

PARALLELS BETWEEN IMRT AND FUS

Mark Carol, M.D.
Chief Development Officer
SonaCare Medical
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Ablation Complementary to Existing Therapies

RADIATION THERAPY

RADIATION THERAPY

Best suited for microscopic disease that infiltrates tissue

HIFU

Best suited to treat macroscopic (gross) disease

HIFU used to treat gross disease in single session followed by a short course of RT to treat infiltrative disease

Added Plus: Reduces number of RT fractions; RT infrastructure to support HIFU

ROBOTIC SURGERY

Surgical Robot

Used to deliver precisely surgical tools to regions of interest

HIFU

A tool to destroy selected regions of interest

HIFU used as tool to destroy selected region of interest accessed by the Robot

Added Plus: Use of HIFU in place of “knife” will reduce blood loss and reduce time

RT and Ablation

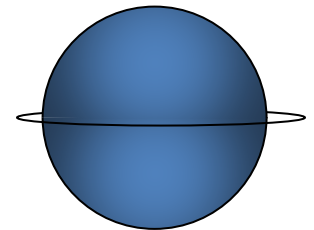
- RT and Ablation use the same three principles - inverse planning, modulated energy delivery, image guidance - to deliver focal therapy



- The difference between the two is not just semantics. There are fundamentally different biological principles guiding their rationale and use

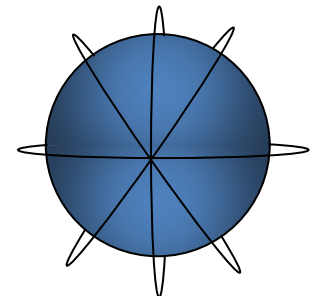
Radiation Therapy

- Makes use of the biological property that healthy cells will recover more readily from radiation injury than tumor cells. The dose given at each fraction is sufficient to kill a percentage of the tumor cells, while giving healthy cells time to recover between treatment sessions.
- *Similar to using Ortho "Weed-Be-Gone" on lawn. With the appropriate amount and correct dosing schedule, weeds are killed gradually over time while grass recovers and prospers*
- Used:
 - To control post-surgical disease
 - To treat tumors that cannot be removed by surgery
 - To treat medically inoperable tumors
 - As an alternative to surgery for well defined medium to large tumors
- Normal Fractionation: 20 – 40 fractions
- Hypofractionated Radiation: 6 – 20 fractions with precision targeting



Focal Ablative Therapy

- Thermal Ablation, Electrocoration, Cavitation, Radiosurgery
 - Treats cancerous and normal cells the same, delivering enough dose in a short enough period of time to kill everything
 - *Similar to using “Roundup” Herbicide – kills everything it touches; weeds and grass*
 - Used:
 - As an alternative to surgery for well-defined small to medium tumors
 - As an alternative to conventional RT for small well defined target volumes
 - Treat non-cancer conditions like AVMs and functional disorders of CNS
 - Investigated for other uses: atrial fibrillation and renal hypertension
 - Requires extremely precise localization and delivery in order to limit damage to target only
 - RS/Thermal Ablation: single fraction
 - SRS: 2 -5 fractions



IMRT vs FUS

- RO has the advantage over ablative modalities of a developed infrastructure including physicists, dosimetrists, therapists
- Ablative modalities have advantages over ionizing energy sources that make them ideally suited for focal therapy:
 - They tend to be deterministic rather than statistical in impact
 - They can be guided easily using real time imaging
 - Real time impact can be assessed using noninvasive thermometry
 - Can be repeated (no “tissue memory”)
- Regardless, it can be argued that ablative therapies will need the same set of tools and resources as exist in RT if they are to compete successfully

Cornerstone #1

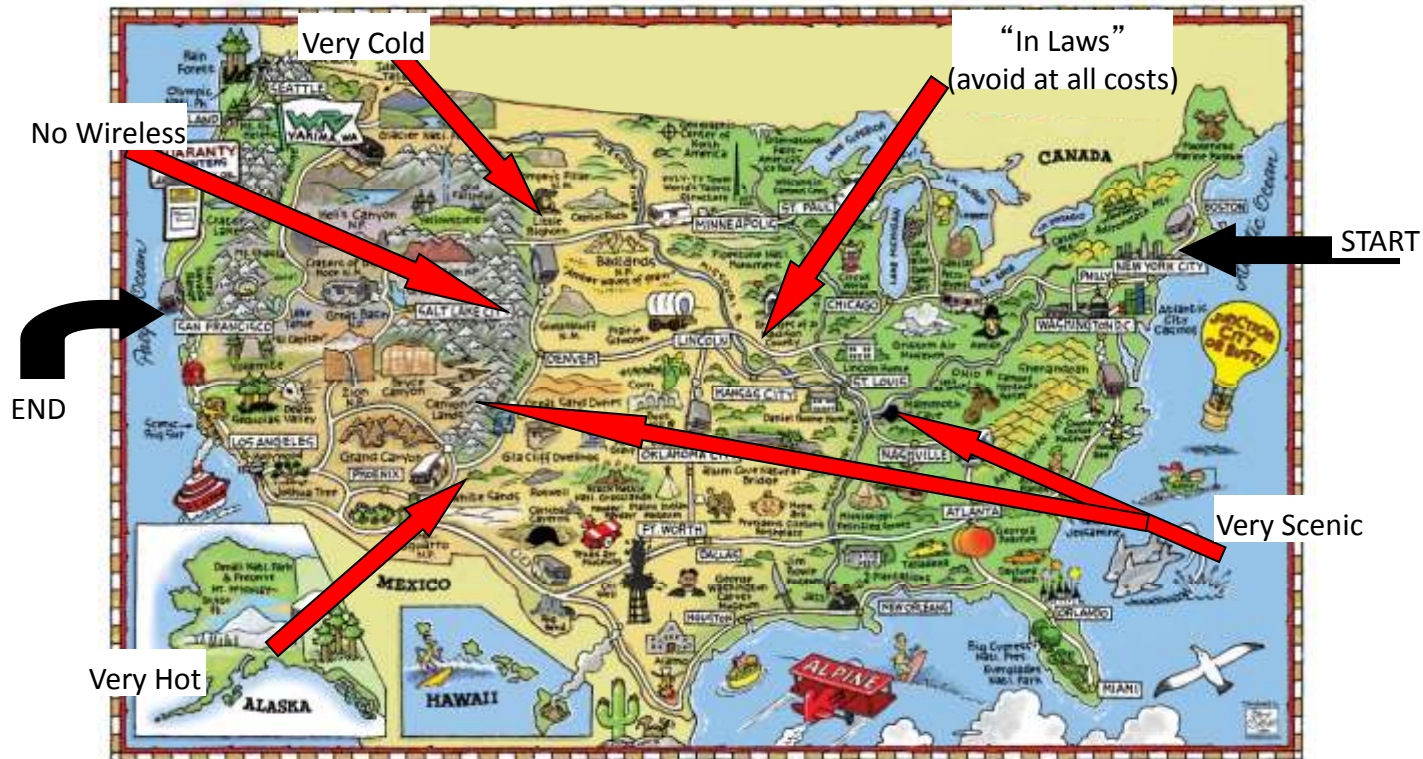
How does one create an optimized plan: As much target volume as possible receiving desired dose, as little avoidance structure volume as possible reaching limits



Principle RT Inverse Treatment Planning

Similar to using your GPS system where you can select from:

- shortest route
- most scenic
- fewest highways
- shortest time
- (avoid all traffic police)
- least gas



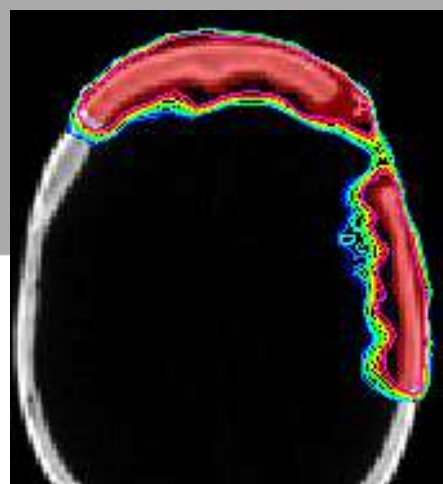
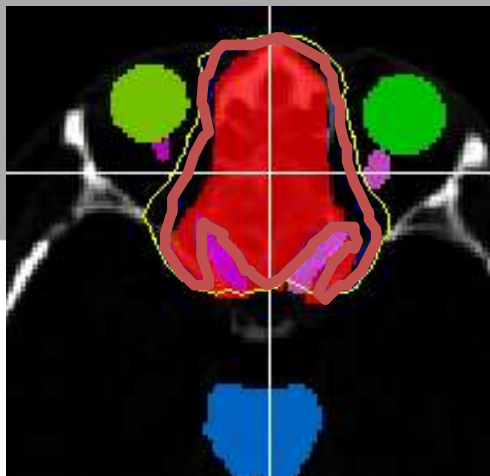
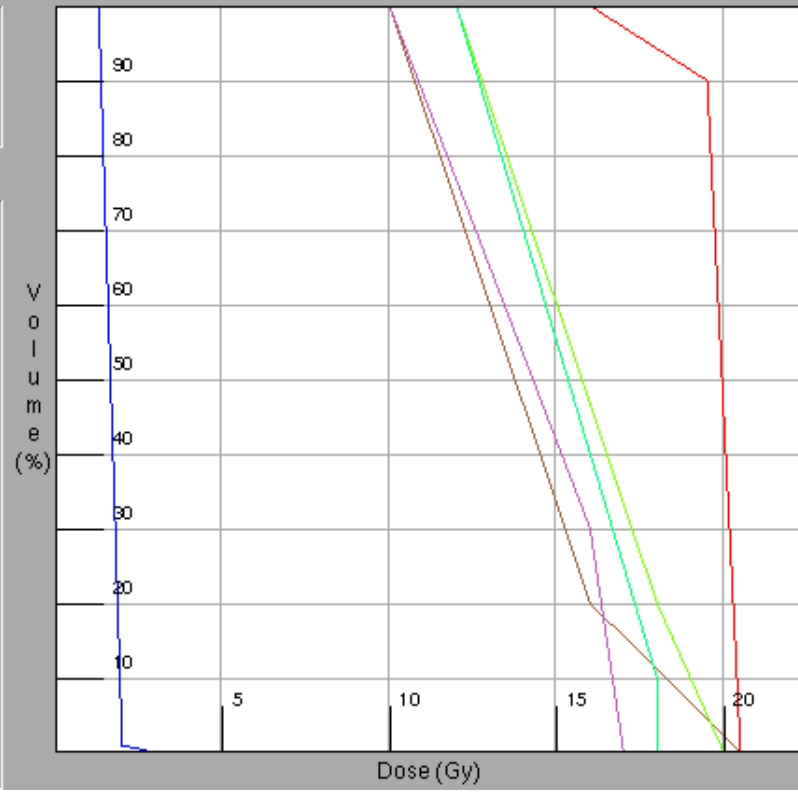
If you could weight each of these you would have a cost function that determines how “expensive” is any given solution, thus allowing you to select the least “expensive” solution.

Driving the RT Result

(“Sensitive” structure avoidant treatments)

Target Name	Goal (Gy)	Vol Below Goal (%)	Min (Gy)	Max (Gy)	AG	
target	19.5	10	16.0	20.5	<input type="checkbox"/>	<input checked="" type="checkbox"/>

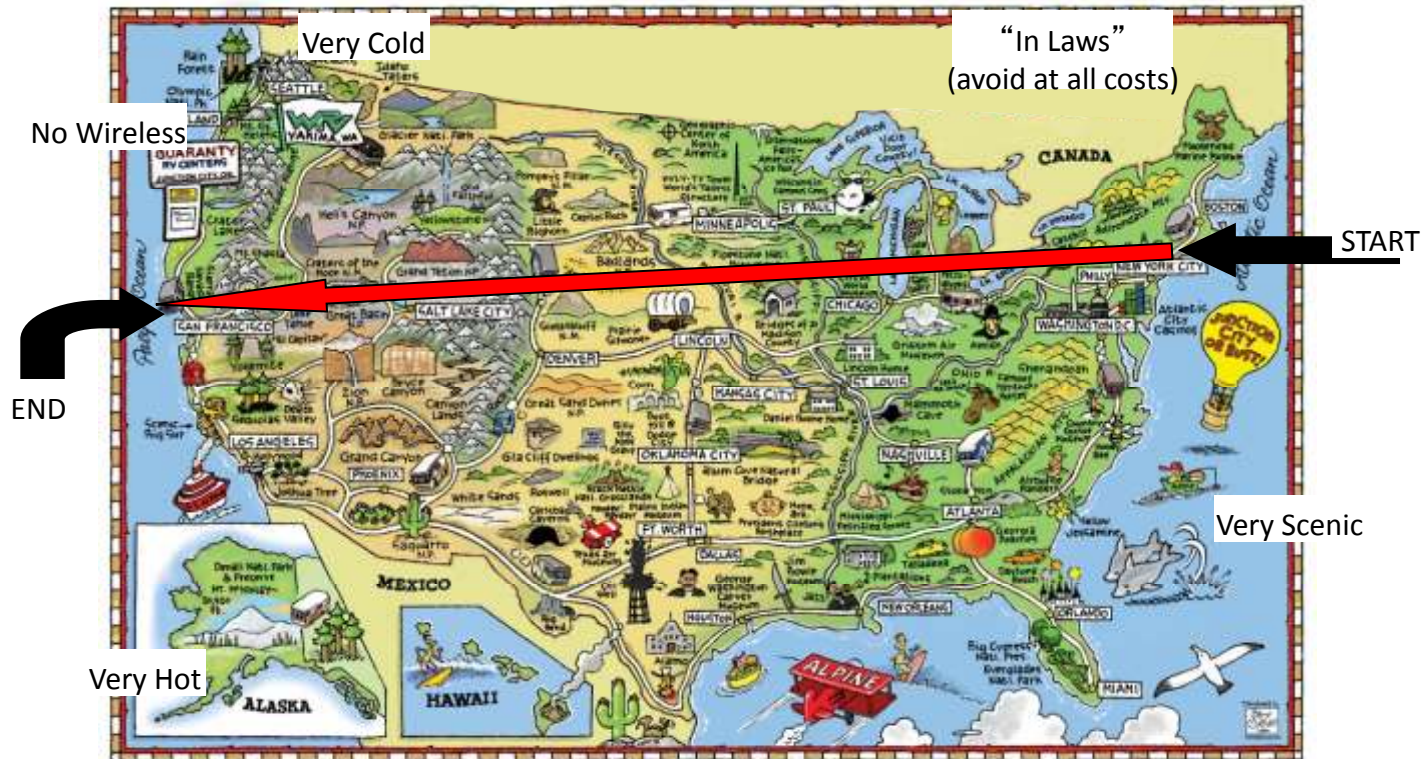
Sensitive Structure Name	Limit (Gy)	Vol Above Limit (%)	Min (Gy)	Max (Gy)	BU	BP	I	
Tissue	16.0	20	10.0	20.5	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Kidney (L)	18.0	20	12.0	20.0	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Kidney (R)	18.0	10	12.0	18.0	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Liver	16.0	30	10.0	17.0	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Spinal cord	2.0	1	1.3	3.0	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>



Principle FUS Inverse Treatment Planning

Similar to using your GPS system where you can select from:

- most direct route



Since each shot is delivered so quickly, there is essentially no effect on intervening tissue, and dose falloff is so rapid that efficiency becomes the only real cost

Driving the FUS Result ("spindle packing")

The screenshot displays the Sonablate 500 Simulator software interface, which is used for planning focused ultrasound (FUS) treatments. The interface is divided into several sections:

- Top Left:** A large ultrasound view showing a sector scan of the prostate with a red dotted line indicating the treatment zone. The distance is marked as $\#34 @ 2.75 \text{ cm}$.
- Top Right:** A smaller ultrasound view showing a different angle of the prostate with a red dotted line. The distance is marked as $\#91 @ 0.5^\circ$.
- Bottom Left:** A zoomed-in view of the treatment zone, showing a dense grid of red dots. The distance is marked as $\#79 @ 3.90 \text{ cm}$.
- Bottom Right:** A 3D visualization of the prostate and the treatment zone, showing the spatial arrangement of the treatment shots.
- Checklist:** A task list on the right side of the interface, detailing the steps for creating and refining a treatment plan. The checklist includes:
 - 1. Create rough plan for a single-focus zone
 - 1. Gather sector images to cover entire prostate
 - 2. Mark the left and right edges of the prostate on each sector image
 - 2. Refine plan for a single-focus zone
 - 1. Gather new sector and linear images at treatment spacing to cover entire prostate
 - 2. Identify nearby critical structures
 - Identify bladder neck
 - Identify rectal wall
 - Identify pubic bone
 - 3. Identify neurovascular bundles
 - 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 neurovascular bundles on as many sector images as possible
 - 4. Remove or add treatment shots as necessary:
 - To cover the desired portion of the treatment zone
 - While avoiding critical structures
 - Avoid bladder neck
 - Avoid rectal wall
 - Avoid pubic bone
 - Avoid neurovascular bundles
 - 3. Zone treatment plan complete

- Layout:** A panel on the right side of the interface, showing a grid of icons for different views and tools.
- Stack/Live:** A panel on the right side of the interface, showing a green indicator and a scan button.
- Planning Method:** A panel on the right side of the interface, showing a red indicator and a green indicator.
- Adjust Area:** A panel on the right side of the interface, showing a grid of icons for adjusting the treatment area.
- Add or Remove Treatment Shots:** A panel on the right side of the interface, showing a red plus sign, a white minus sign, and buttons for Undo and Reset.

Driving the FUS Result

("focal" normal tissue avoidant treatments)

SN1001 Sonablate® 500 Simulator Version 0.0.0[0.0] [special build "SonaPlan-Demo4t4UA-1005"] Copyright © 2000-2013 Focus Surgery, Inc. a subsidiary of SonaCare Medical, LLC

Checklist

- 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 pulse zone
- 3. Identify neurovascular bundles
 - 1. Open the RGB - Display for Neurovascular Bundle Detection tool
 - 2. Rotate staples and choose live sector imaging
 - 3. Move the display gate to identify the neurovascular bundles on as many sector images as possible
- 4. Outline and plan the prostate on the R-Mode image
 - Choose the polygon sector in the Planning Method box
 - Use the mouse to draw the outline of the prostate
 - Single mouse clicks add points to the outline
 - Click-and-drag near a point marked with "V" moves the point
 - Click-and-drag near a segment adds a point
 - Double-click near a point deletes the point
 - Clicking on the open 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

Layout

Stack/Live: [Live] [Stack]

Scan: [Scan] [Pause]

Planning Method: [Polygon] [Staple] [Staple]

Adjust Area: [Adjust Area]

Add or Remove Treatment Shots: [Add] [Remove] [Undo] [Redo]

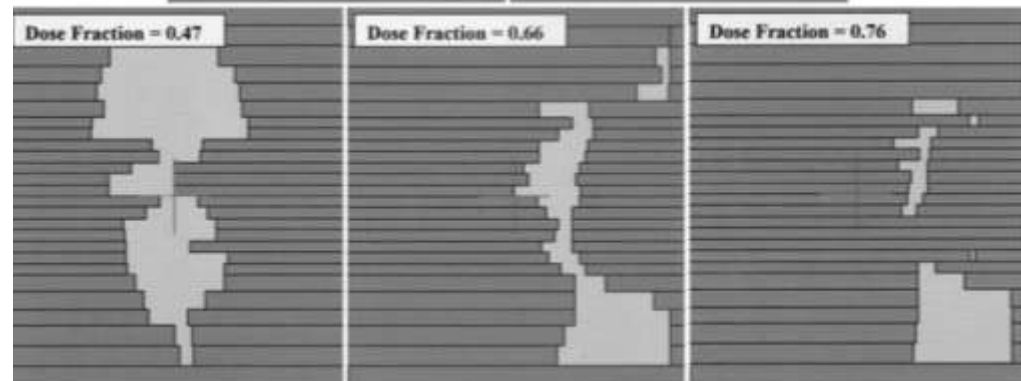
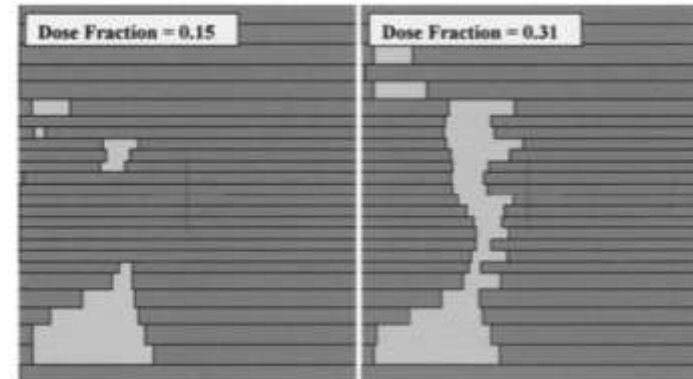
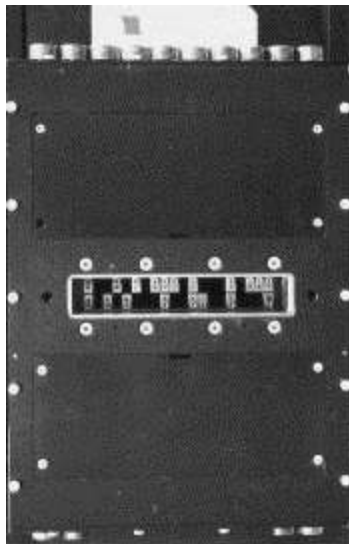
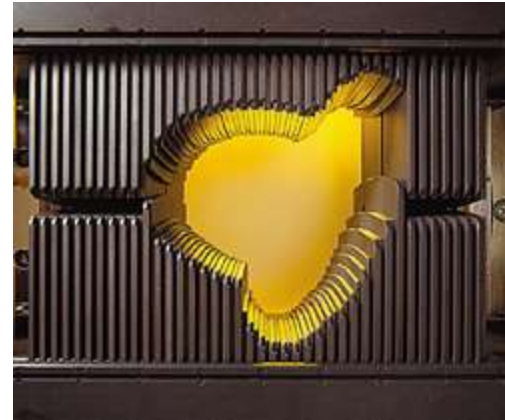
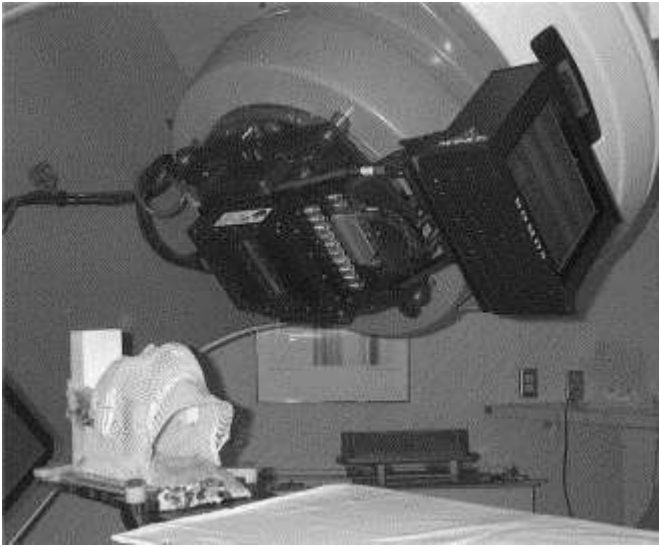
Status: Saving files...done

Cornerstone #2

How do we deliver an intensity modulated treatment plan ?



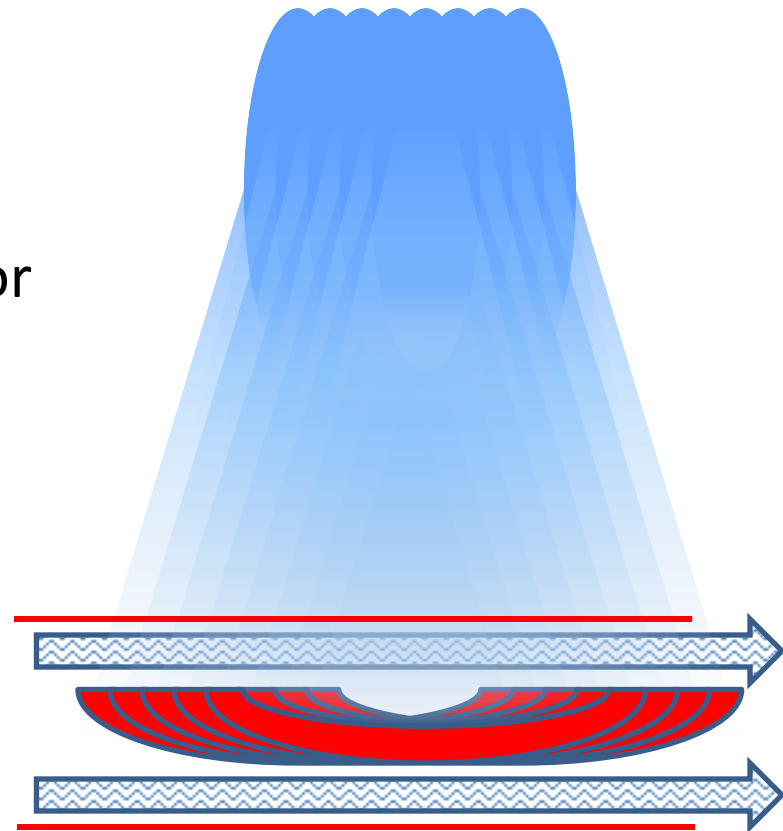
Delivering Modulated RT Treatments



HIFU

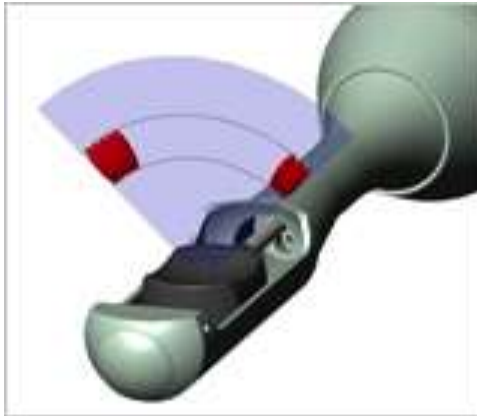
Discrete Delivery

- **Most HIFU systems deliver a series of discrete ablations or “shots”**
- Each shot is delivered in 3 seconds
- 3 - 6 second pause after shot allows for imaging and tissue cooling
- Staggered pattern of shot dispersion allows cooling of tissue
- Probe cooled with chilled water

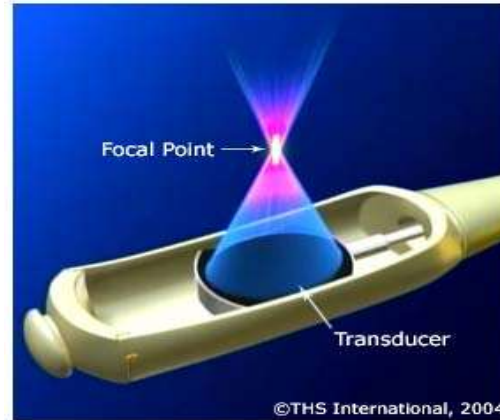


Delivering Modulated FUS Treatments

See



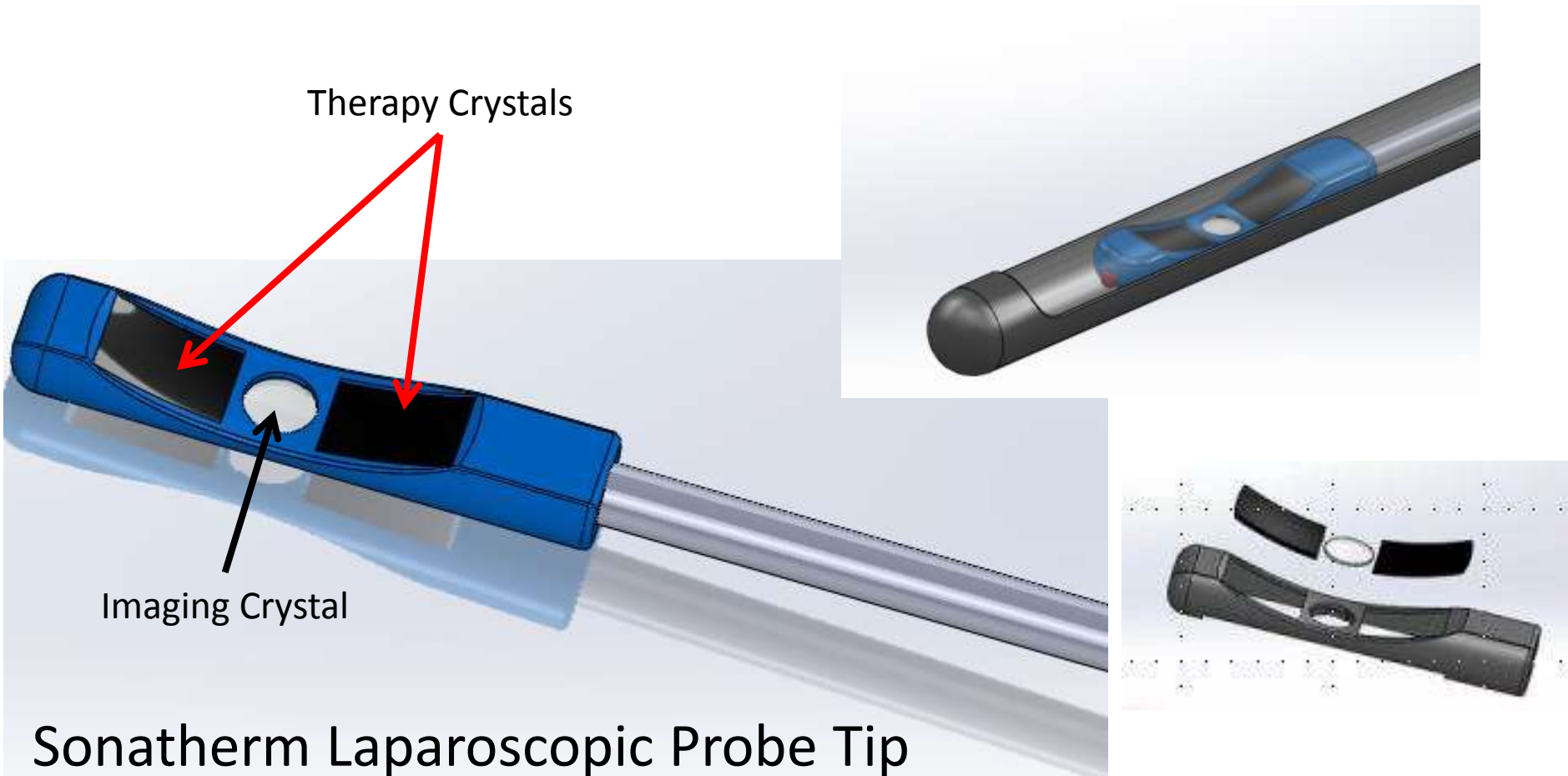
Treat



Track



Delivering Modulated FUS Treatments



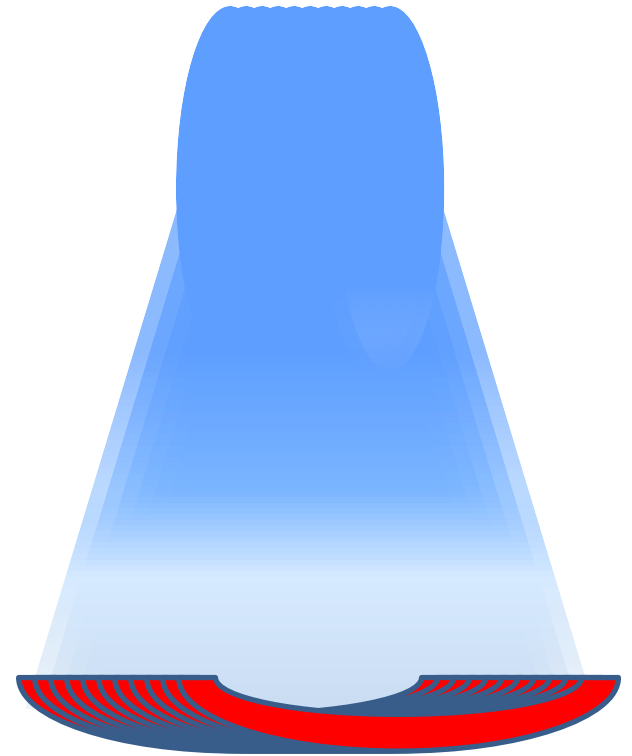
Sonatherm Laparoscopic Probe Tip

- Three (3) distinct operating crystals (one imaging and two therapy)
- Robotic scanning of transducers for volumetric imaging & ablation

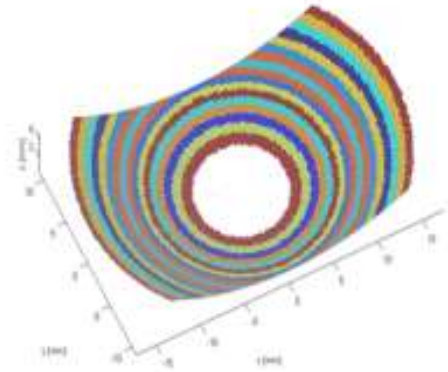
HIFU

Continuous Delivery

- It is possible to deliver heat continuously, moving the focal point over volume of tissue to be ablated
- Tissue back to surface of the probe is destroyed eliminating need for probe cooling and pauses for cooling
- Elimination of “active” cooling results in a more efficient treatment delivery (3 – 6x)



Depth Modulated FUS Treatments



25 mm

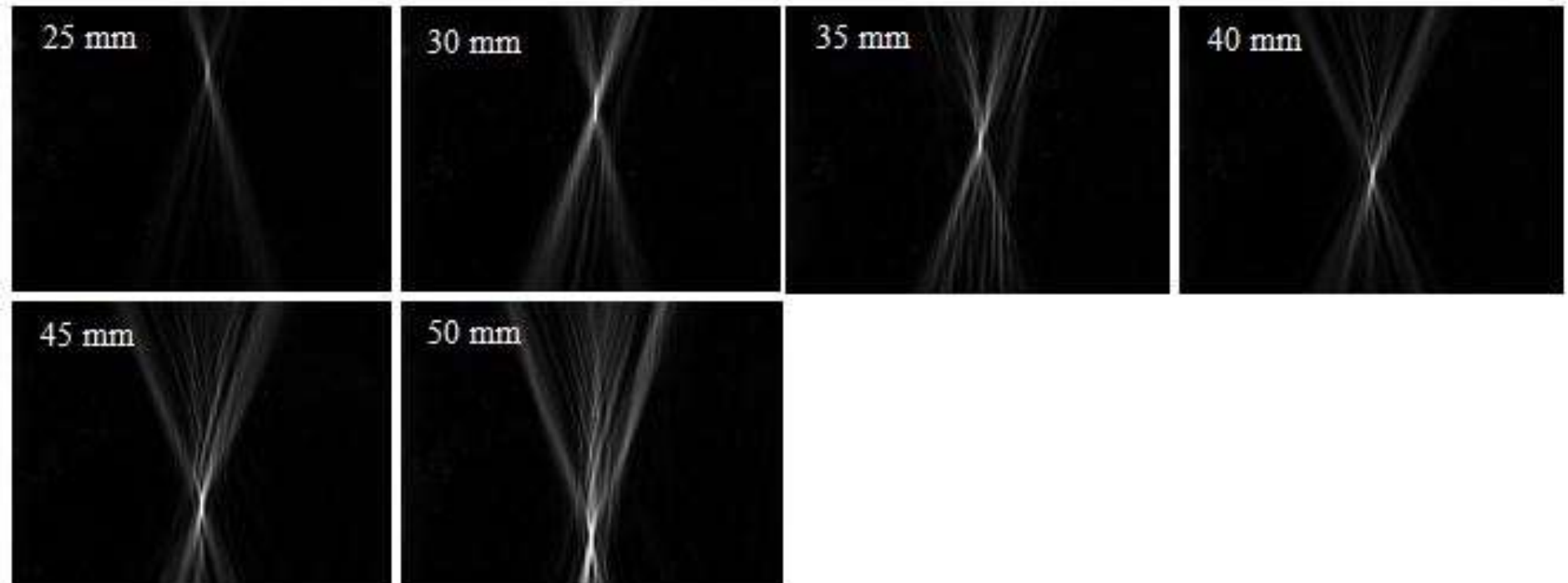
30 mm

35 mm

40 mm

45 mm

50 mm



Cornerstone #3

As we get better at limiting size and shape of region we treat, the potential for, and risk from, geographic miss increases



"Dang. I must've hit the juggler vein."

Localizing Target at Time of Treatment

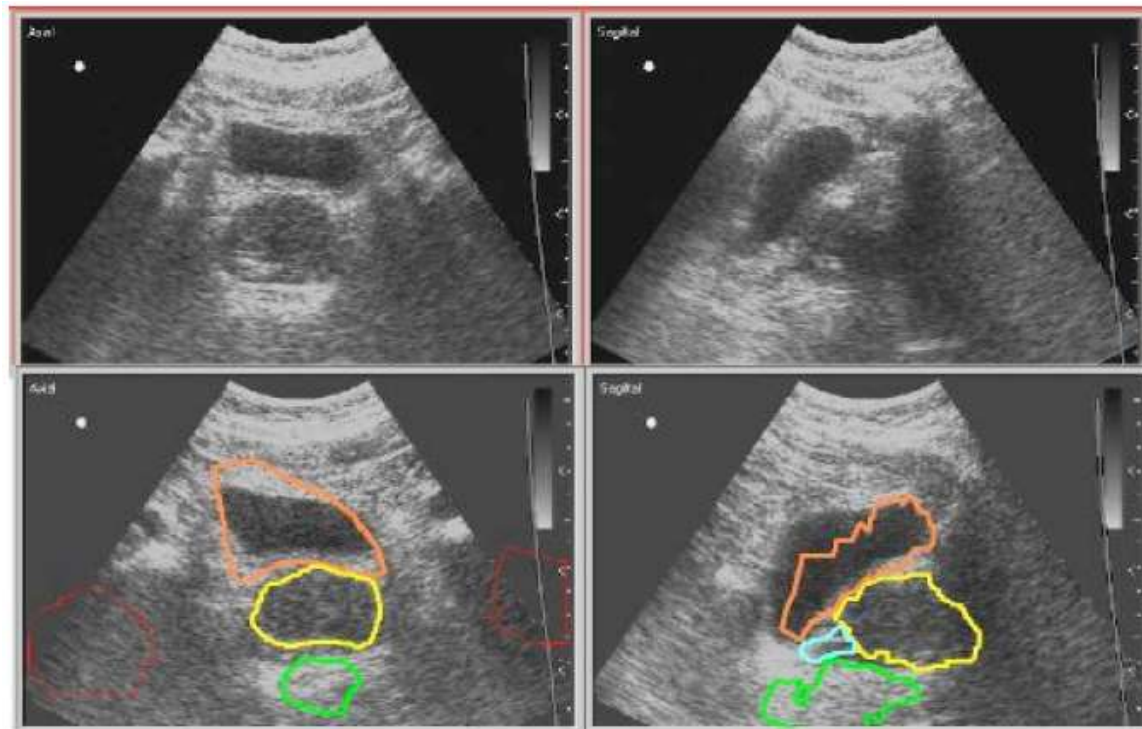


Localizing Target at Time of RT Treatment

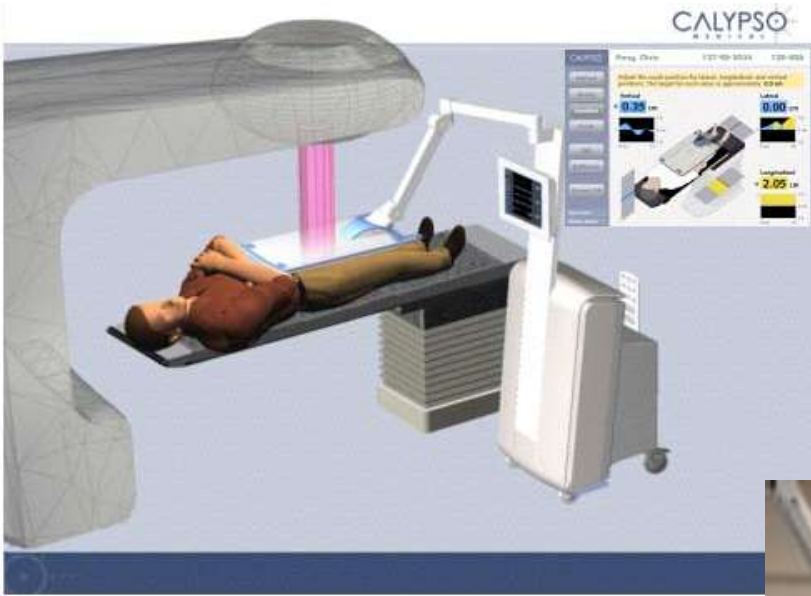
- Traditionally, localization was done to surface anatomy, as determined by skin tattoos, or to bony anatomy, as identified by x-rays. - Worked great for brain as well as head & neck.
- Outside the skull many targets move relative to skin or bony anatomy, such as is the case with prostate and lungs?
- *How does one take a precise dose distribution and put it in the correct location on each of up to 40 treatments spread out over 8 weeks, knowing that if one doesn't the potential for recurrence and for complications increases?*

Localizing Target at Time of RT Treatment (Step 1)

Enter concept of Image Guidance



Localizing Target at Time of RT Treatment (Step 2)



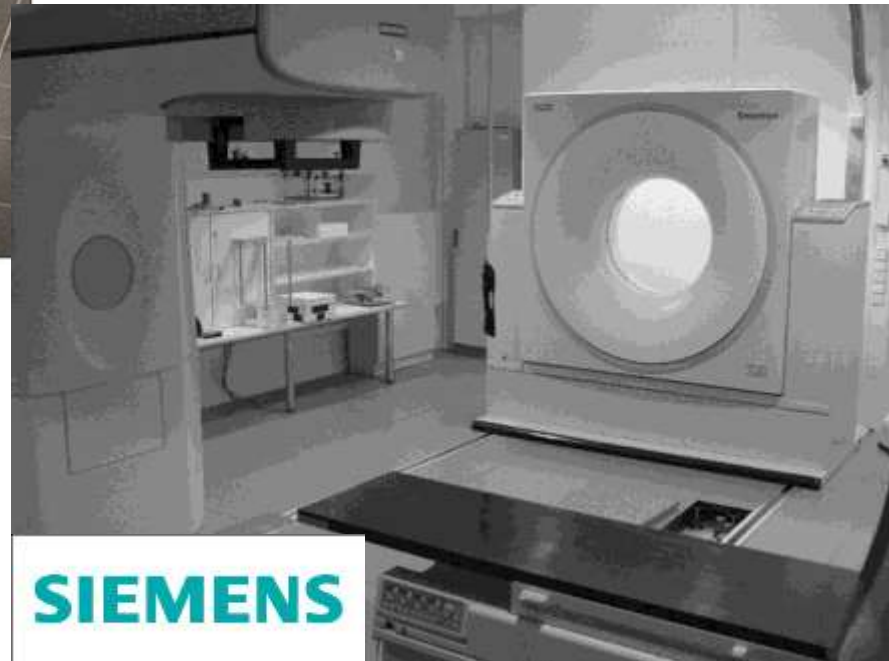
Implanted Markers



Localizing Target at Time of RT Treatment (Step 3)



3D Imaging



Localizing Target at Time of FUS Treatment

- RT has benefit of fractionation, which allows one, to some degree, to make up tomorrow for that missed today
- Ablation is delivered in a single fraction – if one misses it today it is missed for good.

Localizing Target at Time of FUS Treatment



3D (MRI) Imaging

Localizing Target at Time of FUS Treatment

Real Time US
Imaging
at site of treatment



Target Volumes Move During Treatment



"Sorry about that, the firing squad prefers a moving target"



Modeling Movement During RT Treatment

Planning Goals & Optimization

Planning Set
 Prostate +U

Optimizer
 Continuous Annealer

Immobilizer & Localizer

Immobilizer
 Pelvis-styrofoam body cast

Localizer
 BAT

Treatment Machine & Delivery Options

Treatment Machine
 Siemens 6MV MLC IMFAST [Siemens Coordinates]

Delivery Options
 6 Fields revised

IMMOBILIZATION UNCERTAINTY (mm)

Uniform A/P R/L S/I U ✓

LOCALIZATION UNCERTAINTY (mm)

Overlap Localized Organ Uniform A P R L S I U ✓

TOTAL UNCERTAINTY (mm)

A P R L S I

Target Name	Overlap Priority	Localized Organ	Uniform	A	P	R	L	S	I	U	A	P	R	L	S	I
Prostate - target	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	2.0	2.0	2.0	2.0	2.0	2.0	✓	2.8	2.8	2.8	2.8	2.8	2.8

Sensitive Structure Name

Sensitive Structure Name	Overlap Priority	Localized Organ	Uniform	A	P	R	L	S	I	U	A	P	R	L	S	I
Tissue	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	7.3	7.3	11.4	11.4	7.3	7.3	✓	7.6	7.6	11.6	11.6	7.6	7.6
Bladder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	30.5	2.0	31.7	31.7	30.5	2.0	✓	30.6	2.8	31.8	31.8	30.6	2.8
Femoral Heads	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	5.7	5.7	10.4	10.4	5.7	5.7	✓	6.0	6.0	10.6	10.6	6.0	6.0
Rectum	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	2.0	7.3	11.4	11.4	2.0	7.3	✓	2.8	7.6	11.6	11.6	2.8	7.6

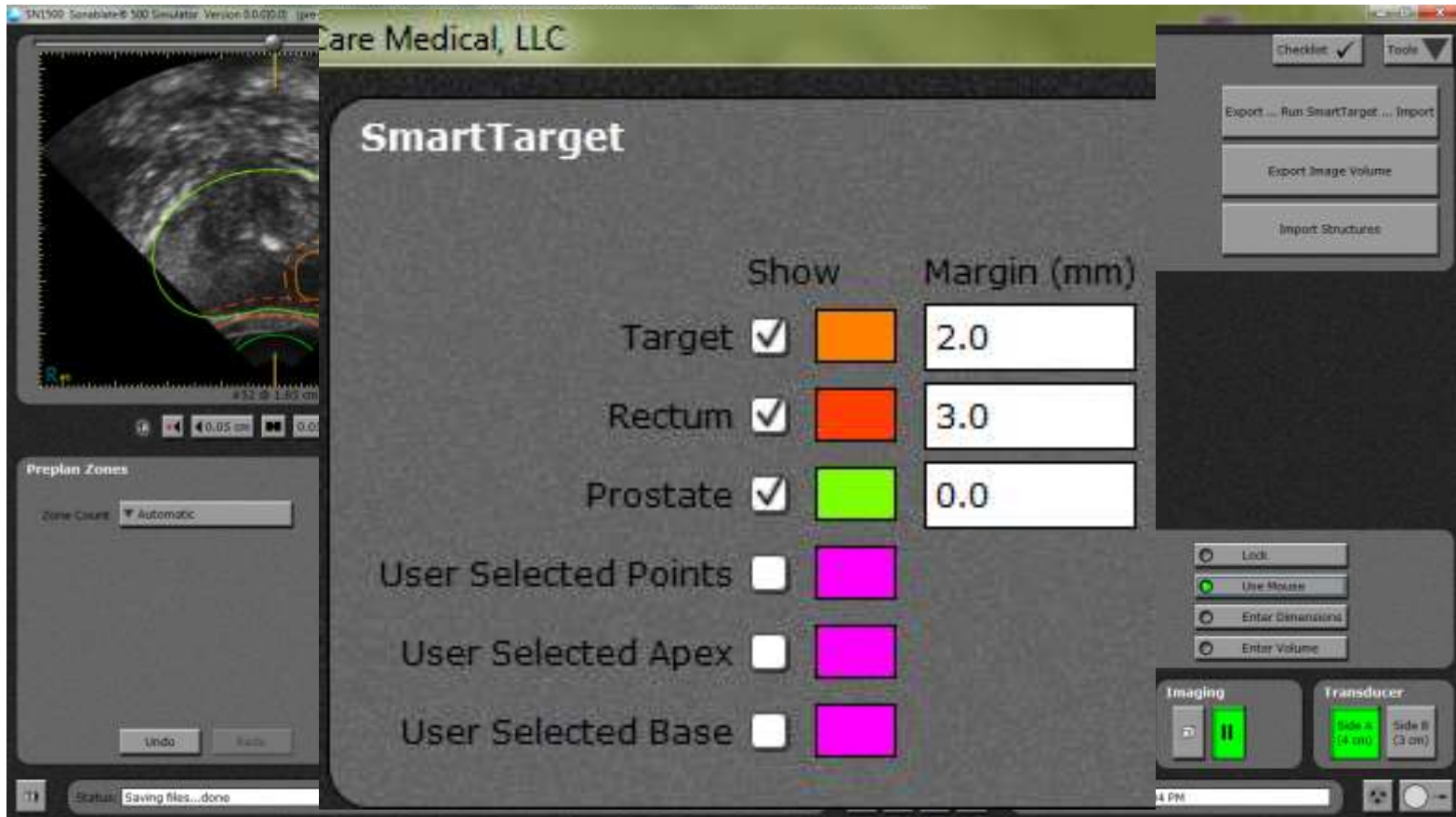
Modeling Movement During RT Treatment



Patient Setup and Tracking



Modeling Movement During FUS Treatment



By imaging immediately for 1 sec after each shot, the next shot can be positioned to compensate for any movement

DIRTY LITTLE SECRETS

x



SWEARS LIKE A
SAILOR



EATS OUT OF THE CAT
BOX



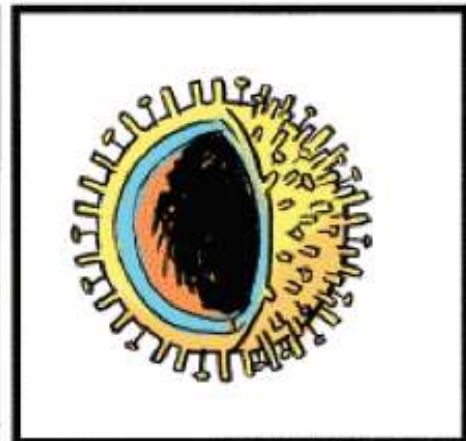
M.C. ESCHER TATTOO
ON BELLY



VOTED FOR NADER,
TWICE



POURS 2% MILK INTO
SKIM MILK CARTON

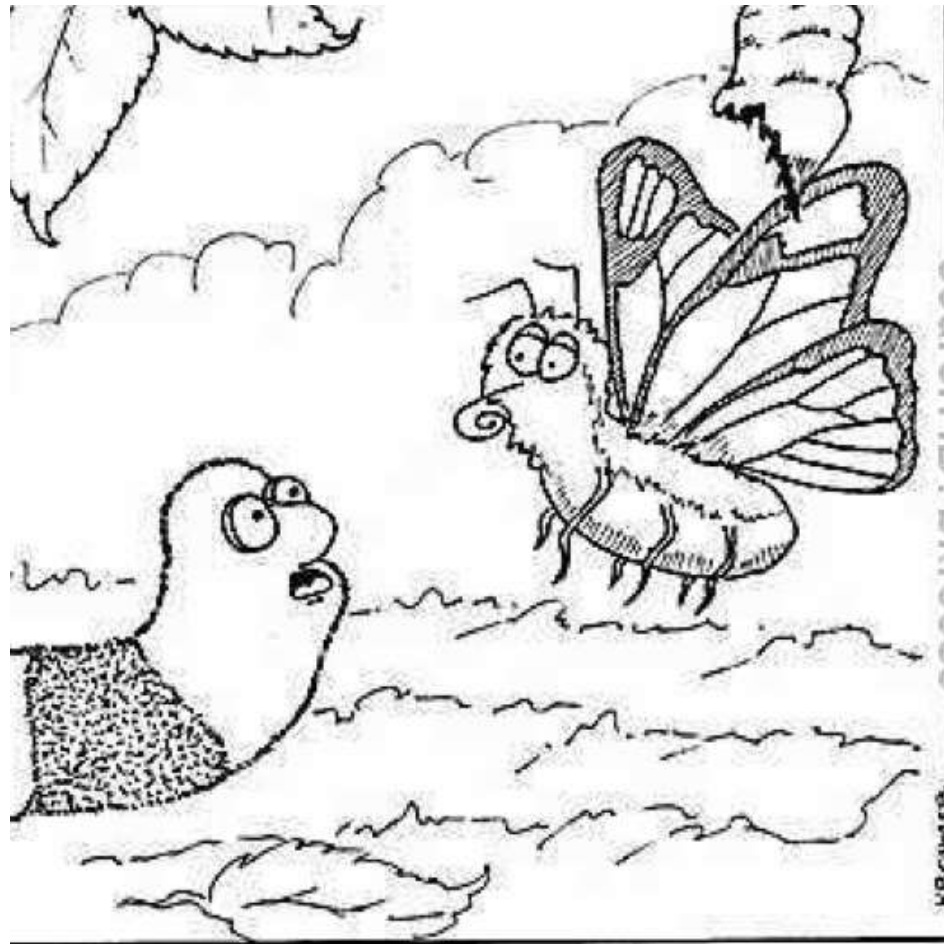


CAUSES
INFLUENZA

© 2008 Stiness

Dirty Little Secret #1

Target Volumes Change Shape and Size Day-to-Day



I KNOW THAT YOU HAVE CHANGED IRENE,
BUT I STILL THINK WE CAN WORK THINGS OUT

Adaptive Radiation Therapy

- Typical standard is one treatment plan at beginning of course of RT good for entire course of treatment
- BUT...targets shrink and sometimes may even grow over course of therapy
- While changes in size and shape are common from day to day, they are relatively rare during the course of a treatment
- Adaptive Radiation Therapy therefore teaches reimaging patient before (after) each fraction in order to create a modified or new treatment plan for consideration for each fraction

Adaptive Radiation Therapy



*Image of adjusting contours to match the anatomy changes with RealART Real-Time Treatment Planning.

STAT SBRT: A TomoTherapy based proposed approach to real time treatment planning and quality assurance

East Coast CT-Directed IGRT Symposium
Long Branch, New Jersey April 18, 2009

Paul W. Read, M.D. Ph.D.
University of Virginia
Department of Radiation Oncology



Adaptive Thermal Ablation

- Daily changes in size and shape are not a problem with thermal ablation since there is only one day
- However, the introduction of heat into tissue causes the tissue to change size and shape during treatment
- This change is variable, occurs throughout treatment to varying degrees, and is difficult to model upfront
- Since treatment planning is essentially real-time, and since tissue can be imaged in real-time, continuous correction by using continuous real-time replanning / plan modification is possible

Dirty Little Secret #2

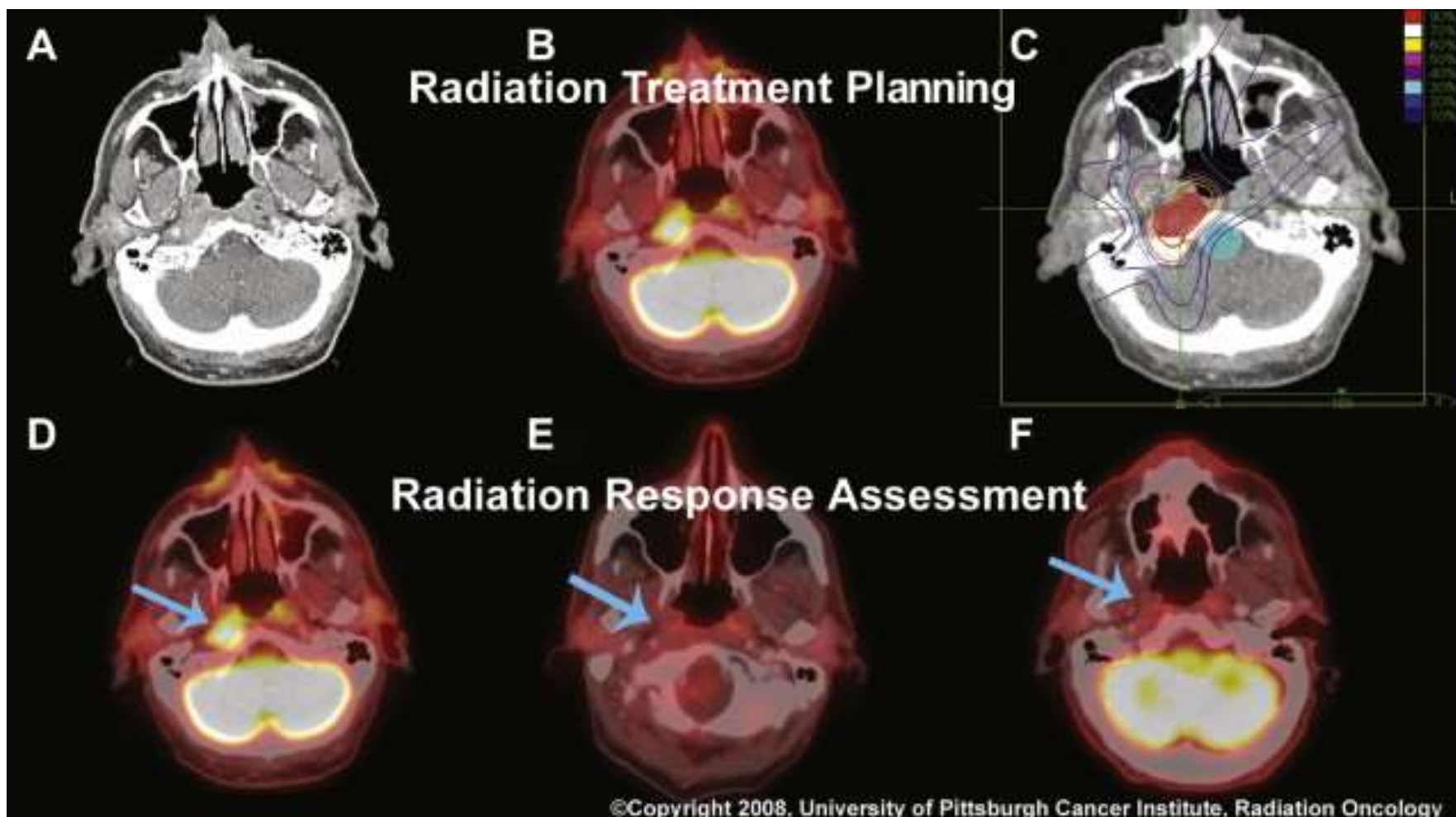
We delivered
"How much, and to what?"

**"Formula for success:
under promise and
over deliver"**

Thomas J Peters

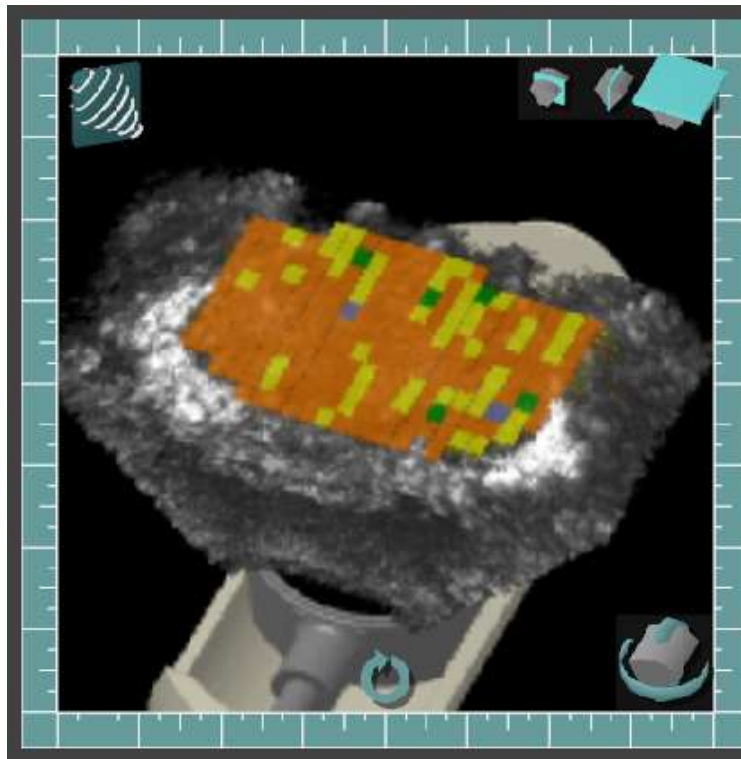


Assessing RT Treatment Delivery

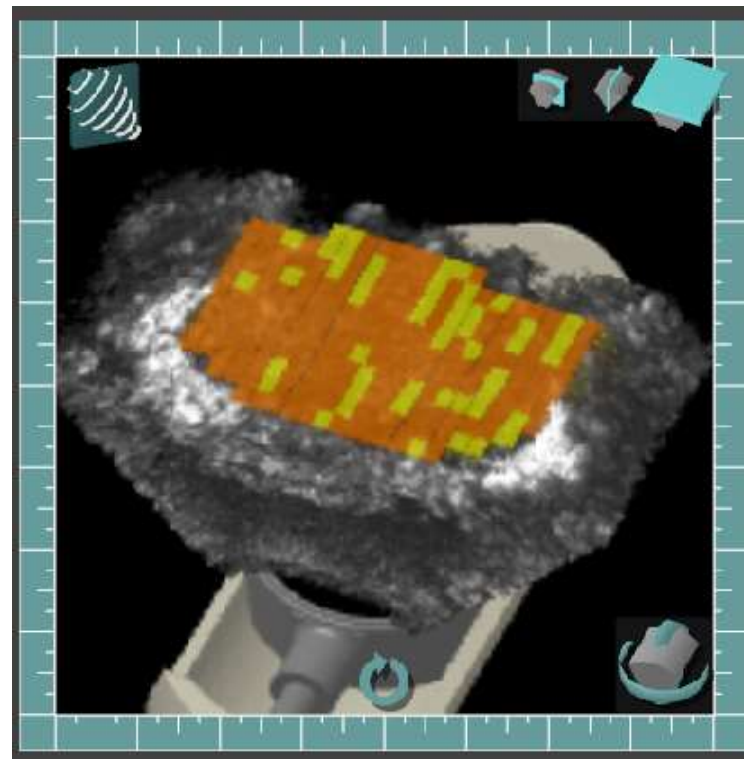


Assessing FUS Treatment Delivery

Temperature Change Monitoring (TCM)



First Pass



Second Pass

Assessing FUS Treatment Delivery

Phantom Validation

SN1001 Sonablate® 500 -- HIFU Therapy Version V5 TCM /Rev4/ [3.3] Copyright © 2000-2006 Focus Surgery, Inc.

Site: Hospital Doctor: Dr. X Patient name Patient Probe: SN5236 4.0/3.0

PREPARE IMAGE PLAN VOLUME THERAPY MANAGE

The interface displays four ultrasound images in a 2x2 grid. The top-left image is timestamped 11:38:05 AM and shows a red vertical oval. The top-right image is timestamped 11:38:07 AM and shows a red horizontal rectangle with a yellow and green gradient. The bottom-left image is timestamped 11:22:32 AM. The bottom-right image is timestamped 11:22:51 AM and shows a yellow horizontal rectangle. A central vertical slider is set to 9 watts. The right-hand side contains a control panel with a 'STATUS' section showing 0:01:30 total, 0:01:30 elapsed, and 0:00:00 remaining. Below this is an 'ENERGY' section with a 22.0 °C temperature display and a 'reflectivity index' of 0. The 'STACK' section shows 'HIFU amplifier' at 0 watts and 0.0 seconds. The 'VOLUME STACK' section has a 'Display' option with a 'Save' button. The 'TCM' section shows 'Last reading' at 0.775 (Orange), 'Total cycles' at 10, and a breakdown: Green (4, 40%), Yellow (2, 20%), Orange (4, 40%), and Grey (0, 0%). At the bottom, there are 'Start HIFU' and 'Pause HIFU' buttons, and a status bar at the very bottom showing 'Image: Jul 26, 2013 11:38:07 AM'.

Image verification: never Therapy verification: never

Status: Image: Jul 26, 2013 11:38:07 AM

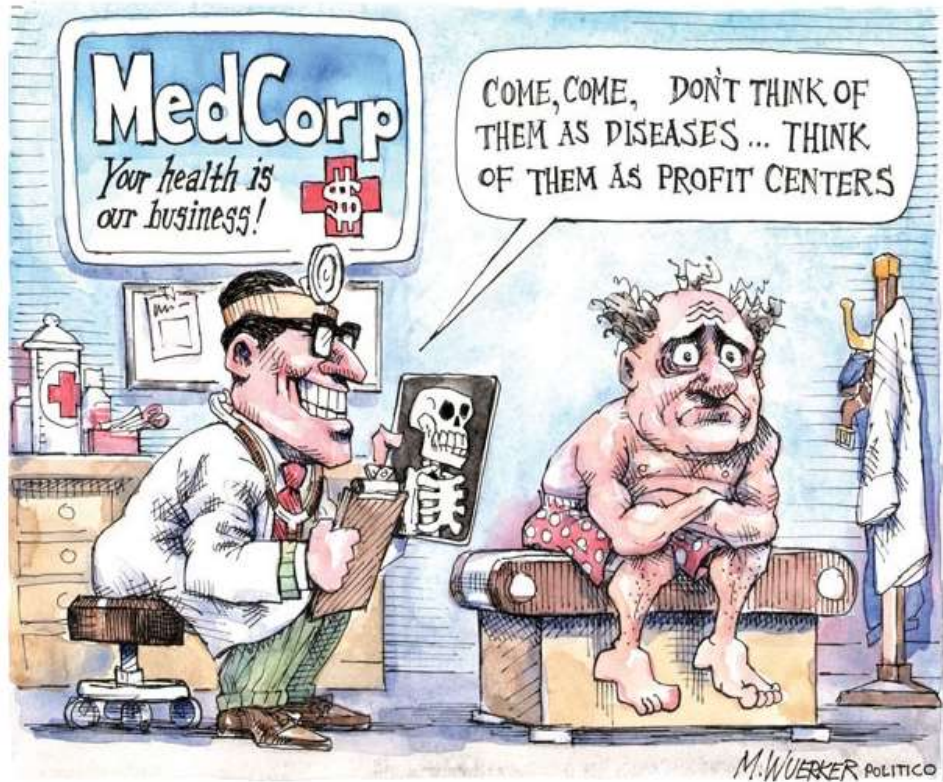
Problems Secondary to Today's Economic Environment

Longstanding bias in medicine that more expensive technology is better technology. But...

- Less money available to develop new solutions
- Less “reward” for successful solutions
- Fewer willing to risk tackling less mainstream solutions
- Time to develop is continually increasing



“I call my invention ‘The Wheel,’ but so far I’ve been unable to attract any venture capital.”



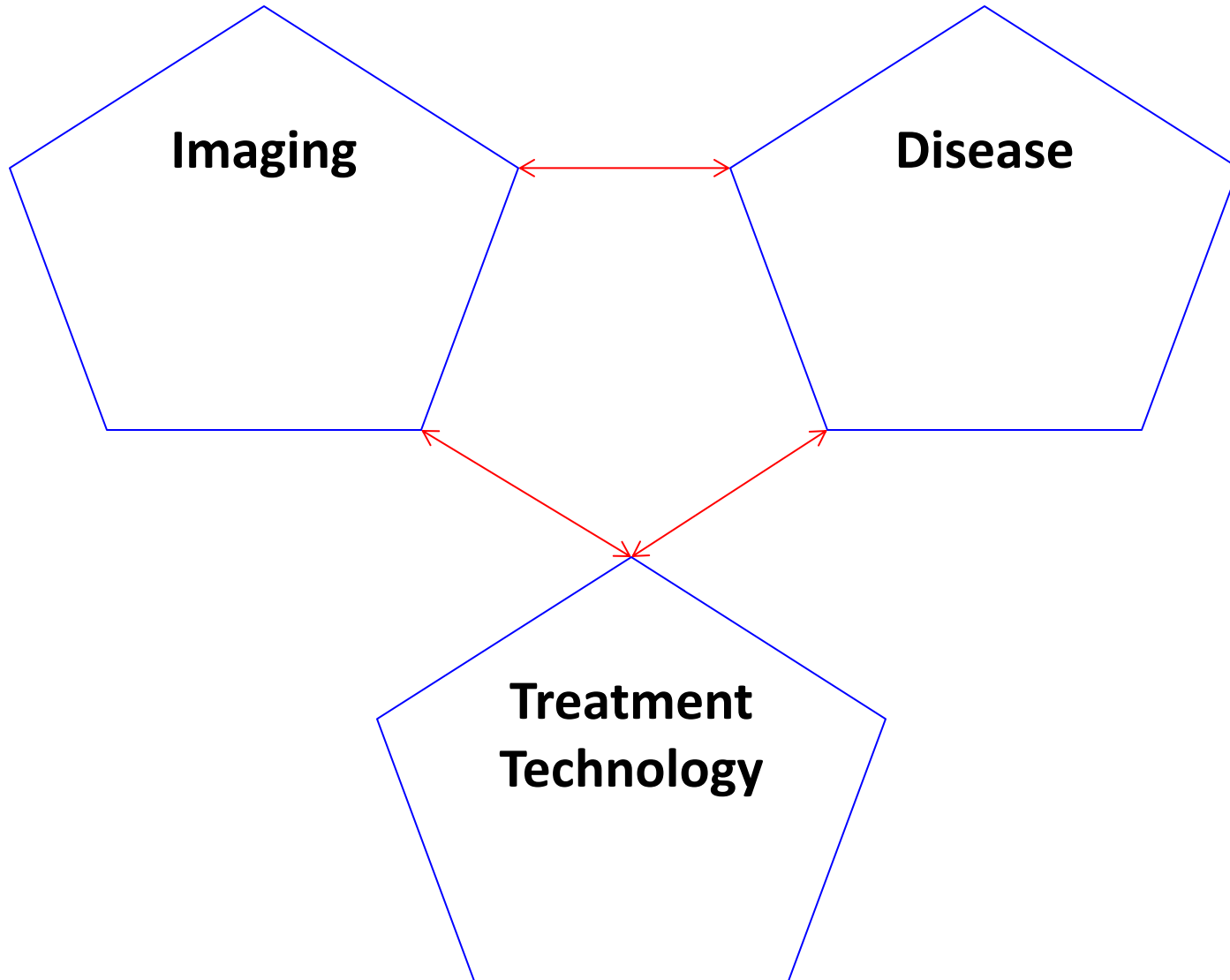
Summary

- Radiation therapy has undergone a continuous evolution where a clinical and biologic understanding of disease, advances in imaging, and advances in treatment planning and delivery, have each driven developments in the other two
- We are now at a point where the concept of focal treatment is more dominant, accepted, and appropriate than ever
- This should drive the development of tools for delivering focal therapies that are by their very nature volumetric imaging dependent, progressively less invasive than surgical alternatives, but will require image guidance for their utilization
- Nonionizing energy sources have distinct advantages over ionizing energies: their delivery can be easily monitored and assessed in real time and that the results can be characterized and controlled precisely
- Nonionizing ablative therapies should be viewed as an alternative to surgical intervention yet complimentary to ionizing interventions

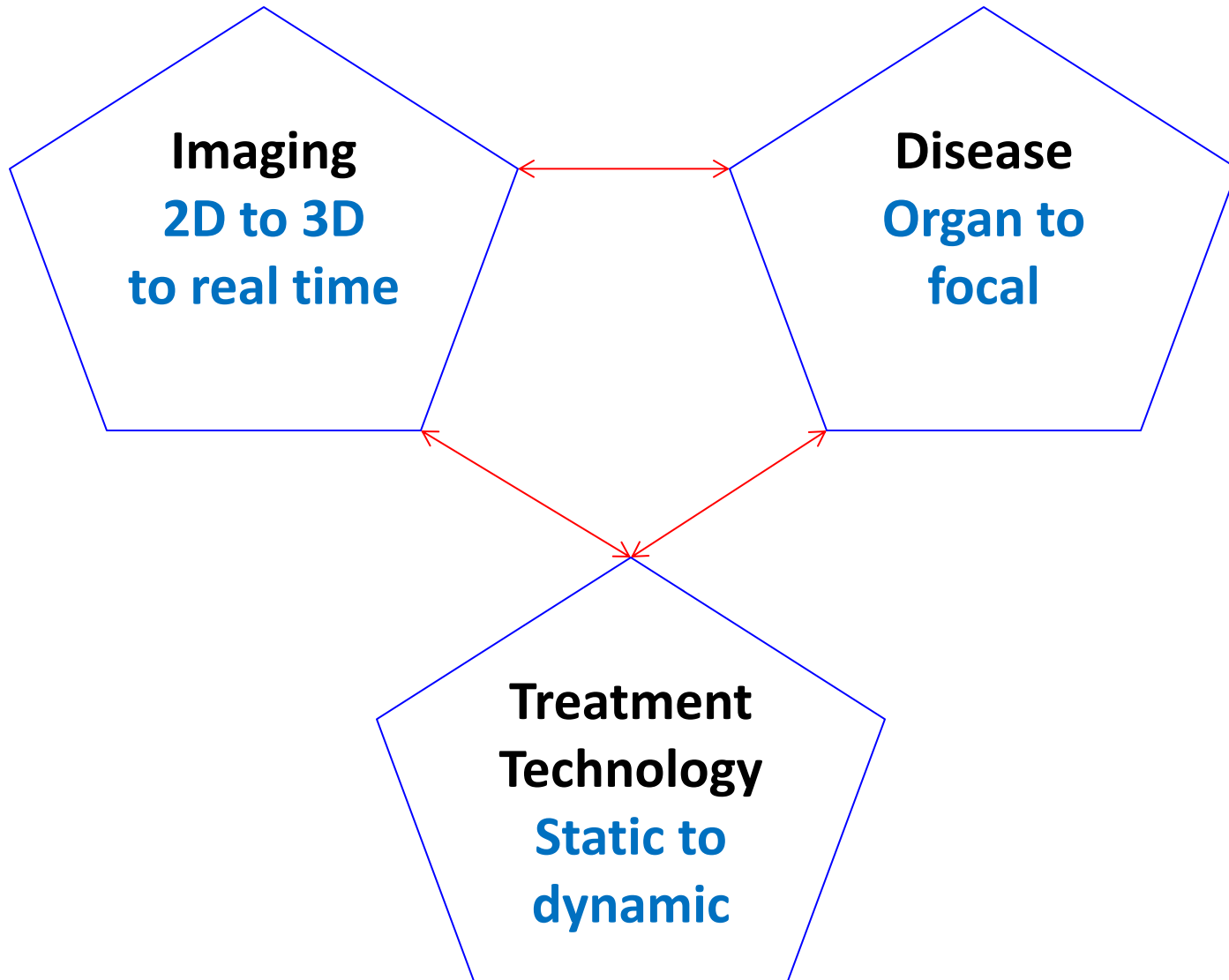
Take Home Message

- FUS is "just" another form of radiation that can be used to impact human disease.
- FUS is built upon the same foundation of image guidance, inverse planning, modulated delivery, and dose verification that characterizes RT
- As such it would benefit from the same physics infrastructure support and oversight that characterizes RT

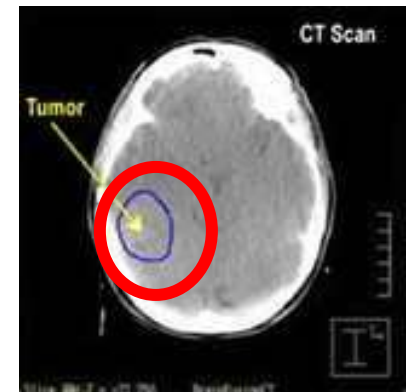
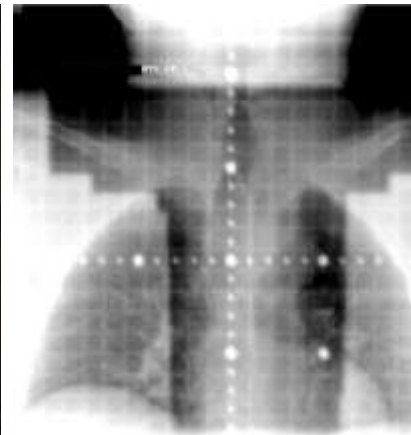
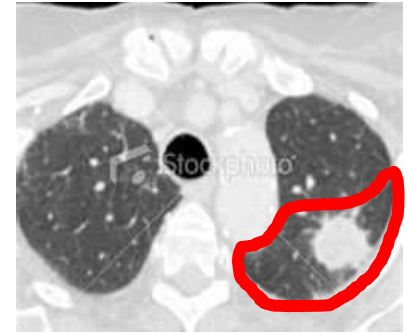
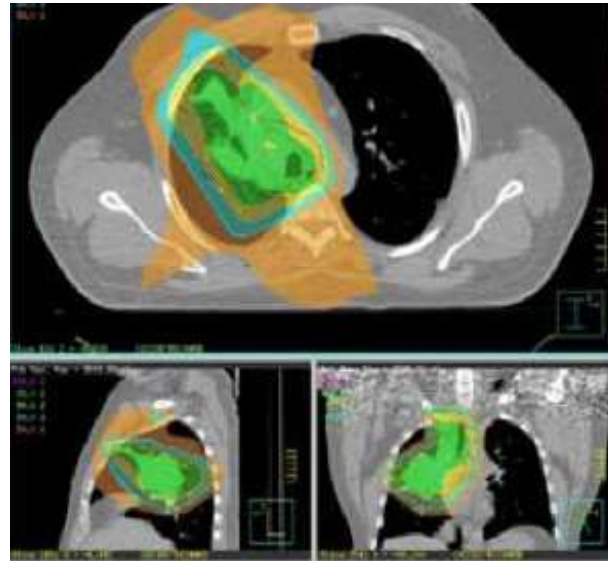
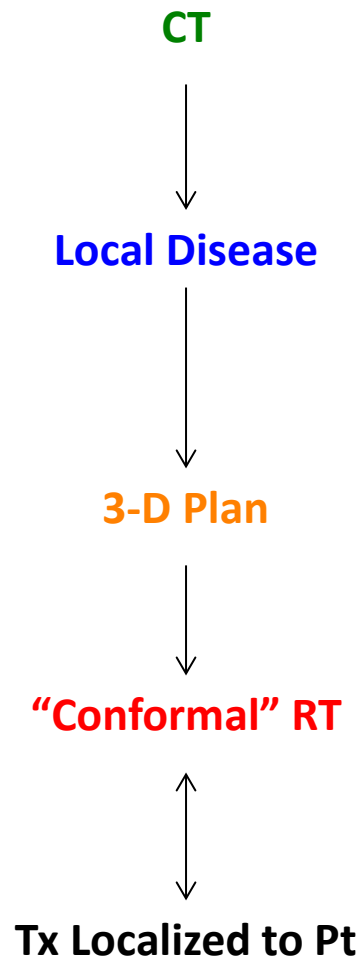
Medicine and Technology Have Changed Over Time in a Synchronized Manner



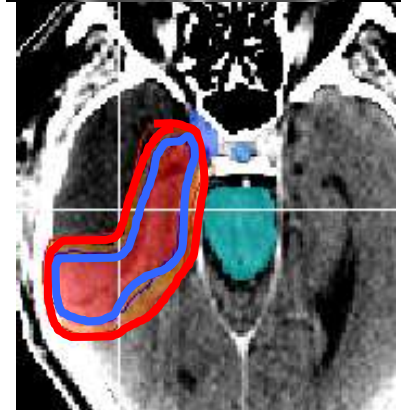
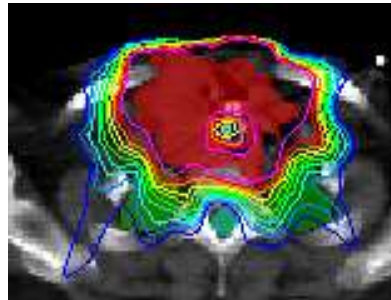
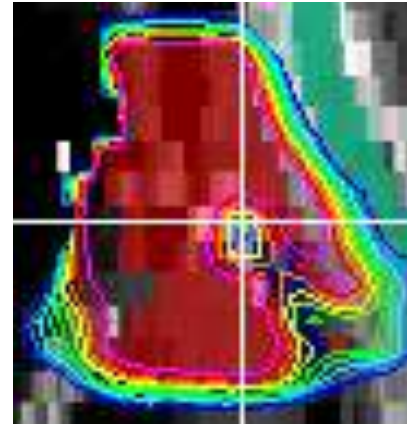
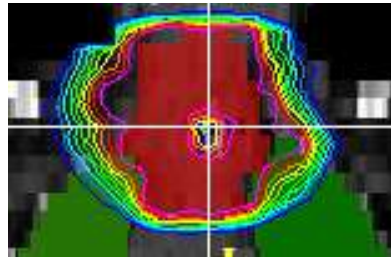
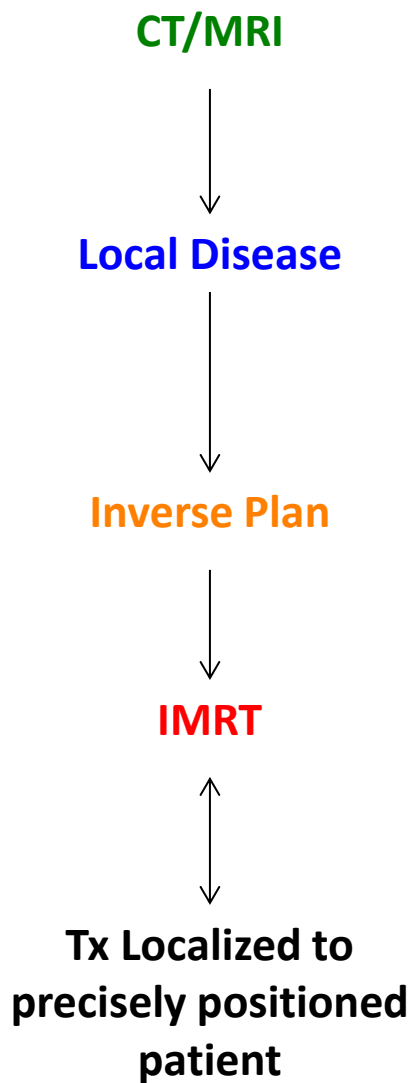
Medicine and Technology Have Changed Over Time in a Synchronized Manner



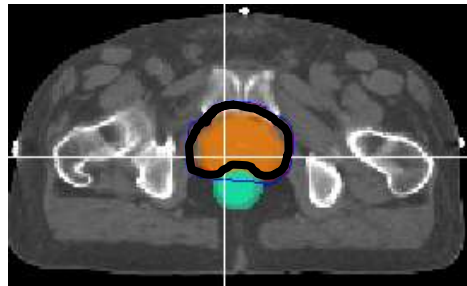
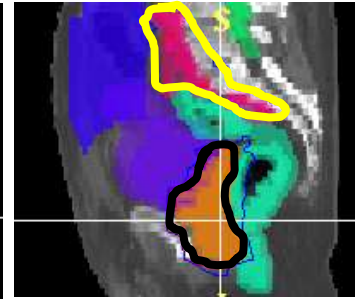
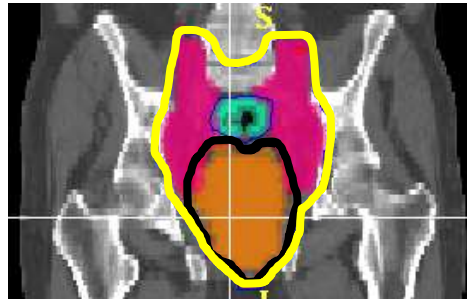
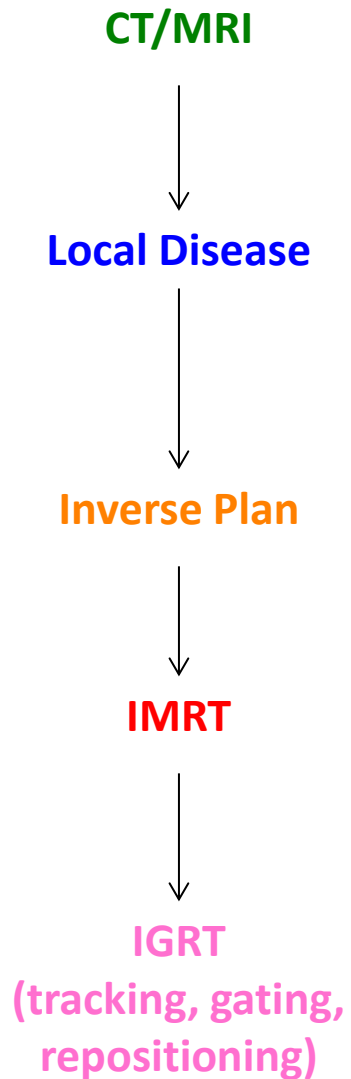
Radiation Therapy Circa 1990



Radiation Therapy Circa 1995



Radiation Therapy Circa 2000



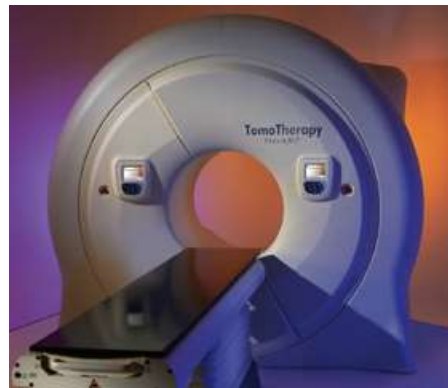
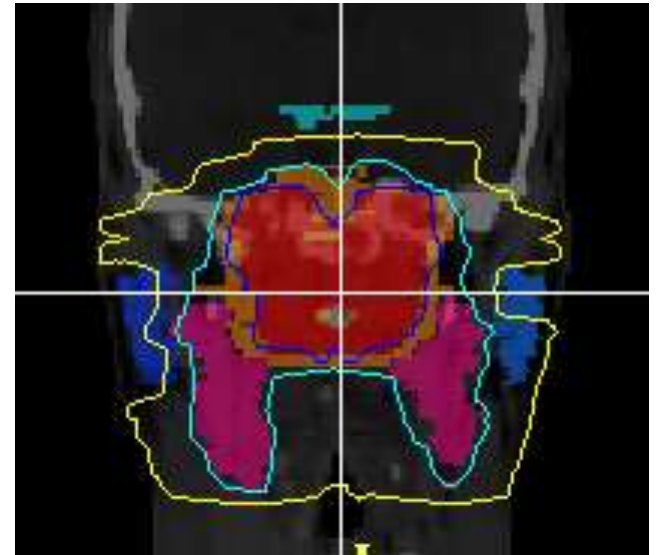
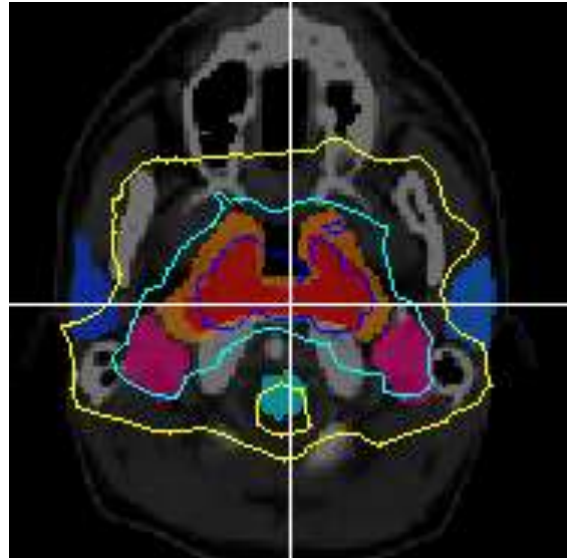
Radiation Therapy Circa 2020

Daily Assessment of Changes in Position and Shape
Daily CT/MRI

↓
Identify Changes

↓
**Replan
(if required)**

↓
IMRT/IGRT



HIFU Ablation Circa 1990

