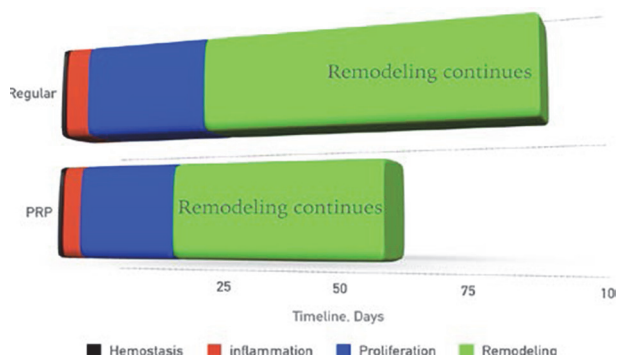
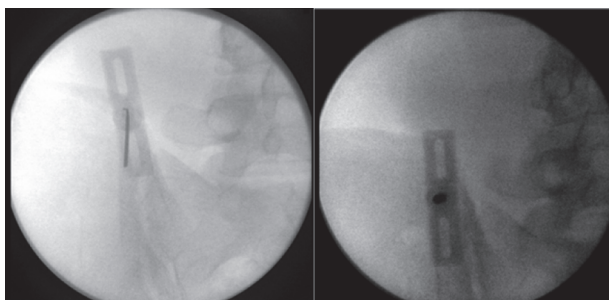


Abstract SP6 Figure 1 Naturally occurring healing process with the 3 phases, inflammatory, proliferative and remodeling varying from 3 days to more than 1 year.



Abstract SP6 Figure 2 Effects of the Platelet Rich Plasmas (PRP) on the healing process.



Abstract SP6 Figure 3 Aspirate of the stem cells via a Jamshidi needle placed in the left iliac crest of a patient, optimally identified using fluoroscopic guidance

Conclusions Regenerative medicine is a novel, advancing way of treating chronic pain. There are limited studies currently, but evidence is evolving for the use and efficacy of regenerative medicine techniques as powerful tools in treating chronic pain

Indications for the PRP and BMC vary widely and are based on the regenerative technique and substance used. As such, platelet rich plasma (PRP) is more often used in musculo-skeletal conditions while use of mesenchymal stem cells have been reported to effectively treat intervertebral disc pathology.

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SP7

CRYONEUROLYSIS OF CUTANEOUS NERVES: WHAT SHOULD WE KNOW?

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Neuropathic pain after surgery and trauma can be severe and debilitating and lead to low quality of life. The frequency of persistent neuropathic pain after surgery and trauma is as high as 10–50% depending on the type of surgery.^{1,2} Very often the pain problem remains unsolved despite extensive and thorough investigation of possible medical, surgical and traumatic causes of the pain problem including exploratory surgery and other interventions.

A main generator of persistent postsurgical neuropathic pain is cutaneous neuropathy, which is due to injury of peripheral nerves innervating the skin and the pain is localized in the skin area innervated by the injured nerve. Thus, neuropathy can appear in any skin area innervated by a nerve injured by surgery or trauma. Injury of cutaneous nerves during surgery cannot be avoided as the entire skin is innervated by a dense network of ramifications of cutaneous nerves. Often the injured nerve regenerates and normal sensation is reestablished. When this does not happen, the injured nerve endings start constant or intermittent firing of pain signals. Cutaneous neuropathy typically feels intense, burning, sharp, or like electric shock.

Cryoneurolysis for the treatment of neuropathic pain after surgery and trauma is approved by in the States and Europe³: A purpose-made double-barrel needle (gauged 1–2 mm) is inserted until the needle tip touches the target nerve. The cryoneurolysis system makes the needle tip generate a few-mm-wide ice-ball that interrupts the nerve fibers. The ice-ball is generated by gas (typically carbon dioxide, CO₂) driven by high pressure through the inner needle to an opening at the tip of the inner needle. The gas expansion instantly cools the gas (Joule-Thomsons effect) and the needle tip is cooled down to minus 60–80°C depending on the choice of gas. The gas is vented back to the cryoneurolysis system via the outer needle. Thus, the cryoprobe is designed as a 'closed circuit', and the gas stays contained inside the double-needle.⁴ The duration of the freezing is typically two minutes creating the few mm thick ice-ball at the tip of the needle. Repetition of the freeze/thaw cycle can increase the thickness of the ice-ball.⁴

The virtue of cryoneurolysis with carbon dioxide as opposed to globally neurodestructive techniques such as radio-frequency ablation (RFA) and glycerol injection and surgical transection is that cryoneurolysis with carbon dioxide selectively interrupts the axons in the target nerve and their myelin sheaths but leaves the connective tissue skeleton of the nerve intact securing normal regeneration of the axons and their sheaths.⁵ This relieves the neuropathic pain for 4–12 months, while normal nerve fiber regeneration is ongoing.^{5,6}

The neurodestructive effect of extreme cold is well-established. Sunderland expanded Seddon's classification of nerve injury due to cold from three to five categories in 1953.^{7,8}

Together, the five categories make a continuum of increasing severity of nerve injury from no macroscopic structural injury to irreversible destruction of the entire nerve trunk. The target of therapeutic cryoneurolysis is the category axonotmesis. This is selective destruction of axons and myelin sheaths leaving the connective neural tissue skeleton intact by freezing the target thoroughly in the temperature range from minus 20 to minus 100 degrees Celcius. Temperatures exceeding this range would lead to neurotmesis, which is irreversible total neurodestruction.⁶

Cryoneurolysis with carbon dioxide never reach temperature lower than minus 78 degrees Celcius as this is the boiling point of the gas. The phase transition from gas to a solid occurs when carbon dioxide is cooled below the boiling points. Consequently, a cryoneurolysis system using carbon dioxide is safe guarded against the irreversible nerve destruction of neurotmesis.⁶

The only adverse events associated with cryoneurolysis using carbon dioxide are rarely occurring incidents of short-duration localized pain, minor swelling, bleeding or infection at the site of intervention. No studies have reported any serious or persistent adverse effects even after repeated cryoneurolysis.^{9,10} Cryoneurolysis can be repeated as the maintained integrity of the endoneurium (axonotmesis) allows uncomplicated normal axonal regeneration.

Clinical cryoneurolysis studies have been carried out on a range of cutaneous nerves: the lateral femoral cutaneous nerve,^{11,12} the intermediary femoral cutaneous nerves,¹³ the posterior femoral cutaneous nerve,¹⁴ the genitofemoral,¹⁵ the pudendal nerve,¹⁶ the sural nerve,¹⁷ the occipital nerve,^{18–20} the intercostal nerves,^{21,22} the intercostobrachial nerve,²³ the ilioinguinal and iliohypogastricus nerves,^{24,25} and the saphenous nerve.^{26,27} In addition, a study of cryoneurolysis has been carried out on large mixed sensori-motor nerves such as the femoral, sciatic and obturator nerves.²⁸ Follow-up demonstrated complete regeneration of muscle strength in the innervated muscles.²⁸

Most of the studies cited above present data of significant pain relief with cryoneurolysis of cutaneous nerves – but the results are heterogenous and flawed by high incidences of failure of pain relief.

The first cause of failure of cryoneurolysis is lack of knowledge about cutaneous nerves and cutaneous nerve territories. Consequently, many cutaneous nerves that are relevant for cutaneous neuropathy after surgery and trauma are never attempted to be targeted. The second cause of failure is lack of direct visual ultrasonographic identification of true target nerve. The third cause of failure is inaccuracy of needle tip placement exactly adjacent to the target nerve. The fourth cause of failure is the small diameter of the ice-ball capable of generating freezing below -20 degrees Celcius, as the -20 degrees Celcius isotherm is just a few millimeters from the surface of the tip of the cryoprobe when CO₂ is the gas of choice.

During the last 20 years ultrasound has become a pervasive tool for visualization and localization and local anesthetic blockade of peripheral nerves in clinical anesthesiology. However, the resolution of conventional 'high-frequency ultrasound' (up to 20 MHz) just allows visualization of the large mixed sensori-motor nerves and major sensory nerves (eg. the lateral femoral cutaneous nerve). Thus, the caliber of the ubiquitous small skin nerves has so far been too small to be

visible and possible targets using conventional high-frequency ultrasound as interventional guidance. In order to solve this problem cryoneurolysis has been applied either on the few large and sensory nerves visible with ultrasound or cryoneurolysis has been applied along 'treatment lines' in presumed locations of small invisible neuropathic nerves. This has compromised the success rate of cryoneurolysis.

Conclusion In summary, persistent painful cutaneous neuropathy is frequent after surgery and trauma. However, (1) the specific skin area of neuropathy is rarely localized, (2) the specific associated neuropathic nerves are not identified and visualized, (3) cryoneurolysis is an effective and safe technology for focused and specific treatment of cutaneous neuropathy, but the applicability is limited by lack of techniques and technology for ultrasound guided visualization of many small cutaneous nerves, (4) the applicability of cryoneurolysis with CO₂ is limited by the narrow action radius from the surface of the tip of the cryoprobe to the -20 degrees Celcius isotherm.

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SP8 CRYONEUROLYSIS OF CUTANEOUS NERVES

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Severe, persistent neuropathic pain after surgery and trauma occurs as frequent as 10–50%.^{1,2} The pain is typically due to cutaneous neuropathy, which is due to injury of skin nerves.

Cryoneurolysis can be used to treat cutaneous neuropathy³: A double-barrel needle is inserted until the needle tip touches the target nerve. A few-mm-wide ice-ball is generated and interrupts the nerve fibers. The needle tip is cooled down to minus 60–80°C when using carbondioxide (CO₂). The cryoprobe is a ‘closed circuit’.⁴

Cryoneurolysis with CO₂ interrupts the axons and their myelin sheaths but leaves the connective tissue skeleton of the nerve intact securing normal neural regeneration.⁵ This relieves the neuropathic pain for 4–12 months.^{5,6} Cryoneurolysis with CO₂ never reach temperature lower than minus 78 degrees Celcius as this is the boiling point of the gas. Thus, the nerve is safe-guarded against irreversible destruction, which occurs when the freezing exceeds minus 100 degrees Celcius.⁶

No serious or persistent adverse effects have been reported even after repeated cryoneurolysis.^{9,10} Clinical cryoneurolysis studies have been carried out on various cutaneous nerves. Most of these studies present data of pain relief with cryoneurolysis of cutaneous nerves – but the results are heterogeneous and flawed by high incidences of failure of pain relief.

The causes of failure are: (a) Lack of knowledge about specific cutaneous nerves and cutaneous nerve territories; (b) lack of direct visual ultrasonographic identification of true target nerve; (c) inaccuracy of needle tip placement exactly adjacent to the target nerve; (d) a very small diameter of the ice-ball capable of generating freezing below -20 degrees Celcius.

Conclusion In summary, persistent painful cutaneous neuropathy is frequent after surgery and trauma. However, the applicability of cryoneurolysis with CO₂ is limited by a range of technical problems.

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SP9 OPTIMAL PERIPHERAL NERVE BLOCKS FOR TOTAL KNEE ARTHROPLASTY – 2ND OPINION

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Total knee arthroplasty (TKA) generates moderate to severe pain especially the first postsurgical days – unless the pain is managed efficiently. Multimodal analgesia (MMA) and local anaesthetics can solve the pain problem the critical first 24 postsurgical hours.

The first step of efficient pain management after TKA is MMA: Paracetamol, NSAIDs, intravenous dexamethasone, and escape opioid. The second step is local analgesics. That is mainly a choice between intraoperative local infiltration analgesia (LIA) by the surgeon or peripheral nerve blocks by the anaesthesiologist.

Complete anaesthesia of the genicular innervation would require nerve blockade of the femoral, obturator and sciatic nerves. The femoral nerve innervates the anterior knee region. The obturator and sciatic nerves innervate the posterior knee region.

Complete block of the three nerves would impede ambulation. A better strategy is analgesia of the relevant peripheral nerve branches.¹

The posterior genicular innervation is due to the popliteal plexus (the posterior branch of the obturator nerve and the tibial nerve). It can be anaesthetized either by LIA or an iPACK block or a popliteal plexus block (PPB).

The most important branch of the femoral nerve for TKA is the medial vastus nerve that innervates the medial retinaculum and the capsule. In addition, the anterior femoral cutaneous nerves and the infrapatellar saphenous nerve branch innervate the integumentum of the surgical incisional field. All these femoral nerve branches can be anaesthetized by a proximal femoral triangle block.²

The anterior inferomedial and inferolateral genicular innervation is due to tibial and peroneal nerve branches respectively. They are of occasional relevance for analgesia after TKA.

In summary, effective analgesia after TKA can be conducted by two different strategies:

- (a) MMA + LIA + escape nerve blocks.
- (b) MMA + nerve blocks (iPACK or PPB for the posterior innervation and proximal femoral triangle block for the anterior innervation)

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