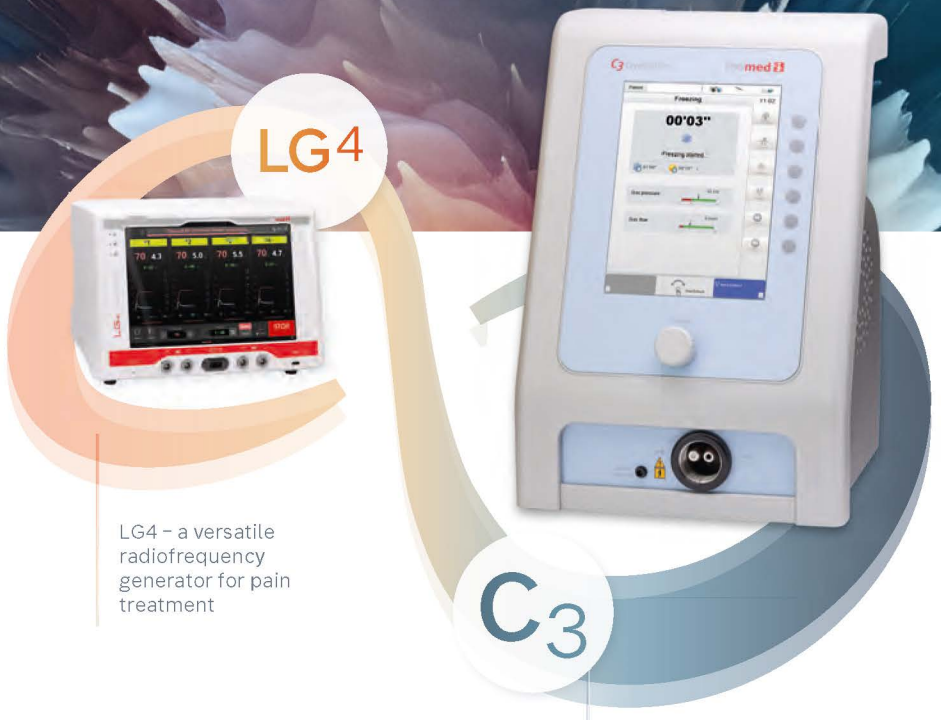


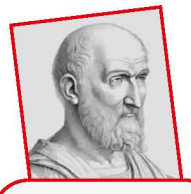
LG4 – a versatile radiofrequency generator for pain treatment

C3 – a dedicated cryoneurolysis system

Fire & Ice

inomed is the only company to offer both radiofrequency & cryoanalgesia systems

inomed



Hippocrates first to treat pain with ice

~ 420 BC

~ 1000

Avicenna of Persia used cold for preoperative analgesia and to manage postoperative pain

John Hunter found tissue killed by cold healed with no scaring

1777

1822

Jean Larrey noted that soldiers exposed to extreme cold had less pain during limb amputation procedures

Arnott succesfully treated cancer and nerve pain

1848

1961

Cooper developed first cryoprobe for liquid nitrogen achieving temperatures of - 190 °C

Trendelenburg noted frozen tissue nerves regenerated without neuroma

1917

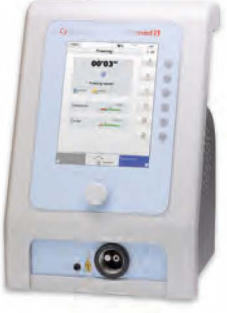
Amoils developed a cryoprobe that used CO_2 and N_2O and reached temperatures of -70 °C

1967

Humanity has been using cold to relieve pain for millennia

1977

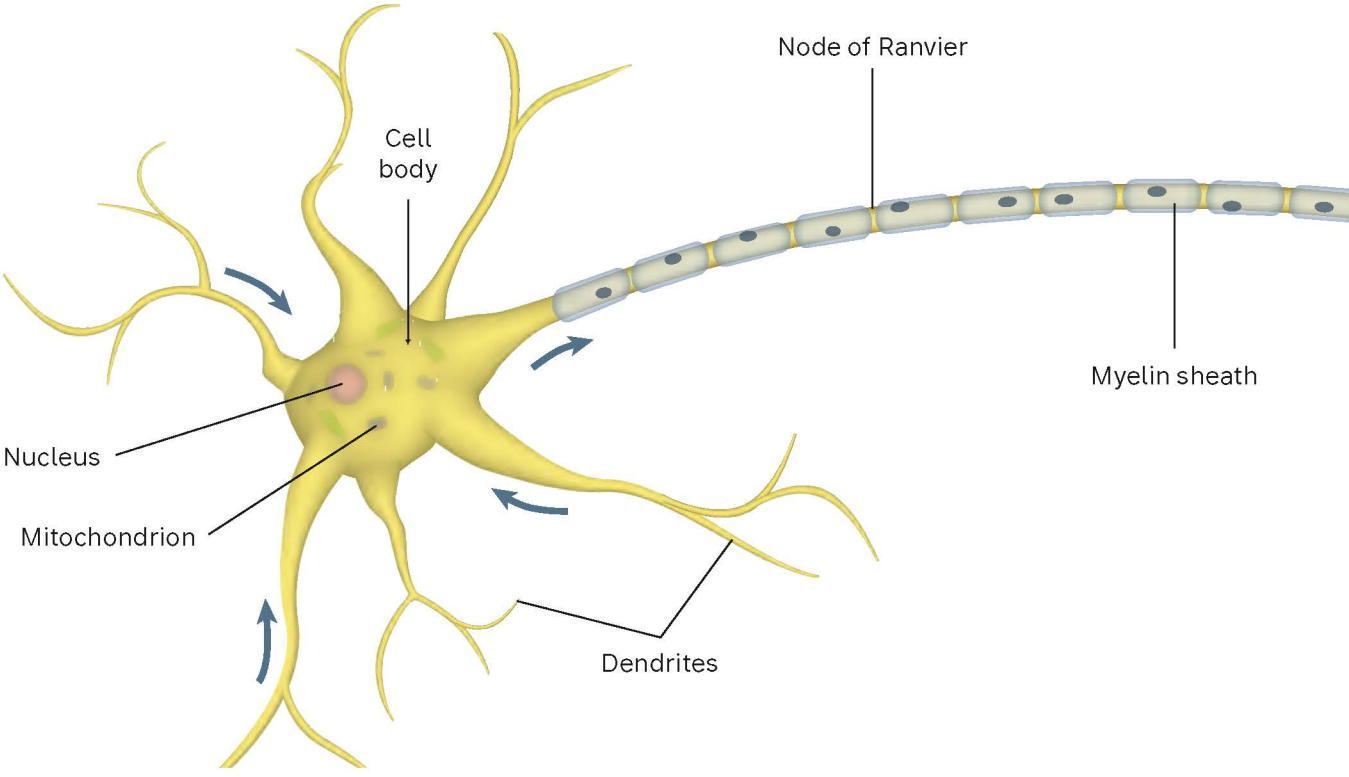
Lloyd coined the term cryoanalgesia in a paper published in "The Lancet" claiming this technique was superior because it is not followed by neuritis or neuroma



2013

inomed introduces the first C3 CryoSystem

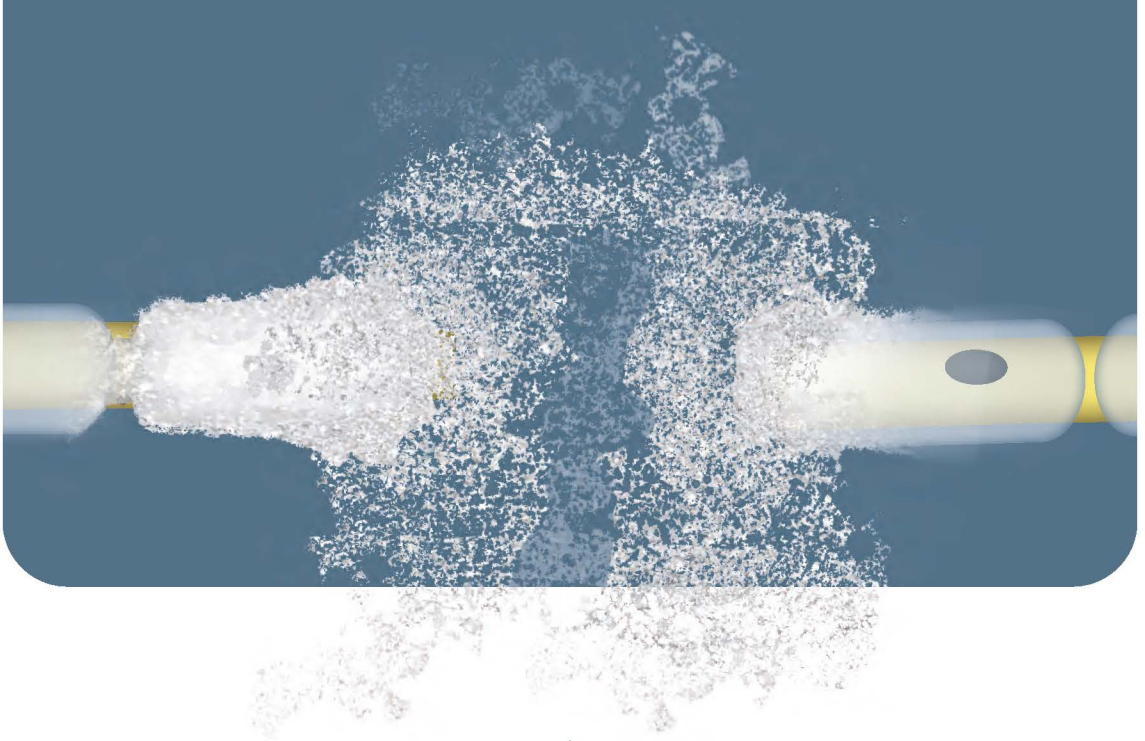
What is cryoanalgesia and how does it work?

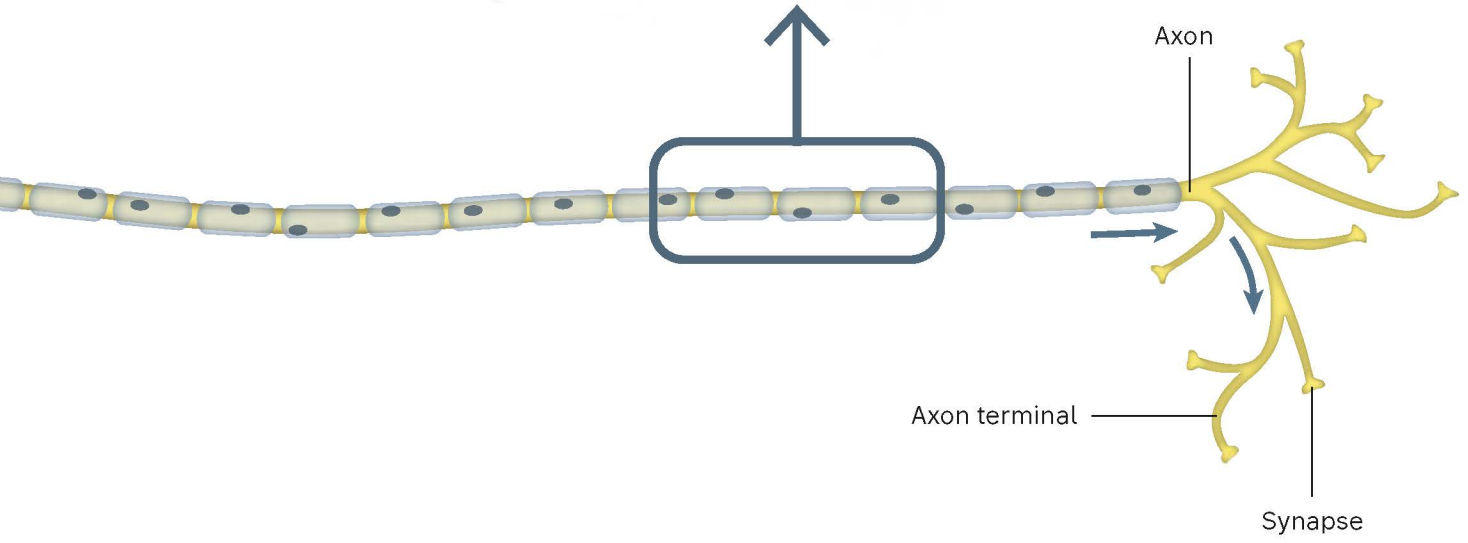


Cryoanalgesia is a specialised technique for providing long-term pain relief where peripheral nerves are partially destroyed by extreme cold in order to create a conduction block and stop the pain signal.

Although cryoanalgesia is an old-established technique, it is gaining a resurgence as an interventional pain technique as the lesion size is comparatively much larger than a radiofrequency heat lesion. It is also reversible and hence a repeatible technique.

The ice crystals created during the procedure disrupt the axon causing Wallerian degeneration distal and slightly proximal to the lesion. The ice crystals only affect the axon and myelin sheath.

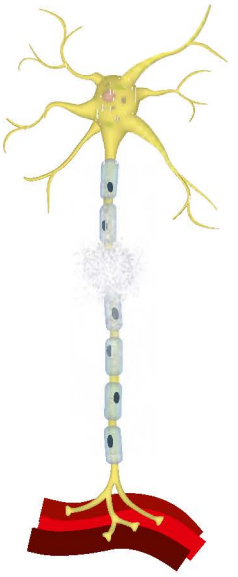



Axon
Axon terminal
Synapse

Cryoanalgesia is ideally suited to treat large myelinated sensory or mixed nerves that are responsible for peripheral pain

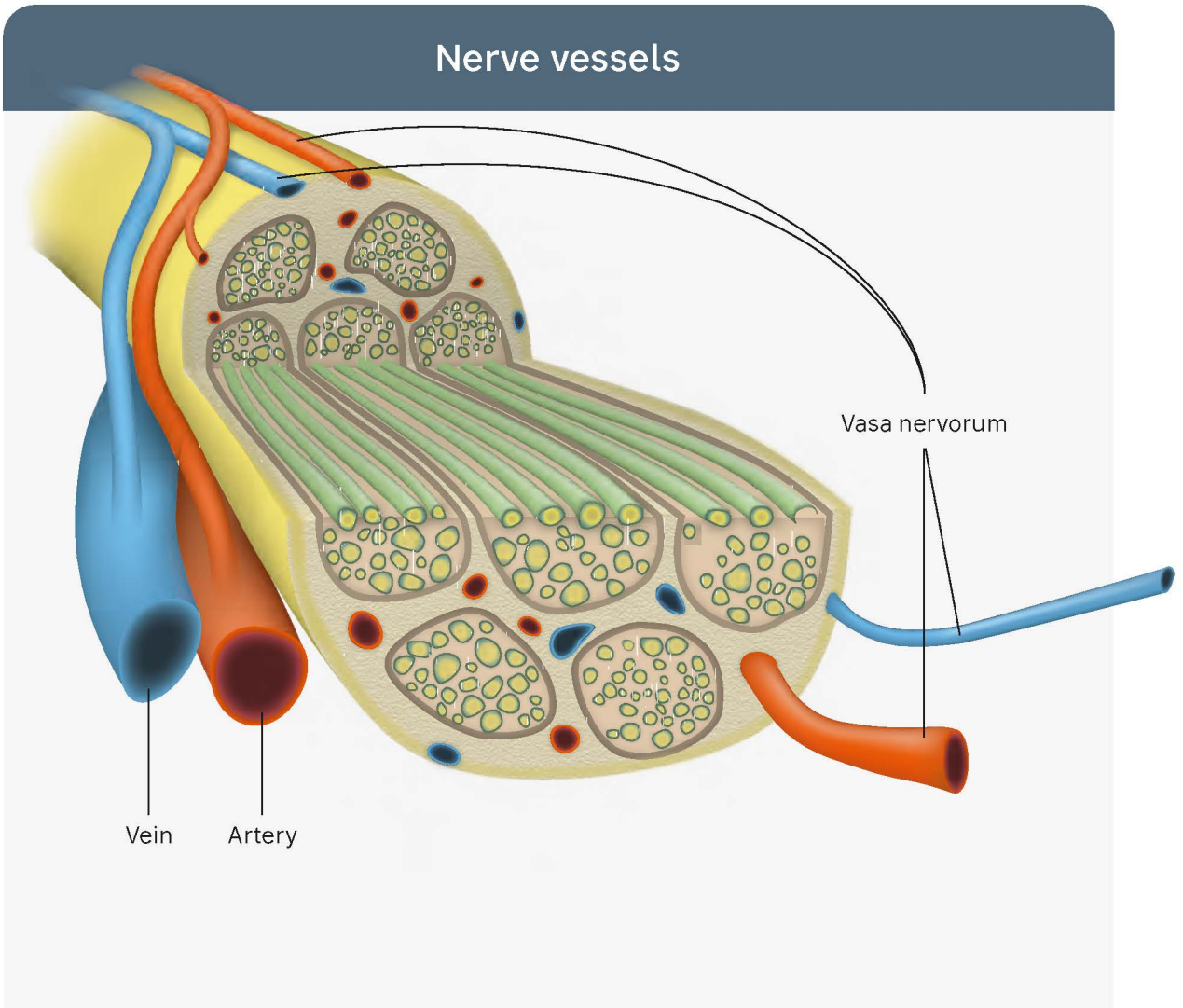
The cells regenerate at a rate of 1 mm per day and the analgesic effect is temporary and dependent on the quality of the freezing. Although the analgesic effect continues after the axon has regenerated, the duration of pain relief felt by the patient is comparable to that of a radiofrequency procedure.

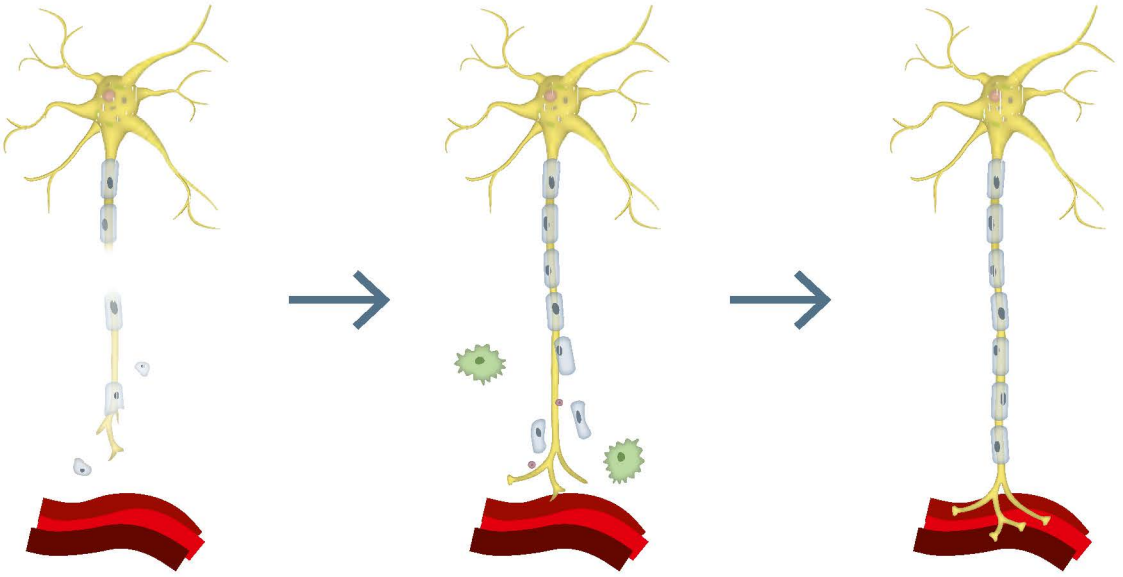
The long term analgesic affect is due to the fact that ice crystals, which destroy the axon, also create vascular damage to the vasa nervorum, which produces a severe endoneural oedema.



1. Ice ball formation

An ice ball is formed around the targeted nerve, freezing induces either a neuropraxic or axonotmesis injury depending on the temperature attained.





2. Degeneration

When temperatures of more than -20 °C are reached, Wallerian degeneration of the axon ensues.

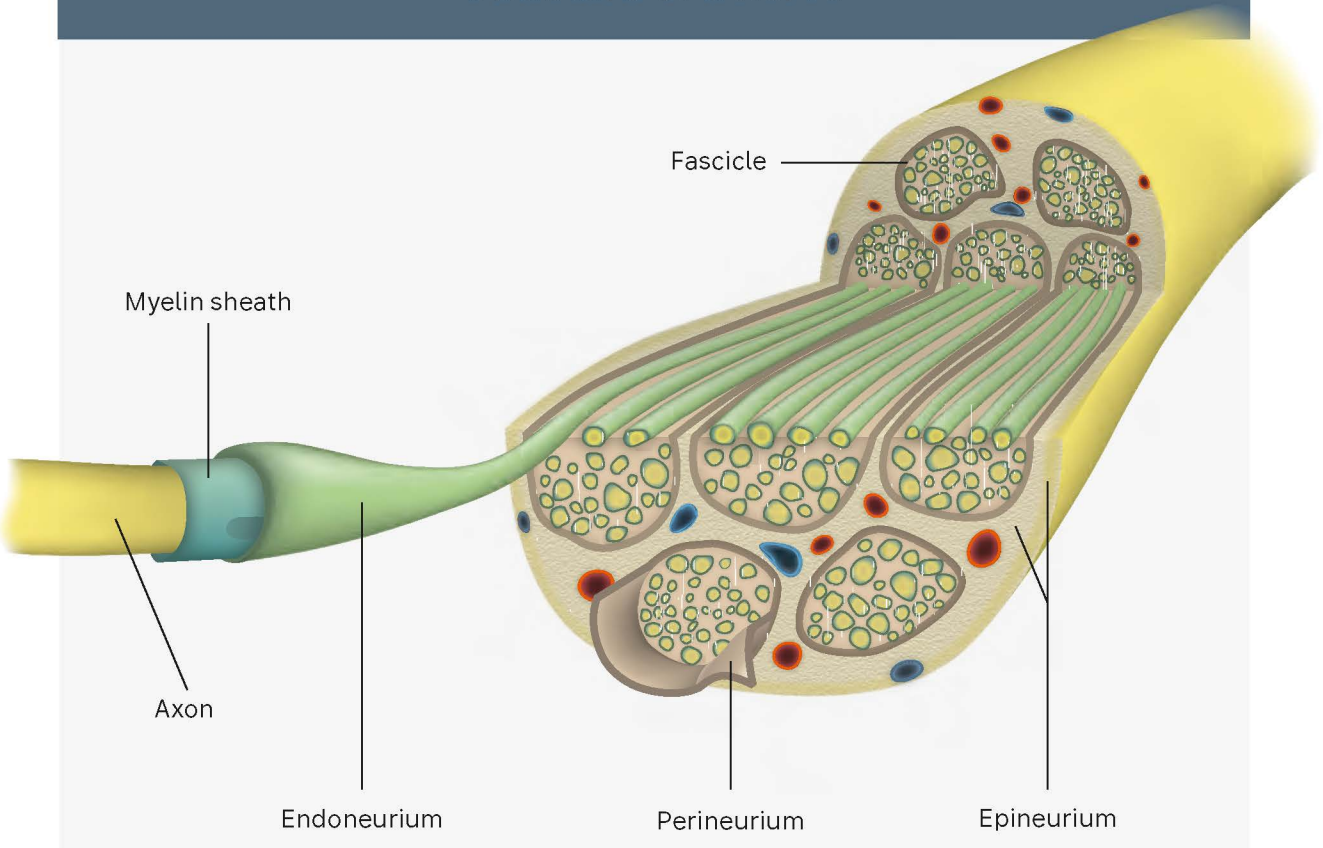
3. Regeneration

The axon regenerates at a rate of 1 mm per day.

4. Reinnervation

The axon is fully regenerated. The analgesic effect is maintained even when the nerves have fully regenerated.

Structure of a nerve



James Prescott Joule

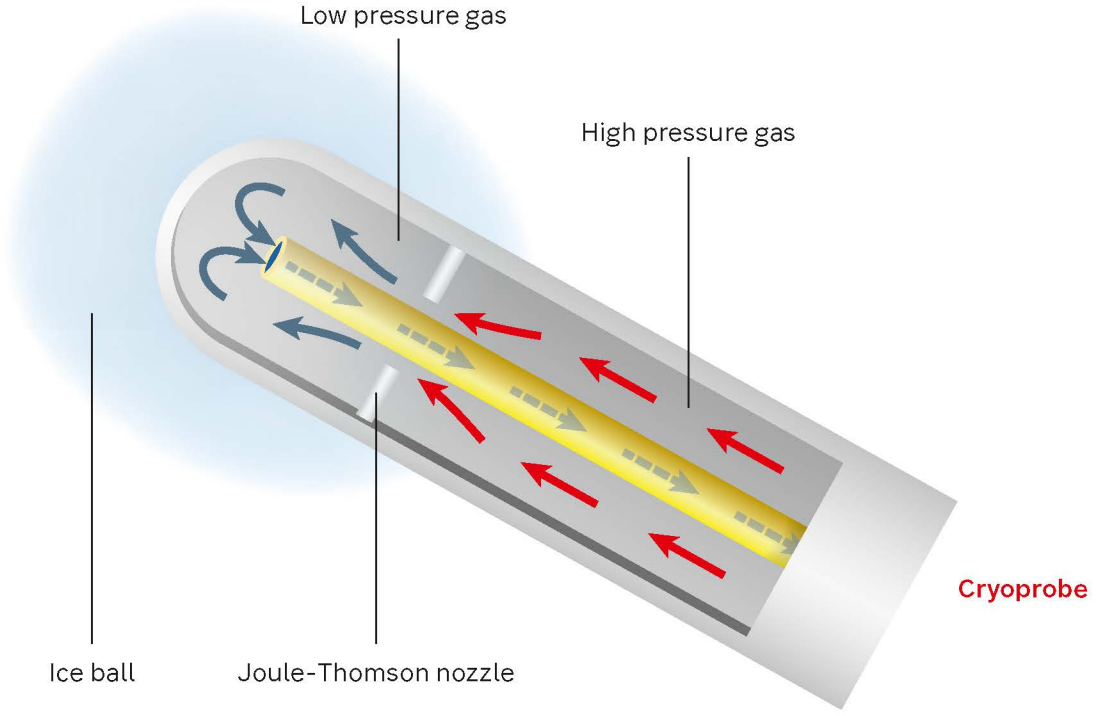
William Thomson

Two British physicists who developed the thermo-dynamic principles that the cryoprobe utilises in order to create an ice ball

Physics behind a cryoanalgesia cryoprobe

A cryoanalgesia cryoprobe works by using the Joule-Thomson effect: a compressed gas, either carbon dioxide (CO_2) or nitrous oxide (N_2O), is passed through a narrow tube and then suddenly allowed to expand at the tip of the outer sealed probe.

The pressure drop from 650–800 psi to 80–100 psi results in a rapid decrease in temperature and a cooling of the probe tip. Absorption of heat from surrounding tissues accompanies expansion of any gas, according to the principles of general gas law; this is the adiabatic principle of gas cooling extraction or the Joule-Thomson effect.
The tissue around the probe rapidly cools and an ice ball is formed. The ice ball varies in size depending on probe size, freeze time, tissue permeability to water and the presence of any vascular structures, which may cause a heat sink. Precise levels of gas flow through the cryoprobe are essential for maximum efficiency. Inadequate gas flow does not freeze tissue, excessive gas flow results in freezing down the stem of the cryoprobe.

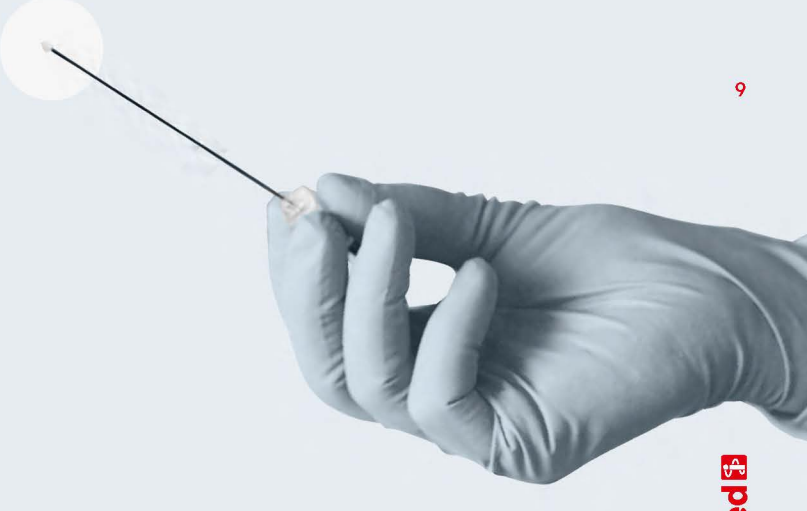


Is it possible to cause permanent damage to the peripheral nerve?

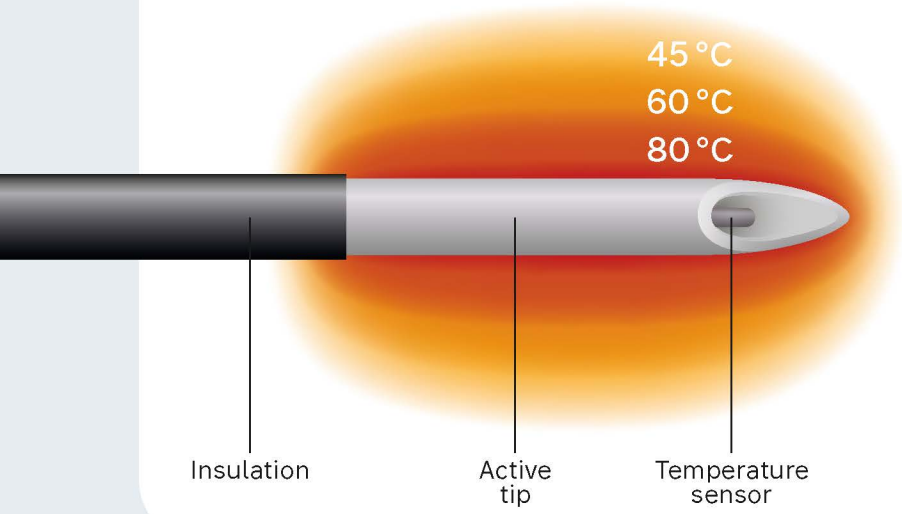
The Sunderland classification of peripheral nerve injury, which was developed from the earlier Seddon classification, outlines the grading of nerve injuries. The application of extreme cold to a nerve root creates a 2nd degree injury or axonotmesis.

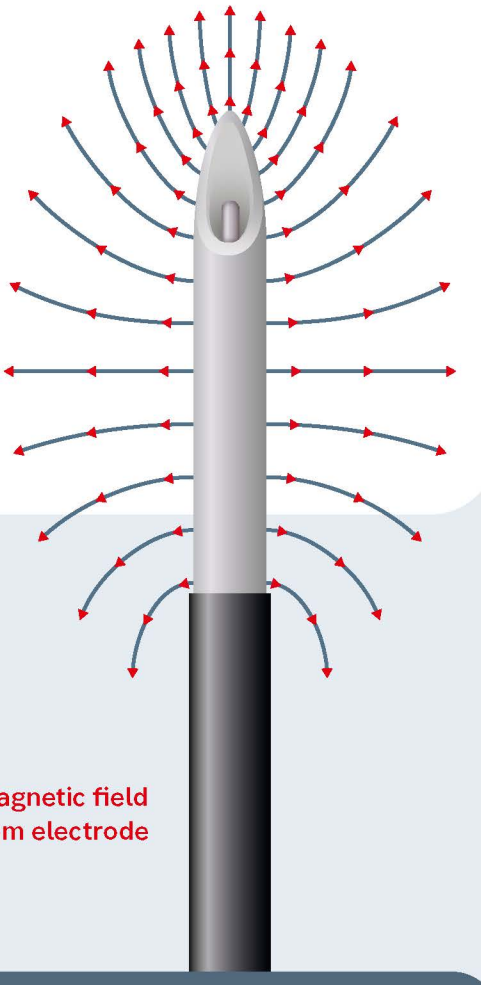
The C3 CryoSystem utilises carbon dioxide (CO_2), which has a cryo boiling point of -79 °C or nitrous oxide (N_2O), which has a cryo boiling point of -88 °C. This means that the C3 CryoProbe can never create a non-reversible cryolesion (Sunderland grade 3 and above), as the temperature at the probe tip cannot be lower than the cryogenic boiling point of the gas used to create the ice ball.

Reversible		
1st degree	Neuropraxia – interruption of conduction, short recovery time	+10 °C to -20 °C
2nd degree	Axonotmesis – loss of continuity of the axon; Wallerian degeneration; preservation of endo-, peri- and epineurium	-20 °C to -100 °C C3 CryoSystem
Non-reversible		
3rd / 4th degree	Neurotmesis – loss of continuity, and colder some loss of continuity of epineurium and perineurium	-140 °C
5th degree	Transection (severe neurotmesis) – gross loss of continuity	



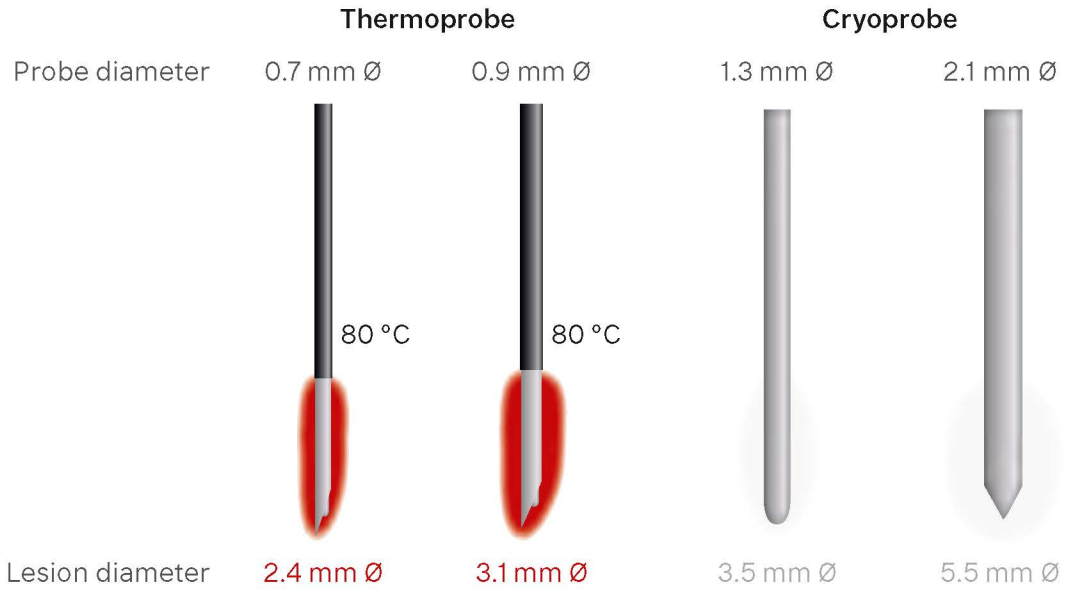
CRF isotherm showing temperature dissipation





PRF electromagnetic field radiating from electrode

Comparison of CRF heat lesion and cryo ice ball lesion



What is the difference between RF lesion and cryolesion?

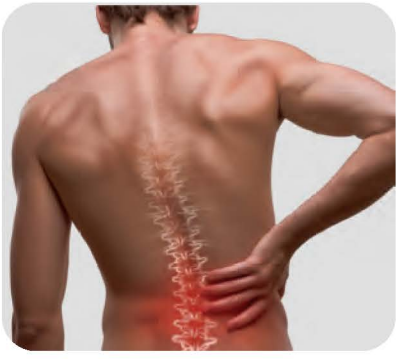
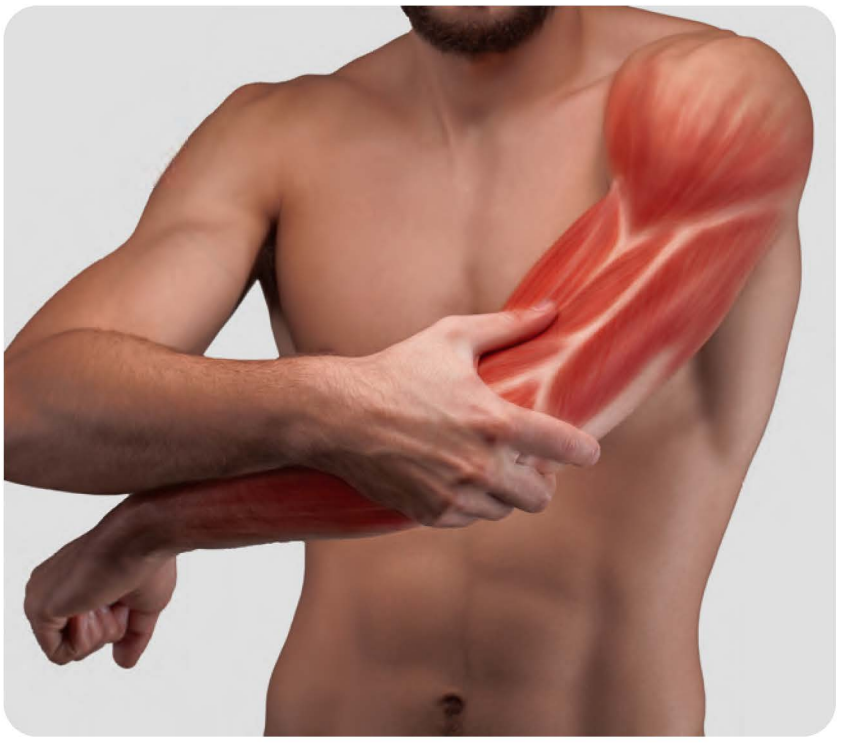
Continuous radiofrequency (CRF) lesion is achieved by prolonged application of continuous electrical current which heats the tissues to neurodestructive temperatures of 60–80 °C. This causes coagulative necrosis of both cellular and acellular structures. Histologically, both axonal degeneration and collagen fibre destruction of the endoneurium, perineurium and epineurium structures occurs. CRF produces a 3rd or 4th degree nerve injury with Wallerian degeneration and associated potential for neuroma and neuritis. CRF is a highly versatile technique, that creates relatively small lesions, which require a high degree of placement acurracy of the cannula and subsequent electrode placement.

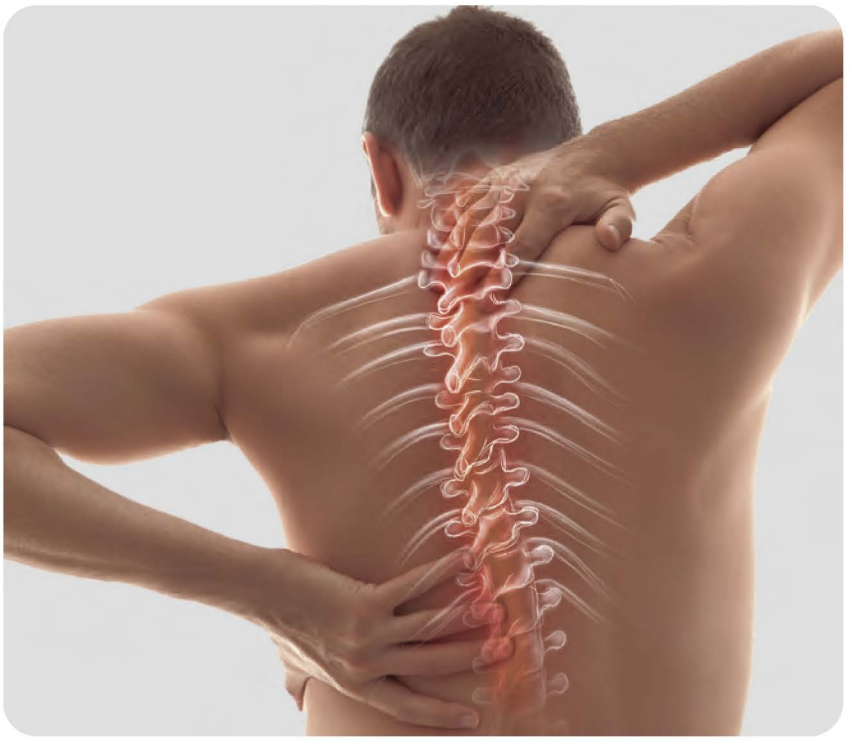
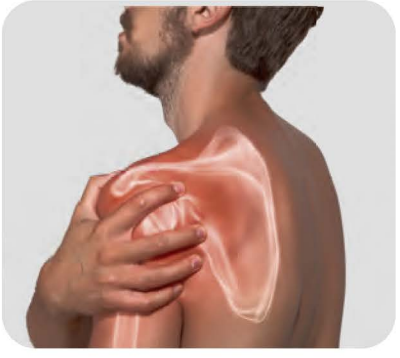
Pulsed radiofrequency (PRF) induces a temporary electromagnetic field, which creates cellular changes that favourably alter the transmission of pain signals, although the true mechanism of how this is achieved remains unclear. The popular view is that PRF alters gene expression, neuronal membrane function and cytokine regulation. PRF does not fit into the Sunderland classification as it is not known how the nerve is altered to suppress the pain signal. PRF creates no tissue destruction and as such it does not have any risk of neuroma formation. The pain relief from PRF is of a shorter duration when comapared to CRF or cryoanalgesia. In addition, the way in which PRF works is not sufficiently understood, which has led to significant differences in its application, calling into question the effectiveness of the procedure.

Cryoanalgesia utilises extreme cold to create a reversible pain conduction block. This is achieved by the formation of an ice ball around the target nerve. The ice crystals create an axonotmesis injury, which creates a reversible lesion that can be easily seen via ultrasound. Cryo ice ball lesions are comparatively much larger than CRF lesions and, as as in the case of PRF, can also be used on mixed sensorimotor peripheral nerves, since cryoneurolysis does not cause any long-term motor deficts. This has led to cryoanalgesia being utilised as a treatment for spasticity as clinicians are able to treat pure motor nerves, pure sensory nerves and mixed sensorimotor nerves.

inomed is the only company that can offer radiofrequency and cryoanalgesia interventional pain treatment solutions



Unique benefits from cryoanalgesia treatment

- Direct visualisation of lesion under ultrasound
  → Can be performed in clinical setting
- In contrast to surgical, chemical or heat ablation, cryoneurolysis does not disrupt the epineurium, endoneurium or perineurium
  → No risk of procedural neuritis
- Reversible → Procedure can be safely repeated
- Low risk treatment option
- Wide range of clinical applications
- Large elliptical lesion compared to radiofrequency
- Immediate pain relief
- Pain relief from 6 months to 2 years
- Effective treatment option for spasticity
- Can be used preoperatively to reduce postoperative pain and opioids in arthroplasty

Clinical applications for cryoanalgesia

Craniofacial pain

- Supraorbital neuralgia
- Infraorbital neuralgia
- Mandibular neuralgia
- Mental neuralgia
- Auriculotemporal neuralgia
- Trigeminal neuralgia
- Posterior auricular neuralgia
- Glossopharyngeal neuralgia

Abdominal and pelvic

- Iliohypogastric neuralgia
- Ilioinguinal neuralgia
- Subgastric neuralgia
- Genitofemoral
- Sacral neuralgia
- Pudendal neuralgia
- Post-thoracotomy neuromas
- Persistent pain post rib fracture
- Thoracic post-herpetic neuralgia

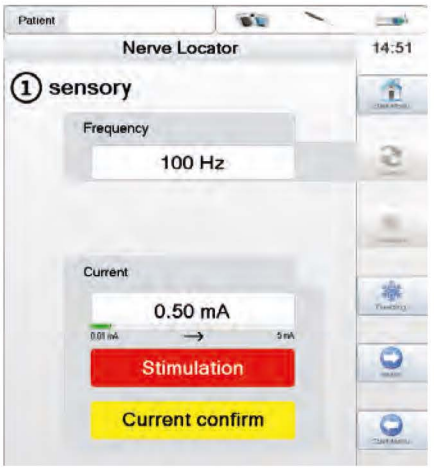
Low back and lower extremity

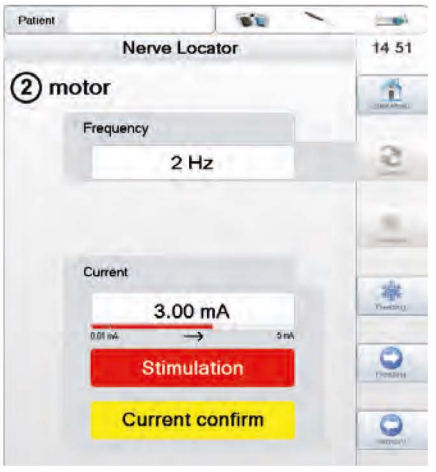
- Facet joint pain
- Interspinous ligament
- Pseudosciatica
- Superior gluteal nerve
- Sacroiliac joint pain
- Cluneal neuralgia
- Lower extremity pain
- Obturator nerve
- Deep peroneal nerve
- Medial & lateral calcaneal nerves
- Peripheral neuropathy
- Phantom limb pain

Upper extremity pain

- Suprascapular nerve
- Superficial radial nerve

Indications Reference – Cryoanalgesia in interventional pain management. Pain Physician 2003 Jul;6(3):345-60 - Dr A. Trescot MD, DABBIPP, FIPP, CIPS – Past President of American Society of Interventional Pain Physicians.


Patient
Nerve Locator
14:51
1 sensory
Frequency
100 Hz
Current
0.50 mA
Stimulation
Current confirm


Patient
Nerve Locator
14 51
2 motor
Frequency
2 Hz
Current
3.00 mA
Stimulation
Current confirm


1
2
3
4
5
6
C3 CryoSystem
inomed
Patient
Emergency Patient
Freezing
14 41
00'42"
Freezing started...
MANUAL
00'15"
Gas pressure
40 bar
Gas flow
18 l/min
Start Defrost
Control

Features of the C3 CryoSystem

The C3 CryoSystem generator is a compact single-channel device that features an easy-to-follow, intuitive graphic display. The C3 has been designed to be used with carbon dioxide (CO_2) and nitrous oxide (N_2O) from a non-siphoned gas cylinder.

The C3 has a list of key features that enhance the end users experience when delivering a cryoneurolysis treatment.

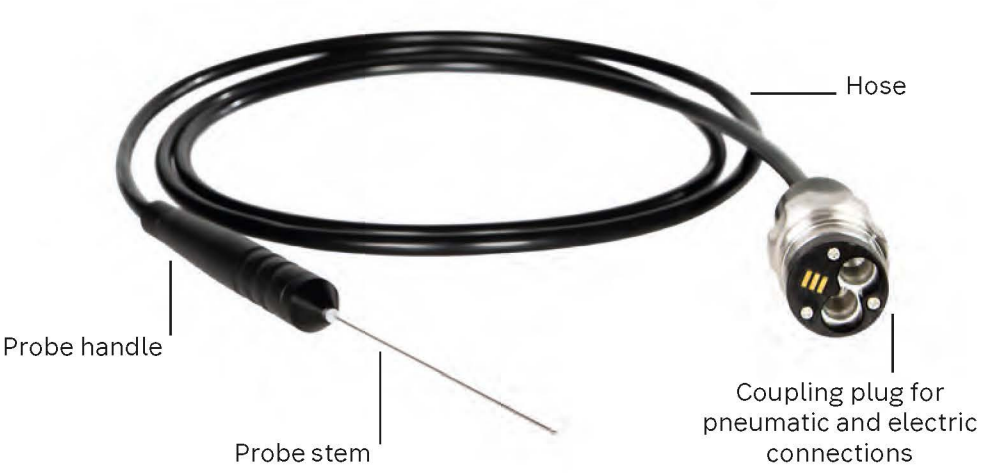
1. Automatic control and regulation of gas flow and pressure
2. Sensory and motor stimulation
3. Six soft key function buttons
4. Central rotary control knob
5. Neutral electrode connection
6. CryoProbe connection port

Additional features include

- Probe recognition
- USB data flash drive
- Barcode reader for patient identification
- Creation of treatment reports
- Acoustic signal to indicate freezing and defrosting cycle

Features of the C3 CryoSystem: C3 CryoProbes

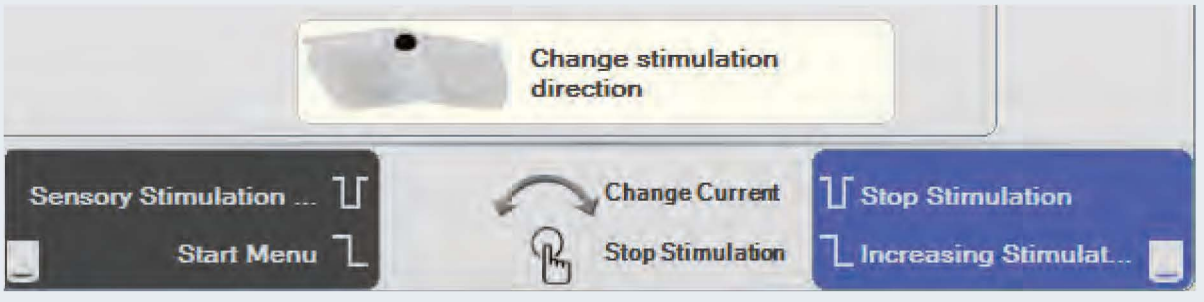
The C3 CryoProbes have been specifically designed to deliver a targeted cryogenic ice ball to peripheral nerves for the purpose of providing prolonged pain relief.
The probes feature a coupling plug, which incorporates various types of connections to the C3 CryoSystem.
The C3 CryoProbes also have an integrated memory that contains the information about the probe type, the required probe pressure and usage information.



Features of the C3 CryoSystem: Foot switch

The C3 CryoSystem has a an optional foot switch that enables the CryoSystem to be operated independently by the clinician. The foot switch is operated by short and long presses on the three switches.

The foot switch functions are displayed at the base of the C3 CryoSystem display screen.

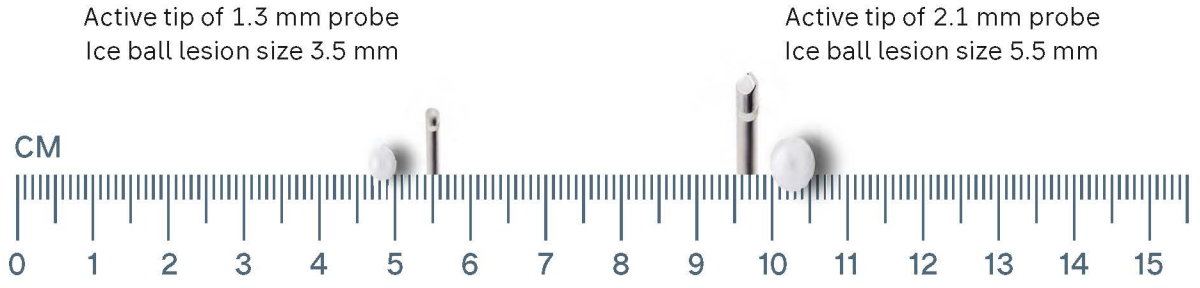


In order to generate an ice ball, the C3 CryoProbes use the Joule-Thomson effect of gas expansion. Cryogenic gas is forced at high pressure to the tip of the probe, where is passes through a Joule-Thomson nozzle, allowing the gas to expand. The resultant pressure drop causes the cryogenic gas to cool rapidly, which freezes the water content in the adjacent tissue.

Rapid defrost is achieved by equalising the pressure on either side of the Joule-Thomson nozzle. Once the defrost is completed, the cryoprobe can be safely removed without any fear of tissue adhesion to the cryoprobe.

The C3 CryoProbes have a built-in nerve stimulator for precise targeting of the nerve. They are monopolar and require a neutral surface electrode positioned on the patient's body to complete the electrical circuit.

The C3 CryoProbes are reusable and available in two sizes: 1.3 mm blunt (15 gauge) and 2.1 mm sharp (12 gauge).



Cannulas

Art. No.	Name	Description
217604	Disposable cannula 15Gx45 with mandrin	Suitable for C3 CryoProbe 1.3 mm (217100) With depth marking for orientation Overall length 74.6 mm, working length 45 mm Outside diameter 1.8 mm (15G) Single use product, EO sterilised
217606	Disposable cannula 15Gx65 with mandrin	Suitable for C3 CryoProbe 1.3 mm (217100) With depth marking for orientation Overall length 94.6 mm, working length 65 mm Outside diameter 1.8 mm (15G) Single use product, EO sterilised
217609	Disposable cannula 15Gx95 with mandrin	Suitable for C3 CryoProbe 1.3 mm (217100) With depth marking for orientation Overall length 124.6 mm, working length 95 mm Outside diameter 1.8 mm (15G) Single use product, EO sterilised
217660	Disposable cannula 12Gx62 with mandrin	Suitable for C3 CryoProbe 2.1 mm (217200) With depth marking for orientation Overall length 96.3 mm, working length 62.5 mm Outside diameter 2.6 mm (12G) Single use product, EO sterilised
217680	Disposable cannula 12Gx92 with mandrin	Suitable for C3 CryoProbe 2.1 mm (217200) With depth marking for orientation Overall length 126.3 mm, working length 92.5 mm Outside diameter 2.6 mm (12G) Single use product, EO sterilised

CryoProbes

Art. No.	Name	Description	
217100	C3 CryoProbe 1.3 mm blunt for C3 CryoSystem	Diameter 1.3 mm, blunt tip Stem length 133 mm Handle length 140 mm Hose length 2 m	
217200	C3 CryoProbe 2.1 mm sharp for C3 CryoSystem	Diameter 2.1 mm, sharp tip Stem length 133 mm Handle length 140 mm Hose length 2 m	

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