Treatment of Localized Prostate Cancer

Robert G. Pugach, M.D

Medical Director

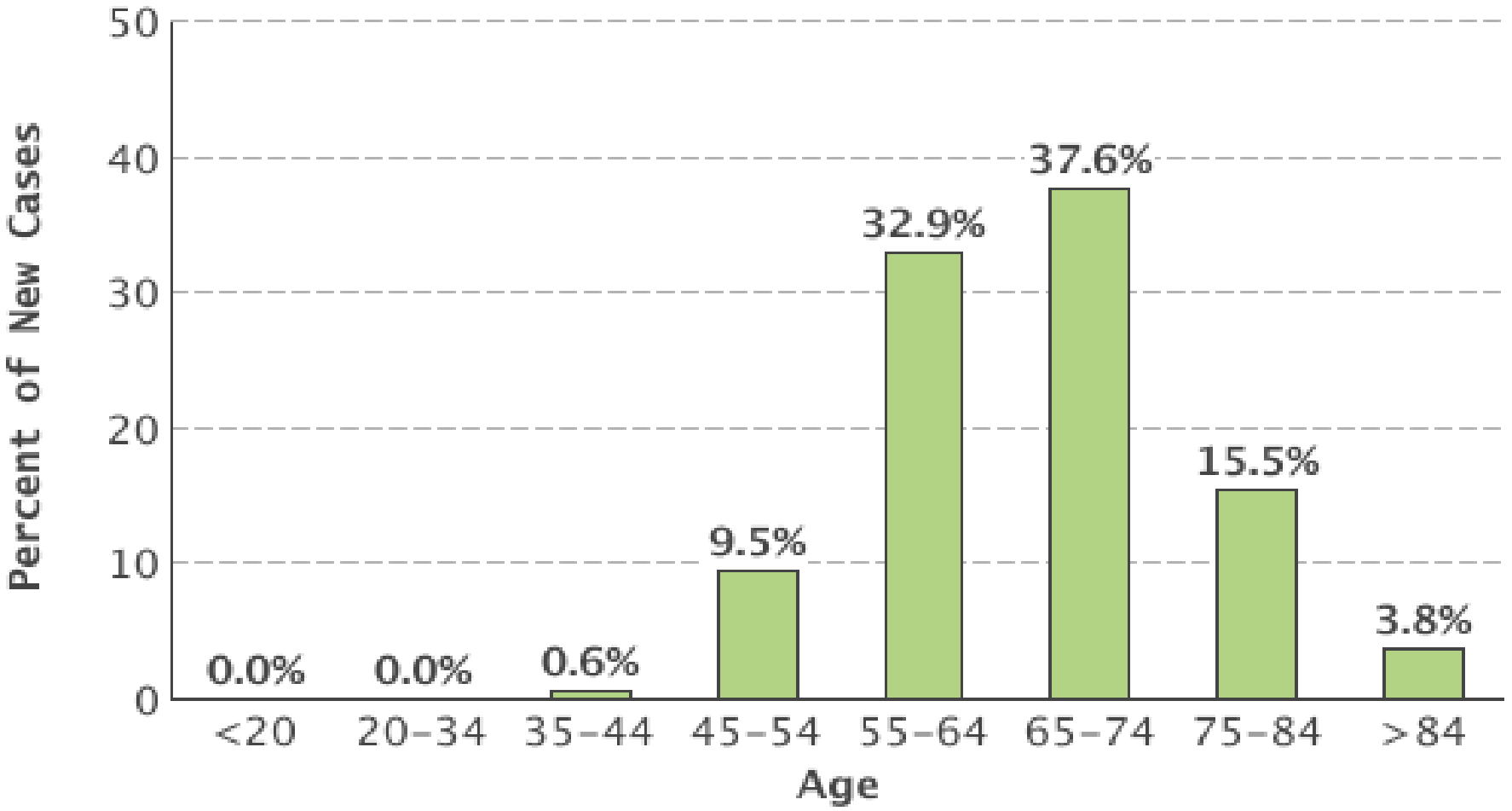
Western States HIFU

&

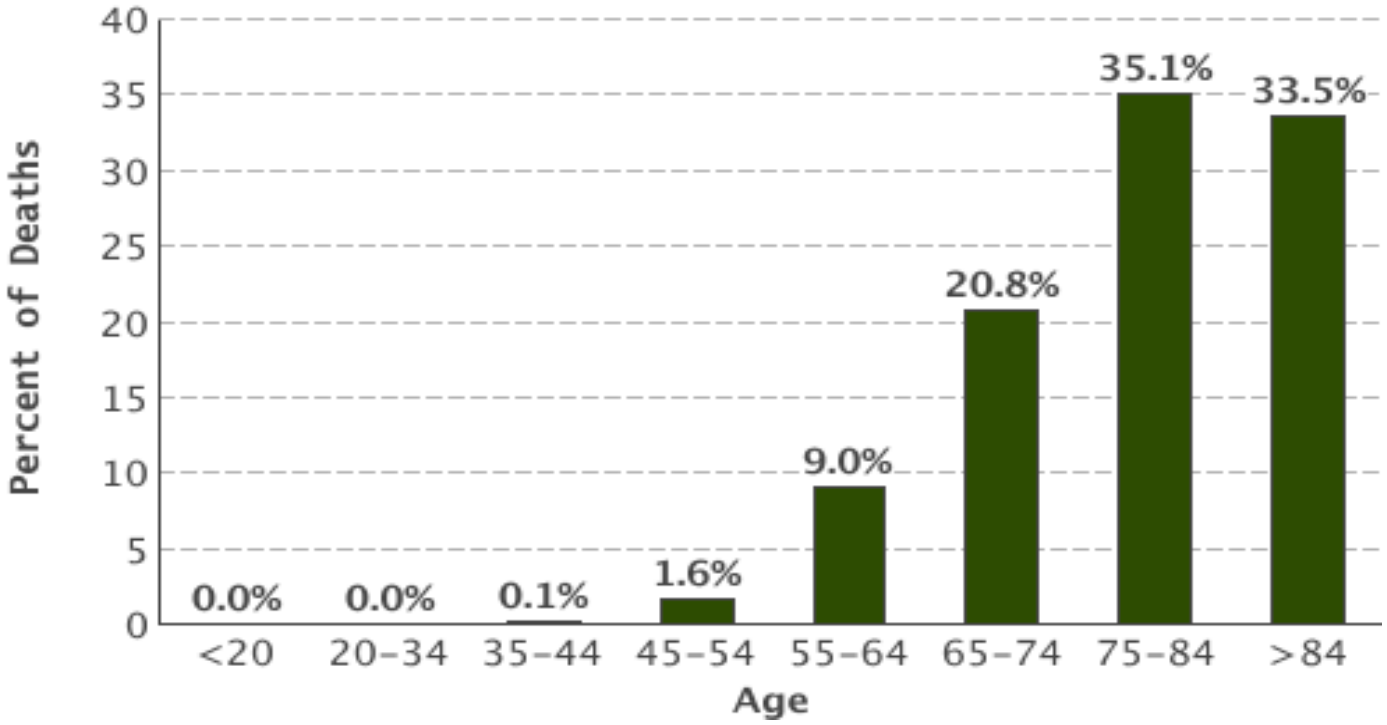
Pacific Coast Urology Medical Center

November 5, 2016

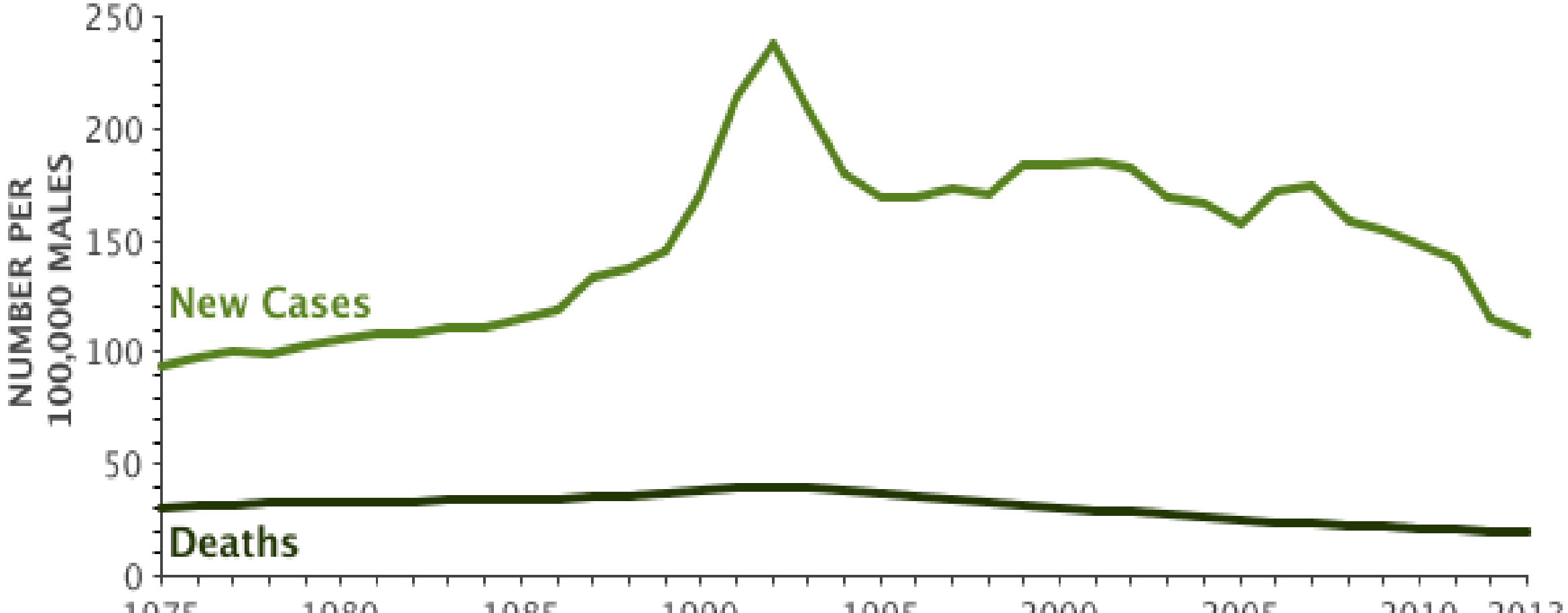
Percent of New Cases by Age Group



Percent of Deaths by Age Group



New Cases/Deaths 1975 - 2013



Decreased Screening by Primary Care

- Vanderbilt University investigators reported that new diagnoses of prostate cancer in the United States declined 28% in the year following the USPSTF's draft recommendation against routine PSA screening.

    - *Journal of Urology* (June 15, 2015).

Decreased Screening by Primary Care

- A study presented at the AUA annual meeting focusing on PSA utilization by primary care providers at Oregon Health & Science University found a significant 50% decrease in PSA testing since the release of the 2012 recommendation. Also at the AUA, a survey of primary care providers from the University of Massachusetts showed 75% have changed their PSA practice patterns based on the recommendation

CA-P Incidence and Gleason Grade at Dx

- The prostate cancer diagnosis rate increased from 39.7% in 2010-2011 to 41.4% in 2013 and 45.4% in 2015. The percentage of positive cores per positive prostate biopsy rose from 31.4% in the pre-USPSTF cohort to 33.3% in 2015, and the percentage of men diagnosed with Gleason 8-10 cancers increased from 15.5% in 2010-2011 to 24.5% in 2015.

CA-P Incidence and Gleason Grade at Dx

- Newly diagnosed cancers are presenting with increased tumor volume and grade, which may translate into an increase in prostate cancer-related mortality; unfortunately, we may not see that effect for another 5 to 10 years. Although we can't establish an absolute causal link to USPSTF from a single study, it is absolutely astonishing to see that the migration to more aggressive disease has happened so quickly after the recommendation—particularly since our protocols have been stable. While we didn't specifically study this, evidence from other recent studies shows an increase in the percentage of disseminated disease at diagnosis since the USPSTF recommendation, which is very ominous.

Icahn School Of Medicine, Mt. Sinai, NY

Early Detection

Annual Screening

- Prostate Specific Antigen (PSA)
- Digital rectal exam (DRE)

If either of these are abnormal, the next step is a 10 minute biopsy procedure done in the office.

- A **biopsy** is the only way to diagnose prostate cancer.
- A **multiparametric MRI** may also be recommended.

Western States HIFU
Experience Counts!

Prostate Cancer Symptoms

- Blood in your urine
- Dull pain in your lower pelvic area
- General pain in your lower back, hips or other bone areas
- Urgency of urination
- Difficulty starting urination
- Pain during urination
- Loss of appetite and weight
- Painful ejaculation
- Persistent bone pain
- Weak urine flow and dribbling

To Treat or Not To Treat

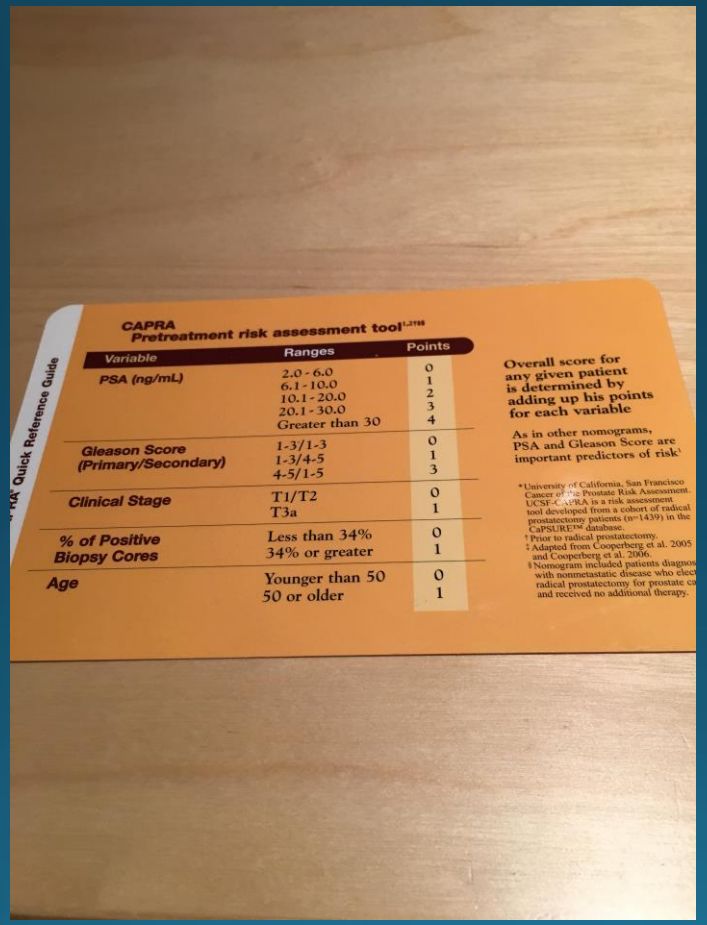
Recent debate on whether you should treat prostate cancer or wait… "active surveillance/watchful waiting."

What are you waiting for?

At *Western States HIFU,* we believe that prostate cancer should be treated before it can spread outside of the prostate and is no longer curable.

Western States HIFU
Experience Counts!

CAPRA Data Points



CAPRA Quick Reference Guide

CAPRA Pretreatment risk assessment tool[1,2†‡]

Variable	Ranges	Points
PSA (ng/mL)	2.0 - 6.0	0
	6.1 - 10.0	1
	10.1 - 20.0	2
	20.1 - 30.0	3
	Greater than 30	4
Gleason Score (Primary/Secondary)	1-3/1-3	0
	1-3/4-5	1
	4-5/1-5	3
Clinical Stage	T1/T2	0
	T3a	1
% of Positive Biopsy Cores	Less than 34%	0
	34% or greater	1
Age	Younger than 50	0
	50 or older	1

Overall score for any given patient is determined by adding up his points for each variable

As in other nomograms, PSA and Gleason Score are important predictors of risk[1]

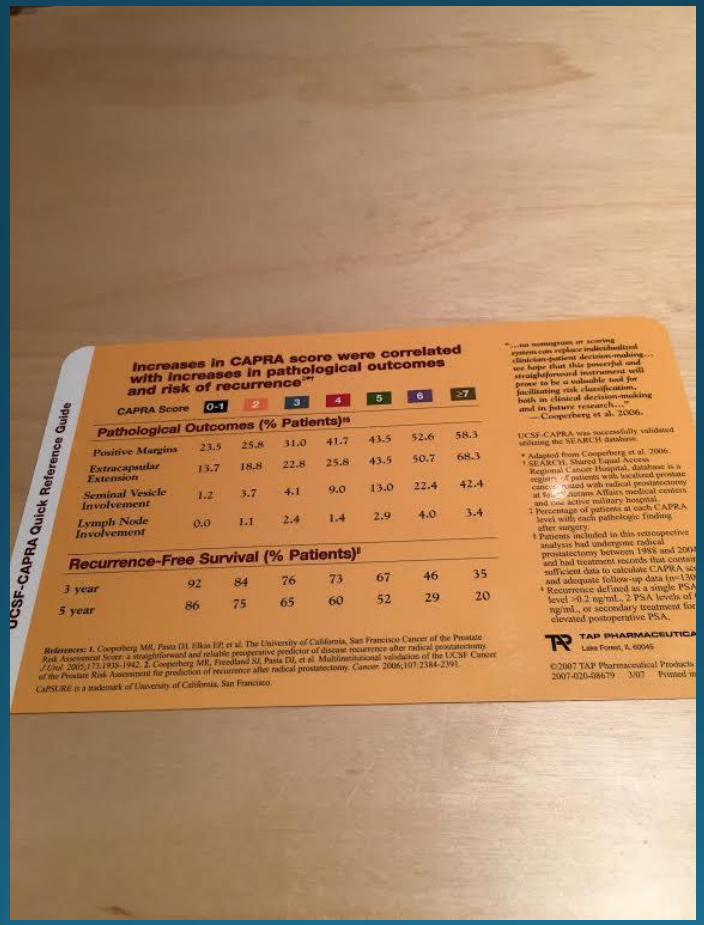
*University of California, San Francisco Cancer of the Prostate Risk Assessment. UCSF-CAPRA is a risk assessment tool developed from a cohort of radical prostatectomy patients (n=1439) in the CaPSURE™ database.

†Prior to radical prostatectomy.

‡Adapted from Cooperberg et al. 2005 and Cooperberg et al. 2006.

§Nomogram included patients diagnos with nonmetastatic disease who elec radical prostatectomy for prostate ca and received no additional therapy.

CAPRA Significance



HIFU Treatment For Prostate Cancer

Non-invasive cancer treatment focused on preserving quality of life.

Western States HIFU
Experience Counts!

HIFU PROSTATE SERVICES
Preserving Quality of Life
Non-Invasive Cancer Treatment

Brief History of HIFU

- HIFU research began in the 1950s in Indianapolis, IN.
- Over the years HIFU has evolved with dramatic technical advances and the ability to treat multiple cancers and diseases.
- In 2004, U.S. HIFU opened multiple Sonablate HIFU centers outside of the United States.

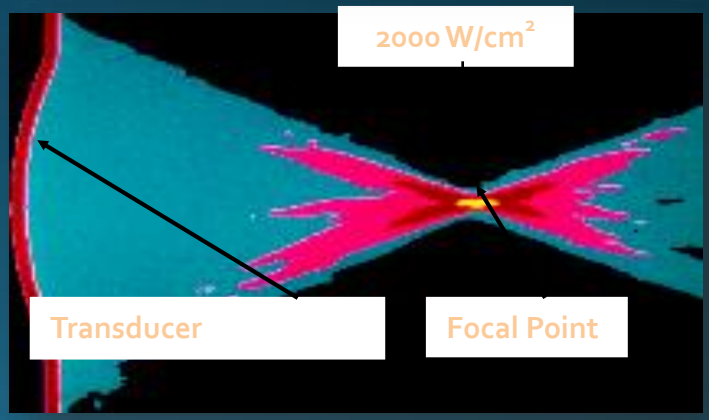
New Technology?

- In use worldwide for 17 years
- Approved in 49 countries
- 65,000+ treatments
- U.S.FDA approval October, 2015

What is HIFU?

High Intensity Focused Ultrasound

- Minimally invasive therapy that focuses sound waves to create heat.
- Similar to the way light travels through a magnifying glass to create heat.
- Temperature raises in the target tissue to 195° degrees Fahrenheit for 2-3 seconds.
- Destroys the targeted tissues where sound waves cross



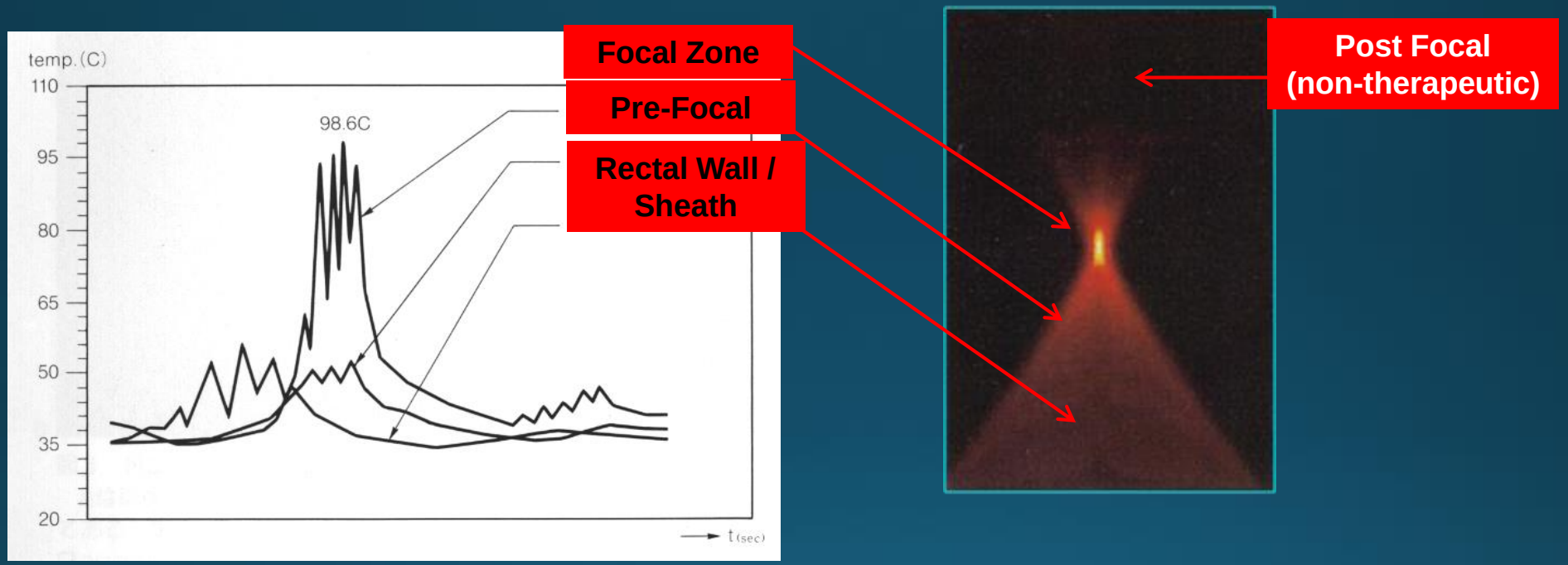
What is HIFU?

Basic Science and Physics

- Non-Invasive acoustic ablation technique that uses intersecting, precision- focused ultrasound waves
- Raises the temperature of the target tissue to 92 - 100 degrees Celsius
- Destroys the targeted tissues at the focal intersection
- Rapid heat dissipation past focal point

Basic HIFU Principles

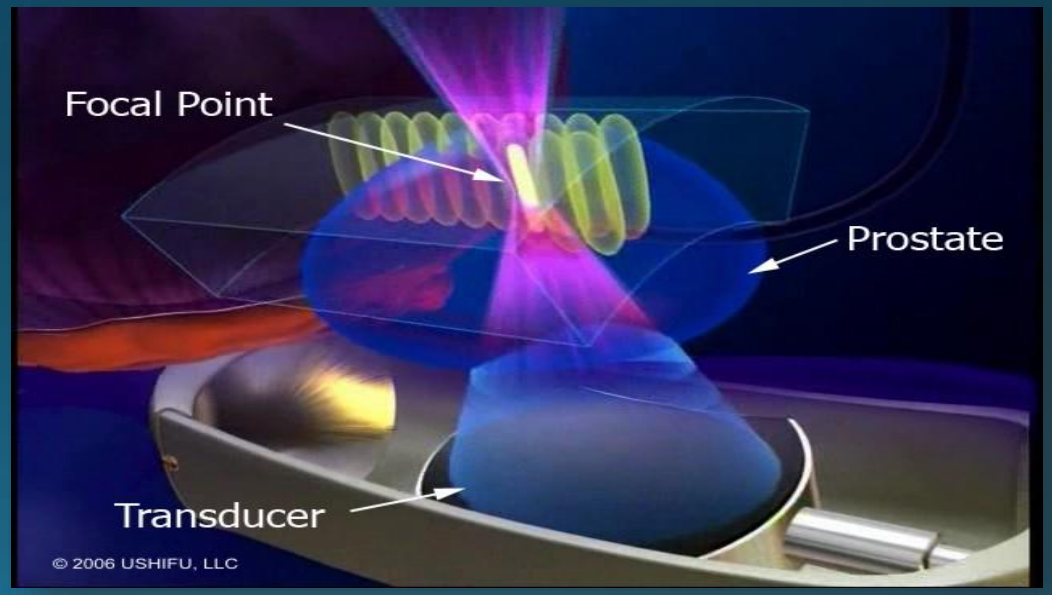
Thermal Energy Distribution within the Ultrasound Beam



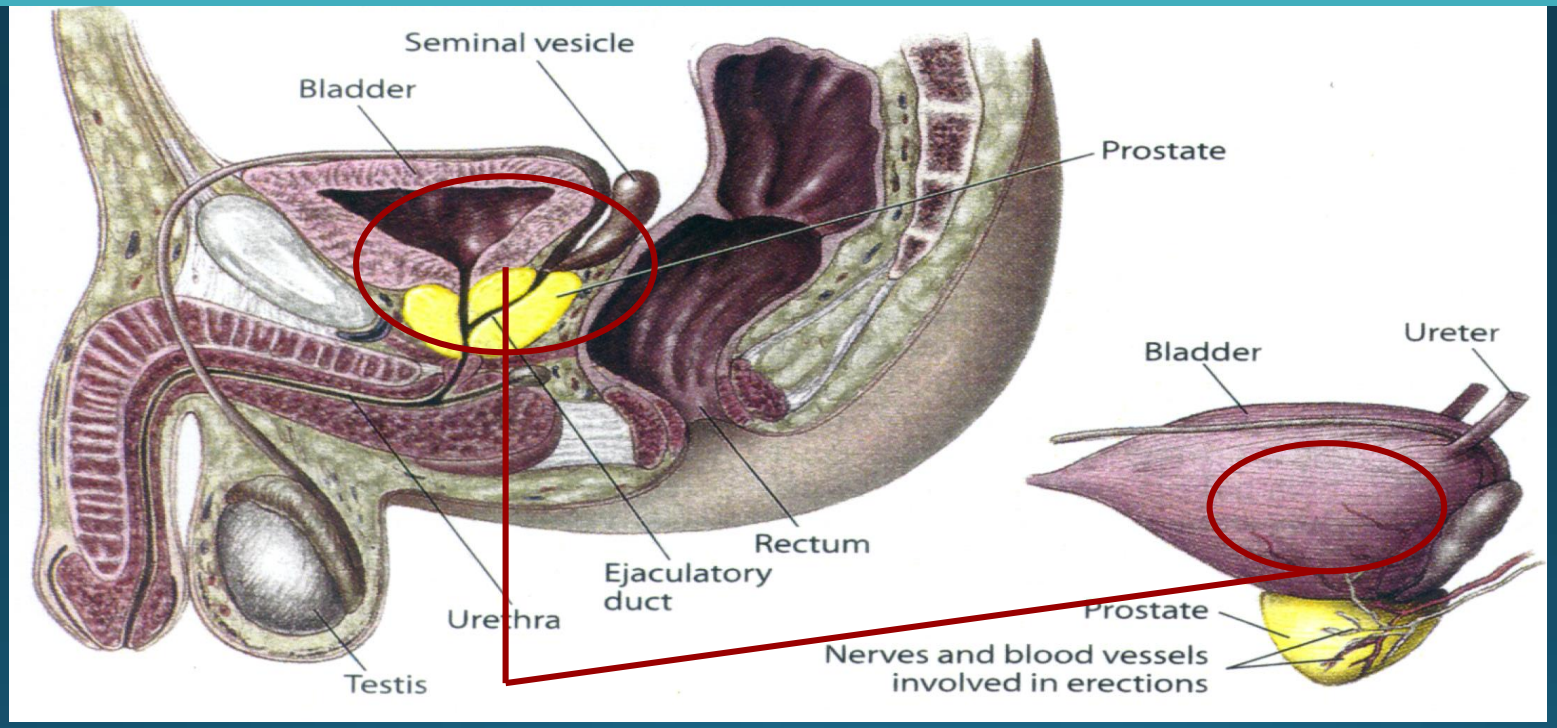
- By focusing high-energy ultrasound in tissue, it is possible to destroy tissue in the focal zone without damage to intervening and surrounding tissue
- After delivery of each treatment lesion, there is a short cooling period to allow heat dissipation to allow for better controlled delivery of energy
- Circulating chilled water in the probe sheath serves to protect the rectal wall

Sonablate 500 HIFU

The Sonablate 500 is a technically advanced medical device that uses HIFU to thermally ablate the prostate using a transrectal probe.

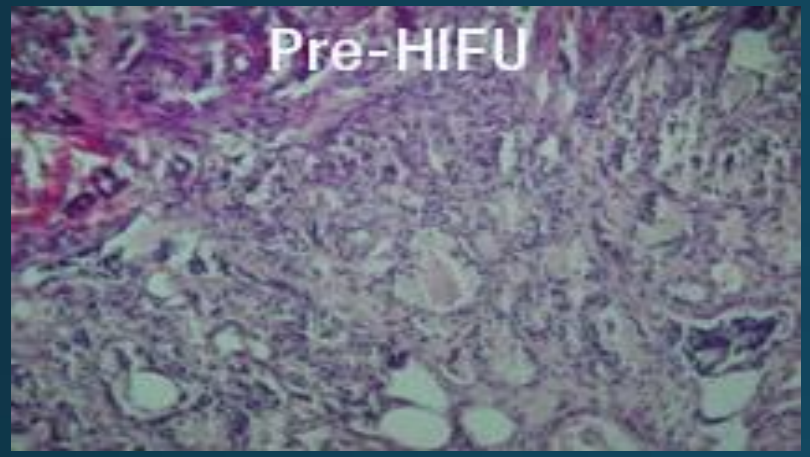


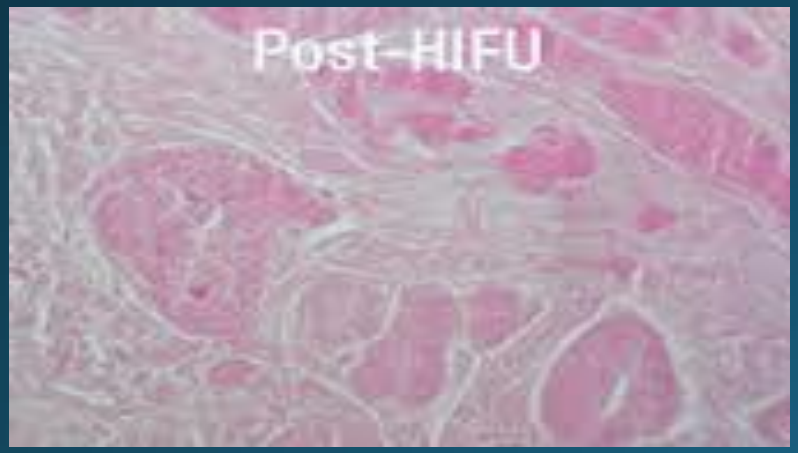
Prostate Anatomy



Goal: Cancer control with minimal side effects.

Physiology Of HIFU Ablation





- Ultrasound energy is absorbed and converted to heat in the focal zone
- Temperature elevation depends on tissue absorption coefficient and thermal response of tissue
- Biologic response depends on maximum temperature and duration of exposure (thermal dose)
- Temperature elevation, if sufficient, melts lipid membranes, denatures proteins, produces vascular endothelial cell damage, and ultimately leads to coagulative necrosis

HIFU – A New Treatment Paradigm

Targeted/Focal HIFU ablation offers a clinical option between surveillance and surgery.

Western States HIFU
Experience Counts!

Preferred HIFU System- Sonablate

Sonablate®

Trans-rectal HIFU probe
for prostate ablation

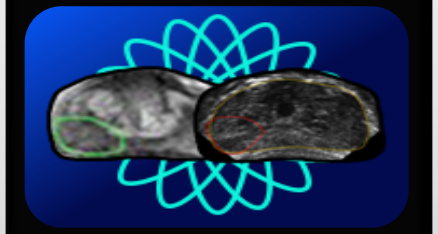
Sonablate® has 510(K) clearance in the U.S. under a De Novo regulatory classification.
Caution: Federal (USA) law restricts the sale and use of this device by, or on the order, of a physician.

Sonablate® 500 Probe

- The probe consists of a double-sided transducer and two internal drive motors which precisely position the transducer under software control
- The probe is connected to the Sonachill via water path tubing which is utilized to circulating chilled degassed water to cool the transducer and rectal wall
- The transducer is composed of two distinct crystal sets: one for imaging and one for delivering therapy

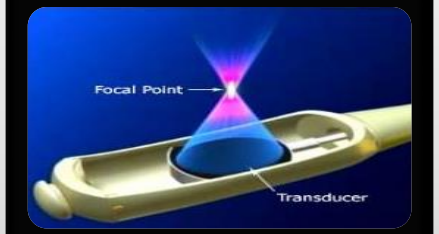
Sonablate A3 Technology

AIM



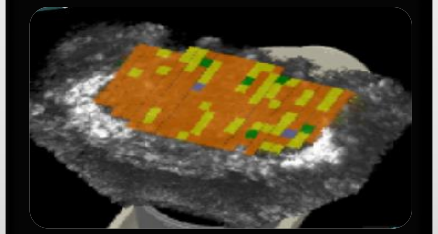
US Imaging
MRI Fusion

ABLATE



HIFU Ablation

ANALYZE



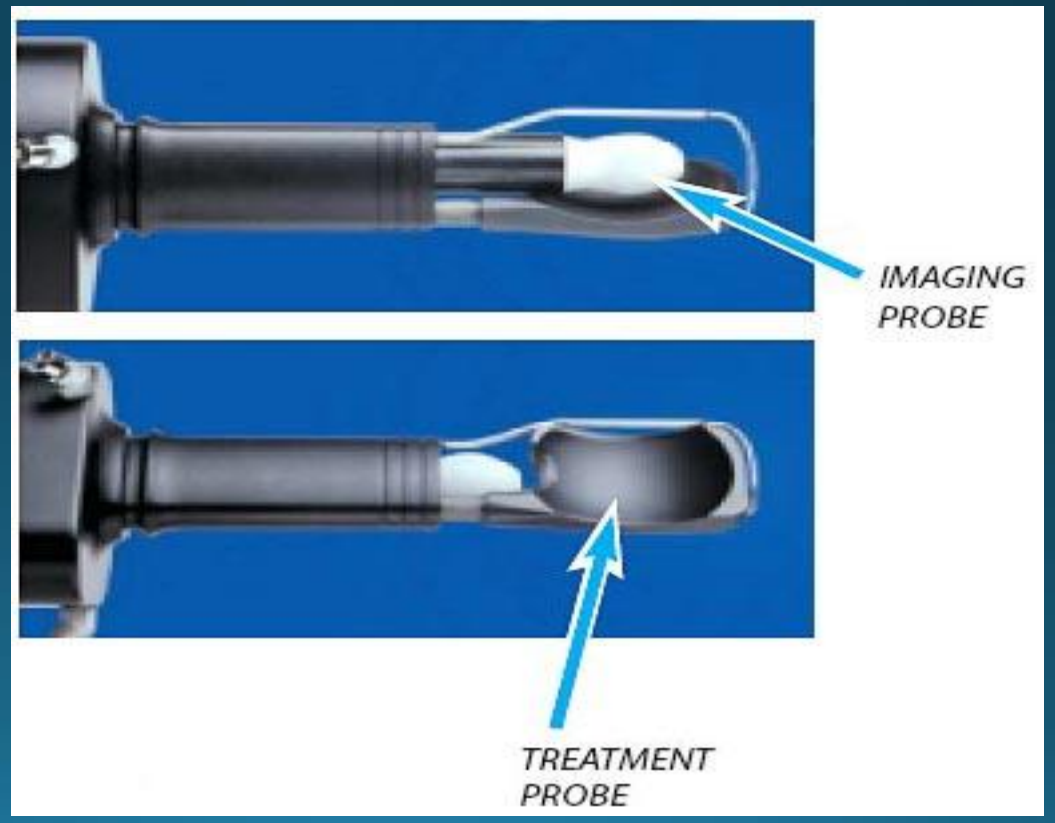
Tissue change monitoring

CONTINUE

COMPLETE

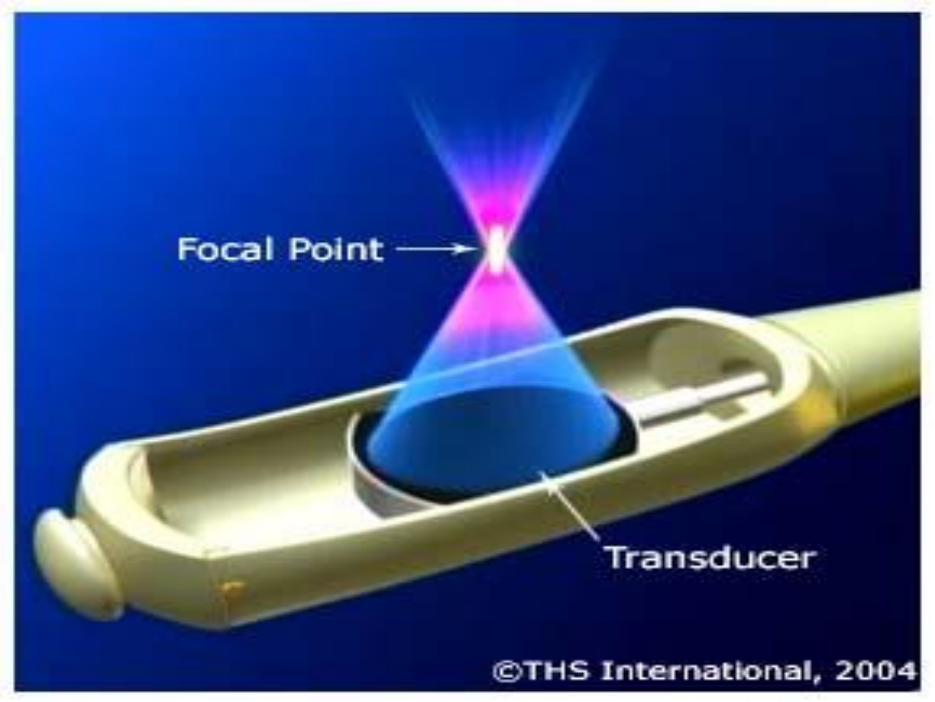
Sonablate® 500 HIFU
3X-Probe Image, Treat, Confirm

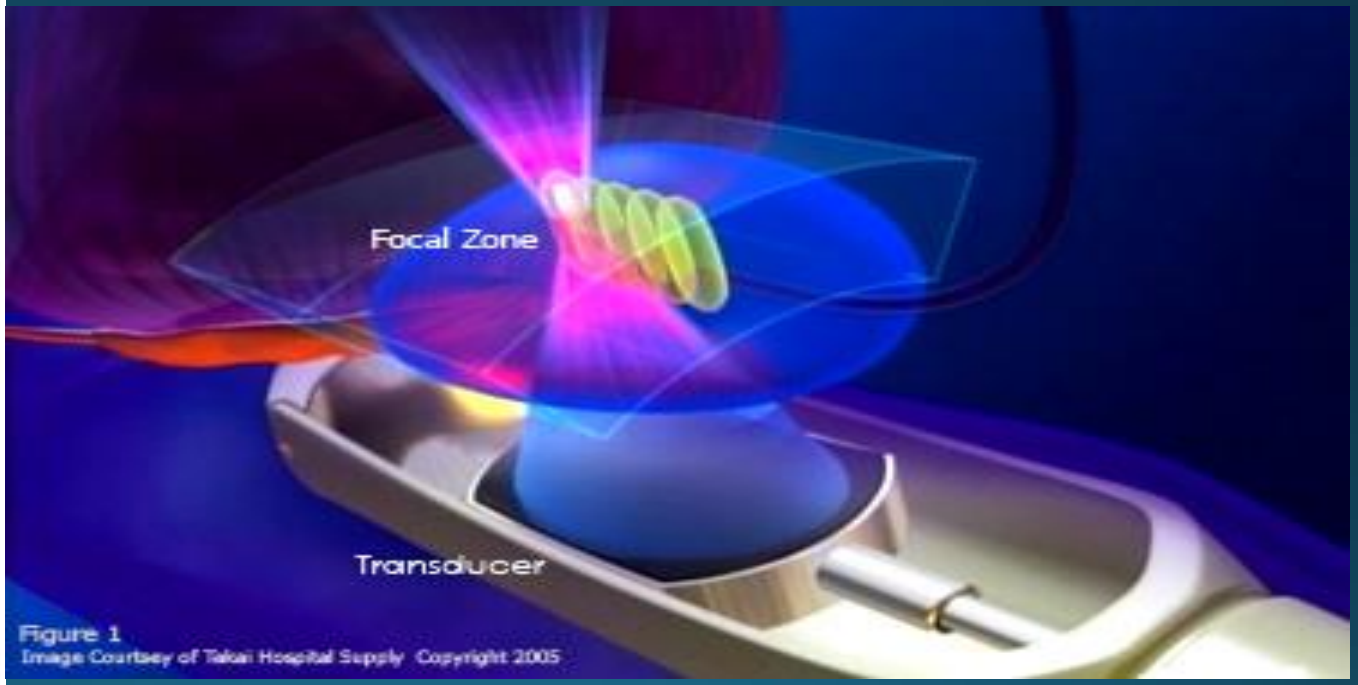
Imaging



Sonablate® 500 HIFU
3X-Probe Image, Treat, Confirm

Treatment





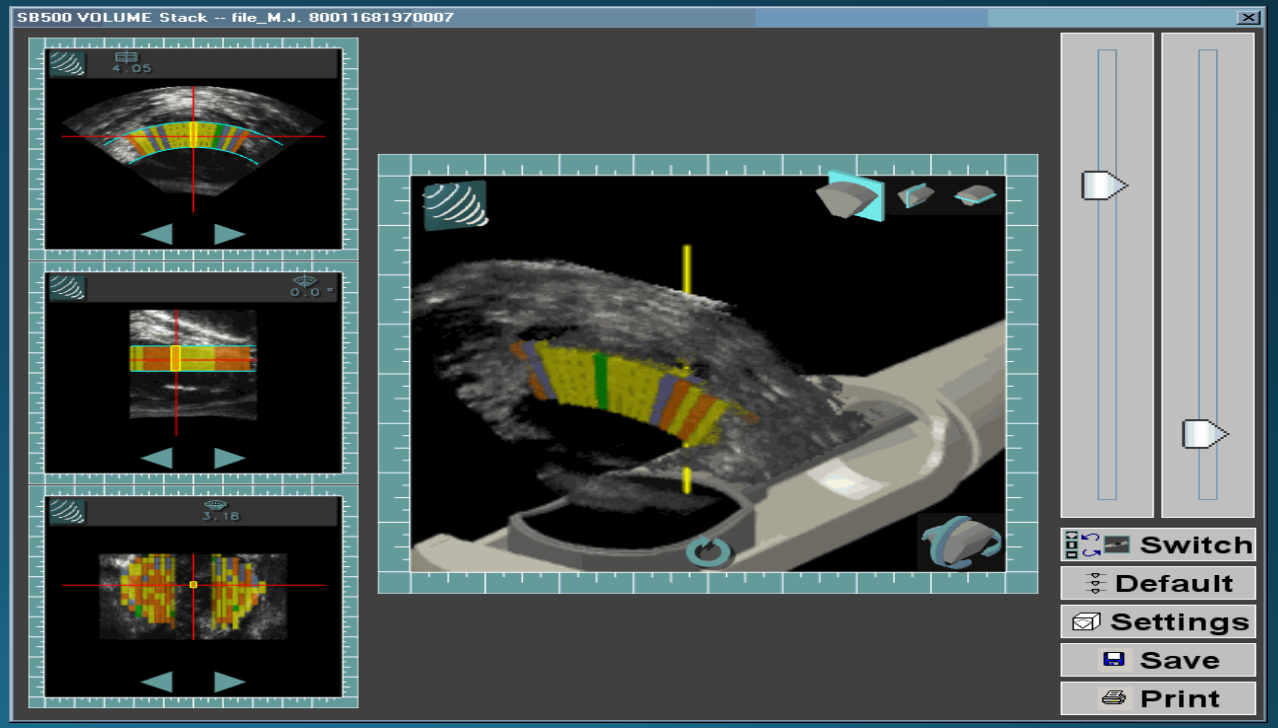
Sonablate® 500 HIFU
3X-Probe Image, Treat, Confirm

Confirmation

Tissue Change Monitoring

(TCM) Sonablate software

Compares tissue changes before and after treatment to confirm ablation the HIFU treatment site.

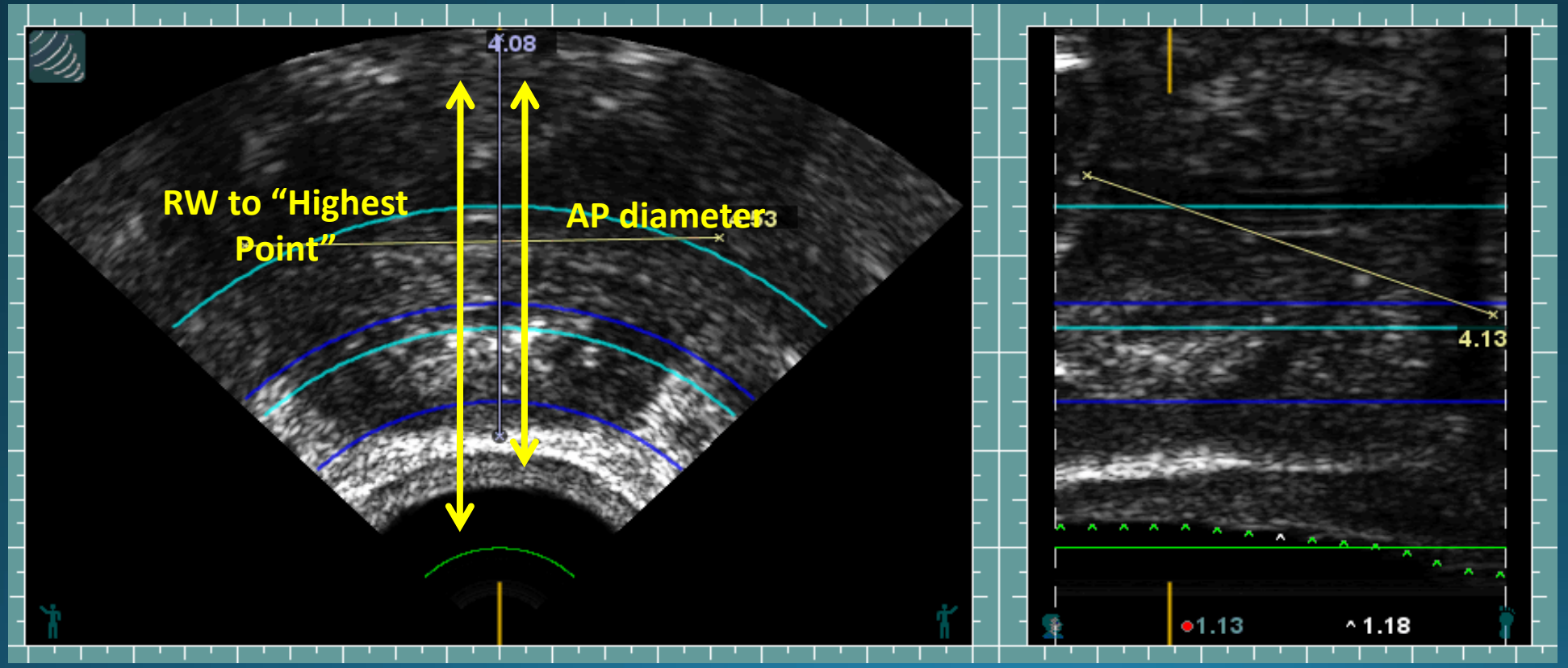


Sonablate® 500 HIFU
Advanced Computer Controls

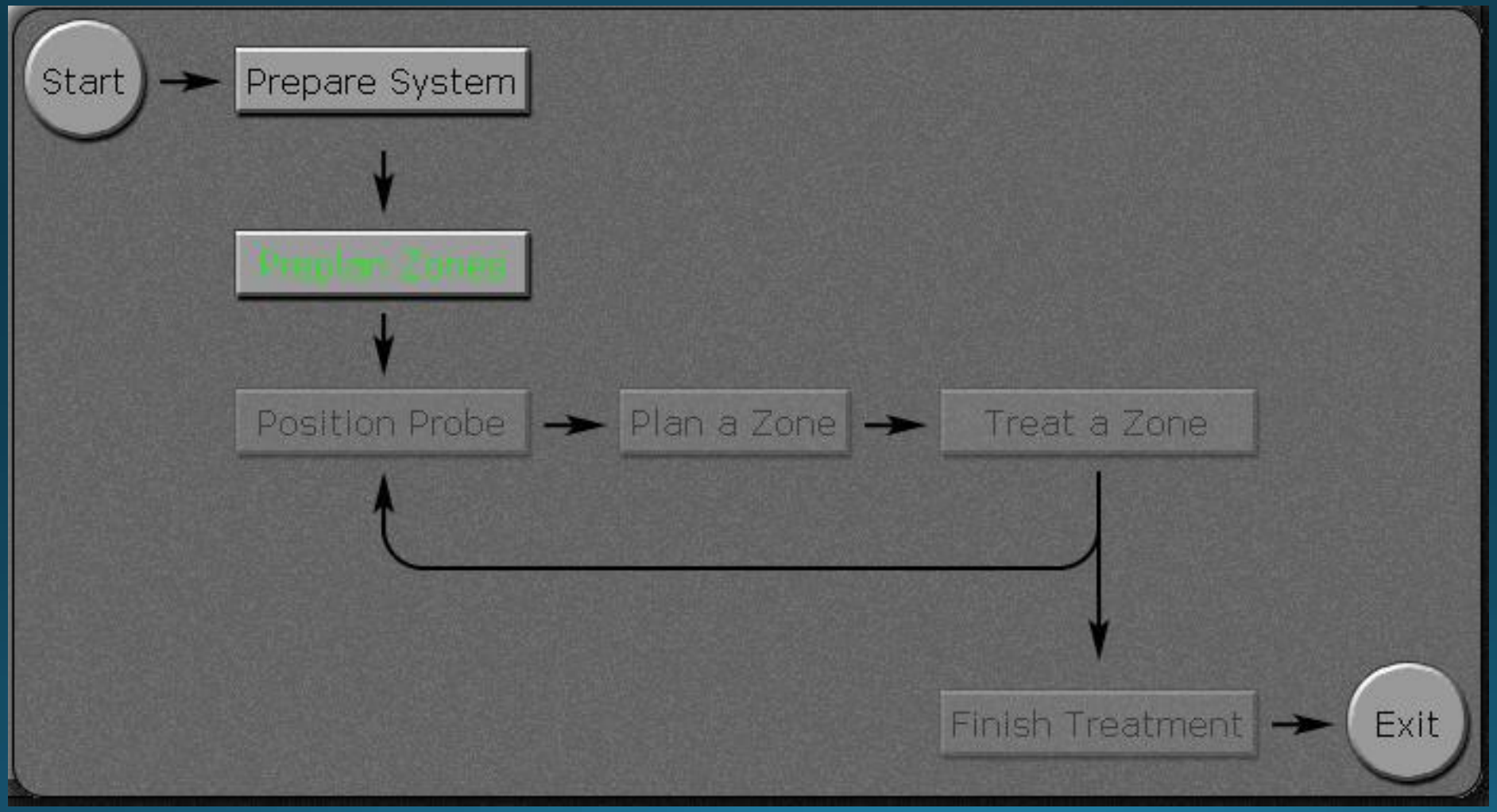
The rotation and positioning of the transducer is controlled by the computer and the physician on the computer screen

Prostate Size

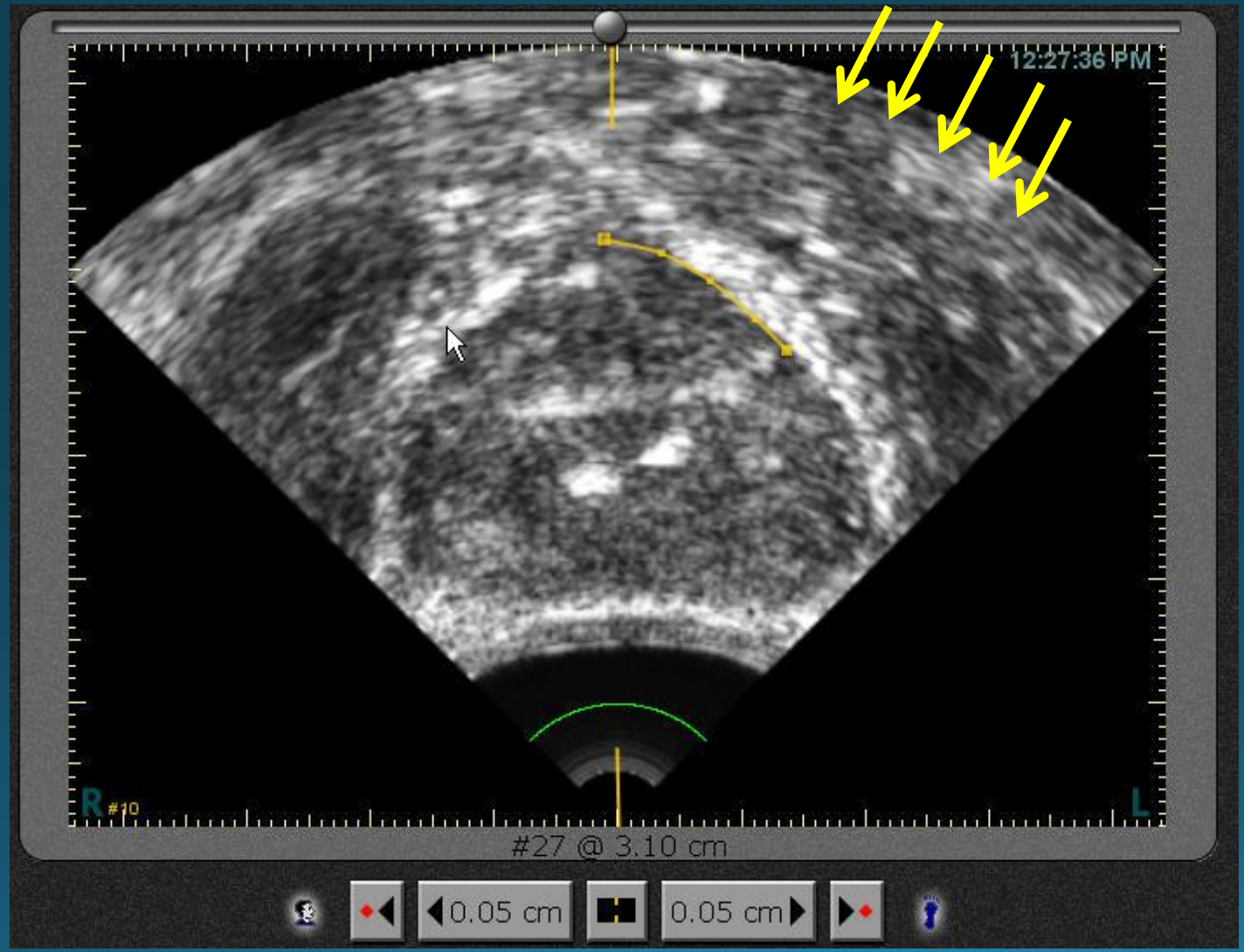
- The prostate size is important because the prostate must fit inside the treatment window in order to be fully ablated.
- AP Diameter vs. Rectal Wall to Highest Point
  - AP Limitations ≤ 4.0 cm
  - Size = Time: 10cc = 1hr



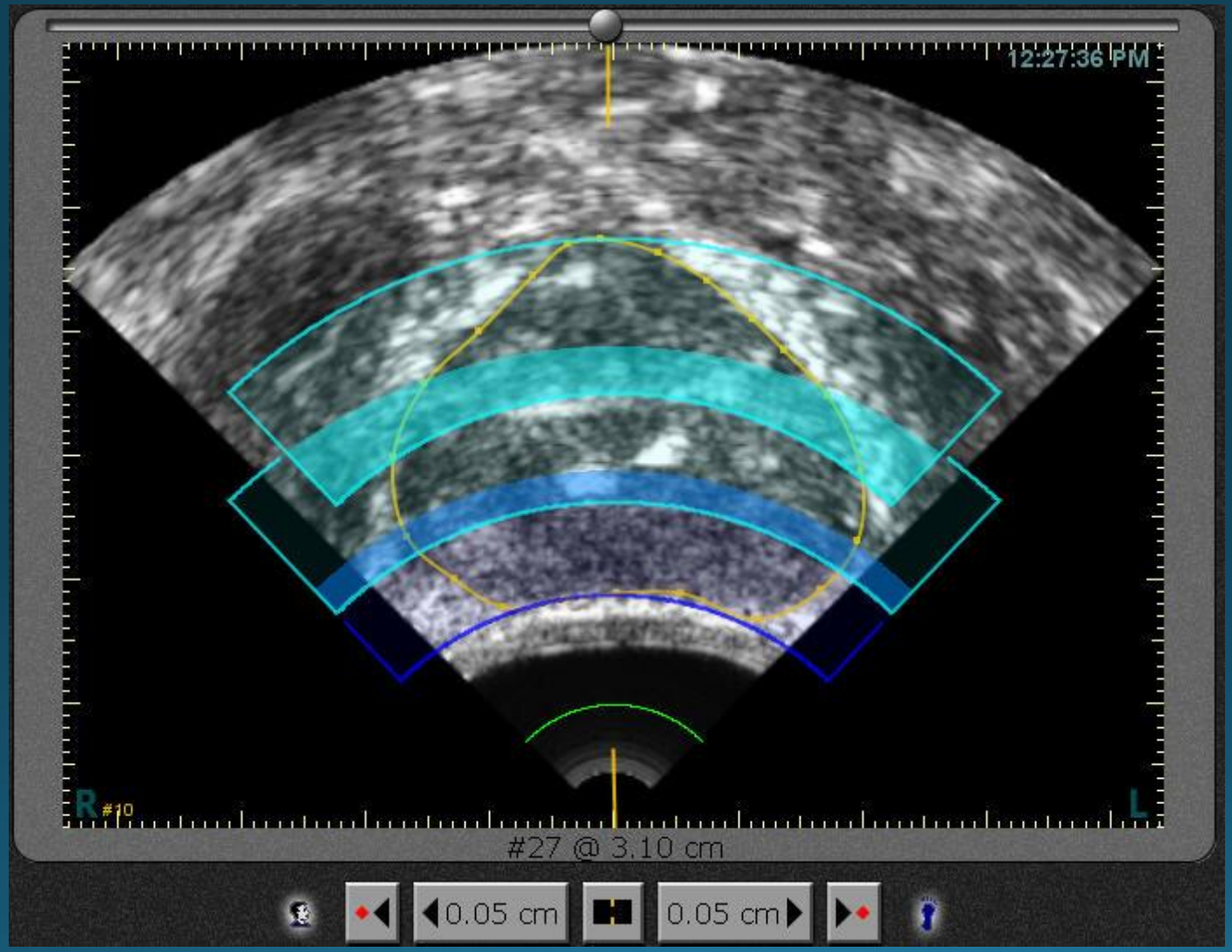
Treatment Flow Chart



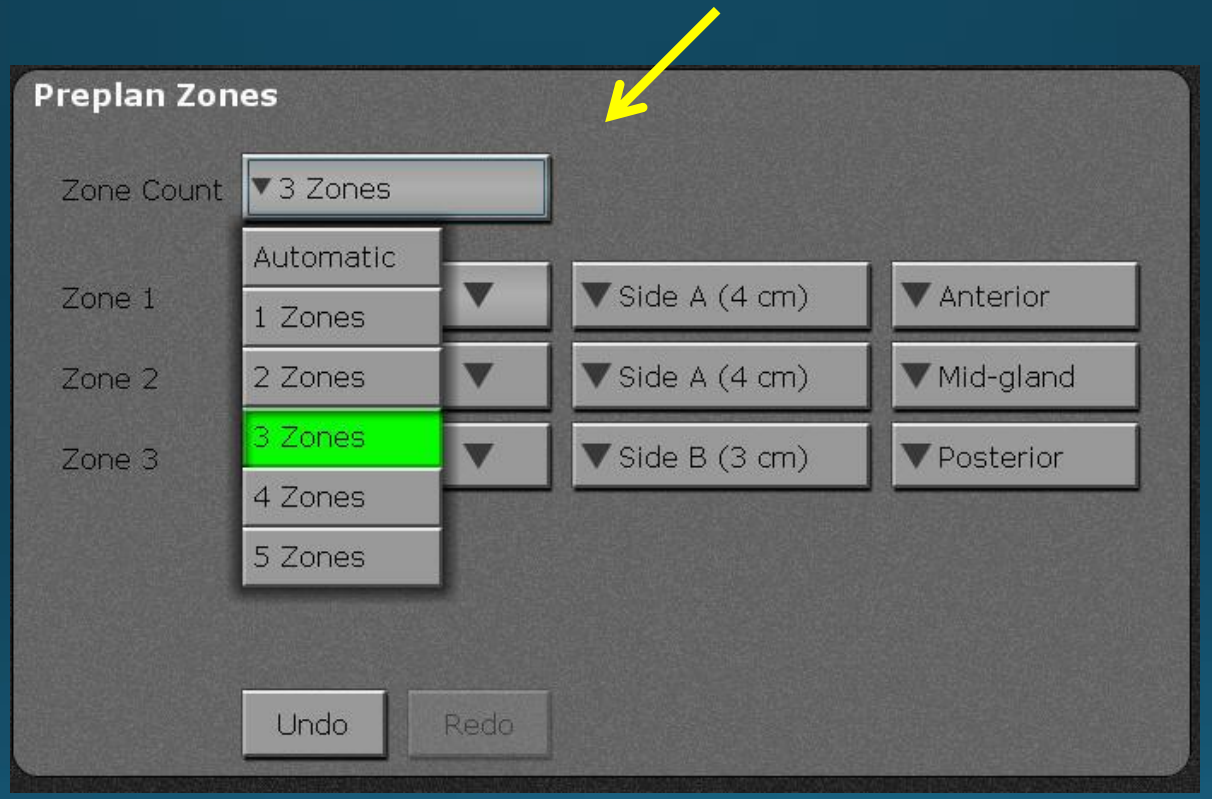
Preplan Zones - Outline gland perimeter to determine number of treatment zones

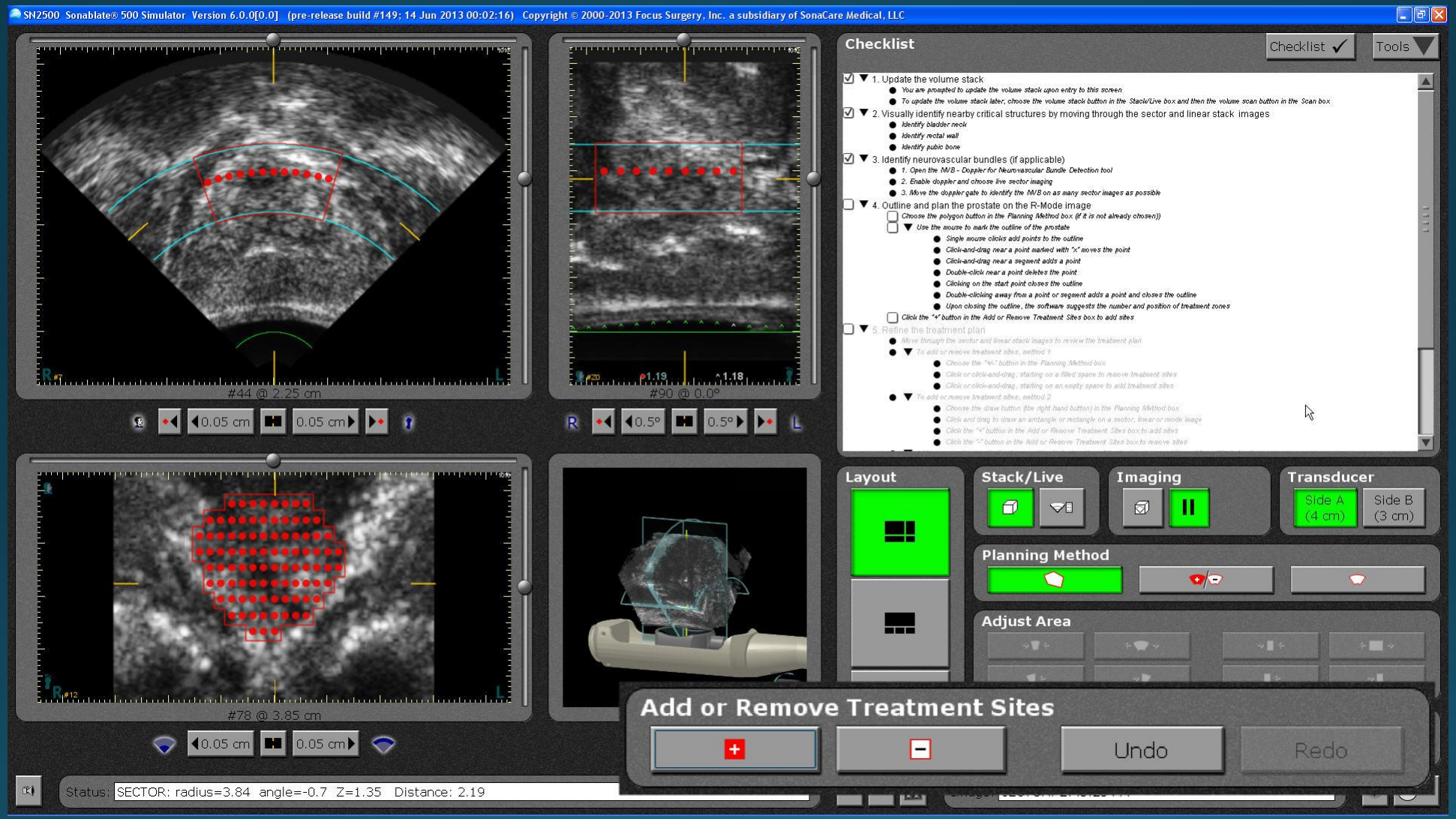


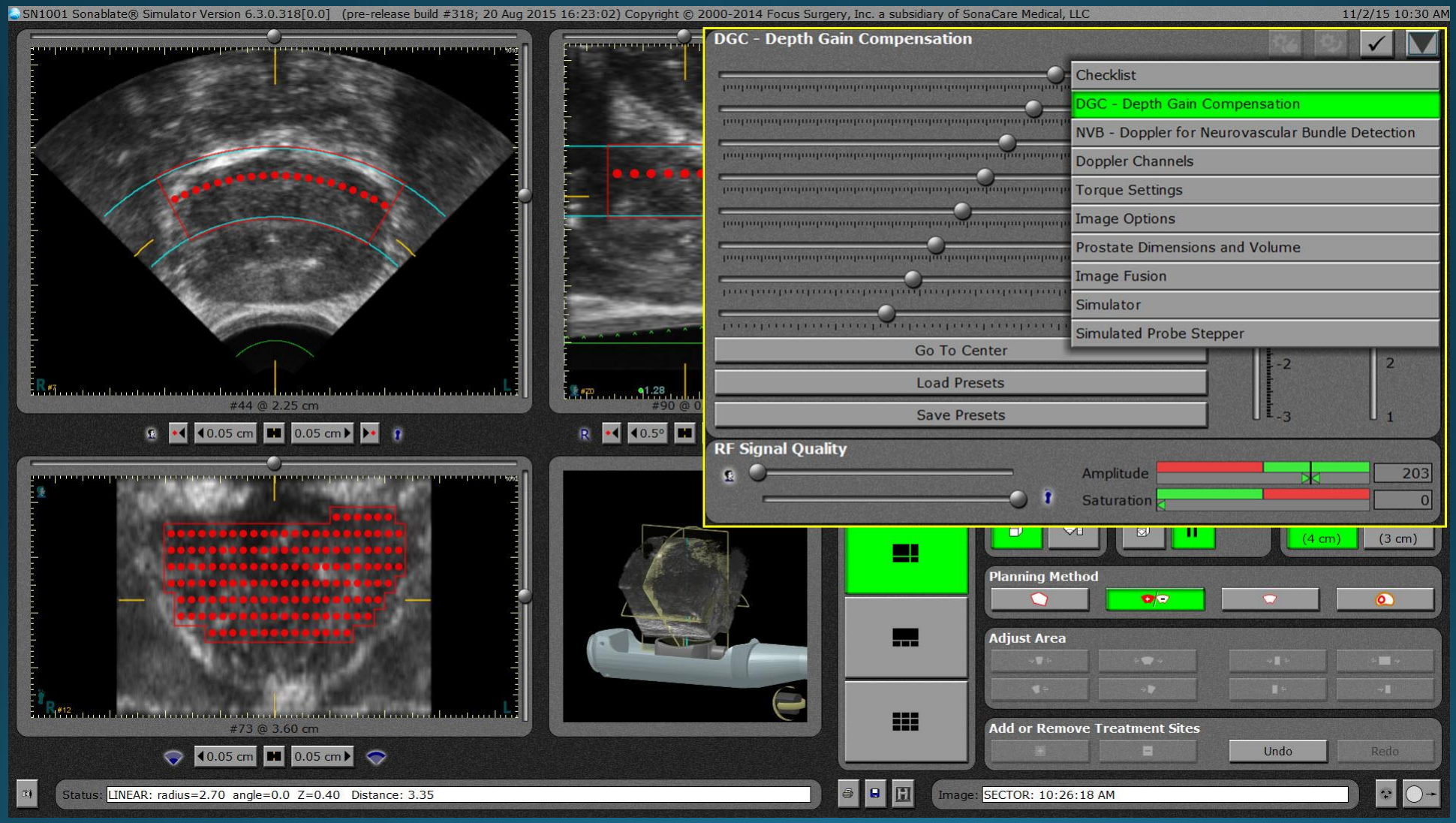
Preplan Zones



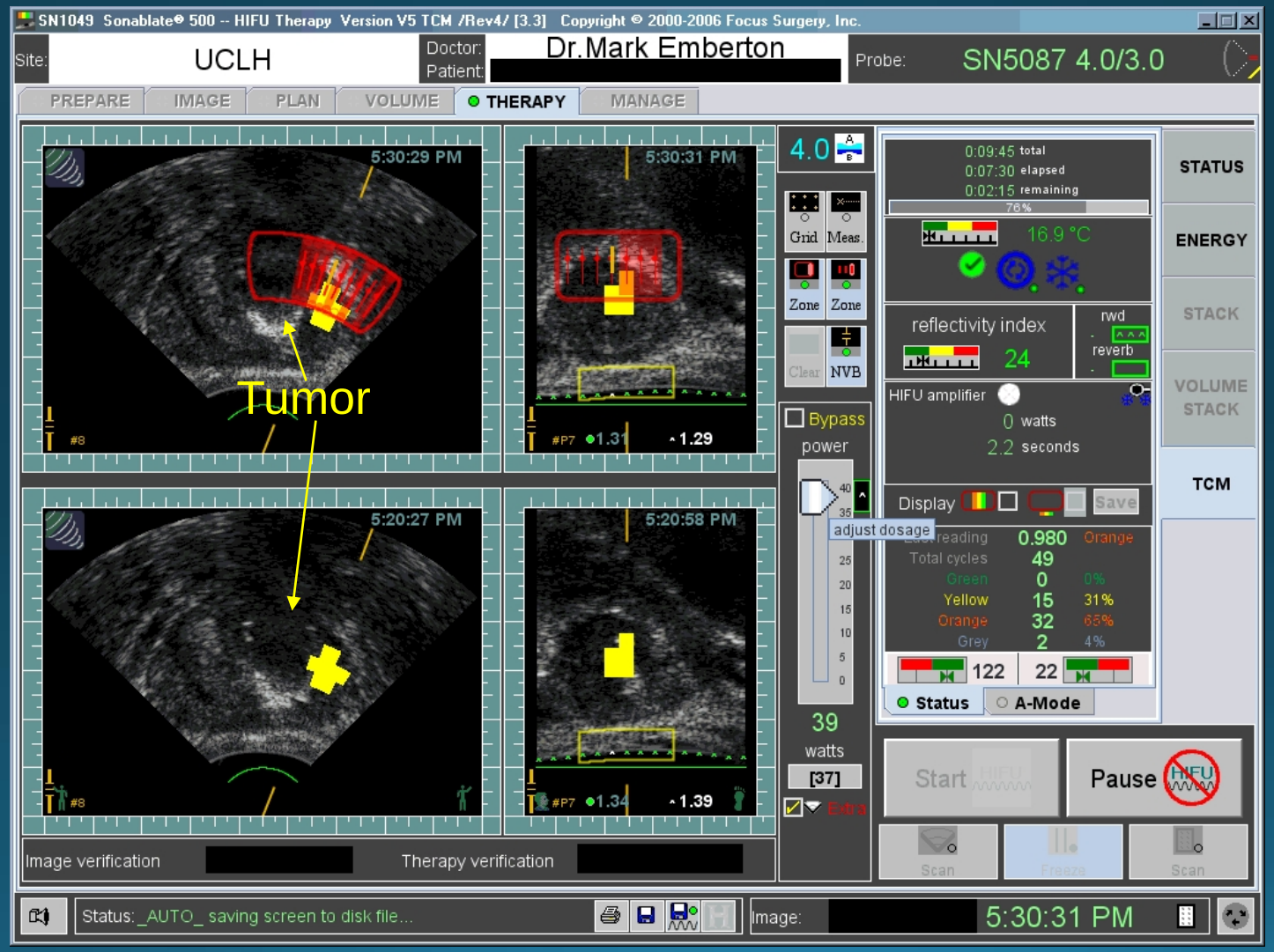
Preplan Zones

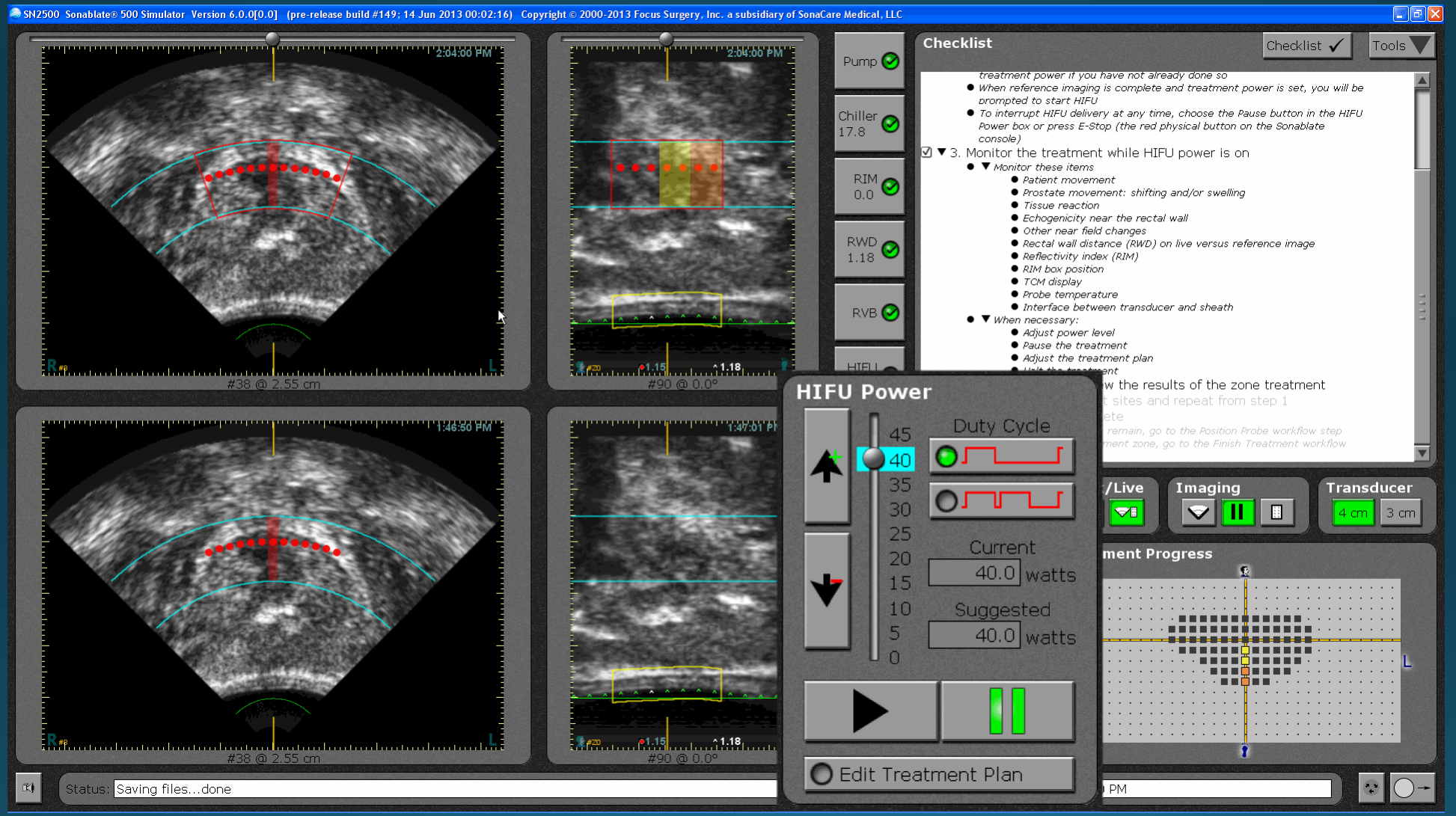



SN2500 Sonablate® 500 Simulator Version 6.0.0[0.0] (pre-release build #149; 14 Jun 2013 00:02:16) Copyright © 2000-2013 Focus Surgery, Inc. a subsidiary of SonaCare Medical, LLC
#44 @ 2.25 cm
#90 @ 0.0°
#78 @ 3.85 cm
0.05 cm
0.05 cm
0.5°
0.5°
Checklist
Checklist
Tools
1. Update the volume stack
You are prompted to update the volume stack upon entry to this screen
To update the volume stack later, choose the volume stack button in the Stack/Live box and then the volume scan button in the Scan box
2. Visually identify nearby critical structures by moving through the sector and linear stack images
Identify bladder neck
Identify rectal wall
Identify pubic bone
3. Identify neurovascular bundles (if applicable)
1. Open the NVB - Doppler for Neurovascular Bundle Detection tool
2. Enable doppler and choose live sector imaging
3. Move the doppler gate to identify the NVB on as many sector images as possible
4. Outline and plan the prostate on the R-Mode image
Choose the polygon button in the Planning Method box (if it is not already chosen))
Use the mouse to mark the outline of the prostate
Single mouse clicks add points to the outline
Click-and-drag near a point marked with "x" moves the point
Click-and-drag near a segment adds a point
Double-click near a point deletes the point
Clicking on the start point closes the outline
Double-clicking away from a point or segment adds a point and closes the outline
Upon closing the outline, the software suggests the number and position of treatment zones
Click the "+" button in the Add or Remove Treatment Sites box to add sites
5. Refine the treatment plan
Move through the sector and linear stack images to review the treatment plan
To add or remove treatment sites, method 1:
Choose the "+/-" button in the Planning Method box
Click or click-and-drag, starting on a filled space to remove treatment sites
Click or click-and-drag, starting on an empty space to add treatment sites
To add or remove treatment sites, method 2:
Choose the draw button (the right hand button) in the Planning Method box
Click and drag to draw an rectangle or rectangle on a sector, linear or mode image
Click the "+" button in the Add or Remove Treatment Sites box to add sites
Click the "-" button in the Add or Remove Treatment Sites box to remove sites
Layout
Stack/Live
Imaging
Transducer
Side A (4 cm)
Side B (3 cm)
Planning Method
Adjust Area
Add or Remove Treatment Sites
Undo
Redo
Status:
SECTOR: radius=3.84 angle=-0.7 Z=1.35 Distance: 2.19


SN1001 Sonablate® Simulator Version 6.3.0.318[0.0] (pre-release build #318; 20 Aug 2015 16:23:02) Copyright © 2000-2014 Focus Surgery, Inc. a subsidiary of SonaCare Medical, LLC
11/2/15 10:30 AM
DGC - Depth Gain Compensation
Checklist
DGC - Depth Gain Compensation
NVB - Doppler for Neurovascular Bundle Detection
Doppler Channels
Torque Settings
Image Options
Prostate Dimensions and Volume
Image Fusion
Simulator
Simulated Probe Stepper
Go To Center
Load Presets
Save Presets
RF Signal Quality
Amplitude
Saturation
203
0
#44 @ 2.25 cm
#90 @ 0
#73 @ 3.60 cm
0.05 cm
0.05 cm
0.5°
(4 cm)
(3 cm)
Planning Method
Adjust Area
Add or Remove Treatment Sites
Undo
Redo
Status: LINEAR: radius=2.70 angle=0.0 Z=0.40 Distance: 3.35
Image: SECTOR: 10:26:18 AM

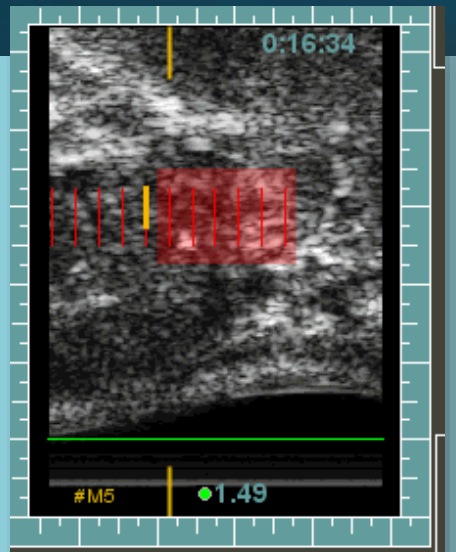
Targeted HIFU therapy using the Sonablate® 500

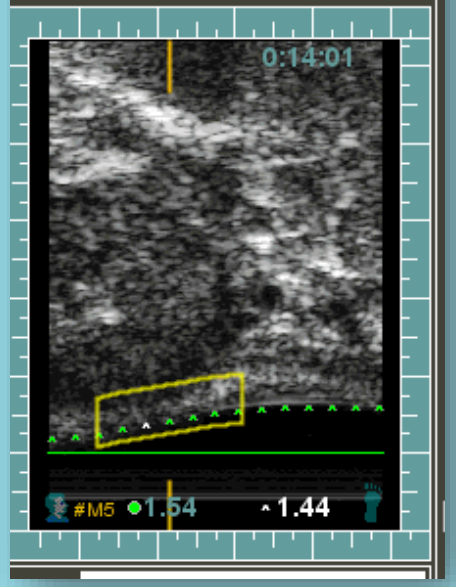



SN2500 Sonablate® 500 Simulator Version 6.0.0[0.0] (pre-release build #149; 14 Jun 2013 00:02:16) Copyright © 2000-2013 Focus Surgery, Inc. a subsidiary of SonaCare Medical, LLC
2:04:00 PM
#38 @ 2.55 cm
#90 @ 0.0°
1:46:50 PM
1:47:01 PM
Pump
Chiller 17.8
RIM 0.0
RWD 1.18
RVB
Checklist
Tools
treatment power if you have not already done so
When reference imaging is complete and treatment power is set, you will be prompted to start HIFU
To interrupt HIFU delivery at any time, choose the Pause button in the HIFU Power box or press E-Stop (the red physical button on the Sonablate console)
3. Monitor the treatment while HIFU power is on
Monitor these items
Patient movement
Prostate movement: shifting and/or swelling
Tissue reaction
Echogenicity near the rectal wall
Other near field changes
Rectal wall distance (RWD) on live versus reference image
Reflectivity index (RIM)
RIM box position
TCM display
Probe temperature
Interface between transducer and sheath
When necessary:
Adjust power level
Pause the treatment
Adjust the treatment plan
w the results of the zone treatment
t sites and repeat from step 1
ete
remain, go to the Position Probe workflow step
ment zone, go to the Finish Treatment workflow
HIFU Power
45
40
35
30
25
20
15
10
5
0
Duty Cycle
Current
40.0 watts
Suggested
40.0 watts
Edit Treatment Plan
/Live
Imaging
Transducer
4 cm
3 cm
ment Progress
Status: Saving files...done
PM

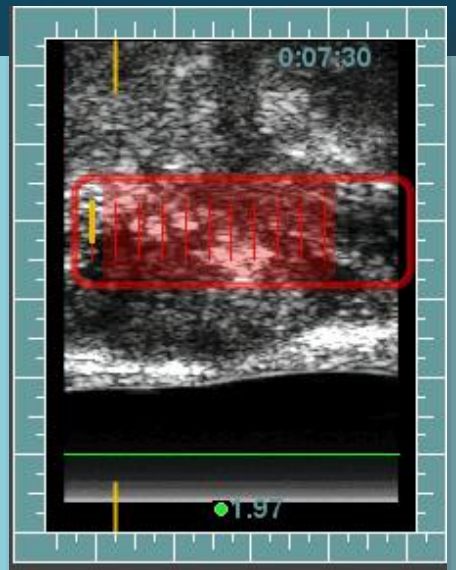
Popcorn

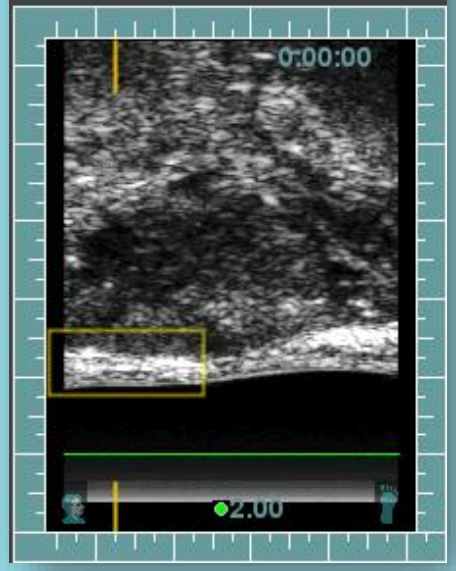
Grade 1



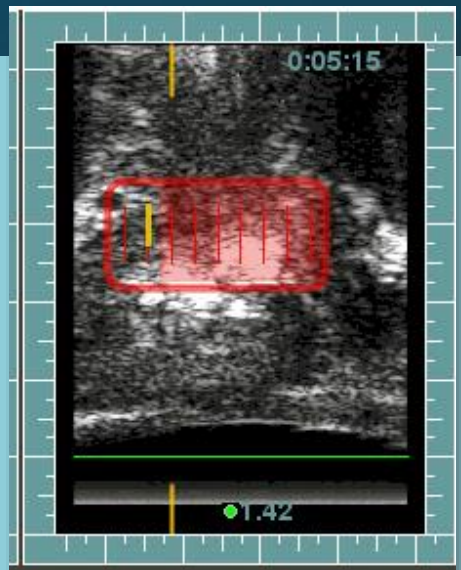


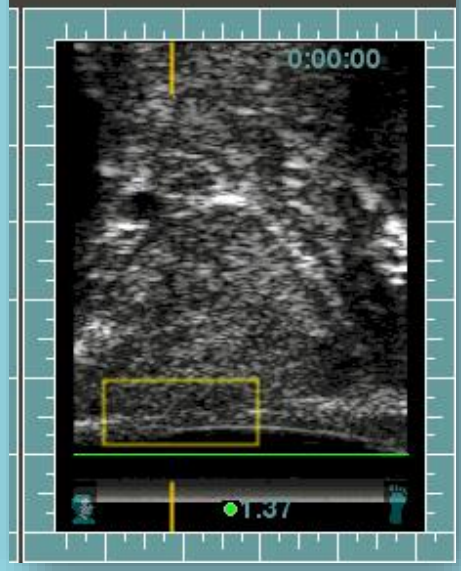
Grade 2



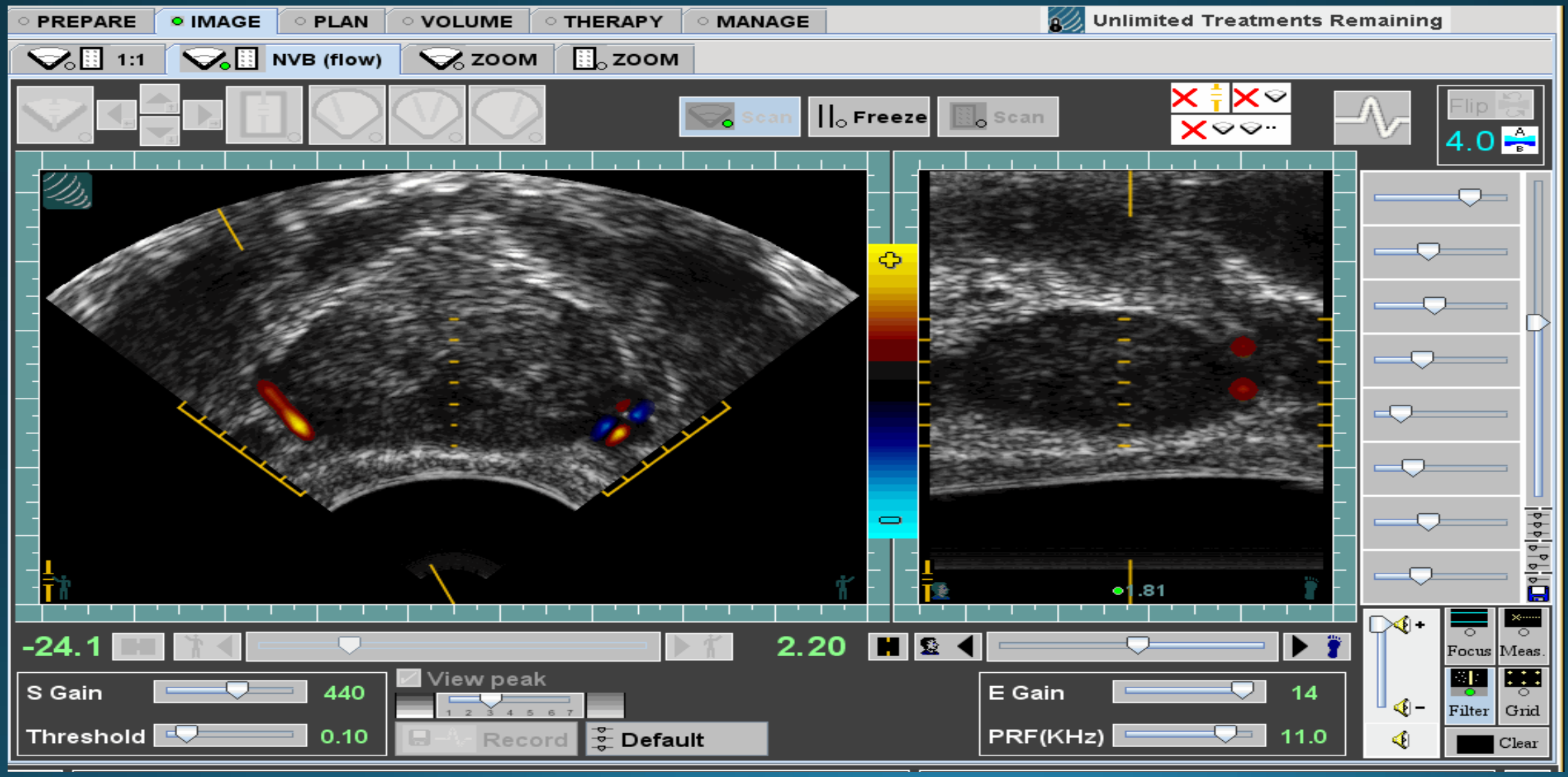


Grade 3

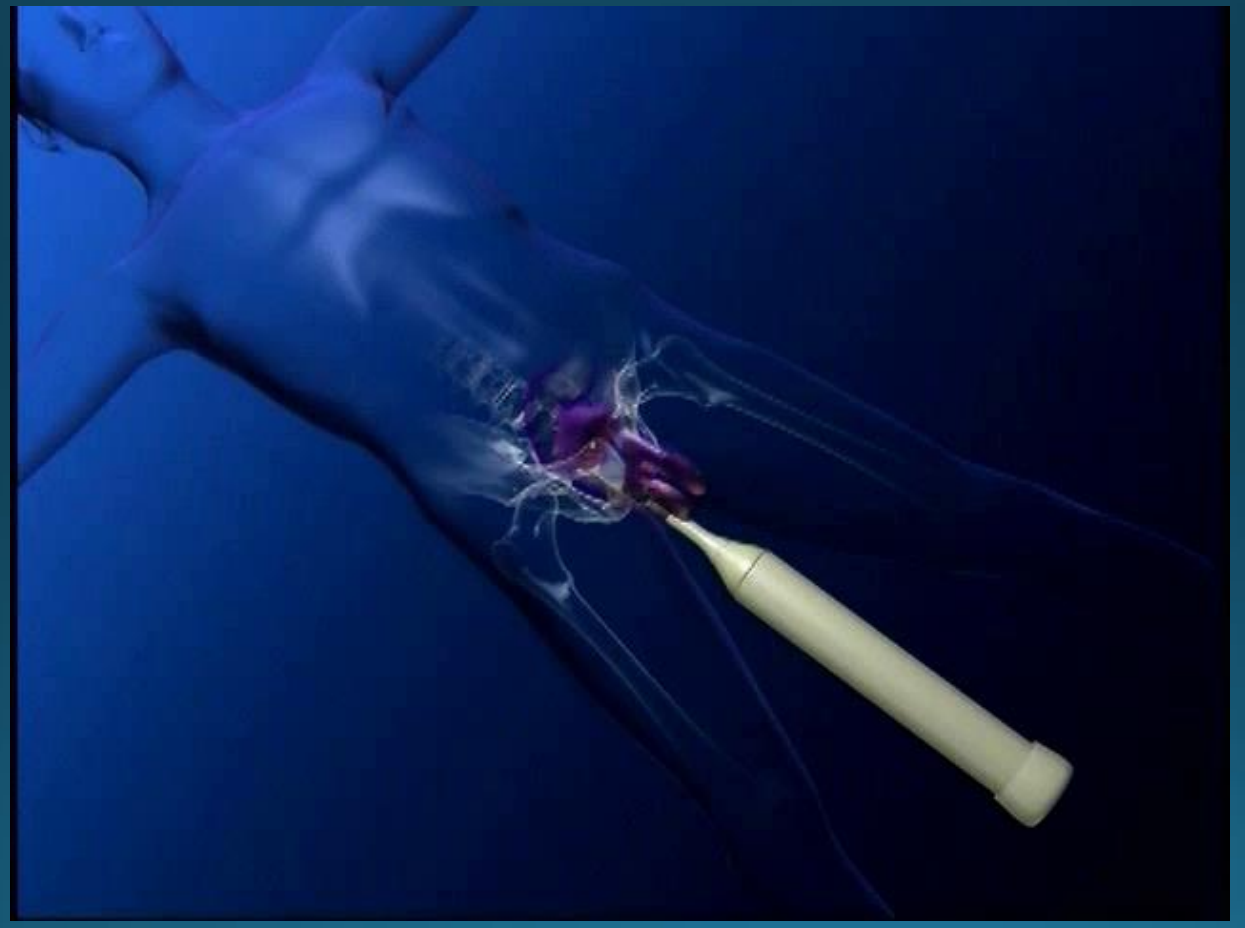




Neurovascular Bundle Detection



HIFU Animation



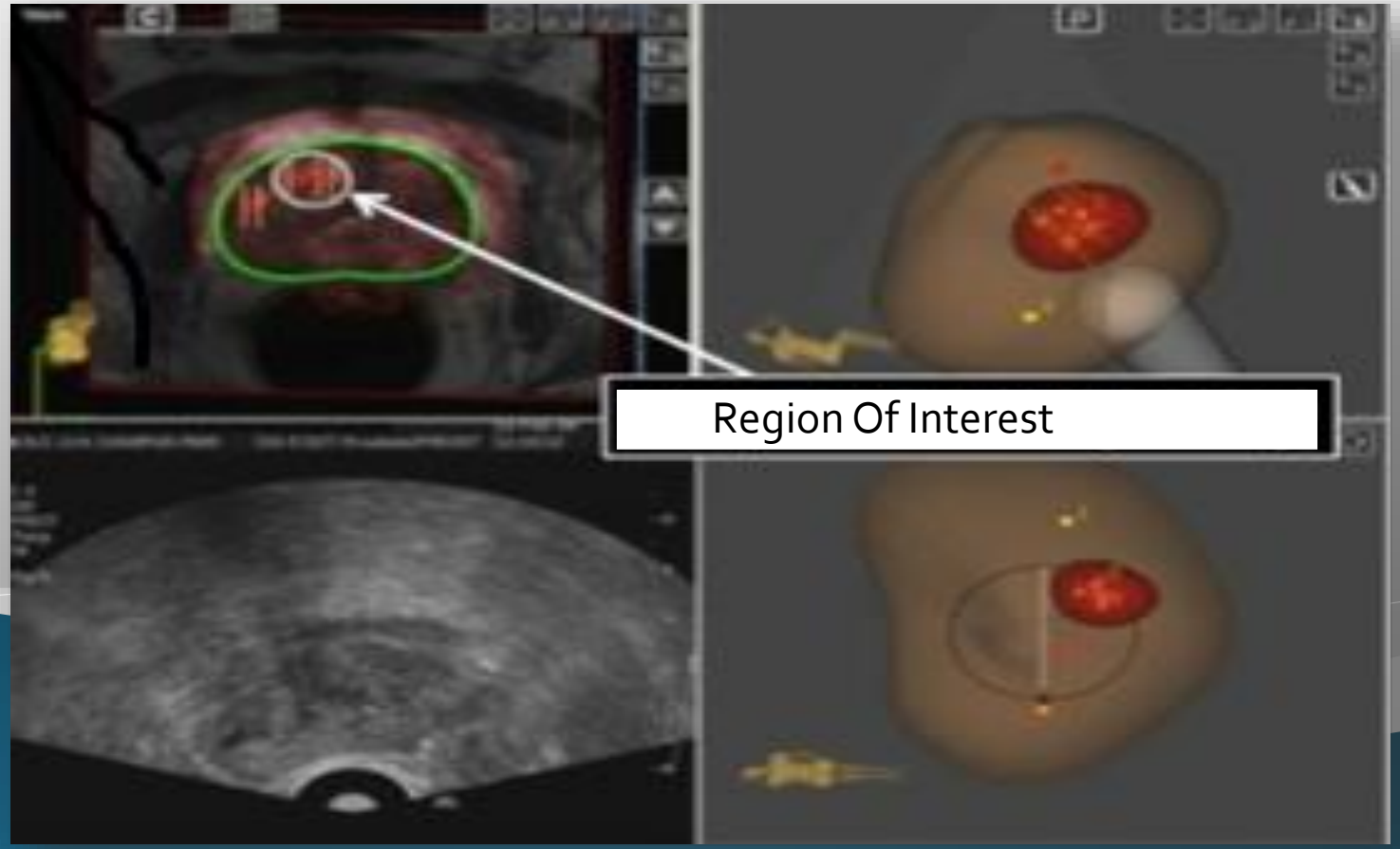
Sonablate 500
Long Term Data: Uchida

- Biochemical Free Survival: Phoenix ASTRO
- BFSR overall at 8 years: 59%
- BFSR at 8 years : S200: 55% S500: 56%
- BFSR at 4 years: S 500 V4: 84%

Software Version	# patients	Biopsy negative	Low Risk BDFS rate	Mod Risk BDFS rate	High Risk BDFS rate
S200	**33**	~~97%~~	**75%**	**54%**	**43%**
S500	**406**	**79%**			
S500 V4	200	94%	93%	72%	58%
S500 TCM	19	100%			

MRI / Ultrasound Fusion

Combines the specificity and sensitivity of mpMRI with the ease of use of ultrasound imaging



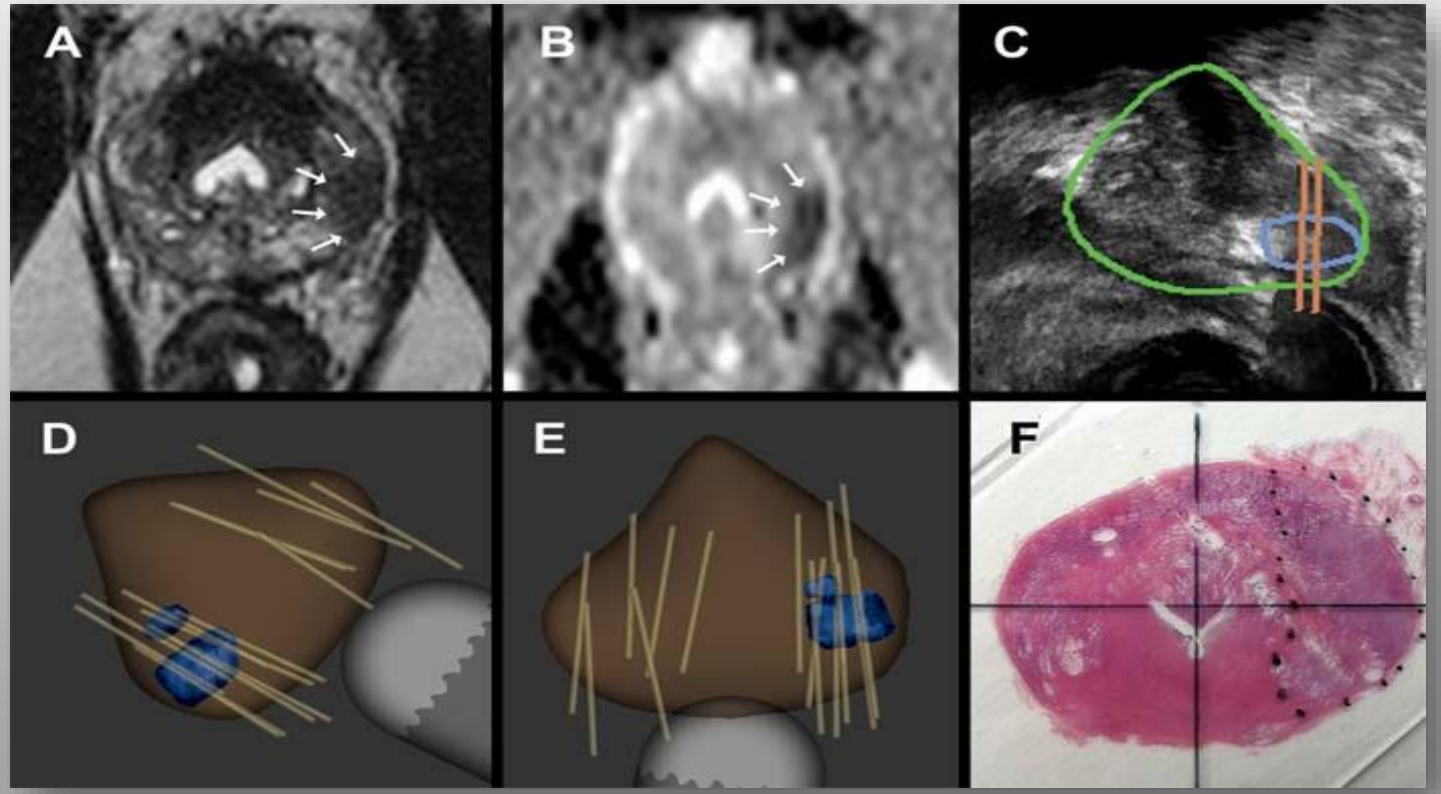
Western States HIFU
Experience Counts!

MRI / Ultrasound Fusion Guided Biopsy

MRI/US fusion combines mpMRI and live ultrasound to improve the biopsy needle guidance

MRI/US Fusion Bx Advantages

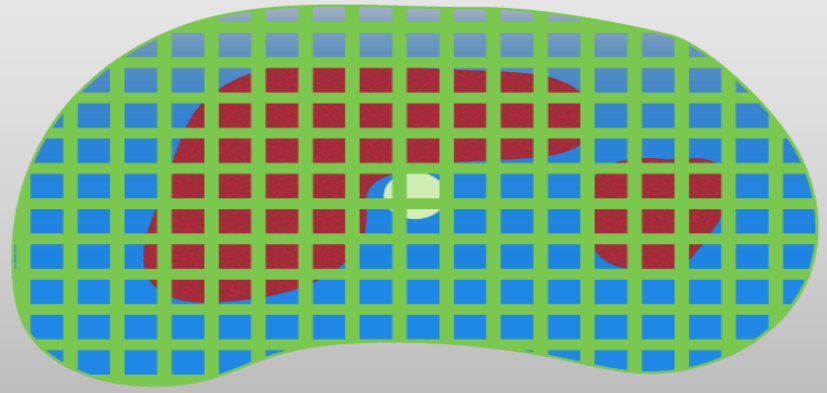
- Targeted biopsy compared to standard 12 core
- Enhanced patient outcomes
- More cost *effective than MR guided biopsy*



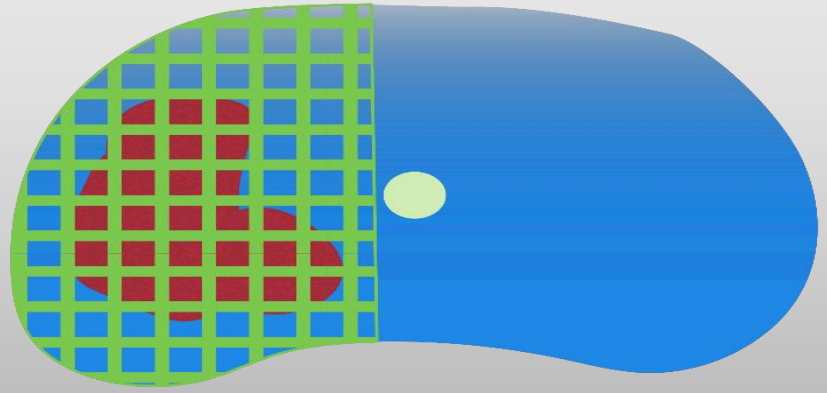
Western States HIFU
Experience Counts!

Sonablate Prostate Ablation

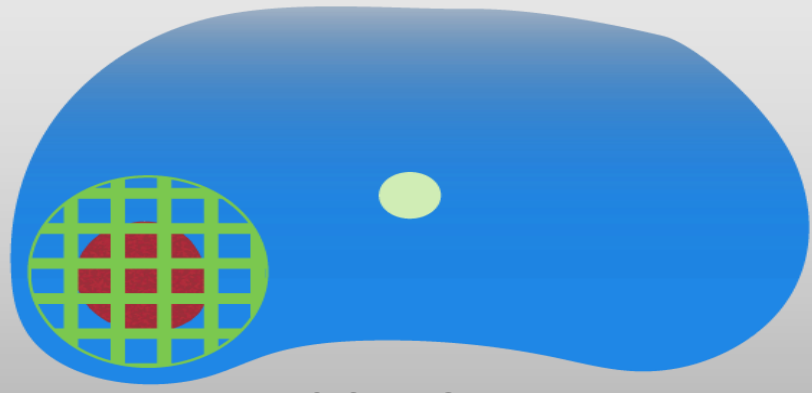
Sonablate® software allows for a customizable and targeted ablation plan tailored to each patient's prostate.



WHOLE GLAND



HEMI GLAND

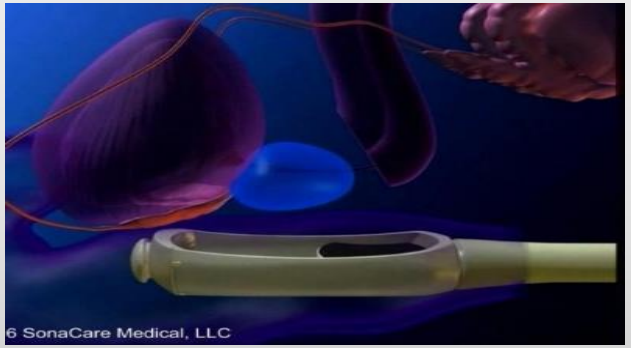


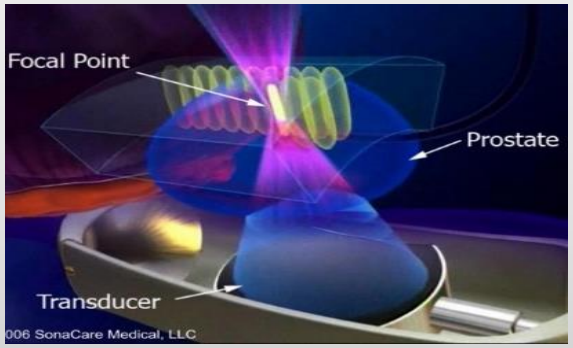
FOCAL GLAND

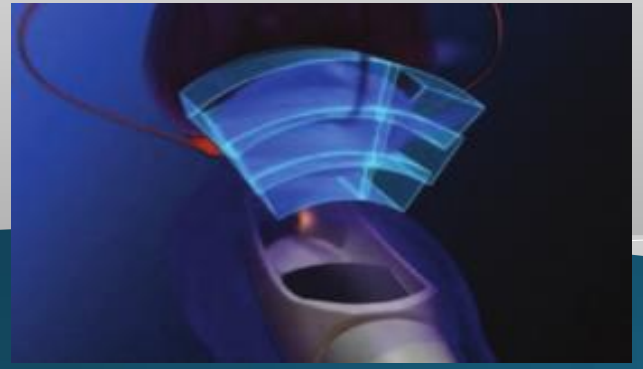
This tailored ablation plan allows the user to perform a whole or partial gland ablation.

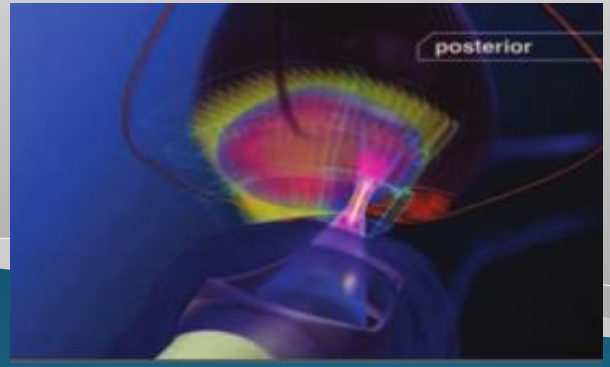
Western States HIFU
Experience Counts!

Sonablate Prostate Ablation









HIFU can deliver targeted, non-invasive ablation to specific prostate tissue regions

Western States HIFU
Experience Counts!

Sonablate Whole Gland Ablation

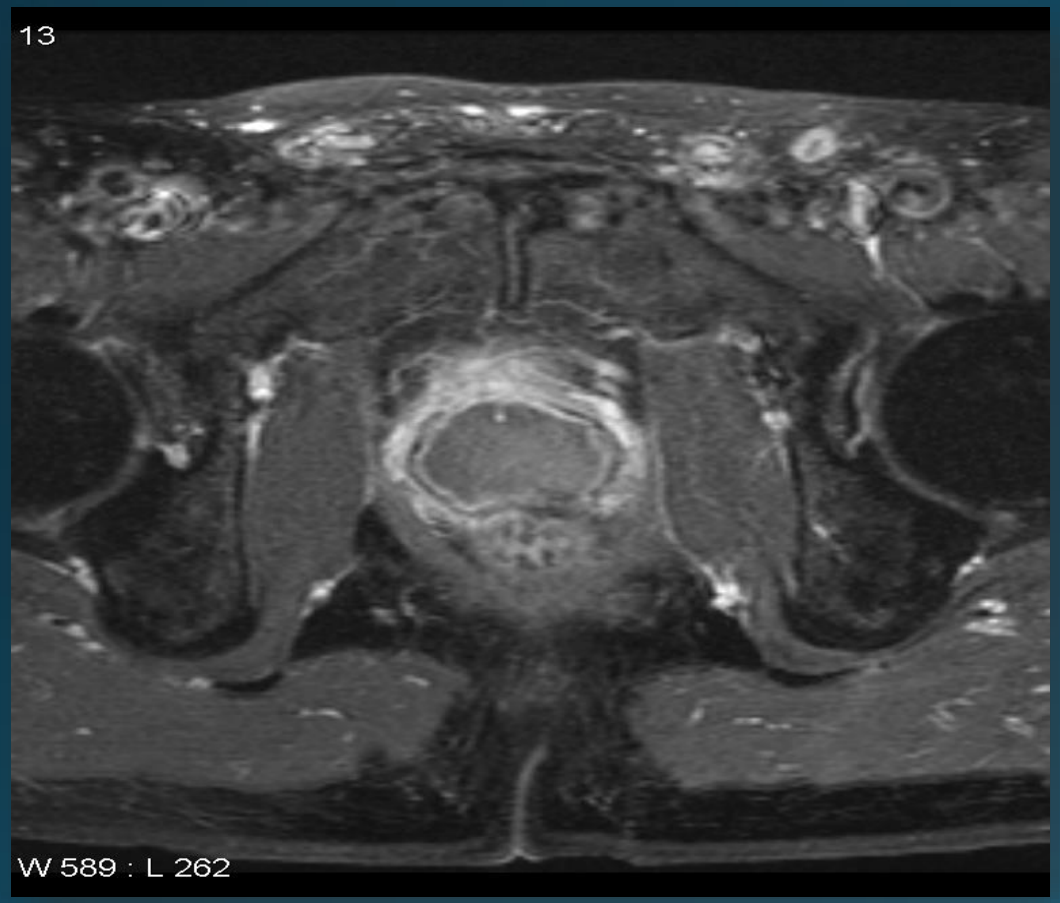
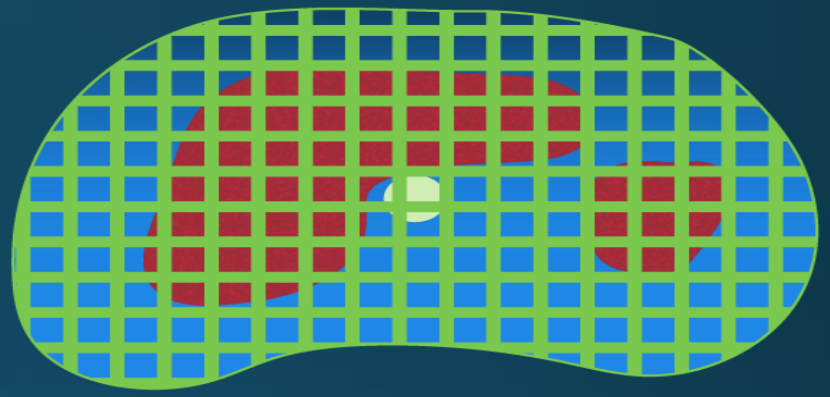


Image courtesy of Professor Mark Emberton, University College London

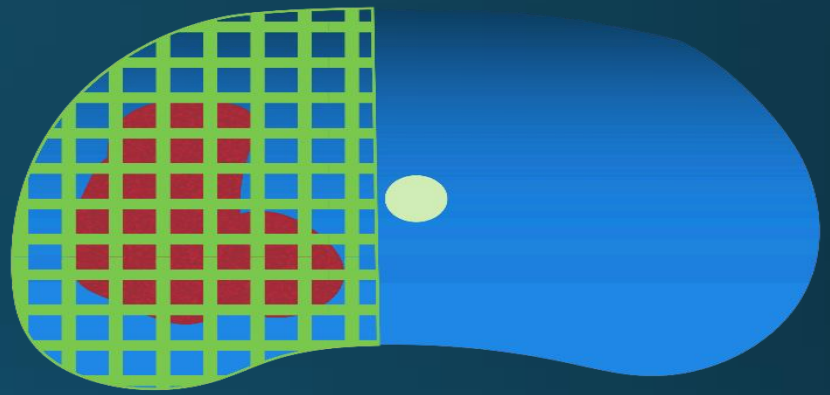


Two months post HIFU

- Shrinkage of necrotic volume through mixture of sloughing, resorbtion and fibrosis
- T1W axial MRI
- 1 min post gadolinium contrast

Sonablate Prostate Hemi Ablation

Image courtesy of Professor Mark Emberton, University College London



Prostate HIFU Hemi Ablation of the patient's left lobe performed at University College of London

T1-weighted gadolinium enhancement at 1 week post Left Hemi-HIFU

Western States HIFU
Experience Counts!

Sonablate Prostate Focal Ablation

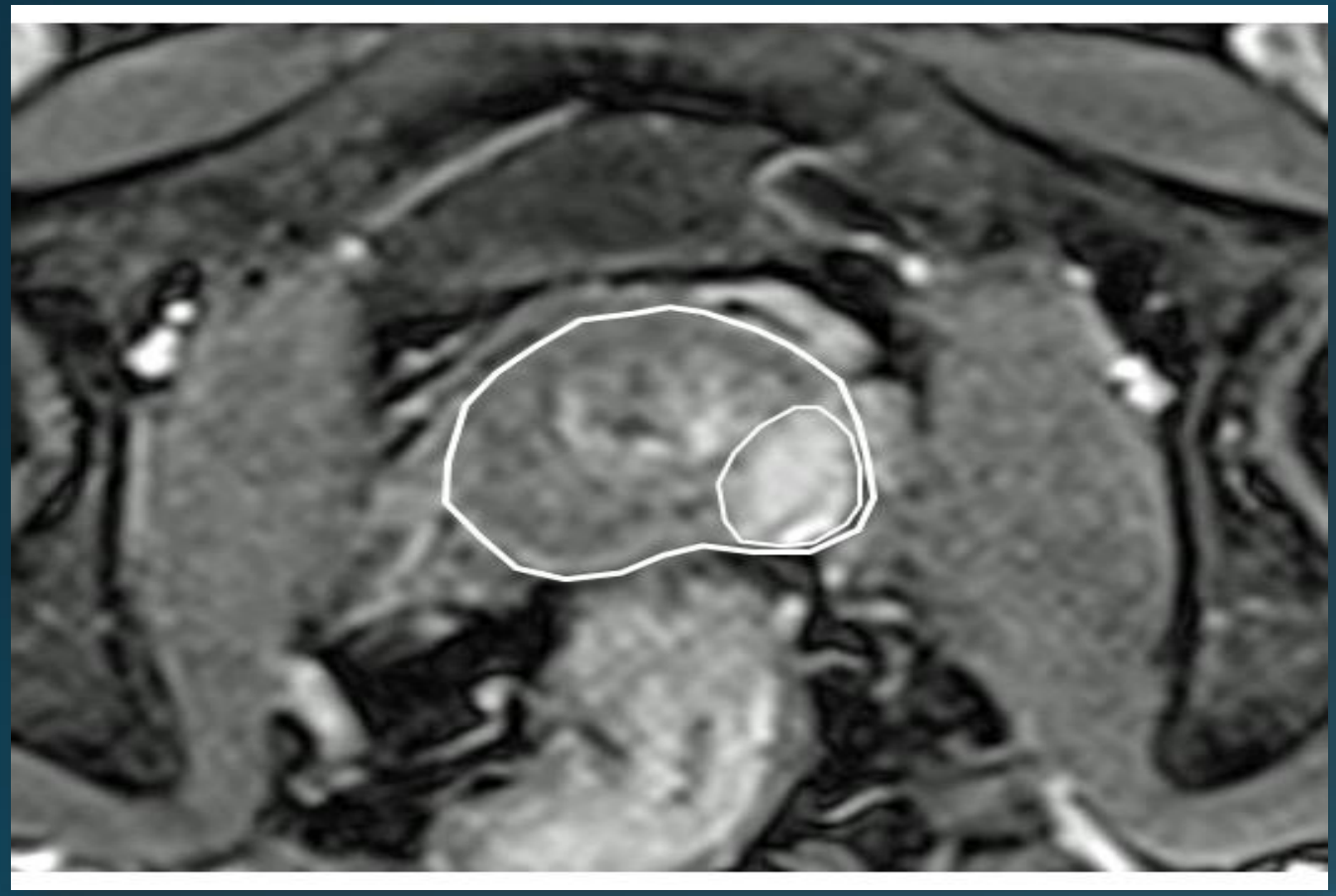
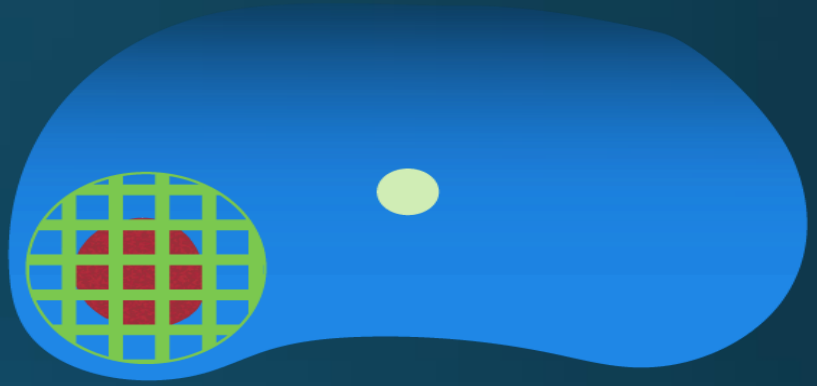


Image courtesy of Professor Mark Emberton, University College London



Prostate HIFU Focal Ablation of focal site on the patient's left side

MRI study following-up using DCE /gadolinium shows positive ablation results

Quality of Life Outcomes after Focal Therapy

	Radical Surgery	Radiotherapy	Whole Gland HIFU	Focal Therapy HIFU
Hospital stay length/visits	2-5 days	45 visits	1 outpatient visit (2-4 hrs)	1 outpatient visit (1 hr)
Return of normal urine flow	6-12 months	3-6 months	14-21 days	2-7 days
Incontinence at 6 months (requiring pads)	30%-60%	20%	2%	0%
Impotence	50%-90%	60%	15%	<5%

Treatment of Localized Prostate Cancer

Robert G. Pugach, M.D.

Medical Director,

Western States HIFU

&

Pacific Coast Urology Medical Center

November 5, 2016