PARALLELS BETWEEN IMRT AND FUS

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Ablation Complementary to Existing Therapies

**RADIATION THERAPY**
- Best suited for microscopic disease that infiltrates tissue

**HIFU**
- Best suited to treat macroscopic (gross) disease
- Used to treat gross disease in single session followed by a short course of RT to treat infiltrative disease

**ROBOTIC SURGERY**
- Surgical Robot
  - Used to deliver precisely surgical tools to regions of interest

**HIFU**
- A tool to destroy selected regions of interest
  - Used as tool to destroy selected region of interest accessed by the Robot

Added Plus:
- Reduces number of RT fractions; RT infrastructure to support HIFU
- 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
Thermal Ablation, Electrocorporation, 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

"Best of all, this baby has a GPS that finds the cheapest gas."
Similar to using your GPS system where you can select from:

- shortest route
- shortest time
- most scenic
- (avoid all traffic police)
- fewest highways
- 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)
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")
Driving the FUS Result
("focal" normal tissue avoidant treatments)
Cornerstone #2

How do we deliver an intensity modulated treatment plan?
Delivering Modulated RT Treatments
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
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
Cornerstone #3

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

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<th>Overlap</th>
<th>Localized</th>
<th>Priority</th>
<th>Organ</th>
<th>Uniform</th>
<th>A</th>
<th>P</th>
<th>R</th>
<th>L</th>
<th>S</th>
<th>I</th>
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Modeling Movement During RT Treatment
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

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

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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

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

A: Radiation Treatment Planning

D: Radiation Response Assessment

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Assessing FUS Treatment Delivery

Temperature Change Monitoring
(TCM)
Assessing FUS Treatment Delivery

Phantom Validation
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.”
THE NOBEL PRIZE FOR MEDICINE WAS AWARDED TO DR. QUENTIN R. OWSELY, WHO DEVELOPED AN ANESTHETIC THAT LEAVES PATIENTS CAPABLE OF WRITING CHECKS.

COME, COME, DON'T THINK OF THEM AS DISEASES ... THINK OF THEM AS PROFIT CENTERS
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

- Imaging: 2D to 3D to real time
- Disease: Organ to focal
- Treatment Technology: Static to dynamic
CT

Local Disease

3-D Plan

“Conformal” RT

Tx Localized to Pt

Radiation Therapy Circa 1990
Radiation Therapy Circa 1995

CT/MRI

Local Disease

Inverse Plan

IMRT

Tx Localized to precisely positioned patient
Radiation Therapy Circa 2000

CT/MRI

Local Disease

Inverse Plan

IMRT

IGRT (tracking, gating, repositioning)
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

US

Target Organ

3-D Plan

“Conformal” RT

Tx Localized to Organ