

Probe-Free Method for Long-Lasting Sensory Analgesia Using an Injectable and Neural Selective Ice Slurry: Cooling Capacity Characterization



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INTRO

- Today's commercially available cryoneurolysis devices are not simple to use [1]. They require meticulous probe placement to create a perineural ice ball at temperatures between -20°C and -100°C to incite nerve degeneration.
- Recent published pre-clinical work shows that milder temperature ranges (at -9°C) can also reduce myelinated nerve fiber density WHILE sparing unmyelinated nerve fibers & without damage to surrounding skin and muscle tissues [2].

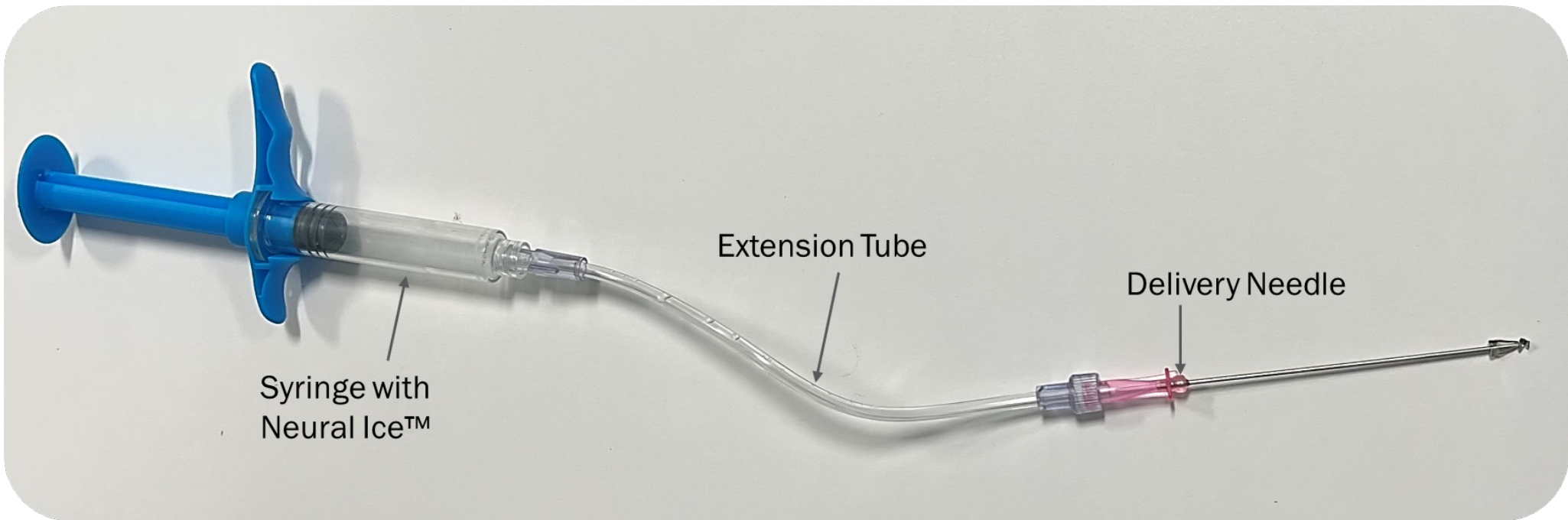
METHODS

- The cooling system is comprised of two major components: Neural Ice™ and a delivery system (Coolio; Brixton Biosciences, Cambridge, MA).

Neural Ice



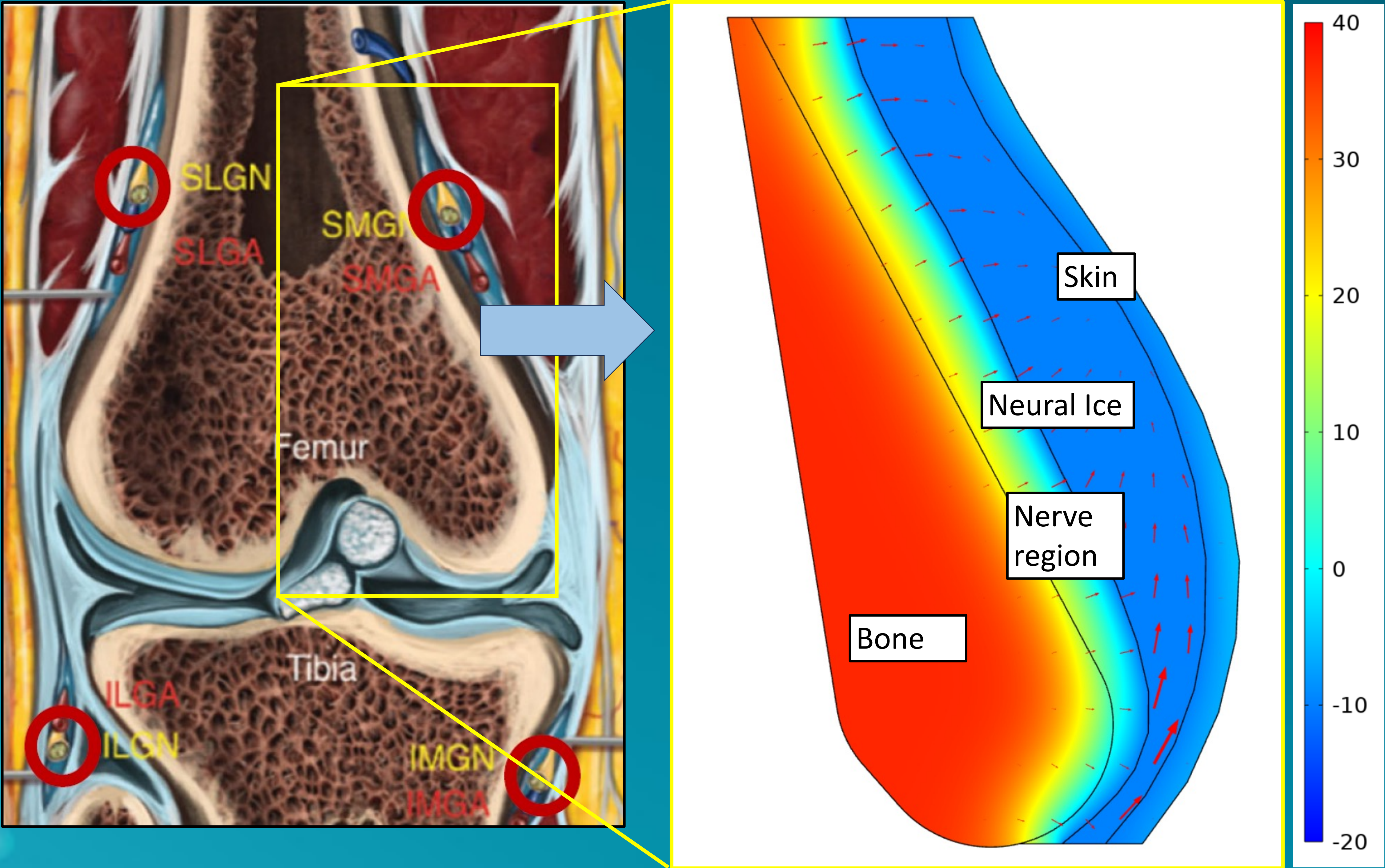
Neural Ice Delivery System



- The tissue cooling effect was characterized using benchtop calorimetry, coupled with finite element thermal fluid models to predict, pressure, velocity, shear rate, and temperature along the delivery system (COMSOL).
- For benchtop testing, a characterization fixture was designed with a tissue analog that has an initial temperature of 40°C.
- Neural Ice was injected into the insulated analog and temperature was recorded until thermal equilibrium was reached, defined as a temperature difference of ~1°C.
- Neural Ice injectate treatment zone was modeled and characterized through gross dissection of stained injections around cadaveric knees.



Injectable Neural Ice creates large cooling zones for ease of use



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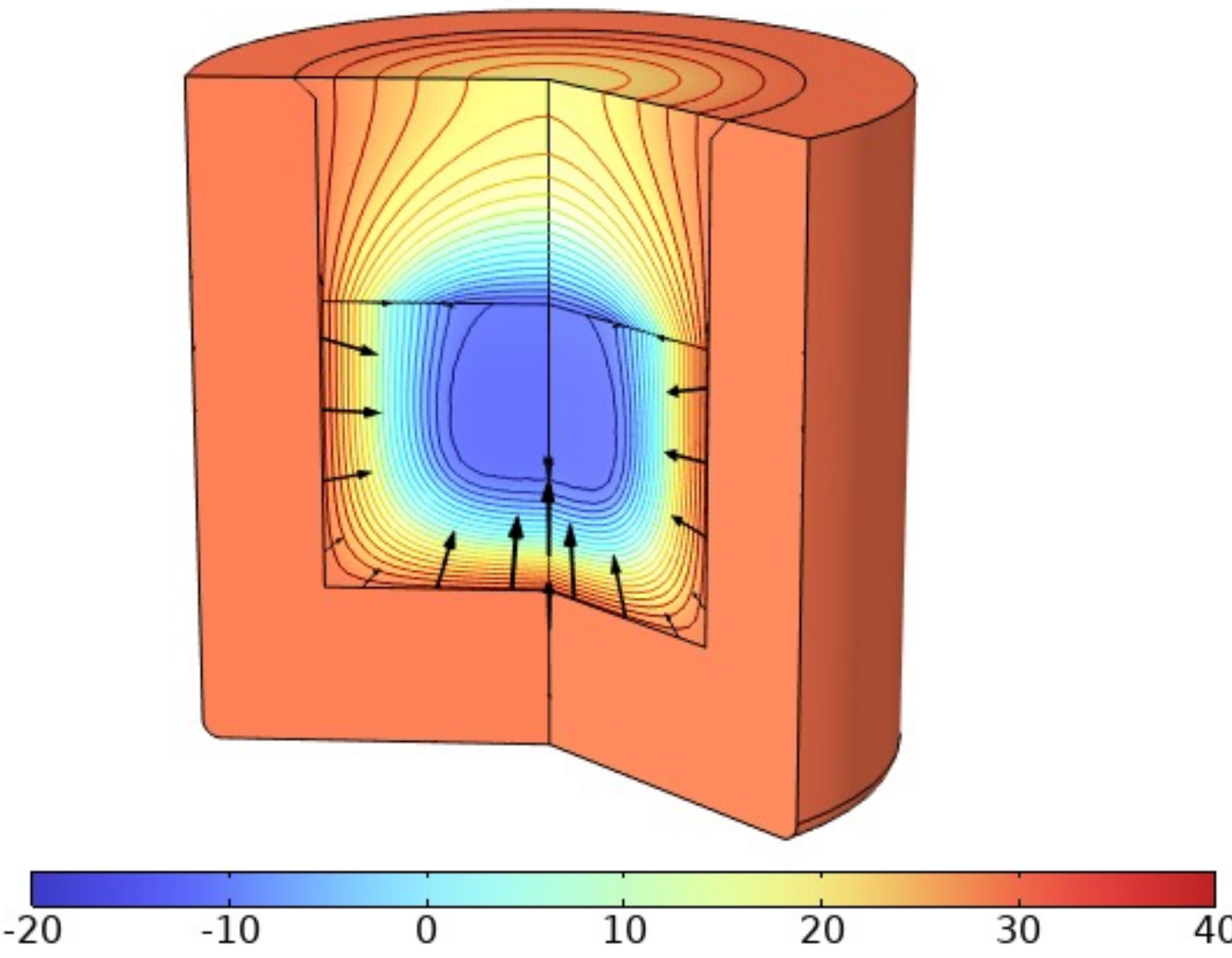
Thermal modeling of the superomedial genicular nerve (red circle) region. Temperature is in degrees Celsius. Arrows show heat flux away from warm tissue into Neural Ice at time = 120s. [3]

Neural Ice is part of an investigational device that has not been approved or cleared for marketing by the FDA

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RESULTS

Neural Ice Calorimetry 120 seconds After Injection



DISCUSSION

- Clinical studies are underway to evaluate the safety and effectiveness of Neural Ice injections as long-lasting analgesia to address chronic pain arising from knee osteoarthritis.
- The presented technique for mild temperature, nerve-selective sensory analgesia is expected to create a larger effective treatment zone with a wider margin of safety compared to probe-based cryoneurolysis.
- **The advantage of performing nerve-selective injection compared to today's probe dependent methods is that direct contact with nerves is not necessary.**
- The landmark-based injection technique compared to probe-based cryoneurolysis, may enable a broader range of providers to utilize regional cold therapy with less of a learning curve for pain treatment and may improve reliability of hitting nerve targets that could improve patient outcomes.
- The presented mechanism of action relies on:
 - Due to its fluid-solid structure, Neural Ice can easily infiltrate the target treatment zone, flowing around & surrounding nerves.
 - The critical thermodynamic property that empowers the Neural Ice is water's large heat of fusion (334 J/g), the required thermal energy to melt ice per unit mass.
 - This melting process draws thermal energy from nerves in the treatment zone, allowing Neural Ice to produce rapid, diffuse, nerve cooling, triggering degeneration.

REFERENCES

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2. Garibyan, L. et al. Neural Selective Cryoneurolysis with Ice Slurry Injection in a Rat Model. *Anesthesiology* **133**, 185–194 (2020).
3. Genicular Nerve Blocks, <https://www.nysora.com/nysora-com-genicular-nerve-blocks/>, Accessed 2024-02-21.