKA: conservative management which may include corticosteroid injections or oral medications for osteoarthritis (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 with a VAS or NRS. The Oxford Knee Score is scaled between 12 and 60, with 12 representing the best outcome. Quantifiable pre - and post-treatment 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.

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

In 2019, Walega et. al. performed a sham-control prospective clinical trial with six-month follow-up for genicular nerve radiofrequency ablation (GN-RFA) to assess if preoperative GN-RFA would improve postoperative pain outcomes following TKA. Refractory chronic knee pain from osteoarthritis (OA) is commonly treated with total knee arthroplasty (TKA). TKA can be associated with severe postoperative pain and persistent postsurgical knee pain. Poorly controlled postoperative pain can negatively affect functional outcomes following TKA, and effective opioid-sparing analgesia is key to the ideal recovery. Genicular nerve radiofrequency ablation (GN-RFA) has been shown in several trials to be clinically effective in patients with severe refractory knee pain from OA. This sham-control prospective clinical trial which blinded participants were randomized to image-guided GN-RFA or simulated sham procedure 2-6 weeks prior to elective TKA. Outcomes were assessed at 48 hours and 1, 3 and 6 months

following TKA. Seventy participants enrolled in this study. As compared with sham controls, GN-RFA had no treatment effect on postoperative consumption, pain or functional measures at any time point. The authors concluded cooled RFA of the superior lateral, superior medial and inferomedial genicular nerves, when performed 2-6 weeks prior to elective TKA as part of a multimodal postoperative pain management regimen, had no measurable effect on postoperative opioid use, analgesia use or function in the 48 hours following surgery. In addition, we found no longer term effect on outcome measures 1, 3, or 6 months after TKA.

Radnovich et. al. (2017) reported on a randomized, double blinded, sham-controlled, multicenter trial with a 6-month follow-up in patients with mild to moderate knee osteoarthritis, to evaluate the efficacy and safety/tolerability of cryoneurolysis for reduction of pain symptoms associated with knee osteoarthritis. The patients were randomized 2:1 to cryoneurolysis targeting the infrapatellar branch of the saphenous nerve (IPBSN) or sham treatment. Cryoneurolysis was administered using the iovera device and the sham treatment consisted of cryoneurolysis using the iovera device but did not allow a freezing zone to form and had no therapeutic effect. The primary endpoint was the change from baseline to Day 30 in the Western Ontario and McMaster Osteoarthritis Index (WOMAC) pain score adjusted by baseline score and site. Secondary endpoints, including Visual Analogue Scale (VAS) pain sore and total WOMAC score, were tested in pre-defined order. A total of 180 patients were enrolled (active treatment n=121 and sham treatment n=59). Compared to the sham group, patients who received active treatment had a statistically significant greater change from baseline in the WOMAC pain subscale score at Day 30 (P=0.0004), day 60 (P=0.0176) and day 90 (P=0.0061). Among patients who continued to have a benefit at day 120 and day 150, respectively, those who received active treatment had statistically significant lower WOMAC pain score at day 150 but not day 180 than those who received sham treatment. Most expected side effects were mild in severity and resolved within 30 days. The incidence of device or procedure related adverse events was similar in the two treatment groups with no occurrence of serious or unanticipated adverse side effects. Several limitations should be noted. Although allocation to treatment group was initially well concealed, patients began to more accurately guess their treatment group assignment based on their response to treatment over time, which may have affected patient-reported outcomes and biased results in favor of active treatment. There is a lack of consensus about how OA treatment responders should be defined. The study was conducted at multiple sites with different investigators applying treatment, lending greater weight to the robustness and generalizability of results, the trial should be replicated to ensure reproducibility of findings. The authors concluded cryoneurolysis of infrapatellar branch of the saphenous nerve (IPBSN) resulted in statistically significant decreased knee pain and improved symptoms compared to sham treatment for up to 150 days and appeared safe and well tolerated.

In 2016, Dasa et. al. completed a retrospective chart review of 100 patients who underwent total knee arthroplasty (TKA) to assess the value of adding perioperative cryoneurolysis to a multimodal pain management program. The treatment group

consisted of the first 50 patients consecutively treated after the practice introduced perioperative (five days prior to surgery) cryoneurolysis as part of its standard pain management protocol. The control group consisted of the 50 patients treated before cryoneurolysis was introduced. Outcomes included hospital length of stay (LOS), post-operative opioid requirements, and patient reported outcomes of pain and function. A significant lower proportion of patients in the treatment group had a LOS of > 2 days compared with the control group (6% vs 67%, $p < 0.0001$) and required 45% less opioids during the first 12 weeks of surgery. The treatment group reported a statistically significant reduction in symptoms at the six- and 12-week follow-up compared with the control group and within-group significant reductions in pain intensity and pain interference at two- and six-week follow-up, respectively. This study had several limitations, including its retrospective, nonrandomized and lack of blinding of patients and investigators, which may have biased results and limits the generalizability of findings. Selection bias may have influenced results as the control group was comprised of the first 50 patients with complete WOMAC responses treated prior to the initiation of preoperative cryoneurolysis. These patients may have been different from less compliant patients who did not complete the questionnaire and were excluded from the control group. In addition, differences between the control and treatment groups may be attributable to history or other confounding factors, rather than the study intervention. Because the treatment group underwent TKA more recently than the control group, and there has been a trend towards reducing post-operative LOS in the U.S, it is possible that the shorter LOS observed in the treatment group may be an artifact of history. The authors concluded perioperative cryoneurolysis in combination with multimodal pain management may significantly improve outcomes in patients undergoing TKA. Promising results from the preliminary retrospective study warrant further investigation of this novel treatment in prospective, randomized trials.

A retrospective chart review of 48 patients, 24 patients undergoing total knee arthroplasty (TKA) prior to March 31, 2014, comprised the control group and 24 patients undergoing TKA following cryoneurolysis comprised the cryoneurolysis treated (Cryo) group. It was hypothesized that a pre-operative cryoneurolytic block 5 days prior to surgery would decrease TKA postoperative pain. Subjects in the treated group received a cryoneurolysis treatment to the infrapatellar branch of the saphenous nerve (ISN) and the anterior femoral cutaneous nerve (AFCN) five days prior to TKA. Subjects in the control group received standard pre-operative care. Patient reported outcome measures were collected using the KOOS, Oxford Knee Score, SF12 and PROMIS scales at baseline (pre-cryoneurolysis), and at the 2-, 6- and 12-weeks postoperative visits. KOOS Pain score demonstrates that patients in the Cryo group had KOOS pain scores that were significantly higher (a higher KOOS Pain score indicates less knee pain) ($p < 0.05$) than those of the control group at both 6- and 12-weeks post-operation. The average difference in KOOS Pain score between the two groups at 6- and 12-weeks post-operation were 11.2 and 13.4 respectively. There were no significant differences in average scores for all additional outcomes measures (KOOS, Oxford Knee Score, SF12, and PROMIS) for any of the follow-up time points. The authors concluded cryoneurolysis to block the ISN and AFCN prior to the TKA appears to be an effective

method for reducing postoperative narcotic use and length of hospital stay. Additional research is required to further establish this method as a viable preoperative practice for patients undergoing TKA.

Makovtich et. al. reported on a case report for painful stiffness following total knee arthroplasty using cryoablation of the infrapatellar branch of the saphenous nerve. Injury to the infrapatellar branch of the saphenous nerve can result of knee trauma or iatrogenic (complication) causes during a total knee arthroplasty. Patients may complain of poorly localized, sharp and burning anteromedial knee pain especially with movement. Cryoablation of the IPBSN creates a reversible second-degree nerve injury, which results in a conduction block that provides prolonged pain relief. A 75-year-old woman presented with persistent knee pain and stiffness at 3 months post TKA despite 33 sessions of physical therapy. She reported a functional decline with disturbed sleep as well as a constant sharp, anterior knee pain (10/10) with a dull leg ache, all of which worsened with movement. Her x-rays demonstrated a well-fixed and aligned TKA without identifiable pathology for the knee pain. On exam she exhibited an antalgic gait with a flexed knee posture. Patient underwent consultation with PM&R and Orthopaedics, after the PM&R evaluation the consensus was to attempt cryoablation of the IPBSN prior to manipulation surgery. Cryoablation of the nerve (temp -22 °C to -88 °C) was performed at locations both proximal and distal to the bifurcation of the IPBSN using iovera cryotherapy system. The patient reported a pain score of 0/10 at 15 minutes post procedure, and she allowed aggressive manipulation of the knee and was able to ambulate in the clinic without pain. At 10 weeks post treatment the patient reported that she was pain-free and could actively participate in aggressive home exercises. Her active knee range of motion improved from 15 degrees to 105 degrees. Concluded that cryoablation of the IBSN should be considered in patients with refractory anterolateral knee pain after TKA.

Technical Issues
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 (e.g. ultrasound or using anatomic landmarks) also needs to be established.

Summary of Evidence
Based on review of the peer reviewed medical literature, the literature includes randomized controlled trials (RCTs), retrospective studies and a case report. While these studies may have shown promising results in the treatment of refractory knee pain from osteoarthritis (OA) using cryoablation, there continue to be several technical issues that 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 (e.g., ultrasound or using anatomic landmarks) that need to be established. Also, regarding the assessment of preoperative genicular nerve radiofrequency ablation (GN-RFA) improving postoperative pain outcomes following total knee arthroplasty (TKA), a prospective randomized sham-

controlled trial with six-month follow-up completed by Walega et. al. (2019) concluded that cooled RFA of the superior lateral, superior medial and inferomedial genicular nerves, when performed 2-6 weeks prior to elective TKA as part of multimodal postoperative pain management regimen had no measurable effect on postoperative opioid use, analgesia uses or function in the 48 hours following surgery. In addition, no long-term effect on outcome measures 1, 3 and 6 months after TKA were found. Further randomized, double-blinded studies to include comparing cryoablation (cryoneurolysis, cryotherapy, cryoanalgesia) against other neurolytic modalities are needed to establish this neurolytic modality is effective in the treatment of chronic pain associated with osteoarthritis (OA) of the knee to include assessing the effectiveness of this treatment modality as a preoperative and postoperative practice undergoing TKA to improve postoperative pain outcomes and effect on opioid use. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Chemical Neurolysis
Osteoarthritis is a common source of pain in the hips and knees, there is a significant impact on mobility. A joint replacement is a remedy for many patients, but comorbidities may prevent this as an option. Chemical neurolysis (phenol, alcohol, glycerol) may be an option to provide pain relief and maintain mobility. Chemical neurolysis causes nerve destruction and has a local anesthetic effect on smaller nerve fibers.

Based on review of the peer reviewed medical literature the evidence is very limited, no controlled studies were identified on the use of chemical neurolysis (phenol, alcohol, glycerol) of the treatment of osteoarthritis of the knee. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Osteoarthritis of the Hip
Osteoarthritis of the hip is a common condition that many people develop during middle age or older, though it may occur in younger people too. Osteoarthritis can occur in any joint in the body, but most often develops in weight-bearing joints, such as the hip. Osteoarthritis develops slowly and the pain it causes worsens over time and there is no cure. Osteoarthritis has no single specific cause, but there are certain factors that may increase an individual's risk for developing to include: increasing age, family history of osteoarthritis, previous injury to hip joint, obesity, and improper formation of the hip joint at birth, a condition known as developmental dysplasia. Osteoarthritis can still develop despite not having any of these risk factors. In osteoarthritis of the hip joint, the hip joint gradually wears away over time. As the cartilage wears away, it becomes frayed and rough and the protective joint space between the bones decreases. This can result in bone rubbing on bone. To make up for the lost cartilage, the damaged bones may start to grow outward and form bone spurs (osteophytes). The most common symptom of hip osteoarthritis is pain around the hip joint. Over time, painful symptoms may occur more frequently, including during rest or at night. Additional symptoms may include: pain in the groin or thigh that radiates to the buttocks or knee, pain that flares up with vigorous activity, stiffness in the hip joint that makes it difficult to walk or bend, locking or sticking of the joint and a grinding noise (crepitus) during movement caused by loose

fragments of cartilage and other tissues interfering with the smooth motion of the hip, and decreased range of motion in the hip that affects the ability to walk and may cause a limp. The treatment of osteoarthritis (OA) is directed towards reduction of symptoms and improve function. Nonsurgical treatment includes lifestyle modifications: minimizing activities that aggravate the condition, such as climbing stairs, switching from high impact activities to lower impact activities, losing weight can reduce stress on the hip joint, resulting in less pain and increased function; physical therapy; assistive devices (cane, crutches, walker); medications (acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids either orally or injected into the painful joint. Surgical treatment may include osteotomy, hip resurfacing or total hip arthroplasty.

When an individual exhibits hip pain, the pain signals can be generated from the peripheral nerves innervating the hip including the femoral and obturator nerves, an ablative procedure using radiofrequency ablation (conventional, pulsed or cooled); chemical neurolysis or cryoneurolysis (cold) of these nerves may be performed to restore function and alleviate hip pain as an alternative therapy. Surgical treatment may not be an option for patients with multiple comorbidities, these ablative procedures have been proposed as an alternative for the treatment of chronic hip pain.

Radiofrequency Ablation

Clinical Context and Therapy Purpose
The purpose of radiofrequency ablation (RFA) in patients with osteoarthritis (OA) of the hip who have severe refractory pain is to provide a treatment option that is an alternative to non-surgical treatment which includes lifestyle modifications: minimizing activities that aggravate the condition, such as climbing stairs, switching from high impact activities to lower impact activities, losing weight can reduce stress on the hip joint, resulting in less pain and increased function; physical therapy; assistive devices (cane, crutches, walker); medications (acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids either orally or injected into the painful joint; or to surgical treatment which may include osteotomy, hip resurfacing or total hip arthroplasty.

Patients
The relevant population of interest are patients with hip OA.

Comparators
The following therapy is currently being used to treat OA: lifestyle modifications: minimizing activities that aggravate the condition, such as climbing stairs, switching from high impact activities to lower impact activities, losing weight can reduce stress on the hip joint, resulting in less pain and increased function; physical therapy; assistive devices (cane, crutches, walker); medications (acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids either orally or injected into the painful joint.

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). Quantifiable pre- and posttreatment measures of functional status are also used, such as the12-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 Randomized controlled trials (RCTs) are needed to determine whether outcomes are improved with interventions for pain.

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.
Rivera et. al. (2012) completed a prospective study of 18 patients with chronic hip pain with several contraindications for total hip arthroplasty (THA). Predenervation diagnosis was osteoarthritis in 16 patients and prolonged post-operative hip pain in 2 (1 THA, 1 Girdlestone). The hip pain was treated by percutaneous radiofrequency lesioning of the sensory branches of the obturator and femoral nerves. Six-month follow-up data revealed a statistically significant decrease in Visual Analog Scale (VAS) scores and Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) scores, and a statistically significant increase of Harris Hip Score. Before radiofrequency and at 6-month follow-up, mean VAS scores were 9.52 (range 7-10; standard deviation 0.79) and 6.35 (range 3-10; standard deviation 2.17), respectively; mean Harris Hip Scores were 28.64 (range 19-41; standard deviation 6.98) and 43.88 (range 23.71; standard deviation 16.38), respectively; and mean WOMAC scores were 75.70 (range 92-59; standard deviation 9.70) and 63.70 (range 78-44; standard deviation 11.37), respectively. All values were statistically significant ($P<.05$) for Student's t test and Wilcoxon signed-rank test. Eight patients reported > 50% pain relief at 6-month follow-up. No side effects were reported. The authors concluded the use of this technique for hip pain control is controversial. In our experience, percutaneous radiofrequency lesioning of the sensory branches of the nerves innervating the hip joint can be an option for patients with intractable hip pain.

Chye et. al. (2015) completed a prospective comparative study of 29 patients with chronic hip pain that were divided into two groups, pulsed radiofrequency (PFR) and conservative treatment. Fifteen patients received PRF of the articular branches of the femoral or obturator nerves, and 14 patients received conservative treatment. Visual Analog Scale (VAS) score, Oxford Hip Scores (OHS) and pain medications were used for outcome measurement before treatment and at 1 week, 4 weeks, and 12 weeks after treatment. Results at 1 week, 4 weeks and 12 weeks after treatment initiation, improvements in VAS were significantly greater with PRF. Improvements in OHS were

significantly greater in the PRF group at 1 week, 4 weeks and 12 weeks. Patients in the PRF group also used less pain medications, eight subjects in the conservative treatment group switched to the PRF group after 12 weeks and six of them had > 50% improvement. The authors concluded pulsed radiofrequency (PRF) of the articular branches of the femoral and obturator nerves offers a treatment option with good outcomes for patients suffering from chronic hip pain. When compared with conservative treatment, it offers greater pain relief and can augment physical functioning. Although this study produced promising results, caution is advised in drawing conclusions from this single study. Controlled, randomized investigations with longer observation periods are necessary to further clarify the role of pulsed radiofrequency (PRF) in the treatment of chronic hip pain.

In 2018 Bhatia, et. al. completed an evidence-based narrative review regarding radiofrequency procedures to relieve chronic hip pain. Chronic hip pain from osteoarthritis and other degenerative conditions is a common problem. A few publications have recently reported analgesic success of radiofrequency (RF) procedures on nerves innervating the hip, but interpretation is hampered by lack of clarity regarding indications, clinical protocols, anatomic targets, and longevity of benefit from RF procedures. For this evidence based narrative review the following medical literature databases for publications on RF procedures on the hip joint for chronic pain: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Google Scholar through February 28, 2017. Existing knowledge on innervation of the hip joint was synthesized. Data on analgesic and functional outcomes and adverse effects measured at any time points following the interventions were also collected, analyzed and reported in this narrative review. Fourteen publications on ablative RF treatments of innervation of the hip joint were identified. A high success rate of these procedures in relieving chronic pain of the hip joint was reported at 8 days to 36 months after the procedures, but none of the publications were randomized controlled trials. There was evidence for improvement in function and a lack of serious adverse events of RF treatments. The authors concluded radiofrequency treatments for the sensory innervation of the hip joint have the potential to reduce pain secondary to degenerative conditions. Ongoing concerns remain regarding the anatomic targets, as well as quality, procedural aspects, and monitoring outcomes in publications on this topic. Randomized controlled trials of high methodological quality are required to further elaborate the role of these interventions in this population.

Kapural et. al. (2018) conducted a retrospective chart review in an interventional pain management urban private practice. Chronic hip joint pain is a common condition with an estimated prevalence of 7% in men and 10% in women, in a population sample aged over 45. Conservative treatment can include physical therapy, weight loss, a variety of pharmacologic agents ranging from nonsteroidal anti-inflammatory drugs (NSAIDS) to opioids, and intraarticular injections with various substances. Definitive treatment of hip pain, however, has primarily centered on hip arthroplasty. Data on 52 radiofrequency (RF) ablations of the hip in 23 patients were retrospectively collected. RF ablation was conducted with patient supine and under guidance of fluoroscopy and ultrasound (US).

While fluoroscopy was used to place RF probes to appropriate landmarks, sole purpose of using US was to avoid femoral neurovascular bundle. Data were collected on needle placement, stimulation parameters, and short- and long-term complications. A total of 62 patients underwent 2 diagnostic blocks. Fifty-two of them had greater than 50% relief and agreed to RF ablation. Until now, the ablation was conducted in 23 patients. There were no adverse events, except one case of neuritis. Expectedly, the needle approach to the lateral articular branches of the femoral nerve was easily achieved with more than a 1 cm passage distance from the femoral nerve in all 52 RF cases (median 2.5 range 1-3.5 cm). Placement of the second trocar to the incisura acetabuli was more challenging; in 21 RF cases the passing distance was less than 1 cm (range 0.5 to 1.9 cm, median 0.8). Motor stimulation (2 Hz) at less than 1 V was positive for the obturator nerve in 26 cases, which resulted in electrode repositioning more laterally (2-5 mm). Change in the pain scores was from the baseline 7.61 ± 1.2 to 2.25 ± 1.4 after the RF ablation ($P < 0.01$). The time interval of pain relief was much longer for RF ablation. Limitations of this retrospective, observational study include lack of blinding and absence of a comparator group.

Summary of Evidence
Based on review of the peer reviewed medical literature the literature is limited regarding radiofrequency ablation (RFA) (conventional, pulsed and cooled) for the treatment of osteoarthritis of the hip. Although these limited studies may have shown promising results, further randomized clinical trials (RCTs) are needed to include studies with larger sample sizes, longer follow periods and double blinding to establish the overall effectiveness of these procedures and to compare their outcomes against one another. The evidence is insufficient to determine the effects of this technology on net health outcomes and therefore is considered investigational.

Cryoneurolysis (Cryoanalgesia, Cryotherapy, Cryoablation)
Based on review of the peer reviewed medical literature the evidence is very limited, no controlled studies were identified on the use of cryoneurolysis (cryoablation, cryotherapy, cryoanalgesia) to treat osteoarthritis of the hip. Most studies are related to osteoarthritis of the hip and cryoneurolysis. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Chemical Neurolysis
Osteoarthritis is a common source of pain in the hips and knees, there is a significant impact on mobility. A joint replacement is a remedy for many patients, but comorbidities may prevent this as an option. Chemical neurolysis (phenol, alcohol, glycerol) of the obturator nerve may be an option to provide pain relief and maintain mobility. Chemical neurolysis causes nerve destruction and has a local anesthetic effect on smaller nerve fibers.

Based on review of the peer reviewed medical literature the evidence is very limited, no controlled studies were identified on the use of chemical neurolysis (phenol, alcohol, glycerol) of the treatment of osteoarthritis of the hip. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Chronic Shoulder Pain
Shoulder pain is a common musculoskeletal complaint often stemming from multiple factors and underlying pathology. Shoulder pain can occur at any age and be aggravated by many common daily activities including manual labor, physical activity and general repetitive motions.

The suprascapular nerve innervates the supraspinatus and infraspinatus muscles. Suprascapular nerve injury causes a peripheral neuropathy that is estimated to account for 1 to 2 percent of pathologic shoulder conditions. Injuries to the suprascapular nerve arise most often from mechanical compression, occasionally caused by cysts or tumors. Suprascapular neuropathy causes pain, progressive atrophy, and weakened abduction and external rotation of the shoulder and can be difficult to distinguish from rotator cuff tears. Initial management usually includes activity modification, physical therapy and nonsteroidal anti-inflammatory drugs. Surgical intervention includes decompression of the suprascapular nerve for symptoms refractory to conservative measures.

Axillary nerve palsy, axillary nerve dysfunction or neuropathy of the axillary nerve is a neurological condition in which the axillary nerve has been damaged, it can cause weak deltoid and sensory loss below the shoulder. Signs and symptoms may include pain to the area of the deltoid and anterior shoulder, loss of movement and/or lack of sensation in the shoulder area. Causes of axillary nerve dysfunction include blunt trauma or excessive stress on the nerve over a long period, other body structures putting pressure on the axillary nerve or trapping it against another body part, penetrating injury or exceeding the normal range of motion which can occur with a hyperextension injury to the shoulder. Conservative management includes physical therapy and anti-inflammatory medications and for severe pain the physician may prescribe an opioid medication. In some cases, surgery may be required to repair areas around the axillary nerve.

Glenohumeral osteoarthritis represents wear and tear of the articular cartilage of the glenoid, labrum and humeral head. It is an uncommon problem that is generally preceded by trauma, although the injury may have occurred years earlier. Injuries that are associated with the development of osteoarthritis include previous dislocation, humeral head or neck fracture, large rotator cuff tendon tears (loss of musculotendinous support), and rheumatoid arthritis. Patients complain of the gradual development of anterior or deep shoulder pain and stiffness over a period of months to years. Both active and passive motion particularly abduction and external rotation, become diminished as articular degeneration grows more severe. Conservative management is aimed at relieving pain and preserving range of motion. Options include anti-inflammatory medications, corticosteroid injections, and physical therapy.

Nerve ablation relieves chronic pain by preventing the transmission of pain signals. In general, it is a safe procedure in which a small part of the nerve is destroyed or removed in order to interrupt the pain signal. Nerve ablation can be done in different ways, using cold, heat or even chemicals. Ablative procedures such as radiofrequency ablation (RFA),

cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis have been proposed as an alternative for the treatment of chronic shoulder pain.

Clinical Context and Therapy Purpose
To provide at treatment option that is an alternative to or an improvement on existing therapies.

Patients
The relevant population of interest are patients with chronic shoulder pain.

Interventions
The therapy being considered is radiofrequency ablation (RFA), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis.

Comparators
The following therapy is currently being used to make decisions about treating chronic shoulder pain: conservative management is aimed at relieving pain and preserving range of motion, options include anti-inflammatory medications, corticosteroid injections, and physical therapy

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 time for follow-up is within days to determine procedure success and at least six months to a year to evaluate durability.

Radiofrequency Ablation
In 2012, Simopoulos et. al. retrospectively evaluated the analgesic effects of continuous radiofrequency lesioning of the suprascapular nerve (SSN) for chronic shoulder pain. This study was a case series involving patients with unremitting shoulder pain that lasted for at least 12 months. Patients were selected if they showed a reduction of at least 50% in pain intensity during the anesthetic phase after SSN block, no additional motor weakness of the shoulder and pain relief lasting for less than two months after separate treatments of the SSN with corticosteroids and pulsed radiofrequency. Nine patients were referred to the Arnold Pain Management Center. Of these nine patients, six patients who had significant chronic shoulder pain unresponsive to oral medications and intra-articular injections and who were not considered surgical candidates were selected. These patients were treated with a single radiofrequency lesion of the SSN at 80°C for 60 seconds. The primary outcome was a reduction in pain intensity by 50%, as determined by the numeric rating scale, and duration of this effect. The secondary outcome was improvement in either the passive or the active range of motion (ROM). Patients were

also monitored for adverse effects such as weakness or increased pain. The pooled mean numeric rating scale score before the procedure was 7.2 ± 1.2; this fell to 3.0 ± 0.9 at 5–7 weeks post procedure. The duration of pain relief ranged from 3 to 18 months, and all patients underwent at least one additional treatment. The change in baseline ROM improved from an average of 60 degrees ± 28 degrees (flexion) and 58 degrees ± 28 degrees (abduction) to 99 degrees ± 46 degrees (flexion) and 107 degrees ± 39 degrees (abduction). No adverse side effects were observed. The authors concluded continuous radiofrequency lesioning of the SSN seems to be an effective treatment for chronic shoulder pain. There can be improved ROM of the shoulder following this treatment. More formal, controlled studies are required to confirm these observations.

In 2019 Orhurhu et. al. completed a systematic review on the use of radiofrequency ablation (RFA) for the management of shoulder pain. The treatment options for the management of shoulder pain are broad but evolving process. Modalities for controlling shoulder pain have commonly focused on pharmacotherapy, physical therapy, rehabilitation, and invasive procedures (surgical procedures, surgical, intra-articular steroid injections, many times, being sub-optimal). The use of radiofrequency ablation (RFA) for managing shoulder pain is on the rise. This review investigated the evidence for the use of RFA in the management of shoulder pain. a review of the literature was conducted using Medline, PubMed, and Cochrane Database of Systematic Reviews from 1966 to 2018. Our study included RCTs, open non-randomized control studies, prospective studies, retrospective studies, case series, and case reports. We limited our search to patients with chronic shoulder pathologies. Our initial search identified 96 articles for initial review. This was narrowed down to 31 articles, which met our inclusion criteria, with only 18 articles remaining after our exclusion criteria was applied. This systematic review suggests that shoulder RFA may provide a safe and significant benefit in the management of chronic shoulder pain. There were a few high-quality RCTs included in our study.

In 2020, Eckmann et. al. discussed articular nerve block and radiofrequency ablation (RFA) for the treatment of chronic shoulder joint pain. Generally, degenerative disease of the shoulder includes: 1) cartilaginous injury, osteoarthritis, and inflammatory arthridities, 2) soft tissue disorders such as tendinitis, bursitis, tendinopathy, tendon tear, and adhesive capsulitis, 3) instability and impingement disorders. Advanced shoulder disease rarely manifests in a sole anatomic location and often presents with a constellation of joint and soft tissue findings. Treatments for chronic shoulder pain are as diverse as the etiologies. Exercise and physiotherapy are important foundations of treatment. Besides NSAIDS and other forms of medical management, steroid injections of the shoulder are a common treatment for musculoskeletal causes of shoulder pain. Both thermal and pulsed radiofrequency ablation (RFA) of the suprascapular nerve have been described to treat chronic shoulder pain, but there is a theoretical concern of post-ablation weakness in the supraspinatus and infraspinatus muscles. The safe zones for ablation have been defined as the area lateral to the spinoglenoid notch posteriorly (suprascapular branches), at the inferior-posterior portion of the greater tubercle (axillary branches), and over the coracoid process (lateral pectoral branches). Ideal patients for

articular sensory denervation should have clinical evidence of symptomatic osteoarthritis. Candidates may have chronic shoulder pain of suspected peripheral origin (ie, not of central origin) that has persisted despite rational multimodal therapy, especially if they are not good surgical candidates. Diagnostic blocks should be performed to identify patients who should proceed to have ablation. This is standard with other ablation techniques of the spine and major joints. A patient with greater than 50% pain relief is considered to have a positive diagnostic block. Further studies are needed to determine the ideal number of blocks, block relief threshold, and volume of injectate for the diagnostic block. Inadvertent intra-articular injections are possible with this procedure. While intra-articular injections have diagnostic value, they probably have less prognostic value for RFA success; this phenomenon has been observed in other anatomic structures such as the lumbar zygapophyseal joint. Nerve selection should follow zones of pain perception. Deep posterolateral pain would suggest that the suprascapular and axillary nerve should be targeted. Anterior pain may suggest that the lateral pectoral nerve and nerve to subscapularis should be targeted. Safety considerations for both diagnostic blocks and RFA share commonalities with other pain interventions of low to intermediate risk. There is a low but possible risk of vascular, nerve/plexus injury, and joint infection. Extra caution must be taken for patients with implanted cardiac devices. The authors concluded clinical success in the ablation of fibers from the suprascapular, axillary, and lateral pectoral nerves has been reported. The nerve to subscapularis is a possible target for anterior shoulder pain. Ablation procedures of the shoulder should be performed with attention to anatomy, safety, and consideration of patient-centered risks and benefits in accordance with medical societal guidance. Additional research is warranted to improve patient selection, technique, pain relief, and functional outcomes.

In 2021, Eckmann et. al., reported on the current understanding and gaps in nerve ablation for chronic shoulder pain. The review provides a summary of relevant neuroanatomy, proposed ablation targets, safety and efficacy concerns for ablation targets, and current research gaps. Radiofrequency ablation (RFA) of peripheral sensory nerves is a well-established treatment for chronic joint and spine pain, but it is relatively nascent for shoulder pain. Cadaveric studies demonstrate the shoulder joint is innervated by articular branches of the suprascapular nerve, axillary nerve, lateral pectoral nerve, and upper and lower subscapular nerves. Shoulder articular branch RFA appears to be a safe and effective treatment for chronic shoulder pain, but there are currently no widely accepted protocols for ablation targets. There are also no randomized controlled trials (RCT) assessing safety and efficacy of proposed targets or the prognostic value of articular blocks. Future research studies should prioritize categorical data, use appropriate functional measures as primary endpoints, and would ideally include a large-scale RCT.

Summary of Evidence

Based on review of the peer reviewed medical literature the literature is limited regarding radiofrequency ablation (RFA) (conventional, pulsed and cooled) for the treatment of chronic shoulder pain. Although these limited studies may have shown promising results, further randomized clinical trials (RCTs) are needed to include studies with larger sample sizes, longer follow periods and double blinding to establish the overall effectiveness of

these procedures and to compare their outcomes against one another. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Cryoneurolysis (Cryoanalgesia, Cryotherapy, Cryoablation)
Cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) the use of cold to provide analgesia has been utilized for the treatment of chronic shoulder pain. The effectiveness of this therapy is dependent on proximity of the probe to the nerve, size of the probe, rate and duration of freezing and temperature of the tissues in proximity to the probe.

Per review of the peer reviewed medical literature, the literature is limited related to cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) for the treatment of chronic shoulder pain. Further randomized clinical trials (RCTs) to include prospective double blinding randomized controlled studies with larger sample sizes and longer follow periods are needed to determine the efficacy of cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) in the treatment of chronic shoulder pain. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Chemical Neurolysis
Chemical neurolysis is the use of a chemical using phenol, alcohol, glycerol or a hypertonic saline to cause destruction of nerve(s) by causing a temporary degeneration of the nerve(s) fibers to interrupt the transmission of nerve(s) signals for pain relief.

For patients with chronic shoulder pain no published literature was identified in-regards to patients receiving chemical neurolysis (alcohol, phenol, glycerol) for the treatment of this condition. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Intercostal Neuralgia
Intercostal neuralgia refers to a neuropathic condition involving the intercostal nerves, manifesting as intense dysesthetic pain, e.g., sharp, shooting or burning in quality radiating around the chest wall. Intercostal nerves are peripheral nerves that run along with the vascular bundle on the inferior surface of each rib. The pain usually begins at the posterior axillary line and radiates anteriorly into the distribution of the affected intercostal and sub costal nerves. Deep inspiration or movement of the chest wall may increase the pain of intercostal neuralgia slightly but much less compared with the pain.

Intercostal neuralgia occurs due to a number of reasons such as nerve entrapment, a traumatic or iatrogenic (caused by a complication) neuroma, persistent nerve irritation, or herpes zoster. The pain of the intercostal neuralgia is the result of a damage or inflammation of the intercostal nerves and can be localized in one or more of the intercostal spaces. Although it is commonly seen and recognized in patients with chronic chest wall pain after thoracotomy, intercostal neuralgia has been reported in patients after breast and abdominal surgery, trauma and infection. There are several treatment options available, including systemic medications, topical or invasive nerve blocks, cryoablation and radiofrequency ablation (conventional and pulsed).

A definite treatment protocol is yet to be suggested for patients with intercostal neuralgia, as the efficacy of the proposed treatments is difficult to evaluate. Small sample sizes, difficulty in assigning control groups, and ambiguous outcome parameters are the main factors that affect the outcome. The initial choice of therapy should be guided by the patient's comorbidities, adverse effects of drugs and patient preference. Based on the findings of the pain questionnaires, additional diagnostics and/or multidisciplinary treatment interventional pain treatment may be considered that includes radiofrequency ablation and cryoablation (cryoneurolysis). Radiofrequency ablation to include pulsed radiofrequency has generated interest in the treatment of neuropathic pain. Cryotherapy (cryoneurolysis) involves another way of interrupting the peripheral nerve's ability to transmit pain by freezing it. Cryotherapy has been used on neuromas and the involved intercostal nerves.

Clinical Context and Therapy Purpose
To provide at treatment option that is an alternative to or an improvement on existing therapies.

Patients
The relevant population of interest are patients with intercostal neuralgia.

Interventions
The therapy being considered is radiofrequency ablation (RFA), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis.

Comparators
The following therapy is currently being used to make decisions about treating intercostal neuralgia: systemic medications, topical or invasive nerve blocks.

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 time for follow-up is within days to determine procedure success and at least six months to a year to evaluate durability.

Radiofrequency Ablation
Radiofrequency ablation to include pulsed radiofrequency ablation has been studied in the treatment of chronic intercostal neuralgia pain. Based on review of the literature which includes retrospective and prospective studies and case series/case reports, there is very limited evidence in the literature. Most studies are limited in patient size and of limited long-term follow-up. There is a need for further double blinded randomized trials to further elicit the efficacy of radiofrequency ablative therapy in the treatment of chronic

intercostal neuralgia pain. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Cryoneurolysis (Cryoanalgesia, Cryotherapy, Cryoablation)
Cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) the use of cold to provide analgesia has been utilized for the treatment of chronic intercostal neuralgia pain. The effectiveness of this therapy is dependent on proximity of the probe to the nerve, size of the probe, rate and duration of freezing and temperature of the tissues in proximity to the probe. Based on review of the literature which includes retrospective and prospective studies and case reports, the literature shows mixed results. While some studies have shown promising results of reduced pain, numerous studies yielded concerns about study quality, small study sizes and patient follow-up. Further randomized clinical trials (RCTs) to include prospective double blinding randomized controlled studies with larger sample sizes and longer follow periods are needed to determine the efficacy of cryoablation (cryodenervation) in the treatment of chronic intercostal neuralgia. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Chemical Neurolysis
Chemical neurolysis is the use of a chemical using phenol, alcohol, glycerol or a hypertonic saline to cause destruction of nerve(s) by causing a temporary degeneration of the nerve(s) fibers to interrupt the transmission of nerve(s) signals for pain relief and has been proposed in the treatment of chronic intercostal neuralgia.

Based on review of the peer reviewed medical literature, the literature is limited on the use of chemical neurolysis for the treatment of chronic intercostal neuralgia. Randomized clinical trials (RCTs) are needed to determine the efficacy of chemical neurolysis for the treatment of chronic intercostal neuralgia to include studies with large sample sizes and longer follow periods to establish the overall effectiveness of this procedures compared to other alternative treatments. The evidence is insufficient to determine the effects of this technology on net health outcomes

Inguinal Neuralgia
Chronic inguinal neuralgia involving the ilioinguinal and iliohypogastric nerves is a frequent complication of surgical procedures involving a lower abdominal incision such as hernia repair, appendicitis surgery, caesarean section and may also occur with trauma to the lower quadrant of abdomen or inguinal region. Chronic inguinal neuralgia is a chronic persistent pain in the pelvic and/or groin region caused by nerve dysfunction. Treatment modalities for inguinal neuralgia include nonsteroidal anti-inflammatory medications (NSAIDs), nerve block, nerve ablation, surgery, and nerve stimulation. Ablative procedures such as radiofrequency, cryoneurolysis and chemical neurolysis have been proposed as an alternative for the treatment of chronic inguinal neuralgia pain.

Clinical Context and Therapy Purpose
To provide at treatment option that is an alternative to or an improvement on existing therapies.

Patients
The relevant population of interest are patients with chronic inguinal neuralgia involving the ilioinguinal and iliohypogastric nerves.

Interventions
The therapy being considered is radiofrequency ablation (RFA), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis.

Comparators
The following therapies are currently being used to make decisions about treatment chronic inguinal neuralgia: nonsteroidal anti-inflammatory medications (NSAIDs), nerve block, nerve ablation, surgery, and nerve stimulation.

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 measured with a visual analog scale (VAS) or numeric rating scale (NRS).

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

Radiofrequency Ablation
Based on review of the peer reviewed medical literature, the literature is limited to one randomized trial, retrospective studies and case series, for radiofrequency ablation (conventional and pulsed) for the treatment of chronic inguinal neuralgia.

In 2012, Kastler et. al. completed a retrospective study to evaluate and compare ilioinguinal and iliohypogastric radiofrequency neurolysis and local injection for the treatment of chronic inguinal neuralgia. Forty-two patients suffering from chronic inguinal pain refractory to specific medication were included. A total of 18 radiofrequency neurolysis (RFN) procedures (14 patients) and 28 injections (28 patients) were performed. Pain was assessed in both groups using Visual Analog Scale (VAS) scores measured immediately before and after the procedure at one, 3, 6, 9 and 12 months after the procedure. Mean duration of pain prior to the procedure and mean duration of pain relief were noted. Moreover, mean maximum early pain relief was assessed. All procedures were ambulatory under computed tomography (CT) guidance. Injections contained 1.5 mL of cortivazol and 3 mL of lidocaine-ropivacaine (30%-70%). Radiofrequency neurolysis was performed using a Neurotherm RF Generator. The mean age in both groups was 48.7 years. Forty-two patients presented with post-surgical inguinal pain which occurred after hernia repair. All included patients that had undergone previously unsuccessful pain therapies. Mean VAS scores were 7.72 in the RF group and 7.46 in the infiltration group. Maximum early pain relief did not statistically differ (77% in the RFN group and 81.5% in the injection group). Mean duration of pain relief was statistically significant (P=.005) in the RF group (12.5 months) compared to the

infiltration group (1.6 months). Mean VAS scores during the year following the procedure were all significantly in favor of radiofrequency neurolysis management. Limitations of this study include small study samples and retrospective study. The authors concluded that radiofrequency neurolysis appears to be significantly more effective than local nerve infiltrations. It is a safe and effective treatment for chronic inguinal pain. Local steroid injection along with local injection of anesthetic should be used as a confirmation of ilioinguinal neuropathy before performing radiofrequency neurolysis.

In 2015, Makharita et. al. completed a randomized, double-blind controlled trial to evaluate the efficacy of pulsed radiofrequency in management of chronic inguinal neuralgia. Chronic inguinal neuralgia has been reported after inguinal herniorrhaphy, caesarean section, appendectomy and trauma to the lower quadrant of the abdomen or inguinal region. Twenty-one adult patients aged between 20 and 60 years were allocated into 2 groups. Group 1 received 2 cycles of pulsed radiofrequency (PRF) for each nerve root. In Group 2, after stimulation, the same time was spent to mimic PRF. Both groups received bupivacaine 25% plus 4mg dexamethasone in 2mL for each nerve root. Visual Analogue Scale (VAS) was assessed. Duration of the first block effective pain relief was reported. Repeated PRF blockade was allowed for any patient who reported a VAS > 30 mm in both groups during the one-year follow-up period. The number and duration of blocks were reported, and adverse effects were reported. Significantly longer duration of pain relief was noticed in Group 1 (P=0.005) after the first block, while the durations of pain relief of the second block were comparable (P=0.59). In Group 1 the second PRF produced pain relief from the twenty-fourth week until the tenth month while in Group 2, pain relief was reported from the sixteenth week until the eighth month after the use of PRF. All patients in Group 2 received 3 blocks (the first was a sham PRF) during the one-year follow-up period. Meanwhile, 2 PRF blocks were sufficient to achieve pain relief for patients in Group 1 except 4 patients who needed a third PRF block. No adverse events were reported. Limitations include small sample size, and the study was not powered. The authors concluded for intractable chronic inguinal pain; pulsed radiofrequency represents a promising treatment modality. It is superior to local anesthetic and steroid injection. It provides pain relief for about 20 weeks, and it can be repeated.

Summary of Evidence
Based on review of the peer reviewed medical literature, the literature is limited to one randomized trial, retrospective studies and case series, for radiofrequency ablation (conventional and pulsed) for the treatment of chronic inguinal neuralgia. While these studies may have shown promising results, further prospective randomized clinical trials (RCTs) are needed to determine the efficacy of radiofrequency ablation (conventional, pulsed, cooled) to include studies with larger sample sizes, longer follow periods and double blinding to establish the overall effectiveness of these procedures and to compare their outcomes against one another. The evidence is insufficient to determine the effects of this technology on net health outcomes

Cryoneurolysis and Chemical Neurolysis
Nerve ablation using cryoneurolysis (cryoablation, cryotherapy, cryoanalgesia) and chemical neurolysis (phenol or alcohol) have been proposed as an alternative treatment for the treatment or chronic inguinal neuralgia for patients who have failed other non-surgical management. There is little published evidence related to the use of cryoneurolysis and chemical neurolysis in the treatment of chronic inguinal neuralgia. Alcohol or phenol injection have been tried to reduce chronic inflammation and destroy the offending nerve ending(s). Cryoablation (cryoneurolysis) destroys the nerve fibers by coagulation at very low temperatures, have been shown to give some temporary pain relief. Typically following these procedures pain recurred due to nerve regeneration. Definitive evidence for their effectiveness is lacking. Further randomized clinical trials are needed to determine the effectiveness of cryoneurolysis and chemical neurolysis for the treatment of chronic inguinal neuralgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Plantar Fasciitis
Plantar fasciitis is one of the most common causes 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 may persist, 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 is unclear, although repetitive injury is suspected. Possible risk factors for the development of plantar fasciitis include obesity, prolonged standing or jumping, flat feet and reduced ankle dorsiflexion. Although heel spurs often coexist with plantar fasciitis, it is unclear whether they have a causal role and may instead represent a secondary response to an inflammatory reaction. Most cases of plantar fasciitis are treated with conservative therapy, including stretching exercises for the plantar fascia and calf muscles; decreasing physical activities that are causative or aggravating (running, jumping, dancing); avoiding the use of flat shoes or barefoot walking; prefabricated over the counter arch supports/heel cups; molded shoe inserts (orthotics); night splints; nonsteroidal anti-inflammatory drugs (NSAIDs); and injecting tender areas of the plantar region with glucocorticoids and a local anesthetic. Improvement may take up to 1 year in some cases. Ablative procedures to include radiofrequency ablation, cryoneurolysis (cryoablation, cryoanalgesia, cryotherapy) and chemical neurolysis have been proposed as an alternative for the treatment of chronic heel pain associated with plantar fasciitis.

Clinical Context and Therapy Purpose
To provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Interventions
The therapy being considered is radiofrequency ablation (RFA), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis.

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, randomized controlled trials (RCTs) are needed to determine whether outcomes are improved with interventions for pain.

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

Radiofrequency Ablation
Several case series and an RCT (randomized controlled trial) were identified that evaluated radiofrequency ablation (RFA) for the treatment of chronic heel pain. In all studies, radiofrequency ablation (RFA) used constant radiofrequency application with the intent to ablate nerve endings.

Landsman et. al. (2013) reported the only randomized study of RFA. Seventeen patients were enrolled in a double-blind crossover trial, with crossover to the alternative treatment at 4 weeks. Patients must have failed a least 3 prior types of treatments, have had pain for more than 3 months, and rated pain at least 6 on a 0 to 10 VAS. The sham treatment consisted of all aspects of the actual RFA procedure, which included stimulation of sensory nerves in an awake patient, except for the delivery of RF energy at the final step. Outcomes assessed weekly were a pain VAS reported at the first step in the morning, average pain level, and peak pain in the heel region. It was observed that statistically significant improvement of plantar fasciitis in patients actively treated with radiofrequency ablation and no significant improvement in the sham-treated group. Those treated with sham subsequently demonstrated improvement after subsequent RFA treatment. The authors concluded using a prospective, randomized study with sham treatment and crossover, this study demonstrates the efficacy of radiofrequency ablation for the treatment of plantar fasciitis.

Erken et. al. (2014) reported on two-year follow-up evaluating the results of radiofrequency ablation of the calcaneal branches of the inferior calcaneal nerve on 35 feet in 29 patients with plantar heel pain between 2008 and 2011. All of the patients who were treated had been complaining of heel pain for more than 6 months and had failed conservative treatment. All of the patients were evaluated using the average 10-point Visual Analog Scale (VAS) and the American Orthopedic Foot and Ankle Society Scale (AOFAS) scores assessed before treatment, as well as their 1 month, 1 year and 2 year follow-up after the procedure. The average VAS score of the feet was 9.2, 1.2 at 1 month, 1.5 at 1 year and 1.5 at 2 years. In addition, 85.7% of the patients rated their treatment as successful or very successful at 1- and 2-year follow-up. The mean AOFAS scores (score range 1-100) in 20 patients were 66.9 before treatment, 95.2 at 1 month, 93 at 1 year, and 93.3 at 2 years. The authors concluded these findings suggest that radiofrequency ablation of the calcaneal branches of the inferior calcaneal nerve was an effective pain treatment option for chronic heel pain associated with plantar fasciitis that did not respond to other conservative treatment options.

Wu et. al. (2017) completed a prospective, randomized, double-blinded controlled trial (12-week follow-up) to evaluate the therapeutic benefit of ultrasound-guided pulsed radiofrequency (PRF) stimulation at the posterior tibial nerve (PTN) in patients with recalcitrant plantar fasciitis (PF). Thirty-six patients underwent randomization, and all were included in the final data analysis. Patients in the PRF group were treated with 1 dose of ultrasound guided PRF stimulation at the PTN, and those in the control group received 1 dose of 2% lidocaine, 0.5mL, injected at the PTN under ultrasound guidance. The visual analog scale (first step and overall pain), American Orthopedic Foot-Ankle Society (AOFAS) ankle-hindfoot scale, and ultrasonographic thickness of the plantar fascia were evaluated at 1, 4, 8, and 12 weeks after treatment. Thirty-six patients (20 feet per group) completed the study. The PRF group had a significantly larger improvement in first-step pain, overall pain, and AOFAS score (all $P<.001$), as well as plantar fascia thickness ($P<.05$), compared with those of the control group at all observed time points. The authors concluded, this study showed that ultrasound guided PRF stimulation at the PTN is effective for treating recalcitrant PF and this simple reproducible method could be a novel strategy for managing recalcitrant PF.

The largest case series with the longest follow-up is by Cozzarelli et.al. (2010). This study reported on 12 years follow up of 82 patients who had undergone radiofrequency ablation (RFA) for heel pain. Patients had undergone RFA between 1994 and 1995 and had been interviewed at 5-, 10- and 12-years post procedure. An evaluation of medical records was performed as a means of inclusion in this study. A standardized telephone interview was done, and subjectively scored responses of the patients were recorded and analyzed. Of 99 patients potentially eligible to be interviewed, the study evaluated 82 patients and 89% reported no recurrence of pain after 5-, 10- and 12-years post procedure.

Cione et. al (2009) reported case series of 75 patients with recalcitrant plantar heel pain caused by calcaneal neuritis, treated with radiofrequency ablation. The median age of the cohort was 55 (range 24 to 83) years, 25 (33.3%) of the patients were male, 50 (66.7%) of the patients were female, and 15 (20%) of the patients were treated for bilateral heel pain caused by medial calcaneal neuritis. The median pre-procedure VAS score was 9 (range 2 to 10), whereas the post procedure VAS score was 1 (range 0 to 8). Five (6.7%) of the patients experienced recurrent heel pain, over a median follow-up duration of 18 months. Overall, 93.3% of the patients experienced satisfactory pain relief with radiofrequency lesioning for the treatment of recalcitrant plantar heel pain caused by medial calcaneal neuritis.

Liden et. al. (2009) published a retrospective case series of 22 patients treated with radiofrequency nerve ablation with a history of prolonged moderate to severe heel pain associated with plantar fasciitis to determine if ablation of sensory branch of the medial calcaneal nerve would result in symptomatic relief. Participants in this study were given subjective questionnaires and Visual Analog Scales (VAS) in order to rate their symptoms before and after the ablation using radiofrequency energy. The mean pain VAS decreased from 8.12 to 3.26 1 week after treatment. At a mean follow-up duration of 8 months, pain VAS scores decreased to 1.5, 2.0, and 2.1 at 1 month, 3 months and 6 months post procedure. Adverse events were minor and transient in most cases. One adverse event was called persistent post-static dyskinesia which probably represents nonresponse to treatment. The authors concluded that the findings support radiofrequency nerve ablation may be considered as an alternative to repetitive corticosteroid injections or open surgical intervention for the treatment of recalcitrant plantar heel pain.

Summary of Evidence

Radiofrequency ablation of peripheral nerves may be performed for the treatment of chronic heel pain associated with plantar fasciitis and the literature on the use of this is limited. The evidence for radiofrequency ablation of peripheral nerves in individuals who have plantar fasciitis includes case series studies and 1 randomized controlled trial (RCT). The case series generally have small sample sizes, and many have methodologic deficiencies such as retrospective assessment of pain. The single RCT evaluated only 17 patients, and randomized outcomes could only be assessed out to 4 weeks post-treatment. Although the studies report that radiofrequency ablation reduces heel pain, the quality of the evidence is poor. Because of the variable natural history of plantar fasciitis and the subjective nature of the outcome measures, randomized clinical trials (RCTs) are needed to determine whether outcomes are improved with interventions for pain. Trials should include homogenous population of patients with defined clinical condition, use standardized outcome measures to include longer follow up periods and define clinically relevant outcome measures for pain treatments which includes measures of pain severity and functional limitations. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Cryoneurolysis (Cryoablation, Cryoanalgesia, Cryotherapy)
Cryoneurolysis (cryoablation, cryoanalgesia, cryotherapy) is a relatively new treatment modality using cold (freezing) for the treatment of plantar fasciitis who have failed prior conservative therapy. The most important aspect of this treatment modality is locating the exact area of heel pain as the target area for the tip of the cryoprobe is the central area of the greatest pain. The cryoneurolysis procedure provides ablation of the divisional branches of the medial calcaneal nerve medially and the branches of the lateral calcaneal nerve laterally.

Per review of the peer reviewed medical literature, the literature is limited related to cryoneurolysis and the treatment of plantar fasciitis. Prospective studies and retrospective case series/case reports were found, no randomized controlled trials were found. Some studies may have shown promising results in- regards to decreased pain, however, study quality, small study sizes and patient follow-up limit the applicability of any specific study to clinical practice. Further randomized clinical trials (RCTs) are needed to determine the efficacy of cryoneurolysis (cryoablation, cryoanalgesia, cryotherapy) to include studies with larger sample sizes, longer follow periods and double blinding to establish the overall effectiveness of this procedure and include comparative studies against other treatments. The evidence is insufficient to determine the effects of this technology on net health outcomes

Chemical Neurolysis
For patients with plantar fasciitis no published literature was identified in-regards to patient receiving chemical neurolysis (alcohol, phenol, glycerol) for the treatment of this condition. The evidence is insufficient to determine the effects of this technology on net health outcomes.

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

Clinical Context and Therapy Purpose
To provide treatment option that is an alternative to or an improvement on existing therapies.

Patients
The relevant population of interest are patients with peripheral neuromas.

Interventions
The therapy being considered is radiofrequency ablation (RFA), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis.

Comparators
The following therapy is currently being used to make decisions about treating peripheral neuromas: pharmacotherapy and steroid 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 measured with a visual analog scale (VAS) or numeric rating scale (NRS).

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

Based on review of the peer reviewed medical literature the evidence is very limited, no controlled studies were identified on the use of ablative procedures (chemical neurolysis, cryoablation and radiofrequency ablation to include conventional, pulsed, or cooled RF) to treat painful peripheral neuromas other than Morton neuromas. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Chronic Orchialgia
Chronic orchialgia, may also be referred as one of the following: testicular pain syndrome; testialgia; chronic testicular pain; chronic scrotal content pain (CSCP); post-vasectomy orchialgia; post-vasectomy pain syndrome (PVPS); and congestive epididymitis. Chronic orchialgia is defined as intermittent or constant testicular pain, 3 months or longer in duration that significantly interferes with the daily activities of the patient. Treatment typically includes nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, particularly when there is evidence of infection. Antidepressants such as amitriptyline or nortriptyline may be used to reduce neuropathic pain. Nerve blocks as a single injection or in a series with or without steroids. Other interventions may include cryoablation, surgical neurectomy and orchidectomy. A nonsurgical technique being considered as a treatment modality of chronic orchialgia is pulsed radiofrequency (PRF) ablation to the ilioinguinal nerve and the genital branch of the genitofemoral nerve if the patient receives temporary relief from a spermatic cord block (SCB).

The iliohypogastric ilioinguinal, genitofemoral and pudendal nerves originate from L1-L2 and S2-S4 nerve roots and are responsible for innervation of the testes, epididymis and scrotum. These nerves innervate the scrotal content and travel through the spermatic cord. An injury to the testes or other scrotal content structures is typically the precursor to chronic orchialgia. This acute pain leads to nerve sensitization, resulting in modulation of the nerve pathways, causing hypersensitivity around the spermatic cord. This hypersensitivity has been proposed to follow neural injury, with resulting Wallerian degeneration (WD) in these peripheral nerves. WD is characterized as an auto-destructive change in both the proximal and distal axonal stump by the fusion of axolemmal vesicles around the injured axon endings.

Any organ that shares the same nerve pathways with the scrotal content (L1-L2 and S2-S4) may refer pain to this area. Lower back pain due to irritation of the nerve root of T10-L1 may radiate to the testicle, as they share the same innervation. Pain arising in the ureter due to obstruction, hip pain and intervertebral disc prolapse, or pudendal neuropathies can all result in chronic orchialgia. The pain could also be part of chronic prostatitis/chronic pelvic pain syndrome for which up to 50% of men have reported to also have pain in the testes.

Clinical Context and Therapy Purpose
To provide treatment option that is an alternative to or an improvement on existing therapies.

Patients
The relevant population of interest are patients with chronic orchialgia, may also be referred as one of the following: testicular pain syndrome; testialgia; chronic testicular pain; chronic scrotal content pain (CSCP); post-vasectomy orchialgia; post-vasectomy pain syndrome (PVPS); and congestive epididymitis.

Interventions
The therapy being considered is radiofrequency ablation (RFA), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis.

Comparators
The following therapy is currently being used to make decisions about treating chronic orchialgia: nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, particularly when there is evidence of infection; antidepressants such as amitriptyline or nortriptyline may be used to reduce neuropathic pain; and nerve blocks as a single injection or in a series with or without steroids.

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 measured with a visual analog scale (VAS) or numeric rating scale (NRS).

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

Pulsed Radiofrequency Ablation

Hetta et. al. (2018) evaluated the analgesic effect of pulsed radiofrequency (PRF) applied to the ilioinguinal nerve and the genital branch of the genitofemoral nerve for patients suffering from chronic post-surgical orchialgia in a prospective, double-blind, sham-controlled, randomized trial. The inclusion criteria were patients with chronic scrotal pain (orchialgia) that fulfilled the following criteria: pain intensity > 5 on the visual analog scale (VAS); pain that lasted more than 3 months after groin surgeries; failed conservative treatment with non-steroidal anti-inflammatory drugs (NSAIDs); and showed more than 50% reduction of their orchialgia on the VAS for at least 6 hours following spermatic cord block with 6 mL of lidocaine 2%. Seventy patients complaining of chronic post-surgical orchialgia were randomized into 2 groups: PRF group (n = 35), received pulsed radiofrequency on the ilioinguinal nerve and genital branch of the genitofemoral nerve, or sham group (n = 35). The percentage of patients that showed > 50 % reduction of their visual analog scale (VAS) pain score as well as the percentage of patients that did not require additional analgesic drugs was assessed. The VAS pain score and the global perceived effect (GPE) were reported during the 3-month follow-up period. The percentage of patients that showed > 50% reduction of their VAS pain score was 80% (24/30) in the PRF group versus 23.33% (7/30) in the sham group. The percentage of patients that did not require analgesic drugs was 50% (15/30) in the PRF group versus 3.3% (1/30) in the sham group. There was a significant reduction of the mean post-procedural VAS pain score at 2, 4, 6, 8, and 12 weeks (P = 0.001) in the PRF group in comparison to the sham group. Likewise, there was a significant improvement of the GPE in the PRF group in comparison to the sham group (P = 0.00). This study was limited by the follow-up period, which was only 3 months. The authors concluded for patients suffering from chronic post-surgical orchialgia, PRF applied to the ilioinguinal nerve, and the genital branch of the genitofemoral nerve is an effective treatment modality. It provides long-lasting pain relief and decreases the demand for pain medications.

The use of pulsed radiofrequency (PRF) ablation in the treatment of chronic groin pain and orchialgia has been reported in limited case series with short-term temporary pain relief up to 20 weeks based on visual analog scores.

Summary of Evidence

Based on review of the peer reviewed medical literature the evidence is limited to one randomized controlled trial and limited case series. While the randomized controlled trial may show promising results, this trial was limited by the follow-up period which was only 3 months. These preliminary findings need to be validated by well-designed controlled studies with longer follow-up to determine the safety and efficacy of pulsed radiofrequency ablation for the treatment of chronic orchialgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Cryoneurolysis and Chemical Neurolysis
Based on review of the peer reviewed medical literature nerve ablation is performed in a similar manner to nerve block except that a neurolytic solution such as phenol or alcohol is injected instead of local anesthetic. Alcohol or phenol injection destroys the offending nerve ending and reduces chronic inflammation. Alternative technique of percutaneous nerve ablation also includes cryoablation. The outcomes of percutaneous nerve ablation are less favorable than surgical nerve excision as the nerve ablation only destroys the offending nerve ending(s), and recurrent pain may develop after subsequent nerve regeneration. Randomized controlled trials (RCTs) are needed to better define the role of cyroneurolysis (cryoablation) and chemical neurolysis for patients with chronic orchialgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Miscellaneous Conditions

Postherpetic Neuralgia
Acute herpes zoster typically presents with a rash that is painful but self-limited. Some patients may continue to experience pain for months to years after the resolution of the rash, a condition known as postherpetic neuralgia (PHN). Inflammation associated with acute herpes zoster may induce fibrosis and other structural changes in nerves that result in spontaneous activity capable of maintaining pain in the absence of ongoing tissue damage. PHN refers to pain persisting beyond four months from the initial onset of the rash. The probability of developing PHN increases with age. The major risks for PHN are:

- Age > 60 years
- Severe or incapacitating pain with acute herpes zoster
- More severe rash with acute herpes zoster

Older age is also associated with increasing severity and persistence of PHN symptoms.

Multiple medications have shown benefit in reducing PHN symptoms. However, PHN can be difficult to treat, and some patients require multimodal therapy to manage symptoms. The choice among treatments for PHN should be individualized according to the severity and location of pain, comorbid conditions, medication side effect profile, treatment cost and availability, and patient values and preferences. Because the pain of PHN may be chronic, long-term therapy is often required. Cryotherapy has been considered for patients with refractory symptoms who do not respond to other therapies.

Cryotherapy is an ablation technique that involves freezing peripheral nerves. A small, unblinded study of cryotherapy for facial pain failed to show a significant benefit in patients with PHN. The authors did not provide inclusion criteria, concomitant therapies, or information on how the response was assessed. By contrast, a second trial reported "considerable" relief in 11 of 14 patients with cryotherapy to the intercostal nerves for PHN. In most cases, however, the duration of relief was less than two weeks as assessed

by questionnaire. Larger studies are needed to better define the role of cryotherapy for patients with PHN.

Based on review of the peer reviewed medical literature the evidence is limited on the use of radiofrequency ablation (conventional, pulsed or cooled), cryoablation or chemical neurolysis for the treatment of postherpetic neuralgia. Additional randomized controlled trials (RCTs) are needed to better define the role of these interventions for this indication. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Practice Guidelines and Position Statements

American College of Foot and Ankle Surgeons
In 2018, the American College of Foot and Ankle Surgeons issued a clinical consensus statement on the diagnosis and treatment of adult acquired infracalcaneal heel pain. The panel determined that the following statement were uncertain – neither appropriate nor inappropriate:

- Other surgical techniques (e.g., ultrasonic debridement using microtip device, cryosurgery, and bipolar radiofrequency ablation) are safe and effective options for chronic, refractory plantar fasciitis.

These treatment options have very little long-term data or peer reviewed studies. Further research is needed to determine the effectiveness.

American College of Rheumatology and Arthritis Foundation
In 2019, the American College of Rheumatology and Arthritis Foundation issued a guideline on the management of osteoarthritis of the hand, hip and knee that included the following recommendation:

Several studies have demonstrated potential analgesic benefits with various ablation techniques but, because of the heterogeneity of techniques and controls used and lack of long-term safety data, this recommendation is conditional.

This recommendation was based on evidence of a potential analgesic benefit, but the studies used heterogeneous techniques and there was a lack of long-term safety data.

Regulatory Status
A number of radiofrequency (RF) generators and probes for the peripheral nervous system have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process, some examples are listed in the below table.

In 2014, the iovera system (Myoscience, Inc) received 510K clearance from the U.S. Food and Drug Administration (FDA). It is cleared to be used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in

peripheral nervous tissue by application of cold to selected site for blocking of pain. The iovera device is not indicated for the treatment of central nervous system tissue.

In 2017 the U.S. Food and Drug Administration (FDA) cleared for marketing COOLIEF cooled radiofrequency (Cooled RF) probe (Avanos, previously known as Halyard Health) to be used in conjunction with a radiofrequency generator to create lesions in nervous tissue (K163461). One of the indications is specifically 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."

Radiofrequency and Cryoneurolysis Devices

Device	Manufacturer	Date
SInergy®/Bayless Pain Management Probe	Kimberly-Clark/Baylis	2005
NeuroTherm® NT 2000	NeuroTherm	2011
iovera	Myoscience4	2014
COOLIEF® Cooled Radiofrequency Kit	Avanos, previously known as Halyard Health	2016
COOLIEF® Cooled RF Probe	Avanos, previously known as Halyard Health	2017
Rulo(TM) Radiofrequency Lesion Probe	Epimed International	2019

PRIOR APPROVAL

Prior approval is recommended.

POLICY

See Related Medical Policies:

- 07.01.66 Ablative Treatments of Occipital Neuralgia, Chronic Headaches and Atypical Facial Pain*
- 07.01.41 Pulsed Radiofrequency Ablation
- 07.01.58 Radiofrequency Ablation and Alternative Ablative/Denervation Methods for Chronic Facet Joint Mediate Neck, Back and Sacroiliac Joint Pain*

Ablative procedures of the peripheral nerves including but not limited to the following:

- Radiofrequency ablation (RFA)
- Cooled radiofrequency ablation to include but not limited to COOLIEF cooled RF (Avanos, previously known as Haylord Health)
- Pulsed radiofrequency ablation *(Refer to medical policy 07.01.41 Pulsed Radiofrequency Ablation)*

- Cryoneurolysis (cryoablation, cryotherapy, cryoanalgesia) to include but not limited to iovera system (Myoscience, Inc)
- Chemical neurolysis (alcohol, phenol, glycerol); **and**

The ablative procedure(s) above are being performed to treat pain for any indication, including but not limited to the following is considered **investigational**:

- Chronic knee pain/Osteoarthritis of the knee
    - As a treatment prior to partial or total knee replacement
    - As a treatment following partial or total knee replacement
    - As a treatment for individuals who are not candidates for partial or total knee replacement surgery
- Chronic hip pain/Osteoarthritis of the hip
    - As a treatment prior to partial or total hip replacement
    - As a treatment following partial or total hip replacement
    - As a treatment for individual who are not candidates for partial or total hip replacement surgery
- Chronic orchialgia (may also be referred to as one of the following: testicular pain syndrome; chronic testicular pain; testialgia; chronic scrotal content pain (CSCP); post-vasectomy orchialgia; post-vasectomy pain syndrome (PVPS); congestive epididymitis)
- Chronic shoulder pain
- Inguinal neuralgia
- Intercostal neuralgia
- Peripheral neuromas
- Plantar Fasciitis
- Postherpetic neuralgia

Based on review of the peer review medical literature the evidence is insufficient to determine the efficacy of these ablative procedures (radiofrequency ablation [RFA], cryoneurolysis [cryoablation, cryoanalgesia, cryotherapy], chemical neurolysis) of the peripheral nerves to treat various types of pain. While some studies may have shown promising results in the treatment of severe refractory peripheral nerve pain, there continues to be several technical issues that have yet to be resolved, including the optimal number of applications for each nerve, the duration of treatment, for cryoablation the duration of thawing before moving the cannula, and the most effective method for determining the location (e.g., ultrasound or using anatomic landmarks) that need to be established. Also, there is no literature that currently demonstrates which ablative modality can provide better and longer pain relief. Also, a prospective randomized sham-controlled trial assessing if genicular nerve cryoablation provided preoperatively would improve postoperative pain outcomes following total knee arthroplasty (TKA) concluded cooled RFA of the superior lateral, superior medial and inferomedial genicular nerves when performed 2-6 weeks prior to elective TKA had no measurable effect on postoperative opioid use to also include no long-term effect on outcome measures at 1, 3 and 6 months after TKA. Further randomized, double blinded studies are needed to establish the overall effectiveness of these ablative treatment modalities and to compare

their outcomes against one another. The evidence is insufficient to determine the effects of this technology on net health outcomes.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 64620 Destruction by neurolytic agent, intercostal nerve (destruction by a neurolytic agent may include chemical (e.g., alcohol, glycerol, phenol), cold, or radiofrequency techniques)
- 64624 Destruction by neurolytic agent, genicular nerve branches including imaging guidance, when performed
- 64640 Destruction of neurolytic agent; other peripheral nerve or branch (destruction by a neurolytic agent may include chemical (e.g., alcohol, glycerol, phenol), cold, or radiofrequency techniques)
- 0440T Ablation percutaneous cryoablation includes imaging guidance upper extremity distal/peripheral nerve
- 0441T Ablation percutaneous cryoablation includes imaging guidance lower extremity distal/peripheral nerve
- C2618 Probe/needle cryoablation

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POLICY HISTORY		
Date	**Reason**	**Action**
March 2022	Interim Review	Policy Revised
January 2022	Annual Review	Policy Revised
January 2021	Annual Review	Policy Renewed
January 2020	Annual Review	Policy Revised
January 2019	Annual Review	Policy Revised
January 2018	Annual Review	Policy Revised
January 2017		New Medical Policy

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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