UNIVERSITY of MARYLAND
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Roles of in vivo dose verification in proton therapy

AAPM 2017

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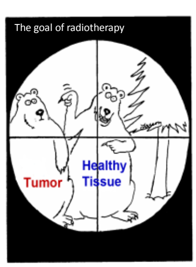
Disclosures

Research Funding: National Institutes of Health National Cancer Institute award R01CA187416.

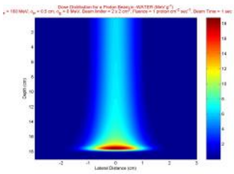
- Prompt gamma imaging for proton radiotherapy treatment verification.

Overview

- Uncertainties in proton dose delivery
- Effect of uncertainties on distal and lateral dose delivery profiles
- In vivo verification methods
- Conclusions



Overview

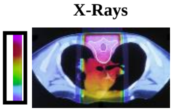


- **Protons Stop!**
- **Photons don't.**

- **Maximum Proton dose at target**
- **Maximum Photon dose dose at d_{max}.**

Overview

X-Rays



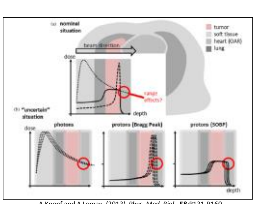
PROTONS

This gives many pictures of how wonderful Protons are.......... in a perfect world.

In reality there are many uncertainties in Proton treatment delivery due to a wide range of factors:

- Treatment setup,
- CT# conversion,
- Tumor motion,
- Tissue response to proton irradiation
- Etc.

Overview



A Knopf and A Lomax, (2013), *Phys. Med. Biol.*, **58**:R131-R160.

Proton beam range uncertainties:

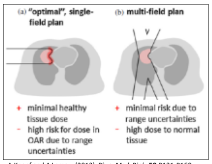
- setup errors,
- tissue inhomogeneity
- CT# to tissue conversion
- changes to internal anatomy
- etc.

Dose *Within* and *Distal* to tumor

Photons: little effect

Protons: significant effect

Overview



A Knopf and A Lomax, (2013), *Phys. Med. Biol.*, **58**:R131-R160.

Consequences for proton therapy

- Limit usable beam angles.
- Increase dose to normal tissue
- Decrease dose uniformity in tumor volume

Managing Uncertainties

1. **Dose Calculation**
2. **Treatment Delivery**

Source of range uncertainty in the patient	Range uncertainty without Monte Carlo	Range uncertainty with Monte Carlo
Independent of dose calculation		
Measurement uncertainty in water for commissioning	± 0.3 mm	± 0.3 mm
Compensator design	± 0.2 mm	± 0.2 mm
Beam reproducibility	± 0.2 mm	± 0.2 mm
Patient setup	± 0.7 mm	± 0.7 mm
Dose calculation		
Biology (always positive) ^	+ ~0.8%	+ ~0.8%
CT imaging and calibration	± 0.5%[a]	± 0.5%[a]
CT conversion to tissue (excluding I-values)	± 0.5%[b]	± 0.2%[g]
CT grid size	± 0.3%[c]	± 0.3%[c]
Mean excitation energy (I-values) in tissues	± 1.5%[d]	± 1.5%[d]
Range degradation; complex inhomogeneities	−0.7%[e]	± 0.1%
Range degradation; local lateral inhomogeneities *	± 2.5%[f]	± 0.1%
Total (excluding *, ^)	2.7% + 1.2 mm	2.4% + 1.2 mm
Total (excluding ^)	4.6% + 1.2 mm	2.4% + 1.2 mm

Paganetti, *PMB*, ***57*** (2012)

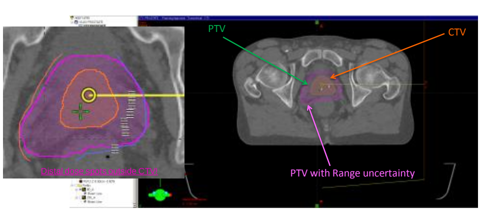
Range uncertainty formula:

~3.5%*(beam range) + 1-2 mm

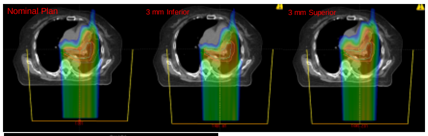
Managing Uncertainties

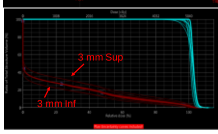
- Currently expand margins

~3.5%*(beam range) + 2 mm



Distal Range Uncertainties



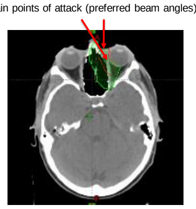


- Reduce coverage to the ITV
- "Over range" into heart
  Increasing dose to heart

Lateral Profile Uncertainties

What about tumors with critical structures lateral to target volume

Main points of attack (preferred beam angles)



- Water Equivalent Path length (WEPL): *2 – 4 cm*
- Oblique angle path is mostly homogeneous.
- Range uncertainty near eye < 3 mm

However,

- A patient shift to the left by only ~2 mm would result in full dose to eye!!

Distal and Lateral Profile Uncertainties

How would we treat this?

Holliday et al, *IJROPB* 2016.

- Use eye-deviation technique to avoid dose to lens/cornea.
- Conform dose distally to avoid optic nerve
- Deviation of < 2 mm could result in full dose to lens/cornea.
- Range over shoot of ~2 mm gives Full dose to optic nerve.

Managing Uncertainties: in vivo dosimetry methods

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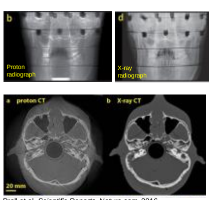
Paganetti, *PMB*, ***57*** (2012)

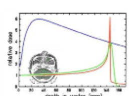
- Pre-treatment delivery
  - proton radiography/CT
- During treatment delivery
  - induced ultrasound
  - in room PET imaging
  - prompt gamma imaging
- Post-treatment delivery
  - in room PET imaging
- Follow up assessment
  - MRI imaging

Managing Uncertainties: Pre-treatment



Prall et al, *Scientific Reports, Nature.com*, 2016

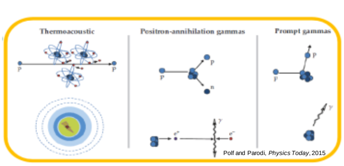
Ion radiography / tomography for:
- Direct (integral) SPR determination
- Daily, low-dose image guidance



pre-treatment verification of:
- Water equivalent path length
- Stopping power ratio

Managing Uncertainties: pre/during/post treatment

- Induced secondary emission

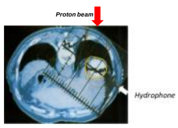


Polf and Parodi, *Physics Today*, 2015

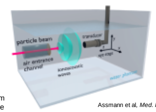
Induced ultrasound imaging | In room PET imaging | Prompt gamma imaging

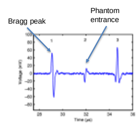
Managing Uncertainties: pre/during/post treatment

- Induced Ultrasound imaging
- Prompt gamma imaging

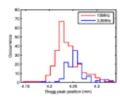


Hayakawa et al, *Rad Onc. Invest.* 1995.





Assmann et al, *Med. Phys.*, 2015

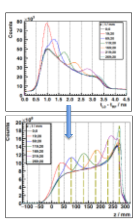


Managing Uncertainties: pre/during/post treatment

- Induced Ultrasound imaging
- Prompt gamma imaging

Prompt gamma timing

Hueso-Gonzalez et al, *Frontiers in Oncology* (2016)



- Measure time of prompt gamma arrival with respect to beam on time.

- Convert time-profile to depth profile using stopping power information from CT

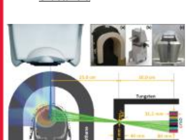
- Compare measured depth profile to Monte Carlo/analytical calculations

- Initial prototype testing in clinical beams.

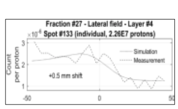
Managing Uncertainties: pre/during/post treatment

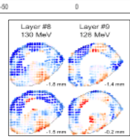
- Induced Ultrasound imaging
- Prompt gamma imaging

Slit camera



Xie et al, *IJROBP* (2017)





- Measure 1D profile of PG emission

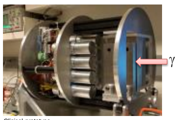
- Compare measured 1D profile to Monte Carlo/analytical calculations

- Clinical trials underway.

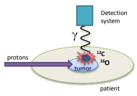
Managing Uncertainties: pre/during/post treatment

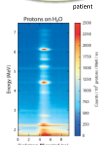
- Induced Ultrasound imaging
- Prompt gamma imaging

Prompt gamma spectroscopy



Clinical prototype developed at MGH





- Measure emitted prompt gamma spectra

- Determine concentration of ^{16}O and ^{12}C.

- Compare PG spectra to calculations Of Nuclear reaction models to determine Range of proton beam

- Clinical trials to start soon.

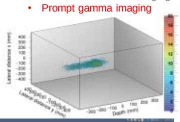
J. Verburg, T. Ruggieri, F. Hueso-Gonzalez, M. Rabe, T. Bortfeld
Department of Radiation Oncology, Massachusetts General Hospital

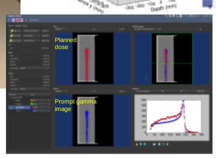
Managing Uncertainties: pre/during/post treatment

- Induced Ultrasound imaging
- Prompt gamma imaging

Compton imaging

Mackin et al, *PMB* (2012)





- Reconstruct 3D image of PG emission

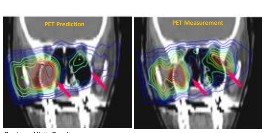
- Register to CT images.

- Compare and analyze dose delivery

- Clinical prototype testing underway.

Managing Uncertainties: during/post treatment

- In room PET imaging



Courtesy of Katia Parodi

- A prediction of the expected induced PET isotope distribution is generated

- The induced PET isotope distribution is then measured with patient of the table

- Differences in the measured and predicted distributions are used to determine changes in the day-to-day dose delivery.

Managing Uncertainties: during/post treatment

- In room PET imaging

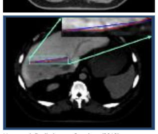
- On line PET imagers: connected to gantry

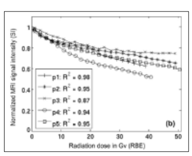
- Off line PET imagers: in room, separate from gantry

Courtesy of Katia Parodi

Managing Uncertainties: Follow up verification

- Follow up MRI



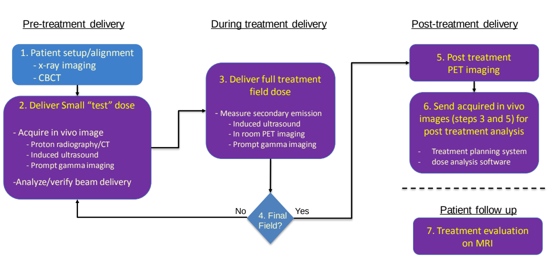


After completion of treatment course

- changes in appearance of tissues in MRI scans shown to correlate to dose delivery in vivo.

Yuan et al, *Radiotherapy Oncology*, (2013)

Managing Uncertainties: Workflow



Summary

- Advantage of protons:
  Protons Stop!   This allows delivery of extremely conformal dose distributions.

- Small Uncertainties in our ability to determine in vivo range limit our ability to take full advantage of this fact.

- Therefore, there is a need for in vivo dosimetry/imaging to verify proper treatment delivery with respect to *both*:

  - the distal beam range

  AND

  - lateral extent of dose profile

Questions