Ultra High-Field MRI as a Therapeutic Modality for the Treatment of Brain Metastases with Comparison to MR Guided Focused Ultrasound

Joshua de Bever, PhD
Department of Radiology
Stanford University
Overview

• Brain Mets: Motivation and Challenges

• MR guided Focused Ultrasound (MRgFUS)

• Ultra High-Field (UHF) MR Hyperthermia
  • “Focused RF”
Brain Mets: Motivation and Challenges

• Most common type of brain tumors
  • ~200,000 cases per year (USA)
  • > all intracranial tumors

• Treatment options
  • Surgical resection
  • Whole-brain radiation therapy (WBRT)
  • Corticosteroids
  • Stereotactic Radiosurgery (SRS)

• Median overall survival:
  • Untreated: 1 month
  • With treatment: 3-11 months

T1w - Gd
Ultra High-Field MRI

- MRI w Gd leads in BM detection
- 66-75% of patients who present with a single lesion on CT actually have multiple lesions
- Higher Field = More Signal
- Increase: Resolution, speed, etc

Fink et al, SNI, 2013
Ultra High-Field MRI: Challenges

SPGR
TR=4000ms
FA = 30°

FA error (%)

Local SAR MIP (W/kg)

BIRDCAGE MODE

Sagittal  Coronal  Axial

Courtesy of: Mehrir Pendse, ISMRM 2015 #573
Ultra High-Field MRI: Challenges

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Grissom, MRM 2012;68:1553–1562

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IMPULSE

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Local SAR MIP (W/kg)

Measured ΔT

0.45°C

0.86°C

0.51°C

BIRDCAGE MODE

SAR UNAWARE

IMPULSE

Coronal

5

-100

0

100

-100

Local SAR MIP (W/kg)

Sagittal

Coronal

Axial

Sagittal

Coronal

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Sagittal

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Q: Can this undesired heating been turned into something positive?
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• PhD – Robotics
  • NSF IGERT Award

• Dennis Parker
• Robert Roemer
• Doug Christensen
• John Hollerbach
MR Guided Focused Ultrasound

FUS creates *localized* intense heating

MRI provides anatomical imaging and monitoring
Cancer Therapy Wish List: MRgFUS

- ✔ Non-Invasive
- ✔ Free of Ionizing Radiation
- ✔ Free of Toxic Chemicals
- ✔ Monitoring: MR thermometry
MRgFUS Cancer Therapy

• Treatment goals:
  • Kill all cancerous tissue
  • Protect healthy tissue
  • Minimize treatment time

Ultrasound transducer (US) produces localized intense heating.
Treat next location in tumor by electronically steering beam.
Multiple pulses needed to treat entire tumor.
Phased-Array allows 3D focal spot steering *without* physical movement of transducer
MR Thermometry
Robotics

Perception -> Cognition -> Action
Robotics

Perception → Cognition → Action
Robotics

Perception → Cognition → Action
Adaptive Model-Predictive Controller (AMPC)
Control Loop

MRI → Ethernet → Controller (Matlab) → Fiber → US Generator

1. Temperature Measurement
2. US command
Control Challenges

• Protect healthy tissue

• Conform treatment to tumor shape, may be surrounded by complex anatomy

• MRgFUS treatments take a long time

• Faster heating makes control more difficult
Thermal Dose and Tissue Damage

- 240 CEM = Tissue Necrosis
- Dose rate **doubles** every 1°C rise

\[ CEM_{43} = \int R^{(T(t)-43)} dt \]

\[ \begin{align*}
T \geq 43^\circ C : R &= 2 \\
T \leq 43^\circ C : R &= 4
\end{align*} \]

CEM: Cumulative Equivalent Minutes @ 43°C

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Time to Deliver 240 CEM</th>
</tr>
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<tbody>
<tr>
<td>43 °C</td>
<td>240 min</td>
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<tr>
<td>44 °C</td>
<td>120 min</td>
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<tr>
<td>50 °C</td>
<td>~2 min</td>
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<tr>
<td>55 °C</td>
<td>~3.5 sec</td>
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</table>
Treatment Without Prediction

- Haven’t reached 240 CEM target dose. US beam stays on.
- 200 CEM
- 1,000 CEM!
- 2,000 CEM!!

Discrete MR Measurement
True Temp.

Time
Temperature
Adaptive Model-Predictive Control

- Discrete MR Measurement
- Model Prediction

Temperature vs. Time graph with predicted stop times at 180 CEM and 240 CEM.
Adaptive Model-Predictive Controller

• Patient specific model derived and adapted in real-time
  • Reduced setup time, adapts to changing tissue environment

• Protect normal tissue w. configurable temperature constraints

• Conform treatment using any path or treatment scheme
Prediction Model

- Every treatment voxel modeled by:
  - Exponential Heating
    \[
    T_{\text{heat}_i}(t) = A \left( 1 - e^{-t/\tau_{\text{Heat}_i}} \right) + C
    \]
  - Exponential Cooling
    \[
    T_{\text{cool}_i}(t) = -A e^{-t/\tau_{\text{cool}_i}} + C
    \]
Adaptive Model-Predictive Control

Predicted Stop Time

Time

Temperature

Discrete MR Measurement

Model Prediction

240 CEM
Normal Tissue Safety

Controller starts US

Controller stops US

43 °C

41 °C

Controller starts US

Controller starts US
Results: Simulation

Prediction saves time!

AMPC can protect healthy tissue
Results: Simulation

- Prediction **Disabled**
  - Median: 886 CEM
  - 44 safety violations

- Prediction **Enabled**
  - Median: 450 CEM
  - 30 safety violations

Prediction delivers target dose more accurately. Improved safety, time saved.
In Vivo: Experiment Setup

Sagittal Slice

Coronal Slice
Results: In Vivo - Efficacy
Transcranial FUS
Transcranial FUS
FUS Through Skull Flap

No Correction

After Phase Correction

Courtesy of Scott Almquist – Univ. Of Utah
Essential Tremor

PRE-TREATMENT

POST-TREATMENT
Treating Brain Metastases
Transcranial FUS
Transcranial FUS: Challenges
Multiple Brain Metastases

Fink, SNI, 2013
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Coronal

Axial

Courtesy of: Mehir Pendse, ISMRM 2015 #573

\(^1\)Grissom, MRM 2012;68:1553–1562
Q: Can this undesired heating been turned into something positive?
A: We’re going to find out....
Configuration 1: Dedicated Applicator

Advantages:
- Applicator is close to anatomy; better spatial control
- Thermometry and hyperthermia can occur simultaneously
- Frequency of applicator can be different from imaging frequency

Disadvantages
- More hardware, cables
- Coupling between two transmitters is possible

Courtesy of: Mihir Pendse, ISMRM 2015 #3224
Configuration 2: All-In-One

Advantages
• Single piece of hardware: fewer cables and coupling issues

Disadvantages
• Only possible at ultra-high-fields
  • Need high Larmour frequency to achieve focal heating
• Must interleave hyperthermia & imaging
• Spatial control is limited by size and frequency of pTx coil

pTx coil used as RF applicator

Courtesy of: Mihir Pendse, ISMRM 2015 #3224
Optimize for MAX-SAR instead of MIN-SAR
Max SAR Algorithm: Focused RF

- 8ch pTx coil for 7T (298 MHz)
  - Loop height = 16 cm
  - Loop width = 5 cm
  - Coil diameter = 28.5 cm

Courtesy of: Mihir Pendse, ISMRM 2015 #3224
<table>
<thead>
<tr>
<th>Target 1</th>
<th>SAR Maximum Intensity Projections</th>
<th>W/kg</th>
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Complex Channel Weightings
Potential

• FRF has all the positives of MRgFUS
  • Non-invasive, monitoring, free of ionizing radiation, etc.

• Hyperthermia
  • Can improve outcomes of radiation and chemotherapy
  • Treat multiple metastases

• Ablation - Direct cell death
  • May not be possible
  • Increase local SAR via Tumor-Targeted Nanoparticles?

• BBB Opening
Road Map

• Investigate optimal coil designs
  • Sim4Life – Realistic body models

• Simulate treatments
  • Integrate adaptive model-predictive controller

• Experimentally verify simulations with 8-Ch pTx coil on 7 T MRI
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