
Past, Present and Future of Therapeutic
Applications of
High Intensity Focused Ultrasound
[HIFU]
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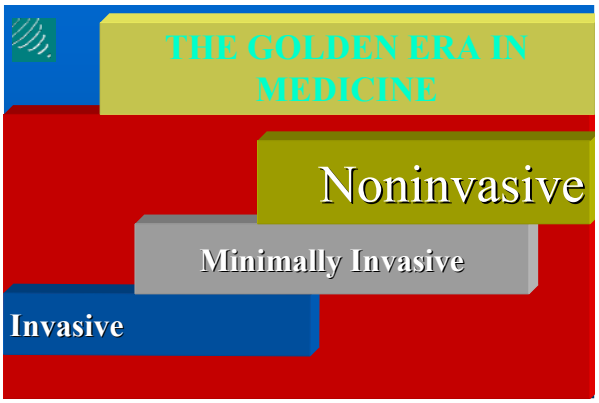
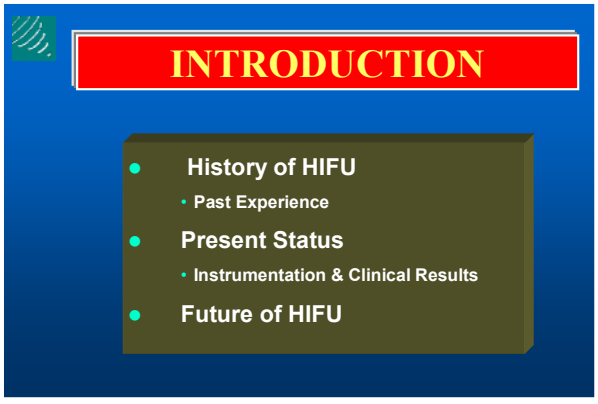
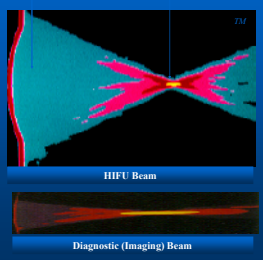

THE GOLDEN ERA IN MEDICINE
Noninvasive
Minimally Invasive
Invasive


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

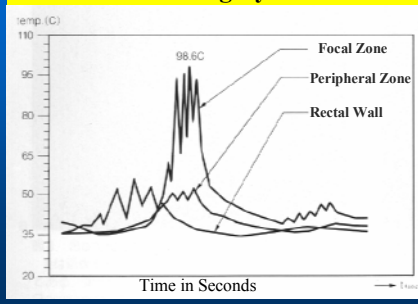

Features of Advanced Medical Technology for Noninvasive Treatment
Image Guided ---- [See What , Where & When You Treat, i.e. Must have FeedBack]
Plan Treatment At The Patient Table
Control Energy To Create Desired Effect
No Residual Effect On Treated Organ and Surrounding Tissues
Must be Easy To Use

ULTRASOUND -- ADVANTAGES



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

Temperature at Focus Region for Prostate Surgery with HIFU



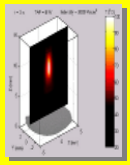
HIFU MECHANISMS

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

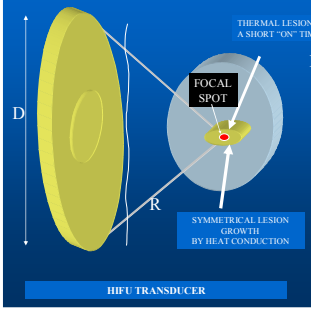
Basics of
High Intensity Focused Ultrasound
[HIFU]

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 = Radius (R) / Aperture (D) < 2

$I_{focus} = (I_0 * e^{-A^* \text{ Tissue Depth}})^* GF$

GF = Transducer Area / Focal Area

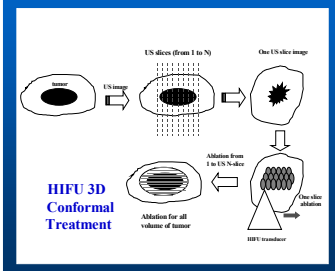
Temperature Rise = $I_{focus} * T_{on}$

Lesions In Turkey Tissue

HIFU Unique Features

- 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



line

slice

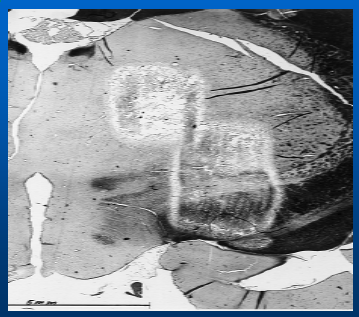
solid

Solid (section)

How & When HIFU Started

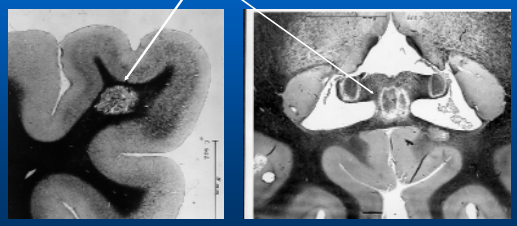
- 1927 Wood & Loomies: Biological Effects of Ultrasound
- 1942 - Lynn et al: Proposed Focused Ultrasound for Tissue Treatment
- 1945 - Fry et al: Brain Treatment

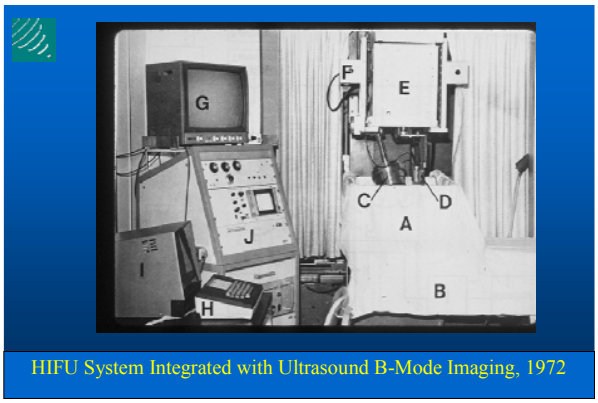
Prof. William J. Fry, Bioacoustic Research Laboratory, University of Illinoise, IL
First HIFU System with four transducers to produce sufficient acoustic power for the treatment of brain disorders.



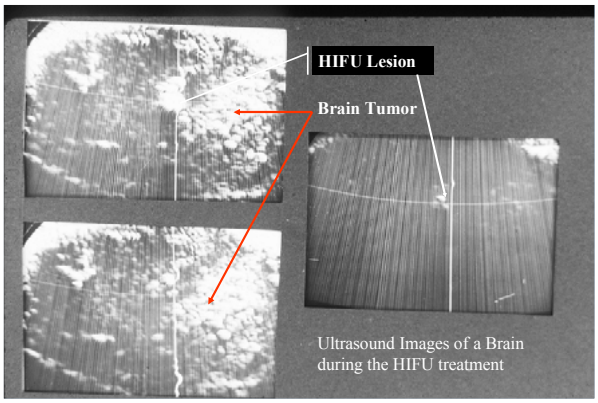
HIFU Lesions of Configurable Size and Shapes in the Cat Brain 1940's

HIFU Lesions in Cat Brain with Greater Precision and Placement Of Selected Tissue Type

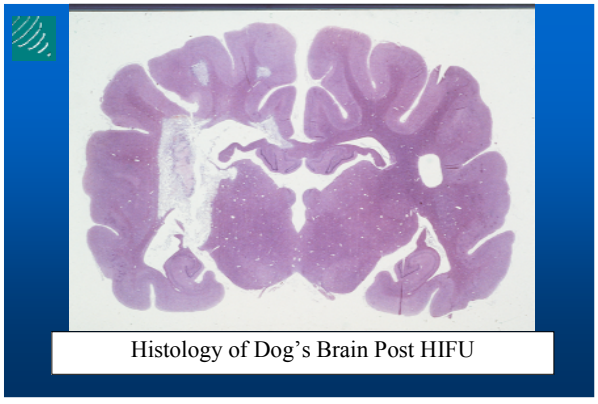




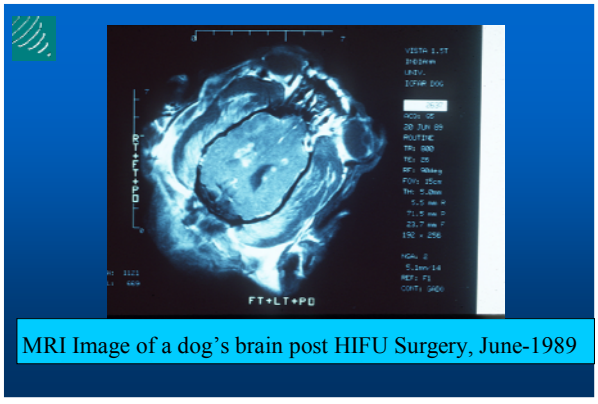
HIFU System Integrated with Ultrasound B-Mode Imaging, 1972



Ultrasound Images of a Brain during the HIFU treatment

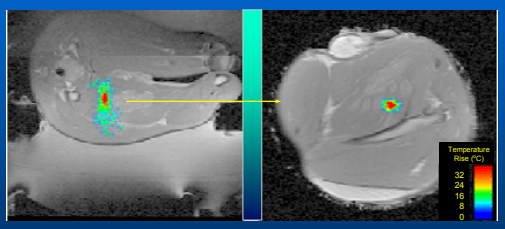


Histology of Dog's Brain Post HIFU



MRI Image of a dog's brain post HIFU Surgery, June-1989

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



Along the Beam Axis Across the Focus

KH 2000

APPLICATIONS OF HIFU
FOR
MALIGNANT TISSUE

FSI TECHNOLOGY BACKGROUND

Illustration of a Prostate HIFU Probe

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

Significance:

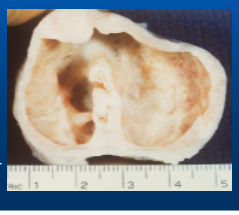
Prostate Cancer
Death 31,000 per Year
Detection 198,000 per Year
(1/11 men @ age 0f 65 has a chance of developing prostate cancer)

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

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

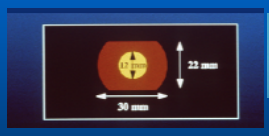
The Sonablate™ 500 platform

Sonablate™ 500

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

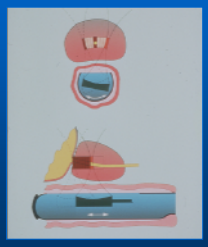
Sonablate™ Probe Technology

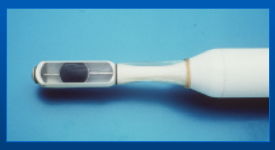
A patented technology that combines both imaging and therapy elements on a single ultrasound crystal.

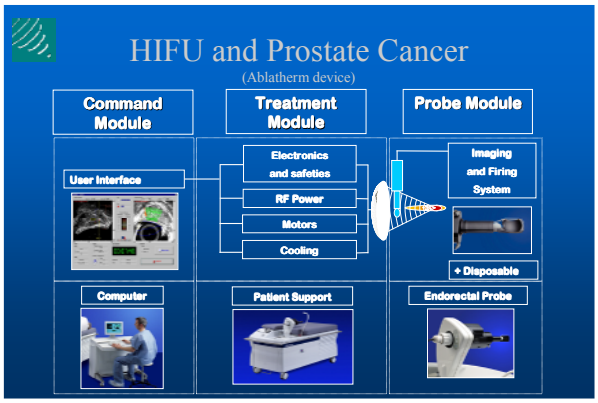


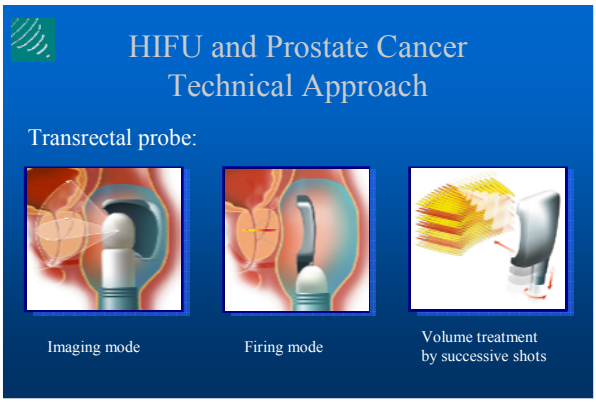
- Therapy Element: 4.0 MHz, Curved Rectangular
- Imaging Element: 4.0/6.0 MHz, Curved Circular

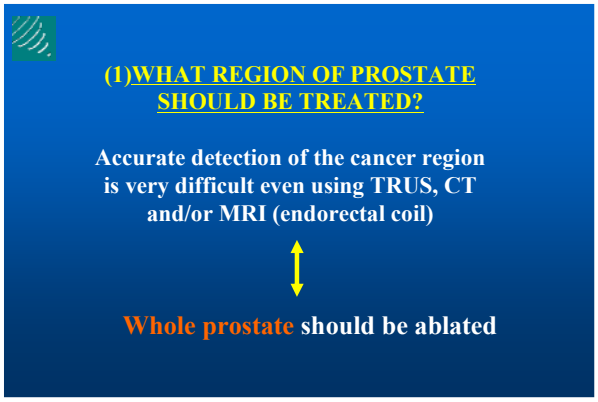
Transrectal HIFU Probe

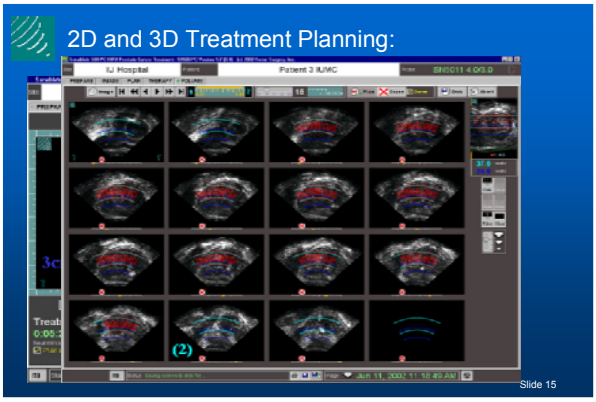


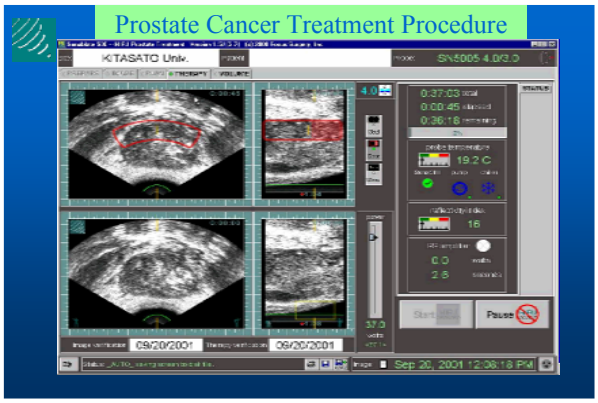


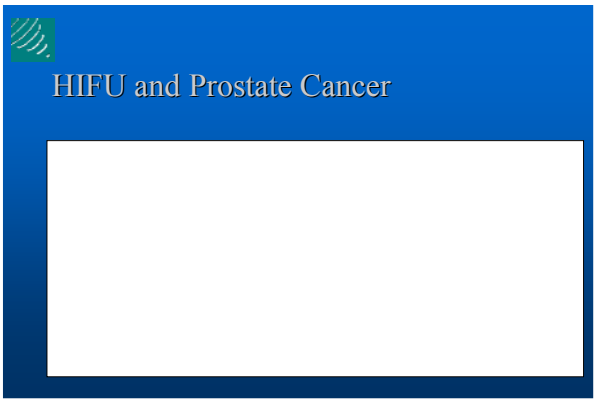

HIFU and Prostate Cancer
(Ablatherm device)
Command Module
Treatment Module
Probe Module
User Interface
Electronics and safeties
RF Power
Motors
Cooling
Imaging and Firing System
+ Disposable
Computer
Patient Support
Endorectal Probe

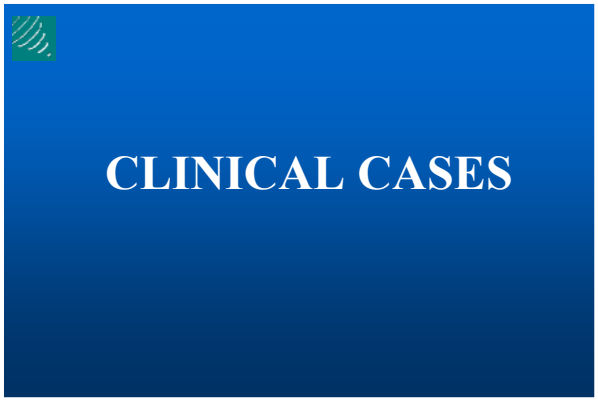

HIFU and Prostate Cancer
Technical Approach
Transrectal probe:
Imaging mode
Firing mode
Volume treatment by successive shots

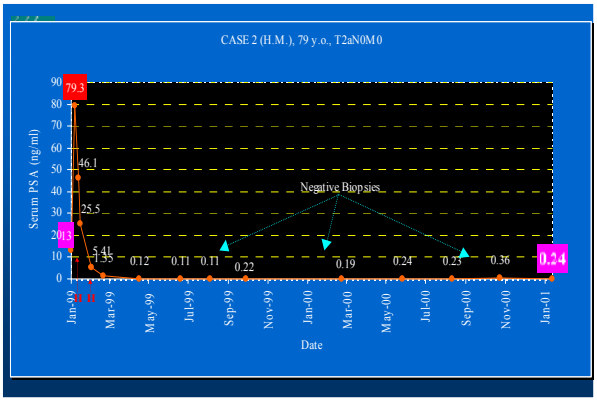

(1)WHAT REGION OF PROSTATE SHOULD BE TREATED?
Accurate detection of the cancer region is very difficult even using TRUS, CT and/or MRI (endorectal coil)
Whole prostate should be ablated

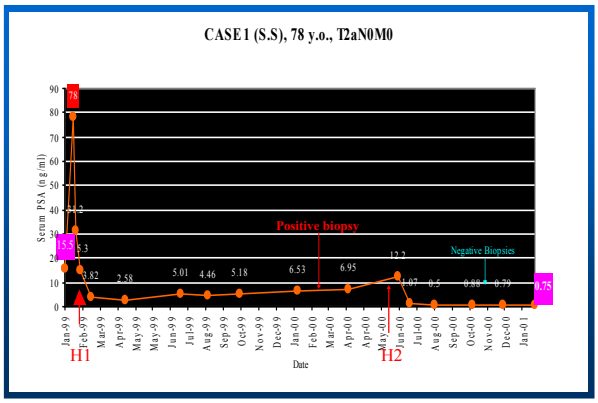

2D and 3D Treatment Planning:
Slide 15

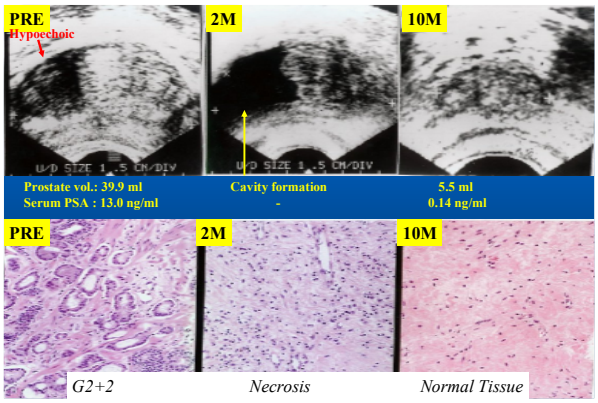

Prostate Cancer Treatment Procedure
KITASATO Univ.
09/20/2001
09/20/2001
Sep 20, 2001 12:06:18 PM

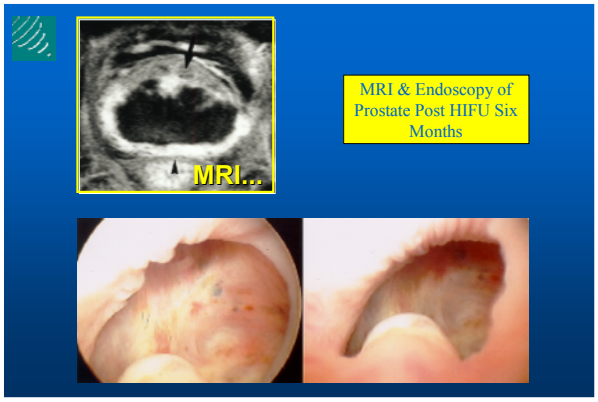

HIFU and Prostate Cancer

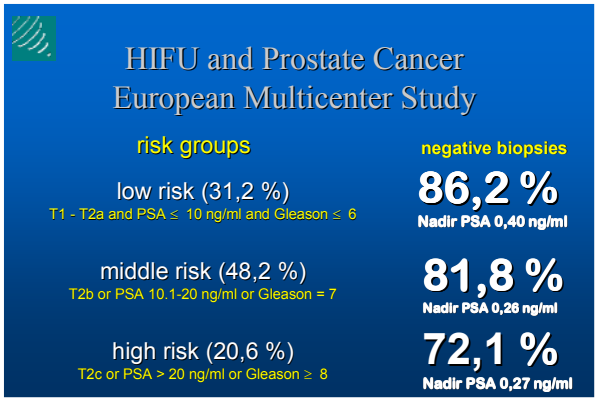

CLINICAL CASES


CASE 2 (H.M.), 79 y.o., T2aN0M0
Serum PSA (ng/ml)
Date
79.5
46.1
25.5
20.3
5.41
1.35
0.12
0.11
0.11
0.22
0.19
0.24
0.23
0.36
0.24
Negative Biopsies
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


CASE 1 (S.S), 78 y.o., T2aN0M0
Serum PSA (n g /ml)
Positive biopsy
Negative Biopsies
H1
H2
Date


PRE
Hypoechoic
2M
10M
Prostate vol.: 39.9 ml
Serum PSA : 13.0 ng/ml
Cavity formation
-
5.5 ml
0.14 ng/ml
PRE
2M
10M
G2+2
Necrosis
Normal Tissue


MRI...
MRI & Endoscopy of Prostate Post HIFU Six Months


HIFU and Prostate Cancer
European Multicenter Study
risk groups
negative biopsies
low risk (31,2 %)
T1 - T2a and PSA ≤ 10 ng/ml and Gleason ≤ 6
86,2 %
Nadir PSA 0,40 ng/ml
middle risk (48,2 %)
T2b or PSA 10.1-20 ng/ml or Gleason = 7
81,8 %
Nadir PSA 0,26 ng/ml
high risk (20,6 %)
T2c or PSA > 20 ng/ml or Gleason ≥ 8
72,1 %
Nadir PSA 0,27 ng/ml

EFFICACY

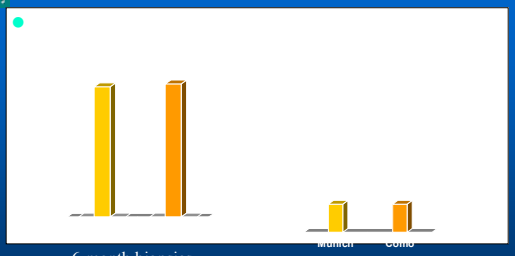
	HIFU Ablatherm®	Radical Prostatectomy	External Beam Radiation	Brachytherapy
Disease free at 5 years	47.5 - 84%	52 - 86%	23 - 88%	7 - 89%

Disease free at 1 year

Sonablate 500
75 - 97%

MORBIDITY

	HIFU Ablatherm®	Radical Prostatectomy	External Beam Radiation	Brachytherapy
incontinence	4 - 9%	5 - 49%	0.7 - 23%	0 - 18%
impotence	22 - 66% (with n. sp. - without n. sp.)	14 - 80% (with nerve sparing)	11 - 67% (short term - long-term)	20 - 50% (short term - long-term)
GI	0%	2 - 4%	14 - 63%	4 - 33%



Münich: 800+ patients - Como: first 127 patients

HIFU and Prostate Cancer State of the Art

Therapeutic benefits	HIFU	Radiotherapy	Brachytherapy	Surgery
Non-Invasive	Y	Y	N	N
Effective	Y	Y	Y	Y
Early Feedback	Y	N	N	Y
Quality of Life	Y	N	Y	N
Repeatable	Y	N	N	N
Adaptable	Y	N	Y	N
No Th. Impasse	Y	N	N	Y
Cost Effective	Y	Y	N	Y

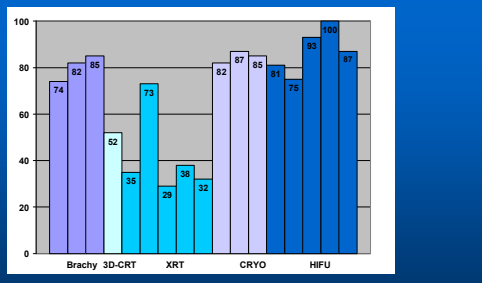


Figure 1. Comparison of negative biopsy results of brachytherapy (Brachy), 3-dimensional conformal radiation therapy (3D-CRT), external beam radiation therapy (XRT), cryoablation (CRYO) and HIFU.

From: John Rucastle, Ph.D. March-2004

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. Seftel**

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 317-541-1580 or visit our web-site:
www.focus-surgery.com

OTHER APPLICATIONS of HIFU

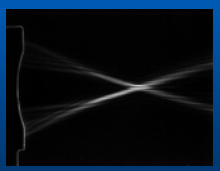
- Tumors --- Liver, Brain,Breast, Pancreas, Rectum
- Heart (TMR-- Trans Myocardial Revascularization)
- Acoustic Hemostasis
- Targeted Drug Delivery
- Blood Brain Barrier

FUTURE PROJECTS

- DEVELOPMENT OF *FOCUSED ARRAY* TRANSDUCERS FOR PROSTAE 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

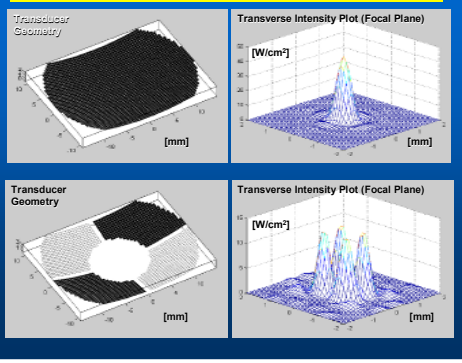
Single and Split Focus Beams

Simple HIFU on Schlieren



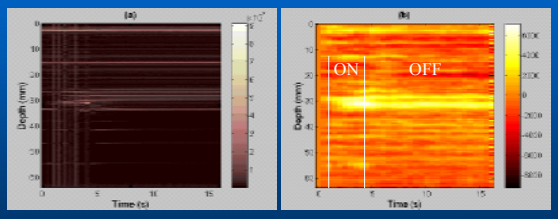
Split Beam on Schlieren

Single Vs. Split Beam Transducer Configurations



Quantitative Lesion Imaging By Relative Attenuation Technique

Color-coded M-mode images of a HIFU-created lesion in the turkey breast tissue

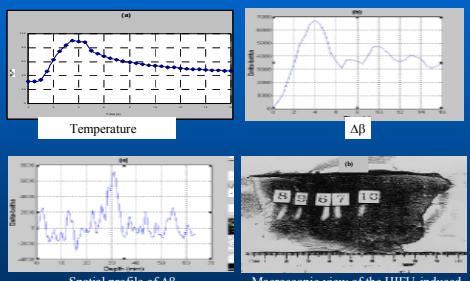


Envelope of the backscattered RF data

Δβ image

Δβ = Relative change in the attenuation coefficient

Results- Continued



Spatial profile of Δβ along the beam axis

Macroscopic view of the HIFU-induced lesions in the turkey breast tissue

Acknowledgments

Indiana University School of Medicine,
Indianapolis, IN

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National Cancer Institute / NIH 1 R 43 CA 83244 - 01

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