INTRODUCTION

- History of HIFU
  - Past Experience
- Present Status
  - Instrumentation & Clinical Results
- Future of HIFU

Features of Advanced Medical Technology for Noninvasive Treatment

- Image Guided ---- [See What, Where & When You Treat, i.e. Must have Feedback]
- Plan Treatment At The Patient Table
- Control Energy To Create Desired Effect
- No Residual Effect On Treated Organ and Surrounding Tissues
- Must be Easy To Use
**Intracavitory Probes for Ultrasound Therapeutic Applications**

**ULTRASOUND – ADVANTAGES**
- US Can do both Imaging and Treatment
- Quick Tissue Destruction
- Bloodless
- Precise and Accurate
- Non-sterile environment

**HIFU MECHANISMS**
- **HIFU Therapy Mechanisms:**
  - Thermal (Coagulative Necrosis)
  - Cavitation
    - (w/wo Chemical Enhancer)
  - Mechanical (Shear / Radiation forces)
    - Changes at molecular level (< 43 C)

**Temperature at Focus Region for Prostate Surgery with HIFU**

**Basics of High Intensity Focused Ultrasound [HIFU]**
**HIFU LESION VOLUME CONTROLLING PARAMETERS**

- **ULTRASOUND FREQUENCY**
- **TRANSDUCER F -- NUMBER**
- **ABSORPTION COEFFICIENT**
- **PEAK INTENSITY**
- **ON Time & OFF Time**

**HIFU – Single Beam Focus Zone**

Lesion Size

\[ F_n = \frac{\text{Radius (R)}}{\text{Aperture (D)}} < 2 \]

\[ \text{Tissue Ablation due to Thermal Effect} \]

- Temperature rise to 70-90 Degrees C in < 4 Seconds
- Lesions are discrete & symmetrical
- No damage to intervening tissue

**Volume Lesions form a single lesion**
How & When HIFU Started

- 1927 Wood & Loomies: Biological Effects of Ultrasound
- 1942 - Lynn et al: Proposed Focused Ultrasound for Tissue Treatment
- 1945 - Fry et al: Brain Treatment

Prof. William J. Fry, Bioacoustic Research Laboratory, University of Illinois, IL. First HIFU System with four transducers to produce sufficient acoustic power for the treatment of brain disorders.

HIFU Lesions of Configurable Size and Shapes in the Cat Brain 1940’s

HIFU Lesions in Cat Brain with Greater Precision and Placement Of Selected Tissue Type
Intracavitary Probes for Ultrasound Therapeutic Applications
Intracavitory Probes for Ultrasound
Therapeutic Applications

APPLICATIONS OF HIFU FOR MALIGNANT TISSUE

MRI Temperature maps (PRF shift) during 10 s sonication in rabbit thigh muscle in vivo

Temperature Rise (°C)

Along the Beam Axis
Across the Focus

KH 2000

APPLICATIONS OF HIFU

For MALIGNANT TISSUE

Based on Success of Lithotripsy in 1984, HIFU Project was Started in 1986 at the Department of Urology, Indiana University School of Medicine, Indianapolis, IN

FSI TECHNOLOGY BACKGROUND

Illustration of a Prostate HIFU Probe

Prostate Cancer
Death 31,000 per Year
Detection 198,000 per Year
(1/11 men @ age of 65 has a chance of developing prostate cancer)

Benign Prostatic Hyperplasia
Over 7 Millions Men suffer from BPH
(Very high probability of developing BPH above the age of 55)

Both diseases are prevalent & costly
Effect Family & Quality of Life

Significance:

Narendra T. Sanghvi
Prostate Cancer

- HIFU Subtotal ablation of the prostate
  - 83% Success Rate After Two Years
  - Over 6000 Patients Treated with HIFU
  - Noninvasive
  - Less Complications
  - Lower Cost

Canine Prostate after HIFU Treatment
Bihrle and Sanghvi et al. 1994

The Sonablate™ 500 platform

- High Frequency & 3D Volume Imaging
- BPH and Prostate Cancer Treatment
- Totally Digital Platform (Windows NT)
- Upgradable Probes & Software
- Multiple Focal Depths / Transducers
- Split-Beam Technology
- Adjustable Power Level During Treatment
- REDUCED TREATMENT TIME

Sonablate™ Probe Technology

A patented technology that combines both imaging and therapy elements on a single ultrasound crystal.

- Therapy Element: 4.0 MHz, Curved Rectangular
- Imaging Element: 4.0/6.0 MHz, Curved Circular

Transrectal HIFU Probe
WHAT REGION OF PROSTATE SHOULD BE TREATED?

Accurate detection of the cancer region is very difficult even using TRUS, CT and/or MRI (endorectal coil)

Whole prostate should be ablated
Prostate Cancer Treatment Procedure

HIFU and Prostate Cancer

CLINICAL CASES

CASE 2 (H.M.), 79 y.o., T2aN0M0

Date

Jan-99
Mar-99
May-99
Jul-99
Sep-99
Nov-99
Jan-00
Mar-00
May-00
Jul-00
Sep-00
Nov-00
Jan-01

Serum PSA (ng/ml)

0.00
0.10
0.20
0.30
0.40
0.50
0.60
0.70
0.80
0.90

Negative Biopsies
CASE 1 (S.S), 78 y.o., T2aN0M0

- Prostate vol.: 39.9 ml
- Cavity formation: 5.5 ml
- Serum PSA: 13.0 ng/ml
- Negative biopsies: 86.2%
  - Nadir PSA: 0.40 ng/ml
- Positive biopsy: 2M
- Hypoechoic: G2+2

MRI & Endoscopy of Prostate Post HIFU Six Months

HIFU and Prostate Cancer European Multicenter Study

risk groups

- low risk (31.2%)
  - T1 - T2a and PSA ≤ 10 ng/ml and Gleason ≤ 6
  - Nadir PSA: 0.40 ng/ml
- middle risk (48.2%)
  - T2b or PSA 10.1-20 ng/ml or Gleason = 7
  - Nadir PSA: 0.20 ng/ml
- high risk (20.6%)
  - T2c or PSA > 20 ng/ml or Gleason ≥ 8
  - Nadir PSA: 0.27 ng/ml

negative biopsies

- 86.2%
- 81.8%
- 72.1%
**EFFICACY**

<table>
<thead>
<tr>
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<th>Radical Prostatectomy</th>
<th>External Beam Radiation</th>
<th>Brachytherapy</th>
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</thead>
<tbody>
<tr>
<td>HIFU Ablatherm®</td>
<td>47.5 - 84%</td>
<td>52 - 86%</td>
<td>7 - 89%</td>
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<tr>
<td>Disease free at 5 years</td>
<td></td>
<td></td>
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<tr>
<td>Sonablate 500</td>
<td>75 - 97%</td>
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**MORBIDITY**

<table>
<thead>
<tr>
<th></th>
<th>Radical Prostatectomy</th>
<th>External Beam Radiation</th>
<th>Brachytherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>incontinence</td>
<td>4 - 9%</td>
<td>5 - 49%</td>
<td>0.7 - 23%</td>
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<tr>
<td>impotence</td>
<td>22 - 66%</td>
<td>14 - 80%</td>
<td>11 - 67%</td>
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<tr>
<td>GI</td>
<td>0%</td>
<td>2 - 4%</td>
<td>14 - 63%</td>
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**HIFU and Prostate Cancer State of the Art**

<table>
<thead>
<tr>
<th>Therapeutic benefits</th>
<th>HIFU</th>
<th>Radiotherapy</th>
<th>Brachytherapy</th>
<th>Surgery</th>
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<tbody>
<tr>
<td>Non-Invasive</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
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<tr>
<td>Effective</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td></td>
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<tr>
<td>Early Feedback</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
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<tr>
<td>Quality of Life</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
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<tr>
<td>Repeatability</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td></td>
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<tr>
<td>Adaptable</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td></td>
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<tr>
<td>No Th. Impasse</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Cost Effective</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
</tr>
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</table>
Intracavitary Probes for Ultrasound
Therapeutic Applications

Figure 1. Comparison of negative biopsy results of brachytherapy (Brachy), 3-dimensional conformal radiation therapy (3D-CRT), external beam radiation therapy (XRT), cryoablation (CRYO) and HIFU.

HIFU and Prostate Cancer
Conclusion

HIFU treatment for prostate cancer is increasingly accepted and used by the medical community. This is a result of a fruitful collaboration between a biomedical company, physicists, and clinicians.

SUMMARY

1. Total prostate should be ablated
2. No severe complications
3. Possible one night stay or outpatient clinic?
4. Non-sterile procedure
5. HIFU can be repeated (Local recurrence after Rd, Px and/or Ho)

Prostate Cancer Clinical Trials

Under the Food and Drug Administration (FDA) Approved Protocol, Phase I clinical studies are conducted at:

Indiana University School of Medicine, Indianapolis, IN
PI: Dr. M. O. Koch and Dr. T. A. Gardner

Case Western Reserve University, Cleveland, OH
PI: Dr. M. Resnick and Dr. A. Sethel

Initially, patients with prostate cancer confined within the gland (T1/T2) or who have recurrent prostate cancer will be treated under these protocols.

For more detailed information about these studies please contact:
Focus Surgery, Inc. at 317-541-1500 or visit our web-site:
www.focus-surgery.com
OTHER APPLICATIONS of HIFU

- Tumors --- Liver, Brain, Breast, Pancreas, Rectum
- Heart (TMR—Trans Myocardial Revascularization)
- Acoustic Hemostasis
- Targeted Drug Delivery
- Blood Brain Barrier

FUTURE PROJECTS

- DEVELOPMENT OF FOCUSED ARRAY TRANSDUCERS FOR PROSTATE TREATMENT
- QUANTITATIVE ULTRASOUND IMAGING & THERAPY SYSTEMS FOR INCREASED EFFICACY AND SAFETY
- DEVELOP SECOND GENERATION HIFU SYSTEMS — UTILIZE CHEMICALS WITH HIFU TO TREAT CANCER TISSUE AT LOWER POWER LEVELS

Single and Split Focus Beams

Simple HIFU on Schlieren  Split Beam on Schlieren

Single Vs. Split Beam Transducer Configurations
Quantitative Lesion Imaging By Relative Attenuation Technique

Envelope of the backscattered RF data

$\Delta\beta$ = Relative change in the attenuation coefficient

Acknowledgments

Indiana University School of Medicine, Indianapolis, IN

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National Cancer Institute / NIH 2 R 43 CA 83244 - 02
National Cancer Institute / NIH 1 R 43 DK 59664 - 01
New Energy Development Organization / MITI, Tokyo, Japan

The Extracorporeal Treatment of Malignant Tumors & Cancers with HIFU

2002.7

CHONGQING HIFU TECHNOLOGY CO., LTD
TAIHAN METRA CORPORATION