Although peripheral neuralgias are treated with a rich range of options, they can be difficult to treat effectively. Conservative management may include physical therapy, topical agents, and neuropathic medications. Interventional techniques include local anesthetic and steroid injections, while radiofrequency (RF) procedures offer another interventional option.
Benefits of Thermal and Pulsed Radiofrequency

All interventional procedures, including RF methods, may offer several benefits. Interventions lack the systemic side effects seen with medications. For RF procedures, therapeutic effects are usually longer lasting than local anesthetic and steroid injections. Recovery is brief. Compared with thermal conventional RF, pulsed radiofrequency (PRF) avoids the possible complications of postprocedure neuritis, motor dysfunction, and deafferentation pain.

Thermal Radiofrequency Versus Pulsed Radiofrequency

Differences between thermal RF and PRF are summarized in the Table.

Technique

Thermal or conventional RF creates a thermal neurodestructive lesion at the active tip of an insulated cannula. A circuit is created with a ground plate, an insulated cannula with an active tip, tissues, and a generator. The generator produces an alternating current and electrical field at the active tip of the cannula. The electrical field causes charged molecules to oscillate, generating heat in the surrounding tissues. Temperatures of 80°C to 85°C at the active tip will heat tissues within a few millimeters to 60°C to 65°C, the temperature at which soft tissues coagulate. The lesion that is created is spheroid in shape with its long axis along the active tip of the cannula; thus, the cannula must be placed parallel to the target nerve. The lesion is created at 80°C to 85°C for 60 to 90 seconds.1

PRF is thought to create a neuromodulatory lesion rather than a destructive thermal lesion. It uses the same circuit as used in thermal RF. However, the current is applied in brief pulses and at temperatures lower than 42°C to avoid heating the target nerve. A current of 50,000 Hz in 20 millisecond pulses is applied at a frequency of 2 per second. The electric field is densest at the tip of the cannula, so the cannula is often placed perpendicular to the target nerve. The lesion is created at a temperature below 42°C for 2 to 6 minutes, depending on the area being lesioned.1

Mechanism of Action

Thermal RF causes neurodestructive lesions. RF of the dorsal root ganglia (DRG) in dogs and goats showed indiscriminate destruction of unmyelinated and myelinated fibers.2,3 Electron microscopy of rabbit DRG treated with RF showed cytoplasmic vacuoles, enlarged endoplasmic reticulum, degenerated mitochondria, and loss of nuclear membrane although the neurolemma integrity was maintained.4 Electron microscopy of rat sciatic nerve treated with RF showed Wallerian degeneration.5

The mechanism of action of PRF is less clear than that of thermal RF. Most animal studies have shown a lack of neurodestruction after PRF. In rabbit DRG treated with PRF, electron microscopy showed no structural pathology in cell membranes, and myelinated and unmyelinated

**Table. Thermal Radiofrequency Versus Pulsed Radiofrequency**

<table>
<thead>
<tr>
<th></th>
<th>Thermal Radiofrequency</th>
<th>Pulsed Radiofrequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism</td>
<td>Neurodestructive lesion</td>
<td>Neuromodulatory lesion</td>
</tr>
<tr>
<td>Cannula placement in relation to nerve</td>
<td>Parallel</td>
<td>Perpendicular</td>
</tr>
<tr>
<td>Temperature setting</td>
<td>80°C-85°C</td>
<td>&lt;42°C</td>
</tr>
<tr>
<td>Duration of lesioning</td>
<td>60-90 seconds</td>
<td>2-6 minutes</td>
</tr>
<tr>
<td>Possible adverse effects</td>
<td>Neuritis, motor dysfunction</td>
<td>Low risk for these side effects</td>
</tr>
</tbody>
</table>
fibers were normal. In rat sciatic nerve treated with PRF, electron microscopy did not reveal any severe degeneration in myelinated axons. A recent study examined rat DRG 1.5 hours after PRF; electron microscopy showed cytoplasmic vacuoles, enlarged endoplasmic reticulum, and degenerated mitochondria. Some myelinated axons appeared damaged, whereas unmyelinated axons were intact. This seems to contradict the above studies showing no histologic damage; however, note that this study examined histology acutely after PRF treatment, whereas the previous studies examined histology 2 to 3 weeks after PRF treatment. Two studies investigated the role of c-fos, an immediate early gene involved in upregulating transcription of a diverse set of genes. In one study, rats were sacrificed 3 hours after PRF was applied to the cervical DRG. Expression of c-fos was increased in the dorsal root and superficial laminae I and II of the dorsal horn. Rats treated with thermal RF did not have increased c-fos expression. In another study, however, in which rats were sacrificed 7 days after treatment, significant increases in c-fos expression in the dorsal horn were observed in both PRF and RF groups compared with sham treatment. In a study using rat hippocampal slices, PRF produced a transient decrease in the amplitude of excitatory postsynaptic potentials, whereas the reduction with thermal RF lasted for the duration of the experiment. In an inflammatory model of pain in rats, analgesic effects of PRF of the sciatic nerve were inhibited by an α2-adrenergic and a serotonin antagonist, suggesting a possible mechanism of action of PRF involving noradrenergic and serotonergic descending inhibitory pathways. In a spared nerve injury rat model of neuropathic pain, the levels of met-enkephalin, an endogenous opioid, were significantly higher in the spinal cord of animals treated with PRF of the DRG than in control and sham groups. Thus, the mechanism of action of PRF has not been clearly elucidated although it is less destructive than thermal RF and may have a neuromodulatory effect.

Lumbosacral Radicular Pain

One of the most common problems seen in the pain medicine specialty setting is chronic lumbosacral radicular pain with a prevalence ranging from 9.9% to 25%. The evidence is mixed concerning RF therapy providing long-term relief to these patients.

Geurts et al conducted a randomized controlled trial (RCT) comparing thermal RF lesioning with sham therapy in 83 patients and did not show any advantage of lumbosacral DRG RF over sham therapy. The primary outcome of the study was success or failure of treatment. Success was defined with a multidimensional decision rule based on reduction in median visual analog scale (VAS) leg pain score, changes in physical activities score, and use of analgesics. Seven of 44 patients (16%) from the RF group versus 9 of 36 (25%) from the control group reported success from treatment at 3 months. There was no difference between the groups with regard to adverse events or side effects.

In a randomized, prospective study by Simopoulos et al, 76 patients with chronic lumbosacral radicular pain were randomized to receive either PRF or PRF followed by continuous thermal RF of the DRG or segmental nerve. Seventy percent of the PRF-only group and 82% of the PRF followed by RF group reported a successful reduction in VAS score at the first follow-up period at 2 months. The authors concluded that the thermal aspects of RF do not add any significant benefit to PRF. A majority of the patients lost the beneficial effect by 8 months. Again, no significant side effects or neurologic deficits were detected.

Considering the relatively short-term benefit that was observed, the authors conducted a follow-up study to investigate whether repeat application provides the same analgesic effect without a higher risk for complications. They retrospectively reviewed 50 patients who reported at least 50% pain relief after PRF followed by continuous thermal RF of the lumbar DRG or segmental nerve. Forty patients underwent a repeat procedure and reported a mean duration of pain relief of 4.7 months. Twenty-eight patients continued on to receive a third treatment after the effect had worn off, and the average duration of relief was 4.5 months. Eighteen patients had 5 or more treatments; the duration of relief and success frequency remained constant after each subsequent RF treatment. There was one report of transient thigh numbness following a second therapy that resolved within a week. It appears that PRF followed by continuous thermal RF may be a time-sensitive pain management modality with minimal risk to patients.

Tsou et al reported on a prospective observational study of PRF for chronic low back pain. In a group of 78 patients with both low back pain and lower limb pain, 47.4% reported greater than 50% pain improvement at 3-month follow-up. At 1-year follow-up, 46% continued to report greater than 50% pain relief. No complications were reported in this study.

Van Boxem et al retrospectively observed 60 consecutive patients who presented for lumbosacral radicular pain and were treated with single-level DRG PRF therapy. Using a 50% reduction in pain relief sustained for at least 2 months, investigators found that 29.5%, 22.9%, and 13.1% at 6, 8, and 12 months, respectively, reported successfully meeting the end point. Mean duration of action was 9.89 months, and there were no differences in success based on age, sex, level, or history of prior back surgery. Secondary end point measures such as daily pain medication intake also were evaluated using
the Medication Quantification Scale III. There was a significant reduction in the success group.\textsuperscript{15} The success rate in the study was considerably lower than in other studies; possible explanations included limiting the therapy to a single intervention or single level, as it has been hypothesized that injury at one level could produce changes in adjacent levels. Another explanation for the low success rate could be a longer follow-up period.

**Chronic Cervical Pain Syndromes**

Van Kleef et al conducted a prospective, double-blind, randomized study on 20 patients with at least 1 year of intractable chronic cervicobrachial pain. The study divided the patients into 2 groups: the RF group, which received a 67°C RF lesion adjacent to the DRG and the sham group, which received sham therapy in which no actual RF lesion was made. Follow-up was conducted at 1 and 8 weeks after therapy, and patients were evaluated using the VAS and McGill Pain Questionnaire. The study demonstrated treatment success in 8 of 9 patients randomized to the RF group and only 1 of 11 in the sham group. There was a 77% chance with conventional RF therapy of burning pain in the associated dermatome, but the symptoms resolved spontaneously by 3 weeks.\textsuperscript{22}

Van Zundert et al performed a prospective review of PRF for cervicogenic headache and cervicobrachialgia. All the patients had therapy targeted at the DRG. Of 18 patients, 13 (72%) showed greater than 50% improvement in pain relief at the 8-week follow-up. Patients who demonstrated positive outcomes at 8 weeks continued to be monitored for long-term effect. The success rate declined to 50% at 3 months and 33% at 12 months, with a mean duration of effect lasting for 9.2 months. No major adverse events were reported.\textsuperscript{20}

The investigators followed up these findings with an RCT evaluating PRF for chronic cervical radicular pain. Twenty-three patients with cervical radicular pain were randomized to PRF of the DRG or sham intervention. The primary outcome was success or failure of treatment; success was defined as at least 50% improvement on the global perceived effect scale and 20-point reduction in pain intensity on a 0 to 100 VAS scale. Nine of 11 (82%) patients in the PRF group reported greater than 50% improvement on the global perceived effect scale after 3 months of follow-up as opposed to 4 of 12 (33%) in the sham group. A 20-point reduction in VAS score was also seen in 9 of 11 patients in the PRF group and 3 of 12 in the sham group. Both these findings were statistically significant. Pain medication intake was less in the PRF group; however, significance was not reached. No side effects were reported.\textsuperscript{21} The study was limited by a small sample size and differences in baseline demographic characteristics of the 2 groups. The PRF group was younger and had a shorter duration of pain. However, the results support the notion that PRF may provide pain relief for carefully selected patients with chronic cervical radicular pain.

**Occipital Neuralgia**

Occipital neuralgia (ON) may be one of the more challenging conditions to treat. Conservative management includes medications, reducing secondary muscle tension, and improving posture with the hope of reducing stress on the nerve. Reported interventional options include nerve blocks, peripheral nerve stimulation, neurolysis, and dorsal root entry zone lesioning. PRF therapy has shown promising results as well.

Vanelderen et al prospectively studied 19 patients with ON who responded favorably to a diagnostic local anesthetic block and subsequently underwent PRF. VAS and Likert scale scores were analyzed in addition to quality-of-life (QoL) and medication intake questionnaires. Substantial pain improvement was reported in 68.4%, 57.9%, and 52.6% of patients 1, 2, and 6 months after PRF, respectively. The authors also noted a significant decrease in medication use and QoL parameters.\textsuperscript{18}

Choi et al prospectively studied 10 patients who underwent PRF for ON for a mean follow-up period of 7.5 months. Mean VAS score, measured on a 10-point scale, dropped from 6.9 to 1.2 and 0.8 at 1- and 6-month follow-up, respectively. The Total Pain Index (TPI), a pain scale that measures the intensity and duration of headaches, also was assessed. The mean TPI score decreased from 232.7 to 53.7 and 40.6 over the same time period. Eight of the 10 patients stopped using analgesics completely, and no complications were observed.\textsuperscript{19}

Huang et al retrospectively analyzed 102 individuals who were treated for ON with PRF in an effort to identify any patient-specific factors that could be predictive of successful therapy. Successful therapy was defined as greater than 50% pain relief on a 10-point numeric scale lasting at least 3 months; 51% of patients met these criteria. Having a history of a previous inciting event, greater ON involvement only (as opposed to having lesser ON or both), requiring lower injectate volumes of local anesthetic during diagnostic workup, and undergoing multiple cycles of PRF were all characteristics associated with good outcomes. In contrast, extensive pain anterior to the scalp apex, pain that contained both neuropathic and nociceptive characteristics, and the possibility of ongoing secondary gain issues all were associated with a negative result. Symptoms radiating above the scalp apex could have been suggestive of confounding pathology such as migraine headaches. Six episodes of complications were noted, primarily temporary worsening of pain, all of which resolved within 3 weeks of onset.\textsuperscript{17}
In patients whose pain has been refractory to other forms of therapy, such as occipital nerve stimulation, neurolysis, or dorsal root entry zone rhizotomy, PRF shows efficacy with fewer complications. Further study is warranted to establish a more concrete consensus on its role.

Intercostal Neuralgia/Chronic Thoracic Pain

Pain in the thoracic region, whether it is intercostal or multifactorial, historically is difficult to treat. Stolker et al reported on 45 patients with chronic thoracic segmental pain who had failed conservative treatment and underwent thermal RF of the DRG. Inclusion criteria included a segmental distribution and temporary relief with an intercostal nerve block using lidocaine. Symptoms were unilateral in all but one of the patients and the duration of symptoms ranged from 6 months to 51 years. The initial follow-up was at 2 months, and 30 patients (66.7%) were pain-free, 11 (24.4%) had greater than 50% improvement, and 4 (8.9%) showed no improvement. Six patients experienced transient burning pain lasting 3 weeks, and 2 patients had slight sensory loss in the corresponding dermatome, which improved after 3 months. No patient suffered any motor loss or a pneumothorax. Long-term follow-up was conducted in 41 patients with a mean follow-up of 25 months. Twenty patients (48.8%) were pain-free, 15 (36.6%) had greater than 50% pain relief, and 6 (14.6%) had no improvement in pain. The authors addressed possible reasons for treatment failure such as a more localized action of the RF lesion compared with the local anesthetic, heat loss from nearby vessels, afferent fibers in the ventral root, ectopic ganglion cells, intersegmental connections, placebo effect of the diagnostic block, or sympathetic maintenance of pain.

Van Kleef et al reported on RF lesioning adjacent to the DRG in 43 patients with chronic thoracic pain. Inclusion and exclusion criteria were similar to those of Stolker et al. Patients were divided into 2 groups. Group 1 included 27 patients with symptoms limited to no more than 2 segments, and group 2 comprised 16 patients with more than 2 segments involved. At the first follow-up period of 8 weeks, 18 of 27 (67%) patients in group 1 had positive outcomes: 6 (22%) had complete relief, 8 (30%) had good relief, and 4 (15%) reported moderate relief. Of the patients in group 1, 52% had long-term pain relief lasting more than 36 weeks. Group 2 did not report such favorable outcomes: 2 (12%) reported complete pain relief, 1 (6%) had good relief, and 3 (18%) stated only moderate relief. Long-term pain relief was achieved in 30% of patients. Fourteen patients experienced transient burning, and 7 had slight hypoesthesia, all of which resolved without therapy after 12 weeks. No other major complications were reported.

Cohen et al retrospectively analyzed data from 49 patients who received either PRF of the DRG, PRF of intercostal nerves (ICN), or conservative medical management for chronic postsurgical thoracic pain. Key inclusion criteria were duration of symptoms greater than 3 months, VAS score greater than 5 on a 10-point scale, and pain deemed to be neuropathic in origin based on history and physical exam. Patients in the pharmacotherapy group received treatment with either a secondary amine tricyclic antidepressant (nortriptyline or desipramine), or an anticonvulsant (gabapentin or oxcarbazepine) titrated to efficacy and side effects. Successful treatment was defined as greater than 50% pain reduction plus an affirmative answer to 2 questions centered on patient satisfaction and functional improvement. Fifteen patients received PRF of ICN, 13 received DRG procedures, and 21 patients were in the pharmacotherapy group. The average number of levels treated was 2.6 in the DRG group and 2.5 in the ICN group. At 6-week follow-up, patients in the DRG, ICN, and medical management groups had 61.5%, 28.6%, and 27.3% success rates, respectively; however, the difference between the DRG and ICN group did not reach statistical significance. At the 3-month follow-up, success rates were 53.8% for the DRG group and only 6.7% for the ICN group; this was a statistically significant difference. Mean duration of relief was
Trigeminal Neuralgia

Trigeminal neuralgia (TN) historically is a difficult condition to treat. Primary treatment is pharmacologic, with carbamazepine being the medication of choice. If patients remain refractory to medication, they may become candidates for surgical microvascular decompression. Other alternatives include balloon decompression, retrogasserian glycerol injection, RF, and PRF. PRF for TN is shown in the Figure.

The largest study with the longest follow-up period for RF therapy in patients with TN was carried out by Kanpolat et al. It followed 1,600 patients for a period of 1 to 25 years. In all, 2,138 procedures were conducted: 1,216 patients (78%) received a single treatment and 384 (24%) received multiple treatments. Acute pain relief was achieved by 97.6%. The recurrence rate was 25.1% over the average follow-up period of 68.1 months (± 66.4 months). Seven hundred and nineteen patients were followed for 5 years; of these, 57.7% had complete pain relief after a single RF procedure, and this rate increased to 92% with multiple procedures. Three hundred and sixty-five patients were followed for 10 years, and 94.2% reported pain control after single or multiple procedures. Thirty-nine patients were followed for 20 years, with 41% reporting pain control after a single procedure. The most common side effects were an absent corneal reflex and masseter dysfunction. The author stressed the importance of clinician experience as well as proper patient cooperation as variables directly related to success rates.

The role of PRF in facial neuralgia has only gained momentum in the past 10 years. Van Zundert et al first reported on 5 patients who received PRF for idiopathic TN. Mean follow-up was 19.2 months at 2-month intervals; 3 of 5 patients reported excellent results. These patients had failed conservative, pharmacologic options. The author did not comment on the pain scoring system; however, the 3 patients who were considered a success all reported they were “pain-free.” The fourth patient required a repeat procedure 15 months into follow-up, which provided complete relief at the last follow-up period, 18 months after the study commenced. No side effects or complications were mentioned.

Erdine et al conducted a prospective, randomized double-blind study comparing PRF with conventional RF therapy in 40 patients. Evaluation criteria included VAS score on a 10-point scale, patient satisfaction using the Patient Satisfaction Scale, additional pharmacologic requirements, and side effects. The results did not support the use of PRF over RF. The preprocedure median VAS score was 9 in both groups, and although the median VAS score was 0.5 at both 3- and 6-month follow-ups in the RF group, it remained 8.5 in the PRF group at 3 months. Only 2 of 20 patients in the PRF group achieved a significant decrease in the VAS score, and in both cases, the pain recurred within 3 months. It was then decided to perform RF therapy on the PRF group as all patients still had intractable pain. At 3-month follow-up, these patients had a median pain score of 1. All patients who underwent RF reported mild hypoesthesia and paresthesia after the procedure. One patient in the RF group developed anesthesia dolorosa that was successfully managed with medication.

Fang et al investigated the efficacy of use of computed tomography (CT)-guided PRF for TN. The 3-dimensional CT-guided PRF therapy allowed for more precise needle positioning. Goals of therapy were pain reduction of 50% for at least 2 weeks using a 10-point numeric rating scale. Of the 20 patients included in the study, only 7 reported a favorable outcome at 2-week follow-up. Of these patients, only 2 did not have a relapse at 1-year follow-up. There were no complications mentioned in the study.

Post-Inguinal Herniorrhaphy Pain

Werner et al conducted a systematic review of the literature to support the use of PRF in the management of chronic pain after inguinal hernia repair. Although only 1% to 3% of patients will develop this complication, this corresponds to an estimate of 6,000 to 18,000 patients every year given the routine nature of herniorrhaphy. Their literature search yielded 4 case reports analyzing 8 patients for efficacy of treatment. Seven of the 8 patients received diagnostic blocks, 3 of the ilioinguinal nerve and 4 of the DRG. Pain relief varied from 63% to 100% with 5 patients reporting at least 90% pain relief; the follow-up period ranged from 3 to 9 months. No adverse effects or complications were noted in any of the studies.

Pudendal Neuralgia

Pudendal neuralgia can present postoperatively but also from repetitive bicycling or without any known provocation. Rhame et al presented a case report of a patient with 1.5 years of sharp pain in the left gluteal and perianal region, which interfered significantly with her QoL. The pain had been refractory to treatment with multiple medications, as well as interventions such as sacroiliac joint, epidural steroid, and piriformis injections. After the patient had a good response to a diagnostic pudendal nerve block, she elected to undergo...
PRF therapy. After the procedure, she was successfully weaned from her multitodalgesic therapy and had improved sitting tolerance. At 1.5 years postprocedure, she continued to report good sitting tolerance and pain relief. There were no side effects or complications of the therapy.

Glossopharyngeal Neuralgia

Glossopharyngeal neuralgia (GPN) is not as common as TN, with an incidence of 0.7 per 100,000. Pain typically is shooting from the oropharynx upward to the Eustachian tube. Surgical treatment has historically been the treatment of choice; however, it is associated with a high chance of complications. Chua et al described 2 case reports of GPN that had been managed successfully with PRF. The patients did not receive diagnostic blocks because of the close proximity of the nerves to major vascular structures. The first patient had a 15-year history of unilateral facial neuralgia. She had been worked up extensively and had been refractory to previous medical management. She reported complete pain relief at the point of her last follow-up at 5 months. The second patient reported her symptoms had persisted for more than 40 years. This patient reported a reduction in pain intensity 2 weeks after the procedure, and at 4-month follow-up she reported lasting pain relief. Although these results show promise, the author highlighted the risk for bradycardia, asystole, and hypotension from vagal stimulation that can occur during the PRF procedure.

Meralgia Paresthetica

Meralgia paresthetica is a sensory mononeuropathy of the lateral femoral cutaneous nerve (LFCN), which produces discomfort in the anterolateral aspect of the thigh. Symptoms often develop because of compression or irritation of the LFCN. Risk factors for the development of meralgia paresthetica include mechanical compression from tight-fitting belts, obesity, pregnancy, or pelvic tumors. The condition also may be idiopathic. The incidence is low, with one study citing 4.3 in 10,000. Symptoms may resolve spontaneously or with the implementation of physical therapy, weight loss, and anti-inflammatory or antiepileptic therapies. Patients who respond to local anesthetic injection typically only benefit from temporary relief and may be candidates for PRF therapy.

Philip et al published the first case report of PRF treatment for meralgia paresthetica in a 33-year-old morbidly obese woman. The patient had achieved temporary relief with multiple nerve blocks but had been refractory to physical and medical therapy. The patient had good pain relief at 6-month follow-up.

Chua et al presented two cases. Both individuals were able to achieve complete pain relief at both 6-week and 3-month follow-up intervals. Fowler et al suggested the added benefit of ultrasound guidance because of the variation in location of the nerve with regard to the anterior superior iliac spine.

Conclusion

Given the safety and emerging evidence, there seems to be a role for RF and especially PRF in the treatment of peripheral neuralgias. Future research should focus on producing well-designed RCTs that compare the effectiveness of RF therapy with current standards of care, especially for some of the less-studied disease processes such as pudendal neuralgia, GPN, and meralgia paresthetica.

Acknowledgment

I acknowledge Dr. John Delfino for providing the image of PRF for TN.

References


