BACKGROUND AND TECHNIQUE

CONVENTIONAL RADIOFREQUENCY

The use of radiofrequency (RF) electrical currents to create quantifiable and predictable thermal lesions has been practiced since the 1950s. The first reported use of RF in the treatment of intractable pain appeared in the literature in the early 1970s, and it involved the use of conventional radiofrequency currents (CRF) to create thermal lesions. The CRF lesions for pain control are created by the passage of RF currents through an electrode placed adjacent to a nociceptive pathway to interrupt the pain impulses and thus to provide the necessary pain relief. The application of RF currents imparts energy to the tissues immediately surrounding the active electrode tip and raises the local tissue temperature, whereas the electrode itself is heated only passively. During CRF application the RF current is switched off once the desired electrode temperature is reached and the repetition of the cycle maintains the selected tissue temperature. Temperatures above 45°C have been known to be neurodestructive, and although selective destruction of unmyelinated C- and A-delta fibers has been suggested, further studies showed indiscriminate destruction of all nerve fiber types during thermal RF application. Therefore, during CRF the tissue temperatures are typically raised well above the neurodestructive levels, but below the point of tissue gas formation (80°C to 90°C). In order to avoid thermal injury to the motor and sensory nerve fibers and the complications of weakness, neuritis, and deafferentation pain, the use of high-temperature CRF has generally been restricted to facet denervation. However, lower temperature CRF, in the range of 55°C to 70°C, has been arbitrarily selected for dorsal root ganglia (DRG) lesioning.

PULSED RADIOFREQUENCY

In a CRF study of DRG lesioning, no difference in the clinical results was found between the CRF lesions made at 40°C C and 67°C. The authors of this study theorized that the electrical currents rather than the temperature determined the outcome. This observation generated immense interest among pain physicians, as the risks of weakness and deafferentation pain could now be obviated by the use of lower temperature CRF. Based on these assumptions, pulsed radiofrequency (PRF) was introduced, which attempted to maximize the delivery of electrical energy by using higher voltage RF currents, while concomitantly minimizing the risk of thermal tissue injury by keeping the tissue temperatures well below the neurodestructive range (42°C C). These conflicting goals were achieved by applying the RF currents in a pulsatile manner to allow time for the heat to dissipate in between the RF pulses.

Sluijter et al. assumed that, because the tissue temperature was kept below the thermal destructive range, thermal tissue injury was avoided. By using mathematical calculations, they further showed that the high-density electrical currents generated at the electrode tip stressed the cellular membranes and biomolecules and caused altered cell function, leading to cell injury. Later investigators, however, suggested a combined role of electrical and thermal tissue injury from PRF application. These authors also ascertained that the slow response time of the temperature-measuring devices used during PRF could not reliably exclude the possibility of brief high-temperature spikes and the likelihood of thermal tissue injury. Although some laboratory studies showed evidence of neuronal activation, cellular stress, and cellular substructure damage after PRF application, others showed that the observed PRF effects were predominantly a function of set temperature, and thus undermined the role of the electrical currents in causing tissue injury. Thus, despite the several claims of its clinical efficacy, the exact mechanism of the clinical effects of PRF hitherto remains unclear, and currently no evidence of the interruption of the nociceptive pathway in response to PRF application exists.

Similarly to CRF, PRF is applied via an electrode placed in the vicinity of the target nociceptive structure. However, unlike CRF, juxtapositioning of the electrode parallel to the target nerve is deemed unnecessary, as the electrical currents, and not the thermal lesion, are considered the source of neuronal dysfunction. During typical PRF application, the RF currents are applied for 20 milliseconds, at 2 Hz, for a total duration of 120 seconds. Therefore, for most of the lesion duration—480–500 milliseconds—no RF currents are applied. The current voltage is controlled in a manner that the maximum electrode temperature achieved remains below 42°C. Variations from this standard PRF protocol have been infrequent, with the exception of longer lesion duration: PRF has been applied for 4, 8, and 20 minutes in some clinical studies.

WATER-COOLED RADIOFREQUENCY

Although water-cooled radiofrequency (WCRF) ablation has been used in cardiac electrophysiology and tumor ablation for some time, its use in the treatment of pain is fairly recent. The basic principle of pain relief during WCRF application is similar to the CRF—a thermal lesion is created by the application of RF energy through an electrode placed in the vicinity of the target neural structure. However, WCRF is applied by using a specialized multi-channel electrode that is actively cooled by the continuous flow of water at ambient temperature (Fig. 60-1). The active cooling prevents the electrode from acquiring the high surrounding tissue temperatures and allows the continued
flow of the RF current, with the consequent heating of a larger tissue volume and the creation of a larger thermal lesion. The resulting WCRF lesion is consequently comprised of a few millimeters of cooled tissue immediately surrounding the electrode, which is surrounded by spherical isotherms of increasing tissue temperature, which in turn are surrounded by lower temperature isotherms at increasing distance from the electrode (Fig. 60-2). Similar to CRF, the size of the WCRF lesion is dependent on the probe size, the electrode temperature, and the duration of RF current applied. If a 50°C isotherm is used as a criterion for the lesion’s edge while using an 18-gauge electrode with a 6-mm active tip with the electrode temperature raised to 60°C, the lesion created would be 8 to 10 mm in diameter. Even though a spherical area of tissue heating is expected, several factors may influence the symmetry of the WCRF lesion created in vivo. Active heat sinks such as cerebrospinal fluid flow in the thecal sac and blood flow in the epidural venous plexus, and passive heat sinks such as the osseous and muscular spinal structures, may determine the eventual shape of the heated tissue.

The larger area of neural destruction with WCRF application increases the probability of successful denervation of a pain generator with numerous and/or variable afferent nociceptive innervation. The preliminary review of the literature on the clinical use of WCRF identified two distinct forms of WCRF techniques, monopolar and bipolar WCRF lesioning. These WCRF lesioning techniques were applied exclusively for the treatment of sacroiliac joint dysfunction (SJD) and discogenic pain (DP), respectively. The unipolar WCRF in the treatment of SJD was applied to S1, S2, and S3 lateral branches and either two or three monopolar lesions were created lateral to each sacral foramen (see Chapter 47). These lesions were created by using a 17-gauge specialized electrode with a 4-mm active tip. The RF current was applied for 150 seconds, and the electrode temperature was raised to 60°C. Due to the larger anticipated lesion size, the introducer needle was kept at a “safe distance” from the sacral nerve roots—8 to 10 mm from the lateral edge of posterior sacral foramen. To avoid injury to the segmental spinal nerve, WCRF was not applied to the L4 and L5 dorsal rami, and CRF was used instead. For the treatment of DP, bipolar WCRF was applied to the posterior-lateral disc annulus by placing two 17-gauge introducer needles and specialized RF electrodes (Fig. 60-3). The electrode temperature was raised to 55°C over 11 minutes, and this temperature was maintained for an additional 4 minutes.

**CRYONEUROLYSIS**

Cryogenic nerve injury is not associated with neuroma formation, hyperalgesia, and deafferentation pain, which are the attributes typical of nerve injury by other physical modalities such as surgical nerve sectioning, thermal radiofrequency lesioning, or chemical neurolysis. Tendaedlenberg first demonstrated that freezing of the peripheral nerves caused nerve disruption without the risk of neuroma formation. Later, Carter et al. and Beazley et al. showed that peripheral nerve injury from extreme cold caused axonal and myelin sheath disintegration and led to Wallerian nerve degeneration without disruption of the endoneurium, perineurium, and epineurium.

The mechanism of cryogenic nerve injury appears to emanate from damage to the vasa nervorum, the resulting endoneural edema and increased endoneural pressure, and consequent axonal disintegration. An autoimmune response triggered by the release of sequestered neural elements has also been implicated in the long-term effects of cryoablation. The spared connective tissue elements and the Schwann cell basal lamina provide a ready substrate for nerve regeneration from intact proximal axons. The axonal regeneration typically occurs at a rate of about 1 to 1.5 mm
per week, and the duration of analgesia from cryoablation depends on the time taken by the proximal axons to reinnervate the end organs (typically weeks to months). Although the local anesthetic-like properties of cold have been known since ancient Egyptian times, tissue temperatures must be lowered to critical levels for adequate duration for the disintegrative nerve changes to occur—a distinction analogous to the difference between cold, numb fingers and frostbite. The critical temperature required to cause such disintegrative nerve changes has been shown to be –20° C. Additionally, the degree and the duration of analgesia is proportional to the severity of the cryogenic nerve damage. It is therefore crucial that the tissue temperatures are maintained below the critical levels for adequate duration during cryolesioning. In addition, the extent of freezing, and therefore the likelihood of the target nerve injury, depends on the probe size, the proximity of the probe to the target nerve, the freezing duration, and the number of freeze cycles applied. Repeat freeze and thaw cycles increase the size of the eventual ice ball formed.

The first cryoneedle, which used liquid nitrogen as refrigerant and lowered the needle tip temperature below –190° C, was developed in 1962. In 1967, the currently used cryoprobe needle (Fig. 60-4) that used the Joule-Thompson enclosed gas expansion principle and lowered the probe tip temperature to between –50° and –70° C was developed. The contemporary cryoprobe is a double lumen aluminum tube that connects to a gas source by flexible tubing, and either nitrous oxide or carbon dioxide is delivered at a pressure of approximately 42 kg/cm² (600 lb/in² [psi]) to the inner cryoprobe lumen. The gas under pressure escapes through a small orifice from the inner lumen near the cryoprobe tip and returns to the console through the outer cryoprobe lumen (Fig. 60-5). The drastic drop in the pressure at the probe tip (from 600–800 psi to 10–15 psi) allows gas expansion and consequent cooling. Heat absorbed from the tissues surrounding the probe tip lowers their temperature and creates an ice ball around the probe tip. Currently available cryoprobe sizes include a 14-gauge (2-mm) probe that roughly forms a 5.5-mm ice ball, and an 18-gauge (1.4-mm) probe that forms a 3.5-mm ice ball.

Meticulous localization of the target nerve is necessary to increase the likelihood of the target nerve disruption. Most currently used cryoprobes are therefore equipped with a built-in nerve stimulator function that allows both motor (2 Hz) and sensory (100 Hz) testing. The probe also has a thermometer incorporated into the tip to precisely monitor the target tissue temperatures. The console unit is equipped with the nerve stimulator controls, temperature and gas pressure gauges, and a gas regulator switch that allows precise control of the gas flows. To ensure safe and effective cryoablation, the gas flows must be precisely regulated—inadequate gas flows are ineffective in lowering tissue temperatures below critical levels, while excessive gas flows may lead to tissue freezing proximally along the probe length and may cause unintended freeze lesions such as skin burns. The cryoprobe should be withdrawn only after the ice ball has thawed, because withdrawing the

![Figure 60-3](image1.png) Water-cooled radiofrequency application for discogenic pain. (Courtesy Baylis Medical Inc. Montreal, Canada)

![Figure 60-4](image2.png) Cryoprobe needle.
probe with the ice ball still present may cause local tissue injury and avulse the nerve segment.

The use of an introducer, such as a large-gauge intravenous catheter, is often recommended during cryoprobe placement. The sharper introducer tip facilitates the placement of the less rigid cryoprobe and affords additional skin protection during cryolesioning of the superficial nerves. Typically, a 12-gauge intravenous catheter is used for the 2.0-mm probe, and a 14- to 16-gauge catheter is used for the 1.4-mm probe.

**CLINICAL USES**

**PULSED RADIOFREQUENCY**

Although PRF has been employed in the clinical practice fairly recently, its use is relatively widespread and it is used for both painful and also for some nonpainful conditions. The growing popularity of PRF is likely due to its perceived safety and clinical efficacy. PRF has been applied to the DRG at all spinal levels in the treatment of multiple pain syndromes, including radicular pains, post-herpetic neuralgia, herniated intervertebral disc, post-amputation stump pain, and inguinal herniorrhaphy pain. It is also applied to a wide variety of peripheral nerves for the following pain syndromes: it is applied to the medial branch nerve for facet syndrome, the suprascapular nerve for shoulder pain, the intercostal nerves for postsurgical thoracic pain, the lateral femoral cutaneous nerve for meralgia paresthetica, the pudendal nerve for pudendal neuralgia, the dorsal penile nerve for premature ejaculation, the saphenous nerve for chronic benign pancreatic pain, the sciatic nerve for phantom limb pain, the obturator and femoral nerves for hip pain, the glossopharyngeal nerve for glossopharyngeal neuralgia, the occipital nerve for occipital neuralgia, and the genitofemoral, ilioinguinal, and iliohypogastric nerves for groin pain and orchialgia. It has also been applied to various central nervous system and autonomic ganglia, including the gasserian ganglion for trigeminal neuralgia, the sphenopalatine ganglion for head, neck, and facial pain, and to the lumbar sympathetic chain in the treatment of complex regional pain syndrome. In some reports, the target neural structure for PRF application has been unclear, such as the sacroiliac joint for sacroiliac joint dysfunction, intradiscally for discogenic pain, myofascial trigger points for myofascial pain, scar neuromas for postsurgical scar pain, the spermatic cord for testicular pain, and intra-articularly for arthrogenic pain.

**WATER-COOLED RADIOFREQUENCY**

Currently, the use of WCRF is confined to pain syndromes in which the pain generator is considered to have numerous and variable sources of innervation. The reported clinical use of WCRF is currently limited to four recently published articles in peer-reviewed journals. In two of these studies, WCRF was used for the treatment of SJD, and the remaining two pertained to the treatment of DP. However, due to its ability to precisely deliver thermal energy to larger tissue volumes, WCRF may be effective where more traditional forms of neuroablation have failed, and its use may be extended to other pain syndromes.

**CRYONEUROLYSIS**

The reported use of cryoablation in the literature is most prevalent for the treatment of post-thoracotomy pain. Cryolesioning for this clinical indication was typically performed intraoperatively under direct vision on the individual intercostal nerves in the intercostal groove. All the intercostal nerves that were likely to be involved in a patient’s pain—from one to two segments above the upper limit of the incision to one to two below the lower limit of the incision or the chest drain—were typically treated. The cryoablation experience with post-thoracotomy pain led to its use in other chronic pain conditions of the chest wall, including postoperative neuroma, costochondritis, post-herpetic neuralgia, and rib fractures.

In the head, neck, and facial region, cryolesioning of several regional nerves is reported in multiple studies. These nerves have included inferior alveolar, mental, lingual, buccal, inferior dental, auriculotemporal, supraorbital, and infraorbital nerves. The painful head, neck, and facial conditions treated with cryoablation included trigeminal neuralgia, post-herpetic neuralgia, atypical facial pain, and various

**FIGURE 60-5** Schematic design of cryoprobe needle.
postsurgical neuralgias. In the majority of these studies, the craniofacial nerves were exposed by open dissection for cryolesioning; however, in a few studies the cryoprobe was placed by a closed technique, either percutaneously or transmucosally. There is one study of cryoablation in the region of tonsillar fossa, in post-tonsillectomy patients, where the exact target neural structure is less clear.60

Cryoablation has also been used in the treatment of spinal and extremity pains. Its use is reported frequently for the treatment of lumbar facet syndrome, where it was applied to the lumbar medial branches.67–69 For extremity pain, its use is reported for the treatment of intermetatarsal space or Morton’s Neuroma.70 Cryolesioning of the ulnar, median, sural, occipital, palmar branch of the median and digital nerves has also been performed for mostly traumatic nerve injuries and for carpal tunnel syndrome.71

Cryoablation has also been used for the treatment of several painful conditions of the abdomen, pelvis, and perineum. The most frequent application in this region has been for the treatment of post-inguinal herniorrhaphy pain, where it was applied to the iliohypogastric and ilioinguinal nerves.72–75 It has been applied to the lower sacral region of tonsillar fossa, in post-tonsillectomy patients, transmucosally. There is one study of cryoablation in the craniofacial nerves were exposed by open dissection for pregnancy-related and post-partum pain in women, cryolesioning of the ilioinguinal nerve was performed for pregnancy-associated symphysis pubis diastasis pelvic pain.81 Cryolesioning of the iliac crest has been performed for donor site pain.82

**CLINICAL EFFICACY**

**PULSED RADIOFREQUENCY**

PRF has been used most frequently for the treatment of lumbar or cervical radicular pains. Seven of the nine studies reporting this PRF use have been observational and reported its successful use.16 There are five randomized controlled trials (RCTs) on PRF (Table 60–1). There is one

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<tr>
<td>Van Zundert et al, 200783</td>
<td>RCT, DB, SCT</td>
<td>23 patients with CRP, 11 had PRF to one level DRG, 12 had ST.</td>
<td>For 3 mos, only patients having favorable response followed for 6 mos. VAS, GPE, SF-36, AU. Success defined as &gt; 50% Δ in GPE and &gt; 20 Δ in VAS</td>
<td>At 3 mos, SS success reported in 9/11 (82%) patients in the PRF group and in 4/12 GPE (33%) and 3/12 VAS (25%) in the ST group. AC: PRF provided SS pain relief compared to ST at 3 mos</td>
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<td>Simopoulos et al, 200884</td>
<td>RCT</td>
<td>76 patients with LRP, 37 had PRF of DRG, 39 had combined PRF and CRF (maximally tolerated temperatures).</td>
<td>2 mos and monthly thereafter; up to 8 mos. VAS. Success defined as reduction in 2 points in VAS for 8 weeks.</td>
<td>Similar decline in VAS scores between the 2 Gps at 2 mos. Similar loss of analgic effect between 2 and 4 mos and return of pain to baseline by 8 month. AC: PRF of DRG was safe and resulted in short-term benefit; the additional application of CRF did not offer any additional benefit</td>
</tr>
<tr>
<td>Tékin et al, 200785</td>
<td>RCT, DB, SCT</td>
<td>60 patients with LFS, 20 had CRF, 20 had PRF and 20 ST.</td>
<td>Followed at 6 hrs, 6 mos and 1 year after the procedure. VAS, ODI</td>
<td>At 6 hrs, SS lower VAS and ODI scores for CRF and PRF Gps compared to ST. At 6 mos and 1 yr. the lower scores maintained only in CRF Gp. AC: CRF and PRF are both useful interventions in the treatment of chronic facet joint pain</td>
</tr>
<tr>
<td>Kroll et al, 200886</td>
<td>RCT, DB</td>
<td>26 patients with LFS, 13 patients had CRF and 13 had PRF</td>
<td>For 3 mos. VAS, ODI</td>
<td>No SS difference between the CRF and PRF Gps in relative improvements in either VAS or ODI scores at three mos. AC: As above.</td>
</tr>
<tr>
<td>Erdine et al, 200787</td>
<td>RCT, DB</td>
<td>40 patients with TN; 20 had PRF and 20 CRF.</td>
<td>For 3 mos, noncomparative follow-up for 6 mos. VAS, PSS, AU</td>
<td>At day 1 and 3 mos all patients in CRF had SS improvement in VAS and PSS. Only 2/20 patients in PRF Gp at day 1 and none at 3 mos had SS improved VAS or PSS. AC: Unlike CRF, PRF is not an effective treatment for idiopathic TN.</td>
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</table>

**TABLE 60–1 Controlled Trials of Pulsed Radiofrequency**

CRP, Cervical Radicular pain; ST, Sham Treatment; RCT, Randomized Controlled Trial; DB, Double-Blinded; SCT, Sham Controlled Trial; VAS, Visual Analogue Scale; GPE, Global Perceived Effect; AU, Analgesic Usage; AC, Author’s Conclusion; SS, Statistically Significant; TN, Trigeminal Neuralgia; PSS, Patient Satisfaction Scale; LFS, Lumbar Facet Syndrome; ODI, Oswestry Disability Index; LRP, Lumbar Radicular Pain
RCT of 23 patients with chronic cervical radicular pains that compared PRF applied to the DRG in 11 patients with a similarly performed sham intervention in 12 patients.\textsuperscript{16} The results of this trial showed statistically significant improvement in pain and patient satisfaction scores at 3 months in the PRF group. However, this was a small sized trial, and it reported only short-term results at 3 months. There is one RCT of 76 patients with lumbar radicular pains that compared PRF to combined PRF and CRF application to the involved DRG.\textsuperscript{85} In both the study groups, the patients experienced significant pain relief at 2 months, but experienced significant loss of analgesic effect after 4 months, and a complete return of pain after 8 months. Although the study results concluded that the PRF of the DRG led to short-term pain relief and no additional benefit was gained by CRF application, this trial compared PRF to a combined PRF and CRF technique not used clinically: CRF was applied until the patient felt radicular pain. As a result, the CRF lesion temperatures and durations were inconsistent.

The second most commonly reported PRF application is in the treatment of facet syndrome (FS). There are two RCTs and three observational studies available on this topic.\textsuperscript{16} In one RCT of 60 patients with chronic lumbar FS, the effects of CRF, PRF, and sham treatment were compared.\textsuperscript{85} The three equal study groups were evaluated immediately and at 6 and 12 months after the procedure. The patients in both the CRF and the PRF groups had lower pain and disability scores immediately after the procedure, compared with the sham group. However, this pain relief and functional improvement was maintained only in the CRF group at 6 and 12 months. The significance of the lower pain scores in the immediate post-procedural period in the PRF group in terms of long-term pain relief, however, is unclear. The second RCT was of 50 patients with lumbar FS of more than 1 month’s duration.\textsuperscript{86} Only 26 patients, of which 13 received CRF and 13 PRF, completed their follow-up evaluations. No significant difference in the pain and disability scores was found at 3 months between the two groups. Several limitations of this trial make its results inconclusive in terms of long-term pain relief: a large dropout rate of 48%, a small study size of 26 patients, short-term results after 3 months, the lack of a placebo control group, and patients with pain duration of only 1 month were included in the trial. The three available observational studies of PRF application for FS all reported its efficacy.\textsuperscript{16} There is one RCT of PRF use: in 40 patients with idiopathic trigeminal neuralgia, the effects of PRF were compared with CRF, both applied to the gasserian ganglion.\textsuperscript{38} At 3 months, patients in the PRF group reported no significant pain relief or improved satisfaction, compared with the CRF group. The results of this study concluded that PRF was not an effective method of treatment for idiopathic trigeminal neuralgia. One criticism of this trial is that multiple CRF lesions were performed in the CRF group, compared with only one PRF application in the PRF group. This trial also lacked a sham treatment group. One additional case series reported the efficacy of PRF in the treatment of trigeminal neuralgia.\textsuperscript{16}

Successful application of PRF to the suprascapular nerve for shoulder pain has been reported in four case reports or case series.\textsuperscript{16} A case report and a prospective case series reported successful application of PRF to the sphenopalatine ganglion for head, neck, and facial pain.\textsuperscript{16} The use of PRF for the remaining clinical conditions described earlier is based on a single case report or case series; almost all of these reports described the successful use of PRF for the condition.\textsuperscript{16}

Thus, although the observational studies almost universally support the use of PRF, the available controlled data is suboptimal and showed variable efficacy for the reported conditions. The efficacy of PRF reported in these RCTs for various clinical conditions was at best short term.

**WATER-COOLED RADIOFREQUENCY**

Of the four available clinical studies of WCRF, only one is an RCT. In this RCT of 28 patients with SJD,\textsuperscript{22} 14 patients received WCRF in the treatment group, while 14 patients in the control group received the placebo treatment (the electrodes were placed similarly to those in the treatment group, but no RF current was applied). Although statistically significant lowered pain and disability scores were reported for the patients in the treatment group, the comparative analysis of the two study groups was performed at one month only. The second study of WCRF for SJD was a retrospective analysis of 27 patients, and it reported the successful use of WCRF.\textsuperscript{23} One study of WCRF use in the treatment of DP is a prospective case series of 15 patients,\textsuperscript{24} and the second publication is a single-patient case report.\textsuperscript{25} Both the studies reported the success of bipolar WCRF in the treatment of DP. Thus, currently the evidence for the clinical efficacy of WCRF is in early rudimentary stages.

**CRYONEUROLYSIS**

The RCTs of cryoablation pertain mostly to its use after thoracic surgery for the relief of postoperative pain (Table 60-2).\textsuperscript{36–46} Although the majority of these trials were published in the 1980s and 1990s, some were published as recently as 2008.\textsuperscript{45} The comparisons made in these trials varied significantly, some comparing cryoablation with no intervention,\textsuperscript{36–40} with local anesthetic blockade,\textsuperscript{16} with continuous intravenous narcotic infusion,\textsuperscript{41,42} and with epidural analgesia.\textsuperscript{41,42} Of the five trials that compared cryoablation with no intervention, three\textsuperscript{36,37,40} reported statistically significant reduced narcotic usage and pain scores after the cryoablation, while two showed no such advantage.\textsuperscript{38,39} The two trials that compared cryoablation with intravenous narcotic infusion showed no advantage of cryoablation.\textsuperscript{41,42} There are three trials comparing epidural analgesia to cryoablation.\textsuperscript{43–45} The results of one trial showed that patients in the epidural analgesia group had significantly better pain scores and pulmonary function tests compared with the cryoanalgesia group.\textsuperscript{45} Results of the other two such trials showed that cryoablation provided postoperative analgesia comparable to the epidural analgesia; however, cryoablation increased the incidence of post-thoracotomy neuropathic pain, and the
<table>
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<tr>
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<tr>
<td>Katz et al, 1980&lt;sup&gt;16&lt;/sup&gt; USA</td>
<td>24 patients, 9 in CA Gp, 9 received either LA intercostals block or no block.</td>
<td>Not blind, randomization only partial; 18 patients; random number selection table.</td>
<td>For up to 5 PODs. 10 point pain measurement scale, AC, PFTs.</td>
<td>CA Gp had SS less pain (student's T test: &lt; 0.001 for day 1, &lt; 0.05 for day 3, and &lt; 0.01 for day 5) and less narcotic usage p &lt; 0.01. No difference for PFTs. Pain relief in CA Gp lasted for 2–3 wks and no AEs at 6 mos.</td>
<td>CA has definite advantages over other forms of therapy for PTP.</td>
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<td>Glynn et al, 1980&lt;sup&gt;17&lt;/sup&gt; UK</td>
<td>58 patients, 29 received CA and 29 did not.</td>
<td>Patients were matched; not randomized or blind.</td>
<td>Narcotic usage and time to mobilization and discharge.</td>
<td>CA patients SS less narcotic usage p &lt; 0.005. No difference for other 2 parameters.</td>
<td>Patients who received CA required fewer narcotics after surgery than those in the control group.</td>
</tr>
<tr>
<td>Roxburgh et al, 1987&lt;sup&gt;38&lt;/sup&gt; UK</td>
<td>53 patients, 23 had CA and 30 did not. Patients in both the Gps had lumbar epidural catheter and epidural methadone.</td>
<td>Randomized and blind</td>
<td>Comparative analysis performed until discharge (14 days). Linear analogue pain scale and AC.</td>
<td>No SS difference at the 5% level between the Gps for either measure.</td>
<td>Addition of CA to standard postoperative regimen produced no significant reduction in postoperative pain or analgesic consumption.</td>
</tr>
<tr>
<td>Müller et al, 1989&lt;sup&gt;19&lt;/sup&gt; Austria</td>
<td>63 patients, 30 CA and 33 CGp.</td>
<td>Randomized and double-blind</td>
<td>For 7 PODs. 0–4 pain scale, AC and PFTs.</td>
<td>None of the measured variables were SS different between the two Gps. In CA Gp 6 patients (20%) had neuralgic pain 6 wks after the operation, which continued for up to 4 wks.</td>
<td>CA provided inadequate pain relief after thoracotomy and advised against its use.</td>
</tr>
<tr>
<td>Pastor et al, 1996&lt;sup&gt;40&lt;/sup&gt; Spain</td>
<td>100 patients; 55 had CA while 45 patients in the CGp did not.</td>
<td>Randomized and double-blind</td>
<td>For 7 PODs. 0–5 pain scale, AC and PFTs</td>
<td>Pain was SS lower in CA Gp; p&lt;0.001, amount of analgesics required was SS lower in the CA Gp; p&lt;0.001). No difference in the PFTs between the Gps.</td>
<td>The authors advocated the use of CA.</td>
</tr>
<tr>
<td>Orr et al, 1981&lt;sup&gt;41&lt;/sup&gt; UK</td>
<td>45 patients. 3 Gps; 15 each. Control, CA, and morphine infusion</td>
<td>Randomized and blind</td>
<td>VAS and analgesic usage</td>
<td>Infusion and CA Gps had similar pain relief p,0.08 and analgesic usage.</td>
<td>This trial did not distinguish between the cryoprobe and morphine infusion.</td>
</tr>
<tr>
<td>Gwak et al, 2004&lt;sup&gt;42&lt;/sup&gt; Korea</td>
<td>50 patients in whom thoracic epidural was not considered. 2 Gps included CIVA and CIVA+CA</td>
<td>Randomized and double-blind</td>
<td>For 7 PODs. Visual analogue pain scale, AC and PFTs. Patients also followed for 6 mos for PTP</td>
<td>No SS difference for the 2 Gps for pain, AC, PFTs, and PTP.</td>
<td>CA was not effective in reducing the incidence of PTP.</td>
</tr>
<tr>
<td>Brichon et al, 1994&lt;sup&gt;43&lt;/sup&gt; France</td>
<td>120 patients, control, epidural and CA Gp</td>
<td>Randomized</td>
<td>Until discharge or up to 12 days. Linear visual analogue pain scale, AC and PFTs</td>
<td>None of the measured variables were SS different between the two Gps. In CA Gp 6 patients (20%) had neuralgic pain 6 wks after the operation, which continued for up to 4 wks.</td>
<td>Pain was SS lower in CA Gp; p&lt;0.001, amount of analgesics required was SS lower in the CA Gp; p&lt;0.001). No difference in the PFTs between the Gps.</td>
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<td>Yang et al, 2004&lt;sup&gt;44&lt;/sup&gt; Korea</td>
<td>90 patients, 45 patients each in Gp, T epidural and T epidural + CA Gp.</td>
<td>Randomized</td>
<td>For 7 PODs. Visual analogue pain scale, AC and PFTs. Patients also followed for 6 mos for PTP.</td>
<td>Epidural-CA patients had less pain on the 7&lt;sup&gt;th&lt;/sup&gt; POD (P 0.036) and less AC on 6&lt;sup&gt;th&lt;/sup&gt; (P 0.044) and 7&lt;sup&gt;th&lt;/sup&gt; (P,0.018) POD. Δ in FVC on 7&lt;sup&gt;th&lt;/sup&gt; POD was greater in epidural+CA Gp than the epidural Gp (P 0.024). The incidence of PTP was similar in the two Gps during the 6-mo follow-up.</td>
<td>Epidural analgesia led to the best pain relief and restoration of pulmonary function after thoracotomy.</td>
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<td>Ju et al, 2008&lt;sup&gt;45&lt;/sup&gt; China</td>
<td>107 patients. T-Epidural Gp and in CA Gp, a subcutaneous catheter placed in the upper back +IVPCA.</td>
<td>Randomized and double-blind</td>
<td>For 3PODs., NRS pain scale, PS. Ts. Patients also followed for 6 mos for PTP.</td>
<td>No SS Δ in NRS scores and PS between the Gps at 3 PODs. Higher incidence of allodynia-like pain in CA Gp with SS on 6&lt;sup&gt;th&lt;/sup&gt; and 12&lt;sup&gt;th&lt;/sup&gt; mos (P &lt; 0.05).</td>
<td>Although CA combined with subcutaneous and IV morphine provided comparable pain control to T Epidural, it could not be recommended due to neuropathic PTP.</td>
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<td>Miguel et al, 1993&lt;sup&gt;46&lt;/sup&gt; USA</td>
<td>45 patients, 4 study Gps; 14 CA, 10 EA (morphine- lumbar), 10 intrapleural analgesia, and 11 CIVA (morphine).</td>
<td>Randomized and double-blind</td>
<td>For 5PODs. VAS and PFTs. Patients also followed for 12 wks by telephone.</td>
<td>Epidural morphine provided superior pain relief than the other modalities. No difference in PFTs was found between the Gps. The number of patients was insufficient to draw definitive conclusions.</td>
<td>PTB is best relieved with epidural morphine, compared to intrapleural analgesia, CA and CIVA.</td>
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</table>

CA, Cryoanalgesia; AC, Analgesic Consumption; SS, Statistically Significant; PTP, Post-thoracotomy pain; AEs, Adverse Effects; VAS, Visual Analogue Scale; CGp, Control Group; POD, Post-operative day; CIVA, continuous intravenous analgesia; PS, Patient Satisfaction; EA, Epidural Analgesia
authors recommended against its use.\textsuperscript{44,45} In one controlled trial of four treatment groups, cryoablation was compared with epidural analgesia, continuous narcotic infusion, and intra-pleural analgesia.\textsuperscript{46} The results of this trial showed epidural analgesia to provide the best relief of the postoperative pain; however, due to the insufficient number of patients enrolled in this trial, the results failed to reach statistical significance. Overall, of the 11 available controlled studies pertaining to the use of cryoablation for the relief of post-thoracotomy pain, only three favored its use.\textsuperscript{36,37,40} This lack of efficacy of intercostal nerve cryoablation has been attributed to unaltered sensitivity of the visceral pleura and the large thoracic wall muscles, such as the latissimus dorsi and serratus anterior.\textsuperscript{39}

Although multiple reports of cryoablation in head, neck, and facial region pain have been published,\textsuperscript{47–66} only one study is a controlled trial.\textsuperscript{66} In this RCT, cryoablation was applied to the tonsillar fossa after tonsillectomy. It reported statistically significant reduced postoperative pain scores in patients receiving cryoablation without evidence of additional complications.

There are three controlled trials of cryolesioning for postoperative pain after herniorrhaphy.\textsuperscript{73–75} In two such trials, isolated cryolesioning of the ilioinguinal nerve was performed at the end of the hernia surgery.\textsuperscript{73–74} One of these trials reported reduced postoperative analgesic usage in the cryoanalgesia group,\textsuperscript{73} while the other trial reported no difference in the pain scores and analgesic consumption between the treatment and the control groups.\textsuperscript{74} In the third trial, cryolesioning of both the ilioinguinal and iliohypogastric nerves was performed intraoperatively and no statistically significant difference in pain scores and analgesic usage was reported between the treatment and the control groups.\textsuperscript{75} This trial also reported increased incidence of sensory disturbances in the patients in the treatment group, and the authors recommended against the use of cryoablation for post-herniorrhaphy pain.

### SIDE EFFECTS AND COMPLICATIONS

Although bleeding, infection, and nerve damage from needle placement and burns from the incorrect placement of the grounding pad have been reported,\textsuperscript{88} no noticeable side effects or complications have been directly attributable to PRF use.

Apart from local transient post-procedural discomfort, none of the four clinical studies of WCRF reported any significant complications.

Despite the claims of reduced risk of neuroma formation and nerve regeneration after cryoneurolysis, the most significant reported adverse effect of cryoneurolysis has been neuropathic pain characterized by hypersensitivity and allodynia.\textsuperscript{44,45,75} Other reported complications from cryoneurolysis are rare and include local tissue injury from the placement of the large-gauge introducer catheter or cryoprobe needle. Patients may report numbness in the territory of the involved nerve, which may be distressful for some patients. A diagnostic local anesthetic block performed prior to the cryoneurolysis allows the patient to experience this numbing effect and judge its tolerability. Alopecia, depigmentation, or hyperpigmentation at the lesion site have also been reported and may especially be of concern when cryolesions are performed in proximity to the face.\textsuperscript{89}

### REFERENCES

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