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Introduction

Cryotherapy is an old therapy but a relatively new technique used to help manage pain in patients with neuralgic pain conditions. Ice and/or Cold forms of analgesia have long been used, and written records go back to the time of Hippocrates for their use. Current models of cryoablation to induce cryoneurolysis rely upon a cryoprobe that produces an ice ball to destroy axons leading to Wallerian degeneration. This nerve damage has led to pain relief across many different diseases. Outcomes have been reported as curative or provided relief from pain for up to months at a time.

Anatomy of the peripheral nerve consists of bundles of axons termed fascicles that are surrounded by different connective tissue layers. The outer layer is called the *epineurium* which surrounds the nerve and helps hold nerve fascicles together. Nerve fascicles are surrounded by the *perineurium* which holds the individual axons within them. Within the fascicles there is a layer which covers individual axons called the *endoneurium*. Blood supply to the nerve comes from the vasa vasorum and is located within the endoneurium and perineurium forming the blood-nerve barrier. Peripheral nerves can be classified as sensory, motor, or mixed.

Given the broad range of injuries that can occur to peripheral nerves in 1943, Sir Herbert Seddon came up with a classification scheme for nerve damage. The scale is eponymously named the Seddon scale which is composed of three types of nerve injury:

- Type 1: Neuropraxia is the most mild of nerve damage that results from nerve compression usually after blunt trauma. The axons remain intact but there is a loss of nerve conduction and some demyelination. Patients usually recover within hours to days, but in some cases, it can take weeks. EMG studies are usually negative.
- Type 2: Axonotmesis occurs when there is complete disruption of the axon and myelin sheath with preservation of the perineurium, epineurium, and endoneurium. Recovery is possible through Wallerian degeneration. EMG studies will show decreased conduction and muscle fasciculations.
- Type 3: Neurotmesis is the most severe and occurs when there is complete transection of the nerve. There is disruption of all three nerve sheath layers. Recovery is unlikely without the help of surgery. EMG studies will show no conduction through the nerve.

Cryoablation results in a nerve injury that falls into the classification as axonotmesis. The ice ball disruption of the nerve results in axon destruction followed by Wallerian degeneration that will occur within 3 weeks post insult. Wallerian degeneration consists of deterioration of the distal axon to the insult and proximal deterioration to the last node of Ranvier. Schwann cells and macrophages remove cellular debris and allow for the proximal axon to form a growth cone and regrow through the intact nerve sheath. Growth rates will vary but usually is considered to be at a rate of between 1 and 3 mm per day. Due to the type of nerve injury, cryoablation may not provide permanent relief in patients, but this can be overcome with changes and optimization of the temperatures that are used.

The exact mechanism for how cryoablation causes nerve insult is not exactly known. Cryoablation has been used to treat several cancers where tissues closest to the probe tip swell and disrupt the cell membranes. The extracellular space then forms a hyperosmotic state which causes peripheral cells to shift their fluid out of the cell. This process is followed by fluid shifts backward into the cells when the cooling process begins leading to disruption of their mem-

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branes. For nerves it is thought that there is damage to the vasa vasorum leading to ischemic necrosis. Temperature range can help to determine what type of lesion and response will occur. At -20°C there is little to no insult made to the nerve, while at temperatures below -140°C , there can be permanent nerve destruction and scar formation. The optimal temperature for nerve ablation ranges between -60°C and -100°C . The cold temperatures also reduce the inflammatory response and destruction of the nerve. Unlike radiofrequency ablation where heat is used to induce nerve lesions, there is a lower risk of neuroma formation.

Background and Historical Perspective

The use of ice or cold for analgesia goes back to the time of Hippocrates and follows a basic principle that when cold is applied to a painful region analgesia is produced. The idea of pain relief with cryotherapy dates back to the twentieth century with the beginning of modern use of cryoprobes coming around in the 1960s. Dr. Irving Cooper a neurosurgeon used a cryoprobe to treat Parkinson's disease by targeted ablation in the thalamus. Further development of cryoprobes came from a South African ophthalmologist Dr. Selig Amoils who invented the first handheld cryoprobe. Cryoprobes now most commonly use nitrous oxide, liquid nitrogen, or argon to form an ice ball in targeted nerves leading to their destruction. One of the first major studies looked at postsurgical thoracotomy pain and the use of cryotherapy. The cryoablation of the nerves showed superior analgesic effect compared to nerve blocks using bupivacaine.

Procedure

Cryoprobes rely on gasses such as nitrous oxide with a micro-pore needle-based delivery system. When delivered the gas is rapidly ejected forming a high pressure system through the needle's micropore where it can expand and form an ice ball. The probe then warms up melting the ice ball and can be safely removed from the patient. Depending upon the probe, they can have a built-in nerve stimulator to identify the nerve and allow for focusing on the targeted nerve. Most probes are covered in Teflon proximally to the tip in order to help with localizing and focusing the temperature to the ice ball at the tip.

Temperature Optimization

Research on rabbit sciatic nerve helped to elucidate the correct temperature that will allow for axonotmesis to occur. The researchers looked at several temperatures, -20°C , -60°C , -100°C , -140°C , and -180°C , which were used

with the cryoprobe. At -20°C there was no change in nerve function. As temperatures were lowered to -60°C , nerve conduction was lost with eventual recovery. At -100°C the nerve lost conduction and underwent Wallerian degeneration with eventual recovery. Further, at -140°C and -180°C , there was necrosis of the nerve and formation of scar tissue forming a more permanent nerve destruction. This study helped to give a recommended range for cryoneurolysis of between -60°C and -100°C to allow for recovery over time while still providing nerve disruption and analgesia.

Benefits and Future Use

Since the early uses of cryotherapy, the positive benefits have continued to show promise with other disease and analgesic uses. Cancers have been treated with insertion of a cryoprobe and frozen from the inside. Targeting of other nerves continues to be expanded upon including the occipital, trigeminal, and pudendal nerves. Being able to localize the nerves and understanding their anatomical landmarks have further enhanced the use of cryotherapy.

When paired with ultrasound, a small cryoprobe can be placed precisely to allow for accurate cryoneurolysis and prevent damage to surrounding tissues. Ultrasound guidance makes procedures easy to be done in the clinic setting without any needed radiographic imaging. Utilizing ultrasound has immense benefits for targeting and providing optimal production results. Ultrasound guidance is covered more in the occipital neuralgia section of this chapter. Analgesia for chronic pain will continue to evolve, and cryoablation has a great potential to be a new and leading treatment modality. Cryoablation has been shown here to be effective at reducing pain related to a myriad of diseases. Cryotherapy leaves patients pain free or without pain for months at a time all with minimal side effects from the procedure.

Uses and Indications

With the current opioid epidemic, it is more crucial than ever to utilize alternative pain management methods like cryoanalgesia. Since Dr. Cooper created the first modern cryoanalgesia probe in 1961, cryoanalgesia has further grown to treat a broad range of different medical conditions that often are debilitating for patients. Alternatives to cryoanalgesia include surgical resection, alcohol and phenol neurolysis, anticonvulsants, and radiofrequency ablation. Before treatment with cryoablation, it is often necessary to have a diagnostic nerve block with a reported 50% reduction in pain in the patient. This pre-procedure test will help to identify if the nerve is truly the etiological cause of the pain and avoid unnecessary procedures.

Table 34.1 Uses and efficacy of cryotherapy in select neuralgia and neurologic disease

Neuropathic condition	Paper	Efficacy as reported by patient
Intercostal neuralgia	Green et al. (2002) Lu et al. (2013)	Chronic pain secondary to thoracic surgery was shown to have a 50% reduction in patient's pain Nondivided intercostal muscle flap and intercostal nerve cryoanalgesia were compared for post-esophagectomy/post-thoracotomy pain, and it was found that up to 6 months, similar pain relief from both modalities was reported by patients
Occipital neuralgia	Kim et al. (2015)	Patients with greater than 75% pain relief from local anesthetic before cryoanalgesia showed increased duration (8.1 months) and greater pain relief than individuals with 50–74% response to local (4.1 months)
Trigeminal neuralgia	Dar et al. (2013) Pradel et al. (2002)	Instant pain relief for palliative pain management of secondary trigeminal neuralgia due to cancer that lasted from 2 weeks to 4 months in the three-patient study Significant pain relief for at least 6 months post cryoablation
Temporomandibular joint pain	Sidebottom et al. (2011)	17 patients with significant TMJ pain that failed medical and arthroscopic management found an average of 7-month pain relief that decreased VAS scores from 6.8 to 2 posttreatment
Hip adductor spasticity and obturator neuralgia	Kim et al. (1998)	2 case reports of patients with hip adductor spasticity resulting in pain and inability to ambulate finding pain relief and ability to walk post cryoablation
Intractable peroneal pain	Evans et al. (1981)	31 out of 40 patients reported improved pain relief for 30 days; and 11 of those patients had complete relief of symptoms
Phantom limb pain	Moesker et al. (2014)	3 out of 5 patients with phantom limb pain had 90–100% resolution of pain
Genitofemoral neuralgia	Fanelli et al. (2003)	10 patients with postherniorrhaphy neuropathic pain received cryoablation of ilioinguinal (4), genitofemoral (1), or combined (5) therapy. Results found an average 77.5% reduction in pain, 80% decrease in analgesic use, and 90% increase in daily function

With improved technique and more research, cryoanalgesia can provide an excellent alternative to current pain therapies. Currently cryotherapy is used secondary to many noninvasive treatments and an effort that effectively saves a patient from untreated pain and allow them to return to a normal life (Table 34.1).

Intercostal Neuralgia

Intercostal neuralgia relating to surgical incision and rib retraction can be debilitating for patients and lead to complications postoperatively. Research by Karmakar et al. in 2004 described post-thoracotomy pain to be likely a result from a combination of trauma to the intercostal nerves and myofascial pain. The group found that up to 50% of patients will develop post-thoracotomy pain syndrome and a further 30% will continue to experience pain 5 years post-op. Patients will mostly describe post-thoracotomy pain as mild, while others experience debilitation with changes to normal daily function.

In treating intercostal neuralgia, another group, Green et al. in 2002 examined 43 patients aged 26–84 who received cryoneurolysis for their chronic pain secondary to thoracotomy pain and postherpetic neuralgia. The group found that 3 months post cryoneurolysis, 50% of their subjects continued to have pain relief.

Cryoneurolysis had a positive patient analgesic report, but a more recent study from Ju et al. in 2008 compared the effectiveness of cryoanalgesia for postoperative thoracic pain to the current gold standard of thoracic epidural analge-

sia. The group used a randomized controlled study that segregated patients into epidural and cryoanalgesia groups. Results found no difference among the two groups in first 3 days post-op followed by an increased incidence of pruritus in the epidural group. In addition, they found high chronic pain incidences of 50 to 60% in both groups at 1 month, 3 months, 6 months, and 12 months post-op. Of note was that the group did find higher incidences of allodynia-like pain, pain intensity, and debilitation of daily activities in the cryoneurolysis group.

Another study by Lu et al. in 2013 compared cryoanalgesia to nondivided intercostal muscle flaps for treating postoperative thoracotomy pain in patients undergoing esophagectomies. In their randomized controlled study, 80 patients received a flap, and the other 80 received cryoanalgesia. Their findings showed that up to 6 months, both groups had no statistical difference in pain scores or the use of oral pain medication. While the flap group showed improved pain treatment at 6, 9, and 12 months, this could show that cryoanalgesia is an option in early pain management up to 6 months postoperatively.

Treating intercostal neuralgia continues to prove that further investigations are required in identifying factors for patients who show good response to cryotherapy. Although Ju et al. has shown debilitation and increased pain intensity, some patients did benefit from cryoanalgesia, which provides an alternative to individuals who are unable to receive a thoracic epidural. Furthermore, cryoanalgesia has been utilized by another group Kim et al. (2016) for Nuss procedures in the treatment of pectus excavatum. The group used thora-

coscopic transthoracic cryoneurolysis to target five intercostal nerves and resulted in 1 month of adequate analgesia. The authors recommend further utilization of this method for Nuss procedure showing the growth of cryoanalgesia.

Occipital Neuralgia

Occipital neuralgia is characterized by the International Headache Society as a unilateral or bilateral paroxysmal, shooting or stabbing pain in the distribution of the greater, lesser, or third occipital nerves. It is commonly associated with tenderness over the involved nerves with patients also reporting feelings of diminished sensation or dysesthesia. Etiology is most commonly idiopathic; however, structural causes including but not limited to trauma, compression of the nerve or nerve roots, and upper cervical cord lesions have been implicated in some cases. It has been complex to treat and no standard of care has been established. Current treatments range from conservative treatment to medical management with severe cases requiring minimally invasive surgery. Conservative treatment includes avoidance of triggers, rest, hot or cold compresses, and relaxation, while medical management ranges from usage of NSAIDs, antiepileptics, TCAs, triptans, and calcium channel blockers. Patient refractory to conservative and medical management often seeks other methods of relief from minimally invasive, such as Botox injections, occipital nerve blocks, and radiofrequency ablation, to invasive surgeries that includes neurectomies or nerve stimulation implants.

Cryoneurolysis has been shown to achieve reliable and long-lasting pain relief in patients with other neuralgias. A positive diagnostic block is mandatory for success using this technique. It is well known that local anesthetic agents inhibit neural activity by interfering with voltage-gated sodium channels resulting in prevention of depolarization. This mechanism of action hinders pain transmission by nociceptive C fibers. An observational study by Kocer in 2016 reported patients who underwent a greater occipital nerve block with lidocaine and saline mixture had a decreased number of attacks with low severity. While these effects were temporary, there was still a significant difference between baseline and 6th month results with MIDAS scores of 31.87 ± 3.98 and 6.75 ± 2.76 . In a retrospective study of peripheral nerve blocks ($n = 64$) utilizing bupivacaine as a local anesthetic, a 60% efficacy rate specifically for patients with occipital neuralgia ($n = 5$) was reported with an endpoint assessment time ranging from 1 to 48 months.

A retrospective study by Kim et al. in 2015 looked at 38 patients divided into 2 groups based on their response to local anesthetic injection. They found individuals who received cryoablation reported a greater than 75% pain reduction which was a statistically significant relief. In addition, they found an increased duration of relief with cryoab-

lation for up to 8.1 months compared to 4.1 months in the group with 50–74% relief response from injectable nerve blocks. In addition, the group found greater relief in women than men; however, the study distribution included 10 men to 28 women. This study supports the reasoning that cryoablation can be utilized for occipital neuralgia. While standards have not been set, even when a patient received a minimal 50% relief, they still found 4 months of pain relief. In the complexity of treating occipital neuralgia, cryoablation provides another treatment option for patients.

Given the superficial nature and consistency of nerve location in relation to bony landmarks, ultrasound can be used to further localize and better target the nerve to cryotherapy. Ultrasound can identify muscles, ligaments, vessels, joints, and bony surfaces and most importantly can have direct visualization of thin nerves when using high-resolution transducers. Using this technique versus landmarks allows for targeting of the occipital nerve more proximally where it has not yet divided. This allows for a greater efficacy not only in diagnostic blocks but also during the cryoneurolysis procedure, ensuring the precise target has been reached. Utilization of Doppler sonography reduces risk of intravascular injection of local anesthetics or injury of vessels during the procedure. Visualization with ultrasound also allows the provider to observe the size of the occipital nerve before and after treatment to observe any changes in nerve size, edema surrounding the nerve (suggested by hypoechoic densities), or other signs of inflammation.

Trigeminal Neuralgia

Trigeminal neuralgia is characterized as an intense stabbing pain that lasts from seconds to minutes most commonly found in the border of the V2 and V3 distribution. It can be triggered by simple movements of the jaw as in eating and make everyday tasks excruciatingly painful. Etiology varies by patients and has been reported to be by entrapment of the nerve root, tumor invasion, cysts, and arteriovenous malformations. Treatment currently includes the use of antiseizure medications, botulinum toxin injections, and surgical decompression for refractory pain; cryoablation can provide an alternative. A group, Dar et al. in 2012 found the use of CT-guided cryoablation for rapid palliative pain relief for patients suffering from trigeminal neuralgia secondary to cancer. They used a selection criteria described by Callstrom and Charboneau that required (1) moderate to severe pain, (2) localized pain to no more than two sites, and painful metastatic lesions accessible to percutaneous ablative devices. Research results found that the three patients of their study had immediate relief lasting between 1 and 4 months based on patient for their trigeminal neuralgia.

Previous studies from another research group, Pradel et al. in 2002 reported 19 patients undergoing cryoablation

who had failed carbamazepine treatment or experienced significant side effects. They found complete pain relief within 5 days of treatment and pain returned for 13 of the 19 subjects after 6–12 months of being without pain. The cryotherapy results show that when medical management has failed, cryotherapy can provide effective management for up to 6 months. The group's results reported that six patients remained pain-free, while the remainder had either repeated cryoablation or returned to lower doses of carbamazepine. Cryoanalgesia can provide significant improvement in patient's daily life with reduced pain, reduced drug dosages, and an effective alternative therapy.

Temporomandibular Joint Pain

Temporomandibular joint pain occurs from muscles of the temporomandibular joint leading to an aching, burning, throbbing, or stiff pain. Treatment includes rest and nonsteroidal anti-inflammatory medication. Treatment can progress to surgical arthrocentesis or open surgery in severe cases. Surgical treatment is mainly indicated when functional disability is also present with the pain. Sidebottom et al. in 2011 performed a retrospective study to investigate the use of cryoablation on 17 patients whose pain did not improve with medical or surgical arthroscopic management. The patients did not qualify for open surgical treatment, and thus cryoablation was attempted. The patients were included if they found adequate relief from nerve block using local anesthetic. Their findings include improved pain relief with a decreased visual analogue scale of 6.8 before treatment to 2 posttreatment. Pain relief was found to last for 7 months on average, and three patients had complete resolution of pain. When patients have exhausted all other treatment modalities, cryoablation shows promise providing adequate pain relief for at least 7 months.

Hip Adductor Spasticity and Obturator Neuralgia

Injuries to the central nervous system can result in chronic muscle spasticity and include stroke, multiple sclerosis, and trauma. Patients can develop chronic pain as a result of the injury and spasticity of their muscles. Treatment approaches include physical therapy, central-acting oral medications, surgical intrathecal pump implantation, injections, or surgery. In 1998 Kim et al. published a case report series that showed the benefits of cryotherapy. One patient suffering from lower limb muscle spasticity found benefit from implanted baclofen pump; however, their hip adductors continued to debilitate their ability to walk. Cryoneurolysis was performed on the obturator nerve and resulted in decreased spasticity with pain relief that lasted for 5 months.

Another patient in this cases series suffered from metastatic breast carcinoma that lead to blastic lesions along their posterior pelvic brim resulting in right medial thigh pain that left them wheelchair bound due to pain on exertion. The patient's analgesia therapy included fentanyl patches and oxycodone as needed with acetaminophen. Cryoanalgesia targeted to their obturator nerves to relieve their hip adductors and resulted in immediate relief and the ability to ambulate for 6 months with a cane. These cases provide evidence that spasticity can significantly interrupt a patient's daily life and cryoneurolysis can be a useful adjuvant therapy for patients who have refractive hip adductor pain or spasticity.

Genitofemoral Neuralgia

Genitofemoral neuralgia results in paresthesias and neuropathic pain distributed along the lower abdomen and medial aspect of the thigh. The painful distribution can include scrotal pain in males and labia majora pain in females. Campos et al. in 2009 used ultrasound-guided cryoablation of the femoral component of the nerve that provided a 47-year-old male immediate relief from his 3 months of left scrotal pain. His pain went from a 4/10 on the visual analogue scale to an acceptable 2/10 at 3-month follow-up. Furthermore, one study by Fanelli et al. in 2003, looked at ten patients with postherniorrhaphy neuropathic pain who had failed to find relief from noninvasive treatment but were able to find relief from cryoablation. Of these individuals, one underwent genitofemoral ablation, five underwent combined ilioinguinal/genitofemoral ablation, and the remaining four underwent ilioinguinal ablation. They found an average of 77% reduction in pain, 80% decrease in analgesic intake, and 90% increase in physical activity in this study group. Of the ten patients, seven found complete relief from cryoablation.

Intractable Perineal Pain

Sacral nerve roots are common sources of perineal pain that can result from many etiologies such as tumor invasion, trauma, osteoarthritis, bone spurs, or even somatized pain resulting from depression. Treatment progressing from conservative to invasive surgeries can now evolve with the addition of cryoablation. A study by Evans et al. in 1981 looked at 40 patients who were divided into 3 groups based on their source of pain: cancer, coccydynia, or perineal neuralgia. The patients had failed other therapies and underwent cryoablation for pain relief. The patients were followed up for 3 months after treatment, and 23 patients required only a single treatment for pain relief, while the rest required additional cryoablations as a result of inadequate pain relief or a return of pain. Seventy-eight percent of their patients found relief with 11 of those patients describing complete pain relief. The

mean duration of relief was found to be 39 days and 16 days for the group that reported complete relief. In some patients, the range of relief lasted up to 180 days. Six patients did not receive adequate relief and underwent a second treatment where three found better pain control. When other pain management strategies fail, cryoablation is an alternative that could be utilized for sacral nerve-related pain.

Phantom Limb Pain

Phantom limb pain is a burning, sharp, pins and needle-type pain a patient may experience following limb amputation. The complexity of treating the pain is a result of the intricate feedback between the peripheral and central nervous systems. Sensory neurons are reported to be hyperexcitable as a result of inflammatory mediators released from local tissue. While the changes occur, standardized treatment has not been found yet. Cryoneurolysis might provide promise in this debilitating condition. A study by Moesker et al. in 2014 involved five patients with phantom limb pain that had their pain localized to the most distal nerve tract that corresponds to their nerve pain. With strong response from local anesthetic, they received cryoablation at the same location. The researchers followed the patients for a minimum of 6 months and two patients up to 5 years. In three of their patients, there was a 90–100% decrease in reported pain. Phantom limb pain has a multifactorial cause of pain that is poorly understood, which includes a psychological component. With the utilization of cryoanalgesia, increased support can be provided to patients suffering from phantom limb pain.

Future Uses

Lateral Femoral Cutaneous Nerve

Pain in the anterolateral thigh is often associated with the disease of meralgia paresthetica. It is caused by compression or entrapment of the lateral femoral cutaneous nerve (LFCN). Meralgia paresthetica presents with pain, numbness, and dysesthesia across the anterolateral thigh. Risk factors for developing the disease include obesity, diabetes, pregnancy, and surgery. Treatment for meralgia paresthetica ranges from conservative to invasive use of nerve ablation. Nerve ablation with radiofrequency ablation has shown promise for relieving persistent and treatment-resistant pain. Due to the success of radiofrequency ablation with meralgia paresthetica, it is likely that cryoablation of the LFCN will result in similar results. Currently cryoabla-

tion has been used with patient-specific success. More studies need to be done, and it is a promising treatment alternative for meralgia paresthetica.

Cryotherapy for Total Knee Arthroplasty Pain

Osteoarthritic knee pain is a chronic problem for many adults and results in nearly 30% of all doctor visits. The treatment options range from lifestyle changes and pharmacological treatment to surgical replacement of the knee. In both non-surgical and surgical management, the use of the cryotherapy has indications for treatment. The sensory nerves that can be targeted include the medial and intermediate femoral cutaneous branches of the femoral nerve along with the saphenous nerve and infrapatellar and sartorial branches. Using anatomical landmarks and the superficial nature of these nerves, a well-targeted cryoprobe can be used to reduce knee pain either without surgery or before and after surgical intervention. Given the nature of the narcotic epidemic, having cryotherapy as an alternative can help to prevent patients from requiring narcotic pain medicine.

Cryotherapy as an Adjunct for Tapering Opioids

Cryotherapy use is also being explored as an adjunct therapy during tapering of opioids in comprehensive opioid addiction treatment (COAT). Opioid therapy is associated with development of physical dependence and addiction. Even with acute low doses of opioids, patients are at an increased risk of developing opioid use disorder (OUD). Analgesic tolerance is linked to opioid-induced hyperalgesia, a paradoxical response where patients may become more sensitive to certain stimuli. Patients may experience pain to non-painful stimuli (allodynia), suggesting involvement of the sensory nerves. Cryoneurolysis has the potential to play a role in relieving pain such as allodynia, eliminating the need to increase opioid dosages in patients. Furthermore, by treating the source of the pain via cryotherapy, it is plausible that tapering of opioids in COAT would have a higher success rate.

Pearls and Pitfalls

- The use of cryotherapy is best done with a well-trained and knowledgeable physician of local anatomy and device use.
- The optimal temperature for targeting nerves is between $-60\text{ }^{\circ}\text{C}$ and $-100\text{ }^{\circ}\text{C}$. This can be adjusted depending

- upon the nerve and pain reduction required which can be upward of -180°C to cause complete nerve destruction.
- Before cryotherapy a test diagnostic block is done using local anesthetic that requires a 50% reduction in pain before the use of cryotherapy is performed. This is done to rule out other causes of pain and increase the likelihood that the cryotherapy will target the right nerve.
 - The procedure is often performed twice for two 2-minute periods of freezing to induce adequate nerve insult. It is important to let the ice ball that forms to thaw before removal of the probe to reduce the risk of complications.
 - As with all procedures, there are risks that can result in complications such as pain, bleeding, infection, or damage to surrounding structures. When used near pleural tissue, there is the risk of pneumothorax. In addition permanent nerve damage can occur that may lead to neuritis, dysesthesia, or numbness of the overlying skin.
 - Future directions for cryoablation include the addition of new diseases such as meralgia paresthetica, the further use of ultrasound guidance, and the use of handheld liquid nitrogen-based portable devices that can be used in clinic.
 - Cryoablation has shown promise in other areas beyond pain and includes the treatment of cancer. Lung pleural tumors show great promise for treatment with cryoablation. Stage I renal cell carcinoma also has shown promise for treatment with cryoablation. Metastatic bone disease has also been treated in a palliative manner.
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