MR Guided Focused Ultrasound Surgery

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Some people talk in their sleep.
Lecturers talk while other people sleep.
Abnormality?
Treatment options

- Medical management for symptomatic relief
- Surgery
- Embolization
- Focused ultrasound
Treatment options

UAE vs Surgery

- Patient selection
  - Better for
    - Menorrhagia
    - Multiple and small and submucosal fibroids
  - Less effective if
    - Large uterus (>22cm)
    - Single and large and subserosal fibroids

- Outcomes
  - 80-95% effective in short to medium term, comparable to surgery
  - Risk of reintervention
    - UAE: 10% at 1 year, 20% at 5 year
    - Myomectomy: 23% at 5 year
  - UAE is not appropriate if want pregnancy
1. Patient Table
   • Docks to GE 1.5T and 3T MR scanners
   • Phased array transducer

2. Operator Console
   • Controls all treatment planning and operation
   • Sits next to GE MR in console room

3. Equipment Cabinet
Patient table: patient cradle

Ultrasound transducer

Motion system
Focused ultrasound physics
Treatment options

HIFU vs UAE
• MR guidance
• Less painful
• Faster recovery
• Similar volume reduction
• Similar symptom relief
• Similar reintervention rate
• Longer procedure
Advantages of MR guidance

Targeting

Thermal dose mapping

Post-procedure target validation
Proton resonant frequency shift
Phase difference

\[ \Delta \Phi = \alpha \Delta T \ 2\pi \ \gamma \ B_0 \ TE \]

\[ \alpha = -0.01 \text{ ppm/°C} \]

Image during heating

Image before heating

Thermal dose

Abnormality?
Clinical impact

• Bone metastases are common
• Poor prognostic sign
• Symptomatic
Treatment options

• Analgesics

• Systemic therapy
  – Chemotherapy
  – Hormonal
  – Radiopharmaceuticals
  – Bisphosphonates

• Localized therapy
  – EBRT
  – Surgery
  – RFA
  – Cryoablation
  – HIFU?
Conformal focused ultrasound probe
HIFU bone vs soft tissue treatment

The absorption coefficient of bone is 20-30x greater than that of soft tissue

**In soft tissue:**
- Narrow, point-shaped focus is required
- High energy density at focal point

**In bone tissue:**
- Wide Beam Approach
- Low energy usage
- Shorter treatment time

Typical Sonication Energy 2500J

Typical Sonication Energy 1500 J
Focal Point - the location of the imaginary targeted focus

Dose Overlay - the region that will be heated above the ablation threshold
MR Thermometry

*MR thermometry provides real-time feedback during treatment, showing regions that have met the thermal dose threshold.*
BM004
Clinical Study Protocol
FDA | G070022

A Pivotal Study to Evaluate the Effectiveness and Safety of ExAblate Treatment of Metastatic Bone Tumors for the Palliation of Pain in Patients Who are not Candidates for Radiation Therapy

Evaluation period: 3 months
A prospective, randomized, single-blind, multiple site, two-arm study

Goal: 148 treated subjects
Stanford is one of 17 sites

BM010
Clinical Study Protocol
FDA | G080206

A Feasibility Study to Evaluate the Safety and Initial Effectiveness of ExAblate MR Guided Focused Ultrasound Surgery in the Treatment of Pain Resulting from Metastatic Bone Tumors with the ExAblate 2100 Conformal Bone System

Evaluation period: 3 months
A prospective, non-randomized, multiple site, single-arm study

Goal: 50 treated subjects
Stanford is one of 3 sites
Evaluate:

- Will 50% of ExAblate-treated patients in the test arm achieve 2 point + improvement from baseline to 3-Months without increase in medication?
- Is there a placebo effect? (FDA)
  - This will require the use of a sham control group. Sham patients who do not see an improvement will be provided with an ExAblate treatment following the placebo effect evaluation.
- Safety (as defined by adverse events)

Eligibility

- Bone mets not suitable for radiation
- Pain score
- Tumor size
- Tumor location
- Tumor visible by MRI and device accessible
- ≤ 5 painful lesions
- Life exp ≥3mo
- KPS optimized 60

Treatment

- most painful lesion treated
- time limited 180mins

Follow-up questionnaires

- 1, 3 d; 1, 2 wk; 1, 2, 3 mo

Sham

- most painful lesion treated
- energy output disabled

“Rescue” Treatment

- for non-responders
Patient’s pain level: VAS (Visual Analog Scale)

- Score from 0 to 10:
  - 0 - no pain at all
  - 10 - worst pain imaginable

Patient’s medications

- Changes in frequency and dosage of analgesic intake

Post treatment and follow up images

- Volume of tissue that shows evidence of treatment effect on contrast enhanced MR images
Criteria for pain palliation treatment outcome according to international consensus on palliative radiotherapy:

**Complete response:**
- Pain score of zero at the treated site with no concomitant increase in analgesic intake

**Partial response:**
- Pain reduction of 2 points or more at the treated site on a 0 - 10 scale without analgesic increase;
- Analgesic reduction of 25% or more from baseline without an increase in pain
Clinical Case

• 78 year old male
• Metastatic melanoma
• Painful osteolytic lesion in right ischium
• Treated with Cyberknife, in September, 2010, with persistent pain
Clinical Case

- 78 year old male with painful metastatic melanoma lesion in right ischium
- MRgFUS procedure was performed on March 24th, 2011
- 19 sonications, up to 1900J, <60 min sonication time
Clinical Case
Overall results to date

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>3 months post</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Max Pain Score</strong></td>
<td>7.3 ± 1.9</td>
<td>2 ± 2</td>
</tr>
<tr>
<td><strong>Avg Pain Score</strong></td>
<td>4.6 ± 1.1</td>
<td>1.4 ± 1.5</td>
</tr>
</tbody>
</table>
Abnormality?
Treatment options

- **Single**
  - <3cm
    - SRS or WBRT + SRS
  - ≥3cm
    - Cerebellar meta. Severe clinical symptoms
      - Ope + WBRT
    - The largest tumor ≥3cm or Severe clinical symptoms
      - SRS or WBRT + SRS (no. of meta. 2-4)
      - WBRT (no. of meta. >4)
- **Multiple**
HIFU of the brain

Thalamic ablation
Thalamic ablation

Thalamic ablation for essential tremor
Thalamic ablation for essential tremor
HIFU as a treatment alternative

Diagnosis?
Treatment options

<T4 < N3 < M1 lesion>

• Breast-conserving surgery w/ XRT and Tamoxifen
• Total mastectomy
• Breast-conserving surgery w/o XRT
• Breast-conserving surgery w/ LND and XRT
• Modified radical mastectomy
• Adjuvant therapy
  • XRT to LN and chest wall
  • Systemic chemotherapy w/ or w/o hormone therapy

>T4 or N3 or M1 lesion

• Systemic chemotherapy followed by surgery with LND and XRT
• Hormone therapy
• XRT a/o surgery for pain relief
• Bisphosphonate
MR-guided system for ablation of breast tumors

Gianfelice et al. Radiology 2003;227:849-855
Sample HIFU ablation
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (n)</th>
<th>Sessions (n)</th>
<th>Assessment methods</th>
<th>Volume of tumor in treated area</th>
<th>Complete ablation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hüber</td>
<td>1</td>
<td>1</td>
<td>Histology and radiology</td>
<td>An entire tumor in the treated area</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td>Gianfelice</td>
<td>12</td>
<td>1</td>
<td>Histology</td>
<td>A tumor partially treated in five patients and entirely treated in seven</td>
<td>2/7 (28.5)</td>
</tr>
<tr>
<td>Zippel</td>
<td>10</td>
<td>1</td>
<td>Histology</td>
<td>An entire tumor in the treated area in all patients</td>
<td>2/10 (20)</td>
</tr>
<tr>
<td>Gianfelice</td>
<td>24</td>
<td>1.2</td>
<td>Histology (core biopsy) and radiology</td>
<td>An entire tumor in the treated area in all patients</td>
<td>19/24 (79)</td>
</tr>
<tr>
<td>Furusawa</td>
<td>30</td>
<td>1</td>
<td>Histology</td>
<td>An entire tumor in the treated area in all patients</td>
<td>15/28 (53.5)</td>
</tr>
<tr>
<td>Wu</td>
<td>23</td>
<td>1</td>
<td>Histology and radiology</td>
<td>An entire tumor in the treated area in all patients</td>
<td>23/23 (100)</td>
</tr>
<tr>
<td>Okuno</td>
<td>10</td>
<td>1.5</td>
<td>Radiology</td>
<td>An entire tumor in the treated area in all patients</td>
<td>9/10 (90)</td>
</tr>
<tr>
<td>Choi</td>
<td>10</td>
<td>1</td>
<td>Radiology</td>
<td>An entire tumor in the treated area in all patients</td>
<td>10/10 (100)</td>
</tr>
<tr>
<td>Wu</td>
<td>22</td>
<td>1</td>
<td>Radiology and histology</td>
<td>An entire tumor in the treated area in all patients</td>
<td>20/22 (90)</td>
</tr>
</tbody>
</table>
Abnormality?
Unresectable pancreatic adenocarcinoma
Unresectable pancreatic adenocarcinoma

- **Resectability criteria include**
  - clear fat plane around celiac and SMA
  - patent SMV and portal vein
  - no distant metastases

- **‘Borderline’ resectable cancer**
  - abutment of a portion of the SMA or celiac axis
  - severe unilateral SMV or portal vein impingement
  - GDA encasement up to origin at hepatic artery
Treatment options

Stage 1 and 2
• Radical pancreatic resection:
  – Whipple procedure
    • Total pancreatectomy when necessary for adequate margins.
    • Distal pancreatectomy for tumors of the body and tail of the pancreas
  – 5-FU or gemcitabine chemotherapy and radiation therapy

Stage 3 and 4
• Palliative
  – surgical biliary and/or gastric bypass
  – percutaneous radiologic biliary stent placement
  – endoscopic biliary stent placement
  – chemotherapy with gemcitabine
  – pain-relieving procedures (e.g., celiac block) and supportive care
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. of patients</th>
<th>Treatment</th>
<th>Pain relief</th>
<th>HIFU related adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xiong et al.</td>
<td>2001</td>
<td>21</td>
<td>HIFU monotherapy</td>
<td>15/17 (88%)</td>
<td>None</td>
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<tr>
<td>Wang et al.</td>
<td>2002</td>
<td>13</td>
<td>HIFU monotherapy</td>
<td>8/10 (80%)</td>
<td>Mild pancreatitis (2)</td>
</tr>
<tr>
<td>Xie et al.</td>
<td>2003</td>
<td>41</td>
<td>HIFU mono vs HIFU + gemcitabine</td>
<td>HIFU mono 66.7% HIFU + gemcitabine 76.6%</td>
<td>None</td>
</tr>
<tr>
<td>Xu et al.</td>
<td>2003</td>
<td>37</td>
<td>HIFU monotherapy</td>
<td>24/30 (80%)</td>
<td>None</td>
</tr>
<tr>
<td>Yuan et al.</td>
<td>2003</td>
<td>40</td>
<td>HIFU monotherapy</td>
<td>32/40 (80%)</td>
<td>None</td>
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<tr>
<td>Wu et al.</td>
<td>2005</td>
<td>8</td>
<td>HIFU monotherapy</td>
<td>8/8 (100%)</td>
<td>None</td>
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<tr>
<td>Xiong et al.</td>
<td>2009</td>
<td>89</td>
<td>HIFU monotherapy</td>
<td>54/67 (80.6%)</td>
<td>2nd degree skin burn (3) Subcutaneous sclerosis (6) Pancreatic pseudocyst (1)</td>
</tr>
<tr>
<td>Zhao et al.</td>
<td>2010</td>
<td>39</td>
<td>HIFU + gemcitabine</td>
<td>22/28 (78.6%)</td>
<td>None</td>
</tr>
</tbody>
</table>
Diagnosis?
Treatment options

- Transplant
- Surgical resection
- Local ablation
  - RFA
  - Cryoablation
- Reduce regional tumor burden (large tumor)
  - TACE + surgery or RFA
Example hepatic ablation
Conformal focused ultrasound probe
Problems with motion
Example hepatic ablation

Abnormality?
Treatment options

- **Watchful waiting**
  - Yearly DRE, PSA, urodynamics and postvoid residual measures
  - Modify behavior

- **Medical management**
  - Alpha adrenergic receptor blockers
  - 5-a reductase inhibitors

- **Invasive management**
  - TURP
  - TUMT
  - TUNA
  - HIFU?
HIFU for BPH

Methods: Transurethral applicators

Images courtesy of Dr. Graham Sommer
What happens to the tissue?

Ablation day

Max Temp 30°C

Contrast Enhanced

10°C

Contrast Enhanced

Axial T2

Gross Specimen

4 weeks later
Prostate cryoablation

<table>
<thead>
<tr>
<th></th>
<th>Pre- MRI cryoablation</th>
<th>10 weeks post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary frequency (daytime)</td>
<td>Every 1.5 hrs</td>
<td>Every 2-4 hrs</td>
</tr>
<tr>
<td>Urinary frequency (nighttime)</td>
<td>Every 1.5 hrs</td>
<td>Once per night</td>
</tr>
<tr>
<td>AUA symptom severity score</td>
<td>23 (severe)</td>
<td>13 (moderate)</td>
</tr>
<tr>
<td>Bother score</td>
<td>4 (&quot;highly dissatisfied&quot;)</td>
<td>1 (&quot;pleased&quot;)</td>
</tr>
<tr>
<td>Peak Flow (mL/sec)</td>
<td>5.1</td>
<td>10.3</td>
</tr>
<tr>
<td>Post-void residual volume (mL)</td>
<td>187</td>
<td>58</td>
</tr>
<tr>
<td>Total volume voided (mL)</td>
<td>110</td>
<td>143</td>
</tr>
</tbody>
</table>
Abnormality?
HIFU for soft tissue tumors

Yellow circles represent planned areas of sonication as seen on this coronal T1 MRI

Avedian, Gold, Ghanouni, P01 Project 1
MR guided HIFU

Images courtesy of Dr. Alessandro Napoli
Abnormality?

Images courtesy of Dr. George Segall
MR guided HIFU

• Noninvasive

• MR image guidance and intervention
  – MR thermometry

• Applications
  – Uterine fibroids
  – Benign and malignant bone tumors
  – Brain – chronic pain, ET, Parkinson’s…. 
  – Prostate cancer and BPH
  – Liver primary and metastatic tumors
  – Pancreatic adenocarcinoma and benign lesions
  – Soft tissue tumors
  – Breast
  – Spinal degenerative pain
  – Thyroid and parathyroid
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Questions and Answers / Discussion
Abnormality?
Treatment options

• Surgical and interventional therapies
  – Parathyroidectomy
  – Percutaneous alcohol ablation
  – HIFU

• Medical therapies
  – Bisphosphonates
  – Maintain calcium intake and vitamin D
  – Raloxifene
  – Cinacalcet
HIFU treatment of the parathyroid

Kovatcheva et al. AJR 2010;195:830-835
HIFU treatment of the thyroid

Esnault et al. AJNR 2010;31:1967-68