Roles of in vivo dose verification in proton therapy

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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

- Protons Stop!
- Photons don’t.
- Maximum Proton dose at target
- Maximum Photon dose at $d_{max}$.

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.

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
2. Treatment Delivery

Range uncertainty formula:

\[-3.5\% \text{(beam range)} + 1-2 \text{ mm}\]

Managing Uncertainties

- Currently expand margins
  
  \[-3.5\% \text{(beam range)} + 2 \text{ mm}\]
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?

- 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

- 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

Paganetti, PMB, 57 (2012)

Managing Uncertainties: Pre-treatment

Ion radiography / tomography for:
- Direct longitudinal SP determination
- Daily localization image guidance

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

Managing Uncertainties: pre/during/post treatment

- Induced secondary emission

Induced ultrasound imaging
In-room PET imaging
Prompt gamma imaging
Managing Uncertainties: pre/during/post treatment

- Induced Ultrasound imaging
- Prompt gamma imaging


Bragg peak Phantom entrance

Managing Uncertainties: pre/during/post treatment

- Induced Ultrasound imaging
- Prompt gamma imaging

Prompt gamma timing

- 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.

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

Prompt gamma timing

- Measure 1D profile of PG emission
- Compare measured 1D profile to Monte Carlo/analytical calculations
- Clinical trials underway.

Xie et al, IJROBP (2017)

Slit camera

- 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

- 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.

Managing Uncertainties: pre/during/post treatment

- Compton imaging

- 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

After completion of treatment course

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

Managing Uncertainties: Workflow

1. Patient setup/alignment
   - x-ray imaging
   - CBCT
2. Deliver small "test" dose
   - Acquire in vivo image
     - Proton radiography/CT
     - Induced ultrasound
     - Prompt gamma imaging
   - Analyze/verify beam delivery
3. Deliver full treatment field dose
   - Measure secondary emissions
     - Induced ultrasound
     - In room PET imaging
     - Prompt gamma imaging
4. Final Field?
   - Yes
   - No

5. Post treatment PET imaging

6. Send acquired in vivo images (steps 3 and 5) for post treatment analysis
   - Treatment planning system
   - dose analysis software

Patient follow up
7. Treatment evaluation on MRI
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
  - lateral extent of dose profile

Questions

\[ Y = -4 \text{ mm} \]
\[ Y = -2 \text{ mm} \]
\[ Y = 0 \text{ mm} \]
\[ Y = +2 \text{ mm} \]
\[ Y = +4 \text{ mm} \]

(a)

(b)