

Narrative Review

Pulsed Radiofrequency Treatment: Evidence for and Applications in Chronic Pain

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Background: Pulsed radiofrequency (PRF) is a neuromodulatory technique that has been widely used for pain management and has recently gained attention as a nondestructive alternative to conventional radiofrequency ablation (RFA), particularly for peripheral neuropathic pain. Over the past decade, PRF has been increasingly investigated for its potential benefits in various chronic pain conditions.

Objective: This review aims to summarize the fundamental principles, mechanisms of action, available evidence, and clinical applications of PRF in chronic pain management.

Study Design: Narrative review.

Methods: A comprehensive literature search was conducted using PubMed, Scopus, and Google Scholar for studies on PRF published up to 2024. Key words included “pulsed radiofrequency,” “pulse radiofrequency,” “pulsed RF,” and “pulse RF.” Relevant case reports, case series, observational studies, randomized controlled trials (RCTs), meta-analyses, systematic reviews, and review articles were included.

Results: PRF has shown promising results in managing various neuropathic pain conditions, particularly radicular pain and postherpetic neuralgia. Clinical evidence also supports its effectiveness in trigeminal neuralgia, occipital neuralgia, cervicogenic headache, chronic migraine, meralgia paresthetica, pudendal neuralgia, and coccygodynia, as well as musculoskeletal conditions such as knee osteoarthritis and shoulder pain. Emerging applications, including intraarticular and transcutaneous PRF, have demonstrated potential benefits. Adjusting PRF settings, such as high-voltage PRF, extended-duration PRF, and pulsed dose radiofrequency, may further enhance treatment effectiveness, though additional validation is needed.

Limitations: This review is narrative in nature and not a systematic analysis. The included studies vary in quality, ranging from case reports to systematic reviews, depending on the availability of research for each condition. Additionally, significant heterogeneity exists in PRF methodologies, treatment parameters, and outcome measures, with a lack of standardized protocols contributing to variability in clinical outcomes.

Conclusion: PRF is a safe, non-ablative technique that modulates pain through electrical fields. It has demonstrated effectiveness in neuropathic pain, particularly radicular pain and postherpetic neuralgia. PRF offers long-term pain relief with minimal risks, though further research is needed to optimize its parameters and expand its applications in chronic pain management.

Key words: Pulsed radiofrequency (PRF), neuromodulation, interventional pain management, pain intervention

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Thermal radiofrequency ablation (RFA) has been applied for cases of chronic pain since 1974 (1). Evidence of the analgesic effectiveness of RFA has been soundly supported by many well-designed, high-quality systematic reviews. There exist pieces of level one-2 evidence in favor of the use of RFA for many chronic pain conditions, such as sacroiliac joint pain, knee osteoarthritis, trigeminal neuralgia and cervical, thoracic, and lumbar facet pain (2-4).

Nevertheless, despite the strong evidence of its effectiveness, thermal RFA can potentially cause undesirable sequelae if it is delivered to mixed somatic nerves, since thermal RFA ablates not only the sensory nerve but also the motor nerve. Similarly, if the pure sensory nerve has a cutaneous branch, ablation of such a nerve may result in neuritis or anesthesia dolorosa (4,5). These possible complications limit the widespread application of RFA.

After the advent of thermal RFA, pulsed radiofrequency (PRF) was developed in 1997 by Sluiter, who applied it to the dorsal root ganglion (DRG) (6). PRF has since been successfully in treating many painful conditions, including radicular pain, axial back pain, postherpetic neuralgia (PHN), and headaches.

The objective of this review is to discuss the fundamental principles of PRF, its applications to common pain conditions, and the supporting evidence for it as a treatment for those conditions.

Basic Principles of Pulse Radiofrequency Treatment

In pain management, radiofrequency (RF) is applied to ablate the nerves, in a process known as radiofrequency ablation (RFA). Conventional RFA consists of the continuous application of an alternating current, which delivers steady energy and thus generates an electromagnetic field, causing adjacent molecules to align and vibrate, leading to frictional energy loss, local heat accumulation, and a rise in temperature. When the temperature exceeds a critical threshold, typically above 45°C for more than 15 minutes, thermal ablation occurs, effectively destroying the targeted nerve (7).

In contrast to conventional RF, PRF involves the delivery of short bursts of current alternating with silent phases between these bursts. The intermittent energy allows heat to dissipate during the silent phase, preventing the surrounding tissue temperature from exceeding 42°C, below the tissue damage threshold. The pulse-like waveform gives rise to the name of the procedure—pulsed radiofrequency (PRF) (8,9). Table 1

illustrates the distinctions between conventional RFA and PRF in the context of pain management.

Mechanisms of Action

When RF energy passes through tissues, it not only increases tissue temperature but also generates 2 types of fields at the tip of the electrode: electric and magnetic. In PRF, the pulse duration constitutes only a small percentage of the time between pulses, resulting in a considerably lower increase in tissue temperature for the same voltage compared to conventional RFA. The thermal effect from PRF is minimal, allowing for the application of higher voltages with a rare chance of the tissue temperature exceeding the denaturation threshold above 45°C.

PRF typically operates at lower frequencies, below 500 kHz, in which the magnetic field is relatively weak compared to conventional RFA. However, due to the brief, high-voltage pulses of PRF, it generates a more intense electrical field than conventional RFA does. It has been suggested that the primary therapeutic effect of PRF is driven by the electrical field rather than the magnetic field (8-10).

The electrical field generated by PRF can induce transmembranous action potential changes, leading to various effects such as disruption in tissue or of ion channels, alterations in resting and threshold potentials, and changes in the axonal membrane due to electroporation. Additionally, the internal electrical field can impact changes in intracellular organelles. Every aforementioned effect induced by the electrical field contributes to the long-term depression of the synaptic transmission of pain signaling, counteracting the long-term potentiation in chronic pain states (10,11).

Park et al categorized the many biological changes observed at subcellular and biomolecular levels to support the potential analgesic mechanism of PRF. These changes were grouped into such categories as alterations at the cellular or molecular level, modifications in neuronal activity, and adjustments in microscopic ultrastructure (anatomical changes) (9).

Numerous molecular changes that support the analgesic effects of PRF include decreases in microglia activation, pro-inflammatory cytokines (TNF- α , IL-6, IFN- γ , COX-2, BDNF), excitatory neurotransmitters (glutamate, aspartate), and the marker of neuropathic pain, c-fos (9,12,13).

Furthermore, PRF selectively reduces post-synaptic evoked potentials in C-fibers while affecting A-fibers minimally, supporting an inhibitory effect on nocicep-

Table 1. *Distinctions between conventional radiofrequency ablation (RFA) and pulsed radiofrequency (PRF).*

Conventional RF	Pulsed RF
Since 1974, documented by Shealy	Since 1997, documented by Sluijter
Continuous current	Repeated short duration of electrical stimulation with resting phase
Constant delivery energy	Delivery energy not constant
Temperature 70-90°C	Temperature below 42°C

tive pathways and enhancing inhibitory pathways. Electron microscopy after PRF procedures shows changes in the myelin sheath, axonal growth, and mitochondrial damage, contributing to temporary pain relief and long-term nerve regeneration (9,12,13).

Besides its analgesic effect, PRF may also promote cellular regeneration and tissue healing. The procedure has been shown to increase the expression of neurotrophic factors, such as the brain-derived neurotrophic factor (BDNF), which are crucial for neuronal survival and repair (14). In vitro studies have demonstrated that low-frequency pulsed electromagnetic fields can stimulate cells to synthesize extracellular matrix components and cytokines, promoting cell proliferation and enhancing the healing of bone, cartilage, and tendon tissues (15,16). Additionally, PRF has been shown to potentiate platelet activation in samples of platelet-rich plasma (PRP), as measured by the secretion of alpha and dense granules under in vitro conditions (17). A synergistic effect on tenocyte proliferation was observed when human tenocytes were exposed to electrical stimulation after the administration of PRP (15). The proposed mechanisms of PRF action are summarized in Table 2.

Distribution of Electrical Field

The intensity of the electrical field is directly proportional to the applied RF voltage. The electrical field forms a spherical shape around the active tip of a monopolar RF electrode, with vectors emanating radially outward and reaching the maximum intensity at the tip. In a study by Cosman et al (18), the intensity of the electrical field was measured using a 5-mm active-tip RF electrode with a peak RF voltage of 45 V, revealing a peak intensity of 187,000 V/m at the ends of the RF tip. The electrical field is notably more intense at the edge of the needle tip (metal boundary) and reaches its maximum at the ends of the tip. When comparing the electrical field at the point 1 mm lateral to the electrode shaft with the point 1 mm forward from the electrode tip, it is observed that the electrical field drops more rapidly from its peak at the point forward from

Table 2. *Proposed mechanism of action of pulsed radiofrequency (PRF).*

Change at Cellular or Molecular Level
<ul style="list-style-type: none"> • Deactivation of microglia at spinal dorsal horn • Reduction of pro-inflammatory cytokines/enzymes/proteins • Reduction of excitatory neurotransmitter • Up-regulation of inhibitory receptor • Increase in level of endogenous opioids precursor • Changes in ion channels • Decrease in level of c-fos
Change in Neuronal Activity
<ul style="list-style-type: none"> • Inhibiting of excitatory nociceptive C-fiber • Enhancing inhibitory pathway
Change in Microscopic Ultrastructure (Anatomical Changes)
<ul style="list-style-type: none"> • Organelle changes • Myelin changes • Changes in neuronal connective tissue
Cellular Regeneration and Tissue Healing
<ul style="list-style-type: none"> • Increasing the expression of neurotrophic factors • Enhancing axonal growth and Schwann cell activity on regeneration after nerve damage • Producing extracellular matrix components and cytokines to promote the healing of bone, cartilage, and tendon tissues

the tip than the field does during the lateral decrease along the shaft. As a result, the electrical field lateral to the shaft begins with a lower maximum intensity but sustains the strength over a longer range. With a 5 mm active-tip electrode and 45 V applied, Cosman et al found the electrical field to be between 10,000-50,000 V/m at 1-2 mm laterally and at 1 mm forward from the electrode's tip (18).

In another study by Ewertowska et al, a computer model was developed to compare temperature and electrical field between a standard protocol and a new high-voltage protocol using a 10-mm active-tip electrode. With a standard PRF setting voltage of 45 V, pulse width of 20 ms, and frequency of 2 Hz, the electrical field measured at various distances (2.5, 5, 7.5, and 10 mm) laterally from the electrode shaft ranged from 4106 to 656 V/m. Similarly, at the same distances forward from the tip, the electrical field measured was between 2329 and 413 V/m. Notably, even at a distance of 1 cm around the shaft, the electrical field remains above 400 V/m, and some studies suggest that even low-intensity electrical fields (200-400 V/m) can initiate the effects of PRF (11,19).

Unlike the well-documented thermal effects of conventional RFA, there is a noticeable gap in studies exploring the influence of RF needle size or the length of the electrode's active tip on the intensity and size of the electrical field. This gap may be attributed to the inherent challenges in measuring the electrical field in vivo. Nevertheless, in theory, a longer active tip of the

electrode should create a larger electrical field, at least in the long axis. A randomized controlled trial study has demonstrated the superior effectiveness of bipolar PRF to its monopolar counterpart in managing chronic lumbosacral radicular pain. Two studies showed favorable response to bipolar PRF in patients whose cervical and lumbosacral radicular pain was refractory to monopolar PRF. As a result, bipolar PRF is suggested to generate denser and larger electrical fields than does monopolar PRF (20-22).

A study demonstrated successful treatment of persistent spinal pain syndrome using epidural bipolar PRF. The researchers in that study aimed to optimize the electrical field to cover the entire dorsal root ganglion (DRG) and increase the density of electrostatic charge by the bipolar PRF technique. This process involved employing 2 needles for access. One targeted the epidural space via a transforaminal approach, while the other accessed it through a caudal epidural approach. The authors speculated that the spherical form of the electrical field created between the 2 needles could cover the entire DRG more effectively than could the electrical field produced by a single monopolar PRF. Furthermore, they noted that the density of the electrostatic charge was inversely proportional to the distribution area of the charge. The distribution area between the 2 RF needles is much smaller than that between monopolar RF and a ground plate, resulting in a higher density of the electrostatic charge in bipolar PRF (19).

Applications in and Evidence for Clinical Use

Clinical evidence supporting the use of PRF has been accumulating steadily over time. The initial study utilizing PRF reported significant pain relief among patients suffering from lumbosacral radicular pain following the application of PRF adjacent to the DRG. An interesting observation from the study was that the RF lesion adjacent to the DRG led to only transient sensory loss, while the relief of pain persisted for a much longer duration (6). Subsequent studies have further reinforced these findings, with positive clinical data emerging mainly in patients with neuropathic pain. A meta-analysis focusing on PRF in neuropathic pain conditions demonstrated favorable outcomes, particularly in post-herpetic neuralgia, cervical and lumbar radicular pain, and cervicogenic headaches (23). As research in this area continues to expand, numerous studies have investigated the effectiveness of PRF for various chronic pain conditions, contributing to a growing body of evidence supporting its clinical utility.

PRF in Radicular Pain

Over the past decade, there has been a wealth of growing evidence supporting the effectiveness of the transforaminal epidural approach of PRF in treating radicular pain, although that evidence is somewhat mixed.

A randomized controlled trial (RCT) compared PRF targeted at the DRG to epidural injections of local anesthetic in patients with lumbar radicular pain and revealed a significant reduction in pain in the PRF group (24). Another RCT compared PRF targeted at the DRG to transforaminal epidural steroid injections (TFESIs) in patients with cervical and lumbar radicular pain from disc herniation and observed no statistically significant difference between the PRF and TFESI groups (25). A meta-analysis focusing on PRF in lumbar radicular pain from disc herniation found no difference between PRF and TFESI at the 4th and 8th week but significant pain reduction in the PRF group at the 12th week (26). Recently, a RCT compared TFESIs alone to a combination of TFESIs and a 10-minute session of PRF in patients experiencing sciatica pain from herniated disc. The patients who received the combination treatment demonstrated greater reduction in leg pain at 4, 12, and 52 weeks (27).

As for the technique of PRF alone, a cohort study of patients with persistent lumbosacral radicular pain demonstrated significant pain relief at one, 2, and 3 months after receiving bipolar PRF subsequently to monopolar PRF (28).

Although there are fewer studies of DRG-targeting caudal PRF than of transforaminal PRF, the available studies have shown that PRF exerts benefits for chronic leg pain in patients with failed back surgery syndrome (29-31).

In conclusion, there is robust evidence that both transforaminal and caudal PRF are effective in treating radicular pain. Comparisons to TFESIs show comparable results for PRF, and combining PRF with TFESI can yield better outcomes. The bipolar technique may be considered for patients who do not respond adequately to monopolar PRF. A summary of clinical evidence on PRF for radicular pain is provided in Table 3 (24-28). Additionally, there is some early evidence to suggest caudal monopolar PRF at the S2-S3 level with the grounding pad at the cervical level can help radicular pain (29).

PRF in Axial Back Pain

An RCT involving lumbar facet joint pain compared conventional RF denervation to the application of PRF

Table 3. Evidence regarding PRF as a treatment for radicular pain (24-28).

Study	n	Population	Comparator	PRF Setting	Outcome
De M et al (2020) RCT	50	Lumbar radicular pain	Epidural LA injection	PRF targeted to DRG; 22G, 10 mm active tip; 45V, 2Hz, 20 ms, 180 sec x 3 cycles	From 2 weeks to 6 months, the PRF group experienced more statistically significant reduction in VAS than did the LA group.
Lee DG et al (2016) RCT	38	Cervical and lumbar radicular pain due to disc herniation	TFESI	PRF targeted to DRG; 22G for cervical, 18G for lumbar, 10 mm active tip; 45V, 5Hz, 5 ms; 240 sec	No statistically significant difference was observed between the PRF and TFESI groups.
Marliana, A et al (2021) systematic review and meta-analysis	81	Radicular pain in lumbar herniated nucleus pulposus (HNP)	Standard radicular pain therapy in lumbar HNP	N/A	No difference between PRF and TFESI at the 4th and 8th week but significant pain reduction in the PRF group at the twelfth week.
Napoli A et al (2023) RCT	351	Sciatica pain due to lumbar disc herniation	Combined PRF vs. TFESI alone	CT-guided PRF targeted to DRG; 22G, 10 mm active tip; 10-minute session. Automatic control of pulse settings, avoiding temperature increases over a specific threshold.	At 4, 12, and 52 weeks, there was greater leg pain reduction ($P < 0.001$) in the combined PRF and TFESI group than in the group who received TFESI alone.
Lee DG et al (2018) prospective cohort	23	Persistent lumbosacral radicular pain after monopolar PRF	Monopolar vs. bipolar PRF	PRF targeted to DRG; 22G, 10 mm active tip; 45V, 5Hz, 5 ms; 360 sec	At one, 2, and 3 months after bipolar PRF, the NRS scores were significantly reduced from the scores before the treatment.

to the medial branch, revealing no significant difference in visual analog scale (VAS) scores at 3 months. However, in the long-term follow-up (at 12 months), the RF denervation group demonstrated superior pain control to the PRF group (32). Additionally, a systematic review comparing PRF to continuous RF for facet joint pain reported greater pain control and better functionality in the continuous RF group (33).

A narrative review aggregating data from 9 studies found that intradiscal PRF offered benefits in patients suffering from discogenic pain. The procedure likely exerted its effects on sinuvertebral nerves (34). A retrospective study that compared intradiscal PRF to intradiscal electrothermal therapy as a treatment for lumbar discogenic pain showed no significant difference in numeric rating scale (NRS) scores between the 2 groups (35). Another retrospective study compared intradiscal PRF for lumbar discogenic low back pain to 2 different duration protocols: 7 minutes and 15 minutes, with no significant difference observed between the 2 groups. Thus, intradiscal PRF has demonstrated effectiveness for discogenic pain regardless of duration (36).

In conclusion, for facet joint pain, PRF exhibits lower effectiveness than does conventional RFA, particularly concerning long-term outcomes. However, for discogenic pain, PRF emerges as a viable treatment option, demonstrating comparable effectiveness to intradiscal electrothermal therapy. Moreover, prolonging the duration of PRF exposure for patients with

discogenic pain does not lead to additional benefits. A summary of clinical evidence on PRF for axial back pain is provided in Table 4 (32-36).

PRF for Postherpetic Neuralgia

There is substantial evidence supporting the use of PRF as a treatment for PHN. A meta-analysis of 6 randomized controlled trials (RCTs) that investigated PRF as a PHN treatment and compared the procedure to sham injections, oral medication, or combined interventions revealed favorable outcomes for PRF. Four studies targeted the intercostal nerve, while the other 2 targeted the DRG. The results favored PRF consistently, with significantly lower pain scores observed in the patients who received PRF at various time points after intervention, including 2-3 days, one week, 2 weeks, 4 weeks, 8 weeks, and 6 months post-treatment (37). Thus, PRF that targets the intercostal nerve and DRG represents one of the strongest bodies of evidence (moderate strength of evidence) among interventional pain management strategies for PHN (38). Furthermore, there is additional evidence supporting the effectiveness and safety of PRF in treating zoster-related trigeminal neuralgia (zoster-related facial pain) (39). There is also some early evidence to suggest that caudal epidural monopolar PRF can improve the ability to control the pain caused by PHN. This case report highlights pain relief following caudal epidural PRF for PHN that affects the L1-4 and T12 dermatomes (40).

A retrospective study assessed the effectiveness of DRG-targeting PRF for both acute herpes zoster (early PRF group within 90 days) and PHN (more than 90 days). The study found that pain intensity decreased after PRF for all patients, with a significantly higher degree of pain reduction, success rate, and medication discontinuation observed in the early PRF group (41).

In a RCT aimed at identifying the appropriate needle tip position when using DRG-targeting PRF to treat herpes zoster-related pain, one group positioned the needle tip inside the pedicle (between the medial and lateral border of the pedicle), while another group positioned it outside the pedicle. The results showed no significant differences between the 2 groups at one and 7 days after therapy. However, the pain score was significantly lower in the inside pedicle group at 30 days (42).

In conclusion, PRF demonstrates good effectiveness in treating PHN and represents one of the strongest bodies of evidence among interventions for PHN. Earlier intervention with PRF appears to be more effective. To achieve optimal outcomes, placing the needle tip between the lateral and medial pedicles to get closer to the DRG is recommended. A summary of clinical evidence on PRF for PHN is provided in Table 5 (37,41,42).

PRF in Trigeminal Neuralgia

The evidence regarding the effectiveness of PRF for trigeminal neuralgia is controversial. An initial RCT that compared PRF to conventional RF for patients with idio-

pathic trigeminal neuralgia reported that PRF was not an effective method of pain treatment. It is noteworthy that conventional RF was eventually performed on the patients in the PRF group after 3 months, since all patients in this group continued to experience intractable pain (43). However, subsequent small retrospective analyses that compared pre- and post-procedure pain levels after trigeminal nerve-targeting PRF in patients with trigeminal neuralgia refractory to conservative treatments showed promising results. These studies reported pain reduction with durations of pain relief ranging from 105 to 1,050 days (44). Moreover, a recent RCT demonstrated that CT-guided PRF to the Gasserian ganglion was more effective than a nerve block. High-voltage PRF was utilized in this study, with the voltage output gradually titrated to the highest tolerable level (mean \pm SD = 77 \pm 11.9 V). The one-year response rate was notably higher in the PRF group (73.8%) than in the nerve block group (32.8%) (45).

In conclusion, evidence for the effectiveness of PRF as a treatment for trigeminal neuralgia is mixed. While initial studies found PRF to be less effective than conventional RFA, later studies, particularly those employing high-voltage PRF, have demonstrated its effectiveness in pain treatment. Therefore, PRF can be considered as an alternative option prior to the administration of more invasive surgical or neuro-destructive treatments. A summary of clinical evidence on PRF for trigeminal neuralgia is provided in Table 6 (43-45).

Table 4. Evidence regarding PRF as a treatment for axial back pain (32-36).

Study	n	Population	Comparator	PRF Setting	Outcome
Li et al (2023) RCT	142	Lumbar facet pain	RF denervation	PRF targeted to lumbar MB; 22G, 10 mm active tip; 45V, 2Hz; 120 sec x 3 cycles	There were no significant differences in VAS at 3 months. In the long-term follow-up, RF denervation was superior to PRF in terms of pain control.
Lopez et al (2019) systematic review (3 RCTs)	103	Facet joint low back pain	Conventional RF (CRF)	N/A	The studies reported greater pain control and better functionality with CRF than with PRF.
Yang et al (2021) narrative review (9 studies)	-	Discogenic back pain	N/A	N/A	Intradiscal PRF effectively alleviated discogenic LBP in all except one study.
Fukui et al (2012) retrospective study	31	Lumbar discogenic pain	Intradiscal electrothermal therapy (IDET)	Intradiscal PRF Diskit II® needle (20 G, 15 cm, 20 mm active tip); 60V, 5Hz, 5 ms; 40°C; 15 min	There were no significant differences in the NRS scores between the 2 groups at one, 3, and 6 months after the treatment.
Park et al (2020) retrospective study	45	Lumbar discogenic low back pain	Intradiscal PRF 7 minutes vs. 15 minutes	Intradiscal PRF; 22G, 10 mm active tip; 60V, 5Hz, 5 ms; 42°C; 7 or 15 min	There were no significant differences between the 2 groups. PRF was shown to be effective for the treatment of discogenic LBP regardless of the duration of the PRF application.

Table 5. Evidence regarding PRF as a treatment for postherpetic neuralgia (37, 41,42).

Study	n	Population	Comparator	PRF Setting	Outcome
Wu CY et al (2020) meta-analysis of RCT (6 RCTs)	420	Herpetic neuralgia	Sham injection, oral medication, or combination of both	PRF targeted to DRG or intercostal nerve; 42°C; 120-240 sec x 2-4 cycles	In all subgroups, the PRF group exhibited significantly lower pain scores in herpetic neuralgia than did the control group at 2-3 days, one week, 2 weeks, 4 weeks, 8 weeks, and 6 months after the intervention.
Kim et al (2017) retrospective study	58	Zoster- related pain	Acute herpes zoster (early PRF) vs. postherpetic neuralgia	PRF targeted to DRG of the involved level; 45V, 2Hz, 20 ms; 42°C; 360 sec	Pain intensity was decreased after PRF in all patients. Degree of pain reduction, success rate, and medication discontinuation was significantly higher in the early-PRF group.
Li et al (2023) RCT	71	Herpes zoster-related pain	Needle tip inside vs. outside the pedicle	45V, 2Hz, 20 ms; 42°C; 120 sec x 3 cycle	No significant differences were found when the 2 groups were compared at one and 7 days after the therapy. However, the pain score was significantly lower in the inside-pedicle group at 30 days.

Table 6. Evidence regarding PRF as a treatment for trigeminal neuralgia (43-45).

Study	n	Population	Comparator	PRF Setting	Outcome
Erdine et al (2007) RCT	40	Idiopathic trigeminal neuralgia	Conventional RF	PRF targeted to trigeminal nerve; 100 mm, 5 mm active tip; 45V, 2Hz, 20 ms; 42°C; 120 sec	PRF is not an effective method of treatment for pain associated with idiopathic trigeminal neuralgia.
Abd-Elsayed et al (2022) retrospective study	21	Trigeminal neuralgia	Pre- and post-procedure	PRF targeted to trigeminal nerve; 21 G, 50 mm, 4 mm active tip; 42°C, 180 sec	PRF can be used as a safe and effective treatment for patients suffering from trigeminal neuralgia that is refractory to conservative measures.
Jia Y et al (2023) RCT	162	Primary trigeminal neuralgia	Trigeminal nerve block with sham PRF	High-voltage PRF targeted to trigeminal nerve; 21 G, 10 cm, 5 mm active tip; 2Hz, 20 ms, 42°C; 360 sec; voltage gradually titrated to highest tolerable output	The proportion of patients who exhibited a positive response at one year after the procedure was significantly higher in the PRF group than in the nerve-block group.

PRF for Headaches

As for occipital neuralgia, the evidence regarding PRF therapy that targets the occipital nerve is limited. However, an RCT that compared PRF to an occipital nerve block using steroids for patients who had occipital neuralgia or migraines with a predominance of occipital pain revealed promising results. The PRF group exhibited a greater reduction in mean occipital pain at 6 weeks, which persisted through 6 months. Additionally, they experienced a greater reduction in their worst occipital pain for up to 3 months (46). Furthermore, case series and observational studies have demonstrated the effectiveness of PRF in improving pain associated with the greater and/or lesser occipital nerves (47,48).

The evidence supporting PRF as a treatment for cervicogenic headaches is relatively limited. While some studies have shown associations between PRF and positive outcomes in pain relief, the variable etiologies of cervicogenic headaches and the diverse targets of PRF complicate the interpretation of results (49-51).

Regarding migraines, PRF has shown promise in

chronic migraine management, based on a few case reports, prospective studies, and RCTs. The targets of PRF in these studies include the greater occipital nerve, C2 DRG, C2-3 posterior medial branch, and transcutaneous electrodes placed over the bilateral neck (GON location). Overall, the results from these studies have consistently demonstrated favorable outcomes with PRF therapy (52-55).

In conclusion, while only a few high-quality RCTs on the use of PRF as a headache treatment are available, several studies have demonstrated the effectiveness of PRF in treating various types of headaches, including occipital neuralgia, cervicogenic headache, and migraines. However, it is essential to note that outcomes vary across studies due to differences in inclusion criteria, targeted nerves, approaches, and settings of PRF. Further research with standardized methodologies and larger sample sizes is warranted to establish a clearer understanding of the role of PRF in headache management. A summary of clinical evidence on PRF for cervicogenic headaches and

migraines is provided in Table 7 (49-51) and Table 8, respectively.

PRF for Other Conditions

PRF has shown effectiveness for various neuro-pathic pain conditions beyond those specifically related to headaches. Reports have indicated the effectiveness of PRF in managing cluster headaches, face and head pain, meralgia paresthetica, gluteal or buttock pain, pudendal neuralgia, chronic idiopathic axonal polyneuropathy, and coccygodynia (56-61).

Moreover, numerous studies support the utilization of PRF to treat joint pain, particularly in the shoulders and knees (62-64). In these cases, PRF targets either intraarticular sites or the articular branch supplying the nerve, which may provide pain relief through the anti-inflammatory effects of PRF. A summary of clinical evidence on PRF for other conditions is provided in Table 9 (56-58,64-75).

A comprehensive table (Table 10) summarizing the clinical applications of PRF and the corresponding targeted lesions would help consolidate the diverse uses of PRF in pain management across different conditions.

Intraarticular PRF

Intraarticular PRF is a treatment for managing chronic joint pain, particularly as manifested in conditions such as osteoarthritis and other inflammatory joint disorders. This technique was first reported by Sluiter ME in a 2008 study (76) in which a needle was inserted into the affected joint space, surrounded by synovium, cartilage, and bone. Rather than directly targeting the sensory nerves around the joint, intraarticular PRF may influence the production of pro-inflammatory cytokines in bone, cartilage, synovium, and the immune system, leading to a decrease of CRP and cytokine levels (77). Exposure to an electric field within the joint space may also stimulate chondrocyte proliferation and ma-

Table 7. Evidence regarding PRF as a treatment for cervicogenic headaches (49-51).

Study	n	Population	Comparators	PRF Setting	Outcomes
Halim et al (2010) retrospective study	86	Pain from lateral atlantoaxial joint	N/A	C1-2 PRF	No. of patients who experienced pain relief > 50%: 2 months: 50% 6 months: 50% One year: 44.2%
Gabrhelik et al (2011) RCT	30	Cervicogenic headache	GON block with steroid (10 mg of 0.25% Marcaine + methylpred, volume 3 mL)	PRF to occipital nerve; 45V; 120 sec x 2 cycles	Significant pain relief at 3 months for both groups In PRF group, pain relief at 9 months
Park et al (2021) prospective observational study	57	Intractable cervicogenic headache (2 diagnostic tests)	N/A	PRF to C3, C4, C5 MB; 42°C; 2 min	Significant pain relief (mean VAS 6.21 >> 1.54 immediately >> 1.77 at 12 months) Pain relief period: 12.4 months

Table 8. Evidence regarding PRF as a treatment for migraines (52-55).

Study	n	Population	Comparator	PRF Setting	Outcome
Yang et al (2015) RCT	37	Chronic migraine (30% pain reduction after ONB)	Sham treatment	PRF to C2-3 posterior MB; 21G, 5 mm active tip; 42°C; 120 sec x 2 cycles	Pain intensity, headache duration, and analgesic dose saw significantly more improvement in the treatment group than in the sham group.
Jun Li et al (2018) case report	1	Chronic migraine in 34-year-old woman	N/A	PRF to C2 (axis) DRG; 22G needle; 45V, 2Hz, 20 ms, 42°C; 900 sec	The patient did not feel a headache after one-year follow-up.
Derya et al (2023) prospective	25	Chronic migraine unresponsive to conservative treatment	N/A	PRF to GON at C2 level; 22G, 5 cm, 5 mm active tip; 45 V, 5Hz, 5 ms, 42°C; 360 sec	VAS, median duration, and number of migraine episodes at the first and third months were significantly lower, shorter, and fewer.
Perdecioğlu et al (2023) RCT	62	Chronic migraine	GON block	Noninvasive PRF with cutaneous electrode over bilateral neck (GON location)	VAS and headache frequency decreased significantly after treatment in both groups. Pre- and post-treatment VAS scores and headache frequencies were similar between the groups.

Table 9. Evidence regarding PRF as a treatment for other conditions (56-58, 64-75).

Study	n	Population	Comparator	PRF Setting	Outcome
Alanbay et al (2020) RCT	30	Hemiplegic shoulder pain after stroke	Suprascapular nerve block	PRF targeted to suprascapular nerve under ultrasound guidance; 21G, 10 cm, 5 mm active tip; 45V, 2Hz, 20 ms; 42°C; 120 sec	PRF combined with physical therapy resulted in greater pain reduction and improved range of motion (ROM) for the shoulder than did the combination of suprascapular NB and physical therapy.
Kim et al (2021) RCT	20	Chronic hemiplegic shoulder pain following stroke	Intra-articular steroid injection	PRF targeted to suprascapular nerve under ultrasound guidance; 21G, 10 cm, 10 mm active tip; 45V, 2Hz, 30 ms, 42°C; 360 sec	Intra-articular corticosteroid injection was more effective than PRF in reducing hemiplegic shoulder pain and improving the ROM for the shoulder.
Abo Elfadl et al (2024) RCT	20	Frozen shoulder pain	Medical treatment (NSAIDs)	PRF targeted to suprascapular nerve under ultrasound guidance; 20G, 5 cm, 5 mm active tip; 2Hz, 20 ms, 42°C; 120 sec	PRF lesioning of the suprascapular nerve significantly reduced pain and improved the ROM in cases of frozen shoulder at 12 weeks after the procedure.
Bergamaschi et al (2024) RCT	40	Chronic shoulder pain	Suprascapular nerve block	PRF targeted to suprascapular nerve under ultrasound guidance; 21G, 70 mm, 10 mm active tip; 50V, 42°C; 180 sec x 2 different points	At 2, 4, and 8 weeks for pain during movement and at 12 weeks for pain at rest, PRF provided better pain relief than did the suprascapular nerve block in cases of chronic shoulder pain.
Han Q et al (2021) RCT (pilot study)	62	Chronic knee osteoarthritis	Passive exercise (PS) alone	PRF targeted to genicular nerve under ultrasound guidance; 22G, 10 cm; 40V, 2Hz, 20 ms; 42°C	The combination of PRF and PS showed superior effectiveness to exercise alone in providing pain relief and improvements in muscle strength and knee function, with sustained benefits over time.
Elawamy et al (2021) RCT	200	Chronic knee osteoarthritis	Intra-articular platelet-rich plasma (PRP)	PRF targeted to genicular nerve under ultrasound guidance; 22G, 10 cm, 5 mm active tip; 42°C, 120 sec x 3 cycles	PRF provided superior, sustained pain relief and a lower osteoarthritis severity index than did intraarticular PRP injections at 6 and 12 months.
Santana-Pineda et al (2021) RCT	188	Knee osteoarthritis	Continuous neuroablative radiofrequency (CNARF)	PRF targeted to genicular nerve under ultrasound guidance; 20G, 10 cm, 5 mm active tip; 45V, 2Hz, 20 ms; 42°C; 360 sec	The CNARF group showed a significantly greater extent and duration of benefits, along with a more substantial reduction in analgesic use.
Horsanali et al (2024) observational study	64	Pain related to knee osteoarthritis	Fluoroscopy-guided intra-articular PRF	PRF targeted to genicular nerve under ultrasound guidance; 22G, 10 cm, 10 mm active tip; 45V, 42°C, 120 sec x 3 cycles	Both groups achieved significant reductions in VAS and WOMAC scores at one and 3 months, with no significant difference in effectiveness between the techniques.
Akbaz et al (2016) retrospective study	27	Head and face pain	N/A	PRF targeted to sphenopalatine ganglion; 20G, 10 cm, 10 mm active tip; 42°C; 120 sec x 4 cycles	PRF provided complete pain relief for 35% of patients and moderate relief for 42%, though 23% experienced insufficient relief.
Philip et al (2009) case report	1	Refractory meralgia paresthetica	N/A	PRF targeted to lateral femoral cutaneous nerve; 20G, 15 cm, 10 mm active tip; 42°C; 120 sec	The patient reported prolonged pain relief at the sixth-month follow-up.
Ghai et al (2018) case series	5	Refractory meralgia paresthetica	N/A	PRF targeted to lateral femoral cutaneous nerve; 22G, 10 cm, 5 mm active tip; 45V, 42°C; extended duration 8 min	All patients reported significant and sustained symptom relief lasting 6 months to 2 years.
Rhame et al (2009) case report	1	Refractory pudendal neuralgia	N/A	PRF targeted to pudendal nerve; 22G, 4 mm active tip; 2Hz, 20 ms, 120 sec	After the procedure, the patient tolerated sitting for 4 to 5 hours, allowing successful weaning from multi-analgesic therapy.
Krijnen et al. (2021) Case series	19	Pudendal neuralgia	N/A	PRF targeted to pudendal nerve; 22G, 5 mm active tip; 45V, 2Hz, 20 ms; 240 sec	At the 3-month follow-up, 79% of patients reported feeling "(very) much better," which increased to 89% at the long-term follow-up.

Table 9 cont. *Evidence regarding PRF as a treatment for other conditions (56-58, 64-75).*

Study	n	Population	Comparator	PRF Setting	Outcome
Atim et al (2011) retrospective study	21	Coccygodynia	N/A	PRF targeted to caudal epidural 10 mm active tip; 42°C, 180 sec	Median VAS score decreased from 8 at the baseline to 2 by the third week and remained at 2 by the sixth month. At 6 months, 57% of patients reported excellent results.
Gopal et al (2014) case series	20	Coccygodynia	N/A	PRF targeted to ganglion impar; 22G, 51 mm, 4 mm active tip; 45V, 2Hz, 20 ms; 42°C; 4 min	PRF treatment of the ganglion impar was successful in 75% of patients, reducing the mean VAS score from 6.53 to 0.93 at 6 and 12 months.

Table 10. *Summary of clinical use of PRF (60,61).*

Clinical Symptoms	Targeted Lesion	Comparators	Supporting Evidence
Radicular pain	Dorsal root ganglia	Epidural LA injection TFESI TFESI	RCT, n = 50 (24) RCT, n = 38 (21) Meta-analysis (26)
Facet joint pain	Medial branches of dorsal rami of spinal nerve	RF denervation	RCT, n = 142 (32)
Discogenic pain	Intradiscal	intradiscal electrothermal therapy N/A	Retrospective study, n = 31 (35) Narrative review (34,36)
Postherpetic neuralgia	Intercostal nerves Dorsal root ganglia	Sham injection or oral medication or combine	Meta-analysis of RCTs (37) Retrospective study, n = 58 (41)
Trigeminal neuralgia	Trigeminal ganglion	Nerve block	RCT, n = 162 (45)
Occipital neuralgia	Occipital nerve (GON, LON)	Nerve block	RCT, n = 81 (46)
Cervicogenic headache	Greater occipital nerve	Nerve block	RCT, n = 30 (50)
Migraine	C2-3 posterior medial branch Greater occipital nerve	Sham treatment N/A	RCT, n = 37 (52) Prospective study, n = 25 (54)
Face and head pain	Sphenopalatine ganglion	N/A	Retrospective study, n = 27 (56)
Shoulder pain	Suprascapular nerve	Nerve block Other treatment	RCT, n = 40 (66) Systematic review of RCTs (62)
Meralgia paresthetica	Lateral femoral cutaneous nerve of thigh	N/A	Case report and case series (57,58)
Knee pain	Genicular nerve	Passive exercise Intra-articular PRP N/A	RCT, n = 62 (68) RCT, n = 200 (69) Systematic review and meta-analysis (63)
Pudendal neuralgia	Pudendal nerve	N/A	Case report and case series (72,73)
Coccygodynia	Ganglion impar Caudal epidural	N/A	Case series (75) Retrospective case series (74)

trix synthesis (78). Clinical studies have demonstrated that intraarticular PRF can provide significant pain relief and improve function in various joints, including the shoulder, knee, sacroiliac, wrist, cervical facet and

atlanto-axial joints, with effects lasting up to 6 months (76,77). Moreover, intraarticular PRF appears to show better outcomes in small joints, such as the trapeziometacarpal and metatarsophalangeal joints, than in larger joints like the shoulder and knee (77). The immediate effect of pain reduction has been observed following the treatment of smaller joints such as atlanto-axial joint, while a later onset of action is seen in the shoulder, knee, and other larger joints (76). Intraarticular PRF treatment was reported to be superior to traditional beta-methasone articular injections for refractory knee osteoarthritis (79). Bipolar intraarticular PRF is more advantageous in reducing chronic knee pain and improving functional recovery than the unipolar method is at 12 weeks post-procedure (80). One systematic review suggested that intraarticular PRF for knee pain exhibited more significant effectiveness than did conservative treatment, although the analgesic effect of intraarticular PRF had a slower onset and shorter duration when compared to cooled RF or RFA on genicular nerves (81). When intraarticular PRF was used for shoulder adhesive capsulitis, the group of patients who received that treatment showed more significant improvements in shoulder function at the second, fourth, and eighth

weeks than did the groups who received intra-articular steroids and ozone therapy (82). However, most studies on intraarticular PRF are retrospective, case reports, or case series. Further research with higher methodological quality is needed to better establish the long-term effectiveness and safety of intra-articular PRF.

Transcutaneous Pulsed Radiofrequency (TCPRF)

TCPRF is a noninvasive application of radiofrequency therapy with evidence supporting both its analgesic and anti-inflammatory effects. The technique offers 2 modes: joint mode and redox mode (83).

The joint mode is primarily used to manage pain in joints such as the shoulder, elbow, wrist, hip, knee, and ankle. Evidence largely highlights the effectiveness of TCPRF for shoulder pain. A retrospective study by Taverner et al (84) demonstrated significant relief from shoulder pain in 14 patients. Additionally, an RCT involving 51 patients compared TCPRF to sham treatment for shoulder pain and reported significant pain reduction and functional improvement lasting up to 12 weeks following a single TCPRF procedure (85). Similar results were observed in studies addressing knee pain (86). Another recent RCT ($n = 50$) found that TCPRF significantly reduced resting pain and improved shoulder function in patients with subacromial impingement syndrome lasted over 12 weeks (87). Furthermore, a pilot RCT ($n = 50$) comparing TCPRF to transcutaneous electrical nerve stimulation (TENS) concluded that TCPRF was superior in alleviating pain and improving general activity (88).

The redox mode offers a systemic anti-inflammatory effect by reducing oxidative radicals in the body, making this mode of TCPRF a potential therapeutic option for managing inflammatory conditions (89).

Setting of PRF in Clinical Use

In clinical practice, the standard protocol for PRF often involves using a voltage of 45 V, a frequency and pulse width of either 2 Hz and 20 ms or 5 Hz and 5 ms, ensuring that the temperature does not exceed 42°C, and a duration of at least 2 minutes. However, there is variation in the setting of parameters:

1. **Voltage:** Voltage settings for PRF can vary among studies, ranging from 45 V to 100 V. Higher-voltage PRF applied to the DRG has shown promising results in animal studies. Retrospective analyses have suggested that higher output voltage and electrical field intensity in PRF procedures may contribute to more effective

pain relief (90). However, questions remain regarding whether higher voltage increases the electrical field, influences outcomes, or raises temperatures above safety thresholds. A computer model study employing a new protocol with higher voltage (55 V) found increased electric field magnitude around 20% without temperature elevation (11). In an RCT comparing standard-voltage (45 V) with high-voltage (60 V) PRF for chronic lumbosacral radicular pain, no statistically significant difference in pain scores was observed at one month, but the high-voltage group reported lower pain scores at 6 months, suggesting potentially enhanced effectiveness with higher voltage (91).

2. **Duration:** Animal studies have yielded inconsistent results regarding the effectiveness of PRF, with different exposure durations ranging from 2 to 12 minutes. While some studies have suggested that longer exposure durations lead to increased antiallodynic effects, others have found no significant differences. Comparative studies on the duration of PRF exposure in humans are limited, with some showing no difference in pain relief between shorter and longer durations (36,92-94).

Regarding the safety of high voltage and prolonged duration for humans, studies employing high voltage (up to 60-90 V) and extended durations (up to 20 minutes) have reported no serious complications in conditions such as discogenic pain, trigeminal neuralgia, and pudendal neuralgia (45,95,96). Kim et al compared the clinical effects between 6-minute and 12-minute PRF therapy in lumbosacral radicular pain and found no significant difference in the intensity of leg pain (97).

3. **Mode of PRF delivery:** The PRF is the initial mode of delivery in which the clinician controls the time of the treatment. Theoretically, the PRF may deliver "empty" pulses if the temperature exceeds the preset temperature to avoid the neuronal damage. Therefore, the actual number of meaningful pulses during the treatment is unpredictable.

The pulsed dose radiofrequency (PDRF) is considered an enhanced mode of PRF delivery in which the clinician controls the number of PRF doses to be delivered. Thus, the clinician can guarantee the delivery of the desired number of pulses to the target (98).

A consensus survey report found, among interventionists who used PRF ($n = 64$), half (53%) reported inconsistent outcomes, and the majority (80%) experienced less-than-ideal pain relief. Of those who used PDRF ($n = 36$), 75% reported consistent outcomes (99).

However, more randomized comparative studies are still required to validate the potential benefits of the PDRF approach.

4. Pulse width and frequency: The default settings of DRG-targeting pulse RFA recommended by Boston Scientific are 2 Hz, 20 ms and 5 Hz, 5 ms (100). However, unlike thermal RFA, there is still no standard consensus on the setting for pulse RFA, which may contribute to the variable results of the studies. Further research is needed to elucidate the effect of parameter setting on the effectiveness of PRF for pain relief in clinical practice.

CONCLUSION

PRF therapy represents a safe and non-ablative approach to pain management. Unlike conventional RFA, PRF operates below 42°C, minimizing the risk of thermal injury. PRF therapy's primary mechanism of action relies on neuromodulation through electrical fields, rather than heat or magnetic fields. This neuromodulatory action triggers long-term depression of pain signaling by altering microscopic anatomy, neuronal activity, and molecular function.

The strongest body of evidence supports the effectiveness of PRF in treating neuropathic pain, particularly radicular pain and postherpetic neuralgia. Clinical studies have demonstrated favorable outcomes with PRF, showing significant pain relief and improved functionality in these conditions.

As for technical considerations, PRF is typically administered using settings such as 45-60 V, 2-5 Hz frequency, and 5-20 ms pulse width, ensuring that the temperature does not exceed 42°C. Higher-voltage settings have been associated with better outcomes, although the benefits of longer exposure durations remain a subject of debate.

Overall, PRF offers a promising alternative for patients suffering from chronic pain, providing long-term relief with minimal risk of adverse effects. Further research is needed to optimize parameters of PRF and expand its applications in pain management.

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