MRI-Guided Focused Ultrasound: Clinical Applications

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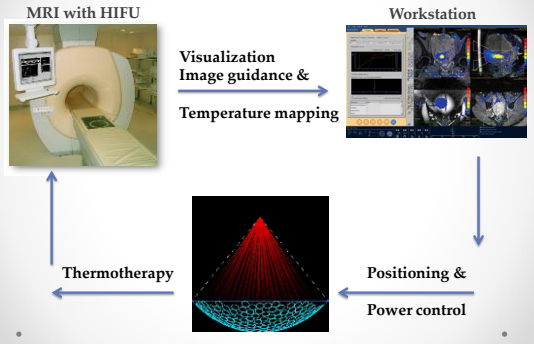
Disclaimer & Disclosure

- Presentation reflects presenter's opinions and not necessarily those of assigned institutions.
- Not an endorsement of products shown.
- Philips Healthcare support of collaborative projects at Johns Hopkins University.

MRI-guided Focused Ultrasound (MRgFUS)



MRI-guided Focused Ultrasound (MRgFUS)

MRI thermometry

- 1960: Hindman, Proton resonance shift of water
- 1983: Parker, Temperature mapping

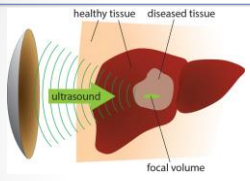
HIFU

- 1940: Lynn, Lele, HIFU hyperthermia
- 1990: Cathignol, HIFU prostate treatment

1990: Hynynen, Jolesz, Mallard
MRI-guided HIFU

C. Moonen

Focused Ultrasound (FUS)



$$I = I_o e^{-2\alpha z}$$

Io, initial beam intensity
α, atten. coeff. [1/dist]
z, distance traveled

Transducer Parameters

- Diameter
- Focal distance
- Frequency (MHz)
- Power (W)

Ultrasound propagation parameters

- Speed of sound in tissues
- Reflection
- Refraction
- Absorption

Pennes Bioheat Transfer Equation

$$\rho C \frac{\partial T}{\partial t} = \nabla \cdot k \nabla T + Q + Q_B + A$$

ρ, density [kg/m^3]
C, specific heat [J/kg°C]
T, temperature [°C]
K, thermal conductivity [W/m°C]
Q, power density [W/m^3]
Q_B, perfusion loss [W/m^3]
A, metabolic heat generation [W/m^3]

US heat: Absorption and Effect

Cumulative Equivalent Minutes
(Sapareto & Dewey; 1984)

$$CEM = \int_{t_0}^{t_f} R^{T-T_{reference}} dt$$

Thermal coagulation:

Thermal dose > 240 CEM43°C

MRI Guidance

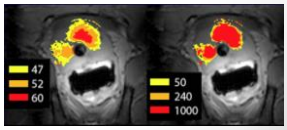
- **Advantages**
  - Soft tissue contrast resolution
  - Temperature sensitivity
  - 3D imaging
  - Multi-parametric
- **Disadvantages**
  - pseudo real-time
  - MR-compatible instruments
  - Workflow

MR PRF Thermometry

$$\Delta\varnothing = \gamma \cdot \alpha \cdot \Delta T \cdot B_0 \cdot TE$$

γ, gyromagnetic ratio
α, rate constant (0.01 ppm/°C)
T, temperature
B_0, magnetic field strength
TE, echo time

Maximum Temp °C | Thermal Dose



Source: Diedrich, Butts-Pauly, et. al.

MRgFUS Range of Clinical Applications

Potential Applications for Cancer

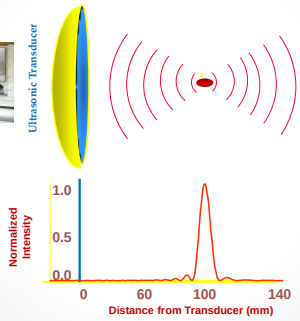
- Complete *in situ* treatment
- Debulking of tumor
- Combined treatments (radiation, chemo, etc.)
- Palliative treatment for pain
- Targeted drug or gene delivery

Current Clinical Systems

InSightec Exablate

Philips Sonalleve

Phased Array Transducer

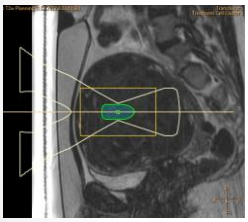


Hynynen (Toronto)

Clinical Workflow

- Patient preparation
  - clear skin entry
- Patient positioning
  - US coupling
- Treatment planning
  - Clearance of bubbles in beam path
- Treatment delivery
  - MR thermometry
- Treatment assessment
  - T2-w imaging and
  - contrast-enhanced T1-w imaging (non-prefused volume ↔ necrosis)

Treatment Planning



Planning based on 3D

- High resolution 3D data set
- See cor, sag and axial simultaneously
- High contrast T2w images

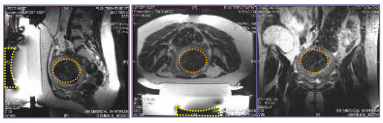
Visualizing geometries

- US beam contour (beige)
- Treatment cell (green) – expected ablation zone
- Region of high attention (Seosa box, yellow)
- Far field safety margin

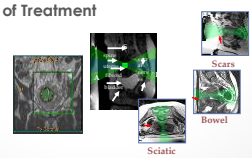
Philips Healthcare

Treatment Planning

I. MR Planning Images



II. Review of Region of Treatment

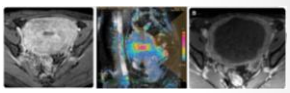


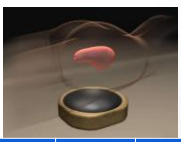
InSightec Inc.

Treatment Delivery

Electronic beam steering:
Outwards-moving concentric circles
4 – 16 mm ø

Uterine Fibroid



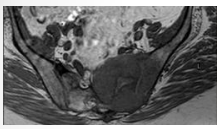


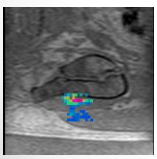
Diameter (mm)	Length (mm)	Volume (ml)
4	10	0.1
8	20	0.6
12	30	2.3
16	40	5.4

Investigational Device

Philips Healthcare

MR-HIFU Bone Mets Pain Therapy





Origin of pain

- Intra-osseous pressure irritates nerve endings
- Malformed bones (lytic lesions) mechanically trigger pain receptors within the bone and surrounding tissue
- Functional pain – blastic lesions causing weakening of the bone

MR-HIFU pain therapy

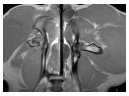
- Treatment of painful Bone Mets
  - Pelvis, Sacrum, Scapula, Ribs, long bones
- Cortical bone – high US absorption, no MR signal
- Metastasis – typically more MR signal than bone
- MR-HIFU pain relief mechanism:
  - Ablation of periosteal nerves may cause immediate pain relief
  - Tumor necrosis → reduced mass effect

Investigational Device

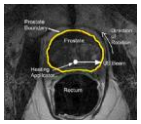
Philips Healthcare

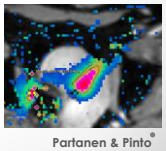
MRgFUS: Prostate

Aim at comparable clinical efficacy as surgery and radiation therapy but with less complications.



Transurethral approach



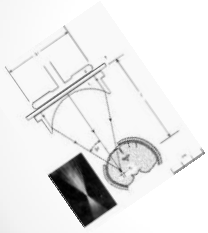


- Investigational Device

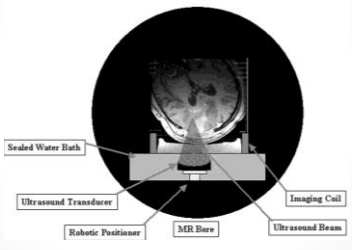
Partanen & Pinto

Early Brain Application

Fry brothers (circa 1955)

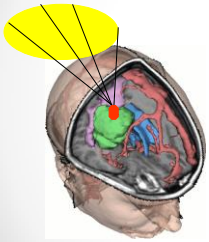


MRgFUS: Craniotomy Study

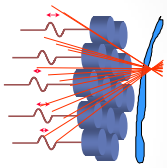


Drs. Mardor and Ram, Sheba Medical Center

MRgFUS: Trans-Skull Phased Arrays



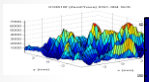
RF signals

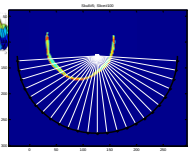


Phase correction to Compensate for Skull thickness

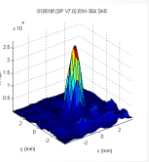
K. Hynynen (Toronto)

Trans-skull Phase Correction



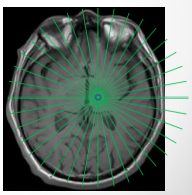


No correction



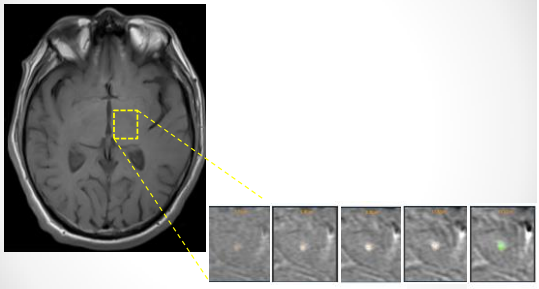
CT based correction

Brain MRgFUS: Prepartion and Planning



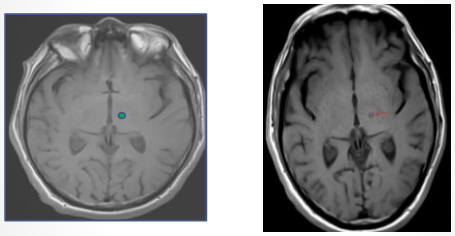
Elias (UVA Neurosurgery)

Brain MRgFUS: Treatment



Elias (UVA Neurosurgery)

Brain MRgFUS: Post-treatment



Elias (UVA Neurosurgery)

MRgFUS: Brain Applications

- Potential benefits for multiple brain indications:
  - Precise and accurate – sharp margins
  - Therapeutic effect is immediate and verifiable
  - Accelerated recovery
  - Reduced risks of infection, of damage to the non-targeted area, and of blood clot formation
  - No exposure to radiation
  - Single treatment
  - No cumulative dose

Non-Thermal Mechanisms & Effects

- Non-Thermal Mechanisms
  - Cavitation (microbubble generation)
  - Radiation pressure (mechanical forces at the focus)
- Tissue Effects
  - Higher energy levels
    - Tissue destruction
    - Hemorrhage
  - Lower energy levels
    - Increased vascular permeability
    - Increased membrane permeability
    - Cavitation enhanced ablation

Potential Brain Applications

- MR Guided Focused Ultrasound for brain indications:

1) Ablation
   a. Essential tremors
   b. Parkinson
   c. Neuropathic pain
   d. Obsessive compulsive disorder
   e. Epilepsy
   f. Tumors
2) Clot-lysis for hemorrhagic and ischemic stroke

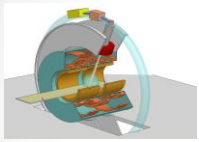
1) Reversible and focal opening of the blood brain barrier
   a. Chemotherapy
   b. Drugs delivery
2) Neuromodulation

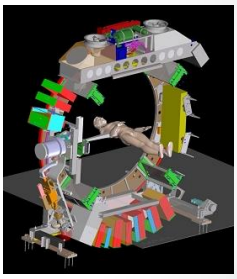
Hananel

Barriers to Clinical Translation

1. Regulatory
2. Reimbursement
3. Competing technologies
4. Need for better dosimetry
5. Need for robust QA

MR-guided Radiotherapy





[Mali, UCM Utrecht]

Summary

- MRgFUS is a powerful non-invasive therapeutic technology capable of treating a potentially wide range of clinical indications
- Clinical applications of MRgFUS range from hyperthermia to drug delivery and thermal ablation
- Wide clinical acceptance will depend on overcoming regulatory, payer (economics), and current technological and workflow challenges
- Emergence of MR-guided radiotherapy may further enable clinical translation of MRgFUS

Acknowledgment

- AAPM TG-241: MRgFUS Task Group
- Philips Healthcare
- InSightec Inc.
- Focused Ultrasound Foundation