Focused ultrasound peripheral neuromodulation for pain suppression

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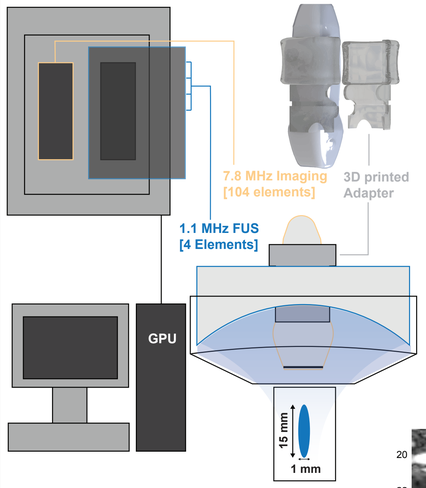
Objectives & Motivation

- A wave of studies have reported that focused ultrasound (FUS) is capable of modulating electrical activity in a wide variety of neural structures: brain circuits, neuronal cells, ion channels, and peripheral nerve fibers[1-11].
- We have shown that FUS can elicit compound muscle activation in mice by stimulating the sciatic nerve[12-13].
- Taken together, the data suggests that FUS may be able to alter somatosensation, yet evidence of pain modulating capabilities is lacking.

Objective:

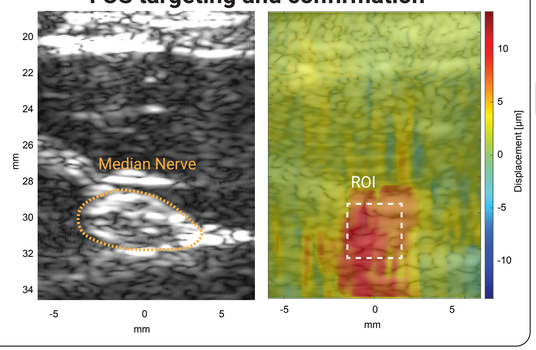
- **Investigate whether FUS nerve neuromodulation is capable of nociceptive and neuropathic pain suppression**

Experimental Setup & Pulse Parameters



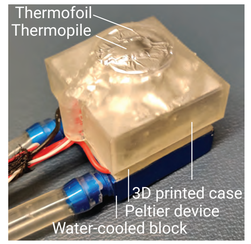
- The system consists of a concentric Imaging transducer (7.8 MHz, Philips) and a FUS transducer (1.1 MHz, Sonic Concepts).
- FUS is driven by a single Verasonics 256 Research Vantage system (128 - Imaging; 128 - FUS; HIFU option).[14]
- The median nerve is identified using compounded plane-wave B-mode and real-time displacement imaging is used to validate delivery to the nerve. [13]
- **5 ms PD, up to 7 MPa, single pulses (study 1) and 10 Hz PRF (study 2) FUS pulses.**

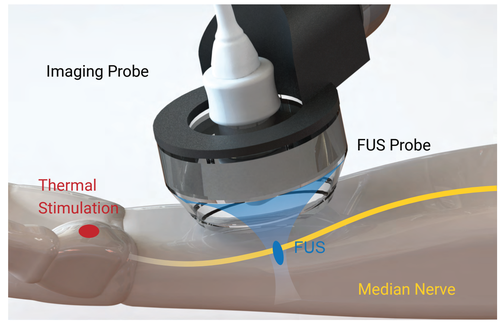
FUS targeting and confirmation



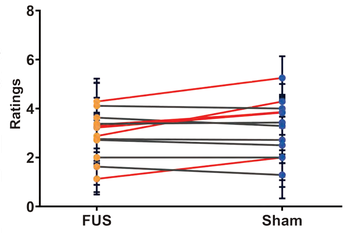
1. B-mode images were used to first target and position the FUS transducer.
2. Displacement imaging, induced by low amplitude FUS pushes, was then used to confirm ultrasound transmission to the nerve and measure nerve displacement.

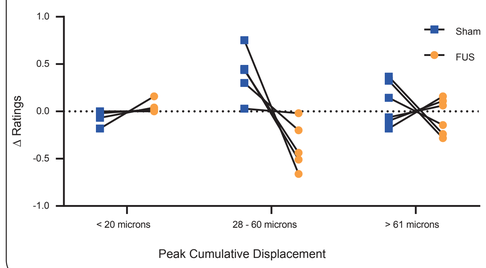
Study 1: FUS suppresses nociceptive pain





- Nociceptive pain was induced using a themo-foil block to generate **painful 2 s thermal heat (60°) at the C6 dermatome.**
- Single FUS and sham pulses were applied to the median nerve during 15 heat stimuli.
- 13 subjects (5 F / 8 M) were employed in this study and asked to rate their pain on the Wong Baker scale.
- 7 of those 13 subjects experienced decreases in percieved nociceptive pain.

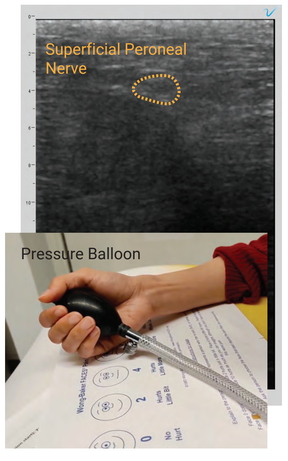


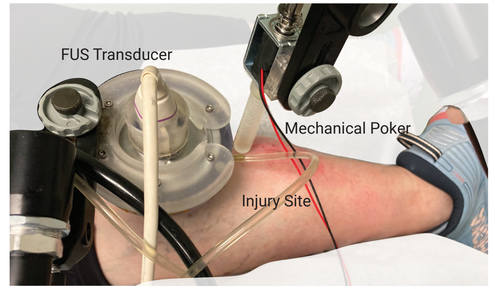


- Rather than FUS transducer driving pressure, changes in pain ratings were associated with measured nerve displacement.
- Nerve displaced between 28-60 microns had higher degrees of pain suppression (average 1.4 units).

Study 2: FUS suppresses neuropathic pain

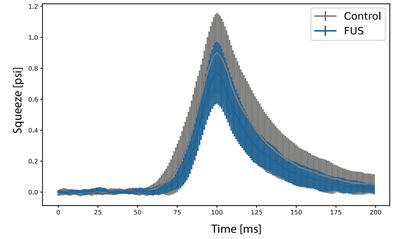
B-mode targeting

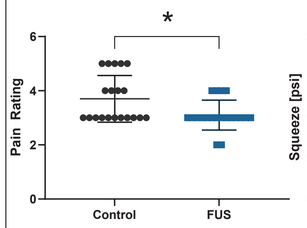




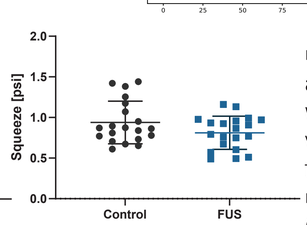
- Patient (n = 1) had a prominent tinel sign at the superficial peroneal nerve as the ankle.
- 40 "pokes" were used to generate reliable neuropathic pain at the injury site.
- FUS/sham pulse trains **(10 s @ 10 Hz PRF)** applied before, during and after pokes

- In addition to Wong Baker pain ratings, the patient was asked to squeeze a pressure sensor balloon in accordance with their perceived pain





0.6 ± 0.2 reduction



0.12 ± 0.07 reduction

- Both pain ratings and peak squeezes were lower for FUS vs sham pulse trains.
- (*) p = 0.0127 (unpaired t-test)

Discussion & Conclusions

- FUS was capable of suppressing nociceptive pain in 53% of healthy volunteer subjects. Moreover, results were linked to effective nerve displacement rather than transducer driving pressures as the same calibrated pressures had displacement variability subject-to-subject.
- Categorization by nerve displacement revealed the optimal range is between 28 and 60 microns. Displacements higher than 60 microns had population of responders and non-responders, indicating there may be more complex effects in this regime.
- Preliminarly, FUS was shown to decrease perceived neuropathic pain from mechanical stimulation in a peroneal nerve entrapment patient.

Future work: Continue the exploration of suppressive FUS on neuropathic pain (sural nerve biopsies, nerve entrapments, and nerve tumors) and investigate multi-biological targeted FUS delivery for pain therapy.

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