Percutaneous Image-Guided Cryoneurolysis

Ross W. Bittman[1]
Gail L. Peters
Janice M. Newsome
Eric B. Friedberg
Jason W. Mitchell
Jacquelyn M. Knight
J. David Prologo

OBJECTIVE. The aim of this article is to review the available evidence regarding image-guided percutaneous cryoneurolysis, with a focus on indications, technique, efficacy, and potential complications.

CONCLUSION. Percutaneous image-guided cryoneurolysis is safe and effective for the management of several well-described syndromes involving neuropathic pain. Additional rigorous prospective study is warranted to further define the efficacy and specific role of these interventions.

The role of the interventional radiologist in the nonoperative local management of painful conditions with the use of image-guided thermal ablation techniques has expanded during recent years [1, 2]. The purpose of this article is to describe cryoneurolysis (CN), an evolving percutaneous image-guided technique for the management of disorders related to peripheral nerves.

The Mechanism of Cryoneurolysis

Cell death after cryoablation results from freezing induced through a metallic probe cooled by the rapid expansion of pressurized gas. The freezing process manifests first in the extracellular space, causing an osmotic gradient to form, leading to cell shrinkage. As the freezing process progresses, intracellular ice crystals form and directly damage organelles [3]. Similar mechanisms result in vascular injury, inducing a coagulative cascade and eventual ischemia-mediated cell damage. During the thaw phase of these procedures, water rushes into previously shrunken cells, causing them to burst. Ablation zone tissues also incur damage through interspersed apoptosis and inflammatory injury [4, 5]. Cryoablation has been found to damage nerves specifically via ice-crystal–mediated vasa vasorum damage and endoneural edema, Wallerian degeneration, direct physical injury to axons, and dissolution of microtubules resulting in cessation of axonal transport [6–9]. The end result of these routes of neuronal damage is decreased pain sensation resulting from conduction cessation, activation of descending inhibition, blockade of excitatory transmitter systems, generalized sodium channel blockade, or a combination of these mechanisms [10].

Clinically, cryoablation affords several advantages over other forms of image-guided thermal or chemical ablation, including direct visualization of the ablation zone, decreased intraprocedural and postprocedural pain, and the ability to simultaneously use multiple probes in variable configurations to create tailored additive overlapping ablation zones [11–13]. In contrast to surgical or heat-mediated ablation, cryoablation does not disrupt the acellular epineurium or perineurium, which reduces the risk of neuroma formation and may allow eventual nerve regeneration [14]. CN also avoids the risk of systemic toxicity associated with chemical nerve ablation [15].

Existing Literature

The first study of CN, published by Nelson et al. [16] in 1974, showed that intraoperative cryoablation of the intercostal nerves resulted in decreased analgesic use after thoracotomy. In 1976, Lloyd et al. [17] published the first study of CN for the relief of preexisting pain, using surgical exposure or percutaneous access and nerve stimulator guidance. Sixty-four patients had a median duration of pain relief of 11 days. More recently, CN without image guidance has been studied as a potential treatment for many syndromes of peripheral nerve dysfunction, including knee

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[1]All authors: Department of Radiology and Imaging Sciences, Emory University Hospital, 1364 Clifton Rd NE, Ste D112, Atlanta, GA 30322. Address correspondence to R. W. Bittman (Ross.bittman@emory.edu).

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TABLE 1: Prospective Trials of Image-Guided Percutaneous Cryoneurolysis

Authors [Reference]	Year of Publication	No. of Patients	Nerve Treated	Symptoms or Condition Treated	Imaging Guidance	Primary Outcome	Complications[a]	Re-treatment[b]
Evans et al. [22]	1981	40	Sacral nerve roots and coccygeal nerve	Perineal pain caused by cancer, coccydinia, or perineal neuralgia	Fluoroscopy	65% Of procedures resulted in complete relief or improvement in pain; the median duration of improvement was 30 days	9 Patients had minor complications, and 1 patient had a prolonged CSF leak	9 Patients received 2 treatments, 6 received 3 treatments, 2 received 5 treatments, and 2 received 6 treatments
Bärlocher et al. [48]	2003	50	Lumbar medial branch nerves	Lumbar facet joint syndrome	Fluoroscopy	One year after the procedure, 31 patients (62%) had complete reduction or greater-than-50% reduction in pain	No complications reported	14 patients received 2 treatments
Staender et al. [23]	2005	76	Lumbar medial branch nerves	Lumbar facet joint syndrome	CT	Mean pain score on VAS decreased from 6.7 preoperatively to 2.9 at 3 days, 3.2 at 3 months, and 3.4 at 6 months after treatment; 40% of patients had pain reduction for 12 months or longer	No complications reported	11 Patients received 2 treatments, 6 received 3 treatments, and 1 received 4 treatments
Birkenmaier et al. [47]	2007	46	Lumbar medial branch nerves	Lumbar facet joint syndrome	Fluoroscopy	Mean low back pain score decreased from 7.7 preoperatively to 3.2 at 6 weeks, 3.3 at 3 months, 3.0 at 6 months, and 4.2 at 12 months after treatment	One patient had a vagus-induced syncope	No patient received multiple treatments
Prologo et al. [73]	2013	24	Dorsal penile nerve	Premature ejaculation	CT	Mean intravaginal ejaculatory latency time increased from 54.7 s at baseline to 256 seconds at day 7, 182.5 s at day 180, and 140.9 seconds at 1 year after treatment	No complications reported	No patient received multiple treatments
Mortell et al. [46]	2014	9	Celiac plexus	Abdominal pain caused by pancreatic adenocarcinoma	CT	5 Patients had a permanent decrease in pain, 2 had immediate posttreatment relief that lasted up to 8 weeks, and 2 did not have pain relief.	1 Patient had a minor complication	No patient received multiple treatments
Prologo et al. [26]	2015	11	Pudendal nerve	Pudendal neuralgia	CT	Mean pain score decreased from 7.6 at baseline to 2.6 at 24 hours, 3.5 at 45 days, and 3.1 at 6 months after treatment	No complications reported	2 Patients received 2 treatments
Yoon et al. [76]	2016	22	Various peripheral nerves	Peripheral neuropathy	Ultrasound	Mean pain score decreased from 8.3 before treatment to 2.3 at 1 month, 3.2 at 3 months, 4.7 at 6 months, and 5.1 at 12 months after treatment	No complications reported	11 Patients received 2 treatments

(Table 1 continues on next page)

TABLE 1: Prospective Trials of Image-Guided Percutaneous Cryoneurolysis (continued)

Authors [Reference]	Year of Publication	No. of Patients	Nerve Treated	Symptoms or Condition Treated	Imaging Guidance	Primary Outcome	Complications[a]	Re-treatment[b]
Prologo et al. [84]	2017	21	Lower extremity ($n = 17$) and upper extremity ($n = 4$) peripheral nerves	Phantom limb pain	CT	Mean pain score decreased from 6.2 at baseline to 2.3 at 45 days after treatment and 2.0 at mean long-term follow-up of 194 days after treatment	6 Patients had minor complications	4 Patients underwent a second treatment

Note—VAS = visual analog scale.
[a]Minor complications include superficial infection, minor bleeding, postprocedural pain requiring analgesics, and spontaneously resolving diarrhea.
[b]In some studies, re-treatment was reserved for patients for whom the first treatment failed, whereas for others it was used to provide further relief for those who had positive results.

pain after arthroplasty, occipital neuralgia, and osteoarthritis [18–21]. Although these studies show the fundamental efficacy of CN, the unique skill set of interventional radiologists broadly expands the potential applications of this treatment.

This article is based on a literature review of all reports of image-guided CN. The methods used for the literature review are described in Appendix 1. Beginning with the use of fluoroscopy in 1981, followed by the use of CT, ultrasound (US), and MRI guidance, image guidance has been used to perform CN of many peripheral nerves for a variety of indications [22–25]. All published reports of image-guided CN are arranged by level of evidence in Tables 1–3.

Technique

CN is performed by placing cryoablation probes under image guidance in the region of the targeted nerve(s), such that the defined ablation zone will include the nerve. Two alternating freeze-thaw cycles are then undertaken, ranging from 6 to 10 minutes and from 3 to 5 minutes, respectively. Multiple probes may be used simultaneously to target multiple nerves; however, the use of multiple probes to target one nerve typically is not necessary. If the targeted nerve is adjacent to skin, gauze soaked in warm saline may be used to protect the skin from cold injury. A diagnostic injection of long-acting local anesthetic, with or without accompanying steroid, before cryoablation (performed on a separate day) may provide critical diagnostic information and define the approach for ablation [26] (Fig. 1). CN is generally performed on an outpatient basis, with the use of conscious sedation and local anesthetic.

There are several types of devices suitable for CN. Large tethered systems work with a wide variety of probes of varying lengths and widths and cryoablation zone shapes and sizes. These systems use compressed gas, typically argon, to provide cryoablation. Smaller battery-powered handheld CN devices utilizing compressed liquid nitrous oxide to provide cryoablation have also become available more recently [27].

Applications of Image-Guided Cryoneurolysis: A Head-to-Toe Approach

Head and Neck

CN has been used to manage a variety of neuropathic conditions involving the face, head, and neck under direct visualization in surgery. As the technique evolved, conditions such as trigeminal neuralgia, supratrochlear neuralgia, and infraorbital neuralgia were safely and successfully treated using landmark guidance, 12- to 14-gauge introducers, and 2- to 4-mm cryoprobes [19, 28–31]. With the addition of image guidance, deeper structures can be safely accessed nonsurgically. For example, Dar et al. [32] reported the successful use of CT guidance to target masses involving the trigeminal nerve in patients with intractable pain secondary to recurrent head and neck carcinoma.

Occipital neuralgia, a well-described painful condition resulting from injury or inflammation of the occipital nerves, has historically been treated using surgical rhizotomy, superficial anesthetic, botulinum injection performed using landmark guidance, implantable neurostimulators, or a combination of these treatments [33]. Several groups have recently described safe approaches using image guidance to target precise segments of the greater occipital nerve for injection of medications for therapeutic, diagnostic, or both purposes in the setting of occipital neuralgia, allowing the safe evolution of percutaneous therapies, including radiofrequency ablation, pulsed neuromodulation, cryoablation, or a combination of these therapies [34–36] (Fig. 2).

Intercostal Nerves

Chronic postthoracotomy syndrome is a pain complex affecting up to 80% of patients who undergo the surgery [37, 38]. The management of postthoracotomy syndrome with CN was well described in the late 1970s and early 1980s, but it was largely abandoned because of unfavorable risk-benefit ratios in the setting of landmark guidance. Despite this, recent reports have described continued efficacy [39]. A variety of techniques have been used to mitigate the pain associated with this syndrome, including pharmacologic regimens, spinal cord stimulation, variable perioperative anesthesia techniques, and acupuncture. Beginning in the late 1990s, intercostal CN was resurrected using image guidance [24, 40–42]. The use of CT, ultrasound guidance, or both decreases the complication rate and favorably shifts the risk-benefit ratio by allowing the operator direct visualization of the ice ball, real-time monitoring of the lung position, and monitoring of potential damage to nontarget structures [41] (Fig. 3).

Celiac Plexus

Neurolysis of the celiac plexus using ethanol as the ablative agent is an effective means for palliation in the setting of painful pancreatic adenocarcinoma. Potential adverse sequelae related to ethanol injection include nontarget distribution of fluid, intractable diarrhea, bleeding, cardioneurological dysfunction, or a combination of these sequelae [15, 43]. In addition, the technique is limited by bulky tumors that impede the dissemination of injected fluid and often necessitate repeat interventions. During recent years, the application of image guidance to endoscopic techniques has proven efficacious for targeting the celiac plexus for alcohol injection [44, 45].

TABLE 2: Retrospective Studies and Case Series of Image-Guided Percutaneous Cryoneurolysis Involving 10 or More Patients

Authors [Reference]	Year of Publication	No. of Patients	Nerve Treated	Symptoms or Condition Treated	Imaging Guidance	Primary Outcome	Complications[a]	Re-treatment[b]
Jones and Murrin [88]	1987	70	Intercostal nerve	Postherpetic neuralgia ($n = 17$), thoracic surgical scar pain ($n = 34$), or other source of intercostal pain ($n = 19$)	Fluoroscopy	Of patients with scar pain, 70% reported some, considerable, or complete pain relief for a median duration of 4–8 weeks; treatment provided little or no relief for patients with postherpetic neuralgia	5 Patients had minor complications	No patient received multiple treatments
Moore et al. [40]	2010	18	Intercostal nerve	Postthoracotomy pain syndrome	CT	Mean pain score decreased from 7.5 before treatment to 1.2 immediately after treatment and 4.1 at a mean follow-up of 51 days	No complications reported	One patient received 2 treatments
Wolter et al. [89]	2011	91	Lumbar medial branch nerves	Lumbar facet joint syndrome	CT	Mean pain score decreased from 7.7 before treatment to 3.7 immediately after treatment and 4.22 at 3-month follow-up; the pain disability index revealed statistically significant improvements[c]	No complications reported	14 Patients received 2 treatments, and 4 received 3 treatments
Friedman et al. [90]	2012	24	Various lower extremity nerves	Stump neuroma ($n = 12$), painful Morton neuroma ($n = 5$), or other ($n = 7$)	Ultrasound	13 Patients had marked or total relief, 4 had moderate or mild relief, and 7 had no relief	No complications reported	7 Patients received 2 treatments
Bellini and Barbieri [91]	2015	18	Various nerves	Lumbar facet joint syndrome ($n = 4$), postarthroplasty knee pain ($n = 4$), or other ($n = 10$)	Fluoroscopy	Mean pain score on VAS decreased from 8 before treatment to 5 at 1-month follow-up and 4 at 4-month follow-up	Complications were not discussed	No patient received multiple treatments
Cazzato et al. [25]	2016	20	Plantar digital nerves	Painful Morton neuroma	MRI	On a per-lesion basis: 14 (78%) were completely satisfied with the results of treatment, 3 were satisfied with minor reservations, 1 was satisfied with major reservations, and 6 were lost to follow-up	One patient had cellulitis around the treatment site	No patient received multiple treatments

Note—VAS = visual analog scale.
[a]Minor complications included lightheadedness, minor swelling at the site of procedure, and mild cough.
[b]In some studies, re-treatment was reserved for patients for whom the first treatment failed, whereas for others it was used to provide further relief for those who had positive results.
[c]The items for which improvement occurred were familial and domestic duties, recreation, social activities, activities related to profession, and vitally indispensable activities.

TABLE 3: Case Series Involving Nine or Fewer Patients and Single Case Reports of Image-Guided Percutaneous Cryoneurolysis

Authors [Reference]	Year of Publication	No. of Patients	Nerve Treated	Symptoms or Condition Treated	Imaging Guidance	Primary Outcome	Complications	Re-treatment
Kim and Ferrante [77]	1998	2	Obturator nerve	Hip adductor spasticity and obturator neuralgia	Fluoroscopy	5 Months of relief of spasticity; 6 months of pain relief	No complications reported	None
Loev et al. [92]	1998	1	Ganglion impar	Chronic anal and perineal pain	Fluoroscopy	Pain relief for 6–12 weeks after each procedure	No complications reported	The patient received 2 treatments
Byas-Smith and Gulati [24]	2006	4	Intercostal nerve	Postthoracotomy pain syndrome	Ultrasound	All patients had pain relief for at least 1 month	No complications reported	None
Campos et al. [58]	2009	1	Genitofemoral nerve	Chronic inguinal pain	Ultrasound	Pain score on VAS decreased from 4 before the procedure to 2 at 3-month follow-up	No complications reported	None
Rhame et al. [87]	2011	1	Sural nerve	Painful neuroma	Ultrasound	Excellent relief for 3 months after each treatment	No complications reported	The patient received serial treatments for 3 years
Connelly et al. [42]	2013	3	Intercostal nerve	Intercostal neuralgia	Ultrasound	Each treatment resulted in reduced pain for 1–9 months	No complications reported	One patient received 2 treatments, and 1 patient received 3 treatments
Dar et al. [32]	2013	3	Trigeminal nerve	Secondary trigeminal neuralgia	CT	4 Months of pain relief ($n = 1$), 1 month of pain relief ($n = 1$), and 2 weeks of pain relief and then lost to follow-up ($n = 1$)	No complications reported	None
Koethe et al. [41]	2014	1	Intercostal nerve	Postthoracotomy pain syndrome	Cone-beam CT	Pain relief for 8 weeks	No complications reported	None
Martell et al. [93]	2016	1	Obturator nerve	Painful peripheral nerve sheath tumor	CT	No pain through 6-month follow-up	No complications reported	None
Mavrovi et al. [85]	2016	2	Iliohypogastric nerve	Painful peripheral schwannoma	Ultrasound ($n = 1$), CT ($n = 1$)	No pain and no residual lesion on 6-month follow-up MRI	Both patients had pain in the treated area, which eventually resolved	None
Ramsook and Spinner [94]	2016	1	Lower extremity nerve (unspecified)	Painful neuroma after traumatic hip disarticulation	Ultrasound	No pain through 6-month follow-up	No complications reported	None
Joshi et al. [78]	2017	1	Posterior femoral cutaneous nerve	Neuralgia	MRI	Symptom-free at 5-month follow-up	Skin paresthesia that gradually improved within weeks	None
Gabriel et al. [95]	2017	3	Intercostal, posterior tibial, and superficial peroneal nerves	Acute pain after surgery or injury	Ultrasound	Pain relief for 14–21 days	No complications reported	None

Note—VAS = visual analog scale.

The addition of CT guidance allows precise targeting of the plexus, real-time monitoring of needle placement, and the addition of neuromodulatory techniques, ablative techniques, or both (Fig. 4). Mortell et al. [46] reported the successful use of CT-guided CN of the celiac plexus in nine patients with pancreatic adenocarcinoma, with only one minor complication occurring. CT-guided CN may be the preferential treatment in this setting because of the inherent control afforded by this modality versus injection of a liquid neurolytic agent. Of note, the costs associated with CT guidance, the equipment necessary for cryoablation, and anesthesia are greater than those associated with fluoroscopically guided alcohol injections. In addition, the larger size of the cryoablation probes compared with spinal injection needles may impact the severity of the potential complication profile (i.e., a bleed or nontarget puncture associated with the cryoablation procedure is likely to be more severe, given the larger size of the probes). Future studies addressing efficacy in relation to these potential pitfalls are necessary.

Lumbar Spine

Osteoarthritis of the lumbar facet joints causes localized pain that may radiate to the proximal lower extremity. CN of the lumbar medial branch nerves using CT or fluoroscopic guidance for the treatment of painful osteoarthritic lumbar facet disease is the most-studied application of image-guided CN (Tables 1 and 2 and Fig. 5). A prospective study of CN of the medial branch nerve for the treatment of painful lumbar facet disease used inclusion criteria of symptoms refractory to conventional therapy (i.e., physical therapy, back braces, nonsteroidal antiinflammatory drugs, analgesics, or a combination of these therapies) for at least 3 months and response to medial branch nerve blockade performed using needle delivery of local anesthetic [47]. The 46 patients treated reported significant improvement of pain using visual analog scale scoring, with scores decreasing from a mean of 7.7 before the procedure to 3.2, 3.3, 3.0, and 4.2 at 6 weeks, 3 months, 6 months, and 1 year, respectively. Additional prospective studies have further shown the efficacy of this therapy [23, 48].

Inguinodynia

The frequency of genitofemoral, ilioinguinal, iliohypogastric, or combined neuralgias approaches 2 million persons per year and includes patients undergoing herniorrhaphy as well as patients with sporadic noniatrogenic cases [49–52]. Patients present with pain in the groin, medial thigh, testes or vagina, or a combination of these locations. Multiple techniques have been used to treat these neuralgias surgically, including mesh removal and triple neurectomy, with mixed results. Periprocedural techniques involving anesthesia (e.g., spinal anesthesia and local bupivacaine injections), neurostimulation, and narcotics have also been studied as treatment in this setting, with largely disappointing outcomes [53–55].

Image guidance techniques have allowed precise targeting of deep and superficial nerves in the pelvis for the purpose of perineural injection of medications, use of neuromodulatory and neuroablative techniques, or a combination of these purposes [56–58]. CT guidance allows safe access to a relatively deep confluence of the genitofemoral and ilioinguinal nerves that is not easily accessible by landmarks or surgery (Fig. 6).

Pudendal Neuralgia

Pudendal neuralgia is a disabling syndrome that may significantly decrease the quality of patients' lives. It is often related to compression, trauma (including gynecologic surgery or traumatic obstetric events), or neuropathy involving the pudendal nerve. Symptoms correspond with the pudendal nerve sensory distribution, are worsened by sitting, do not wake the patient from sleep, and respond to diagnostic blocks [59, 60]. Advanced imaging and nerve stimulator guidance have been used in attempts to improve the outcomes of patients undergoing therapeutic injections [32, 61–67], and neuromodulation techniques have been used with promising initial results [68–70].

CT guidance allows precise positioning of a cryoprobe in the Alcock canal and real-time monitoring of the cryoablation zone (Fig. 1). In 2013, a total of 11 patients were enrolled in a study evaluating percutaneous CT-guided CN of the pudendal nerve for treatment of refractory pudendal neuralgia [26]. All patients were administered the Brief Pain Inventory (BPI) before the procedure and at 24 hours, 45 days, and 120 days after the procedure. The mean BPI score decreased from 7.6 before the procedure to 2.6, 3.5, and 3.1 at 24 hours, 45 days, and 120 days after CN, respectively.

Premature Ejaculation

The cause of premature ejaculation is multifaceted, with contributing factors identified from the cortex (e.g., anxiety, early sexual experience, infrequent sexual experiences, poor ejaculatory control techniques, or evolutionary factors [e.g., faster ejaculation leads to greater reproduction]) to the peripheral nerve (e.g., penile hypersensitivity, hyperarousability, hyperactive ejaculation reflex, endocrinopathy, or genetic predisposition) [71, 72].

In 2012, a total of 24 subjects with refractory premature ejaculation were prospectively enrolled to a trial of percutaneous CT-guided CN of the dorsal penile nerve [73] (Fig. 7). After CN, the subjects had significant improvements in intravaginal latency time and premature ejaculation profile scores up to 360 days after the procedure.

Other Peripheral Nerves

Common causes of peripheral neuropathy include diabetes, radiculopathy, and postherpetic neuralgia. Ultrasound-guided CN has been used to treat a variety of peripheral neuralgias [74, 75]. In 2016, Yoon et al. [76] published a prospective trial of this modality that included 22 patients with neuropathic pain of the lower extremity. The patients had significant pain relief up to 1 year after treatment, with no associated complications. Kim et al. [77] reported the use of fluoroscopy-guided CN of the obturator nerve to relieve hip adductor spasticity in a patient with multiple sclerosis. The application of CT guidance allows CN of deeper nerves for palliative purposes (Fig. 8). Joshi et al. [78] recently described the technique of percutaneous MRI-guided CN for the treatment of sitting pain mediated by the posterior femoral cutaneous nerve.

Postamputation Limb Pain

Much like premature ejaculation, phantom limb pain has a pathophysiologic profile that is complex and variable between individuals [79–82]. CN without image guidance has been safely used in two small series to treat phantom limb pain and residual limb pain associated with stump neuromas. Moesker et al. [7] reported five cases of nerve stump CN, guided by nerve stimulation, with follow-up to at least 2.5 years. Three of the five patients reported 90–100% resolution of their symptoms, one reported 40% improvement, and the remaining patient reported 20% improvement. Neumann et al. [83] reported their experience performing CN guided by nerve stimulation for 10 patients with refractory stump pain. At 3 months after treatment, nine patients reported pain relief, and at 12 months three reported continued relief.

More recently, a prospective single-arm pilot study of 21 subjects undergoing CT-guided percutaneous CN for the treatment of refractory phantom limb pain was conducted [84] (Fig. 9). Disability scores decreased from a mean of 11.3 before treatment to 3.3 at 45-day follow-up. Pain scores decreased from a mean of 6.2 before treatment to 2.0 at long-term follow-up (mean, 194 days after the procedure).

Neuromas and Nerve Sheath Tumors

Neuromas and nerve sheath tumors can be a significant source of localized pain. A 2016 study by Cazzato et al. [25] showed the efficacy of MR-guided cryoablation for the relief of pain secondary to Morton neuroma. Multiple case reports have described the use of ultrasound or CT guidance for the cryoablation of neuromas and nerve sheath tumors (Table 3).

Complications

Percutaneous image-guided CN generally is safe. The available evidence, which is summarized in Tables 1–3, consists of approximately 702 discrete treatments. The exact number of treatments is unknown because some patients received a series of treatments with an unreported exact number of treatments. In the earliest trial of image-guided CN, one patient experienced a prolonged CSF leak after CN of the inferior sacral nerve roots [22]. This was thought to be caused by an extensive bladder carcinoma that had eroded more than half of the sacrum. In another trial, a patient had vagus-induced syncope, which was easily controlled by the administration of atropine [47]. Another patient had pain in the treated area that was managed by a single steroid injection and later resolved [85]. No other complications that might be considered major per Society of Interventional Radiology guidelines were reported [86]. Pain, swelling, superficial infection, or minor bleeding at the treatment site were most common among the 24 reported minor complications. In summary, approximately 702 procedures resulted in three major and 24 minor complications, with no permanent sequelae reported.

Efficacy

Every published report of image-guided CN describes some degree of efficacy, ranging from partial to complete symptomatic relief. The potential for nerve regeneration after CN creates variability in the duration of symptomatic relief. Most studies show maximal pain relief during the first month after treatment, with a gradual return of nerve function occurring over the following months (Tables 1–3). However, all prospective studies that followed patients for 1 year after treatment report continued noting significant reductions in symptoms at that time point. Given the excellent safety profile, CN with repeat treatments as necessary is a viable long-term pain management strategy: One report describes serial CN treatments for a painful sural neuroma over 3 years, with excellent relief occurring for 3 months after each treatment and with no complications noted [87].

The available data regarding the efficacy of image-guided CN are limited by variable outcome measures and time frames and a lack of randomized controlled trials. Large-scale randomized controlled trials comparing CN to either noninvasive treatment or another intervention are warranted on the basis of existing evidence, to further define the role of this treatment and evaluate efficacy in terms of clinically important differences. As with most complex clinical problems in interventional radiology, patient selection, review, and follow-up should be addressed by a multidisciplinary team.

Reimbursement

Reimbursement is an important driver of expanded patient access to health care services, and realistic plans for translation of any new technology must account for payer coverage. A brief discussion of coding options for image-guided CN is located in Appendix 2.

Conclusion

Percutaneous image-guided CN provides a new avenue for the relief of many historically difficult-to-manage pain syndromes. Additional rigorously designed prospective studies are warranted.

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APPENDIX 1: Materials and Methods

A literature search of Ovid MEDLINE was performed in July 2017 to identify relevant articles published in the English language at any point in time. The following search terms were used: "cryoneurolysis," "cryoanalgesia," "cryodenervation," "nerve," "neuroma," "plexus," "neuralgia," "pain," "cryoablation," "cryotherapy," "freeze," "freezing," "cryogenic lesion," "cryoprobe," "cryoanalgesic ablation," "kryorhizotomy," and "cryosurgery." The Boolean operators AND, OR, or both were used to combine terms. The reference lists of relevant articles were screened for additional relevant articles. The archives of the following journals were also individually searched using the aforementioned terms: the *Journal of Vascular and Interventional Radiology*, *Cardiovascular and Interventional Radiology*, *Skeletal Radiology*, and the *American Journal of Roentgenology*. Case reports presented in the form of meeting abstracts or posters and otherwise unpublished may not be included.

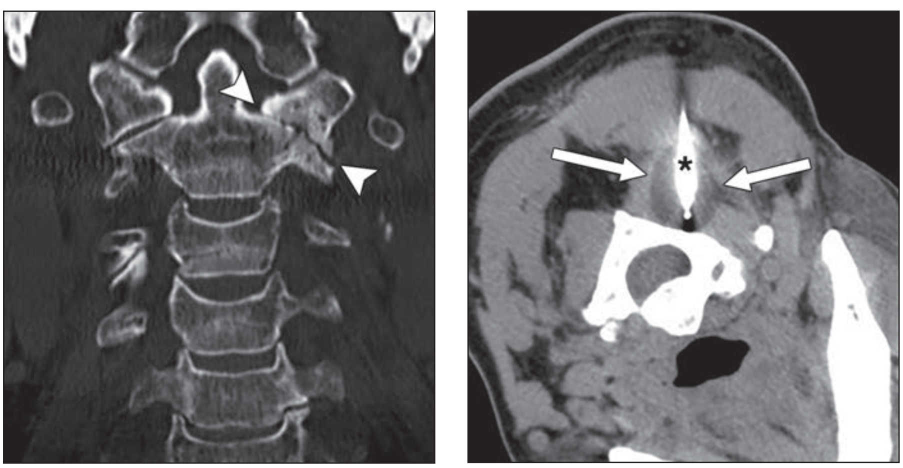
APPENDIX 2: Coding for Image-Guided Cryoneurolysis

The options for coding for image-guided cryoneurolysis begin with guidance codes for CT (77012), ultrasound (76942), or both. Existing neurolysis codes are then applicable, depending on the target nerve. For example, code 64630 corresponds to neurolysis of the pudendal nerve, whereas code 64640 corresponds to neurolysis of "other peripheral nerves or branches." In addition, in October 2015, three new category III Current Procedural Terminology codes were approved specifically for the cryoablation of nerves: 0440T (for ablation, percutaneous, cryoablation [includes imaging guidance and upper extremity and distal peripheral nerve]), 0441T (for ablation, percutaneous, and cryoablation, [includes imaging guidance and lower extremity and distal peripheral nerve]), and 0442T (for ablation, percutaneous, and cryoablation [includes imaging guidance and nerve plexus or other truncal nerve]).

(Figures start on next page)

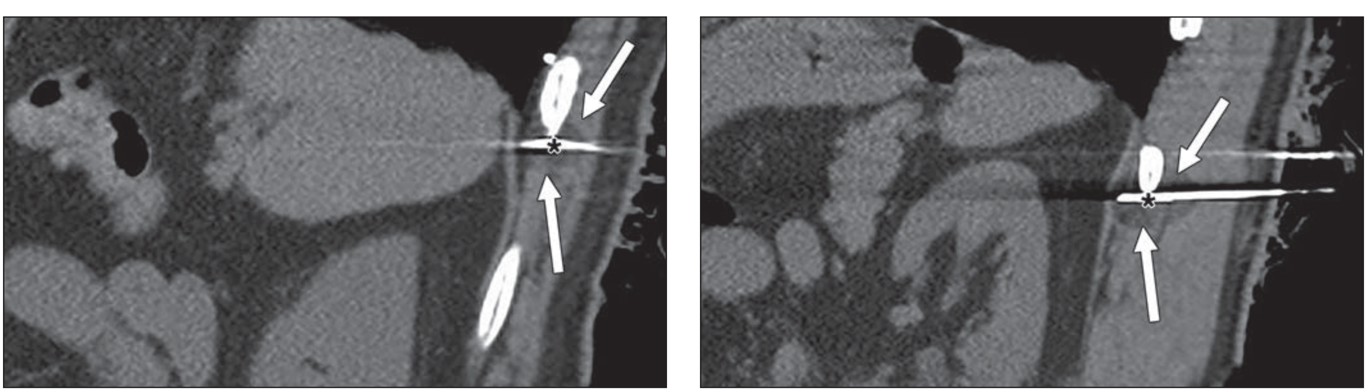
A B C

Fig. 1—36-year-old woman with pudendal neuralgia.
A, Axial CT image at level of Alcock canal. Pudendal vessels and nerve lie within potential space between obturator internus fascia and corresponding muscle (*oval*).
B, Axial CT image obtained after diagnostic injection of bupivacaine and betamethasone shows fluid (*arrow*) and gas (*arrowhead*) within canal.
C, Intraprocedural axial CT image shows cryoprobe and low-attenuation oval-shaped ablation zone (*arrows*).



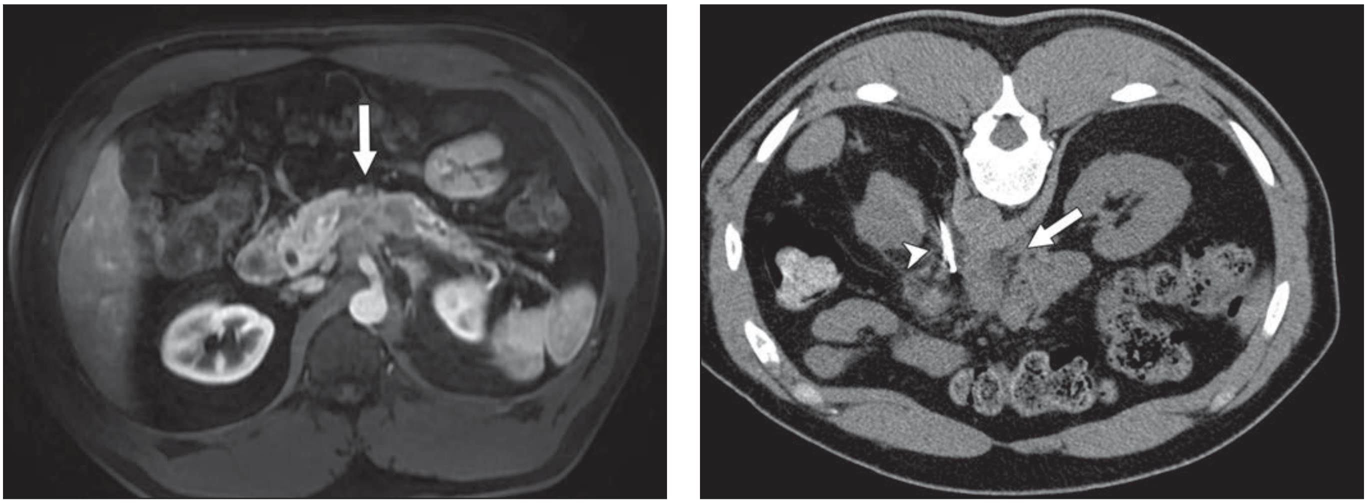
A B

Fig. 2—56-year-old man with occipital neuralgia.
A, Coronal CT image with bone window shows unilateral hypertrophic facet arthropathy at C1–C2 (*arrowheads*).
B, Intraprocedural axial CT image shows cryoprobe (*asterisk*) positioned to include ipsilateral greater occipital nerve in ablation zone (*arrows*).



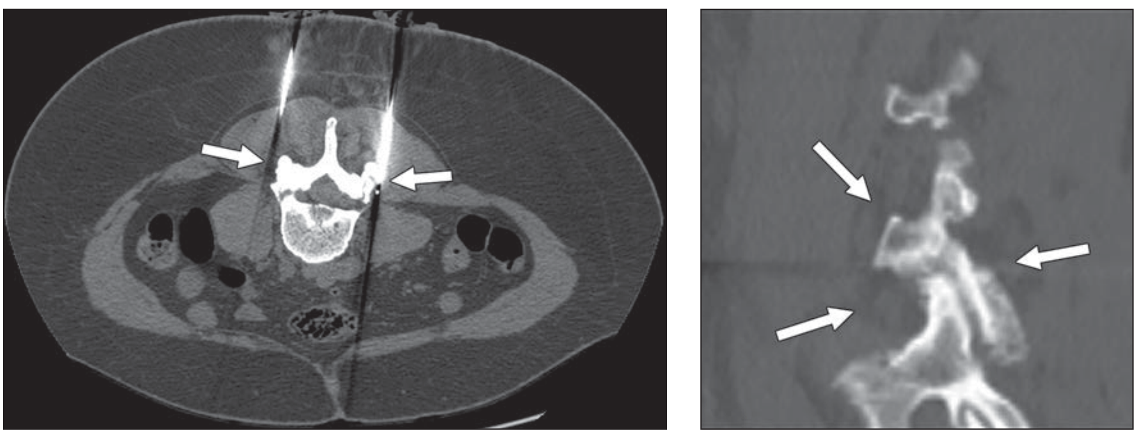
A B

Fig. 3—68-year-old man with primary lung cancer and postthoracotomy pain.
A and **B,** Sagittal CT images show hypoattenuating zones (*arrows*) adjacent to cryoprobes (*asterisk*) placed near intercostal nerves corresponding to patient's pain.



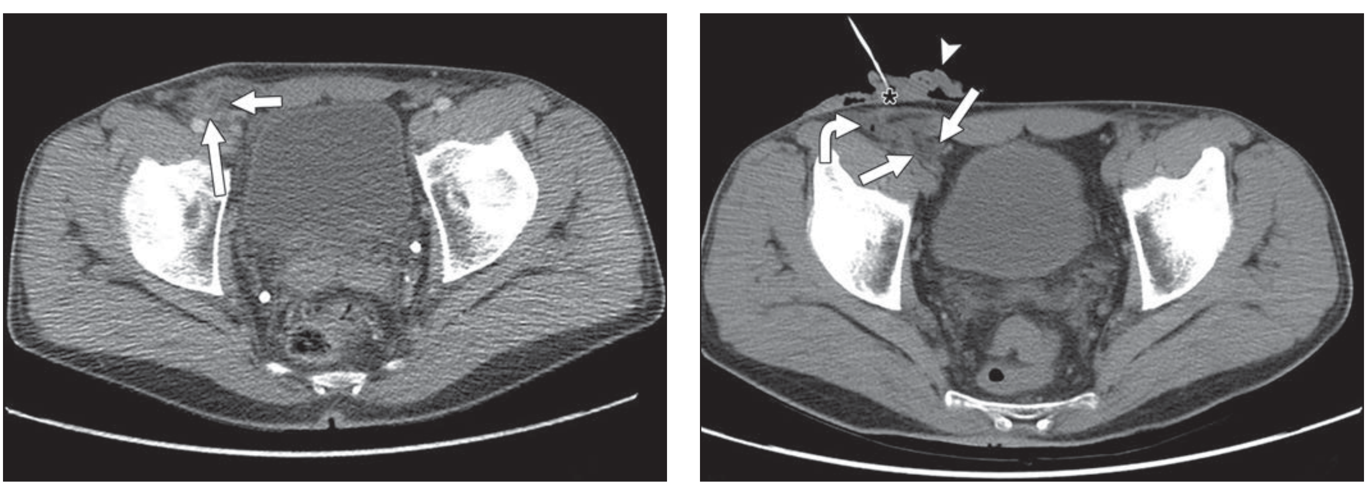
A B

Fig. 4—51-year-old man with pancreatic adenocarcinoma.
A, Axial T1 fat-suppressed contrast-enhanced MR image shows infiltrative mass (*arrow*) in body of pancreas.
B, Intraprocedural axial CT image shows ice (*arrow*) and cryoprobe with surrounding ice (*arrowhead*) targeting celiac plexus.



A B

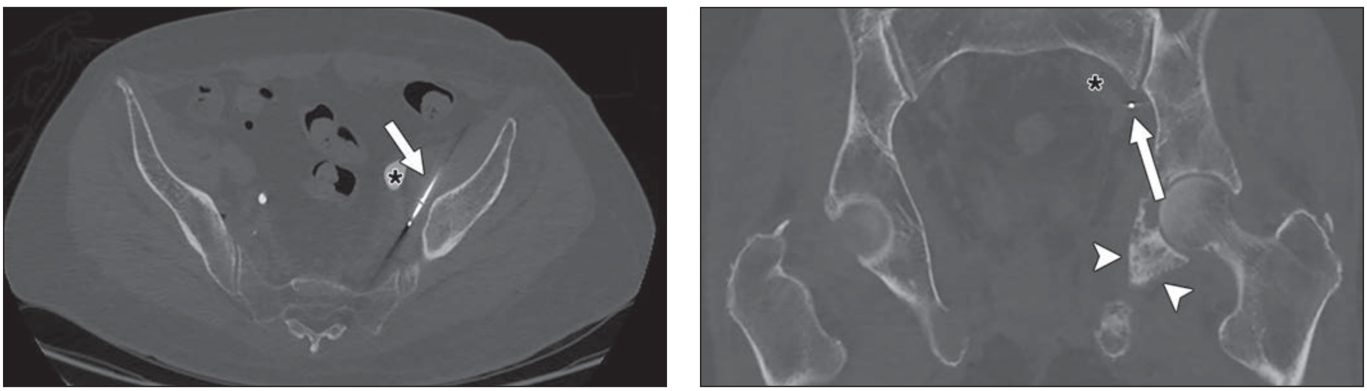
Fig. 5—49-year-old woman with axial back pain.
A, Axial CT image shows two cryoprobes positioned to target medial branch nerves innervating hypertrophic facets (*arrows*) at L3–L4 level.
B, Sagittal CT image shows ablation zone (*arrows*) including defined course of medial branch nerve as it supplies hypertrophic facet in lumbar spine.



A B

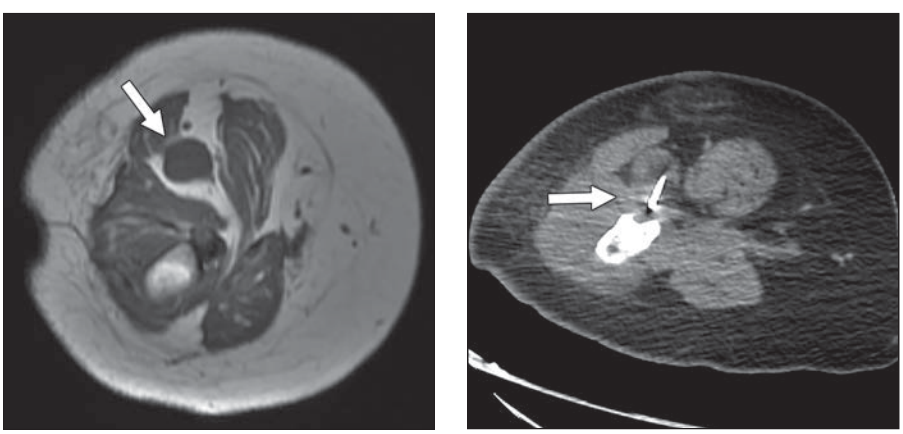
Fig. 6—44-year-old man with inguinodynia after mesh hernia repair.
A, Axial CT image shows inflammatory stranding deep to mesh where genitofemoral and ilioinguinal nerves are entrapped (*arrows*).
B, Corresponding intraprocedural axial CT image shows cryoprobe entry site (*asterisk*), hypoattenuating ablation zone (*straight arrows*), and warm saline-soaked gauze placed at puncture site to protect skin (*arrowhead*). In addition, warmed normal saline was infused with 5-French catheter to dissect away and protect adjacent femoral nerve (*curved arrow*).

Fig. 7—27-year-old man with premature ejaculation. Axial CT image shows cryoprobe (*asterisk*) positioned so ablation zone (*arrows*) includes right dorsal penile nerve as it courses through its defined sulcus along inferior pubic ramus.



A B

Fig. 8—65-year-old man with refractory pain related to sclerotic prostate metastases.
A and **B,** Axial (**A**) and coronal (**B**) CT images show cryoprobe (*arrows*), placed from anterior approach, in position to ablate obturator nerve. Metastases involving ipsilateral acetabulum are apparent (*arrowheads*, **B**). Incidental note is made of adjacent obstructed ureter (*asterisks*).



A B

Fig. 9—31-year-old man with phantom limb pain.
A, Axial T1 prone MR image shows large neuroma (*arrow*) involving distal right sciatic nerve.
B, Corresponding intraprocedural axial CT image shows cryoprobe (*arrow*) in position to ablate neuroma.