NCI/ASTRO/AAPM Joint Workshop Technology for Innovation in Radiation Oncology, June 2013

Innovative Technology

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Henry Ford Health System

Disclosure/COI

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- NIH/NCI
- Varian Medical Systems
- Philips HealthCare

Innovative Technologies: Applications and Challenges

1. Technological advances in software and hardware
2. Multimodality machines incorporating treatment and imaging functionalities, e.g. MR linacs
3. Machines utilizing particles (e.g. protons) – *high performance particles*
4. Nanoparticle Systems

1. Technological advances in software and hardware (David Jaffray)

'Fast physics' and Automation – e.g. use of cloud-based computation and interface technologies, which are automated and *bury the complexity* of the computation, analogy: personal digital assistants (PDAs)

'Fast-physics' and automated approaches will make adaptive treatment approaches feasible, thereby, enabling improvements to the therapeutic ratio to be pursued as the disease responds to radiation therapy

Technological advances: Automation: Example

PHYSICS CONTRIBUTION

AUTOMATED PLANNING OF TANGENTIAL BREAST INTENSITY-MODULATED RADIOTHERAPY USING HEURISTIC OPTIMIZATION

Thomas G. Purdie, Ph.D.,[*†] Robert E. Dinniwell, M.D.,[*†] Daniel Letourneau, Ph.D.,[*†] Christine Hill, B.Sc.,[*] and Michael B. Sharpe, Ph.D.[*†]

[*]Radiation Medicine Program, Princess Margaret Hospital, University Health Network, Toronto, ON, Canada; and [†]Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada

Red Journal 81: 2011

Results: Mean time per plan was ~ 7 min. 157 of 158 plans (99%) were deemed clinically acceptable, and 87% were deemed clinically improved or equal to corresponding clinical plan

Conclusion: …automated tools will improve patient access to *high-quality IMRT* by simplifying the planning process and will *reduce the effort and cost* of incorporating advanced planning into the clinic…

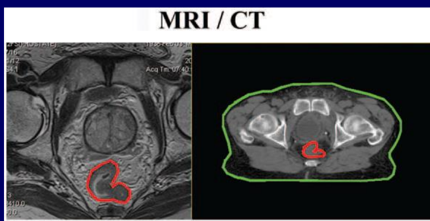
Technological advances in software and hardware

'Fast physics' and Automation (of planning and treatment delivery) will improve efficiency and potentially safety/quality (e.g. automated workflow interfaces: Chan *et al.* "The use of human factors methods to identify and mitigate safety issues in radiation therapy." Radiother Oncol. 97, 2010).

Proper validation and testing is required to ensure safety

2. Multi-modal machines (MRI in RT) (Dan Low)

Soft tissue contrast is improved

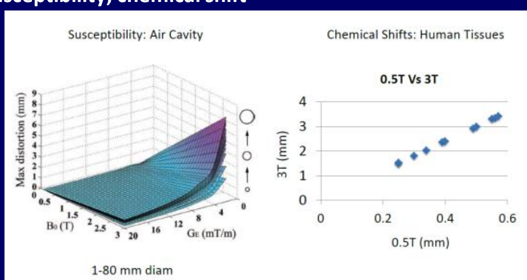


From Devic: "MRI Simulation for Tx Planning" : Med Phys 39 (2012)

Spatial integrity is degraded: B-field inhomogeneity; magnetic susceptibility; chemical shift

MRI in RT

Spatial integrity is degraded: B-field inhomogeneity; magnetic susceptibility; chemical shift



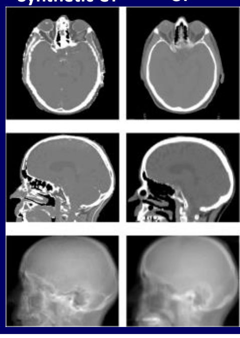
From Dan Low: NCI Workshop, 2013

Management of MRI for RT

Relative to CT, we need to optimize the following for MRI:

- **Bore sizes (70 cm vs. 80- 90 cm bores)**
- **Imaging setup (MRI compatible devices and unobtrusive detector coils**
- **Spatial integrity**
- **Imaging sequences for different anatomical sites**
- **Electron density (from HU)**
- **4D Imaging**
- **Reference kV images (DRR's)**
- **Training**

MRI for RT: Optimal sequences (UTE) and synthetic CT



From Hsu *et al*: "…method for generating synthetic CT models from MRI scans of the H/N…" : Phys Med Biol 58 (2013)

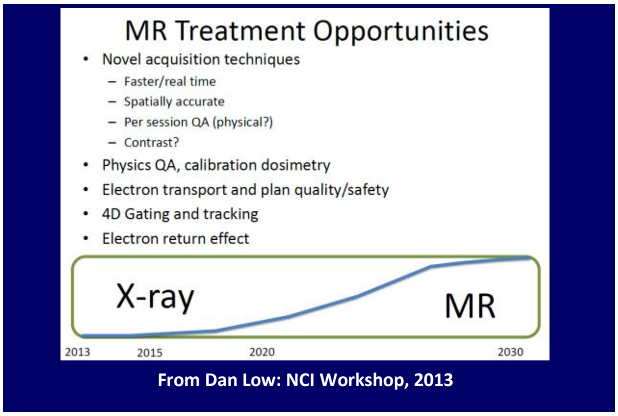
Multi-modal Machines: MRI for RT

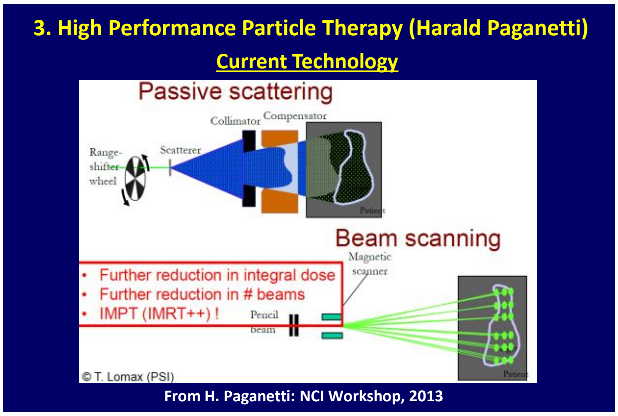
Institution	Radiation source	B field	Magnet type	Beam-field orientation
University of Utrecht	6 MV x-rays	1.5T	Closed	Perpendicular
University of Alberta	6 MV x-rays	0.2T & 0.5T	Split	Inline and Perpendicular
Viewray (Commercial)	^{60}Co g-rays	0.35T	Split	Perpendicular
Australian MRI-linac Program	6 MV x-rays	1.0T	Split	Inline and Perpendicular

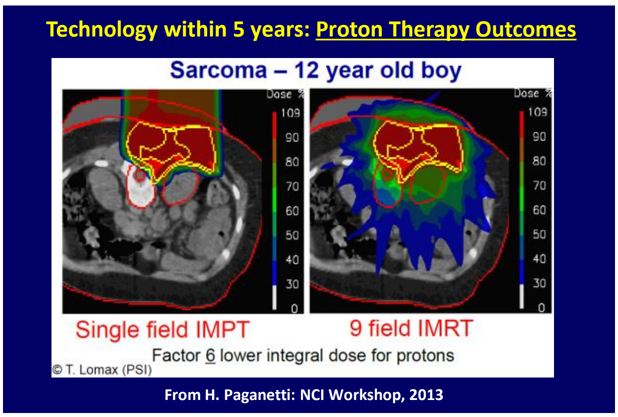
From Dan Low: NCI Workshop, 2013

Magnetic Resonance Guided RT (MRgRT)

Courtesy: Sasa Mutic, Washington U, St. Louis


MR Treatment Opportunities
• Novel acquisition techniques
– Faster/real time
– Spatially accurate
– Per session QA (physical?)
– Contrast?
• Physics QA, calibration dosimetry
• Electron transport and plan quality/safety
• 4D Gating and tracking
• Electron return effect
X-ray
MR
2013
2015
2020
2030
From Dan Low: NCI Workshop, 2013


3. High Performance Particle Therapy (Harald Paganetti)
Current Technology
Passive scattering
Collimator
Compensator
Range-shifter wheel
Scatterer
Beam scanning
Magnetic scanner
• Further reduction in integral dose
• Further reduction in # beams
• IMPT (IMRT++) !
Pencil beam
© T. Lomax (PSI)
From H. Paganetti: NCI Workshop, 2013


Technology within 5 years: Proton Therapy Outcomes
Sarcoma – 12 year old boy
Dose %
109
90
80
70
60
50
40
30
0
Single field IMPT
9 field IMRT
Factor 6 lower integral dose for protons
© T. Lomax (PSI)
From H. Paganetti: NCI Workshop, 2013

Technology within 5 years: Proton Therapy Outcomes

What are the consequences of the integral dose (dose bath) reduction?

1. It depends on the ability to influence where the dose is being deposited

2. Is a small volume of high dose 'better' compared to a large volume of low dose?

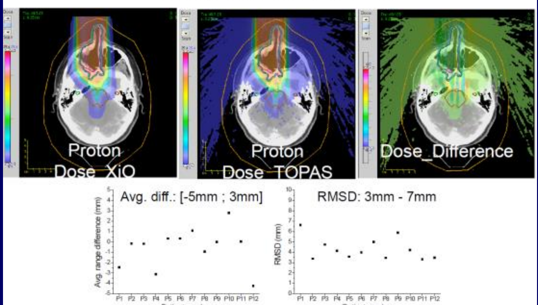
e.g. second cancer induction

e.g. cognitive development in children

From H. Paganetti: NCI Workshop, 2013

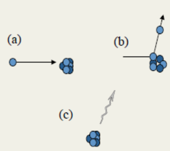
Technology within 5 years: Range Uncertainties

Head & Neck Patient



From H. Paganetti: NCI Workshop, 2013

Technology within 5 years: Prompt Gamma Measurements



- *Prompt* Gamma Ray Emission
  - occurs within 10^{-9} sec of interaction
  - i.e. – "real-time" signal
  - each element emits characteristic gamma-rays with different energies
  - gamma rays only emitted where proton beam interacts in the patient (i.e where dose is deposited)

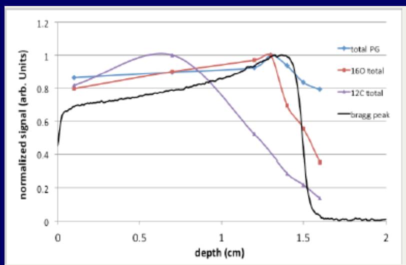
By measuring PG emission, it may be possible to address uncertainties in:

- **delivered proton beam range**
- **(changes to) elemental composition of irradiated tissue**

From J. Polf: AAPM, 2013

Prompt Gamma Measurements of proton range

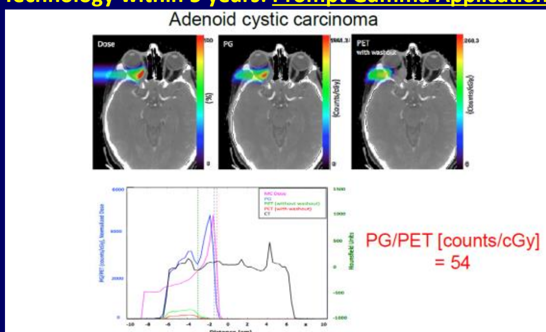
PG emission with depth shown to correlate well to Bragg peak



Polf et al., (2013).

From J. Polf: AAPM, 2013

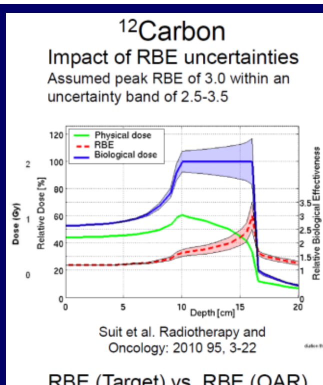
Technology within 5 years: Prompt Gamma Application



Moteabbed M; España S and Paganetti H: Monte Carlo patient study on the comparison of prompt gamma and PET imaging for range verification in proton therapy. Physics in Medicine and Biology 2011 56:1063-1082

From H. Paganetti: NCI Workshop, 2013

Technology within 10 years: *Ion therapy* *C-12: RBE*



From H. Paganetti: NCI Workshop, 2013

Technology within 10 years: Particle beam tracking

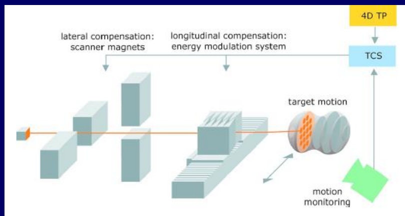
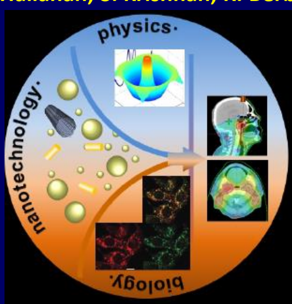


FIG. 4. The particle beam tracking system developed at GSI includes lateral motion compensation using the scanning magnets as well as longitudinal compensation of density changes in the beam path using a dedicated energy modulation system. The energy modulation system consists of opposing wedge shaped absorbers to adapt the primary particle energy. The tracking process determined in 4DTP has been fully integrated in the research version of the TCS.

Reitzel and Bert: Med Phys 37, 2010

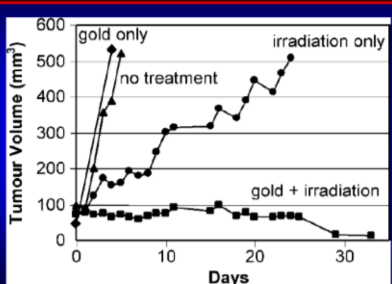
From H. Paganetti: NCI Workshop, 2013

4. Nanoparticle systems (D. Hallahan; S. Krishnan; R. Berbeco)



From S. Krishnan: NCI Workshop, 2013

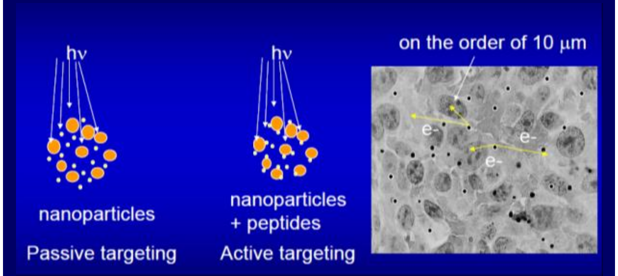
Nanoparticles: Physical dose enhancement



Hainfeld et al. Phys Med Biol 2004; 49: N309-15

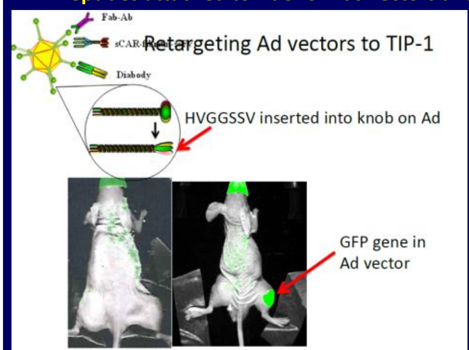
From S. Krishnan: NCI Workshop, 2013

Enhancing physical dose



From S. Krishnan: NCI Workshop, 2013

Peptides attached to Adenovirus vectors and Imaging

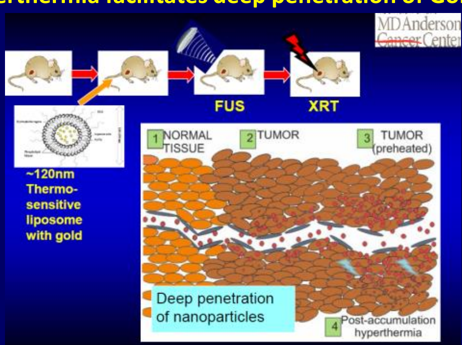


HSGGSSV peptide preferentially targets Tx responsive tumors.

Confirmed by green fluorescence peptide (GFP) imaging

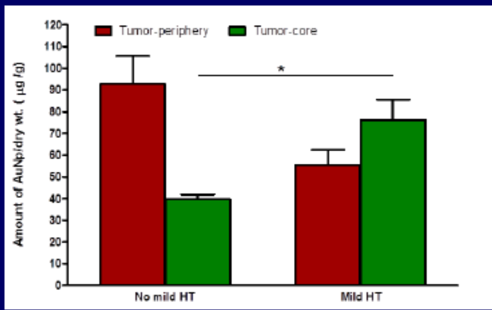
From D. Hallahan: NCI Workshop, 2013

Hyperthermia facilitates deep penetration of Gold NP



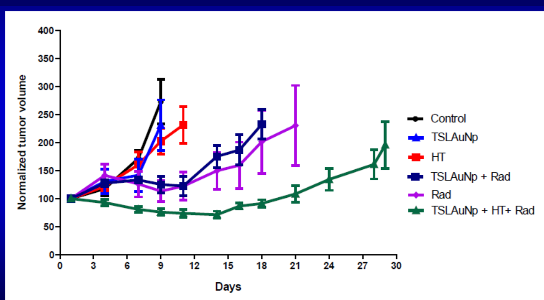
From S. Krishnan: NCI Workshop, 2013

Hyperthermia facilitates deep penetration of Gold NP



From S. Krishnan: NCI Workshop, 2013

Radiosensitization: Gold NP + Heat



From S. Krishnan: NCI Workshop, 2013

Gold Nanoparticles as vascular-disrupting agents during external beam radiation therapy

Ross I. Berbeco [1,*], Houari Korideck [1], Wilfred Ngwa [1], Rajiv Kumar [1,2], Srinivas Sridhar [1,2] and G. Mike Makrigiorgos [1]

[1] *Brigham and Women's Hospital, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA*

[2] *Department of Physics, Northeastern University, Boston, MA*

Hypothesis:

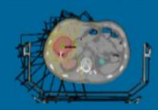
MV irradiation of targeted GNP will cause localized destruction of tumor blood vessels leading to subsequent disruption of tumor viability

From R. Berbeco: NCI Workshop, 2013

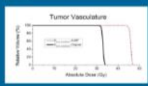
Results and Conclusions

- Theoretical predictions indicate a clinically significant dose enhancement is possible in clinical MV beams
- *In vitro* experiments confirm that dose enhancement will increase in clinical beams for deeper targets and for FFF
- Preferential GNP uptake in tumor has been shown *in vivo*
- Results justify continued investigation of MV + GNP

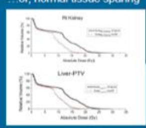
Clinical example: Liver SBRT



Target dose enhancement



…or, normal tissue sparing



From R. Berbeco: NCI Workshop, 2013

Nanoparticles: Opportunities

Understanding the pharmacokinetics/biodistributions

Radiolabeling to image biodistributions

Understanding which peptides are most preferential for tumor targeting in combination with RT; which cancer subtypes show the best radiation-induced binding

Facilitating increased uptake of the NP in tumors

Pre-clinical, animal trials and toxicity profiles

Human Trials: Toxicity analyses; imaging biodistributions; pharmacokinetics

Summary

There are several emerging technologies with strong potential to impact radiation oncology

The NCI/AAPM/ASTRO co-sponsored workshop identified: advances in hardware and software; multi-modality machines; high performance particle therapies and nanoparticle systems as 4 major research areas

Physicists (innovative physics concepts) must collaborate with experts in multi-disciplinary fields to develop and drive the technology forward with the goal of establishing evidence-based efficacy to the patient

Acknowledgements

Mary Martel
Steve Hahn
David Jaffray
Stan Benedict
The entire planning committee

Thank you for
your attention!