UNIVERSITY of MARYLAND SCHOOL OF MEDICINE

Roles of in vivo dose verification in proton therapy

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Disclosures

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- 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



This gives many pictures of how wonderful Protons are......... <u>in a perfect world</u>.

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



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



Consequences for proton therapy

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

Managing Uncertainties

1. Dose Calculation

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	$\pm 0.2 mm$
Beam reproducibility	±0.2 mm	$\pm 0.2 \mathrm{mm}$
Patient setup	$\pm 0.7 \text{ mm}$	$\pm 0.7 \mathrm{mm}$
Dose calculation		
Biology (always positive) *	+~0.8%	+~-0.8%
CT imaging and calibration	±0.5%*	±0.5%*
CT conversion to tissue (excluding I-values)	±0.5%*	$\pm 0.2\%$
CT grid size	±0.3% ^c	± 0.3% ^c
Mean excitation energy (I-values) in tissues	$\pm 1.5\%^{4}$	$\pm 1.5\%^4$
Range degradation: complex inhomogeneities	-0.755	±0.1%
Range degradation; local lateral inhomogeneities *	±2.5% ⁷	±0.1%
Total (excluding ", ")	2.7% + 1.2 mm	2.4% + 1.2 mm
Total (excluding ')	$4.6\% \pm 1.2 \text{ mm}$	2.4% + 1.2 mm

Range uncertainty formula:

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



Distal Range Uncertainties



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?



- 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

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	$\pm 0.3 \text{ mm}$	$\pm 0.3 \text{ mm}$
Compensator design	$\pm 0.2 \text{ mm}$	$\pm 0.2 \text{ mm}$
Beam reproducibility	$\pm 0.2 \text{ mm}$	±0.2 mm
Patient setup	$\pm 0.7 \text{ mm}$	±0.7 mm
Dose calculation		
Biology (always positive) "	$+\sim 0.8\%$	+~0.8%
CT imaging and calibration	±0.5%*	±0.5%*
CT conversion to tissue (excluding I-values)	±0.5%	±0.254
CT grid size	$\pm 0.3\%^{\circ}$	±0.3% ²
Mean excitation energy (I-values) in tissues	$\pm 1.5\%^{4}$	$\pm 1.5\%^4$
Range degradation; complex inhomogeneities	-0.7%*	±0.1%
Range degradation: local lateral inhomogeneities "	±2.5% ¹	±0.1%
Total (excluding ', ')	$2.7\% \pm 1.2 \text{ mm}$	2.4% + 1.2 mm
Total (excluding ')	$4.6\% + 1.2 \mathrm{mm}$	2.4% + 1.2 mm

- 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





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









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- 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



Slit camera



- Measure 1D profile of PG emission

Compare measured 1D profile to Monte Carlo/analytical calculations

- Clinical trials underway.

Induced Ultrasound imaging Prompt gamma imaging Prompt gamma spectroscopy Detection system - Determine concentration of ¹⁶O and ¹²C. - Clinical trials to start soon. Department of Radiation Oncology, Massachusetts General Hospital

Managing Uncertainties: pre/during/post treatment

- Measure emitted prompt gamma spectra

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

Managing Uncertainties: pre/during/post treatment



- 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



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

Managing Uncertainties: Follow up verification



Follow up MRI

p1: R² = 0.98 p2: R² = 0.95 p3: R² = 0.87 p4: R² = 0.94 p5: R² = 0.95

After completion of treatment course

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

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

