UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

# In Vivo imaging in proton therapy

AAPM 2018

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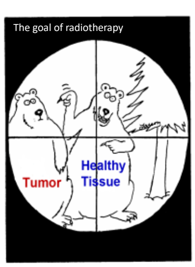
## Disclosures

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

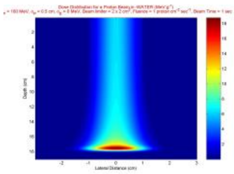
- Prompt gamma imaging for proton radiotherapy treatment verification.

## Overview

- Uncertainties in proton dose delivery
  - What causes them
- Case examples of the effects of uncertainty on patient treatment
- In vivo verification methods
  - Current methods under development
- Future trends in proton therapy
  - In vivo imaging needs.
- Conclusions



## Overview

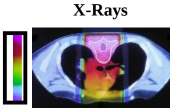


- **Protons Stop!**
- **Photons don't.**

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

## Overview

**X-Rays**



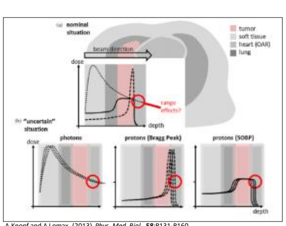
**PROTONS**

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

## 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* (2012)

Range uncertainty formula:

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

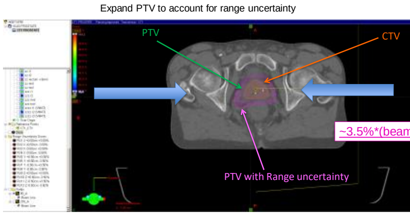
## Treatment Planning Process: Expanding Margins

Define our Clinical Target Volume (CTV): the tumor + microscopic disease

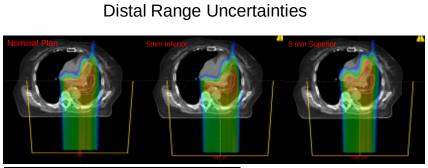
Oncologist writes a prescription: 72 Gy in 40 treatment fractions.

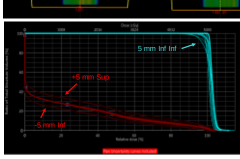
Planning Target Volume (PTV): account for setup uncertainty, etc.

Expand PTV to account for range uncertainty



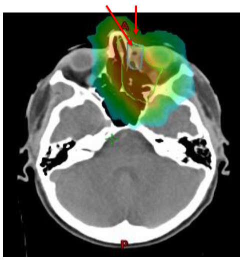

## Distal Range Uncertainties




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

## Lateral Profile Uncertainties



- 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.

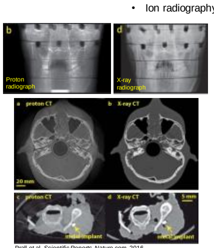
## Managing Uncertainties: in vivo imaging methods

*"In vivo"* = in the room with patient on the table

- Using treatment beam
  - proton radiography/CT
- Using secondary radiation
  - induced ultrasound
  - in room PET imaging
  - prompt gamma imaging

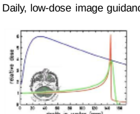
## Managing Uncertainties

- Ion radiography / tomography




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

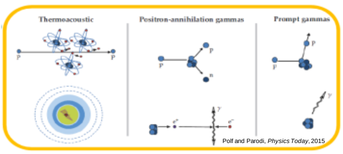
- Direct (integral) SPR determination
- Daily, low-dose image guidance



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

## Managing Uncertainties

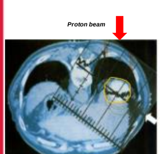
- Induced secondary emission



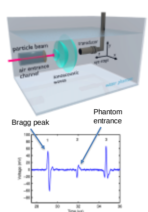

Induced ultrasound imaging | In room PET imaging | Prompt gamma imaging

## Managing Uncertainties

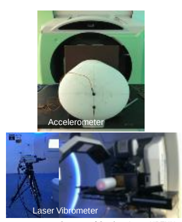
- Induced Ultrasound imaging
- Prompt gamma imaging




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




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




Courtesy of Stephen Avery, UPENN

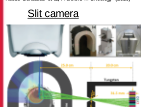
## Managing Uncertainties

- Induced Ultrasound imaging
- Prompt gamma imaging

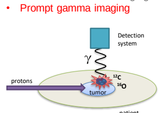
Prompt gamma timing


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

Slit camera



Courtesy of Keawin Teo, UPENN



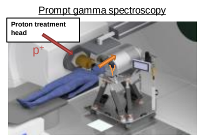

Measure:

- 1D profile of PG emission
- Arrival time of PG
- PG spectra at given position

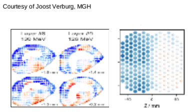
Provide:

- clinical range of a Given proton beam

Prompt gamma spectroscopy

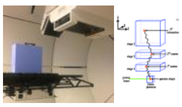


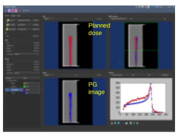

Courtesy of Joost Verburg, MGH



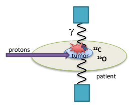
## Managing Uncertainties

Compton imaging






- Induced Ultrasound imaging
- Prompt gamma imaging



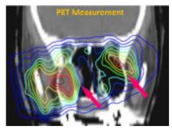

Measure:

- 3D distribution of emission

Provide:

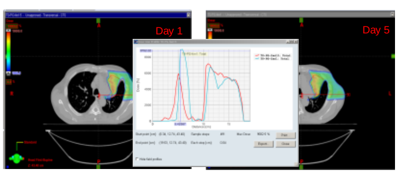
- 3D evaluation of proton dose distribution in patient

PET imaging



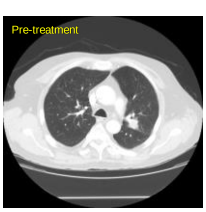

## Future needs: hypo-fractionation

- Current: 1-2 treatments a day for 15 – 45 days → (~2 Gy per treatment)
- Future: 1 treatment a day for 1 – 10 days. → (**10 Gy – 25 Gy** per treatment)

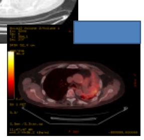



## Future Needs: functional imaging

- Need information about response of tissues to treatment.



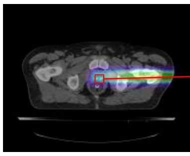


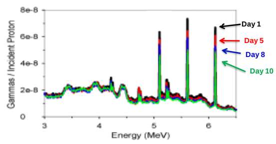


Why does this patient develop pneumonitis. And not the other 100+ lung patients?

## Future Needs: functional imaging

- Need information about response of tissues to treatment.

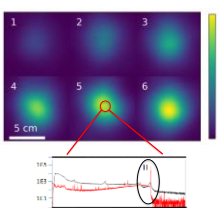




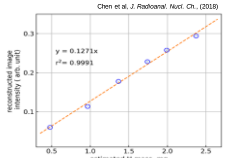

- If change in elemental concentration changes, is it indicative of treatment outcome?
- Would make possible to predict patient response during the course of treatment.
  - Tumor response (changes in Hypoxia)
  - Normal tissue complication

## Future Needs: functional imaging

- NIST prompt gamma activation analysis beamline at NIST Center for Neutron Research
- Imaging specific PG emission lines as a function of elemental mass in the sample.




Chen et al, *J. Radioanal. Nucl. Ch.*, (2018)




## Why no clinical in vivo imaging yet.

- High beam currents [1 – 5 nA at exit of beam nozzle]
- High count rates on the detectors [ up to ~1 Mhz]
- Short irradiation times [ 1 μs - 10 ms per beam spot]

- Detector requirements:
  - Need to handle a high count rate.
  - Fast data processing and image reconstruction
  - "Real-time" data display

## Conclusions: Why do we need in vivo imaging?

- Need to improve the precision of proton treatment delivery.

But Why?

Because we can reduce MARGINS!!!!!

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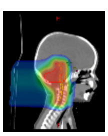
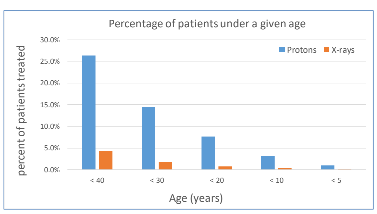


Percentage of patients treated at the University of Maryland School of Medicine (2016 – 2018)
Total number of X-ray patients = 2929
Total number of proton patients = 1000

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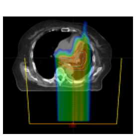
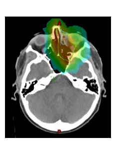


22 year old female
attending college



25 year old male
5 years of military service

1 year old male

Questions