

Overview of Focused Ultrasound

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~~MD~~ Anderson
Cancer Center



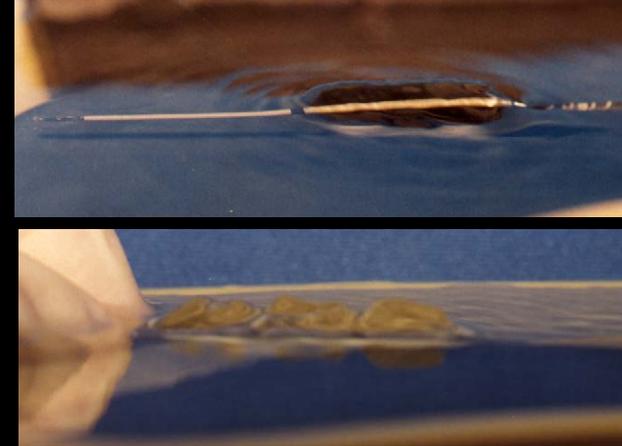
Goals

- The educational goals of this presentation are to provide a brief overview the principles of MR-guided focused ultrasound physics, current and future applications and current clinical status. Off-label use will be discussed.

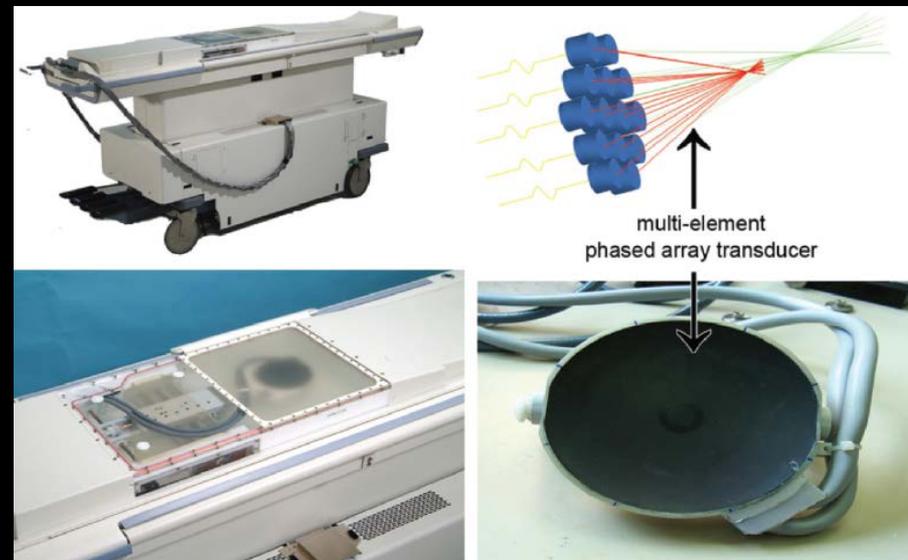
Thermal therapy energy sources

- Cryotherapy
- Radiofrequency
- Microwave
- Laser
- **Ultrasound**

Interstitial multi-element U/S applicators



High Intensity Focused Ultrasound (FUS or HIFU)



Commercial Focused Ultrasound Systems

Ultrasound Guided

Ablatherm®
(EDAP TMS, Lyon, France)



Sonablate® 500
(SonaCare Medical, Charlotte, NC)



ExAblate® OR
(InSightec, Haifa, Israel)



Sonalleve MR-HIFU
(Philips Healthcare, Guildford, UK)

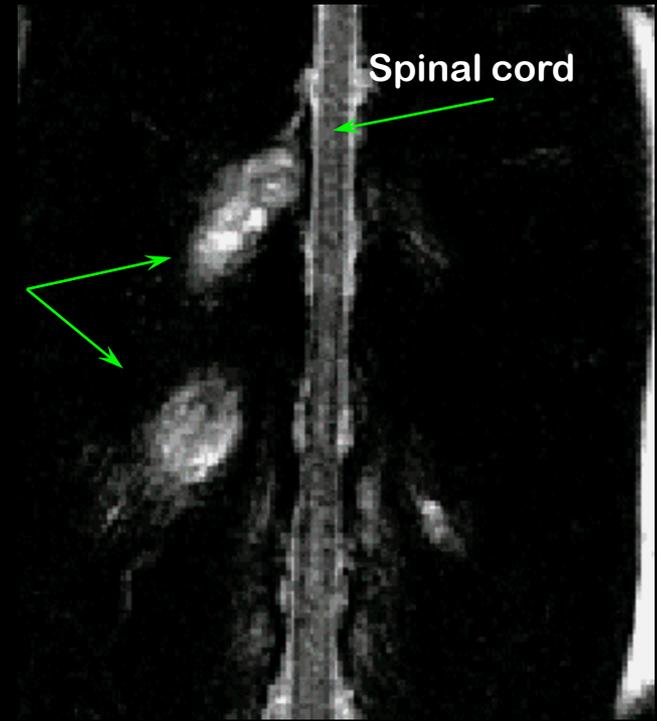


MRI Guided

Role of image guidance in thermal therapy

- Facilitate more optimized treatment
 - planning
 - targeting/localizing
 - **monitoring/control**
 - verification
- Imaging information synergistic with integration of model based simulation
- Endgame
 - increase safety + efficacy
 - **facilitate minimally invasive approaches previously not considered possible/safe**

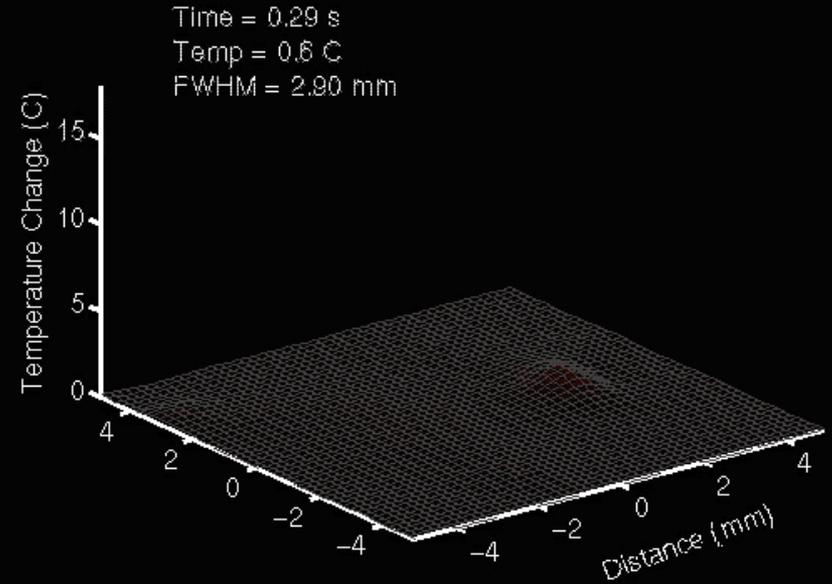
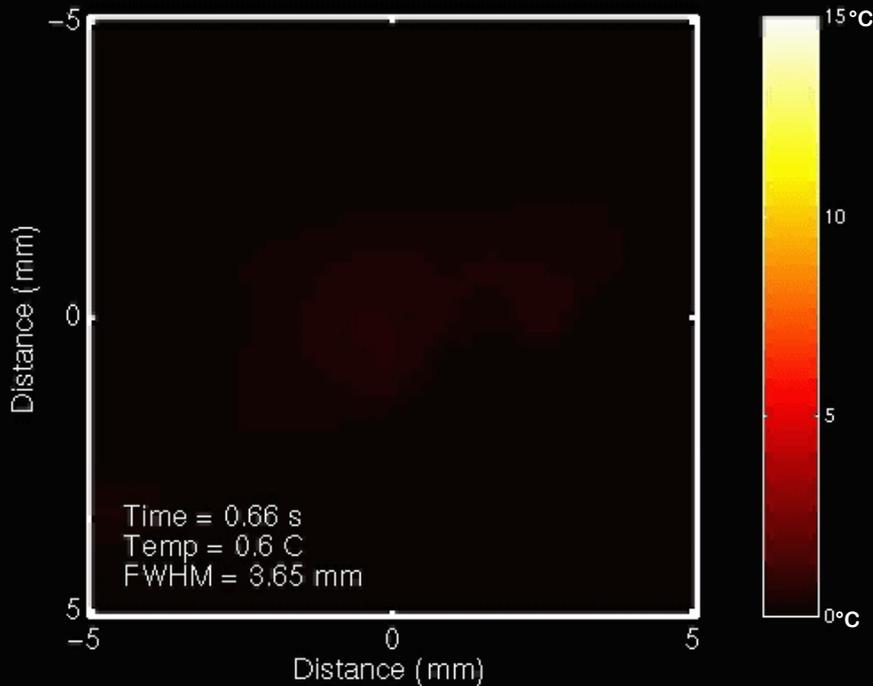
VX-2



HIFU Ablation in Rabbit Paraspinal Muscle @1.5T

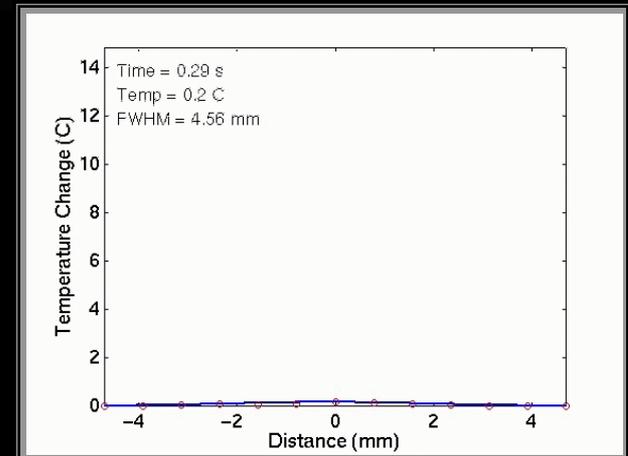
- Treatment prescription
- Prescribed sonication point
- Thermal dose (point)
- Thermal dose (total)

Real-time MRTI for model validation



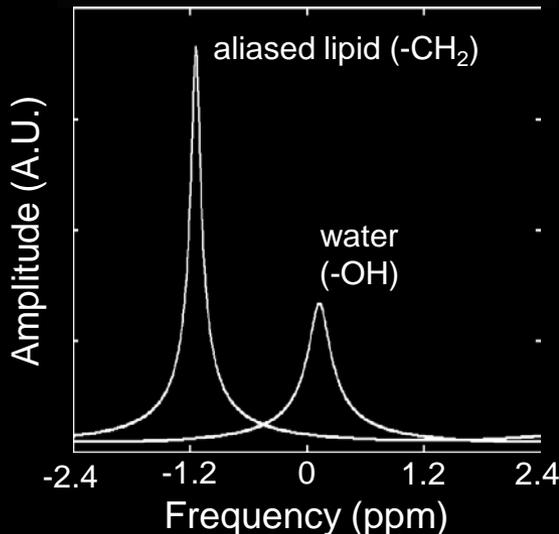
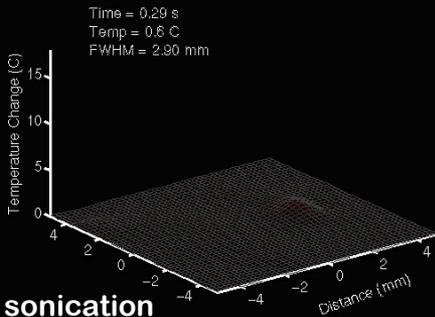
MRTI is a **non-invasive** and **quantitative** means for spatiotemporal characterization of heating and validation of theoretical models used for treatment planning.

Example: Focused ultrasound heating on 1.5T clinical scanner.



MR Temperature Imaging (MRTI)

- Diffusion
- T1-relaxation
- **PRF Shift**
- Proton resonance frequency (PRF) of water shifts linearly with temperature
- Sensitivity: $-0.01 \text{ ppm}/^\circ\text{C}$ (water)



Tissue Type (Canine)	Temp. Range ($^\circ\text{C}$)	Temp. Sensitivity ($\text{ppm}/^\circ\text{C}$)
Brain	25-59	-0.0102 ± 0.0005
Prostate	32-59	-0.0099 ± 0.0004
Kidney	35-54	-0.0103 ± 0.0006
Liver	35-51	-0.0098 ± 0.0002
Bone (femur)	17-57	-0.0109 ± 0.0002

- **Disadvantages**
 - Less sensitive at low field strengths
 - Lipid is insensitive to temperature
 - Sensitive to background field changes
 - Motion, susceptibility, etc

Thermal “Dose” & Risk Assessment

- Thermal damage is cumulative effect
 - Isotherm characterization of bioeffects limited
- Damage as function of exposure can be modeled as an Arrhenius rate process (Ω)

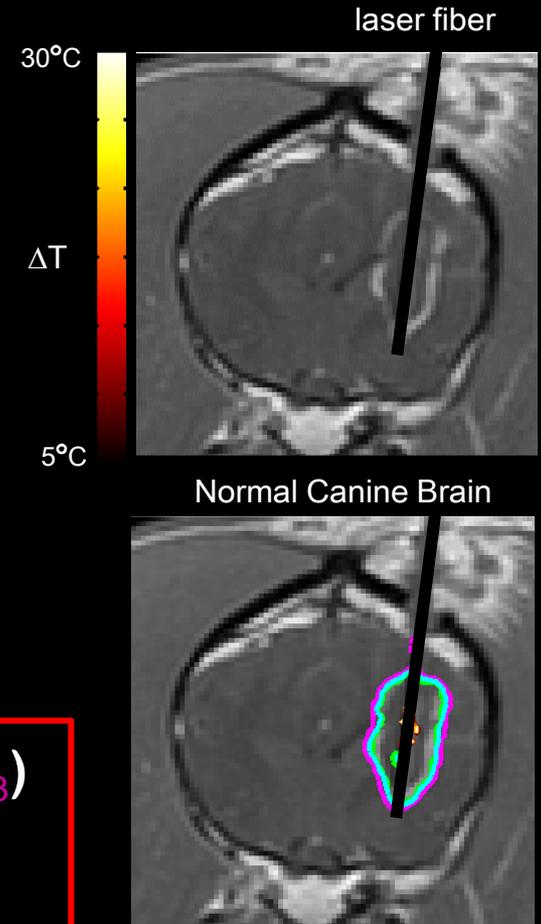
$$\Omega = A \int_0^t e^{\frac{-E_a}{RT(\tau)}} d\tau$$

R = Universal Gas Constant
 A = Frequency Factor ($3.1 \times 10^{98} \text{ s}^{-1}$)
 E_a = Activation Energy ($6.3 \times 10^5 \text{ J}$)
 (Henriques FC, Arch Pathol, 1947; 43: p. 489.)

- Cumulative Equivalent minutes @ 43°C (CEM_{43})
 - Empirically derived from isoeffects observed in low temperature hyperthermia work:

$$\text{CEM}_{43}(t_n) = \sum_{t=0}^{n \cdot \Delta t} R^{(43-T_n)} \cdot \Delta t, \text{ with } R = \begin{cases} 0.25 & T_n < 43^\circ\text{C} \\ 0.50 & T_n \geq 43^\circ\text{C} \end{cases}$$

Sapareto SA, Dewey WC Int. J. Rad. Onc. Bio. Phys. 10: 787-800, 1984.



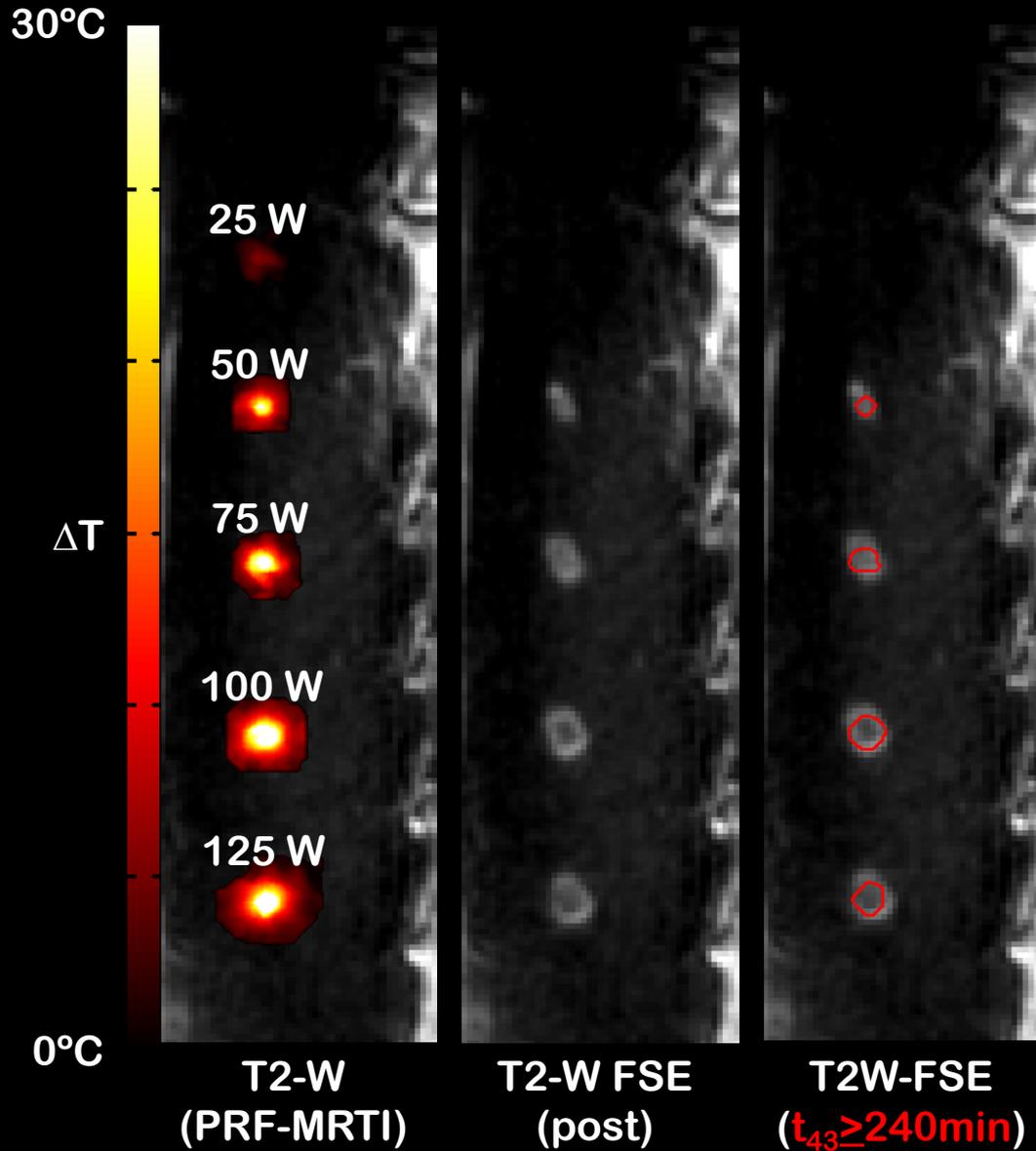
isodose models

$\Omega \geq 1$

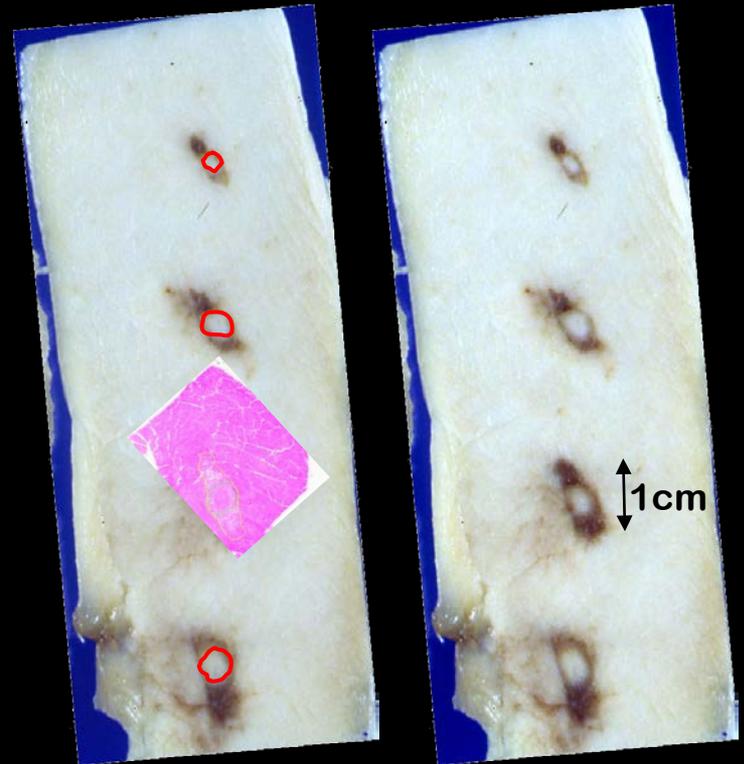
$T \geq 57^\circ\text{C}$

$\text{CEM}_{43} \geq 240 \text{ min}$

Imaging versus Histology

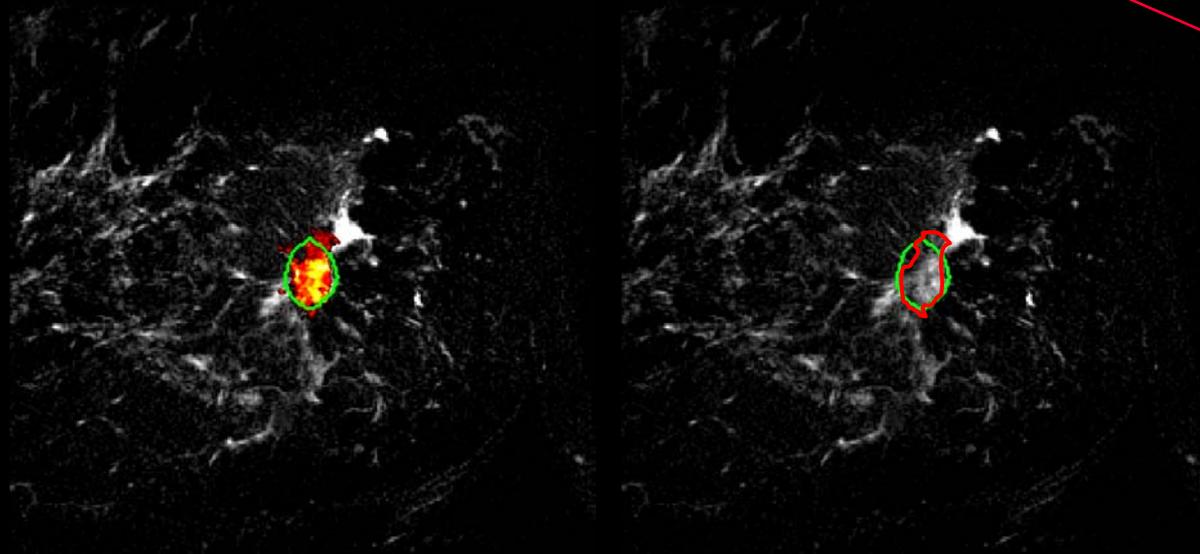
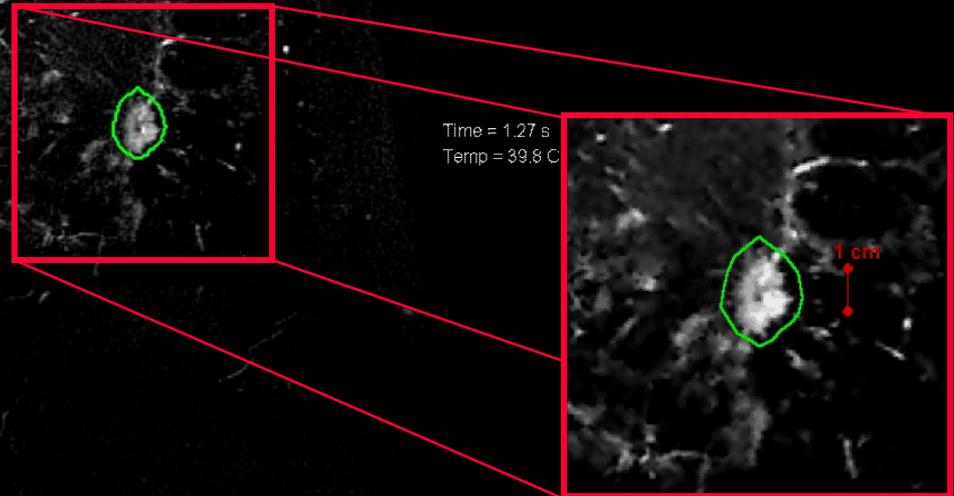
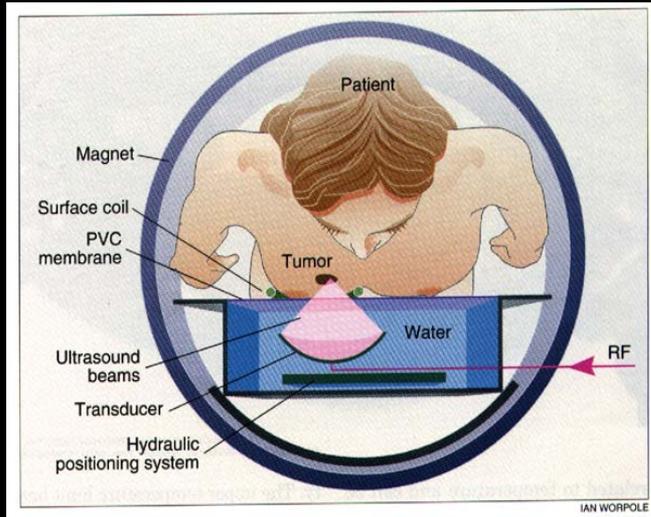


15s FUS exposure *in vivo*
(skeletal muscle)



Pathology/H&E
(Cogulation, Edema, $t_{43} \geq 240 \text{min}$)

Initial studies in breast



Multi-planar, multi-shot EPI MRTI facilitated real-time MRTI with high spatiotemporal resolution, high SNR and lipid suppression

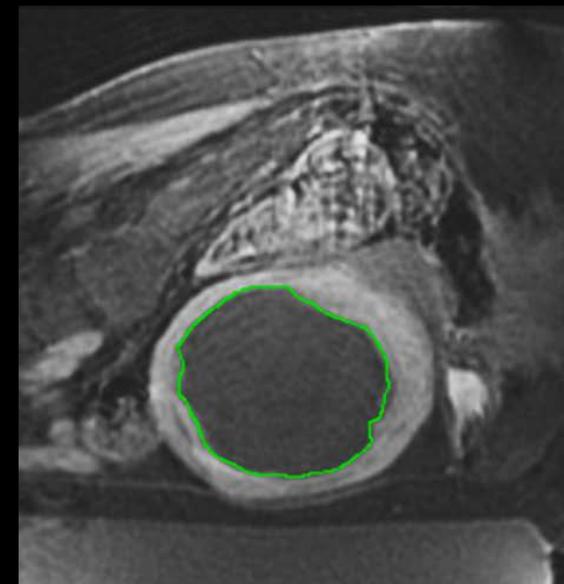
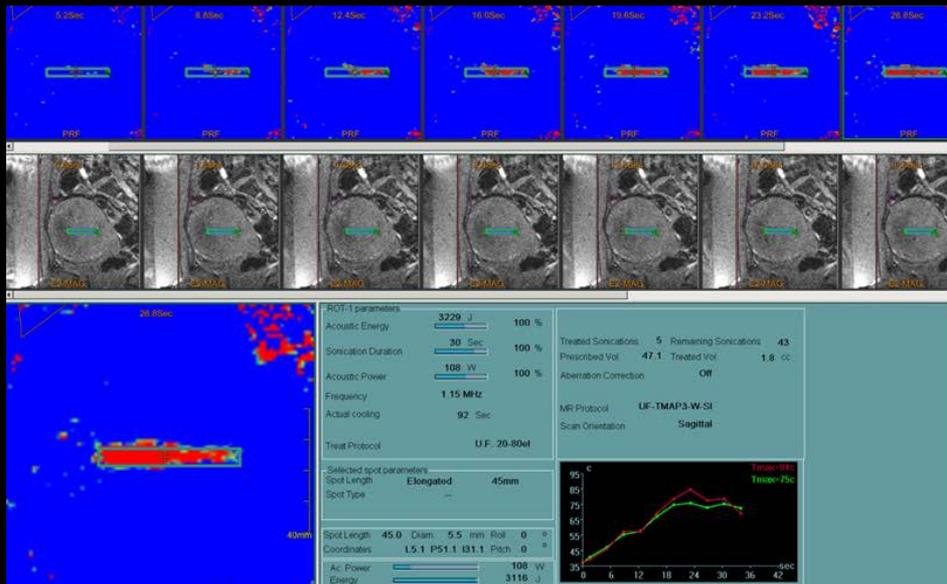
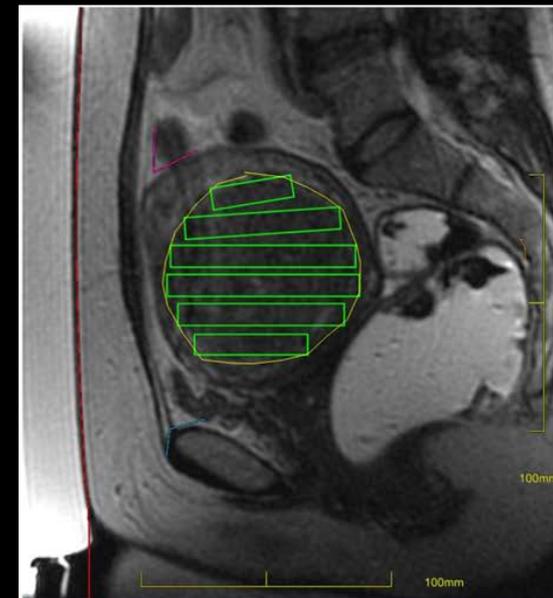
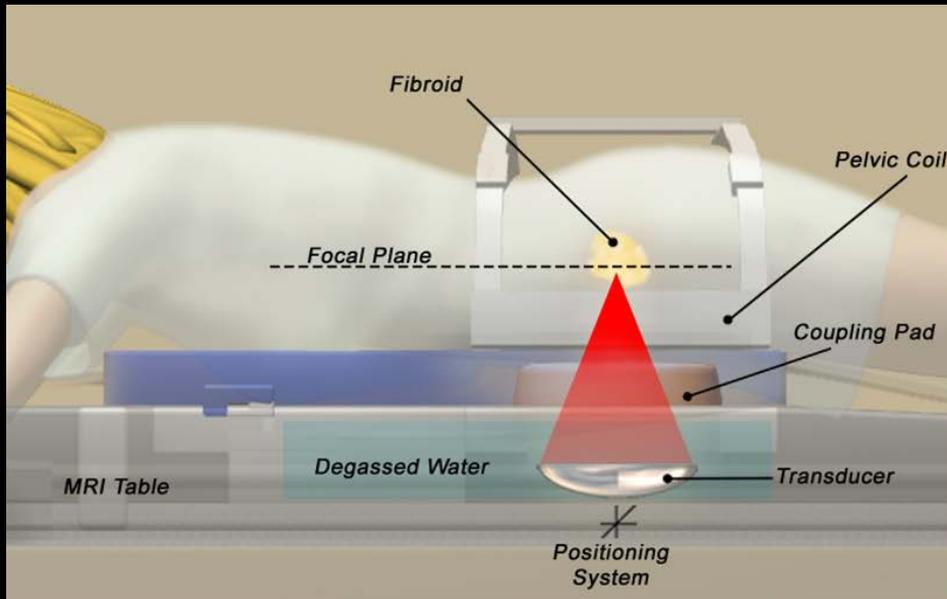
First approved indication: uterine fibroids



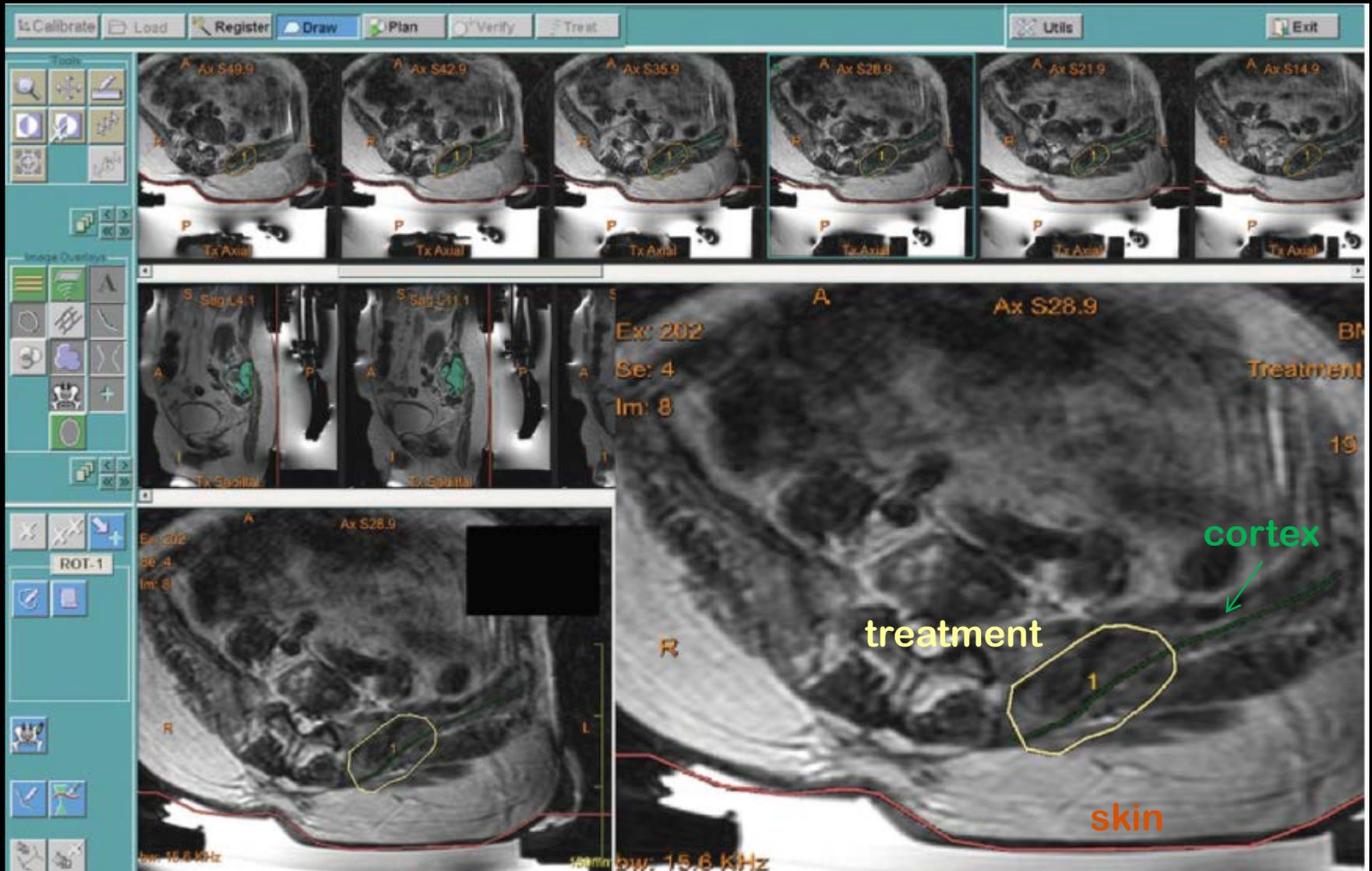
(ExAblate 2000; Insightec, Haifa, Israel)



First approved indication: uterine fibroids



MRgFUS of painful bone mets



Planning: radiologist segmentation

MRgFUS of painful bone mets

The screenshot displays the MRgFUS software interface for treatment planning. The top menu bar includes 'Calibrate', 'Load', 'Register', 'Draw', 'Plan', 'Verify', and 'Treat'. The main workspace is divided into three rows of axial MRI slices, with blue acoustic fields overlaid on the bone metastases. The bottom right panel contains the following parameters:

ROT-1 parameters

- Acoustic Energy: 100%
- Sonication Duration: 20 Sec
- Acoustic Power: 95 W
- Frequency: 1.0 MHz
- Cooling Duration: 57 Sec
- Treat Protocol: Bone

Selected spot parameters

- Spot Energy: 1906 J
- Spot Length: -- Diam: -- mm Roll: 23 °

Treatment Summary

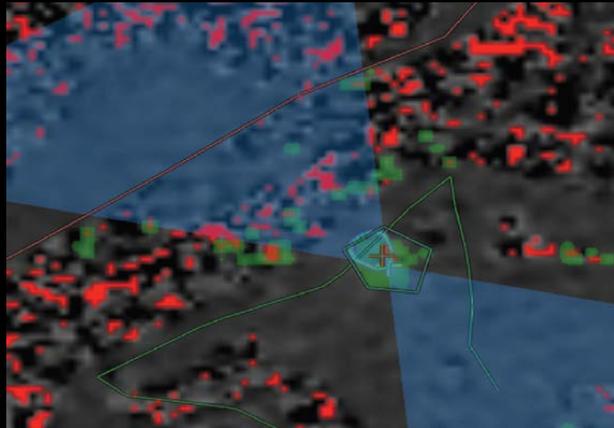
- Treated Sonications: 0
- Remaining Sonications: 12
- Treated Vol: 0.0 cc

Thermal Scan Parameters

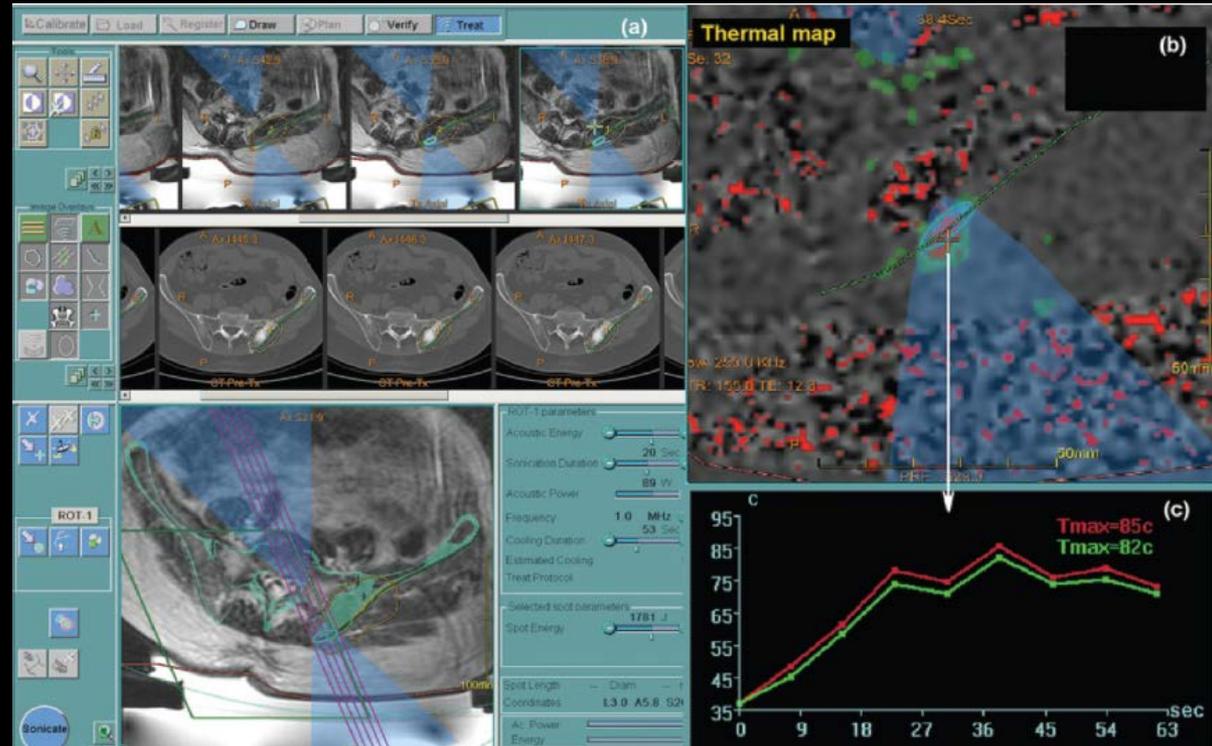
- Path: Beam
- Dir: OSag
- Freq Dir: AP
- Scan Type: MS Auto
- Num. Slices: 5
- Thickness (mm): 3.0
- Spacing (mm): 2.5
- MR Protocol: EPI-TH3-SP2.5-SSL-AP
- Cov: 25.0 mm

Treatment planning: evaluation

MRgFUS of painful bone mets



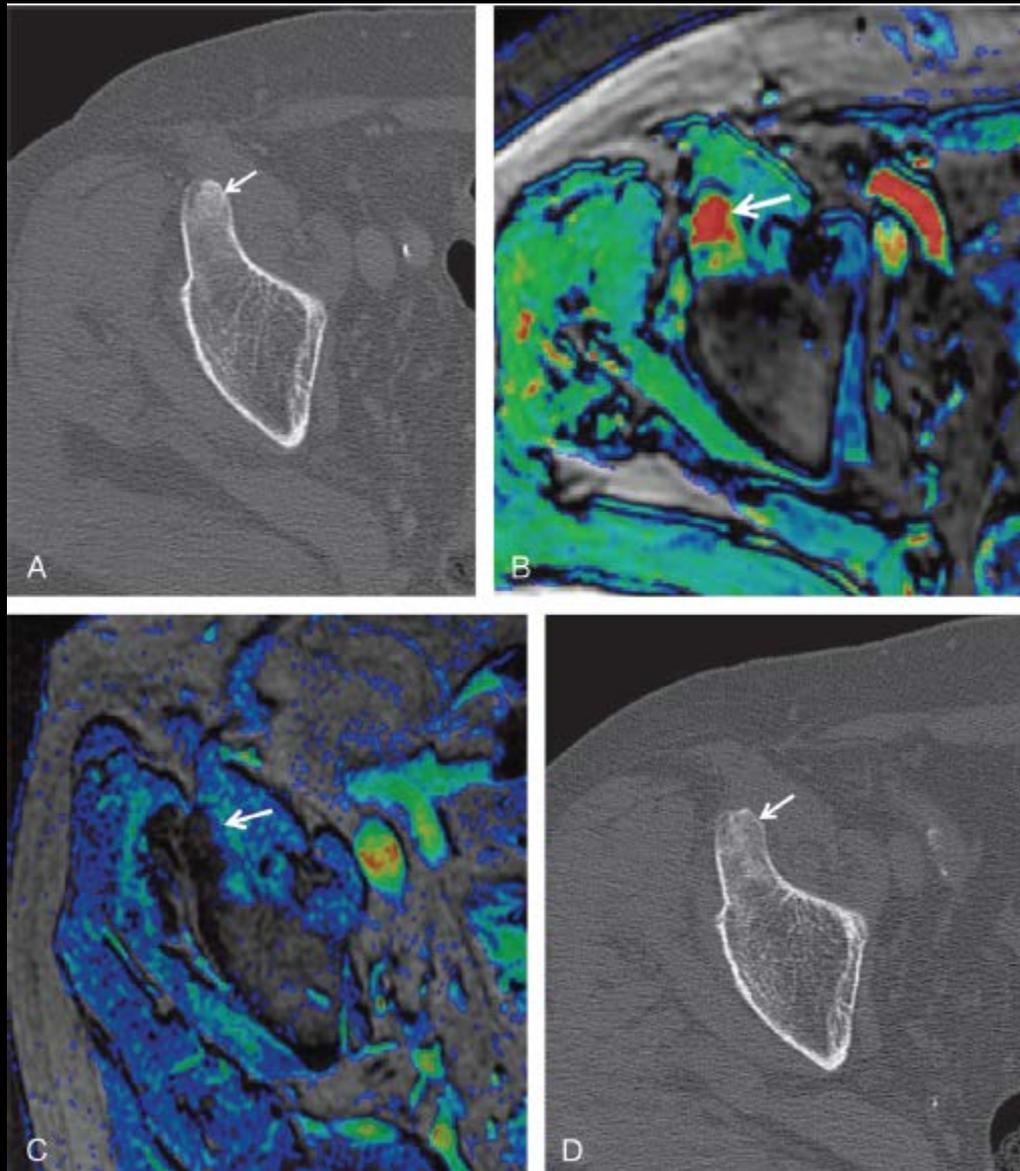
Verification step



Treatment monitoring

Palliation is achieved by spreading the heat across the surface of the bone to ablate the nerves in the adjacent periosteum.

MRgFUS of painful bone mets



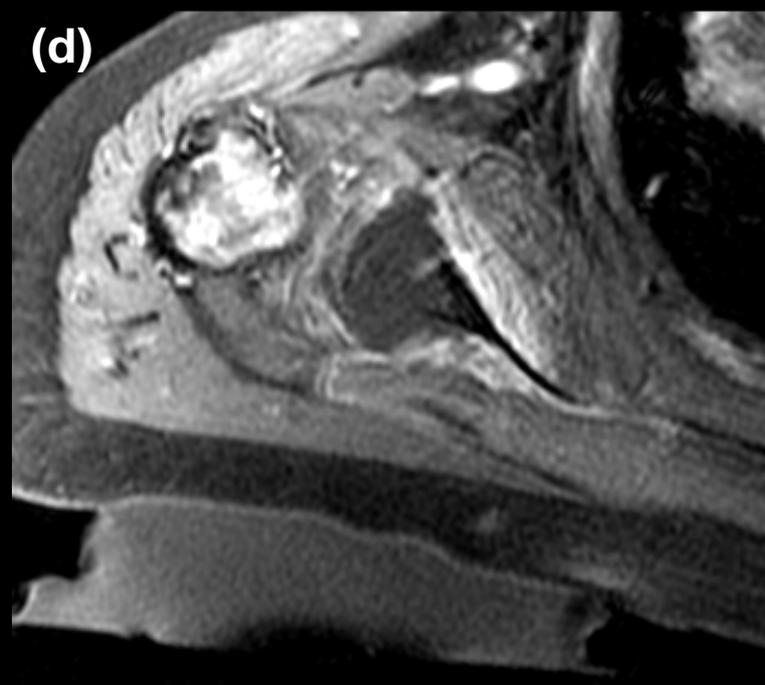
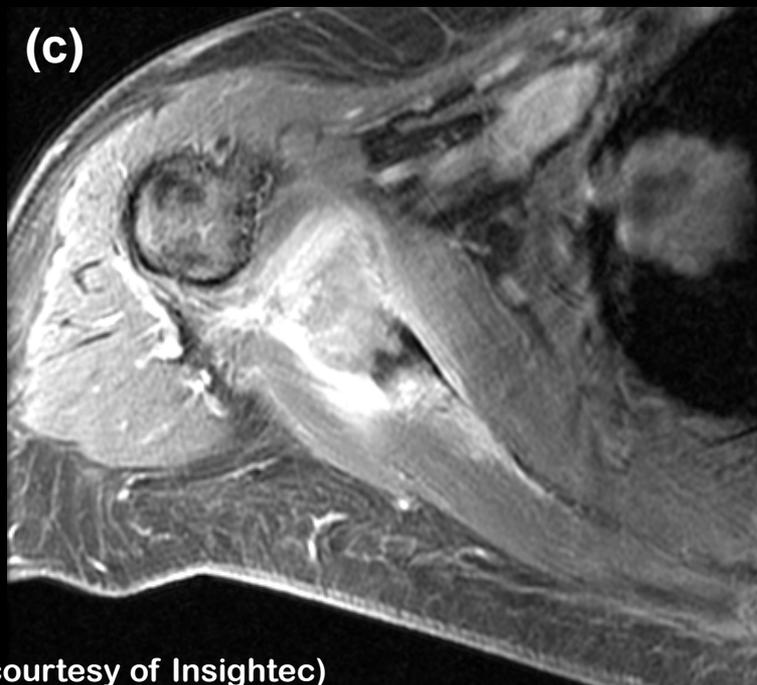
Prostate mets in 63 yo male in right anterior-superior iliac spine

Pre-Treatment:
T1W+C MRI => perfused

Post-Treatment (3 mo):
T1W+C MRI => non-perfused
CT => increased density in treated area and disappearance of nodular pathologic tissue

Patient classified as complete responder (MDACC criteria)

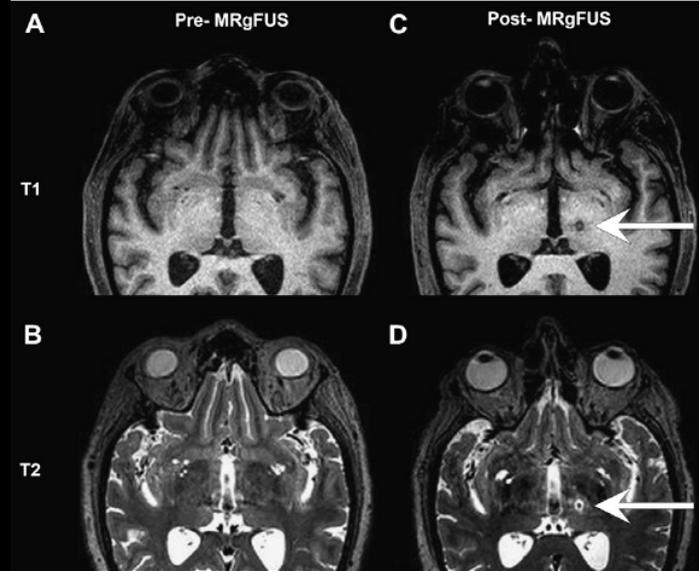
Next stage of development: 'conformal' bone



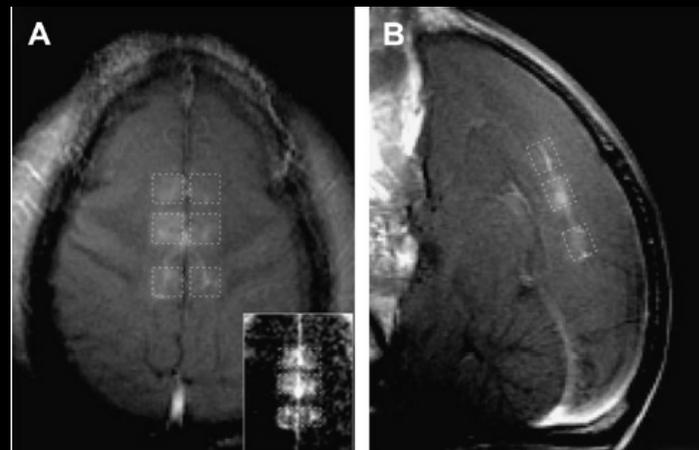
Future applications: transcranial MRgFUS



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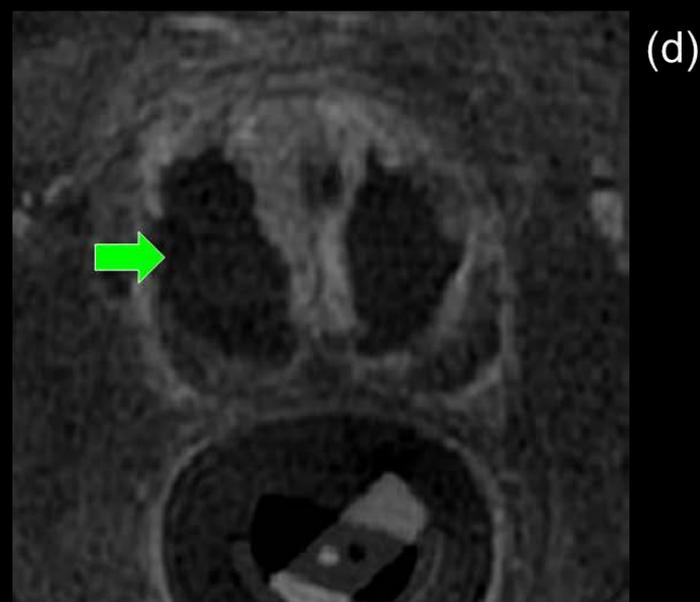
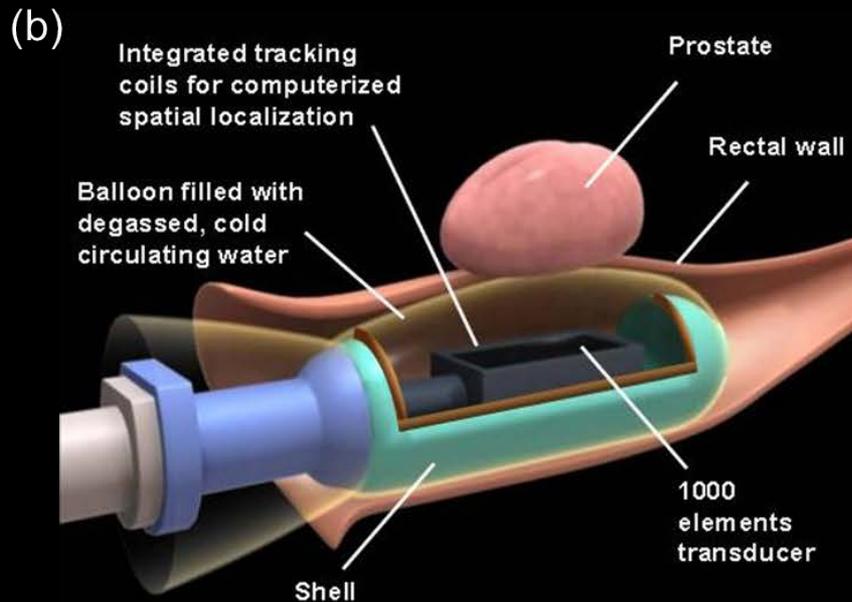
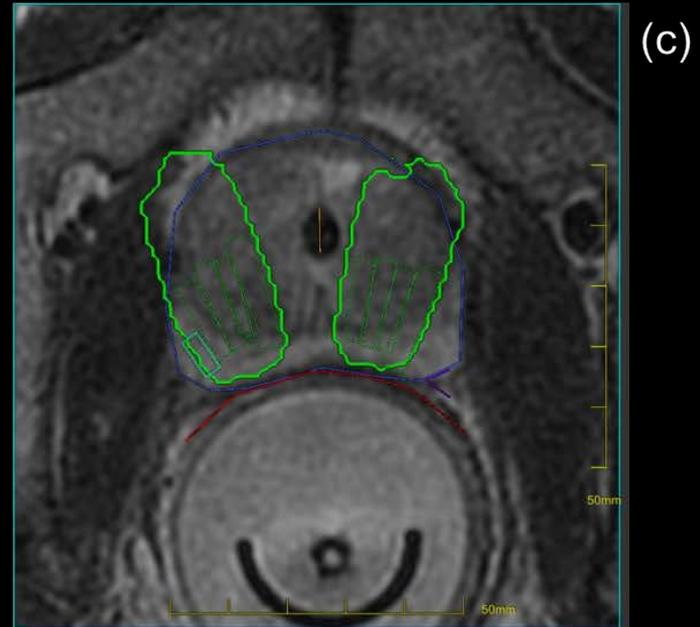


Neuropathic pain: 2-3mm focal lesion in right side of thalamus @ 1 day post-treatment



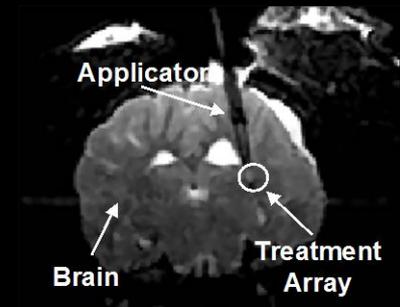
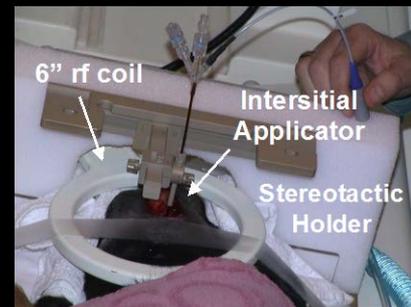
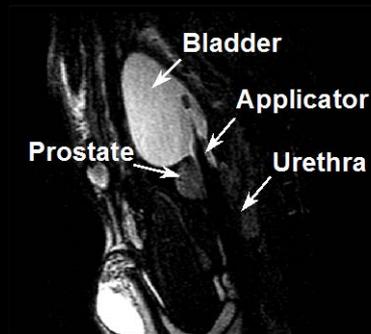
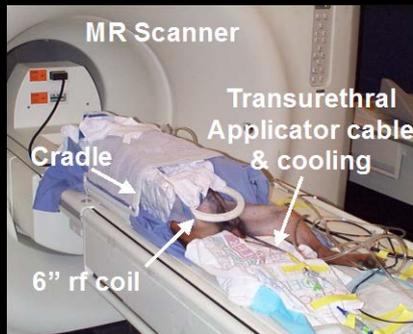
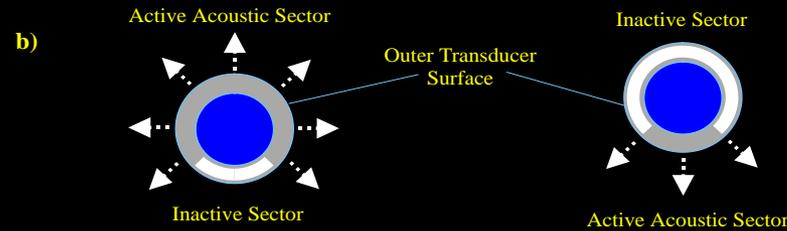
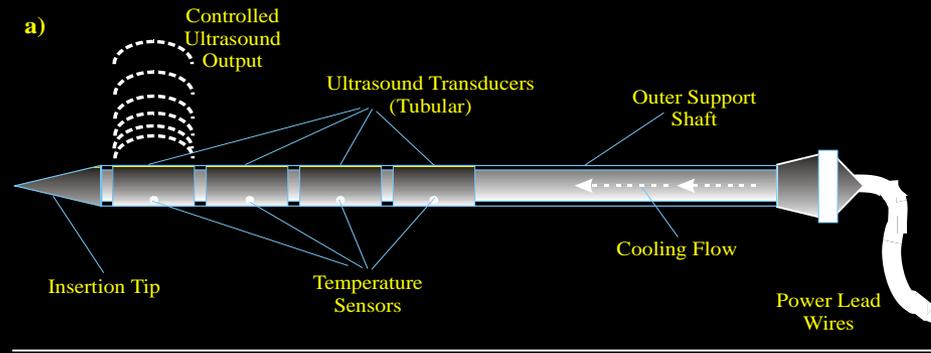
Blood brain barrier disruption (animal model)

Future application: prostate



(Images courtesy Insightec, Inc. and Chris Cheng MD, National Cancer Centre, Singapore)

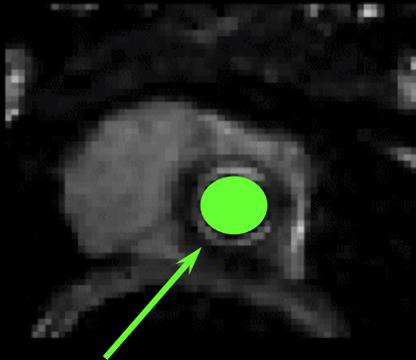
Interstitial ultrasound applicators for MRgTT



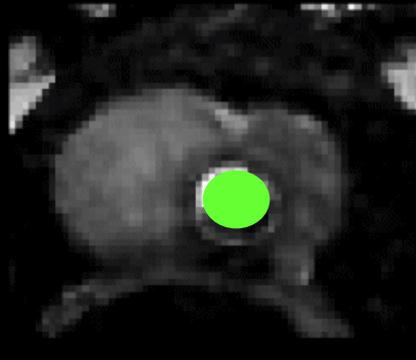
(in collaboration with Christopher Diederich, PhD at UCSF)

MR-guided interstitial ultrasound heating

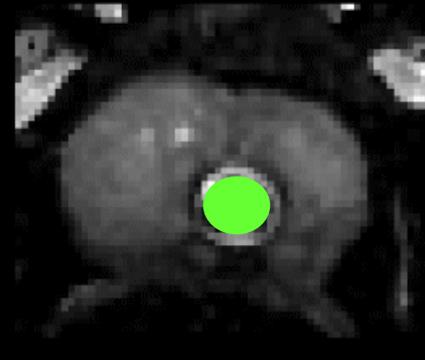
-4 mm



0 mm



+4 mm



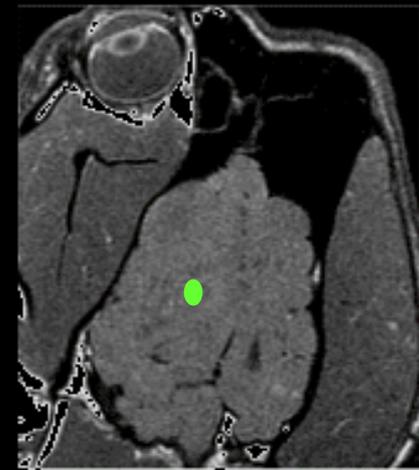
3-element directional
transurethral applicator

45°C



65°C

— Isodose: $t_{43} = 90$ min.



3-element interstitial
applicator

45°C

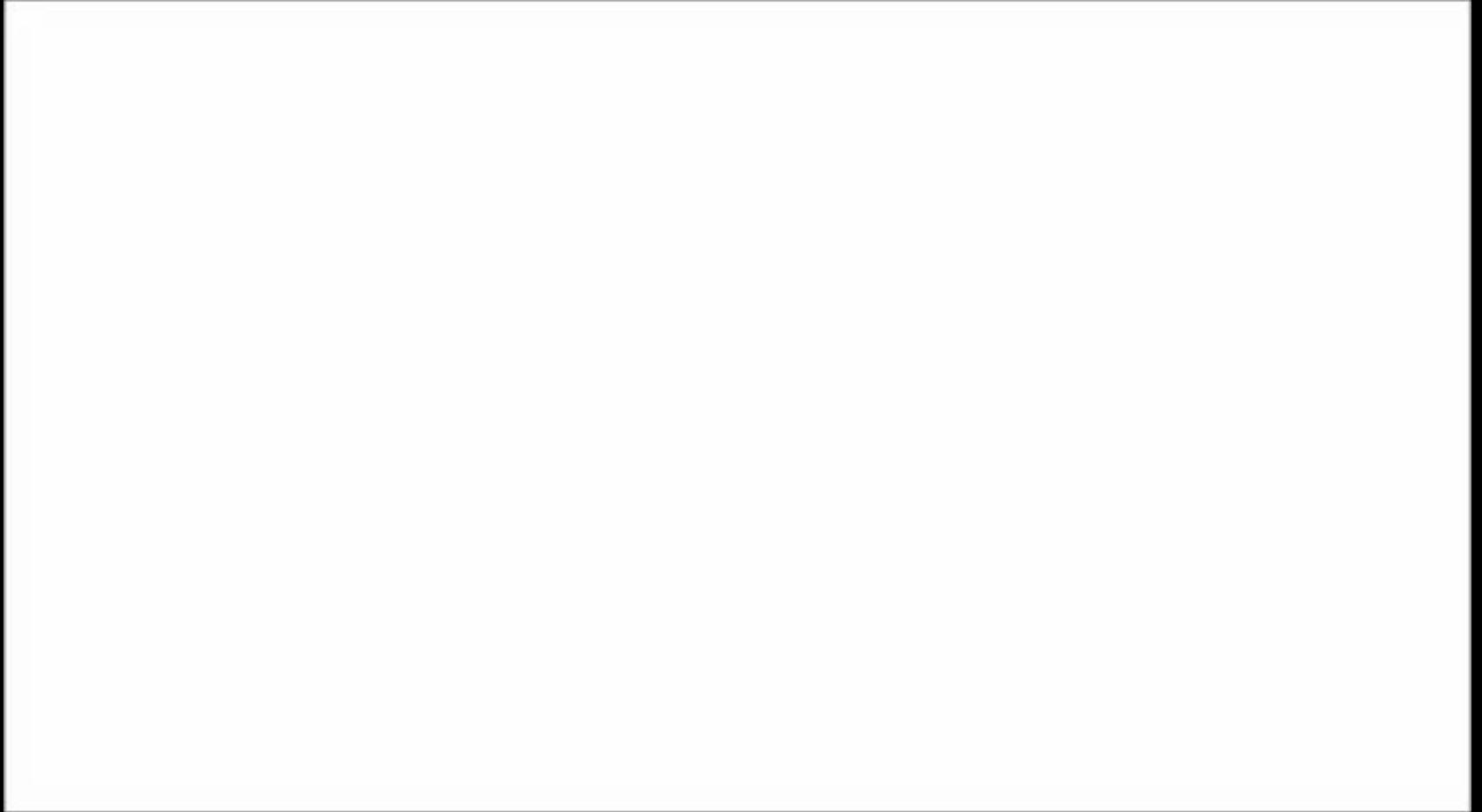


80°C

PID:z001023z3



Transurethral Ultrasound Ablation in Prostate



Task Group No. 241 MR-Guided Focused Ultrasound

Charge

- Identify methodology, phantoms, and software for performance assessment of MRgFUS
- Areas of technical assessment include intrinsic MRgFUS characteristics, quantitative metrics of MRgFUS, and identification of quality assurance measures and procedures

Membership

Keyvan Farahani (NIH)

Rajiv Chopra (UT Southwestern) (Chair)

R. Jason Stafford (UT MDACC) (Co-Chair)

Stanley H. Benedict (UC Davis)

Kim Butts-Pauly (Stanford)

Paul Carson (U Mich)

Lili Chen (FCCC)

Chris Diederich (UCSF)

Arik Hananel (FUS Foundation)

Randy King (FDA)

Nathan McDannold (BWH)

Chrit Moonen (Utrecht)

Eduardo Moros (Moffit)

Dennis Parker (Utah)

Ari Partanen (Philips)

Rares Solomir (Geneva)

Steffen Sammet (U Chicago)

David J. Schlesinger (U Virginia)

Robert Staruch (Philips)

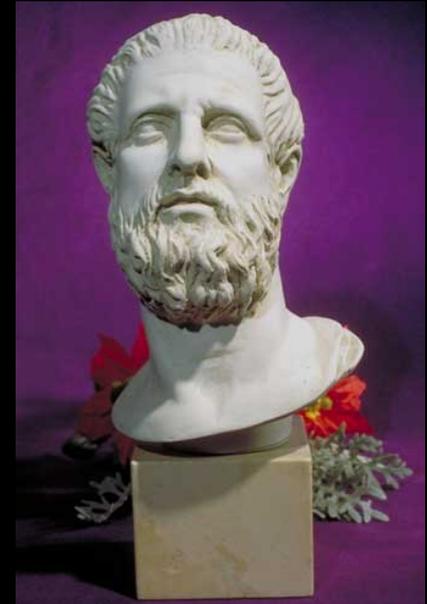
Gail R. ter Haar (Royal Marsden)

Eyal Zadicario (Insightec)



The diseases which medicines cannot cure, excision cures: those which excision cannot cure, are cured by the cautery; but those which the cautery cannot cure, may be deemed incurable.

- Hippocrates Aphorisms (400 BCE)



Thank you for your time!

Email: jstafford@mdanderson.org

Question 1

- The current clinical indications for focused ultrasound are alleviation of
 - A. essential tremor
 - B. uterine fibroids
 - C. pain from bone metastases
 - D. B & C only
 - E. all of the above

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Question 2

- Thermal dose cannot be measured directly, but is calculated from exposure. Currently, the FUS community expresses thermal isoeffective dose as
 - A. the region of tissue perfusion deficit
 - B. the cumulative equivalent time spent at 60°C
 - C. the cumulative equivalent time spent at 43°C
 - D. the average temperature multiplied by exposure time
 - E. the cumulative integral of temperature over time

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Question 3

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 - A. focused through the cortical bone to ablate the tumor using multiple, small, focal ablations.
 - B. focused on the surface of the bone to ablate specific nerves in the periosteum.
 - C. spread across the surface of the bone to ablate the nerves in the adjacent periosteum.
 - D. transmitted at a higher frequency to maximize absorption in bone.
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