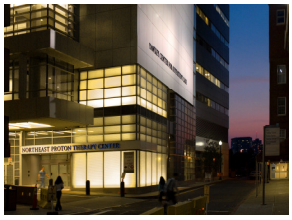
Do uncertainties in proton therapy limit its clinical potential?



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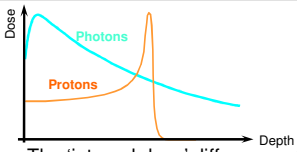
Disclaimer

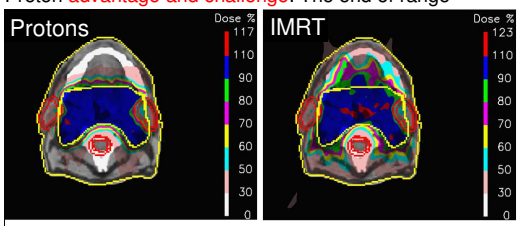
I work for an institution (MGH) which does have a proton therapy facility

Doing research, I do not consider this a conflict of interest ☺

Introduction

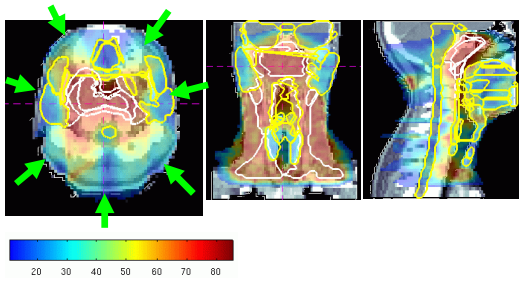


Proton advantage: The 'integral dose' difference : 2-3
Proton advantage and challenge: The end of range



Integral dose

IMRT plan
(7 coplanar photon beams)



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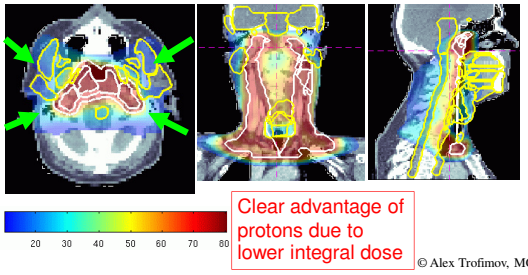
Integral dose

IMPT plan
(4 coplanar proton beams)



Clear advantage of protons due to lower integral dose

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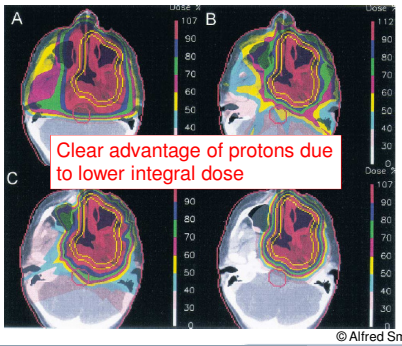
Integral dose

Rhabdomyosarcoma of Paranasal Sinus (7 y old boy)

6 MV Photons (3 field)

160 MeV Protons (2 field)



Photon IMRT (9 field)

Proton IMPT (9 field)

© Alfred Smith (MDACC)

Integral dose

Is the integral dose the decisive parameter?

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

second cancer induction

cognitive development in children (!)

Integral dose

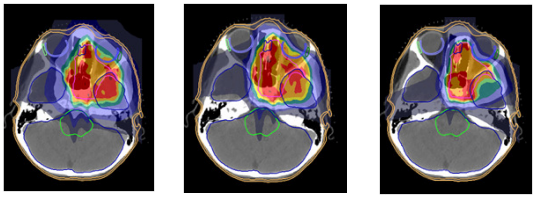
Note:

- To use the 'integral dose' to conclude superiority of protons might be too simplistic. We need to consider the distribution of dose and the distribution of organs at risk !

This affects also the comparison of protons vs. protons !

Integral dose

In beam scanning, spot size matters !



σ=12mm

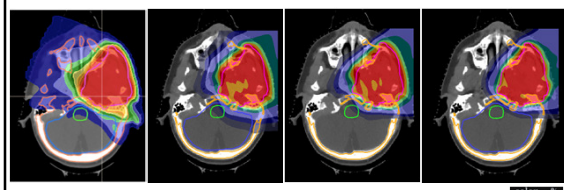
σ=12mm +aperture

σ=3mm

Depending on the beam characteristics, there are considerable differences between different proton beams (potentially showing inferiority compared to photon treatments)

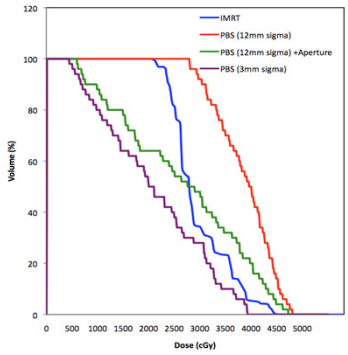
Integral dose

IMRT PBS 12mm PBS 12mm+AP PBS 3mm



Rhabdomyosarcoma
Total dose = 50.4 Gy
Number of proton fields = 2
Number of IMRT fields = 5

Integral dose



Left Lacrimal gland

Integral dose

Note:

- NTCP considerations in treatment planning are based on photon dose distributions
- Organ doses in proton therapy are more heterogeneous. There are no proton specific normal tissue constraints

Integral dose

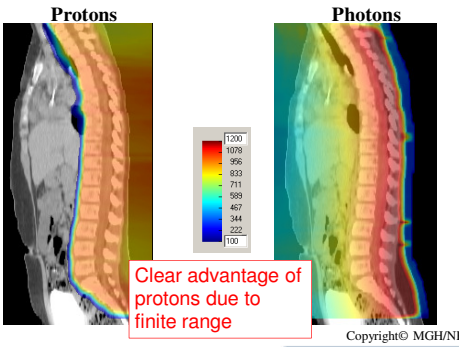
Conclusion I:

The total energy deposited in a patient ("integral dose") is always lower when treating with protons. This, theoretically, should always result in an advantage for proton treatments. However,

- the dose distribution matters
- this may not always result in a significant clinical gain (site dependent; clinical trials?)
- the delivery system matters

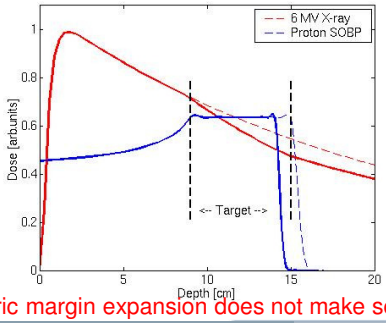
Finite range

Medulloblastoma



Uncertainties when predicting dose

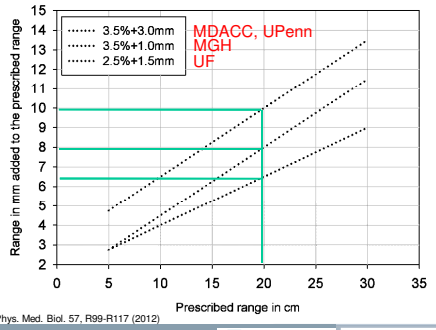
The difference compared to photon therapy: range uncertainties



symmetric margin expansion does not make sense !

Uncertainties when predicting dose

Applied range uncertainty margins for non-moving targets



H. Paganetti: Phys. Med. Biol. 57, R99-R117 (2012)

Uncertainties when predicting dose

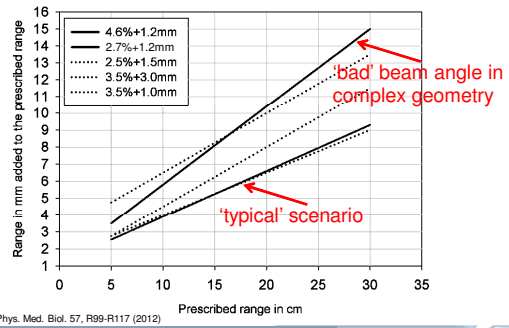
Applied range uncertainty margins for non-moving targets

Source of range uncertainty in the patient	Range uncertainty
Independent of dose calculation:	
Measurement uncertainty in water for commissioning	± 0.3 mm
Compensator design	± 0.2 mm
Beam reproducibility	± 0.2 mm
Patient setup	± 0.7 mm
Dose calculation:	
Biology (always positive)	+ 0.8 %
CT imaging and calibration	± 0.5 %
CT conversion to tissue (excluding I-values)	± 0.5 %
CT grid size	± 0.3 %
Mean excitation energies (I-values) in tissue	± 1.5 %
Range degradation; complex inhomogeneities	- 0.7 %
Range degradation; local lateral inhomogeneities *	± 2.5 %
Total (excluding *)	2.7% + 1.2 mm
Total	4.6% + 1.2 mm

H. Paganetti: Phys. Med. Biol. 57, R99-R107 (2012)

Uncertainties when predicting dose

Applied range uncertainty margins for non-moving targets



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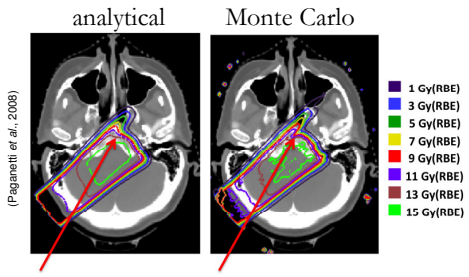
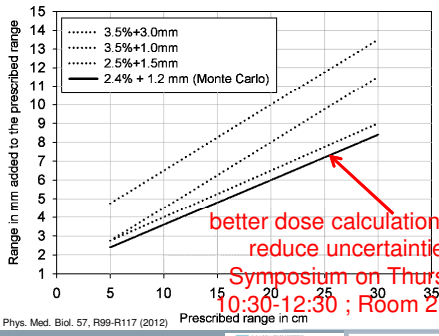
Uncertainties when predicting dose



Uncertainties when predicting dose

Comment



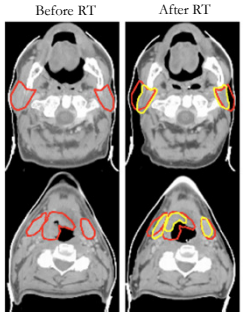
better dose calculation might reduce uncertainties:
Symposium on Thursday 10:30-12:30 ; Room 213CD

H. Paganetti: Phys. Med. Biol. 57, R99-R117 (2012)

Uncertainties when predicting dose

In addition(!): patient geometry changes

Example: Intra-fractional geometry changes



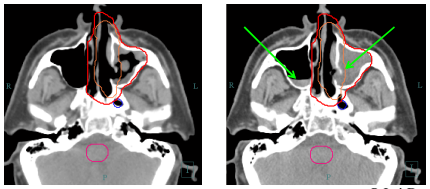
- Parotid glands
- Subm.glands
- Tumor

E. M. Vasques Osorio *et al.*
IJROBP 70: 875-82

Uncertainties when predicting dose

In addition(!): patient geometry changes

- Patient weight gain / loss
- Filling up of sinuses
- (Sub-clinical) pneumonia
- Wet hair / gel / hairspray



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Uncertainties when predicting dose

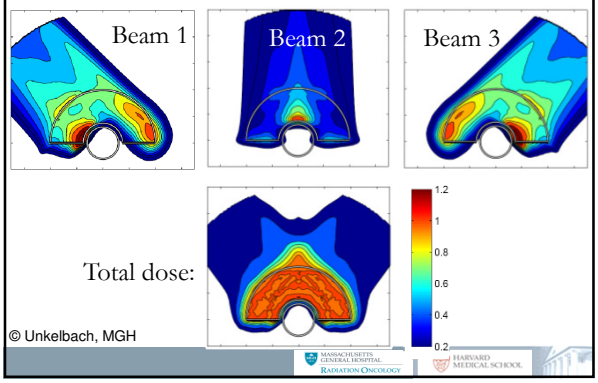
Note:

In proton therapy, generic margin recipes are not sufficient !

Treatment planners need to understand the origin and magnitude of range uncertainties !

Uncertainties when predicting dose

Mitigating range uncertainties using robust planning in IMPT



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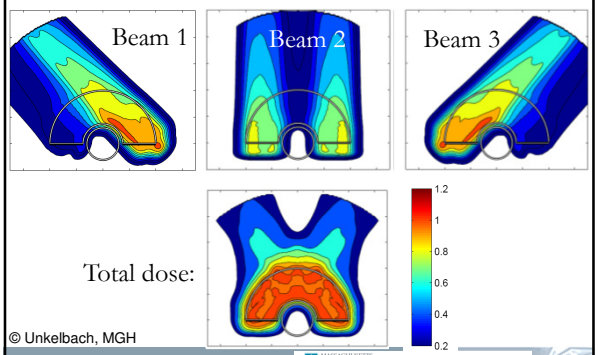
Uncertainties when predicting dose

Mitigating range uncertainties using robust planning in IMPT



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Uncertainties when predicting dose

Range uncertainties sometimes limit our ability to exploit the end of range

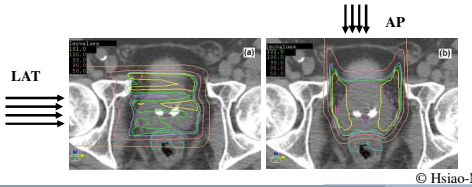
Example: Prostate treatments

Uncertainties when predicting dose

Protons and Prostate Treatments

Current technique: Lateral fields
Use lateral penumbra (10 mm, 50-95%) to spare rectum (penumbra not better than 15 MV photon fields)

Why not AP fields?
Use much sharper distal penumbra (~ 4 mm, 50-95%)



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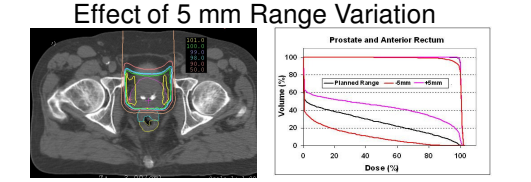
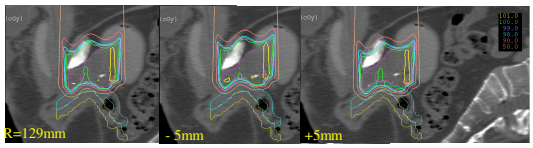
Uncertainties when predicting dose

Effect of 5 mm Range Variation





Correct Range Undershooting Overshooting

Uncertainties when predicting dose

Conclusion II:

- Proton treatment planning needs to be done by experienced planners who understand the impact of range uncertainties.
- For some sites (e.g. prostate) range uncertainties prevent us from exploiting the full potential of proton therapy.

Will Proton Therapy Gradually Replace Photon Therapy?

From a pure physics perspective (putting economic constraints aside and assuming well-trained personnel):

For some sites (e.g. pediatrics), YES (because clear advantages can be expected)
For other sites, POTENTIALLY (we are not there yet), if:

- We can reduce planning and delivery uncertainties (e.g. beam range)
- We understand the impact of 'better' dose distributions (i.e. their clinical significance)
- We use 'optimized' proton delivery systems (e.g. small beam spots in proton beam scanning)

What do you consider the main obstacle in physics before proton therapy can become mainstream?

21% 1. Treatment planning is too complex (need more training)

20% 2. Current range uncertainties are unacceptable and need to be reduced

21% 3. Unproven clinical advantage of a lower integral dose

19% 4. Biological consequences of different dose distributions compared to photons

19% 5. *Proton therapy will never be a mainstream treatment option*