Radiofrequency techniques to treat chronic knee pain: a comprehensive review of anatomy, effectiveness, treatment parameters, and patient selection

Background: The use of radiofrequency ablation (RFA) procedures to treat chronic knee pain has surged in the past decade, though many questions remain regarding anatomical targets, selection criteria, and evidence for effectiveness.

Methods: A comprehensive literature review was performed on anatomy, selection criteria, technical parameters, results of clinical studies, and complications. Databases searched included MEDLINE and Google Scholar, with all types of clinical and preclinical studies considered.

Results: We 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.

Conclusion: 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.

Keywords: Knee pain, osteoarthritis, radiofrequency, ablation, denervation, genicular nerve

Introduction

Knee pain has a lifetime prevalence rate of ~45%, and represents a source of significant disability and reduced quality of life. Risk factors for the development of knee pain include a history of prior injury or surgery, obesity, and advancing age.

The most common cause of chronic knee pain is osteoarthritis (OA), which is characterized by the progressive loss of articular cartilage, with other etiologies including rheumatoid arthritis, trauma, crystal arthropathies, and persistent postsurgical pain.

Available treatments for knee pain vary depending on the etiology and diagnosis, but broadly include physical therapy, oral medications, injections, and surgery. Injections for knee pain consist of several types, and may be directed to the soft tissues of the knee joint or the intra-articular joint space. Intra-articular injections encompass a wide range of medications to include anti-inflammatory corticosteroids,
pro-inflammatory prolotherapy and platelet-rich plasma (PRP) solutions, vicosupplements, and stem cell preparations.4–11 All intra-articular injections require the presence of an intact joint, and are therefore not applicable following total arthroplasty. Knee surgery is similarly heterogeneous and ranges from minimally invasive arthroscopic procedures to open partial or total arthroplasties.12,13 Pain due to severe OA is not reliably responsive to conservative therapies, and chronic pain may persist in over 40% of patients who undergo joint replacement, being characterized as severe in 15% of cases.14–16 Delivery of radiofrequency (RF) energy to the knee’s nerve supply is a relatively new intervention that can be safely done in the presence of an artificial joint, and may offer an alternative to surgery or surgical revision.

Radiofrequency ablation (RFA) entails the discrete delivery of thermal energy produced by an alternating current to neural tissue, thereby degrading its ability to conduct pain signals.17 First described as a treatment for pain in the 1960’s,18 RFA evolved from a therapy primarily employed to alleviate neuropathic pain to one used today predominantly for mechanical joint pain amidst reports of increased pain stemming from deafferentation and neuroma formation. Since the neurosurgeon Norman Shealy adapted its use for the treatment of pain arising from the spinal facet joints in the mid-1970’s,19 the accepted indications for RFA have expanded steadily over the ensuing decades. The advent of cooled radiofrequency ablation (CRFA)20 and the non-ablative pulsed radiofrequency (PRF)21 therapy have further broadened the clinical utility of RF for chronic pain states. Accepted targets for RF treatment now include most neural structures to include major nerves and ganglia.22–24 The use of RF as a treatment for knee pain was first described in a small case series involving the treatment of different types of joint pain by Sluijter et al, who noted complete eradication of pain with intra-articular PRF in a patient with refractory post-traumatic knee pain.25 This area of pain medicine has evolved in the past decade, and though knee RFA has been the subject of numerous publications, high-quality randomized controlled trials (RCTs) remain sparse. The objectives of this publication are to review the relevant neuroanatomy of the knee and the available literature on RFA.

Search strategy

We systematically searched and screened all titles and abstracts from MEDLINE and Google Scholar from inception to February 1, 2018 using the following key words: “knee,” “pain,” “arthritis,” “persistent postsurgical pain,” “chronic postsurgical pain,” “radiofrequency,” “ablation,” “denervation,” and “pulsed radiofrequency.” This initial search yielded 92 trials of varying design, which were then separately reviewed by the authors. For the purposes of this review only randomized and comparative trials were selected, with all other study types being excluded. A total of nine randomized or comparative trials were ultimately identified by independent searches conducted by each author. The literature search was complemented by reviewing the reference lists of the selected publications to search for additional articles missed by our initial electronic search.

**Neuroanatomy of the knee**

The innervation of the knee joint is complex given that genicular nerves arise from branches of three major nerves: the sciatic, femoral, and obturator, all of which are themselves derived from the lumbar plexus.26,27 The sciatic nerve bifurcates into the tibial and common peroneal nerves in the popliteal fossa. The tibial nerve remains in the posterior compartment of the lower leg and gives off the superomedial (SM) and inferomedial (IM) genicular nerves to the posterior aspect of the knee joint. The common peroneal nerve passes into the anterior compartment of the lower leg, and contributes the superior lateral (SL) genicular nerve to the anterior portion of the knee. These genicular branches of the sciatic nerve reliably course in approximation to the periosteum at the medial and lateral junctions of the distal femoral shaft and epicondyles, and at the medial junction of the proximal tibia and epicondyle. The saphenous nerve is a cutaneous sensory branch of the femoral nerve and gives off suprapatellar and infrapatellar (IP) genicular nerves to the anterior portion of the knee. The contribution of the obturator nerve is more variable, but its posterior branch can provide an articular branch to the posterior knee.

The complexity of the knee joint’s innervation has resulted in a disparity in procedural technique among the available controlled and observational studies. Studies report on a range of procedural targets to include the SM, IM, and SL genicular nerves in combination,28–33 the saphenous nerve,34 the sciatic nerve,35 the IP genicular nerve,36 the IP and SM genicular nerves in combination,37 the femoral, tibial, saphenous nerves, and peripatellar plexus in combination,38 and the intra-articular joint space6,25,39–41 (Figures 1 and 2).

**RCTs**

The earliest published RCT is the 2011 study by Choi et al.28 This trial was designed to compare genicular nerve RFA to sham RFA. Nerves targeted in this trial were the SM, IM, and SL genicular branches. Inclusion criteria were age between
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50 and 80 years, presence of refractory knee pain of at least 3 months duration, and at least grade 2 radiographic evidence of OA on the 5-point Kellgren–Lawrence scale. Thirty-eight patients who met the criteria and had a positive response to genicular nerve blocks were randomized to receive either continuous, fluoroscopically guided RFA at 70°C, or sham RFA that consisted of superficial and deep local anesthesia with lidocaine. Primary outcomes were pain level as assessed by visual analog scale (VAS) and the proportion of patients reporting at least 50% pain relief at 12-week follow-up. Overall follow-up was obtained at 1, 4, and 12 weeks post-procedure. The results showed that RFA significantly lowered the VAS at all time periods compared to sham, but both groups showed similar improvement at 1 week, suggesting a temporary improvement with local anesthetic nerve block. Ten of the 19 RFA patients achieved at least 50% pain reduction at 12 weeks, compared to no patients in the control group. Secondary outcomes to include Oxford knee score (OKS) and patient satisfaction were also significantly improved in the RFA group. The limitations of this study are primarily its small size, the large discrepancy between the volume of prognostic blocks and the small electrodes used, the high proportion of positive prognostic blocks (82.5%), and lack of long-term follow-up.

RFA was first compared to intra-articular injections in the 2016 Sarı et al trial. Seventy-three patients with at least grade 2 Kellgren–Lawrence OA were randomized to receive either RFA of the SL, SM, and IM genicular nerves at 80°C for 90 seconds or intra-articular injection of bupivacaine, morphine, and betamethasone. Patients were assessed at baseline, 1 and 3 months for pain level via VAS and function via the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) index. Results showed statistically superior pain relief with RFA at 1 and 3 months, but superiority in the total WOMAC score with RFA only at 1 month. Limitations of the study include the lack of prognostic blocks, the unrestricted and undocumented use of oral analgesics, and the lack of a true control group.
The SM, IM, and SL genicular nerves were also targeted in the 2017 Qudsii-Sinclair et al trial, but in this trial the effect of RFA was examined only in patients with a history of total knee arthroplasty (TKA). Thirty patients with refractory knee pain that persisted at least 6 months following TKA were enrolled in the study, with 28 completing follow-up to 12 months. Patients were randomized to receive either continuous RFA at 80°C or sham RFA that consisted of genicular nerve blocks with local anesthetic and corticosteroid. Both procedures were performed under fluoroscopic guidance. Outcome measures were pain level assessed via a numeric rating scale (NRS), and function assessed via both the OKS and Knee Society Score. Outcomes with respect to function were modest and similar between groups, with most improvements occurring between months 1 and 6, and declining toward baseline by 12 months. Pain also decreased in both groups, but the reduction following RFA peaked at 3 months and persisted at 12 months, while the control group experienced their lowest NRS on day 1 and then steadily increased toward baseline at 12 months. This trial is limited by a small size and the lack of prognostic blocks pre-RFA, which may have led to the inclusion of nonresponders in the RFA group.

The Shen et al trial compared RFA with PRP and sodium hyaluronate (HA) to PRP and HA alone. Inclusion criteria were refractory pain of at least 3 months duration due to OA and pain level of at least 6 on a 0–10 VAS. Both groups received intra-articular injections of PRP and HA weekly for 5 weeks, but the treatment group also received RFA at 70°C, although the timing of the RFA was not described. The precise nerves were also neither named, nor was it specified whether image guidance was used. Twenty-seven patients were randomized to each group and follow-up was obtained at the completion of intra-articular injections and 3 months. Outcome measures included pain intensity as measured on a VAS, life quality as measured on the 36-item Short-Form Health Survey, and function via the American Knee Society Score. Both groups showed improvement in pain and function, although the gains in the RFA group were statistically superior at all time periods. The RFA group also demonstrated significant improvement in quality of life at 3 months, while the control group did not.

The 2018 trial by Davis et al is the largest study and was also the first to employ CRFA. Similar to the Qudsii-Sinclair and Choi trials, the SM, SL, and IM genicular nerves were targeted. Inclusion criteria were the presence of at least grade 2 Kellgren–Lawrence radiographic OA, refractory knee pain of at least 6 months duration, pain of at least 6 of 10 on a NRS, OKS score of at least 35, and at least 50% improvement with genicular nerve blocks. One hundred and fifty-one patients met the inclusion criteria and were randomized to receive either CRFA or intra-articular steroid (IAS) injection. CRFA was performed under fluoroscopic guidance with 17-gage introducers at 60°C for 150 seconds. The primary outcome was the percentage of patients achieving at least 50% pain reduction at 6 month follow-up as measured by a NRS. Secondary outcome measures included function measured on OKS, patient’s overall perception of the treatment, and analgesic usage. Pain relief with CRFA was superior to that obtained with IAS at all time periods, and at 6 month follow-up 74% of the CRFA group had at least 50% relief compared to just 16% of the IAS group. Function and global perception were also superior in the CRFA cohort, although there was no statistical difference between the groups in terms of oral opioid use. The longer duration of relief noted in this study provides evidence for the theoretical benefit of CRFA, namely the creation of larger lesions to reduce the technical failure rate (ie, missed nerves).

The most recent RCT by El-Hakeim et al compared RFA to non-interventional therapy. Sixty patients with at least grade 3 Kellgren–Lawrence OA were randomized to receive either RFA of the SM, SL, and IM branches or conventional treatment with oral acetaminophen and diclofenac. RFA was accomplished with three 90 seconds cycles at 90°C per site, which is a substantially longer duration of RFA than that employed by any other RCT. Patients were evaluated at baseline, 2 weeks, 3 months, and 6 months. Results showed statistically superior pain relief with RFA at all follow-up intervals. Function as assessed by the WOMAC index was improved in both groups at 6 months, but was superior with RFA. Lastly, patient satisfaction as measured on a Likert scale was significantly higher at 3 and 6 month follow-up in the RFA group. However, the study is limited by the lack of pre-RFA prognostic blocks and the lack of patient blinding.

Randomized, non-comparative studies

The 2017 randomized trial by McCormick et al also employed CRFA, but the study was designed to determine the predictive value of pre-RFA nerve blocks, not to compare RFA to other modalities. Fifty-four patients with chronic knee pain due to OA all received CRFA, but 29 did so after prognostic blocks and 25 did not. Notably, only three of 32 (9.3%) patients had a negative block, defined as <50% pain relief. Some patients had the procedure done bilaterally; so a total of 36 knees had CRFA following prognostic blocks and 35 knees proceeded directly to CRFA. Inclusion criteria were...
Consisted only of topical and deep anesthesia with lidocaine; RFA was not performed. Other complementary treatments were withheld for 12 weeks, and assessment was obtained at 4 weeks, 8 weeks, 12 weeks, and 6 months. Outcome measures included the WOMAC functional assessment, VAS pain scores, and a 4-point patient global assessment. Outcomes were overall mixed. The total WOMAC score remained lower in the RFA group throughout the 6-month follow-up, but the difference was not statistically significant. VAS scores were significantly lower in the RFA group at 4-, 8-, and 12-week follow-ups, but the effect tapered off by 6 months. Limitations of the this study include the lack of randomization, lack of prognostic nerve blocks, and the targeting of only two nerve branches (Table 1).

RFA predictors of outcome
Predictors of success or failure with RFA relate to both patient characteristics and procedural technique. This subject has been reported extensively as it relates to other pain interventions, notably lumbar facet and sacroiliac joint (SIJ) RFA. Patient factors predictive of failure with SIJ RFA include age >65 years, higher baseline pain level, and opioid use.46 Patient factors predictive of poor success with lumbar or cervical RFA include advanced age, certain pain referral patterns and physical exam signs, opioid use, prior history of depression, previous back surgery, longer duration of pain, and ongoing legal action.47-49 In individuals with chronic neck pain due to whiplash, low levels of pain catastrophizing and functional disability were found to be predictive of success with cervical RFA.50 In a study evaluating prognostic factors before PRF of the occipital nerves, treatment failure was associated with extension of pain beyond the confines of the targeted nerve distribution, while a lower diagnostic block volume, multiple treatment cycles, and a traumatic precipitating event predicted success.51 Procedural factors that contribute to success with RFA include the type of RF energy applied, the duration and temperature of treatment, and the gage of the RF probe itself. An ex vivo trial compared several types of RF and found that CRFA created larger lesions than either continuous or PRF.52 Within RFA and PRFA groups, larger probes and longer duration of treatment were associated with larger lesions. Results from studies on SIJ RFA have been mixed, with one reporting superior relief with CRFA when compared to RFA,53 one showing a trend toward superiority with CRFA,54 and another demonstrating no difference.55 Orientation of the RF probe parallel to the targeted nerve has also been demonstrated in preclinical studies to create larger lesions,56 but results from uncontrolled trials are mixed.55,57
| Trial            | Study type | Trial size, diagnosis | RF method                  | Anatomic targets | Prognostic block | Follow-up | Results                                                                 | Comment                                      |
|------------------|------------|-----------------------|----------------------------|------------------|------------------|-----------|-------------------------------------------------------------------------|----------------------------------------------|
| Choi et al<sup>18</sup> | RCT        | 38, OA                | RFA (70°C, 90 seconds) + LA vs sham | SM, SL, IM        | Yes              | 12 weeks | RFA > sham for pain and function at 4 and 12 weeks                     | High volume (2 mL) used for prognostic blocks |
| Sarı et al<sup>19</sup> | RCT        | 73, OA                | RFA (80°C, 90 seconds) vs IA steroid, LA, and morphine | SM, SL, IM        | No               | 3 months | RFA superior for pain and function                                       | No prognostic blocks                          |
| Shen et al<sup>20</sup> | RCT        | 54, OA                | RFA (70°C, 120 seconds) + PRP + HA vs PRP + HA | Not specified     | No               | 3 months | RFA superior for pain and function                                       | Nerves targeted not described, unclear if imaging guidance was used |
| Qudsi-Sinclair et al<sup>10</sup> | RCT        | 28, post-TKA           | RFA (80°C, 90 seconds) vs LA + steroid | SM, SL, IM        | No               | 12 months | RFA > nerve block for pain at 12 months; functional relief modest and not different between groups | Significant short-term relief with nerve blocks. Functional improvement modest and not statistically different between groups |
| Davis et al<sup>11</sup> | RCT        | 151, OA               | Cooled RFA (60°C, 150 seconds) vs IA steroid | SM, SL, IM        | Yes              | 6 months | RFA > IA injections for pain and function                              | No difference in opioid usage between groups |
| El-Hakeim et al<sup>12</sup> | RCT        | 60, OA                | RFA (90°C, 270 seconds) vs PO acetaminophen and NSAIDs | SM, SL, IM        | No               | 6 months | RFA superior for pain and function                                       | Patients not blinded                          |
| McCormick et al<sup>13</sup> | RCT        | 53, OA                | Cooled RFA (60°C, 150 seconds) either after or without prognostic nerve block | SM, SL, IM        | Yes/no           | 6 months | Both groups improved in pain and function, no difference between groups | 29 of 32 patients in the nerve block group received RFA |
| Gulec et al<sup>14</sup> | RCT        | 100, OA               | Bipolar vs monopolar IA PRF (42°C, 10 minutes) | IA                | No               | 12 weeks | Bipolar > monopolar RFA for pain relief at 12 weeks                    | No control group                             |
| Ikeuchi et al<sup>15</sup> | CS-P       | 35, OA                | RFA (70°C, 90 seconds) + LA vs LA | SM, IP            | No               | 6 months | RFA > LA for pain at 12 weeks                                          | Not image guided, non-randomized              |

**Abbreviations:** CS-P, case series, prospective; HA, hyaluronic acid; IA, intra-articular; IM, inferomedial; IP, infrapatellar; LA, local anesthetic; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis; PO, per os; PRF, pulsed radiofrequency; PRP, platelet-rich plasma; RCT, randomized controlled trial; RF, radiofrequency; RFA, radiofrequency ablation; SL, superolateral; SM, superomedial; TKA, total knee arthroplasty.
The predictive value of prognostic genicular nerve blocks prior to RFA is similarly questionable. Among the eight RCTs discussed, only three employed positive response to nerve block as a criterion for the performance of RFA. The Choi et al trial, which is the only RCT to compare RFA to sham, required a positive response to prognostic nerve blocks for patients to proceed to the RF portion of the study.28 However, 2 mL lidocaine per site was used to perform the nerve blocks, and a positive response was defined as at least 50% pain relief lasting for 24 hours. Higher volume local anesthetic nerve blocks have been shown to decrease the specificity of prognostic blocks as local anesthetics may spread farther than a subsequent RF lesion,51 and pain relief lasting 24 hours is inconsistent with the pharmacodynamics of lidocaine.

The McCormick et al trial specifically addressed the prognostic value of nerve blocks by comparing RFA outcomes performed after positive genicular nerve blocks to results obtained without the use of prior injections.33 Blocks were performed with 1 mL of lidocaine, with a positive response defined as ≥50% pain reduction persisting for at least 1 hour following injection. Given the lack of statistical difference between the groups, the authors concluded that their method of genicular nerve block has little prognostic value. Methods postulated by the authors to increase the prognostic utility of genicular nerve blocks include the use of a higher threshold for defining a positive response to nerve blocks (90% relief), or using double comparative nerve blocks. However, studies evaluating the effect of using higher cutoffs to select patients for SIJ and lumbar and cervical RFA have mostly found no improvement in outcomes.46,58,59 The use of comparative medial branch blocks with local anesthetics of differing durations of action is also of unclear benefit, having been shown to have marginal sensitivity60 and little impact on lumbar facet RFA outcomes61,62 (Table 2).

### Complications

No major adverse events were reported in any randomized or observational trial. All patients in the RF limb of the Ikeuchi trial noted 2–6 weeks of hypoesthesia in the IP region, but these symptoms self-resolved.37 A review in 2016 discussed the potential adverse effects of knee RFA given the proximity of genicular arteries to the genicular nerves.53 Multiple genicular arteries arise from the popliteal artery, and they course along the epicondyles of the distal femur and proximal tibia in the region where the SL, SM, and IM genicular nerves are normally targeted (Figure 3). Injuries to the genicular arterial system are described in the surgical literature, from both open and arthroscopic procedures, and sequelae include pseudoaneurysm formation, hemarthrosis, arteriovenous fistula formation, and patellar osteonecrosis.65–68 The authors are also aware of several unpublished reports of skin burns, which may arise because of the close proximity of the target nerves to the skin. Other potential complications include those generic to other interventional procedures, namely infection, bleeding, or bruising. Intra-articular approaches also confer the risk of joint sepsis or chondrolysis, but these have not been described following RFA.

### Discussion

Chronic knee pain is a recent addition to the growing list of indications for RF, having first been described only a

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**Table 2** Factors associated with radiofrequency ablation treatment outcomes for knee pain and other conditions

| Predictors of success                  | Predictors of failure                                                                 |
|---------------------------------------|--------------------------------------------------------------------------------------|
| Medial compartment osteoarthritis and concordant pain | Greater disease burden (eg, longer duration of symptoms, greater disability) |
| Large and/or multiple lesions          | Previous surgery                                                                     |
| Controlled prognostic blocks           | Opioid use                                                                            |
|                                       | Psychopathology                                                                      |
|                                       | Diffuse pain symptomatology (fibromyalgianess)                                       |
decade ago. Among the eight RCTs found in the literature, six compared knee RFA to sham or other accepted treatments, but all demonstrated superior pain relief and function with RFA. Fundamental differences between studies make the aggregate body of literature difficult to interpret, as the type of RFA and the anatomic targets vary considerably. However, the preponderance of evidence suggests that RF denervation can be a safe and effective treatment for chronic knee pain, with the duration of benefit similar to that targeting other joints, ranging between 3 and 12 months.

The use of PRF for knee pain is not well supported, and was featured in only one RCT that compared two types of PRF, without a control group. PRF is generally acknowledged as an effective treatment for neuropathic pain based on dozens of preclinical studies and numerous clinical trials. Considering that knee arthritis is a non-neuropathic pain condition, the conceptual basis for the use of PRF in this condition (ie, neuromodulation without significant injury to the neural architecture) is lacking. RCTs comparing PRF to RFA for lumbar facet joint pain have shown greater and more sustained pain relief with continuous RFA, raising further questions regarding its utility for knee pain. Although pain was improved compared to baseline in the PRF groups of both studies, these differences were small and may be attributable to a placebo response. In any case, these results are not easily extrapolated to PRF of the knee given that the targets were neural structures (ie, the medial branch nerves), and not the intra-articular space.

The utility of prognostic blocks prior to RFA is also unclear. Employment of a higher pain relief threshold and the use of comparative local anesthetic blocks may increase the confidence of its benefit. It should be acknowledged that comparisons to and from the spine pain literature regarding RFA are based primarily on the similarity of the intervention, not on similarities in pathology or anatomy. Therefore, in addition to neuroanatomical studies and large multicenter studies that further elucidate the benefit of knee RFA in comparison to sham ablation (ie, placebo-controlled studies), different types of ablation (eg, cooled vs conventional, techniques targeting different genicular nerves and anatomical locations), and alternative treatments (ie, comparative-effectiveness studies), other areas ripe for future research include modification of facet and SIJ RFA trials that have shed light on patient selection criteria, and the effects of prognostic nerve blocks on RFA outcomes.

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