Focused Ultrasound

Brain to Peripheral Nerves to Systems

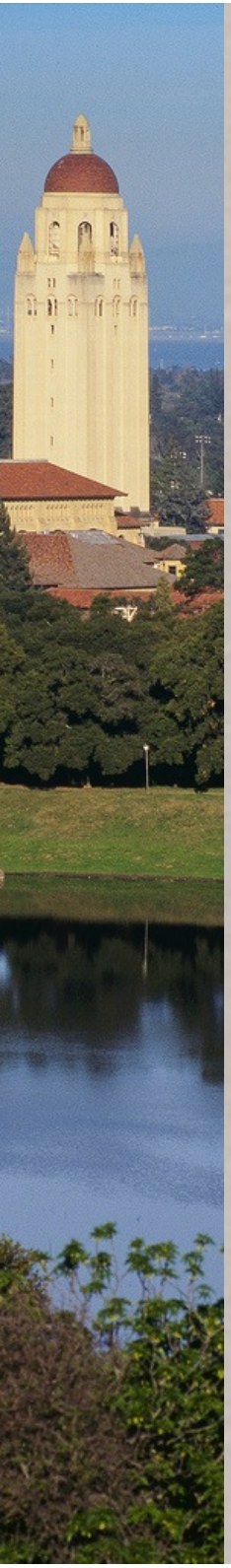
Kim Butts Pauly, Ph.D.

Department of Radiology, BioE, and EE, by courtesy

Stanford University

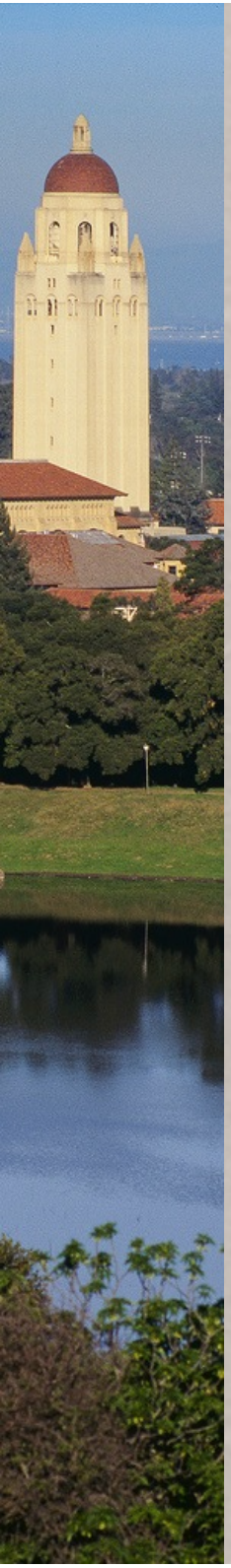
What is Focused Ultrasound?

- large area ultrasound transducer array outside the body
- focused geometrically or electronically
- amplification
- significant intensities deep within the body, without effect in intervening tissues



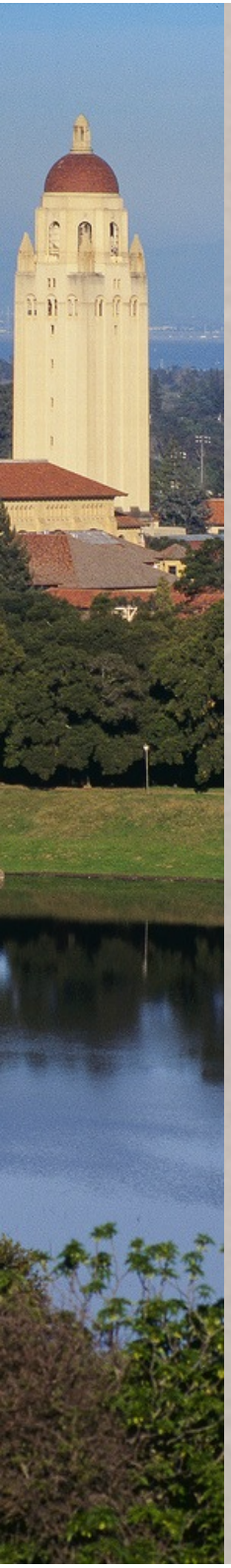
Outline

- Blocks Brain/Peripheral Nerves
- Stimulation Brain/Peripheral Nerves
- Stimulation Organs/Systems



Outline

- Blocks Brain/Peripheral Nerves
  - High Heat: > 55°C (Permanent)
  - Low Heat: < 53°C (Reversible)



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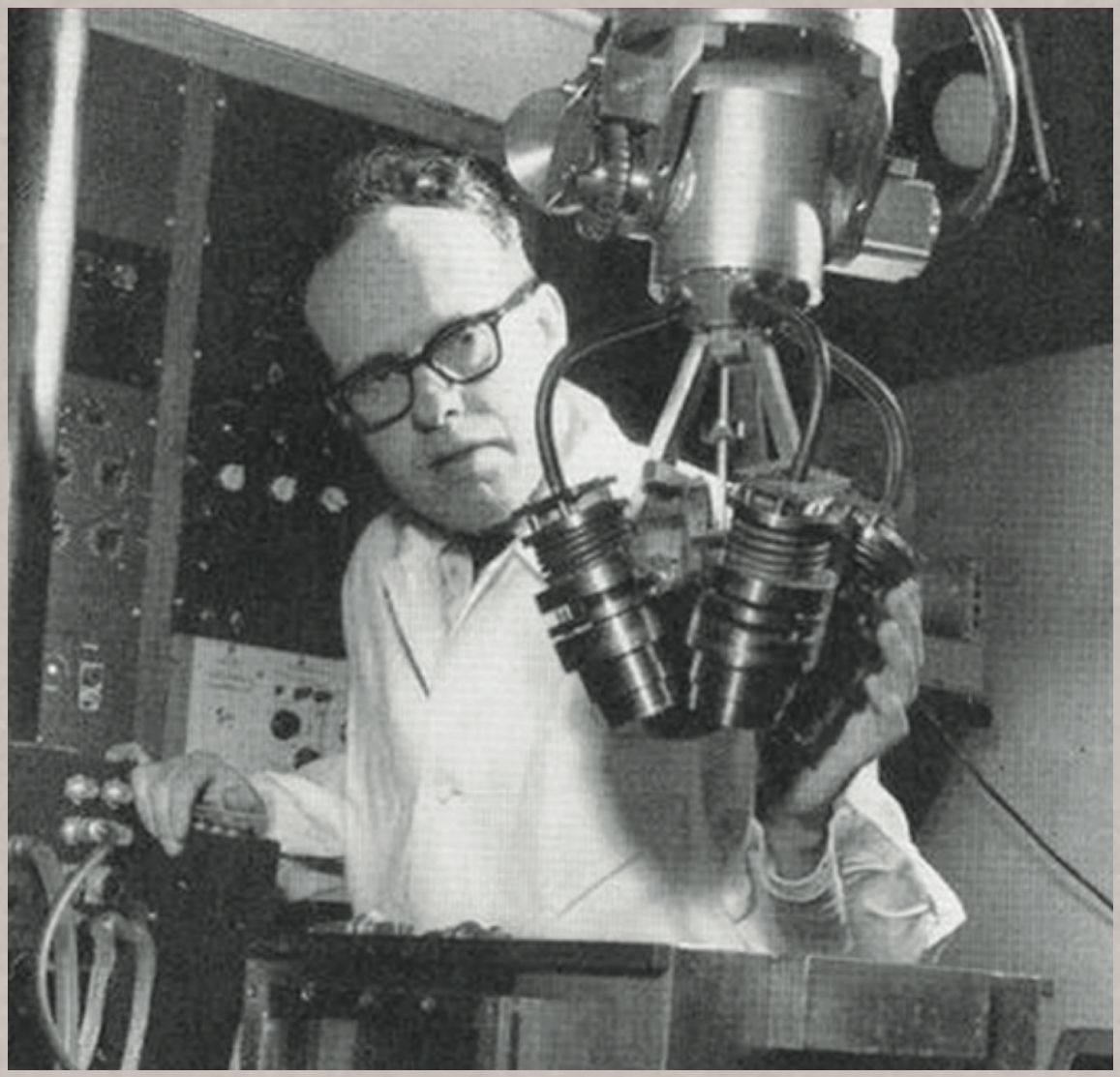
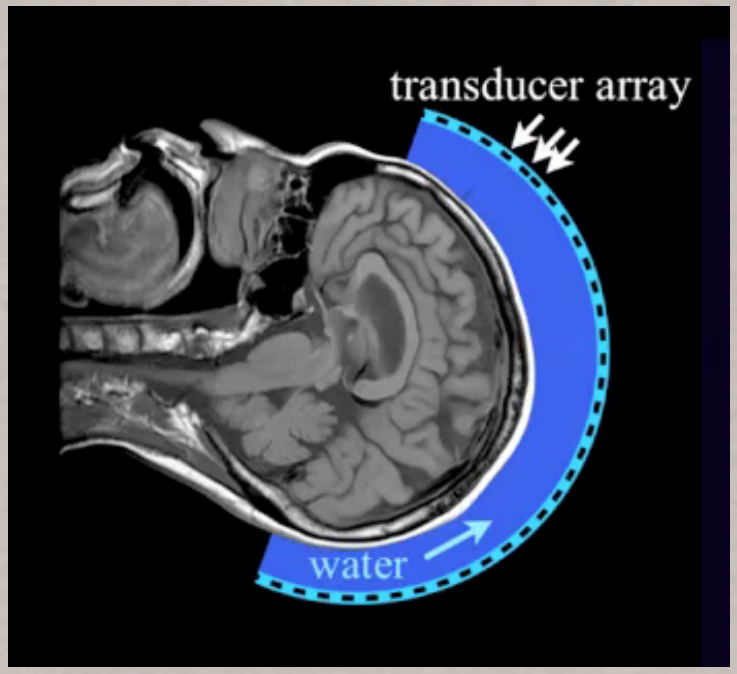


William Fry at the University of Illinois, Champaign, circa 1960, with the early 4-beam high- intensity focused ultrasound (HIFU) applicator for neurosurgery. (from Jagannathan et al. Neurosurgery 64(2), 2009)

Modern System

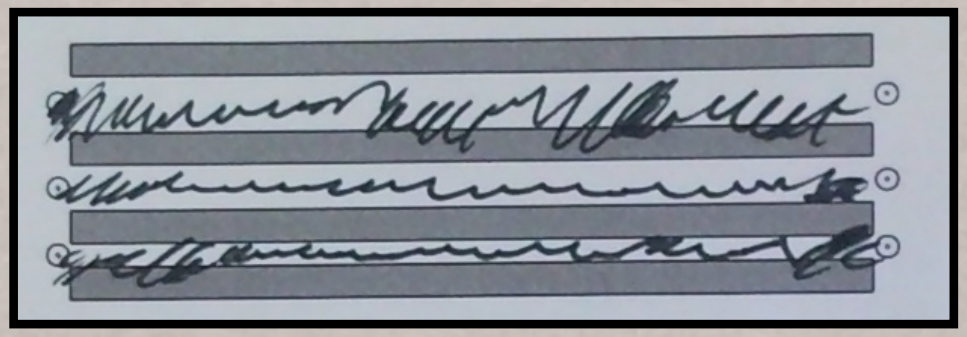


- 1000 elements
- cooled circulating water
- focusing/amplification
- MRI thermometry guidance

Essential Tremor

- 10 million Americans or 3% of the population have an essential tremor.

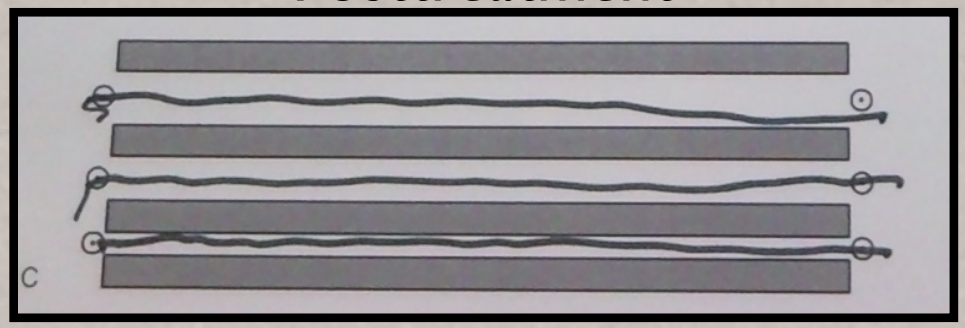
Pretreatment



- Ablate the VIM nucleus in the thalamus

- immediate symptom relief.

Posttreatment



• *Elias WJ, et al. N Engl J Med. 2013 Aug 15;369(7):640-8*

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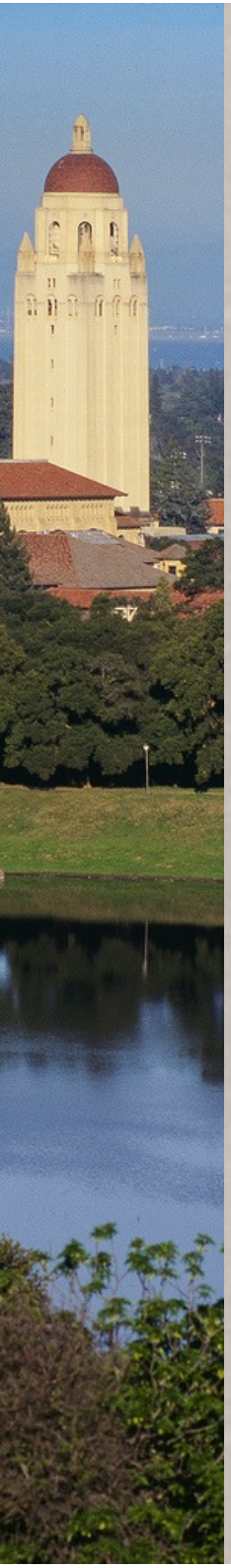
Blocks vs. Electrical Stimulation

- FUS Block has the same effect as DBS

Peripheral Nerve Blocks under High Heat

- Painful Bone Met Nerve Blocks
  - ablating nerves in the periosteum
  - FDA-approved procedure
- Spinal Facet Arthritis Nerve Block
  - similar
  - under investigation
- Nerve Blocks for Treatment of Spasticity
  - *Foley J et al. 2004*
  - sciatic nerves in vivo rabbit
  - complete conduction block in 100% of 22 nerves



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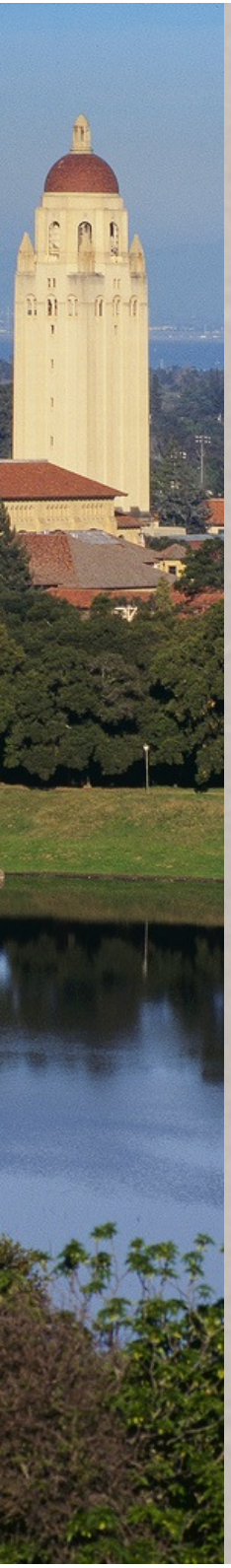
Reversible Effect with Low Heat

~50°C, start to have modulation of symptoms that last for minutes

Nerve Blocks under Low Heat

- Nerve Blocks for Treatment of Spasticity
  - *Foley J et al. 2008*
  - sciatic nerves in vivo rat
  - changed the US protocol
  - For nerves treated with the three lower exposures, CMAPs decreased initially within 4 h or 7 days after HIFU treatment and then recovered to their baseline level at 28 days after treatment.
  - For the highest exposure, however, CMAPs remained absent even 28 days after treatment.



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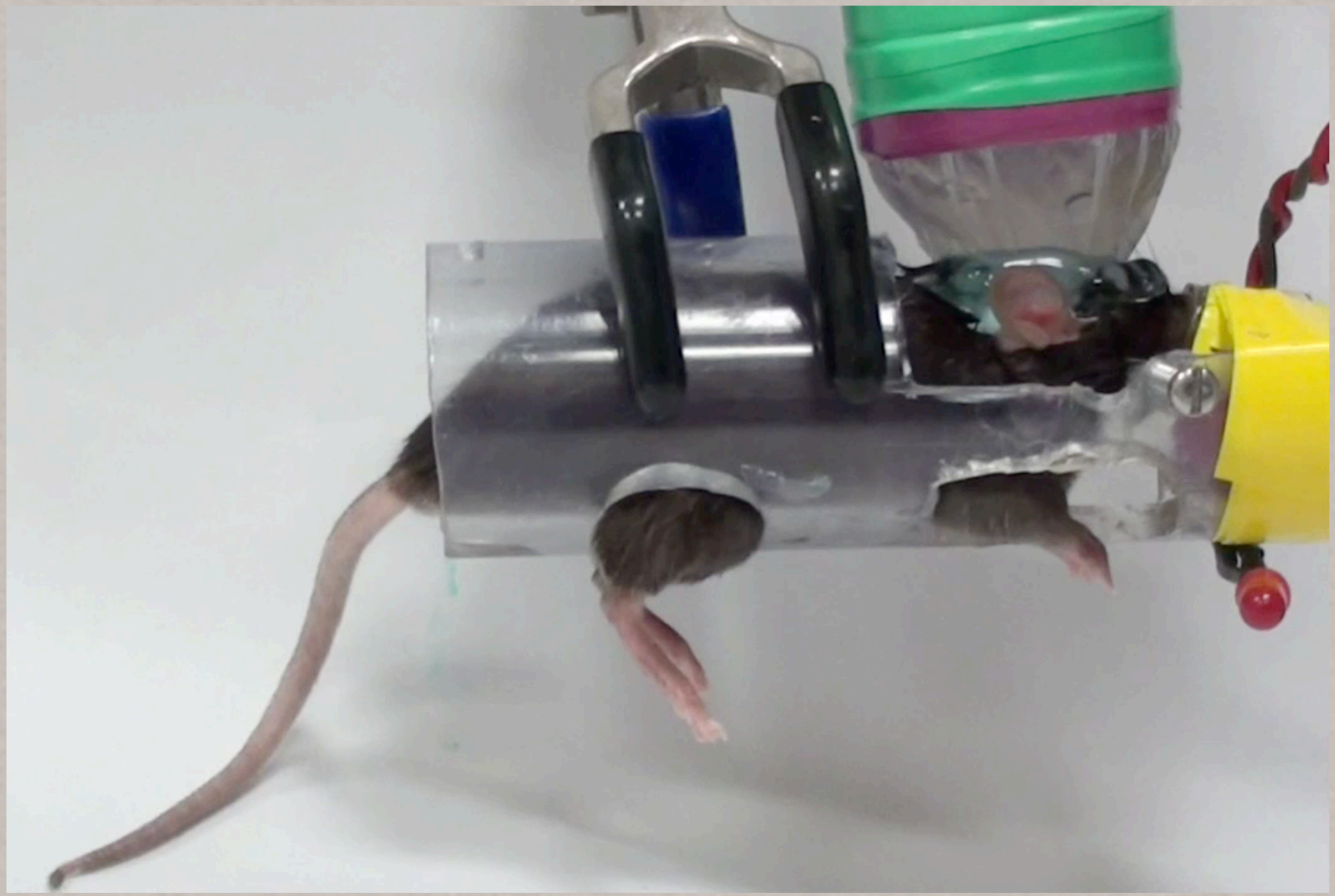
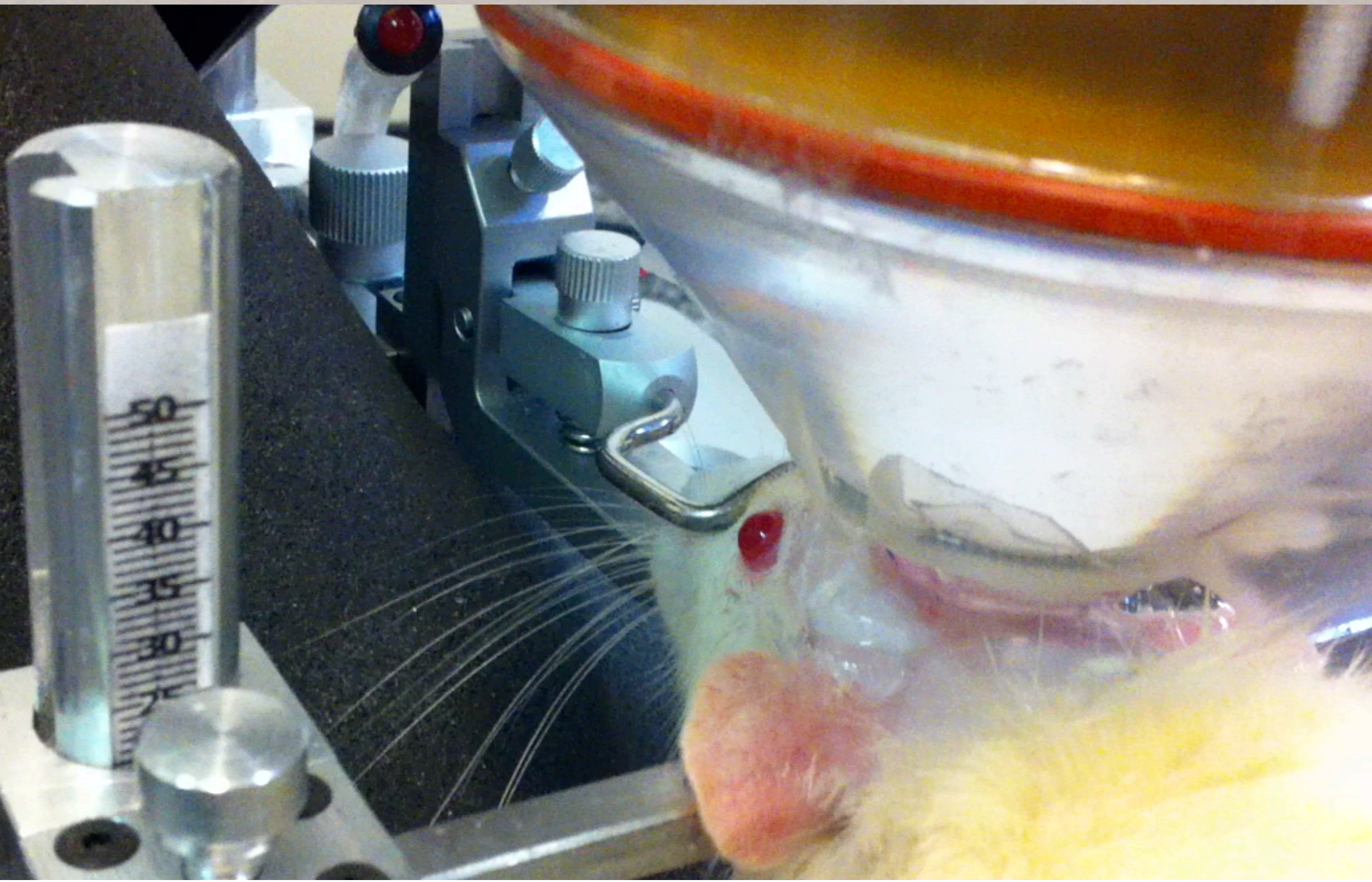
Brain Neuromodulation



King et al. UMB

Whisker

Y. Younan, T. Deffieux,
M. Tanter and J.-F. Aubry
Institute Langevin, Paris



Nerve Stimulation

- *Kim et al, UMB, 2012*
- Stimulation of rat abducens nerve
- controls the movement of a single muscle, the lateral rectus muscle of the eye

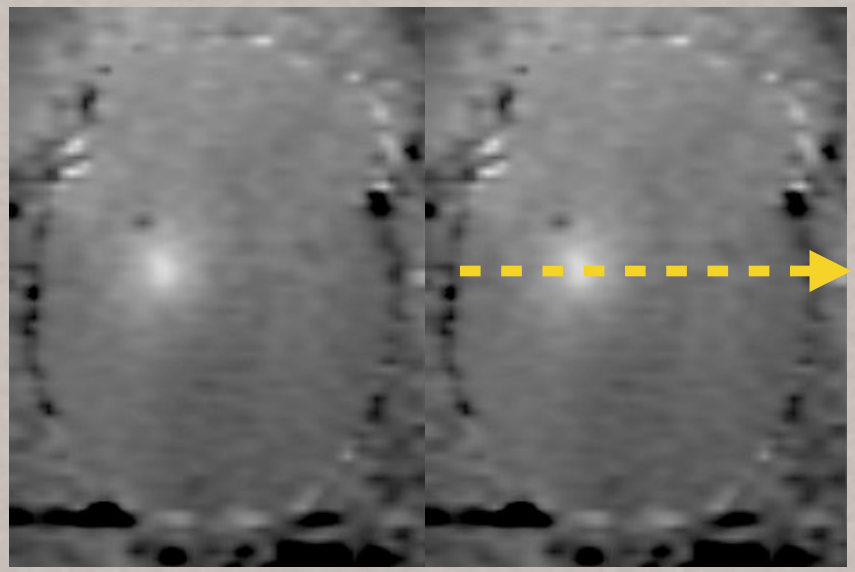
Possible Mechanisms

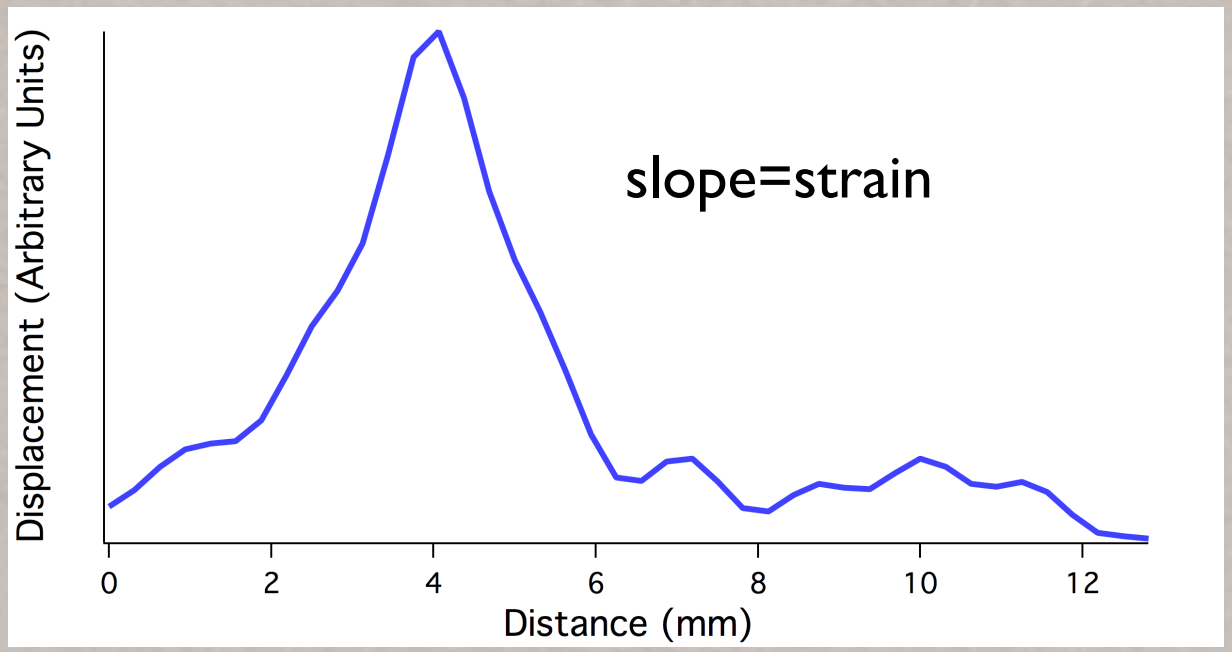
- ~~Heat~~
- Tissue Stretch/Strain
- Cavitation

Tissue Stretch/Strain

- Tissue Stretch/Strain
  - Can stimulate the brain upon touch at surgery
  - Stretch Sensitive Ion Channels
  - Ultrasound can produce local strains
  - We are investigating…

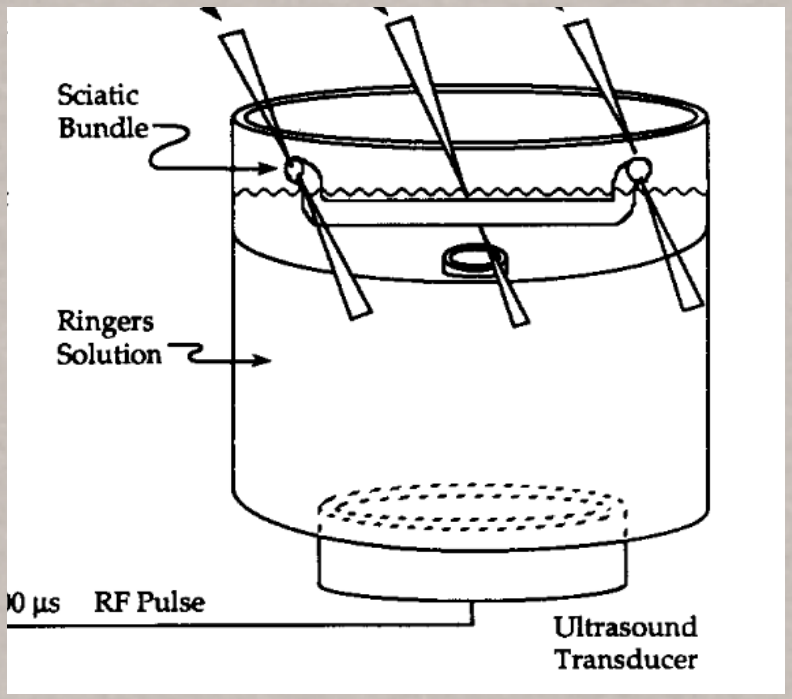
MR-ARFI
Displacement Map





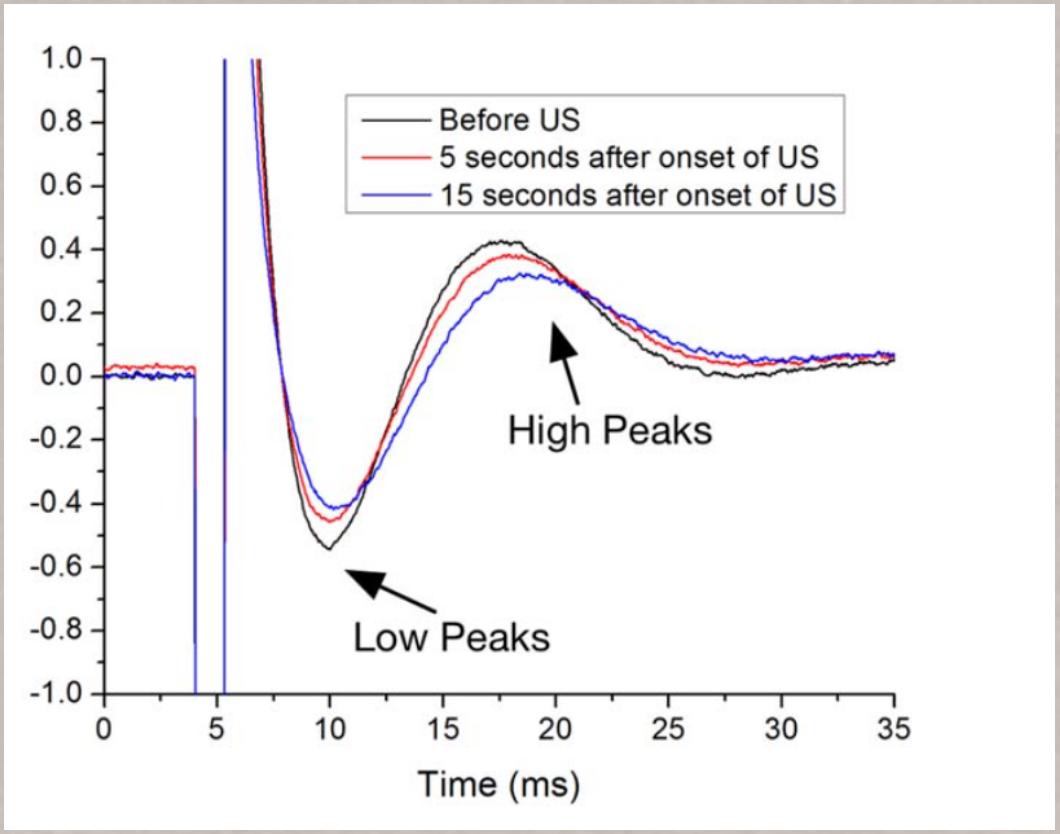
Tissue Stretch/Strain in Sciatic Nerve

- *Mihran et al 1990*
- Frog sciatic nerve, short duration US, heat<0.025°C
- US + electrical stimulus
- changed the excitability of nerve
- the same effect with mechanical stimulus
- hypothesizing stretch sensitive ion channels



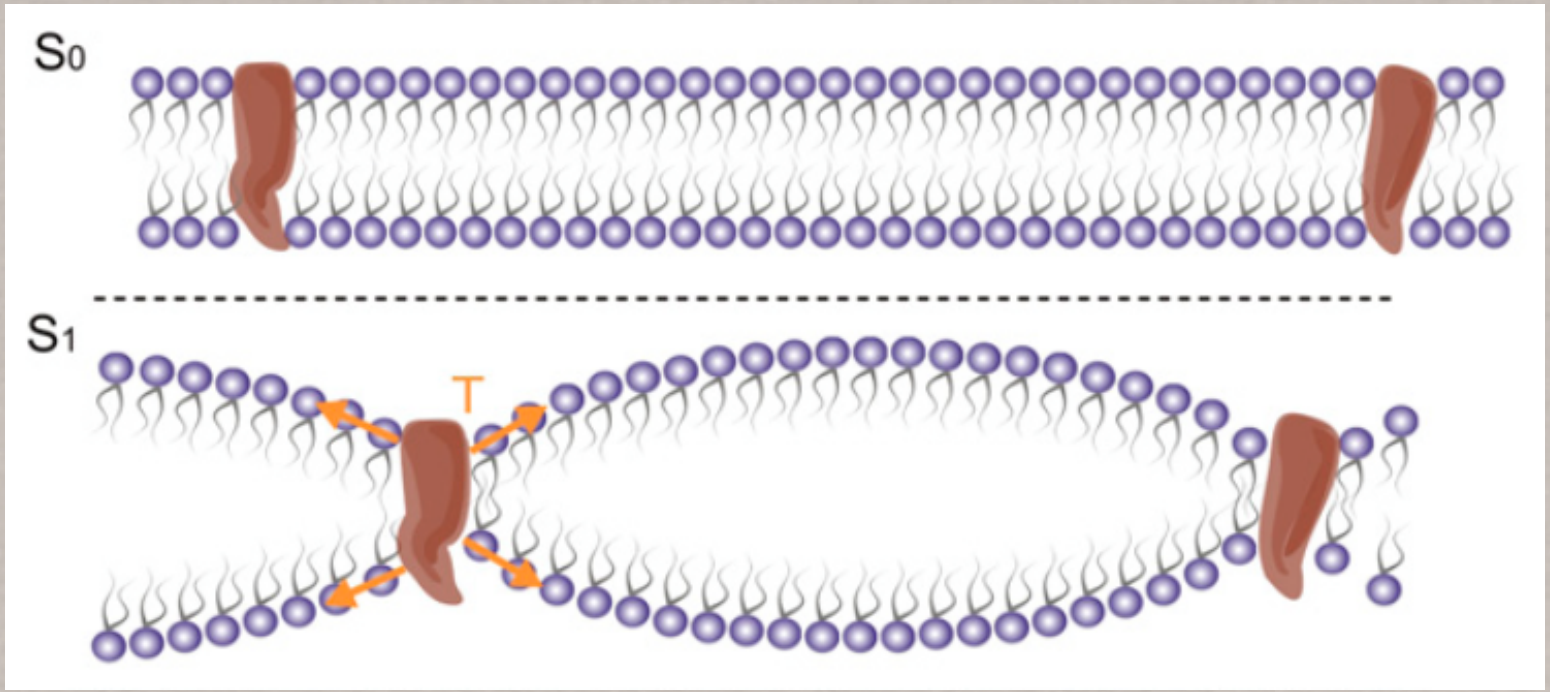
US Modulates Electrical Stimulation in Vagus Nerve

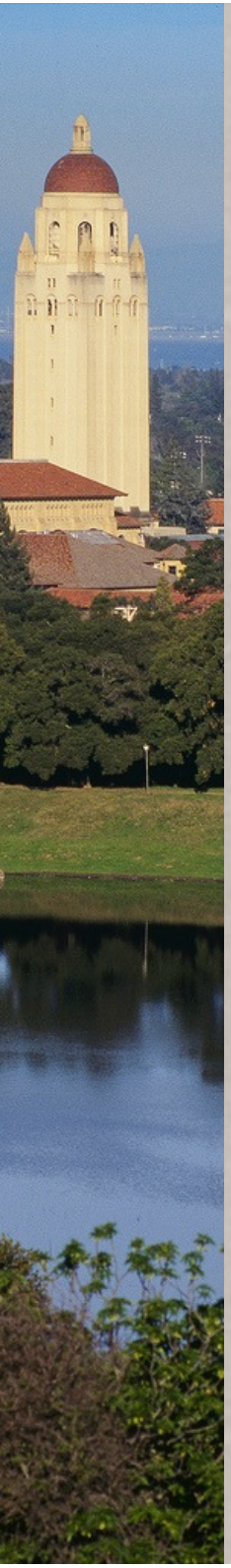
- *Juan et al. Int J Imaging Syst Technol 2014*
- Combined US and Electrical Stimulation
- Suppression of evoked potential amplitude
- Decrease in conduction velocity



Cavitation

- *Krasovitski et al, PNAS 2011*
- *Plaskin et al Physical Review 2014*
- Model of Cavitation within lipid bilayer
- Explaining both stimulation and suppression





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US Stimulation → Systems

- LIPUS: Low Intensity Pulsed Ultrasound
- Immune System Signaling/Upregulation of Signaling Molecules
- Bone and Tissue Healing
- Arteriogenesis

US Stimulation → Systems

- Immune System Signaling/Upregulation of Signaling Molecules

High intensity focused ultrasound ablation and antitumor immune response

Feng Wu[a)]
Institute of Ultrasonic Engineering in Medicine, Chongqing Medical University, 1 Medical College Road, Chongqing 400016, People's Republic of China

J. Acoust. Soc. Am. **134** (2), Pt. 2, August 2013

US Stimulation → Systems

- Immune System Signaling/Upregulation of Signaling Molecules

STEM CELLS 2013;31:2551–2560

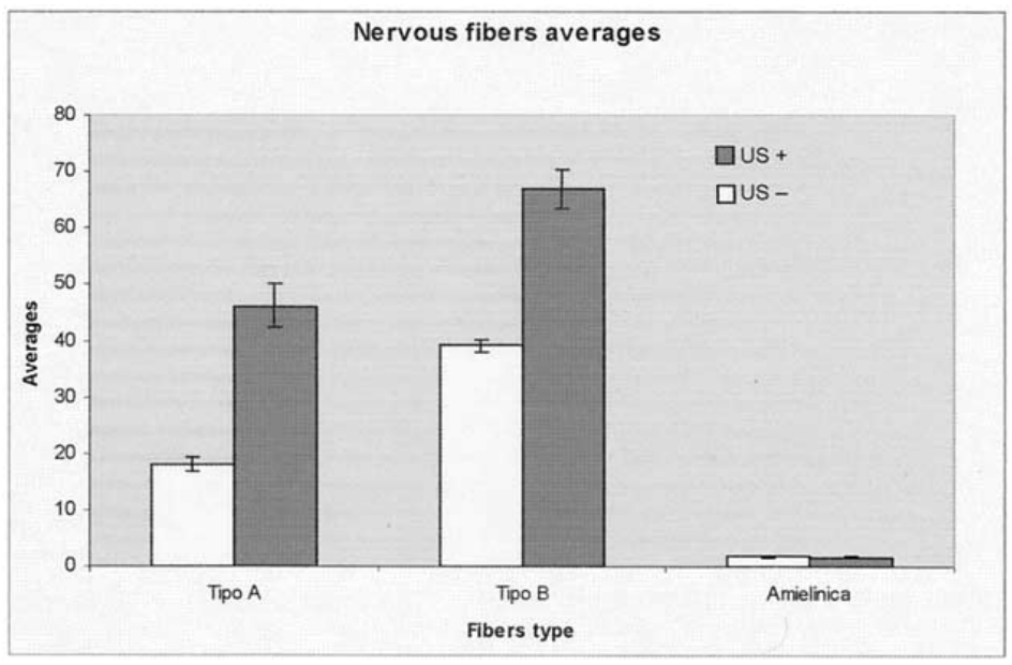
TRANSLATIONAL AND CLINICAL RESEARCH

Noninvasive Pulsed Focused Ultrasound Allows Spatiotemporal Control of Targeted Homing for Multiple Stem Cell Types in Murine Skeletal Muscle and the Magnitude of Cell Homing Can Be Increased Through Repeated Applications

SCOTT R. BURKS,[a,b] ALI ZIADLOO,[a] SAEJEONG J. KIM,[a] BEN A. NGUYEN,[a] JOSEPH A. FRANK[a,c]

Nerve Regeneration

- Low Intensity Pulsed Ultrasound accelerates the regeneration of the sciatic nerve after neurotomy in rats
  Crisci et al, UMB 2002



- Ultrasound improves regeneration of Sciatic Nerves in Rats
  Vanessa Vilela Monte Raso J Neuro M 2005

Summary

- Ultrasound has a neuromodulatory effect
- Both in the brain and peripheral nerves
- Blocks, permanent and temporary
- Stimulation, active area of research
  - mechanical stretch/strain
  - cavitation
- US Stimulation →
  - Bone/Tissue Healing/Arteriogenesis
  - Immune System Signaling
  - Modulation of Stem Cell Homing
  - Nerve Regeneration

Stimulating Peripheral Activity to Relieve Conditions