Current Status of HIFU Therapy for Treatment of Benign and Malignant Tumors of the Abdomen, Pelvis and Bone

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Objectives
- Overview of current HIFU clinical systems
- Overview of current clinical applications
  - Uterine fibroids
  - Pancreatic tumors
  - Liver tumors
  - Renal cell carcinoma
  - Bone metastases
  - Breast cancer
  - Thyroid/parathyroid tumors
- Discuss future clinical applications

Clinical HIFU Systems
US-guided

Ultrasound targeting
- Ultrasound-guided HIFU devices do not provide monitoring of lesion development (other than hyperecho from boiling)
- Methods for estimating in situ intensity exist
- Methods for monitoring HIFU therapy are in development
  - Thermometry
  - ARFI
  - Elastography
Clinical HIFU Systems
MR-guided

Temperature mapping
Proton Resonance Frequency shift

\[ \Delta T = \frac{\Delta \Phi}{\alpha \cdot \gamma \cdot T_E \cdot B_0} \]

- \( \gamma = 2\pi \cdot 42.56 \text{ MHz/T} \)
- \( \alpha = 0.0101 \text{ ppm/°} \)
- \( T_E \approx 20 \text{ ms} \)
- \( B_0 = 1.5 \text{ T} \)

Real Time Feedback
Reliable necrosis volume

Clinical Applications for HIFU Ablation

\begin{itemize}
  \item Indications: Non-invasive ablation of solid benign or malignant tumors
  \item Requirement:
    \begin{itemize}
      \item Acoustic window – critical
      \item Non-oncologic applications
    \end{itemize}
  \end{itemize}
Treatment of Uterine Fibroids with HIFU

Uterine Fibroids

Pre-HIFU
Post-HIFU

Courtesy of Dr. Hu

HIFU of Fibroids - Fertility
- Uterine leiomyomas (fibroids) affect ~25% of women of reproductive age
- Large nonhysteroscopically resectable submucosal and intramural fibroids can cause cavitary distortion impacting fertility
- MRgFUS
  - 54 pregnancies in 51 women
    - Live births (41%)
    - Spontaneous abortion (28%)
    - Elective abortion (11%)
    - Ongoing pregnancies beyond 20 wks (20%)
    - Vaginal delivery rate – 64%

Rabnovidi et al. Fertil Steril 2008

Oncologic Applications for HIFU Ablation
- Oncologic indications:
  - Palliation
  - Local tumor control
  - Poor surgical candidate
  - Patient refuses surgery
- Oncologic applications:
  - Pancreatic cancer
  - Liver tumors (should be below costal margin)
  - Renal cell carcinoma
  - Osteosarcoma/soft tissue sarcomas/bone metastasis
  - Breast cancer
HIFU Ablation for Palliation of Advanced Pancreatic Cancer

Pancreatic Cancer
- 4th leading cause of cancer deaths in the US
- >42,000 new cases – >35,000 deaths in 2010
- 80-90% are “unresectable” when diagnosed
- Poor outcomes
  - Median survival without therapy: 3 months
  - Median survival with therapy: 6-12 months
- Palliation of symptoms is important
  - Pain relief

Treatment of Pancreatic Cancer

Pre-HIFU

6 months post-HIFU
HIFU Ablation of Liver Tumors

- Acoustic window is a problem
- Treatment through the ribs has been reported
- Treatment after rib resection
- Randomized study (Wu et al.)
  - TACE vs. HIFU+TACE (50 patients)
  - HIFU treatment 2-4 weeks following TACE

<table>
<thead>
<tr>
<th>outcome</th>
<th>TACE</th>
<th>TACE+HIFU</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Median survival</td>
<td>4.0 months</td>
<td>11.3 months</td>
<td>0.004</td>
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<tr>
<td>6-month survival</td>
<td>13.2%</td>
<td>80.5%</td>
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<td>1-year survival</td>
<td>0%</td>
<td>42.9%</td>
<td>&lt;0.001</td>
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Liver Tumors

HIFU Ablation of Renal Cell Carcinoma

Pre-HIFU

3 months post-HIFU

Courtesy of Dr. Hu
Renal Cell Carcinoma

- Small renal tumors are being more frequently identified
- Surgical resection has significant morbidity
- Many pts are poor surgical candidates
- Other less invasive procedures are needed

Marberger et al. BJU 2005

HIFU Ablation of Bone Metastasis

Bone Metastasis

- Bone is a common site for metastatic disease
  - Prostate CA and Breast CA
- Pain from bone metastasis is the most common cause of cancer pain
- Current treatment options:
  - Analgesics
  - Chemotherapy
  - Biphosphonates
  - Local therapies:
    - Radiation (no relief in 20-30%)
    - Surgery
    - RFA

Feasibility Study

Patient population:
36 treatments in 31 patients were conducted, targeting 32 metastatic lesions

Patient tumor characteristics:
- Treated bone mets from primary tumor type: renal, colorectal, lung, breast, prostate and other cancers
- Treated lesion locations: iliac bone, ischium bone, sacrum, femur, scapula, humerus, clavicle
- Treated lesion type: both osteolytic and osteoblastic

Bone Metastasis – Palliation of Pain


HIFU Ablation of Breast Cancer

Breast Cancer – Phase II Study Results.

- Evaluation of Safety and Efficacy
- Total 195 patients treated, 30 were treated with contrast enhanced planning images

Mean necrosis of ablated tumor = 96.9 ± 4%
- 15 patients had 100% necrosis
- 3 patients had < 95% necrosis


HIFU Ablation of Thyroid/Parathyroid Tumors
Clinical studies

HIFU: Future

Gross Specimen

The Future of HIFU

- Expanded indications for therapy
- Enhanced tumor-specific immunity
- Drug delivery
  - Targeted delivery (Heat activation)
  - Enhancement of vascular permeability
  - Enhanced penetration
- Improved treatment monitoring
  - Thermometry
  - Elastography
  - Radiation Force Imaging
- Device approvals

Pain control
Summary

- Overview of current clinical systems
- Overview of current clinical applications
  - Uterine fibroids
  - Pancreatic tumors
  - Liver tumors
  - Renal cell carcinoma
  - Bone metastases
  - Breast cancer
  - Thyroid/parathyroid tumors
- Discussed future clinical applications

Thank You