Sonication & Feedback Control Strategies for MRg Hyperthermia with the Insightec Prostate Array

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Presentation Outline

- Introduction
  - Hyperthermia (HT): Clinical significance, delivery, monitoring
  - Overview: Insightec ExAblate system
- Numerical study & preliminary analysis
  - HT-specific operational modifications to prostate ablation array
  - Experiments in phantom
- Real-time MRTI & Control in vivo

Hyperthermia – Clinical Significance

- Typical HT regimen combined with radiation or chemotherapy
  - 40 – 45 °C, $T_{90} = 40.5 \text{ °C}$, CEM43C: 6 – 10 min, time: 30 – 60 min

Compelling Evidence: Recent Randomized Phase III Trials

- Glioblastoma: 2 yr Survival - 15% to 31%
- Melanoma: 2 yr local control - 28% to 46%
- Chest Wall Recurrence (Breast Cancer): CR - 43% to 77%
- Advanced Pelvic Disease: CR - 39% to 55%
- Head & Neck Tumors: 5 yr local control – 24% to 69%
- LA Cervical: 3 yr survival 27 to 51%; local control 41 to 61%
- Sarcoma (HT+CT): disease free survival – 16.2 to 31.7 mo
HT – Emerging Applications

- Targeted drug delivery – liposomes
- Anti-tumor immunity stimulation
- Immune modulation for cancer vaccines
- Hormone therapy

Prostate HT

- Precise delivery of uniform HT to prostate is challenging
- Ultrasound (US) applicators for targeted prostate HT
  - Smith 1999, Nau 2005

MRgHIFU – Drug Delivery

- Recent animal studies of HT with MR-guided HIFU systems
  - Scanned focus for liposome drug release (Staruch 2011, Partanen 2012)
  - Pulsed-HIFU for enhanced docetaxel uptake (InSightec, Mu PMB 2012)
MR Thermometry (MRTI) during HT

- Precise temperature measurement necessary in HT
- Long-term MRTI during HT is challenging
  - Motion, susceptibility changes, phase drift
  - Compensation: Accuracy 0.3 – 1 °C reported during MRgHT
    - Temp. reference fiducials
    - Multi-baseline
    - Referenceless

Prostate Treatment with ExAblate 2100

- Clinical trials for focal tumors → whole gland ablation
- ExAblate prostate array at multiple sites
- Motivation: Fast track prostate HT with ExAblate 2100

Study Objectives

- Implement HT-specific, long-duration sonications
  - Work within ExAblate system constraints
- Real-time MRTI and control for HT with ExAblate prostate array
Models: Identify Array Beamforming

- Hardware and software specs of ExAblate prostate array
  - Proprietary array layout, dimensions
  - Proprietary element interconnection scheme
  - Phase round offs
  - Input power limitations
- Pennes bio-heat model

HT-specific Beamforming Examples

- CW sonications (15 min), time-avg surface intensity = 0.86 W/cm²
- MRTI: 3.0 T, PRFS, SPGR: TE = 16 ms, FOV = 14 cm, FA = 30°

Patient-Specific Models - Feasibility

- Pennes bio-heat transfer equation in 3D
- Patient specific geometry
- Temperatures calculated using commercial FEM solver
**Conformal HT: Multi-foci Sonication**

- **Dominant lesion**
- **Central axial plane**
- **Oblique sagittal plane**
- **Time-avg. surface intensity = 0.85 W/cm²**
- **SAR = 300 W/kg**

**Diverging Sonication: Volumetric HT**

- **Dominant lesion**
- **Central axial plane**
- **Oblique coronal plane**
- **Time-avg. surface intensity = 1.35 W/cm²**
- **SAR overlay: Cylindrically diverging beam**

**Beam-pattern Analysis**

- **Useful illumination patterns for HT**

<table>
<thead>
<tr>
<th>Beamforming</th>
<th>Surface Intensity (W/cm²)</th>
<th>Vol. T&gt;40 °C (cm³)</th>
<th>Vol. T&gt;41 °C (cm³)</th>
<th>Targeting capability and caveats</th>
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</thead>
<tbody>
<tr>
<td>Simultaneous multi-foci focusing (Num of foci + 4 – 8)</td>
<td>0.66 – 0.72</td>
<td>8.8 – 10.8</td>
<td>4.5 – 5.8</td>
<td>Selective heating of small targets. Potential unintended hotspots due to side lobes from shallow or off-axis focusing. Useful for localized conformal HT.</td>
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<tr>
<td>Conlinear focusing (depth = 25 – 50 mm)</td>
<td>0.7 – 0.75</td>
<td>12 – 12.1</td>
<td>6.0 – 6.6</td>
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<tr>
<td>Diverging sonication (Radius of curvature = 10 – 40 mm)</td>
<td>1.05 – 1.2</td>
<td>24.4 – 37.2</td>
<td>13.3 – 21.5</td>
<td>Uniform energy deposition. Suitable for targeting posterior quadrants and deep gland targets. Potential bone heating.</td>
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<tr>
<td>Planar sonication</td>
<td>0.94</td>
<td>35</td>
<td>22.8</td>
<td></td>
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</table>
Development of MRTI with Prostate Array

- **RTHawk** real-time MRI system, GE 3T MR scanner
- **SPGR** pulse sequence
  - TE = 13.4 ms, FOV = 28-32 cm, 3 slices
- **PRFS** thermometry
- 95% CI for baseline temp
  - 0.4 – 1.2 °C (5x5 px ROI)

Feedback Control

- Sharp 4-point focus
  - Focal dist. = 30 mm
  - Foci: 0.5 cm apart
- Mild 4-point focus
  - Focal dist. = 40 mm
  - Foci: 1 cm apart
- Cylindrical diverging ROI: 40 mm

**In vivo Assessment: Swine study**

- Acute study - 28.7 kg female swine
- Respirations: 10 breaths/min
- Heart rate ~87 beats/min
**Conclusions**

- Modifications to ExAblate for HT delivery were successful
- Implemented HT delivery and MRTI/control in vivo
- MRgHT with InSightec prostate ablation system feasible
- Additional work necessary for clinical implementation
  - Dynamic beam patterns (FUSIMO)
  - Multi ROI for volumetric control
  - Extend accuracy of MRTI
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ΔT = 4 °C Dimensions

- 1: Sharp 4-point focusing
- 2: Mild 4-pt focusing
- 3: Diverging

Beam plots – Yuan Zhang, Kim Butts, Stanford University