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

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Objectives

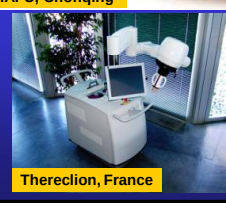
- Overview of current HIFU clinical systems
- Overview of current clinical applications
  - Uterine fibroids
  - Pancreatic tumors
  - Liver tumors
  - Renal cell carcinoma
  - Bone metastases
  - Breast cancer
  - Thyroid/parathyroid tumors
- Discuss future clinical applications

Clinical HIFU Systems
US-guided


YDME, Beijing

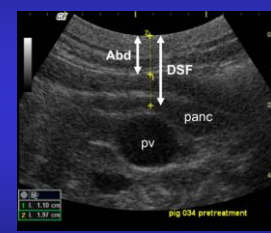

HIAFU, Chonqing


Shanghi A&S


Thereclion, France

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



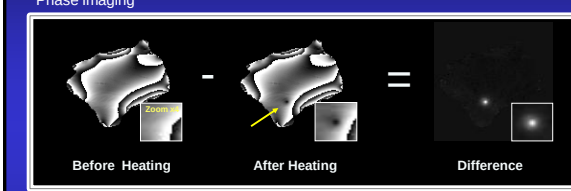
Clinical HIFU Systems
MR-guided

InSightec, Isreal

Philips, US/France

Temperature mapping
Proton Resonance Frequency shift

Phase Imaging



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

$\gamma = 2\pi \cdot 42{,}56$ MHz/T	Gyromagnetic Ratio
$\alpha = 0.0101$ ppm/°C	Water Frequency Shift
$T_E \sim 20$ms	Echo Time
$B_0 = 1.5$ T	Magnetic Field

Courtesy of Philips

Real Time Feedback
Reliable necrosis volume

Thermal map & Dose map

↓

Real time visualization
+ Feedback

↓

T > 57°C* or Dose >240 EM

↓

Stop heating

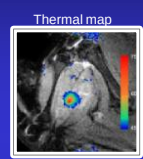
↓

Reliable necrosis volume
No a-priori knowledge needed
Simple and robust

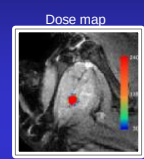
* Applies to the border of the cell. Temperatures at the center are higher, especially for larger cells.

Courtesy of Phiilips

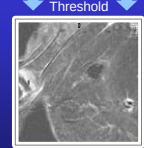
Thermal map



Dose map



↓ Threshold ↓



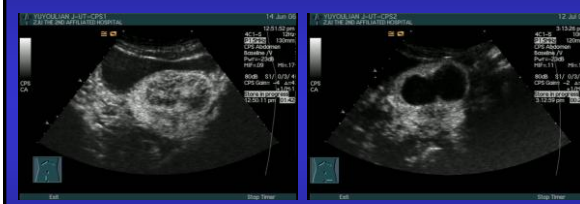
Non-perfused volume

Clinical Applications for HIFU Ablation

- Indications: Non-invasive ablation of solid benign or malignant tumors
- Requirement:
  - Acoustic window – critical
- Non-oncologic applications
  - Uterine fibroids

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%

Hanstede et al. Fertil Steril 2007
Rabinovici 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

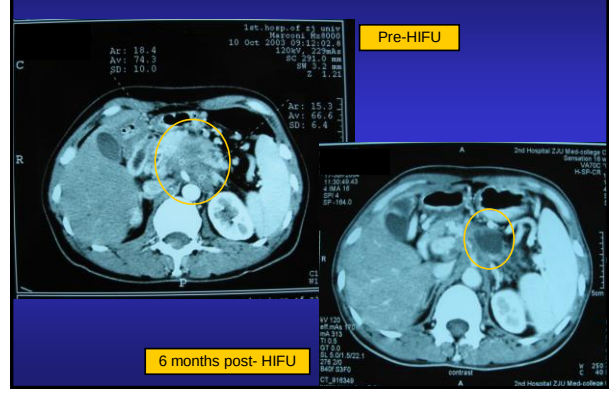
HIFU Ablation for Palliation of Advanced Pancreatic Cancer

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

Pancreatic Cancer



HIFU Ablation of Liver Tumors

HIFU Treatment 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

outcome	TACE	TACE+HIFU	p-value
Median survival	4.0 months	11.3 months	0.004
6-month survival	13.2%	80.5%	0.002
1-year survival	0%	42.9%	<0.001

Liver Tumors

Pre-HIFU

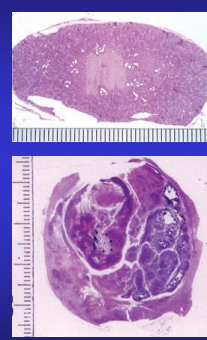
3 months post- HIFU

Courtesy of Dr. Hu

HIFU Ablation of Renal Cell Carcinoma

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

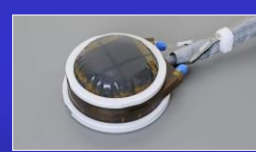


Marberger et al. BJU 2005

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



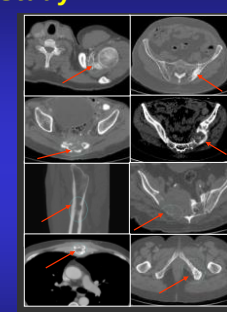
Feasibility Study

Patient population:

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

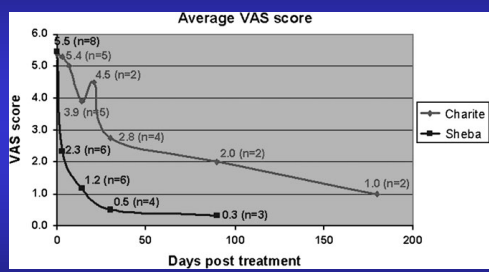
Patient tumor characteristics:

- 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



Liberman B *et al.* Pain palliation in patients with bone metastases using MR-guided focused ultrasound surgery: a multicenter study. Ann Surg Oncol. 2009 Jan;16(1):140-6. Epub 2008 Nov 11.

Bone Metastasis – Palliation of Pain

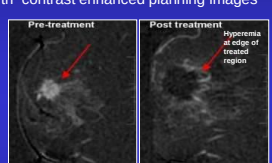


Catane et al. Ann Oncol 2007

HIFU Ablation of Breast Cancer

Breast Cancer – Phase II Study Results.

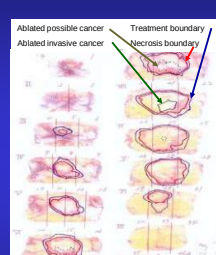
- Evaluation of Safety and Efficacy
- Total 195 patients treated, 30 were treated with contrast enhanced planning images



T1w contrast enhanced subtracted images

Mean necrosis of ablated tumor = 96.9 ± 4%

- 15 patients had 100% necrosis
- 3 patients had < 95% necrosis



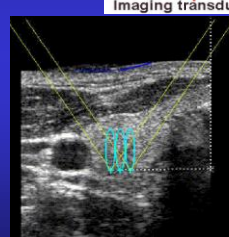
Post-treatment pathologic results

Furusawa H, Namba K, Thomasen S, Akiyama F, Bendet A, Tanaka C, Yasuda Y, Nakahara H. Magnetic Resonance-Guided Focused Ultrasound Surgery of Breast Cancer: Reliability and Effectiveness, J Am Coll Surg, 2006, 203(1):54-63

Courtesy of Breastopia Namba Medical Center, Miyazaki, Japan

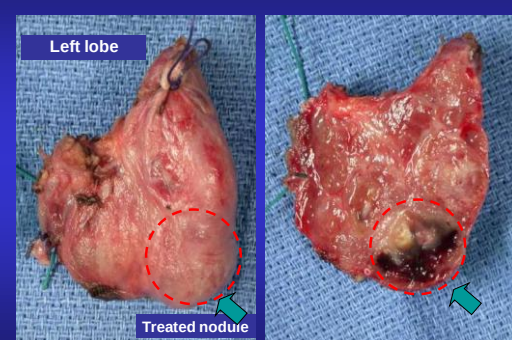
HIFU Ablation of Thyroid/Parathyroid Tumors

Clinical studies



Courtesy of Theraclion

Gross Specimen



Courtesy of Theraclion

HIFU: Future

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

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