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## Introduction

*Cryoneurolysis*, also known as *cryoanalgesia* or *cryoneuroablation*, is a technique that uses extreme cold to provide long-term relief for patients suffering from chronic pain due to sensory nerve involvement. The word is derived from the Ancient Greek “κρύος” (“krúos,” “icy cold,” “chill,” “frost”), “νεῦρον” (neuron, “nerve,” “cordlike structure”), and “lysis” (“loosening,” “dissolving,” “dissolution”).

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## History

The use of cold in pain medicine dates from 1000 years ago when Hippocrates de Cós (460–377 BC) reported that snow had been used over wound with analgesic properties [1]. Avicenna of Persia (980–1037 AD) and Severino of Naples (1580–1656) described the use of ice as an anesthetic technique for surgical procedures [2]. In the nineteenth century, Baron Dominique Jean Larré, Napoleon’s military surgeon, noted that soldiers underwent painless limb amputations during the severe battlefield winter [3]. Trendelenburg was the first to report that cooling nerves produces prolonged and reversible loss of its function [4].

The clinical use of cryoneurolysis started with James Arnott (1797–1883), an English physician, who reported the benefits of cold in treating several diseases, such as headaches, neuropathic pain, and some gynecological cancers [5]. He also developed a cryotherapy device which was presented in

1851 at the Great Exhibition in London as a mode of applying cold as a therapeutic agent [6].

In contemporary medicine, cryosurgery gained popularity in 1961 with the introduction of automated cryosurgical devices by Cooper and Lee that created cryolesions with liquid nitrogen [7]. After this important boost, there was a rapid growth of use of cryosurgeries such as cryohypophysectomy [8], transurethral freezing of the prostate [9], skin cancer ablation [10], treatment of Meniere’s disease [11], hemorrhoidectomy [12], tonsillectomy [13], and even retinal detachment surgeries [14].

It was Lloyd and his colleagues that coined the term *cryoanalgesia* for its use in pain management [15].

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## Technical Aspects and Equipment

The cryoprobe consists of a hollow tube with a smaller inner tube. A high-pressurized gas (usually CO<sub>2</sub> or N<sub>2</sub>O), at 600–800 psi, goes through the smaller tube and is released into the larger, low pressure, outer tube through a microscopic aperture (0.002 mm) (Fig. 2.1). The cryogenic gas (Table 2.1) expands quickly at the distal tip in an adiabatic process fashion, dropping the distal tip to a temperature as low as –70 °C (Joule-Thompson effect) [16], creating an ice ball (Fig. 2.2). The gas then travels back to the machine where it is scavenged through a ventilated outlet, making no contact with the patient tissues.

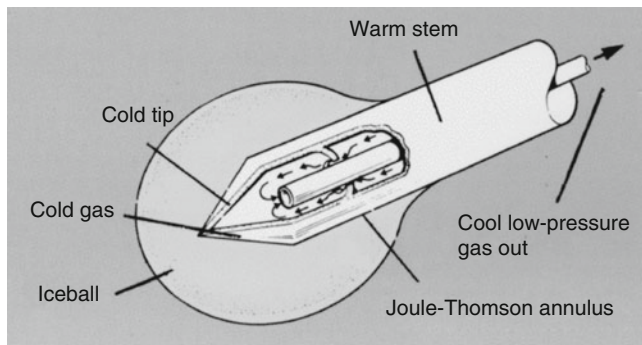
The bigger the tip probe, the bigger the ice ball generated. While the 1.4 mm probe makes a 3.5 mm ice ball, a 2.0 mm probe creates a 5.5 mm ice area. An accurate gas flow is mandatory to create an adequate and safe freezing lesion because a low gas output cannot extract enough heat, and a flow that is too high could result in an excessively cold lesion.

The cryoprobe has a built-in sensory (100 Hz) and motor (2 Hz) nerve stimulator that allows a precise positioning on the target. The freezing (and consequently the nerve damage) depends on:

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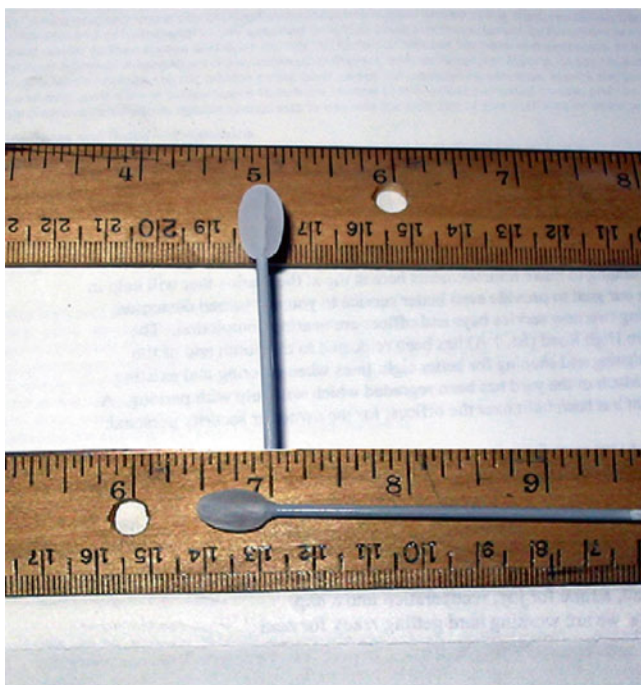
**Fig. 2.1** Anatomy of the cryoprobe (Image courtesy of Epimed®, with permission)

**Table 2.1** Compounds used in cryotherapy

Cryogenic gas	Boiling point (°C)
Dichlorotetrafluoromethane (Freon 114)	3.8 <sup>a</sup>
Dichlorodifluoromethane (Freon 12)	-29.8
Chlorodifluoromethane (Freon 22)	-40.8
Carbon dioxide, solid	-78.5 <sup>b</sup>
Nitrous oxide, liquid	-89.5 <sup>b</sup>
Argon, liquid	-185.7
Nitrogen, liquid	-195.8

<sup>a</sup>When sprayed on skin surface, the fluorinated hydrocarbons yield colder temperatures (Freon 114 approximately -33 °C; Freon 12 approximately -60 °C; Freon 22 approximately -70 °C)

<sup>b</sup>Sublimes at 1 atmosphere



**Fig. 2.2** Ice ball formation (Image courtesy of Epimed®, with permission)

- Correct diagnosis, which requires knowledge of anatomy and clinical syndromes
- Small volume (less than 1 cc) diagnostic injections
- The proximity of the probe to the nerve, which involves landmark, fluoroscopy, CT, or ultrasound guidance as well as meticulous nerve stimulation
- The size of the cryoprobe
- The size of ice ball formed
- The rate and duration of freezing

## Mechanisms of Cold-Induced Cell Injury

It is well established that temperatures below -20 °C are lethal to human cells [17–20], although there are no *in vivo* studies that support this finding. Actually, *in vitro* research offers no data about the local blood flow changes that freezing promotes, which can be important in cell lesioning. It is also believed that mild but prolonged low temperature exposures can result in cell death [21, 22].

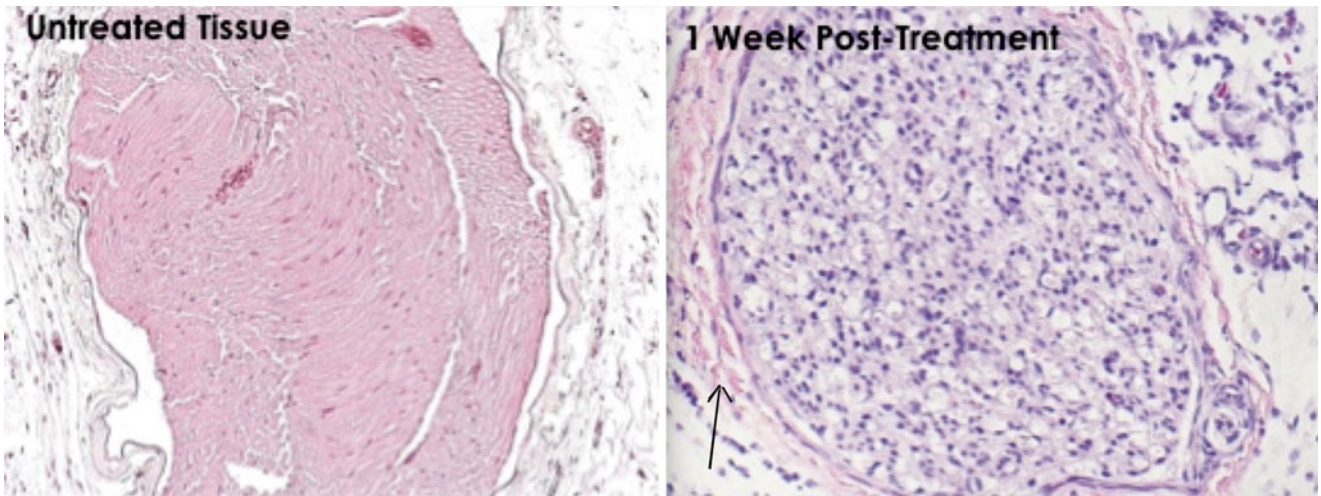
As the tissue temperature goes down, the extracellular fluid gets crystallized, which promotes a hyperosmotic environment leading to severe cell dehydration. As time goes by, the rise of some intracellular ions and intracellular ice generation usually induces cell death, by shrinkage and membrane rupture [23–27].

Cooling directly disrupts the blood supply tissues. There is an initial vasoconstriction and, after thawing, a microcirculatory stasis caused by vasodilatation, endothelial changes, increased vascular permeability, increased platelet aggregation, and microthrombus formation [28–30].

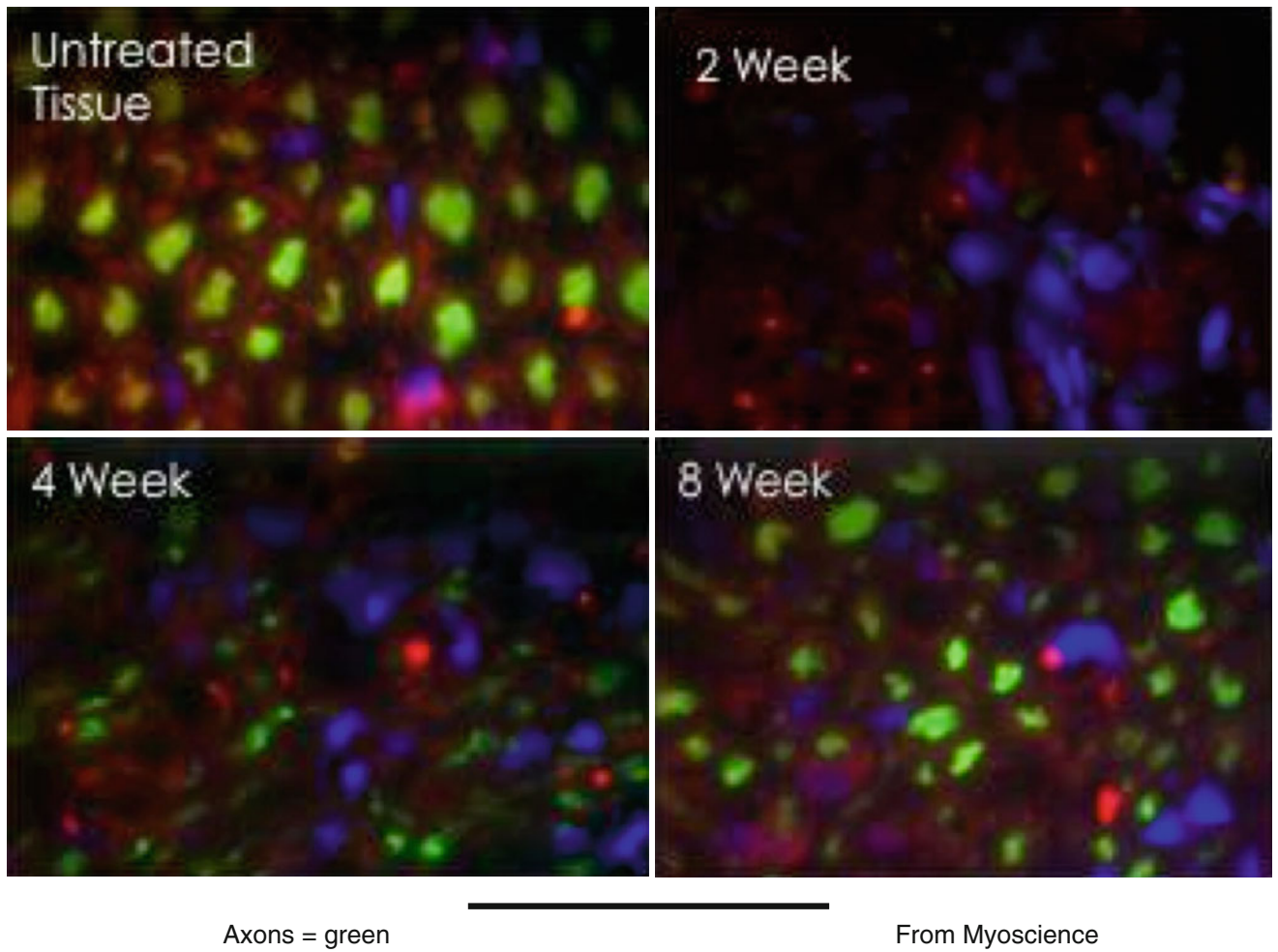
The faster the freezing rate, the bigger is the cell destruction [24, 31]. Regarding the target temperature, studies show that cell death occurs between -5 and -70 °C [24, 32]. As a result, there is damage to the vasa nervorum, which promotes severe endoneurial edema, increased of endoneurial fluid pressure, and a wallerian degeneration (Fig. 2.3) with preservation of the myelin sheath [33]. The Schwann cell basal lamina is preserved, which allows regeneration (Fig. 2.4). When the endoneurium remains uninjured, there is no neuroma formation and the nerve is able to regenerate at a rate of 1–1.5 mm/week [34].

Sunderland described five stages of nerve injury based on histological findings and prognosis [34]:

- First degree (neuropraxia): minimal histological changes with days to months' loss of nerve function.
- Second degree (axonotmesis): loss of axonal continuity without endoneurium injury. This occurs when the nerve is frozen to -20 °C (the range of cryoneuroablation).
- Third, fourth, and fifth degree (neurotmesis): neural and stromal destruction with low regeneration possibility.



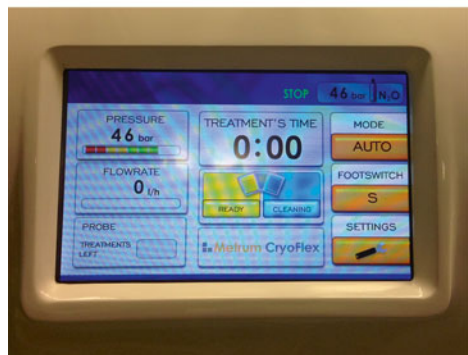
**Fig. 2.3** Histology after cryoneurolysis (Image courtesy of Myoscience®, with permission)



**Fig. 2.4** Regeneration after cryoneurolysis (Image courtesy of Myoscience®, with permission)



**Fig. 2.5** Epimed/Wallach PainBlocker® (Image courtesy of Epimed®)



**Fig. 2.6** Cryo-S cryoneuroablation machine (Image courtesy of Metrum Cryoflex®)

There are several cryoneurolysis machines now available with built-in nerve stimulators, gas flow monitors, and temperature thermistors (Figs. 2.5 and 2.6).

## Techniques

For deeper structures, it is useful to direct the cryoprobe under fluoroscopy or ultrasound guidance, but the use of sensory and motor stimulation to identify nerve structures is key

to success of this technique. Some steps should be followed to perform a safe and effective procedure:

- 1 A sterile prep and drape.
- 2 Skin and subcutaneous local anesthetic.
- 3 A small amount of saline with freshly added epinephrine 1:200,000 is infiltrated for hemostasis.
- 4 A small incision is made on the skin.
- 5 An IV introducer (size 12 or 14 gauge, depending on the size of the probe) is advanced to the target area.
- 6 The stylet is removed and the cryoprobe is then advanced through the catheter.
- 7 Withdrawing the catheter into the subcutaneous tissues exposes the tip of the probe.
- 8 Sensory stimulation (100 Hz), preferably below 0.5 mV, is used to identify the nerve.
- 9 Motor stimulation (2 Hz) is used at 2 mVolts to ensure that the probe is far enough from any motor nerves.
- 10 Gas flow is then turned up to 10–12 liters per minute (for the 2.0 mm probe) or 8–10 liters per minute (for the 1.4 mm probe).
- 11 A series of three 2-minute freezes with a 30-s thawing period between each cycle is performed.
- 12 The patients usually describe a burning pain in the first seconds of the first freezing cycle, which usually resolves within 30 seconds.

Some studies evaluated patients undergoing repeated cryoneurolysis sessions in a long-term fashion and concluded that this treatment demonstrated to provide safe, effective, and reversible outcomes [35–37].

## Craniofacial Pain

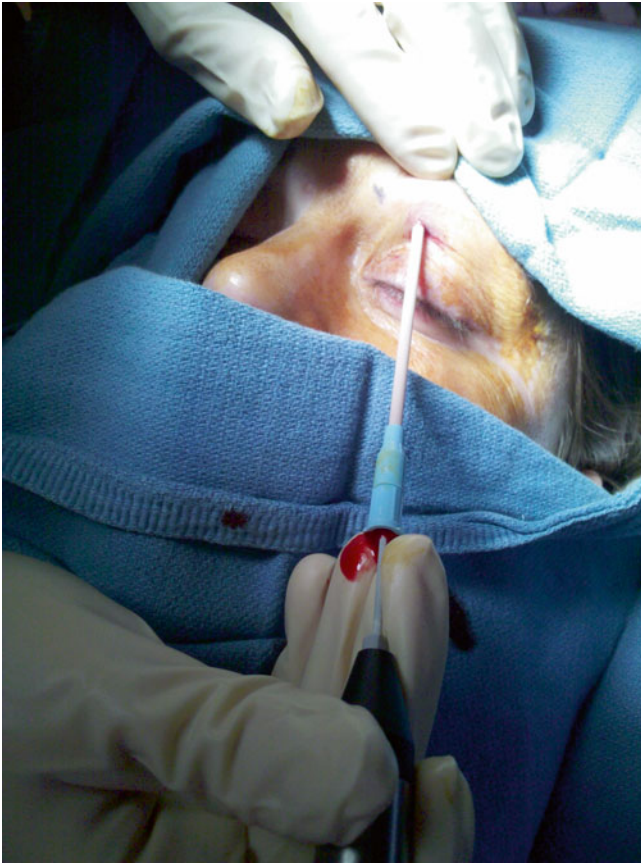
### Supraorbital and Supratrochlear Nerves

The supraorbital and supratrochlear nerves are branches of the frontal nerve all from the first division of trigeminal nerve. They are responsible for the forehead innervation, and their entrapment can cause frontal headache (often misdiagnosed as migraine or sinusitis).

The supratrochlear nerve can be found about 16 mm lateral from the medial orbital border aspect and 7 mm below the orbital upper margin, while the supraorbital nerve exits the supraorbital notch or supraorbital foramen about 29 mm lateral to the midline and 5 mm below the supraorbital upper margin (Fig. 2.7) [38].

### Infraorbital Nerve

The infraorbital nerve (ION), a purely sensory nerve, is a maxillary nerve terminal branch. It is responsible for the cutaneous sensation of the zygomatic, paranasal, and para-orbital areas [39]. After emerging onto the face through the



**Fig. 2.7** Cryoneuroablation supraorbital nerve (Image courtesy of Andrea Trescot, MD)

infraorbital foramen, the ION gives out the inferior palpebral, nasal, and superior labial branches [40, 41]. It can be damaged by trauma (especially malar fractures), surgical procedures, and sinusitis. It can be easily reached by a percutaneous or intraoral approach (Fig. 2.8) just outside the infraorbital foramen, avoiding deeper needle introduction, which can cause global penetration [42].

### Maxillary Nerve

The maxillary nerve neuralgia usually causes upper jaw and cheek pain. The nerve can be entrapped proximal to the infraorbital foramen and can be one of the branches involved in the trigeminal neuralgia, occurring in as many as 80% of the cases. The maxillary can be accessed by the lateral pterygopalatine fossa approach with the probe perpendicular to lateral pterygoid plate.

### Zygomaticotemporal Nerve (ZN)

The ZN is one of the branches of the maxillary nerve. The ZN is responsible for the sensory innervation of a small area of the forehead and the temporal region. It can be squeezed



**Fig. 2.8** Intraoral cryoneurolysis infraorbital nerve (Image courtesy of Andrea Trescot, MD)

at the zygomaticotemporal foramen or by the temporalis muscle (Fig. 2.9).

The ZN can be blocked 10–17.5 mm posterior to the frontozygomatic suture and 22–24.8 mm above the zygomatic arch [38].

### Auriculotemporal Nerve (ATN)

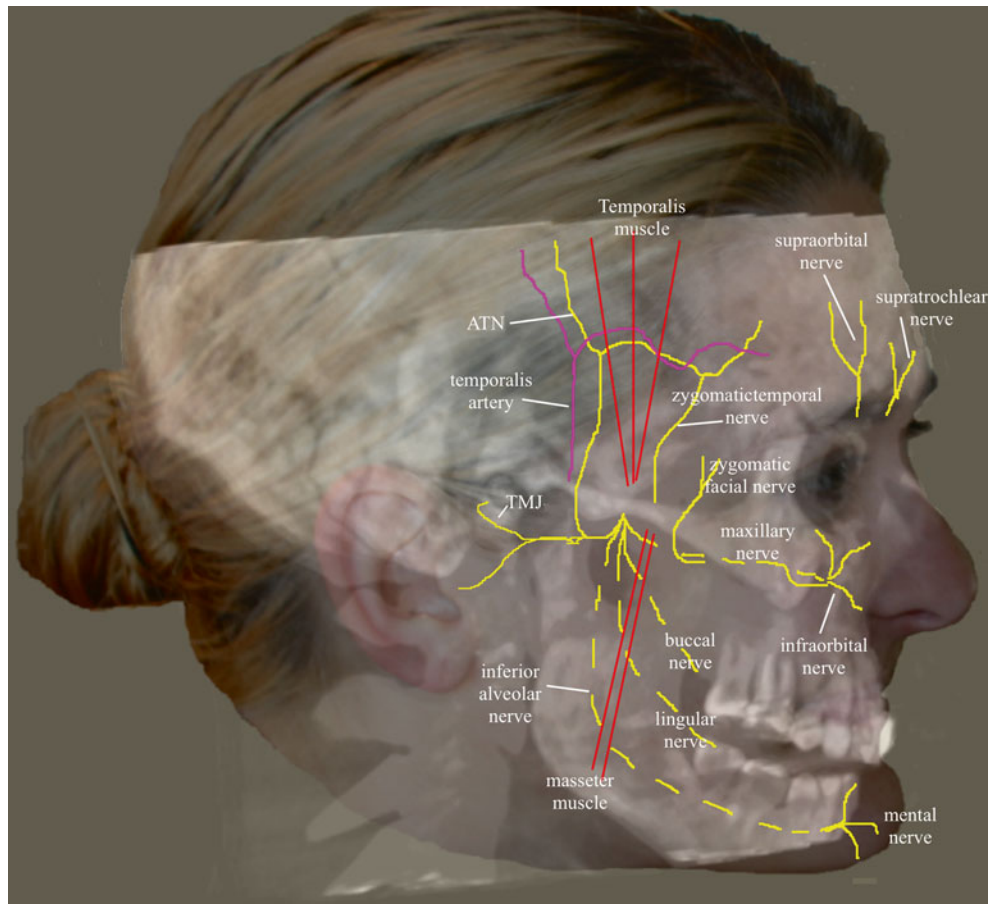
The ATN is a branch of the posterior trunk of the mandibular division of the trigeminal nerve. It is responsible for the sensory innervation of the tragus and the anterior aspect of the ear as well as the temple. In some instances, the ATN can be compressed by temporal artery, which can cause headaches. The ATN can be accessed at a point 10–15 mm anterior to the upper origin of the helix of the ear (Fig. 2.10) [38].

### Mandibular Nerve

The presentation of mandibular nerve (the third trigeminal branch) neuropathy is pain involving the mandibular, dental, and lateral tongue areas. It can be compressed by bone, muscle, and fibrous band [43–45]. In the cryoneurolysis technique, the probe is placed perpendicular to the lateral pterygoid plate and advanced posteriorly [46].

### Inferior Alveolar Nerve

The inferior alveolar nerve, also called inferior dental nerve, is a branch of the third division of the trigeminal nerve. Its involvement produces a clinical picture of lower jaw and dental pain, which usually occurs after jaw trauma or dental surgery [47]. The nerve can be accessed intraorally at the medial aspect at the angle of mandible (Fig. 2.11).



**Fig. 2.9** Anatomy of the facial nerves (Image courtesy of Andrea Trescot, MD)



**Fig. 2.10** Cryoneurolysis of the auriculotemporal nerve (Image courtesy of Andrea Trescot, MD)

### Mental Nerve

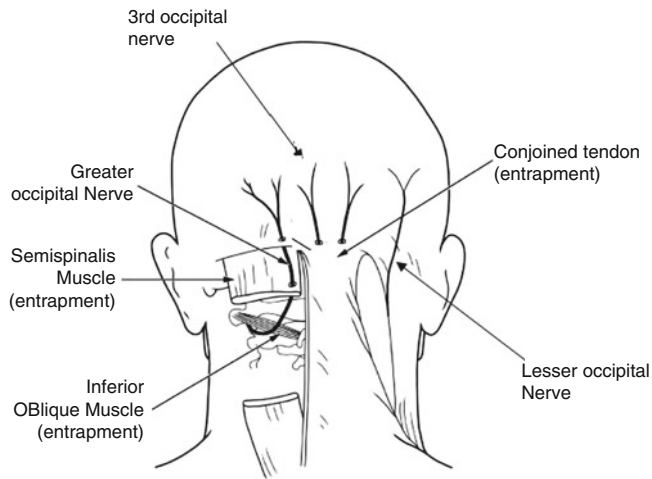
The mental nerve (MN) is a terminal branch of the mandibular nerve. The MN is responsible for the lower chin, lower



**Fig. 2.11** Intraoral inferior alveolar nerve injection (Image courtesy of Andrea Trescot, MD)

incisors, and lower lip sensory innervation, and its damage causes pain and sensory disturbances in those areas. The MN exists at the mandible through the mental foramen, usually at the second premolar level.

The MN can be blocked by the intraoral and extraoral approach, both techniques through the mental foramen.



**Fig. 2.12** Occipital nerve entrapment sites (Image courtesy of EpiMed®)

### Greater Occipital Nerve (GON)

The GON originates from the medial branch of the dorsal ramus of the C2 spinal nerve and also can communicate with branches from the dorsal branch of the C3 spinal nerve [48]. The GON entrapment typically produces occipital pain that can radiate to the frontal and periorbital areas. The GON pierces the trapezius muscle, the semispinalis capitis muscle, and the inferior oblique muscle (Fig. 2.12) in, respectively, 45 %, 90 %, and 7.5 % of cases [49]. These muscles are typical sites of nerve entrapment [50].

The GON blockade is performed blindly or under ultrasound guidance at a point 3–5 cm laterally and 2–3 cm below the inion (Fig. 2.13).

### Lesser Occipital Nerve (LON)

The LON originates from the ventral rami of C2 and C3 nerve roots and travels superiorly along the posterior border of the sternocleidomastoid muscle. Communicating branches with the GON are very common (Fig. 2.14). Lesser occipital pathology usually manifests as a cervicogenic headache; it can be frozen at a point approximately 7 cm lateral to the external occipital protuberance or under ultrasound guidance.

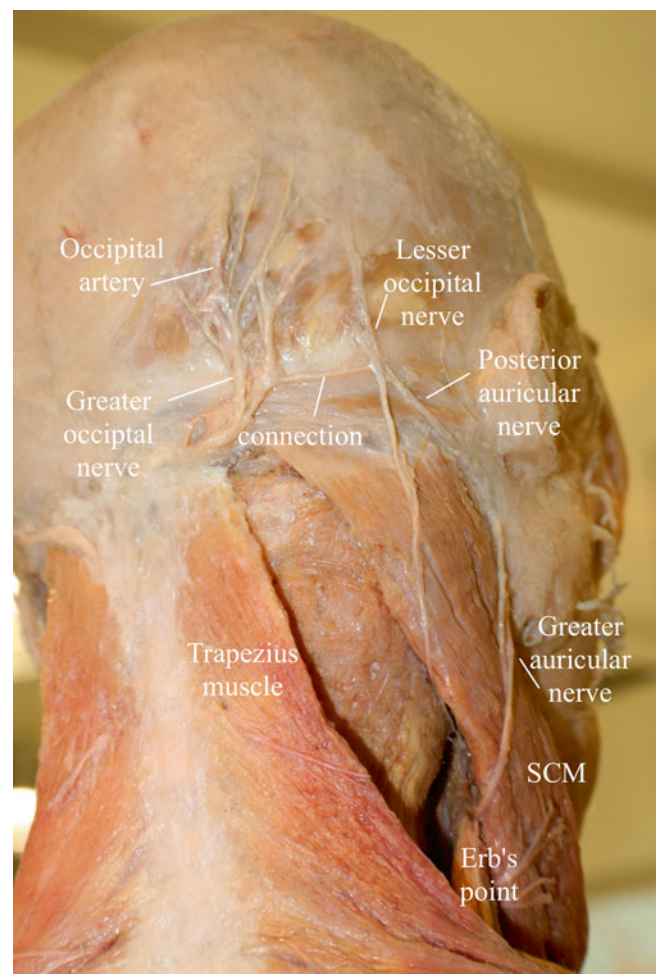
## Upper Extremity Pain

### Suprascapular Nerve

The suprascapular nerve originates from the fifth and sixth cervical nerves and is responsible for the motor innervation of the supraspinatus and infraspinatus muscles as well as the sensory innervation of the shoulder [51]. It can be entrapped



**Fig. 2.13** Occipital nerve cryoneurolysis (Image courtesy of EpiMed®)



**Fig. 2.14** Occipital nerve dissection showing connection between the greater and lesser occipital nerves (Image courtesy of Andrea Trescot, MD, from *Bodies, The Exhibition*, with permission)

by the supraspinatus muscle or by an ossification of the suprascapular ligament [52] and is also a great target for shoulder pain [53] and even chronic headache control [54].



**Fig. 2.15** Cryoneurolysis of the suprascapular nerve (Image courtesy of Andrea Trescot, MD)

The suprascapular nerve can be lesioned with landmark, ultrasound, or fluoroscopic guidance (Fig. 2.15).

## Chest Wall Pain

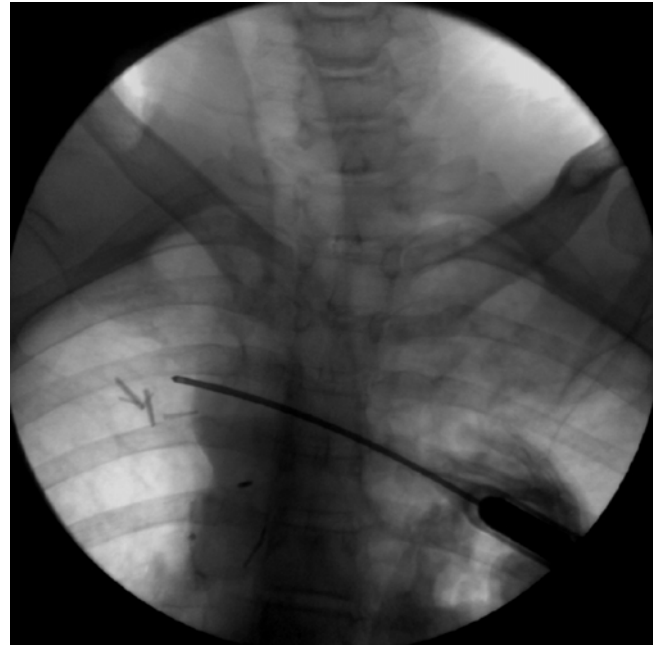
### Intercostal Nerve

The intercostal nerves arise from the ventral roots of thoracic spinal nerves from T1 to T11. They can be injured during thoracotomy or by rib fractures or shingles. The intercostal nerve lies posterior and cephalad to the inferior border of the rib. The cryoprobe should be placed tangentially to the inferior border of the rib, slipping beneath the inferior rib (Fig. 2.16). It is strongly recommended that ultrasound or fluoroscopy guidance be used to avoid pneumothorax [55].

## Abdominal/Pelvic Pain

### Iliohypogastric/Ilioinguinal Nerve

The iliohypogastric nerve arises from the L1 nerve root with a contribution from T12 in some patients. It travels from the



**Fig. 2.16** Fluoroscopic image of cryoneurolysis of the intercostal nerve (Image courtesy of Andrea Trescot, MD)

ventral aspect of the quadratus lumborum muscle (at L1/L2 intervertebral disc level), passing behind the middle or lower pole of the kidney and piercing the aponeurosis of the transversus abdominal muscle above the iliac crest.

The iliohypogastric nerve is frequently injured during inguinal repairs and appendectomies [56] or even during pregnancy (due to traction of the nerve secondary to expanding abdomen) or after Pfannenstiel incision [57]. Patients may complain about neuropathic pain in the skin over the pubis and lower flank region.

The ilioinguinal nerve is also derived from the L1 nerve root with possible contribution from T12. Ilioinguinal injury may also cause lower pelvic and groin pain.

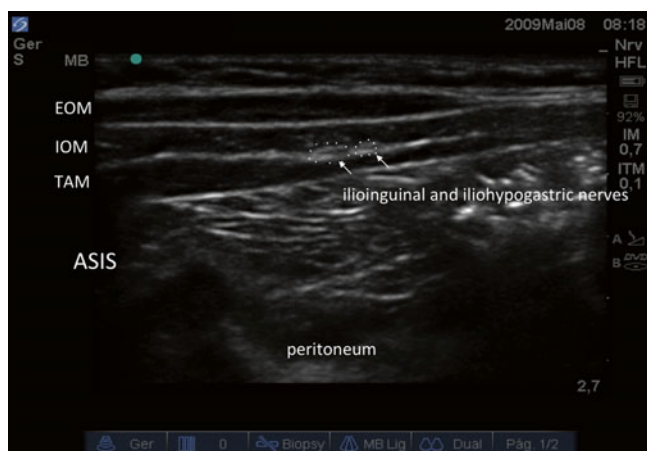
The iliohypogastric and ilioinguinal nerves can be easily visualized under ultrasound (Fig. 2.17) and cryoneurolysis performed with landmark guidance (Fig. 2.18) or ultrasound visualization.

### Genitofemoral Nerve

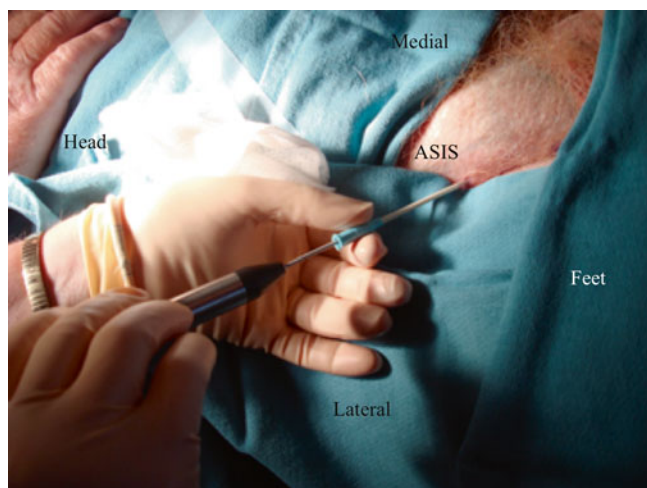
As with the iliohypogastric and ilioinguinal nerves, the genitofemoral nerve arises from the L1 nerve root with T12 contributions in some patients. Its femoral branch provides sensory innervation to a small area on the medial aspect of the thigh, while its genial branch passes through the inguinal canal and is responsible for the sensory innervation of round ligament of the uterus and labia majora in women or the lower part of the scrotum in men.

The genitofemoral nerve can be injured in some surgeries such as appendectomies, inguinal hernia repairs, and cesar-





**Fig. 2.17** Ultrasound images of the iliohypogastric and ilioinguinal nerves (Image courtesy of Thiago Nouer Frederico, MD, modified by Charles de Oliveira, MD)



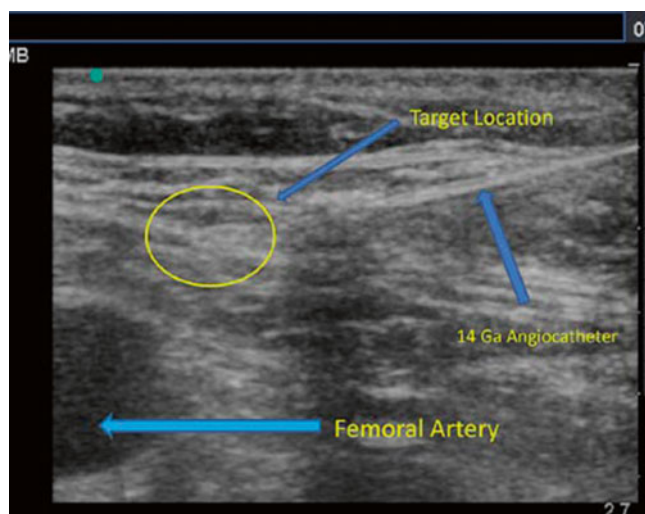
**Fig. 2.18** Cryoneurolysis of the ilioinguinal nerve (Image courtesy of Andrea Trescot, MD)

ean sections. The genitofemoral nerve can be safely accessed by ultrasound guidance in the thigh (Fig. 2.19) [58], or at the pubis (Fig. 2.20) or proximally at the spine (Fig. 2.21) under fluoroscopy.

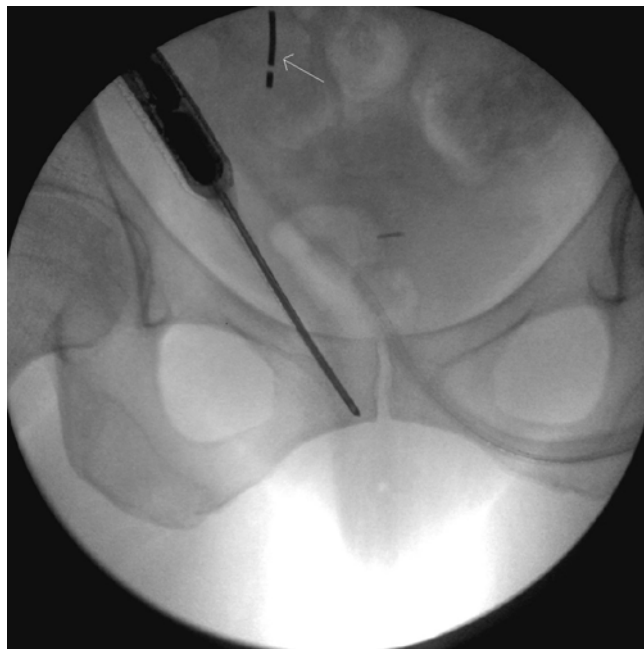
## Pudendal Nerve

The pudendal nerve is derived from the S2, S3, and S4 nerve roots. It leaves the pelvis through the greater sciatic notch around the sacrospinatus ligament and runs through the pudendal canal (Alcock's canal) to innervate the anus, perineum, and scrotum/vagina.

Four primary types of pudendal entrapment syndromes had been described: type I, entrapment at the exit of the greater sciatic notch in concert with piriformis muscle spasm; type II, entrapment at the level of the ischial spine,



**Fig. 2.19** Cryoneurolysis under ultrasound of the femoral branch of the genitofemoral nerve (Image courtesy of John Chiles, MD)



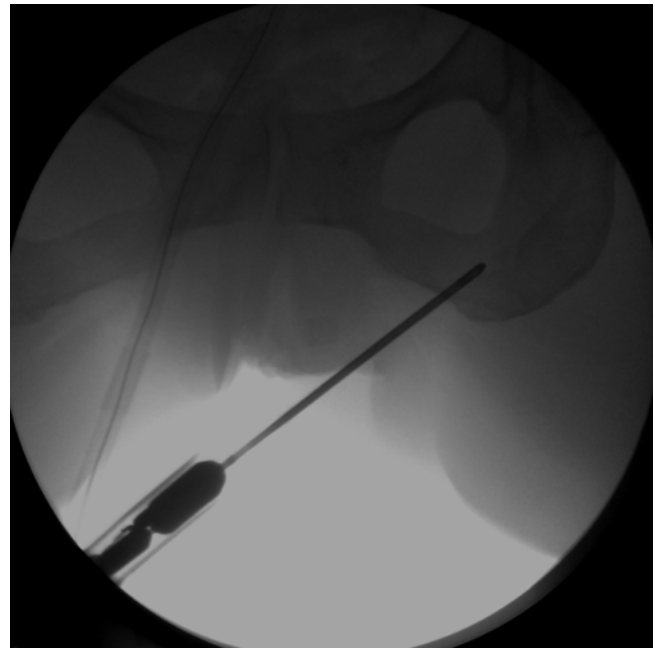
**Fig. 2.20** Cryoneurolysis of the genitofemoral nerve at the pubic tubercle. Note the white arrow showing the Interstim® placed for interstitial cystitis pain that offered no relief (Image courtesy of Andrea Trescot, MD)

sacrospinatus ligament, and lesser sciatic notch entrance; type III, entrapment in association with obturator internus muscle spasm at the entrance of the Alcock's canal; and type IV, distal entrapment of terminal branches [59].

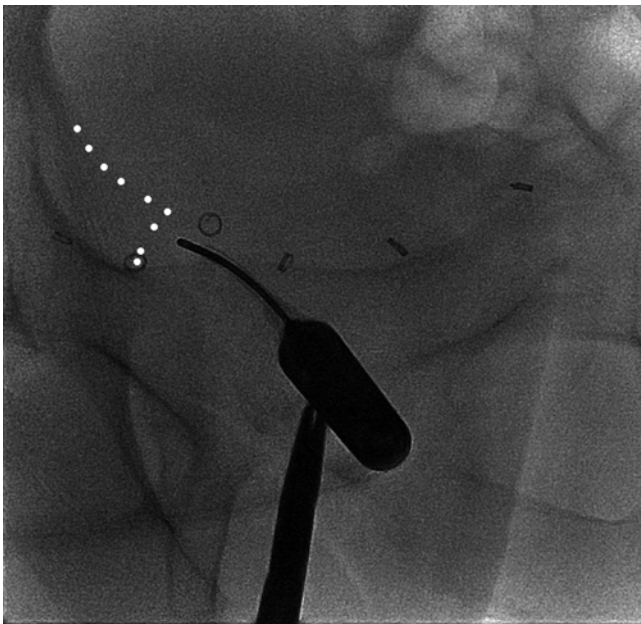
The clinical picture of pudendal nerve entrapment is pain from the anus through the penis or clitoris, usually predominantly experienced while sitting. The presence of sphincter motor disorders suggests more proximal sacral nerve involvement [60].



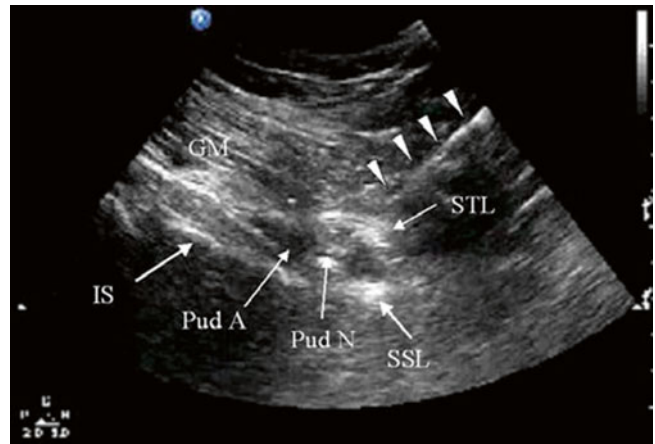
**Fig. 2.21** Cryoprobe positioned on the proximal genitofemoral nerve at L1 (Image courtesy of Andrea Trescot, MD)



**Fig. 2.23** Cryoneurolysis at the pudendal canal (Image courtesy of Andrea Trescot, MD)



**Fig. 2.22** Cryoneurolysis at the ischial spine (outlined in *white*) (Image courtesy of Agnes Stogicza, MD)



**Fig. 2.24** Ultrasound picture of the pudendal nerve during injection. *STL* sacrotuberous ligament, *SSL* sacrospinous ligament, *Pud A* pudendal artery, *Pud N* pudendal nerve, *IS* ischium at ischial spine level, *GM* gluteus maximus. The needle is identified by the *solid arrows* (Image from Peng [89], with permission)

The pudendal nerve cryoneurolysis can be accomplished proximally or distally, by fluoroscopic [61] or ultrasound visualization, with patient in prone or lithotomy position. Figure 2.22 shows cryoneurolysis proximally at the ischial spine, and Fig. 2.23 shows cryoneurolysis at the pudendal (Adcock's) canal, both under fluoroscopic guidance, while Fig. 2.24 shows the pudendal nerve under ultrasound.

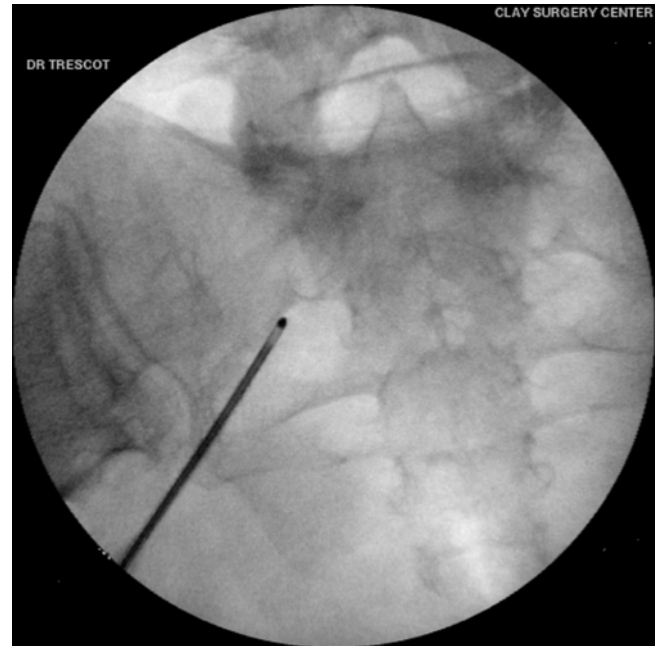
## Lower Extremity Pain

### Superior Cluneal Nerve

The superior cluneal nerve is composed of the cutaneous branches of the dorsal rami of L1, L2, and L3 [62]. Although classically it had been seen as a cause of pain after iliac bone harvest surgery, superior cluneal pathology may occur more frequent as result of a spontaneous entrapment of the nerves as they pass through the thoracolumbar fascia [63]. The



**Fig. 2.25** Location of cluneal nerve entrapment (Image courtesy of Andrea Trescot, MD)



**Fig. 2.27** Cryoneurolysis of the posterior ramus of the sacral nerves (Image courtesy of Andrea Trescot, MD)



**Fig. 2.26** Cryoneurolysis of the cluneal nerve (Image courtesy of Andrea Trescot, MD)

patient usually complains about low back pain that radiates to the gluteal region. The symptoms can be reproduced by manual palpation of the iliac crest at a point approximately 7 cm lateral to the midline (Fig. 2.25). Cryoneurolysis is performed at the iliac crest (Fig. 2.26) or more proximally at the spinal foramen.

## Sacral Nerve

The sacral nerve pathology can produce sacroiliac joint pain with tenderness over the medial aspect of the posterior iliac. Pain can be referred from the buttocks to the foot. The cryoprobe must be placed at the lateral border of the foramen to freeze the posterior ramus of the sacral nerves (Fig. 2.27).

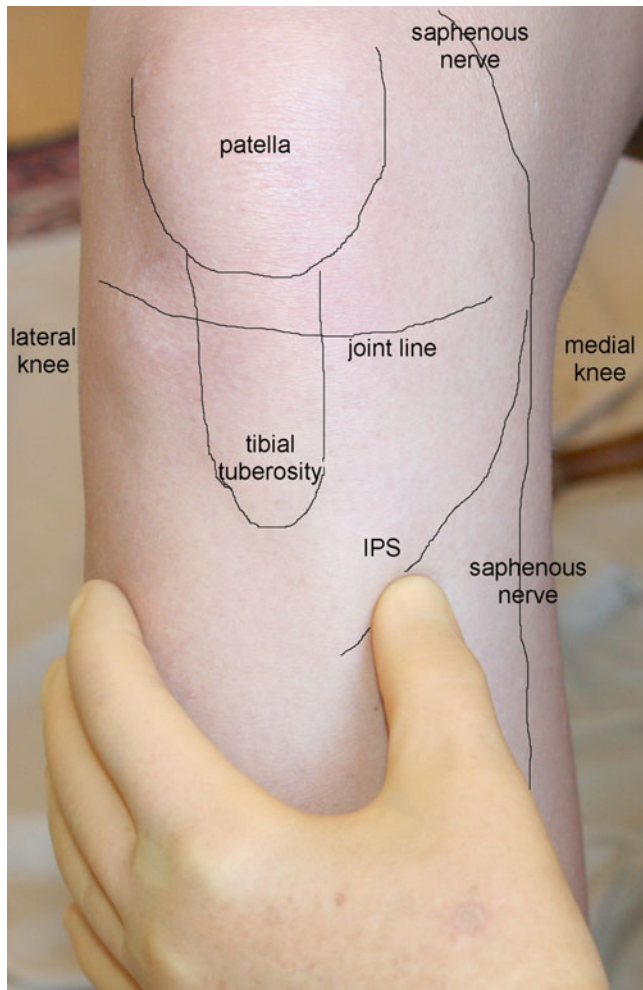
## Infrapatellar Saphenous Nerve

The infrapatellar branch of saphenous nerve (IPS) is a pure sensory nerve that is responsible for the infrapatellar skin and anterior knee capsule innervation [64]. The nerve crosses the inferior knee from medial to lateral (Fig. 2.28) where it could be injured in many surgical procedures such as total knee replacement [65], patellar and hamstring tendon harvest [66], and tibial nailing as well as by anterior knee trauma [67].

The IPS can be cryolesioned at the inferior medial tibial plateau, medial and inferior to the tibial tuberosity (Fig. 2.29). It is useful to palpate and locate the maximum tender point over the nerve. It is important to be prudent and avoid skin freezing since the nerve is superficial.

## Superficial Fibular (Peroneal) Nerve

The superficial fibular nerve (also known as the superficial peroneal nerve) is a branch of the common fibular nerve and



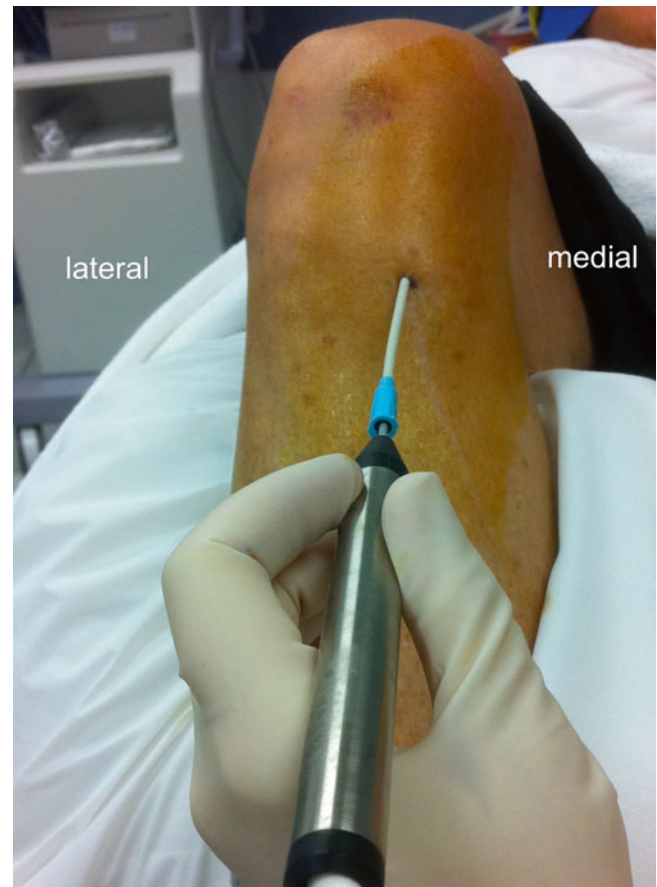
**Fig. 2.28** Physical exam of the infrapatellar saphenous nerve (Image courtesy of Andrea Trescot, MD)

innervates the fibularis longus and fibularis brevis muscles and the skin over the greater part of the dorsum of the foot. The nerve lies between the lateral malleolus and the extensor retinaculum, and it can be injured frequently after inversion foot injuries, mimicking complex regional pain syndrome [68]. The patient may experiment dull lateral ankle pain that radiates to the dorsal of the foot.

The probe should be placed parallel to the nerve, and, since the nerve is quite superficial, one needs to be careful about skin freezing (Fig. 2.30).

### Superficial Saphenous Nerve

The saphenous nerve is the largest branch of the femoral nerve, derived from the L3 and L4 spinal roots. The nerve runs along the adductor canal (also known as subsartorial or Hunter's canal) and becomes superficial as it approaches



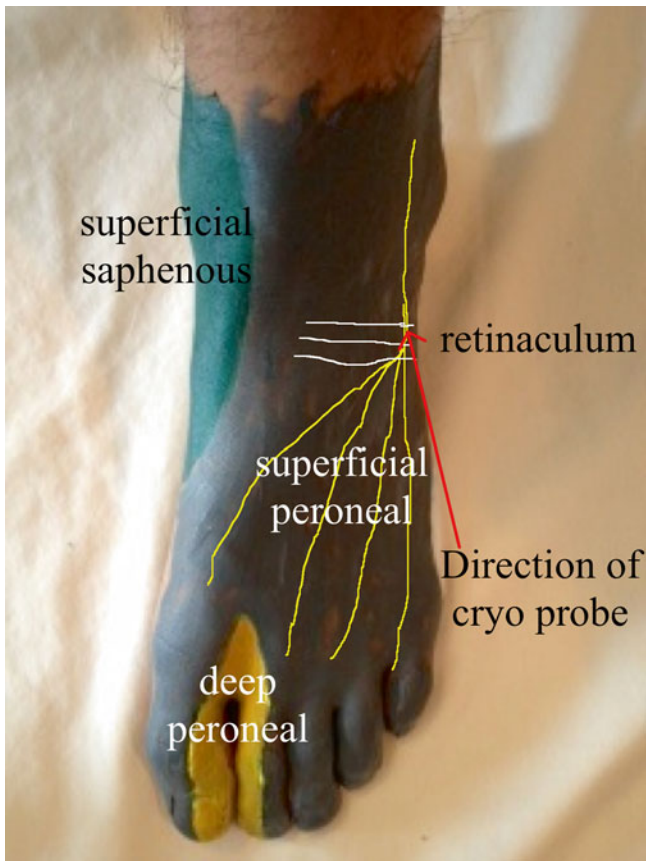
**Fig. 2.29** Cryoneurolysis of the infrapatellar nerve (Image courtesy of Andrea Trescot, MD)

the knee. More distally, the nerve passes anterior to the medial malleolus, the site for cryoneurolysis of the superficial saphenous nerve (Fig. 2.31). The superficial saphenous nerve is frequently injured during saphenous vein surgeries (for aesthetic or vein graft harvest purposes) or after foot eversion injuries. The patient usually complains about a dull medial ankle pain that may radiate down to the great toe.

### Medial and Inferior Calcaneal Nerves

The medial and inferior calcaneal nerves are branches of the posterior tibial nerve, and they are responsible for the medial and inferior heel innervation, respectively (Fig. 2.32) [69]. They can be compressed by tight-fitting shoes or injured by trauma and cause pain in the innervated area.

The medial and inferior calcaneal nerve cryoneurolysis may be useful targets for the recalcitrant plantar fasciitis (Fig. 2.33); inferior calcaneal neuralgia may need treatment



**Fig. 2.30** Site of cryoneurolysis of the superficial peroneal nerve (Image courtesy of Terri Dallas-Prunskis, MD)



**Fig. 2.31** Cryoneurolysis of the superficial saphenous nerve (Image courtesy of Andrea Trescot, MD)

for its own entrapment (also known as Baxter's neuropathy) [70–72].

### Digital Nerve

The plantar digital nerve entrapments can produce a poorly localized foot pain, mainly at the ball of the foot and between the toes. The deep peroneal nerve functions as a digital nerve and is treated the same way. The most common mechanism of entrapment is compression by the metatarsal heads. Cryoneurolysis is an attractive option to alcohol injections and open surgery (Fig. 2.34).

### Outcome Data

Cryoneurolysis is used for non-spinal pain in multiple sites. Although the technique has a great clinical efficacy, the evidence has been scarce. Most of studies are case reports, case series, or observational studies.

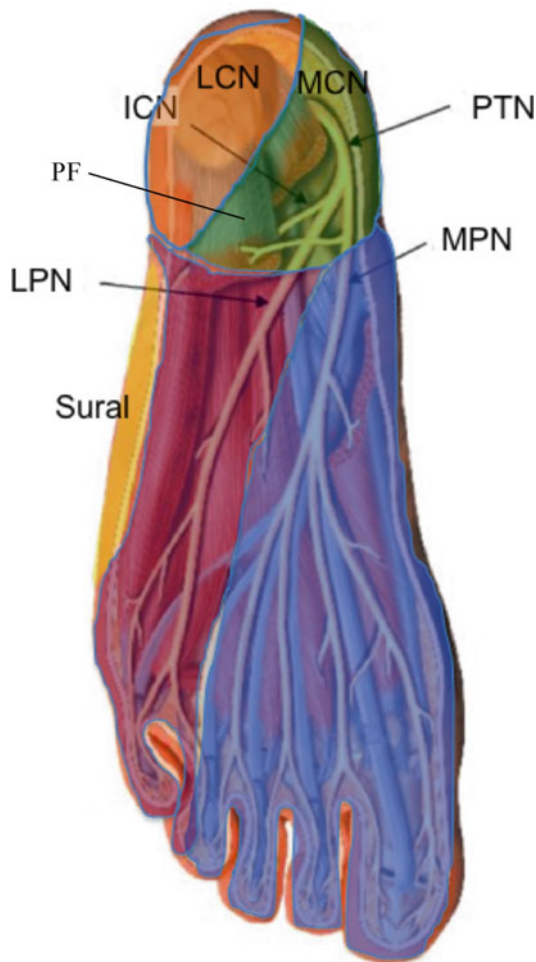
### Craniofacial Pain

Zakrzewska et al. [73] reviewed 475 trigeminal neuralgia patients over a 10-year follow-up period. The patients were subgrouped as follows: 145 submitted to cryotherapy, 265 underwent radiofrequency thermocoagulation, and 65 underwent microvascular decompression. The recurrence probability among the patients submitted to cryotherapy was lower, and none of the cryoneuroablation patients developed anesthesia dolorosa, which occurred in 8 % of patients in the radiofrequency group.

Sidebottom et al. [74] tested cryoneuroablation in the management of intractable pain of the temporomandibular joint (TMJ). They observed a decrease at the visual analogue pain scale from 6.8 (range 4–10) to 2 (range 0–7), after applying the cryoablation at the auriculotemporal nerve region and at the TMJ in 17 patients.

### Thoracic Pain

Cryoneurolysis had been used to treat intercostal neuralgia and even for post-thoracotomy pain control.



**Fig. 2.32** Anatomy of the plantar nerves: *PTN* posterior tibial nerve, *MPN* medial plantar nerve, *LPN* lateral plantar nerve, *ICN* inferior calcaneal nerve, *LCN* lateral calcaneal nerve, *MCN* medial calcaneal nerve, *PF* plantar fascia (Image courtesy of Andrea Trescot, MD)



**Fig. 2.33** Cryoneurolysis of the medial calcaneal nerve (Image courtesy of Andrea Trescot, MD)



**Fig. 2.34** Cryoneurolysis of the deep peroneal nerve (digital nerve) (Image courtesy of Andrea Trescot, MD)

Momenzadeh et al. [75] compared the effects of intercostal cryoneurolysis on post-thoracotomy pain. The postoperative pain was classified in three groups according to the intensity: 0–1 (mild), 2–3 (moderate), and 4–10 (severe). On the second day, the incidence of severe pain was 33 % and 0 in the control and cryoanalgesia groups, respectively. The opioid consumption was significantly lower in the cryoanalgesia group.

Ju et al. [76], in a randomly prospective fashion, compared the efficacy of intercostal cryoablation and epidural analgesia in 107 patients undergoing thoracotomy. They found the same pain relief with lower pruritus incidence in the cryotherapy group.

Green et al. [77] retrospectively studied the effects of cryoneurolysis in 43 patients with chronic chest wall pain due to intercostal neuralgia. The mean VAS score dropped from 8.2 (preprocedure) to 2.7 in a 3-month follow-up. Three months after cryoanalgesia, 50 % of the patients continued to report significant pain relief.

## Lumbar Pain

One of the uses of cryoanalgesia for low back pain is the treatment of lumbar facet pathology. When diagnostic lumbar facet injections (either pericapsular or median branch blocks [78]) have given good but only temporary relief, one option for further treatment is cryoneuroablation of the medial branches (see Fig. 2.35). The American Medical Association (AMA) has confirmed that the facet neurolytic codes (64633/64634



**Fig. 2.35** Cryoneuroablation of the medial branches

and 64635/64636) are appropriate to use for cryoneuroablation of the cervical, thoracic, and lumbar facets.

Wolter et al. [79] retrospectively analyzed 117 cryoneurolysis treatments for zygapophyseal joint pain. All the procedures were done under CT visualization after a positive diagnostic block using local anesthetic.

### Abdominal/Pelvic Pain

Racz and Hagstron [80] studied 15 patients with chronic abdominal pain treated with cryoneurolysis of the ilioinguinal and iliohypogastric nerves. Seven patients (47 %) reported excellent pain relief. Four of the seven patients experienced pain relief lasting between 4 and 30 months, and the other three had permanent pain relief.

Glynn and Carrie [81] reported two cases of successful cryoneurolysis through the caudal hiatus to provide pain relief from the pain caused by diastasis of the symphysis pubis during pregnancy.

Loev et al. [82] reported one case of cryoneurolysis of the ganglion of impar in a patient with severe anal and perineal pain secondary to surgical resection of rectal carcinoma. The procedure was performed after a diagnostic block through the sacrococcygeal membrane.

### Lower Extremity Pain

Hodor et al. [83] reported a successful treatment of the intermetatarsal space neuroma in one patient with a 2-min

cryoneurolysis technique. They found a 38 % VAS decrease after 3-month follow-up and even anxiety and depression scale reduction.

Caporusso et al. [84] prospectively evaluated the cryogenic neuroablation of 32 neuromas in 20 patients. All patients were surgical candidates who had failed prior conservative treatment. After 1 year, 38.7 % of patients were pain-free, 45.2 % reported partial pain relief, and 16.1 % returned to the baseline condition.

Allen et al. [85] did a prospective study testing the efficacy of cryosurgery on painful plantar fasciitis in 59 patients (61 heels). The results were impressive with a mean pain rating dropping from 8.38 to 1.26 during a 12-month follow-up period.

Moesker et al. [86] reported the treatment of five phantom limb pain patients with cryoneurolysis of the affected nerve. The nerve was chosen according to the referred pain location described by the patient and confirmed by diagnostic injection using local anesthetic. Cryoneurolysis was performed at the same location using two cycles of 3-min freezing separated by a 2-min defrost. Three of five patients had excellent outcomes, with 90–100 % pain relief. One patient had 40 % pain decrease, and the other one had 20 % pain relief.

Rhame et al. [87] described an ultrasonographic-guided cryoneuroablation of a refractory sural neuroma with long-term relief.

## Complications

Cryoneurolysis carries a low probability of complications risk. The most frequent complication is hypoesthesia of the innervated area. Puncture-related complications such as bleeding, infection, and pneumothorax can be avoided with a proper technique. Hyperpigmentation or depigmentation is a potential risk as is alopecia at the cryo site (especially the eyebrow).

### Conclusion

Cryoneurolysis is an effective interventional pain management technique, providing short- and long-term analgesia for properly selected patients. A positive diagnostic block is mandatory for the technique success.

We have a scarcity of scientific evidence, not only about the cryoneuroablation but also for many of our interventional pain management techniques.

Nonetheless, in this “evidence vacuum,” we still have a responsibility to treat. Certainly, we must develop better evidence, but our patients cannot wait for that [88].

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