Towards personalized medicine – integration of imaging into therapy

Robert Jeraj
Associate Professor of Medical Physics, Human Oncology, Radiology and Biomedical Engineering
Translational Imaging Research (TIR) Program
University of Wisconsin Carbone Cancer Center, Madison, WI
rjeraj@wisc.edu

Imaging and therapy

100 years later…
Image Guided Radiation Therapy
100 years later…
Image Guided Surgery

100 years later…
What did medical physics contribute?

- **Imaging advances**
  - New imaging modalities: MRI, PET, combined modalities
  - Improved imaging technologies: contrast, resolution, noise, speed, accuracy

- **Treatment advances**
  - New RT technologies: Co-60, linacs, IMRT
  - Surgery: Minimally invasive procedures

- We can be very PROUD of these achievements!

100 years later…
Where is medical physics in Tx chain?

Shore et al 2012, Br J Urol Int, 6: 22
"4 P's of medicine": Individuals respond differently to environmental conditions, according to their genetic endowment and their own behavior. In the future, research will allow us to predict how, when, and in whom a disease will develop. We can envision a time when we will be able to precisely target treatment on a personalized basis to those who need it, avoiding treatment to those who do not. Ultimately, this individualized approach will allow us to preempt disease before it occurs, utilizing the participation of individuals, communities, and healthcare providers in a proactive fashion, as early as possible, and throughout the natural cycle of a disease process.

Elias A. Zerhouni, M.D.
Director, National Institutes of Health (NIH), 2008

Imaging in treatment process
TREATMENT SELECTION

PRE Tx | TREATMENT | POST Tx | TREATMENT

DIAGNOSIS | STAGING | TREATMENT SELECTION | TREATMENT SELECTION

FMISO PET in HN

FMISO PET + (hypoxia) + TPZ boost
FMISO PET – (no hypoxia)
FMISO PET focal uptake mildly larger than bgrd
FMISO PET + (hypoxia) + chemo boost

FMISO PET in HN


FES PET in Breast

LABC or Metastatic Br CA
Primary Tamoxifen Rx

Responders
Non-Responders

Reccurrent or Metastatic Br CA
Aromatase Inhibitor Rx

FES PET SUV=1.5
(P < 0.01 for both)

FES PET in Breast

Linden et al 2006, J Clin Oncol, 24: 2793
DCE/DSc MRI in GBM

Can we image everything - lung?

MICAD: Molecular Imaging and Contrast Agent Database

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But can we really use them all?

1. Credentialing
2. Modality creation
3. Supporting tools
4. Development
5. Clinical trials

Role for medical physics?

Highly interdisciplinary
- Cell/molecular biology
- Chemistry/radiochemistry
- Radiology
- Medical physics
- Pharmacology
- Medicine
- Engineering
- Mathematics
- Material science
- Computer science

Is imaging just an expensive tool?

NO, this makes imaging essential, and complementary

Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing

...branched evolutionary tumor growth, with 63 to 69% of all somatic mutations not detectable across every tumor region...
**Treatment response assessment**

- **WHO (1979, 1981)**
  - anatomic

- **RECIST (2000, 2009)**
  - Response Evaluation Criteria In Solid Tumors
  - anatomic, CT/MR based
  - unidimensional
  - 4 response categories (CR, PR, SD, PD)

**Power of molecular imaging**

- FDG PET response correctly predicts response to Gleevec in majority of patients
- FDG PET response correctly predicts SD and PD, while CT does not
- FDG PET response precedes the CT response (shrinking) by several weeks
- FDG PET response is strongly associated with a longer progression free survival (92% vs. 12% after 1 year) and closely correlated with subjective symptom control

Van der Aarbee 2008, The Oncologist 13(suppl 2), 8
Acute myeloid leukemia


Specificity = 43%
NPV = 64%

Day 14 BMBx
Day 28 BMBx

How early can imaging predict future?

Vanderhoek et al. 2011, Leuk Res 35: 310

Early treatment response assessment

Better than Higgs!!!
Heterogeneity of the response

Pre-treatment FLT PET
Post-treatment FLT PET

SUV Ratio

Imaging vs biopsies

NPV = 64%

Role for medical physics?

ADVANCED IMAGE ANALYSIS

FLT PET
CT Mask
Bone Marrow
FDG PET in NSCLC

HR = 2.27  
(1.70-3.02 95% CI)  
N=1474


PET-based response assessment

- EORTC, NCI Recommendations (1999, 2005) 1,2  
  - SUV-based approach  
  - SUV\textsubscript{mean} and SUV\textsubscript{max}  
  - Response categories with thresholds (CR, PR, SD, PD)

- PET Response Criteria in Solid Tumors (PERCIST) (2009) 3  
  - SUV-based approach  
  - SUV\textsubscript{peak}  
  - Response categories with thresholds (CR, PR, SD, PD)


Images are more than just one number!

- Size measures  
  - Volume  
  - 1D size (axial)

- Standardized Uptake Value (SUV) measures:  
  - SUV\textsubscript{mean}  
  - SUV\textsubscript{max}  
  - SUV\textsubscript{peak}  
  - SUV\textsubscript{mean}

- Uptake Non-uniformity measure:  
  - SUV\textsubscript{sd}  
  - ...

...
Different measures tell different stories

Role for medical physics?

- **SCANNER HARMONIZATION**
  - UW GE DVT S2N2 vs Dis/cc measured for different reconstruction settings
  - NCI Gemini TF S2N2 vs Dis/cc measured for one reconstruction setting
  - Phantom measurements to characterize the scanners
  - Comparative patient data from UW and NCI studied
  - Patient S2N2 data presented using phantom data for reference

TREATMENT SELECTION - AGAIN
EGFR resistance mechanisms

Sequist et al. 2011, Sci Transl Med, 3:75

Origins of treatment resistance

...several lines of evidence support the hypothesis that resistant tumors are a mixture of sensitive and resistant cells...


Role for medical physics?

NEXT TALK
Summary

- Medical physics has been extremely successful, but it has “captured” only a small part of the interface between imaging and therapy – **ENORMOUS POTENTIAL!!!**

- Future of medicine – personalized therapy – is complex, but extremely exciting, don’t wait - **EXPAND HORIZONS!!!**

- **MANY ESSENTIAL ROLES** we should play beyond radiotherapy and diagnostic imaging:
  - Clinical trial design!
  - Molecular imaging chain
  - Advanced image analysis
  - Quantitative imaging
  - Modeling
  - …

CJ’s FUTURE

Pondering her future…... Easy decision…

Courtesy of Stephanie Harmon and her niece CJ, March 2012

Thanks to:

- **Medical Oncology/Hematology**
  - Daniel Liu
  -Invariant Wilson
  - Brad Kahl
  - Anne Taylor

- **Human Oncology**
  - Baran Bentzen
  - Paul Harari
  - Mark Ritter

- **Radiology**
  - Scott Perlmutter
  - Chris Jaskulak

- **Veterinary School**
  - Lisa Foster
  - David Yarr

- **Medical Physics**
  - Rock Mackie
  - Jerry Nicklos
  - Ondre Puleus

- **Phase I Office**

- **Image-guided therapy group**
  - Vikram Adhikari
  - Tyler Stutzman
  - Enrique Cuna
  - Nipun Jhawe
  - Matt La Fontaine
  - Paula Gallow
  - Stephanie Harmon
  - Courtney Malagon
  - Surendra Prajapati
  - Urban Sztukli
  - Peter Sisley
  - Benny Titz
  - Natalie Weiese
  - Krzysztof Ty
  - Stephen Yip
  - Former students…

- **Funding**
  - NIH, POF, UWCCC, Pfizer, AstaZeneca, Amgen, Entrebio
Medical physics and ART

Courtesy of Koala Yp and her mom, January 2012