



Vision for Future Innovative Technology for Radiation Oncology

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Disclosure

Presenter has a financial interest in some of the technology reported here and research collaborations with Elekta, Philips, IMRIS, Varian, Quanta, and Raysearch.

Results from studies using investigational devices will be described in this presentation.

Technology for Innovation in Radiation Oncology: A Summary of the 2013 NCI ASTRO AAPM Workshop

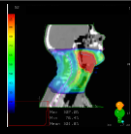
- Main Themes
 - Innovative Technologies
 - Advances in Imaging for Quantitative and Validated Treatment Design
 - Oncology Informatics
 - Evidence Building



From Anatomical to Functional

- Classical Dosimetric Objective:
 - Deliver a uniform dose to the 'clinical target'
 - Minimize or limit the dose to surrounding normal structures

The development of image-guidance technologies addresses the geometric challenges and enables pursuit of functional or molecular sub-targets.



- Biological Objective:
 - Maximize therapeutic ratio
- But what is a valid biological target?

Conceptual Framework for Integration of Functional/Molecular Imaging

1.1 Radiation Oncology • Biology • Physics Volume 47, Number 3, 2000

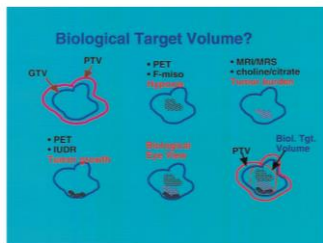


Fig. 2. An idealized schematic illustrating the concept of biological target volume (BTV). Whereas at present the target volume is characterized by the concepts of GTV, CTV, and PTV, biological images as depicted in Fig. 2 may provide information for defining the BTV to improve dose targeting to certain regions of the target volume. For example, regions of low pH level may be derived from PET-¹⁸F-metomidate study, high tumor burden from MR/MRS data of choline/citrate ratio, and high proliferation from PET-¹⁸F-thymidine measurement.

Ling et al., Int. J. Radiation Oncology Biol. Phys., Vol. 47, No. 3, pp. 551–560, 2000

"Incremental to the concept of gross, clinical, and planning target volumes (GTV, CTV, and PTV), we propose the concept of "biological target volume" (BTV) and hypothesize that BTV can be derived from biological images and that their use may incrementally improve target delineation and dose delivery." - Ling et al.

From the '3D Hypothesis' to the 'BTV and 4D Hypotheses'

- **BTV Hypothesis:** Patterning radiation dose according to imaged functional or molecular distributions will increase the TR.
 - A.k.a. 'Biologically Targeted Radiation Therapy'
- **4D Hypothesis:** Adapting to imaged changes in geometry or function during RT will improve the therapeutic ratio.
 - A.k.a. 'Adaptive Radiation Therapy'

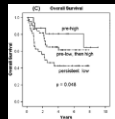
Functional and Molecular Imaging for RT

- Tumour burden, altered metabolism, and clonogen density (e.g. FDG, MRS)
- Tumour hypoxia (e.g. F-MISO, I/FAZA, CAIX, MR-BOLD, HX4)
- Tumour proliferation (e.g. FLT)
- New imaging targets (e.g. FACBC amino acid, EGFR for re-population)
- Functional imaging of crucial healthy tissues (e.g. SPECT/CT/MR derived lung perfusion)
- Vascular and physiological measures (DCE-MR/CT, MR DWI/ADC)

Adapted From 'Theragnostic imaging for radiation oncology: dose-painting by numbers' - S.M. Bentzen - Lancet Oncol 2005; 6: 112-17

Impact of Specific and Sensitive Imaging of Disease on Radiation Therapy

1. Reduce observer-dependent variation in the extent of gross and clinical targets.
2. Enable biologically-modulated targeting of the radiation dose.
3. Enable prediction of response based upon pre- or intra-treatment changes in the image-based biomarkers.



See Steenbakkers 2006, Bentzen 2005, Mayr 2010

Conceptually simple, but execution has been very slow...

- There are signs of progress:
 - MRI. Dominant lesion in multi-focal disease (e.g. DCE/DWI/BOLD definition of dominant lesion in prostate cancer – correlation with pathology)
 - FDG-PET. Targeting regions of elevated metabolism as characterized by FDG-PET
 - Hypoxia. Targeting regions of hypoxia as characterized by F-MISO/FAZA/ATSM agents
- Challenges:
 - Validation of image signal, cost of imaging/pathology correlation, prescription/radiobiology, technical (segmentation, robust imaging, motion compensation, non-specific signal e.g. bladder)

Many scientific questions in the domain of biologically-guided RT.

- What treatment targets are optimal for different tumor histologies and genotypes?
- How to translate from radiobiological heterogeneity to dose heterogeneity?
- What biological changes occur in tumor and normal tissue during therapy and how do we adapt RT to those changes?
- How often do we need to adapt the plans?
- What other biomarkers beyond and in combination with imaging do we need?
- How to integrate radiation therapy with other treatment modalities to increase efficacy? How do we integrate all these RT and other biomarkers?

Technology for Innovation in Radiation



Medical Physicists are capable of inventing, developing, and deploying technology in the clinical setting.



We benefit from a rich array of technology development around us.

Next Gen RT Technologies: Enabled by Better Dose Deposition, Robotics, Computation, Imaging



PET-guided
RT



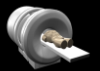
Edmonton
Solution



Utrecht Solution



Protons+



Viewray Solution



Adjacent Solutions

MR-Guided RT

Better dose control, faster imaging, higher CNR,
more responsive in delivery.

Technological Innovation in RT

- From Anatomic to Functional Targeting
 - Validation for Target Delineation
 - Anatomical and Response Adaptation
- Nanotechnology (hot and cold)
 - Modification/Prediction of Response
 - Dosimetry of drug delivery
- A New Breed of Multi-modal Machines
 - Fast Physics that 'Bury the Complexity'
- Our Biggest Treatment Machine Yet
 - Standardization, Automation, Quality, Efficiency, and Evidence



An Apparent Conflict

Radiation Oncology and Medical Physicists are known for creation and adoption of technology.



Technology needs to be better evaluated.

Radiation Oncology and Medical Physicists need to be bridled to assure we have evidence.

An Apparent ~~Conflict~~ Opportunity

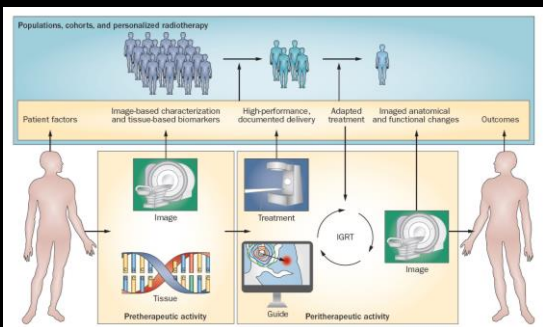
Radiation Oncology and Medical Physicists are known for creation and adoption of technology.



Technology needs to be better evaluated.

Radiation Oncology and Medical Physicists need to turn their creativity to build evaluation into innovation.

RT: A Highly Personalized Cancer Medicine



Jaffray, D. A. Nat. Rev. Clin. Oncol. 9, 688-699 (2012)

A Multi-modal Perspective

Uni-modal biomarkers are not sufficient for informing clinical decisions and the full power of genomics will be only be fully unleashed through integration with multi-modal datasets.

H&N

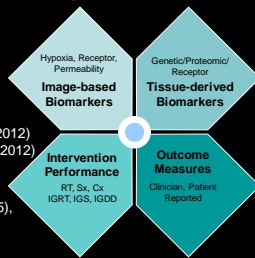
OS<- HPV,p16: 20% (Shi 2009),
DFS<-FAZA-PET: 33% (Mortensen 2012)
LRC<-RT Compliance: 20% (Peters 2012)

Prostate

bPSA<IGRT: 25% (deCresosier 2005),
bPSA<pO2: 25% (Milosevic 2012),
bPSA<Metformin: 10% (Zannella)

NSCLC

LC<-FDG-PET Response: 40% (DeRuyescher, 2012)
OS<-CT Feature: 10% (Aerts 2013)
OS<-RT Technique: 25% (Liao, 2010)
RadPneum<-Cardiac Fn: 2.6 OR (Nalbantov, 2013)



Personalized Cancer Medicine (PCM)

'The right care for the right patient at the right time.'

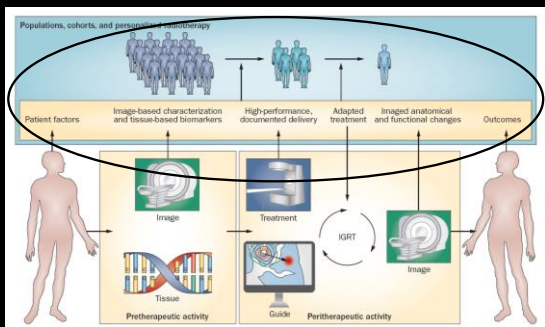
Patients or practitioners?



"If it were not for the great variability among individuals, medicine might as well be a science, not an art."

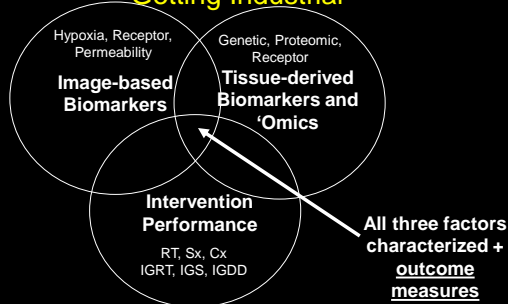
Sir William Osler, 1892

Our Biggest Machine Yet.



Jaffray, D. A, Nat. Rev. Clin. Oncol. 9, 688-699 (2012)

Paradoxically, Getting Personal Requires Getting Industrial



Understanding cancer, developing personalized cancer medicine strategies, and delivering high performance cancer therapy are highly dependent activities.



Medical Physics Efforts Toward 'Industrial Medicine'

- Safety and Quality as Priorities
 - Variance Tracking, Measurement
- Advancing a Nomenclature for RT
 - ICRU 50, 62, 83
- Standardization in Treatment Methods
 - Delineation Standards
- Measuring Outcomes
 - Pay for Performance, Expertise Growth
- Engineering Principles
 - FMEA, Control Charts, Measure and Correct Strategy



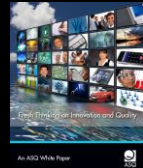
Getting Industrial

- Standards and Nomenclature
 - Communication and Automation
- Precision and Accuracy
 - in our Measurements
 - in our Treatment Delivery
- Collaboration
 - Statistical Strength through Multi-institutional Studies
- Informatics
 - Managing the known unknowns and watching for the unknown unknowns

Are Quality and Innovation Competitive?

Fresh Thinking on Innovation and Quality

An ASQ
White Paper

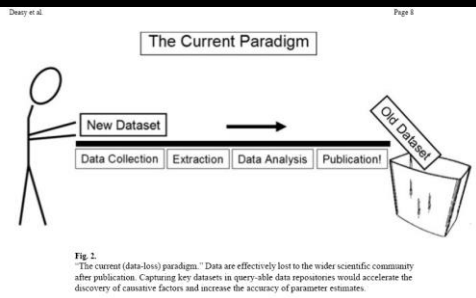


The idea that innovation must embrace both the blue sky and the practical is neither new nor radical, yet we cling to our fascination with the home run.

It makes sense to manage innovation activities with the same management tools and approaches that are used in other major sectors of the business.

ASQ (American Society for Quality) is the world's leading authority on quality and sole administrator of the Malcolm Baldrige National Quality Award.
ASQ 2010

Continuous Expertise/Knowledge Development – Contribute and Benefit



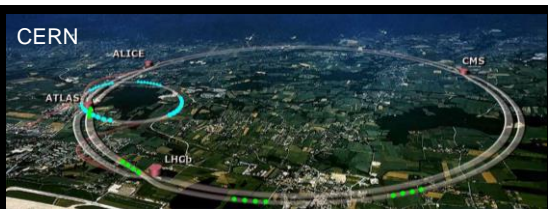
Deasy et al. - Int J Radiat Oncol Biol Phys. 2010 March 1; 76

Converting on the Promise of Personalized Cancer Medicine

- From delivering 'state-of-the-art' care to driving the next generation of care.
 - Radiation Oncology and Medical Physicists have always innovated practice, but this needs to be industrialized to accommodate the complexity of data collection, decision making, and delivery.
- Maximizing intervention performance (quality) to detect sub-populations and evaluate the value of new, more personalized therapies
- Building cancer informatics tools to enable analysis, exploration, and rapid evaluation of novel therapies or stratification.

The Physicist's Approach

- When you want to answer a really big question...
 - you get lots of talented people engaged,
 - you distribute the work,
 - and you build a machine.



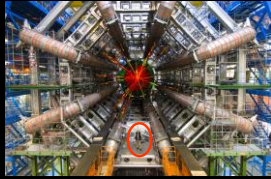
3000 Scientists
174 Universities
38 Countries

Working together on the border of France and Switzerland

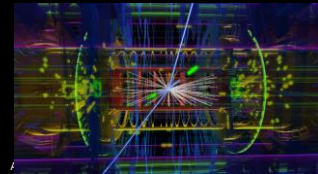
Could translational cancer research become another well-known large-scale science project?

Atlas Detector: Big Data Handling

- >80 million Si pixels
- >100,000 ionization 'straws'
- >100,000 calorimetry channels
- 25 ns resolution
- >350,000 particles/sec/mm²
- 40 million bunch crossings/sec



Dedicated data system filters to 100,000/s (L1), 3000/s (L2), 200/s (L3) – for detailed analysis



What would the 'machine' for seeking the limit of PCM look like?

- It's design would push the limits of our science
 - Drive new technologies and methods from basic science
- It would need to be precise
 - Measurement/Terminology
- It should be accurate
 - Standardized/Validated/Calibrated
- It should be efficient
 - Affordable; large N; statistical power
- Needs to be integrated with healthcare delivery

Isn't this this a remarkably good match for the skills in Radiation Oncology and Medical Physics?

How would it work?

- A steady stream of well-characterized patients colliding with a well-characterized set of interventions.
- Surrounded by certified, calibrated beam control and detection instruments (controlled therapy, imaging, outcomes).
- Data streaming into an appropriately staged real-time and off-line informatics framework.

We just need to build it.

Summary

- Numerous emerging technologies with the potential to impact Radiation Oncology
- Include advances in imaging, nanotechnology, device development.
- Personalized cancer medicine is an emerging medical, scientific, and technical challenge and medical physicists in radiation oncology have a significant role to play.
- Advancing informatics as a central research pillar for the field is timely and appropriate.

