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 with HIFU

Visualization
Image guidance & Temperature mapping

Therapy

Positioning & Power control

Workstation
**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

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**Focused Ultrasound (FUS)**

\[ I = I_0 e^{-2ax} \]

- \( I_0 \): initial beam intensity
- \( a \): attenuation coefficient
- \( x \): distance traveled

**Transducer Parameters**
- Diameter
- Focal distance
- Frequency (MHz)
- Power (W)

**Ultrasound propagation parameters**
- Speed of sound in tissues
- Reflection
- Refraction
- Absorption

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**Pennes Bioheat Transfer Equation**

\[
\rho C \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) + Q + Q_B + A
\]

- \( \rho \): density [kg/m³]
- \( C \): specific heat [J/kg°C]
- \( T \): temperature [°C]
- \( K \): thermal conductivity [W/m°C]
- \( Q \): power density [W/m³]
- \( Q_B \): perfusion loss [W/m³]
- \( A \): metabolic heat generation [W/m³]
US heat: Absorption and Effect

Cumulative Equivalent Minutes
(Sapareto & Dewey; 1984)

\[
C_{EM} = \int_{\text{ref}}^\text{T} R(T - T_{\text{ref}}) \, dt
\]

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

\[
\Delta T = \gamma \cdot \alpha \cdot \Delta T \cdot B_0 \cdot TE
\]

\[\gamma, \alpha, B_0, \text{TE}\]

Maximum Temp °C Thermal Dose

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Source: Diedrich, Buth-Pandy, et al.
MRgFUS Range of Clinical Applications

- Radiation Oncology
- Intervventional Radiology & Oncology
- Thermal Ablation & Surgery
- Hyperthermia + XRT
- IG Drug Delivery

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

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-preserved 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
Treatment Planning

I. MR Planning Images

II. Review of Region of Treatment

Treatment Delivery

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

Uterine Fibroid

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<tr>
<th>Diameter (mm)</th>
<th>Length (mm)</th>
<th>Volume (ml)</th>
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Treatment Delivery

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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

* Philips Healthcare

* Investigational Device

Philips Healthcare

Investigational Device
MRgFUS: Prostate

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

Partanen & Pinto

* Investigational Device

Early Brain Application

Fry brothers (circa 1955)

MRgFUS: Craniotomy Study

Drs. Mardor and Roni, Sheba Medical Center
MRgFUS: Trans-Skull Phased Arrays

Trans-skull Phase Correction

Brain MRgFUS: Preparation and Planning
Brain MRgFUS: Treatment

Brain MRgFUS: Post-treatment

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. Drug delivery
     2) Neuromodulation

Barriers to Clinical Translation

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

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

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