Imaging for Online Control of Particle Therapy

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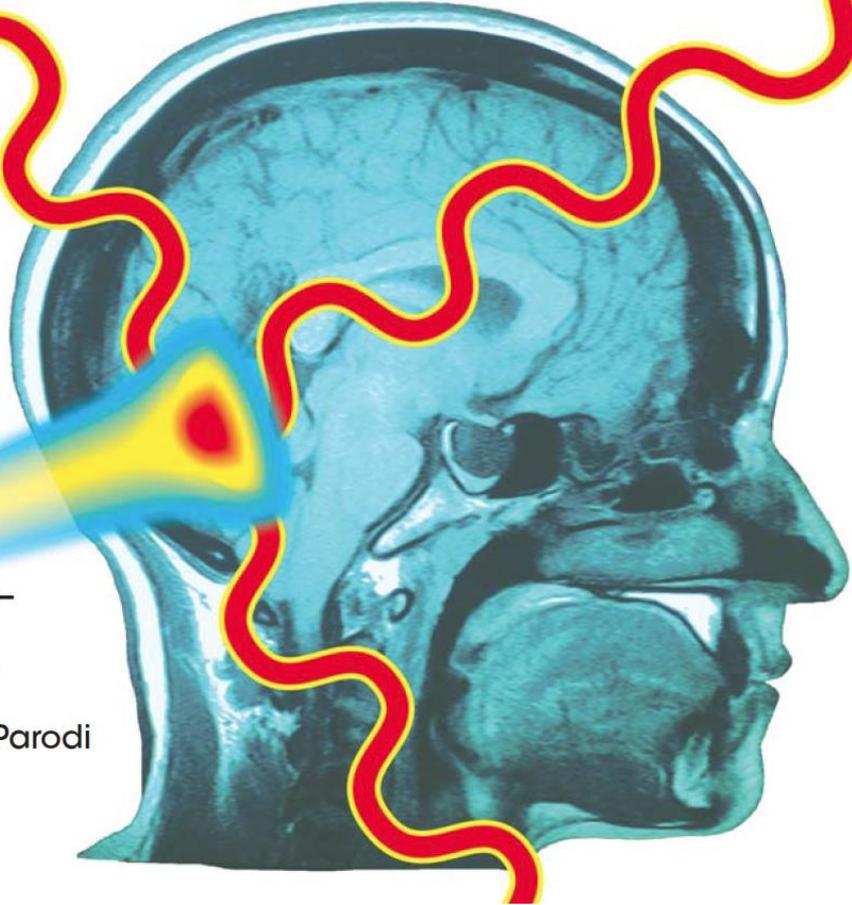
Supported by:

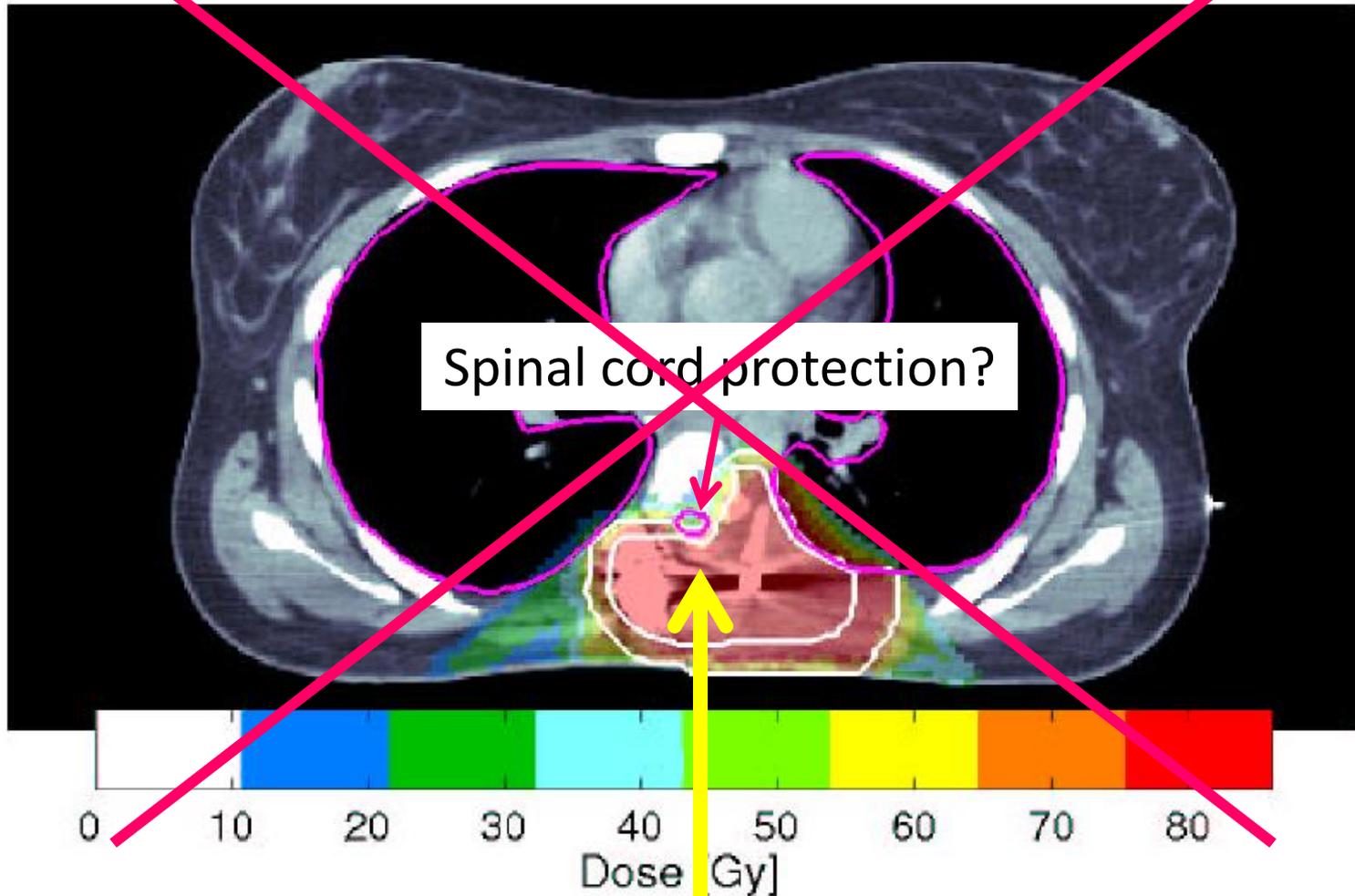MGH-NCI: Therapy Imaging Program (TIP)

ICTR-PHE 2016

Physics Today 68(10), 28 (2015)

Example: Para-spinal

Spinal cord protection?

Proton Beam

Dose [Gy]

0 10 20 30 40 50 60 70 80

Example: Prostate
Have to use lateral beams!

IMRT
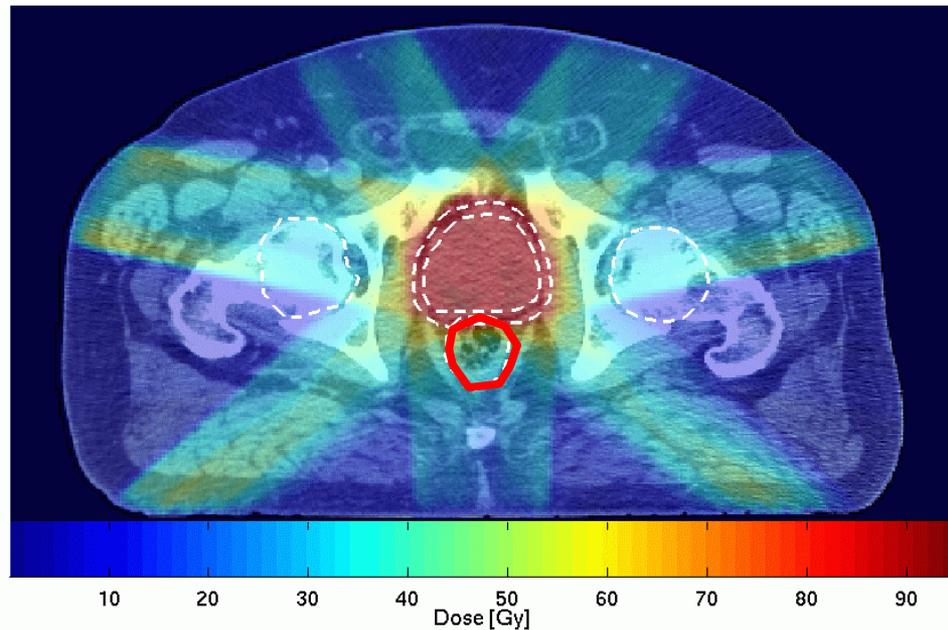
Protons
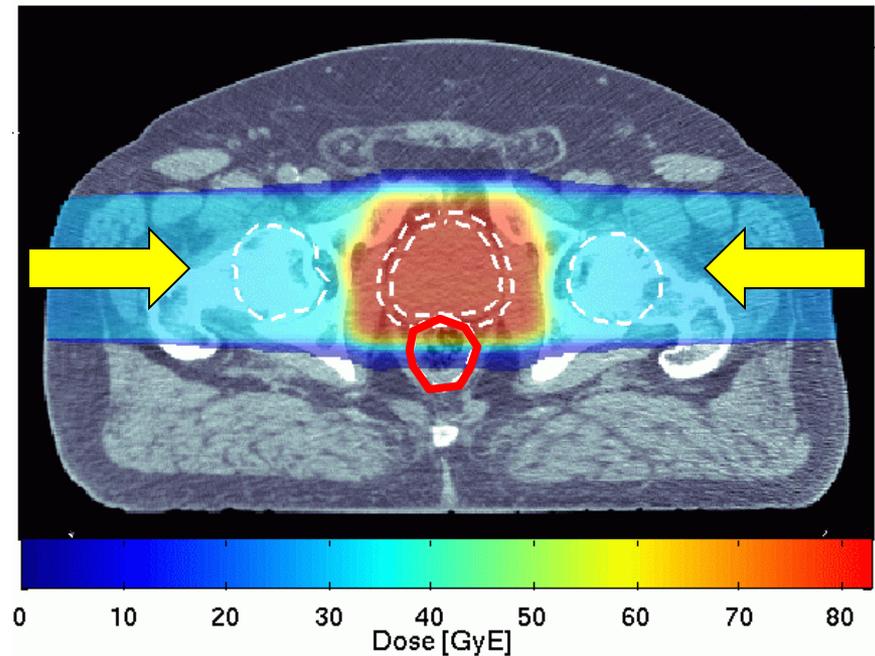
From: Trofimov et al., IJROBP 69(2):444-453, 2007

MGH 1811 MASSACHUSETTS
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RADIATION ONCOLOGY

Example: Lung
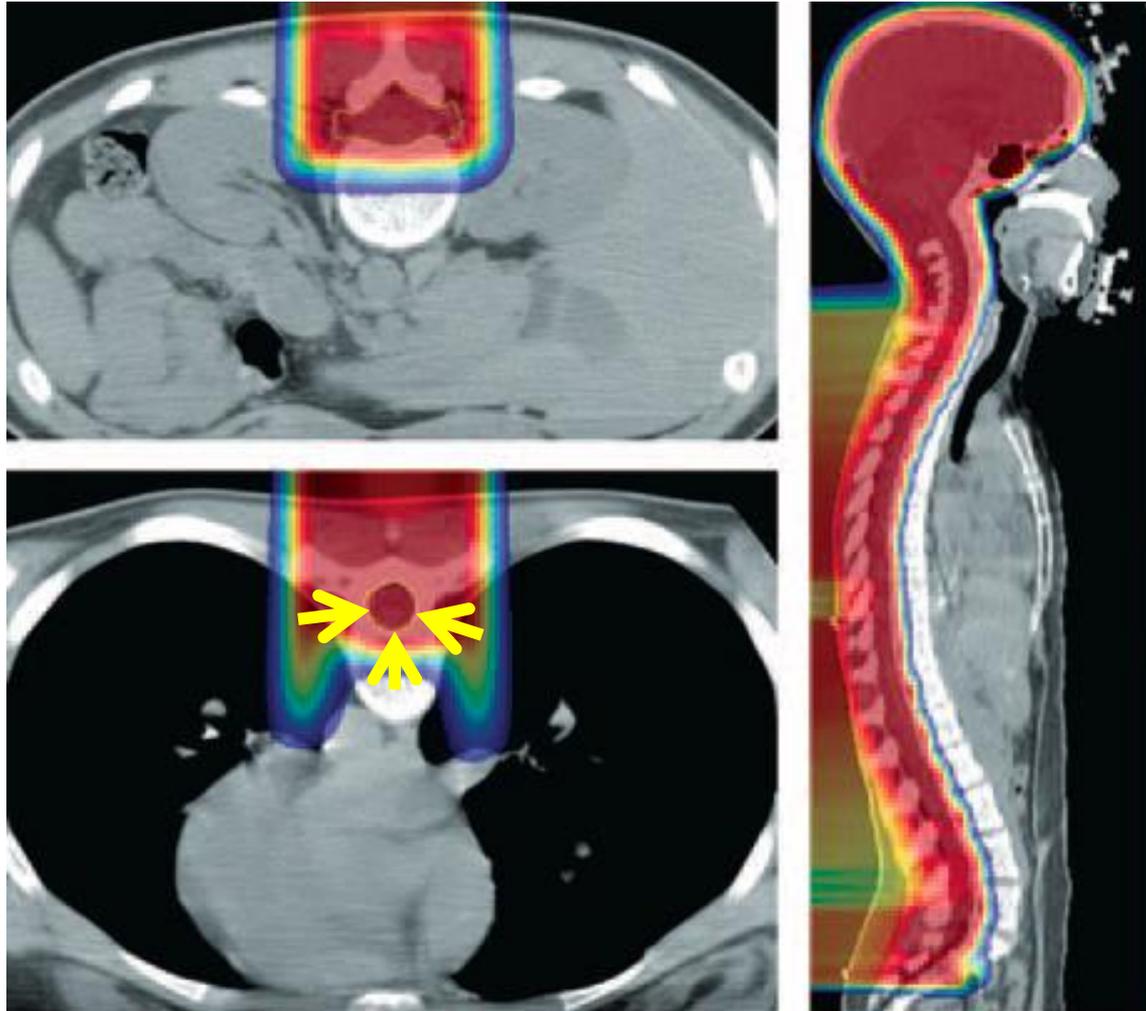# Breathing and range uncertainties
State of the art (2016)
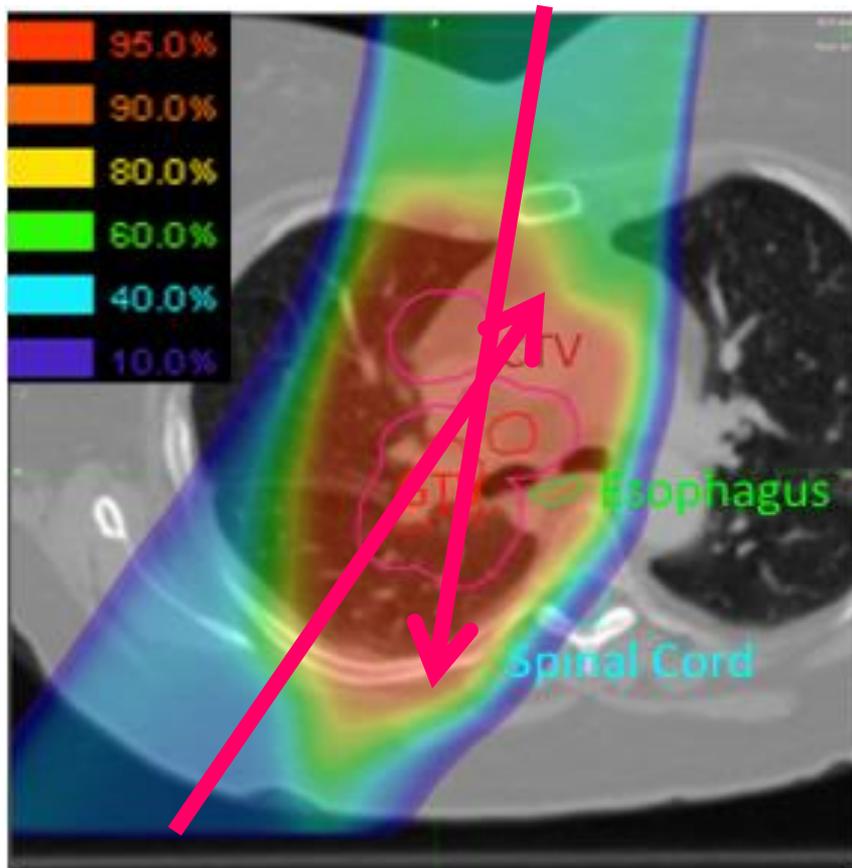
With all margins added, proton plans look like photon plans.

Example: Pediatric, medulloblastoma Thecal-sac-only irradiation?

Range uncertainties and clinical impact: Range margin "recipe"

$$1.5 \times \sqrt{2\%^2 + 1\%^2} + 1\ \text{mm} \approx 3.5\% + 1\ \text{mm}$$

standard deviations
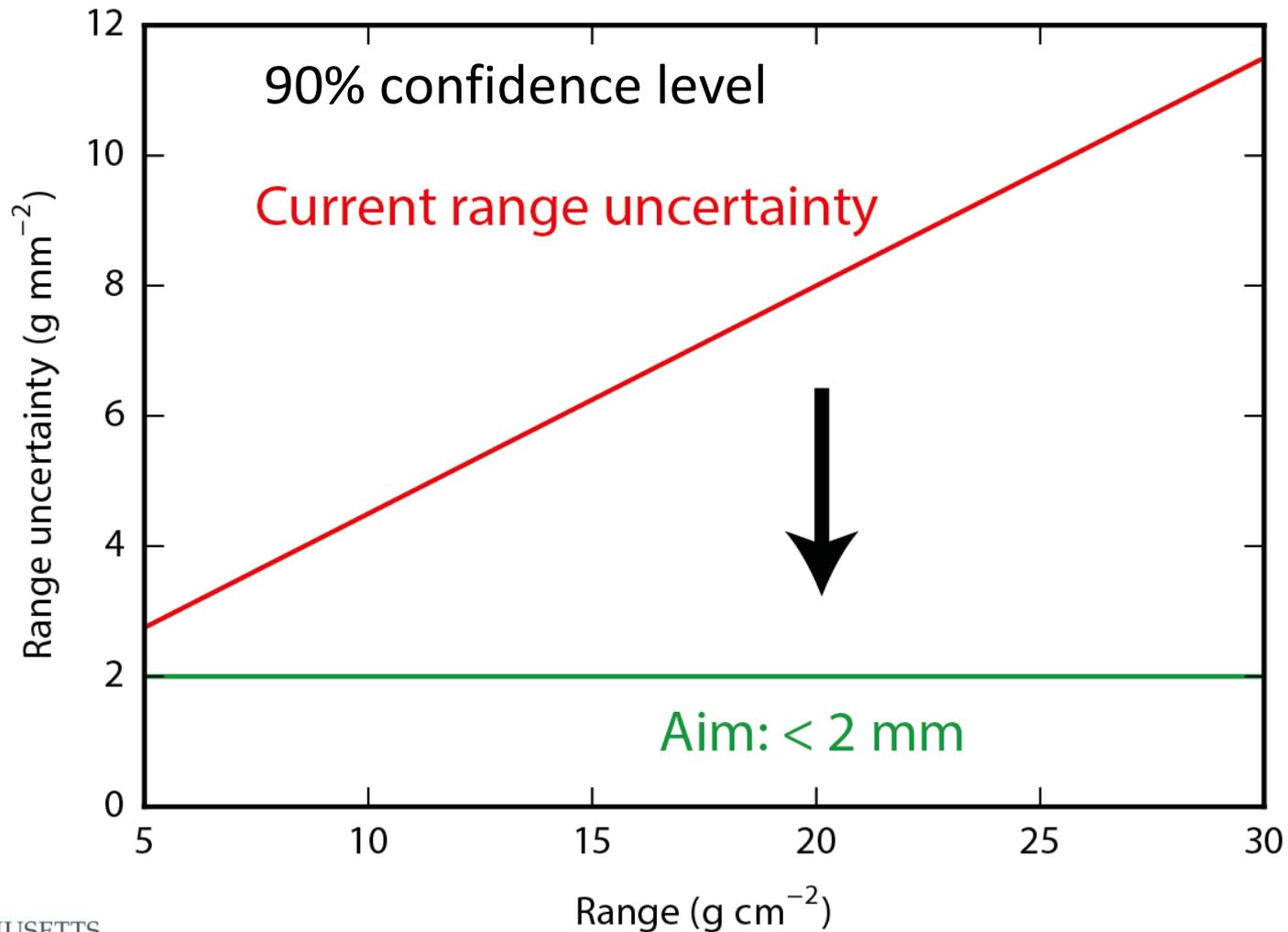
Hounsfield Units (HU)

HU conversion

setup etc.

Michael Goitein 1980

In vivo range verification

Imaging for online control of particle therapy:
A control loop approach
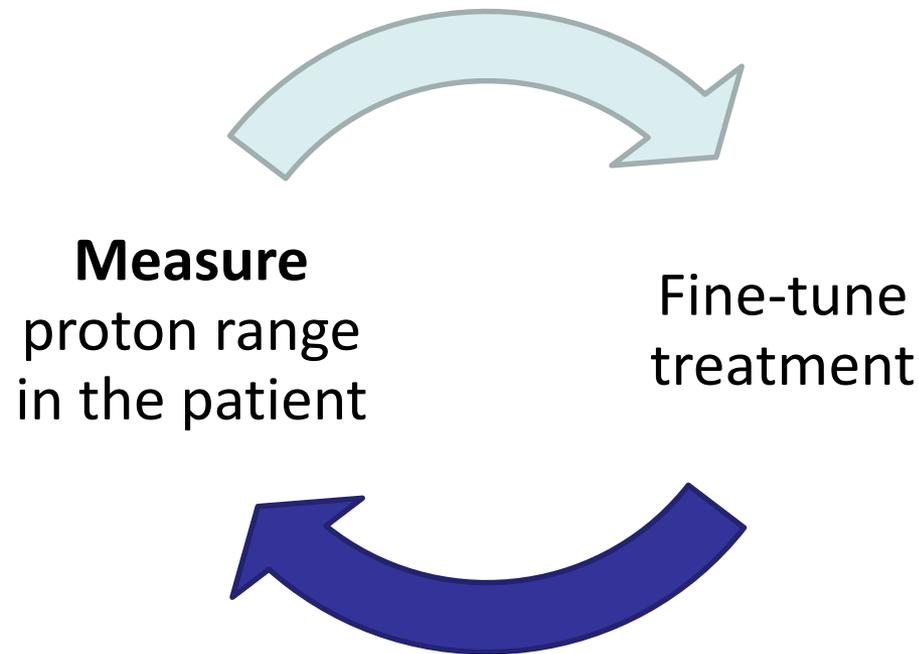
Measure
proton range
in the patient

Fine-tune
treatment

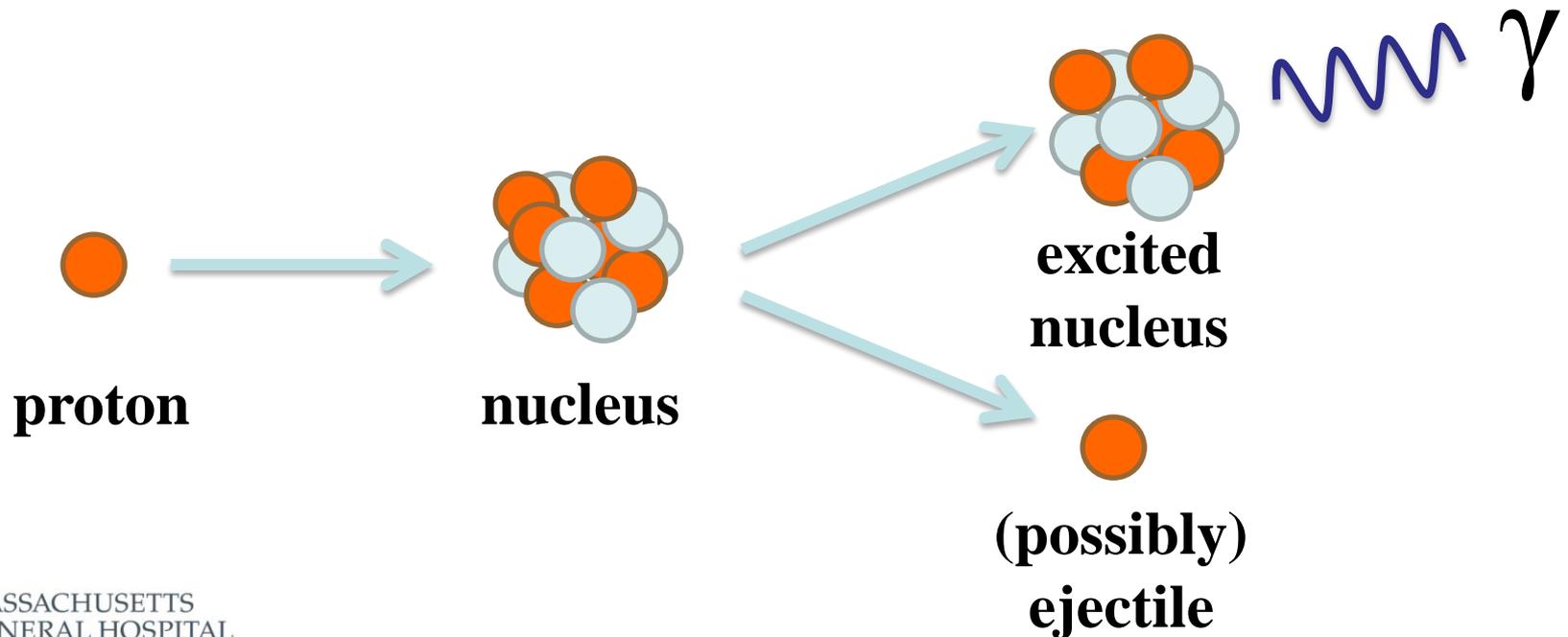# The ideal range "sensor" – requirements:

- Detect range with ~ 1 mm accuracy

- Short response time

- Low dose (< 1 Gy)

- In the patient

- Relative to patient anatomy

Prompt gamma imaging (PGI) – principle

- Measure secondary **prompt gamma radiation** from nuclear reactions of protons with tissue

proton   nucleus   excited nucleus   γ

(possibly) ejectile

Prompt gamma imaging (PGI) – principle
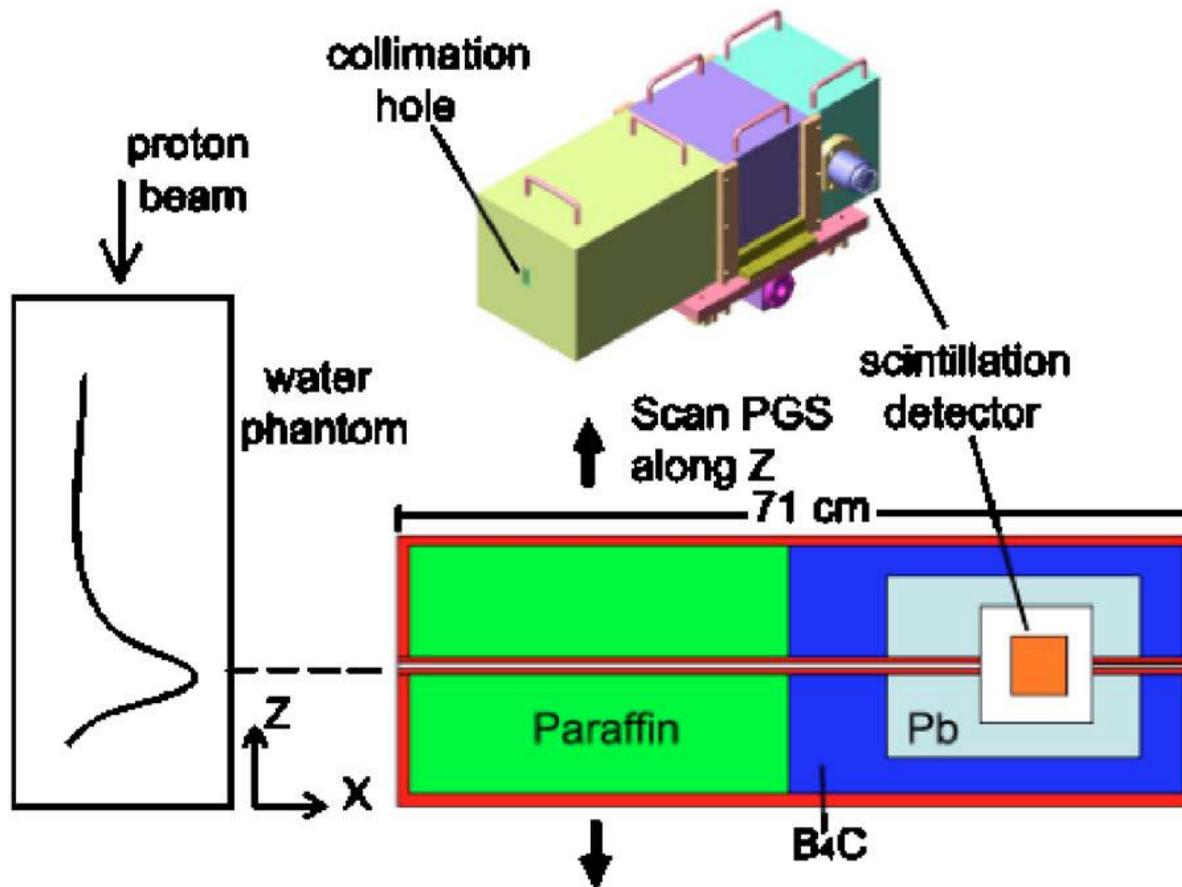
Min et al., Appl. Phys. Lett. 89, 183517 (2006)
Stichelbaut and Jongen (IBA), PTCOG 2003

Potential advantage of **prompt gamma** range imaging over **PET**

Dose

Prompt gamma

PET no washout

PET washout

Moteabbed et al., PMB 2011

Clinical implementation slit camera

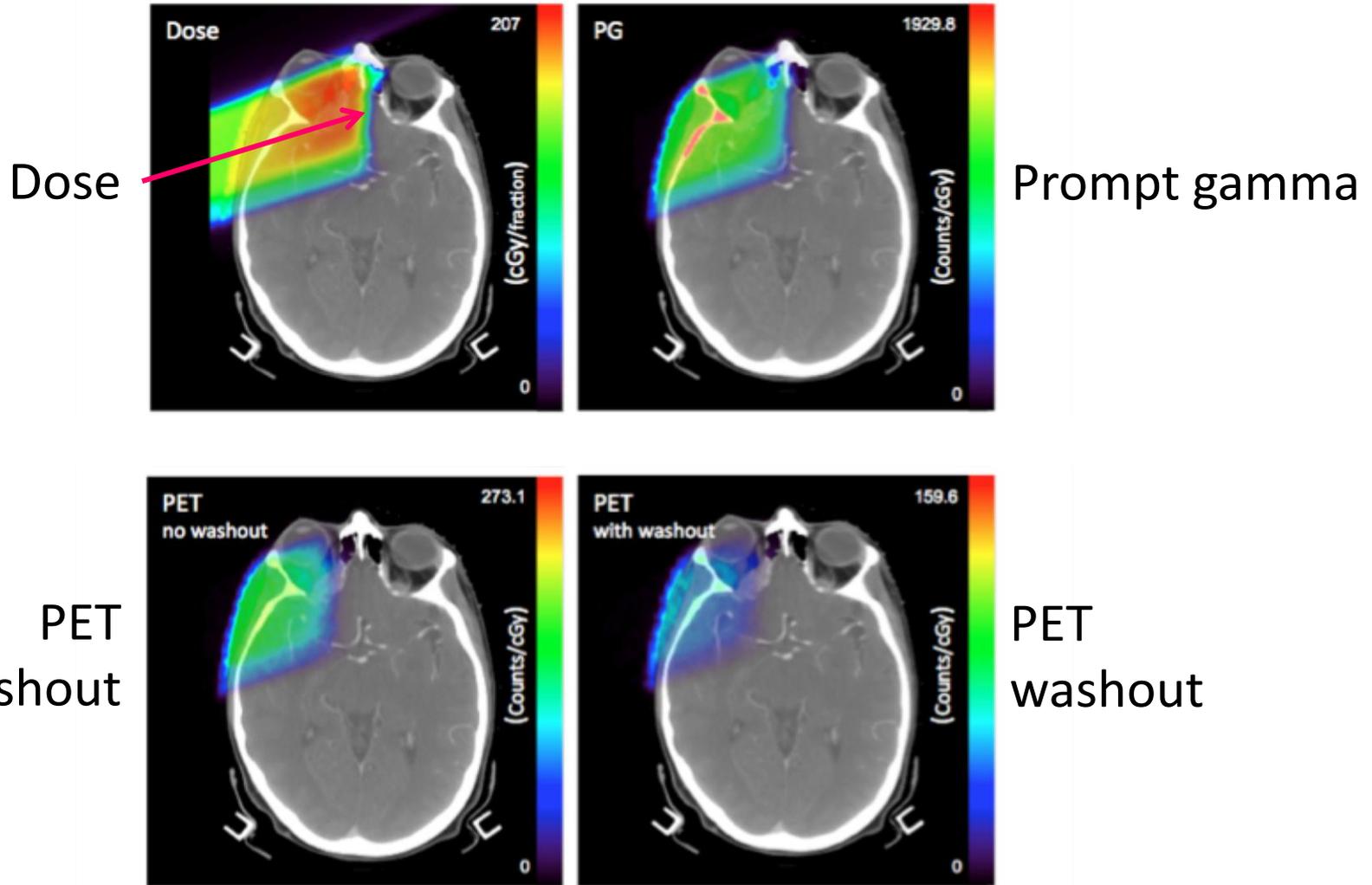- **Prompt γ -ray imaging (PGI):**
  Clinical implementation of IBA slit camera

HPRT,
In vivo dosimetry,
RTTs, clinicians

next talk

- 1st prototype in Dresden since 10/2014

- 1st clinical application 08/2015

- Evaluation of the benefit under clinical conditions

- **Final Goal:** Reduction of range uncertainties and irradiation of normal tissues

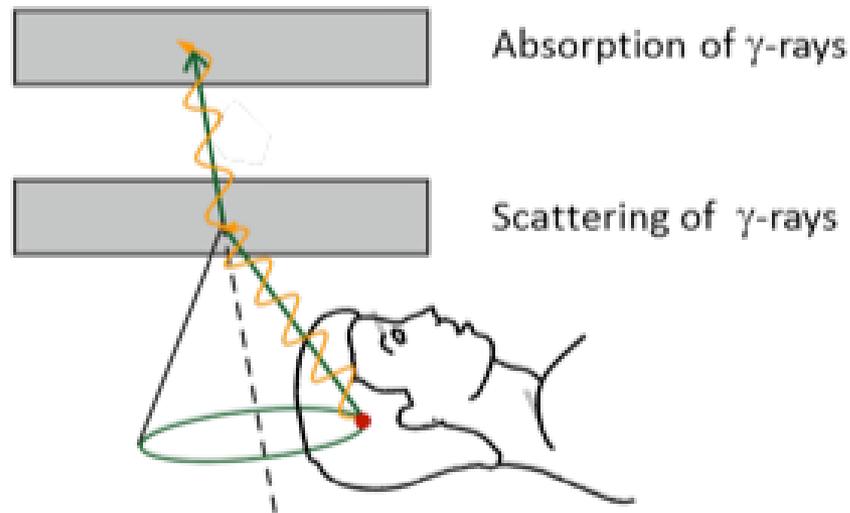Richter et al. Radioth Oncol 2016, ~~Thu 11:45~~

Improvements and extensions of PGI

- Compton camera for "better" geometry
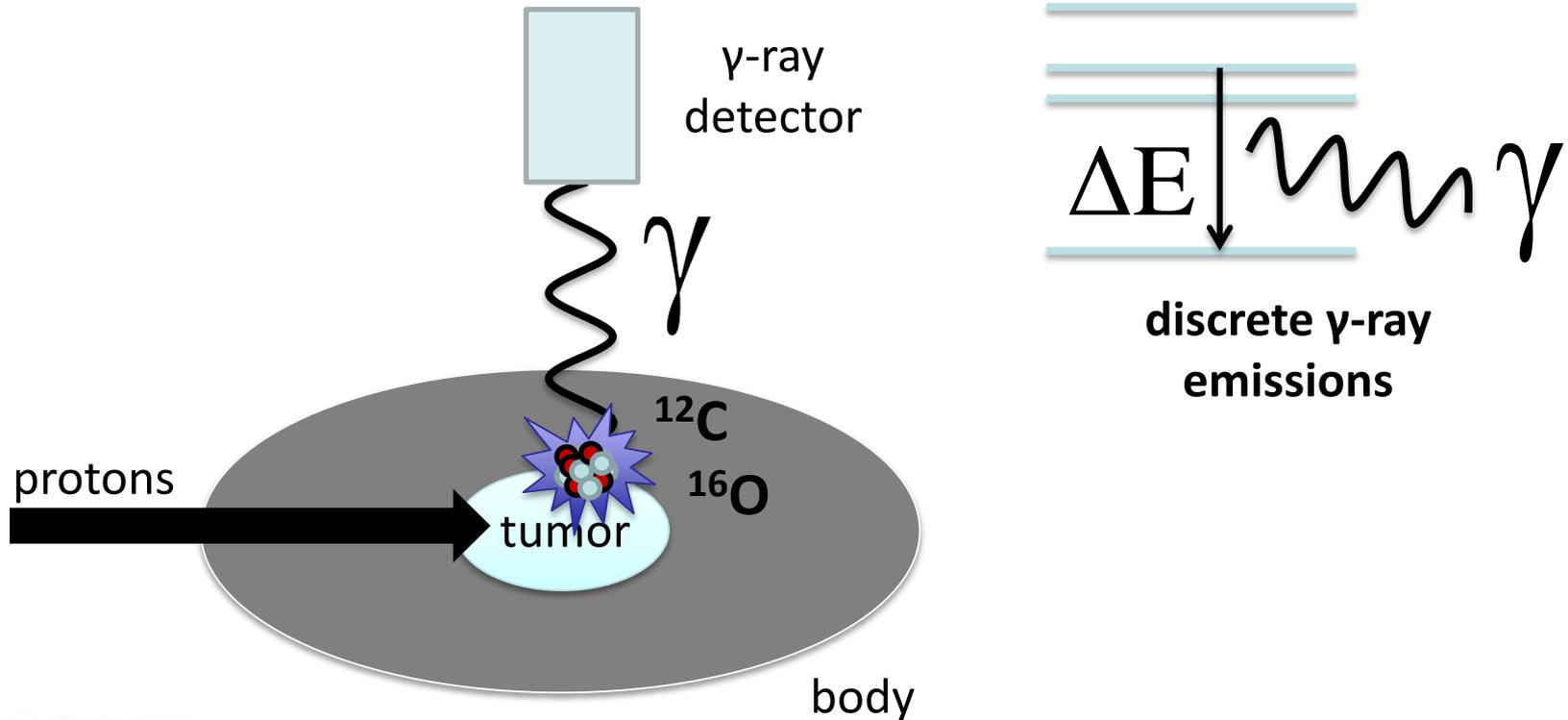

Absorption of γ-rays

Scattering of γ-rays

Improvements and extensions of PGI

- Secondary proton imaging for carbon ion therapy

Prompt γ-ray spectroscopy (PGS)

Unique method to determine the range of proton beams:
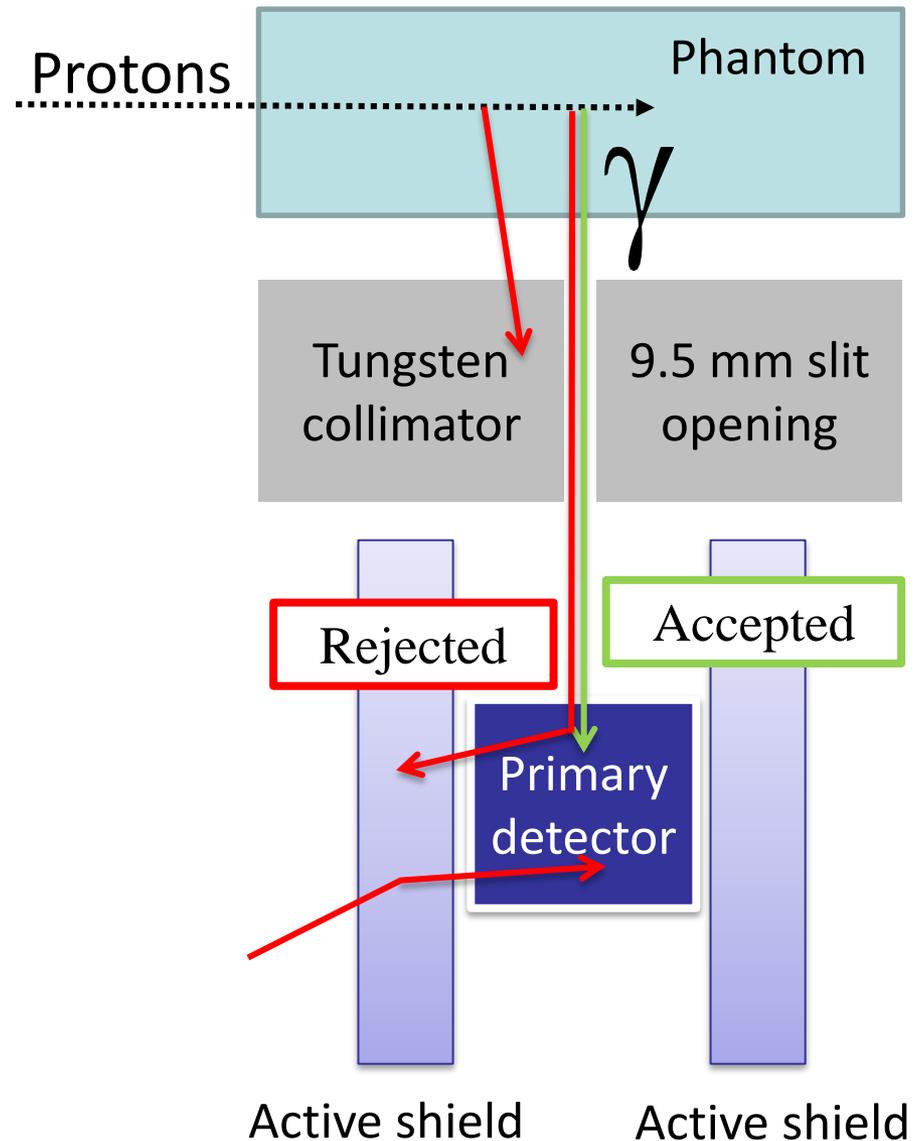*in vivo* **spectroscopy** of proton-induced **prompt γ-rays**

γ-ray detector

γ

^{12}C

^{16}O

protons

tumor

body

ΔE γ

discrete γ-ray emissions

Prompt gamma detector

Prototype design

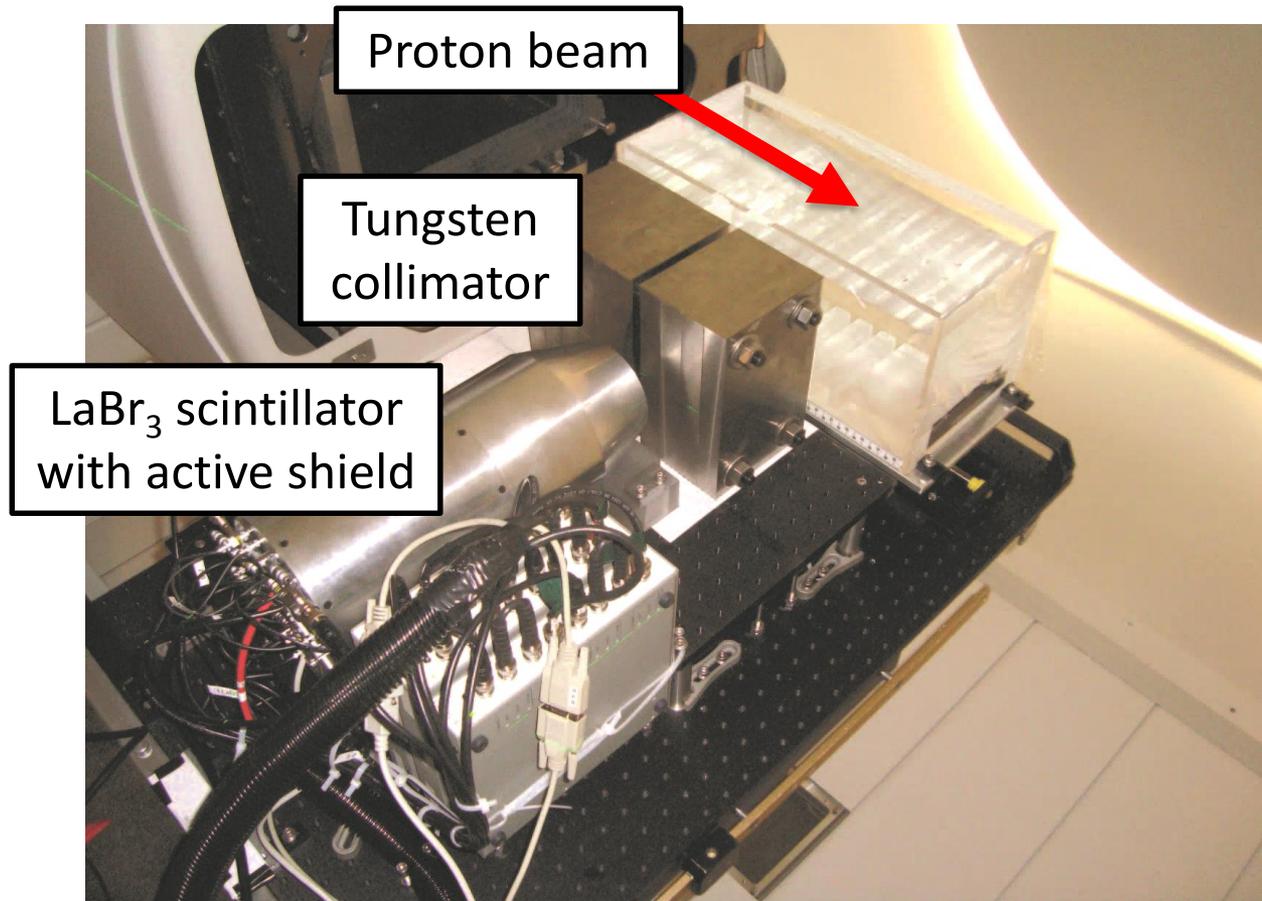7.6 cm LaBr$_3$(Ce) scintillator actively shielded with 4 BGO scintillators

Photomultipliers for detector readout

Tungsten collimator

- High energy resolution for spectroscopy

- Fast timing to separate proton- and neutron-induced reactions

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Experimental setup

Proton beam

Tungsten collimator

LaBr$_3$ scintillator with active shield

Energy- and time-resolved γ detection

p + ^{16}O   p + ^{12}C

Proton-induced γ

Neutron-induced γ
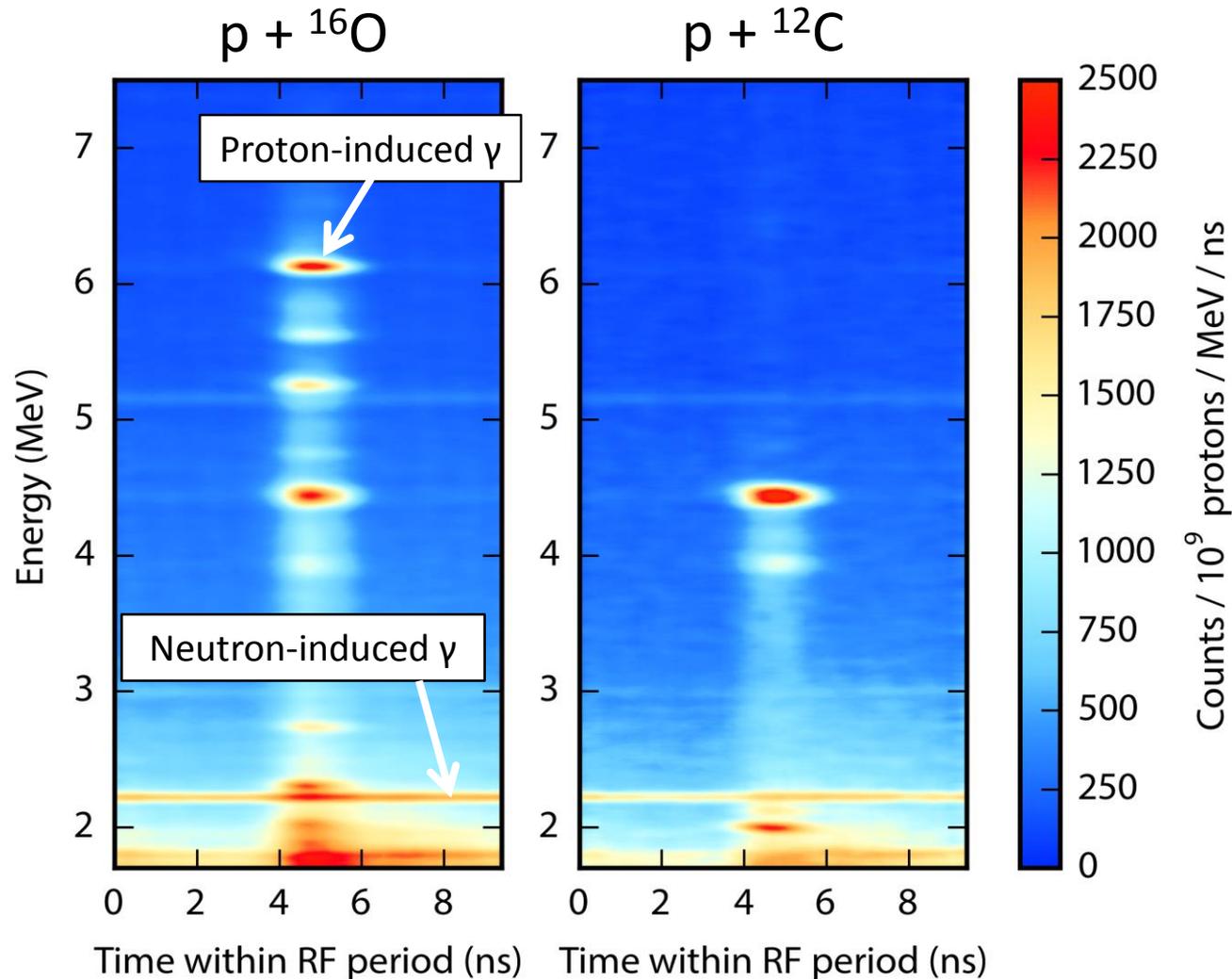
165 MeV proton beam in water, 20 mm upstream of end-of-range

Detection of range shifts

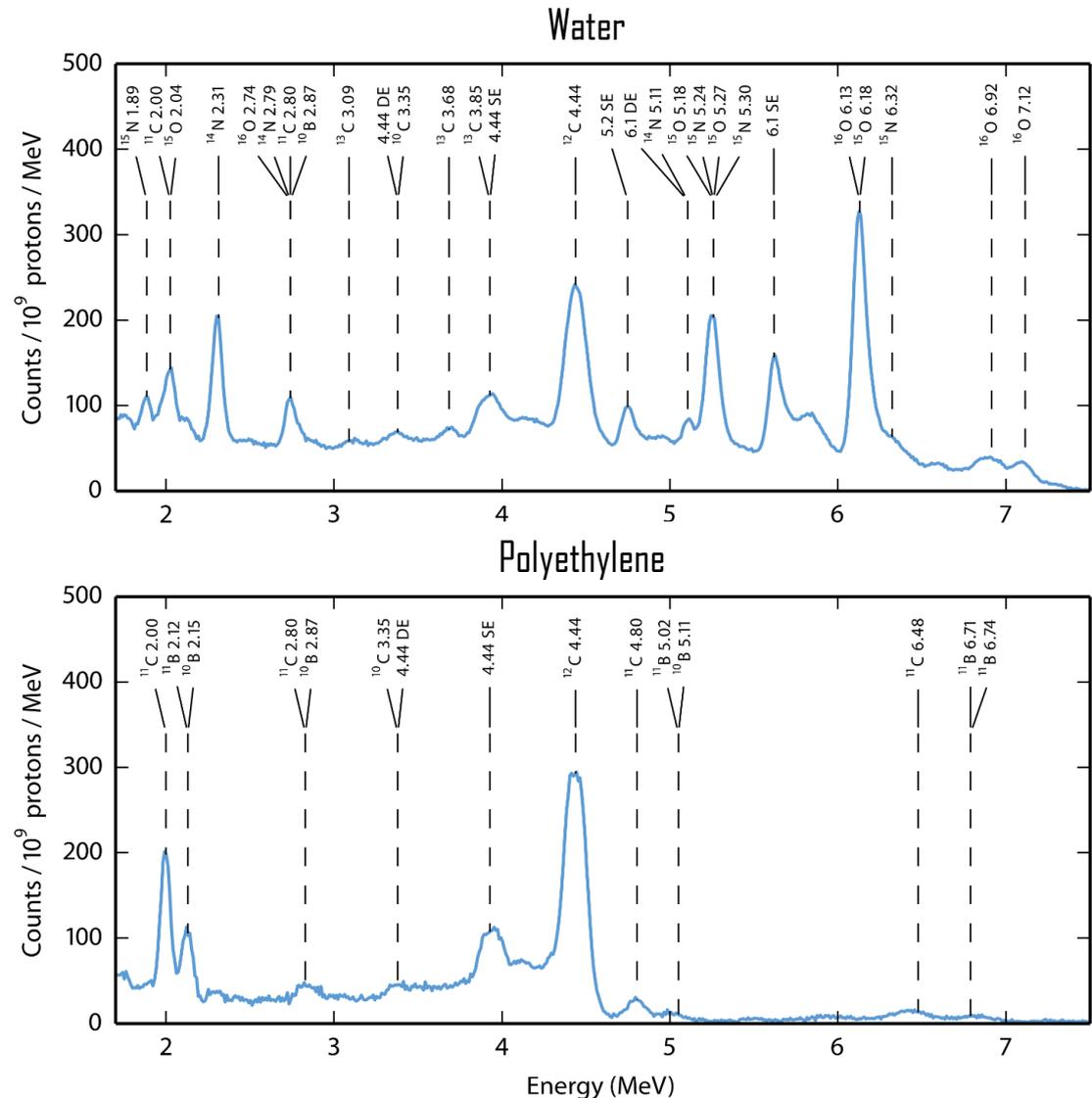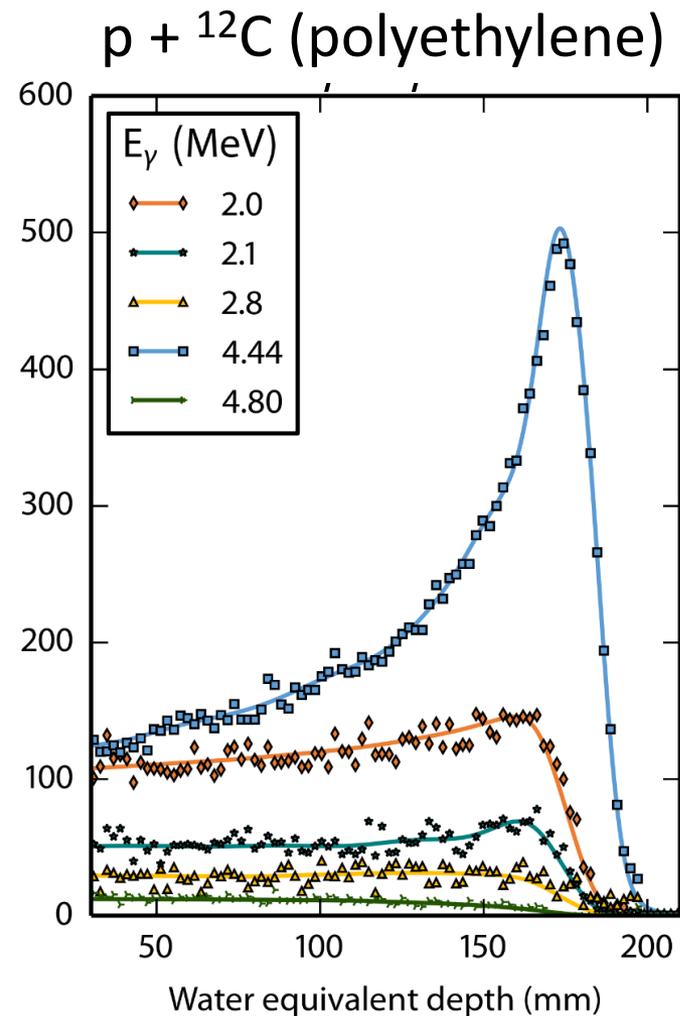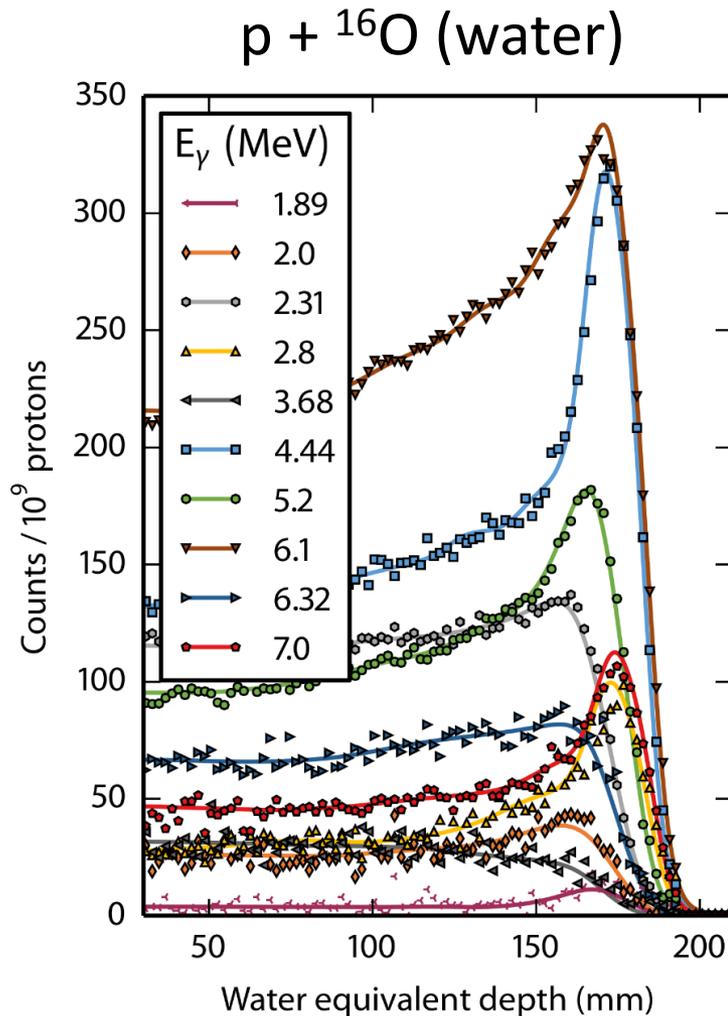151 MeV proton beam in
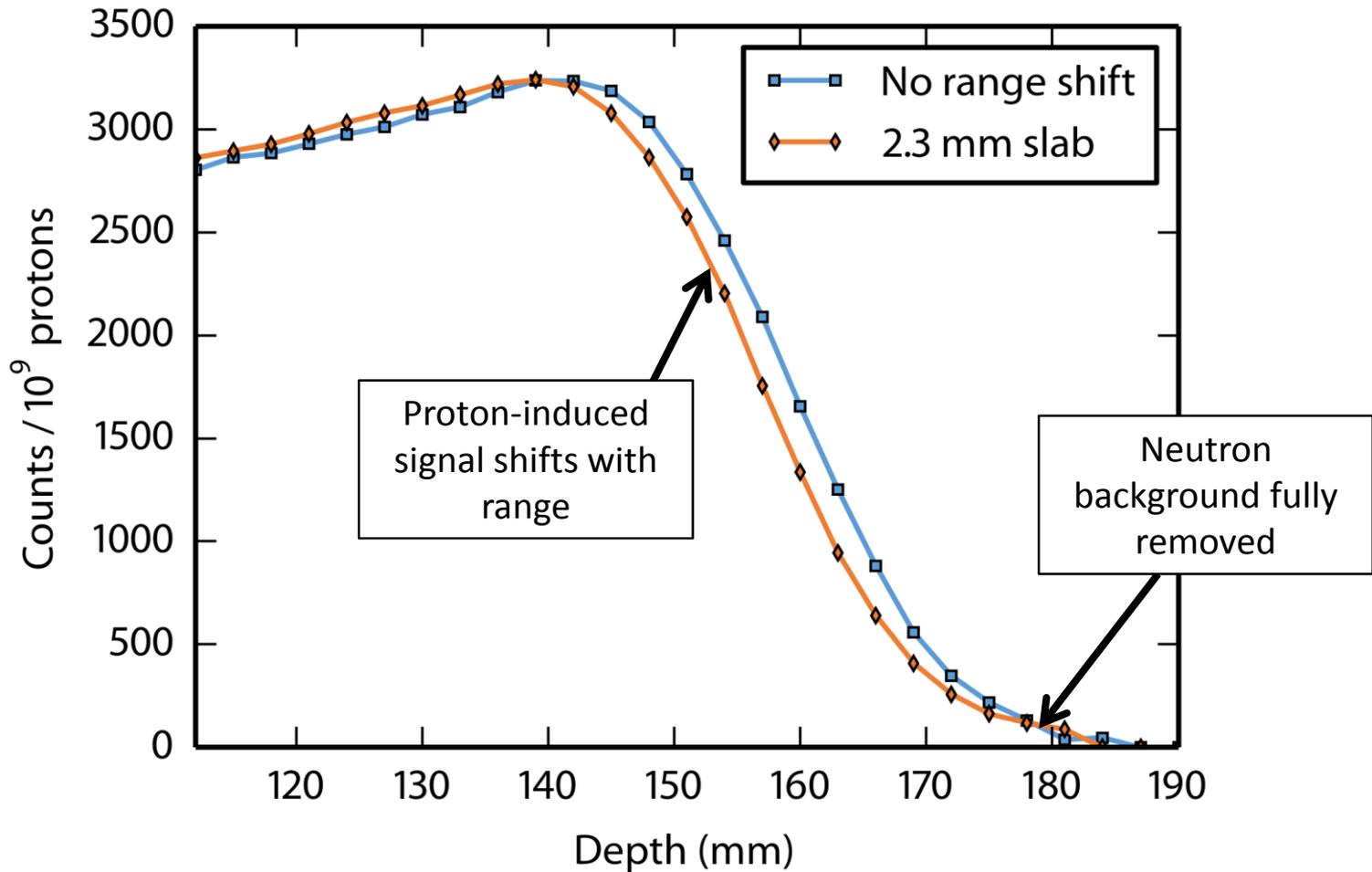
γ-ray energy spectrum

165 MeV proton beam stopped in water (oxygen) and polyethylene (carbon)

Proton-induced component averaged over last 30 mm of range

Discrete γ-ray emissions

p + ^{16}O (water)

p + ^{12}C (polyethylene)

165 MeV proton beam

Range verification method

Optimization parameters

d : Water equivalent depth at detector position

ρ_O , ρ_C : ^{16}O/^{12}C concentrations

$$\underset{d,\rho_O,\rho_C}{\mathrm{argmin}}\left(\sum_{b\in B}\sum_{l\in L}h\left(\rho_O f_{b,l}^{O}(d)+\rho_C f_{b,l}^{C}(d)-\mathbf{m}_{b,l}\right)^2\right)$$

Pencil-beams and gamma lines

Loss function

Reactions with ^{16}O

Reactions with ^{12}C

Prompt gamma model
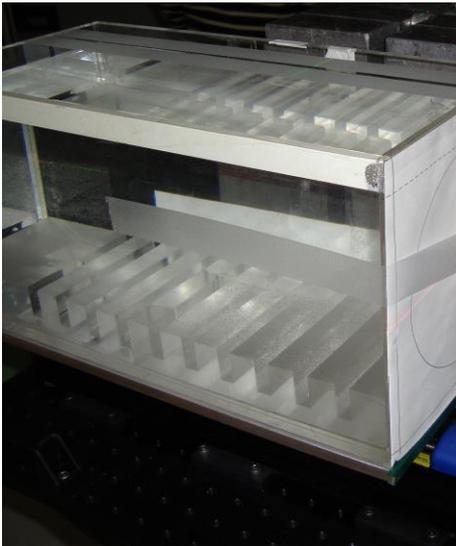
Measurement data

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Range verification of pencil-beams

- Pencil-beam delivered at one position with 5 different energies (R_{80} 15.54 – 17.59 g cm^{-2})
- 2.3 mm / 5.2 mm water equivalent shifters in front of phantom to simulate range error

End-of-range in water
(89% oxygen)

End-of-range in solid water
(21% oxygen, 70% carbon)

Combined **proton range verification** and **elemental composition**

	Detected depth (mm)	Range shift (mm)	Detected ^{16}O (g cm^{-3})	Detected ^{12}C (g cm^{-3})
Water Detector at 156.5 mm (water equivalent), 0.89 g cm^{-3} oxygen				
No range shift	156.3 ± 1.3	0.1 ± 1.3	0.94 ± 0.07	0.05 ± 0.07
2.3 mm shifter	158.6 ± 1.0	−2.2 ± 1.0	0.90 ± 0.07	0.02 ± 0.06
5.2 mm shifter	161.6 ± 1.0	−5.1 ± 1.0	0.88 ± 0.07	0.04 ± 0.06
Solid Water Detector at 157.1 mm (water equivalent), 0.21 g cm^{-3} oxygen, 0.70 g cm^{-3} carbon				
No range shift	157.1 ± 1.4	0.0 ± 1.4	0.17 ± 0.04	0.70 ± 0.07
2.3 mm shifter	159.3 ± 1.4	−2.3 ± 1.4	0.18 ± 0.03	0.70 ± 0.07
5.2 mm shifter	162.4 ± 1.3	−5.4 ± 1.3	0.18 ± 0.04	0.69 ± 0.08

Pencil-beams delivering 5 x 10^8 protons, uncertainties ±1σ,
90 repeat measurements for determination of σ

Planned clinical implementation

- Create **nuclear reaction models** based on treatment plan

- **Prompt γ-ray spectroscopy** at fixed positions near distal end of tumor

- Measurements **fitted to models**, simultaneously optimizing unknown parameters:

  – **Absolute proton range**

  – Elemental composition of irradiated tissue

protons

tumor

collimator

γ-ray detectors
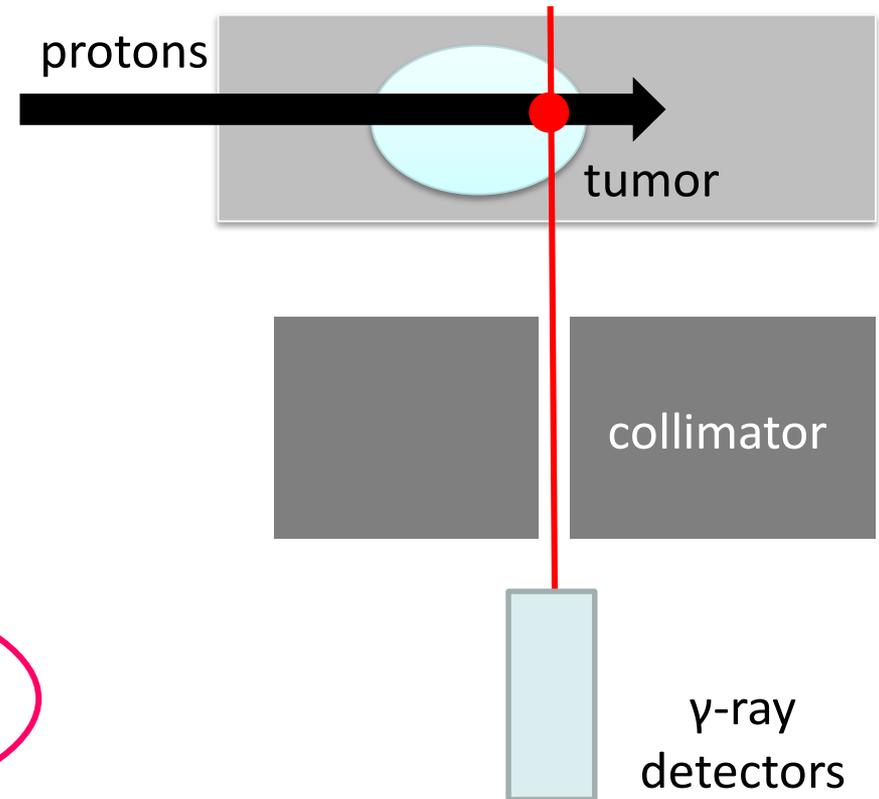
Imaging particle beams for cancer treatment

Jerimy C. Polf and Katia Parodi
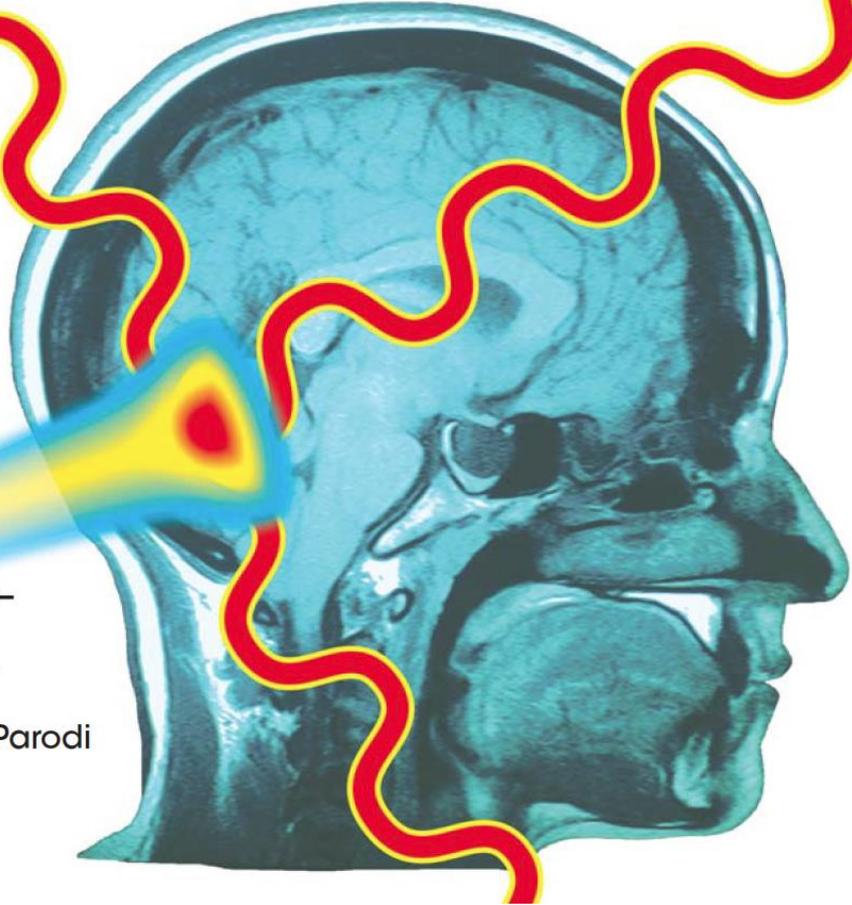
Physics Today 68(10), 28 (2015)

PGI/PGS requires 3D anatomical imaging

Revival of acoustic range measurements

E

Ionoacoustic characterization of the proton Bragg peak with submillimeter accuracy

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Department for Medical Physics, Ludwig-Maximilians-Universität München, Am Coulombwall 1, Garching 85748, Germany

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Institute for Applied Physics and Measurement Technology, Universität der Bundeswehr, Werner-Heisenberg-Weg 39, Neubiberg 85577, Germany

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Institute for Biological and Medical Imaging, Technische Universität München and Helmholtz Zentrum München, Ingolstädter Landstrasse 1, Neuherberg 85764, Germany

K. Parodi
Department for Medical Physics, Ludwig-Maximilians-Universität München, Am Coulombwall 1, Garching 85748, Germany

Acoustic proton range measurement IBA cyclotron (UPenn)
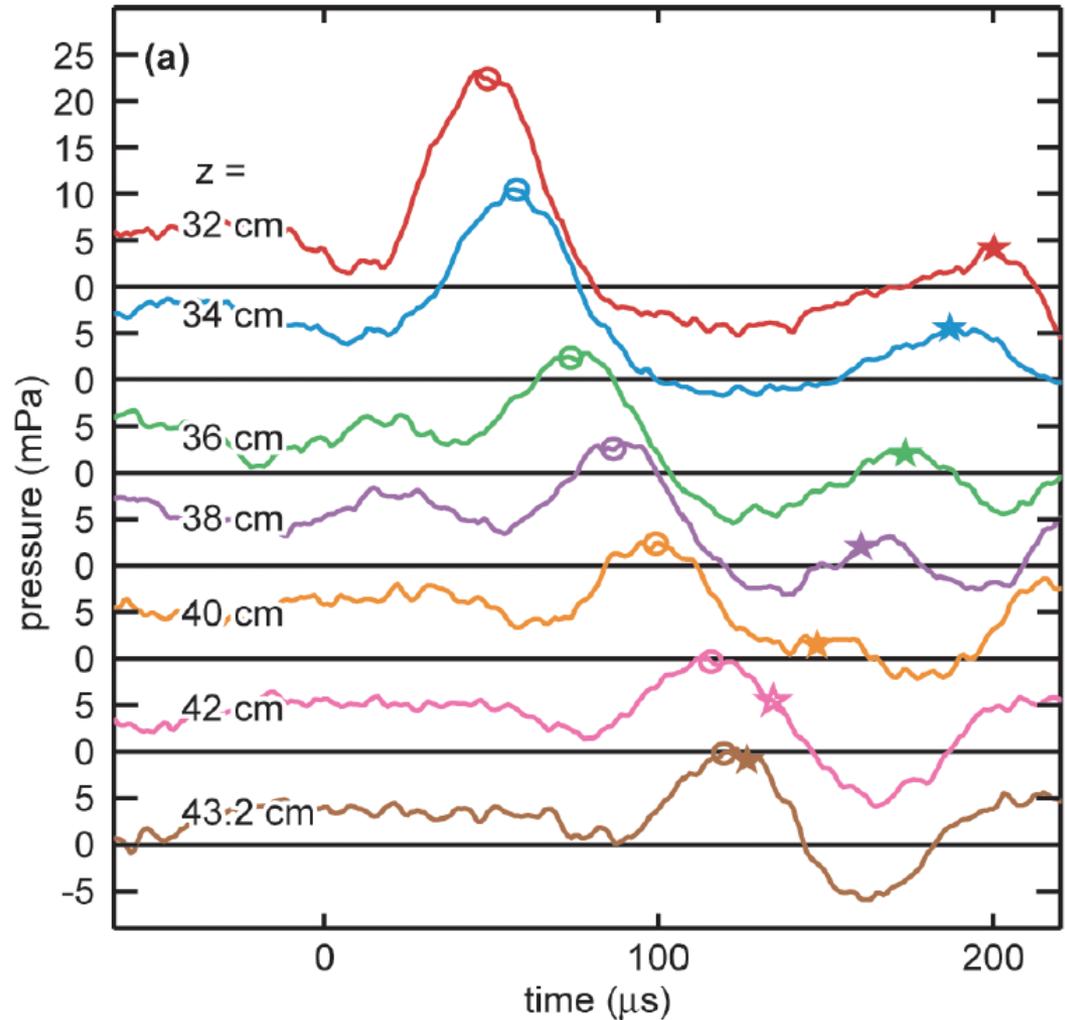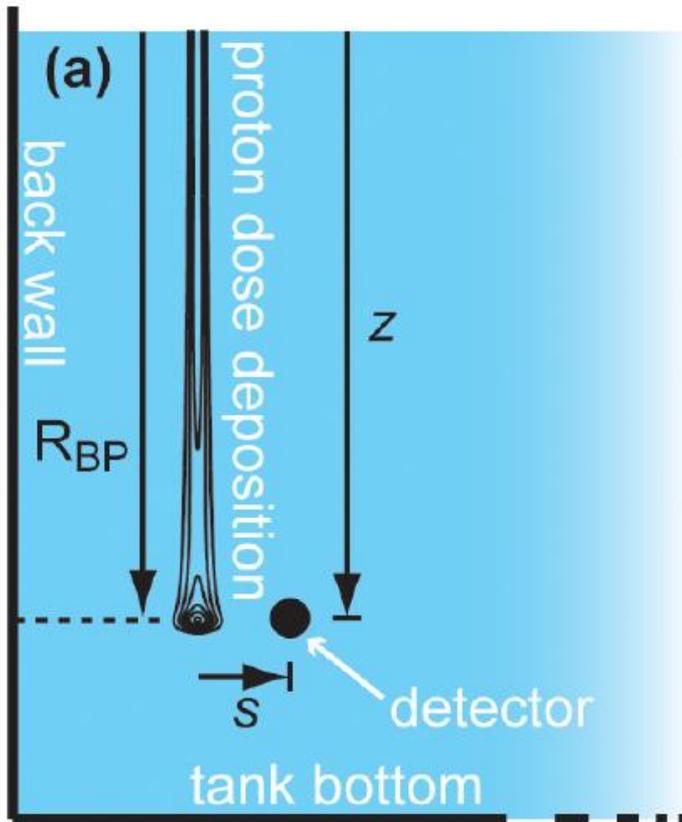
Jones et al., Med Phys 42, 7090 (2015), afternoon session

The ideal range "sensor" – requirements:

- Detect range with ~ 1 mm accuracy

- Short response time

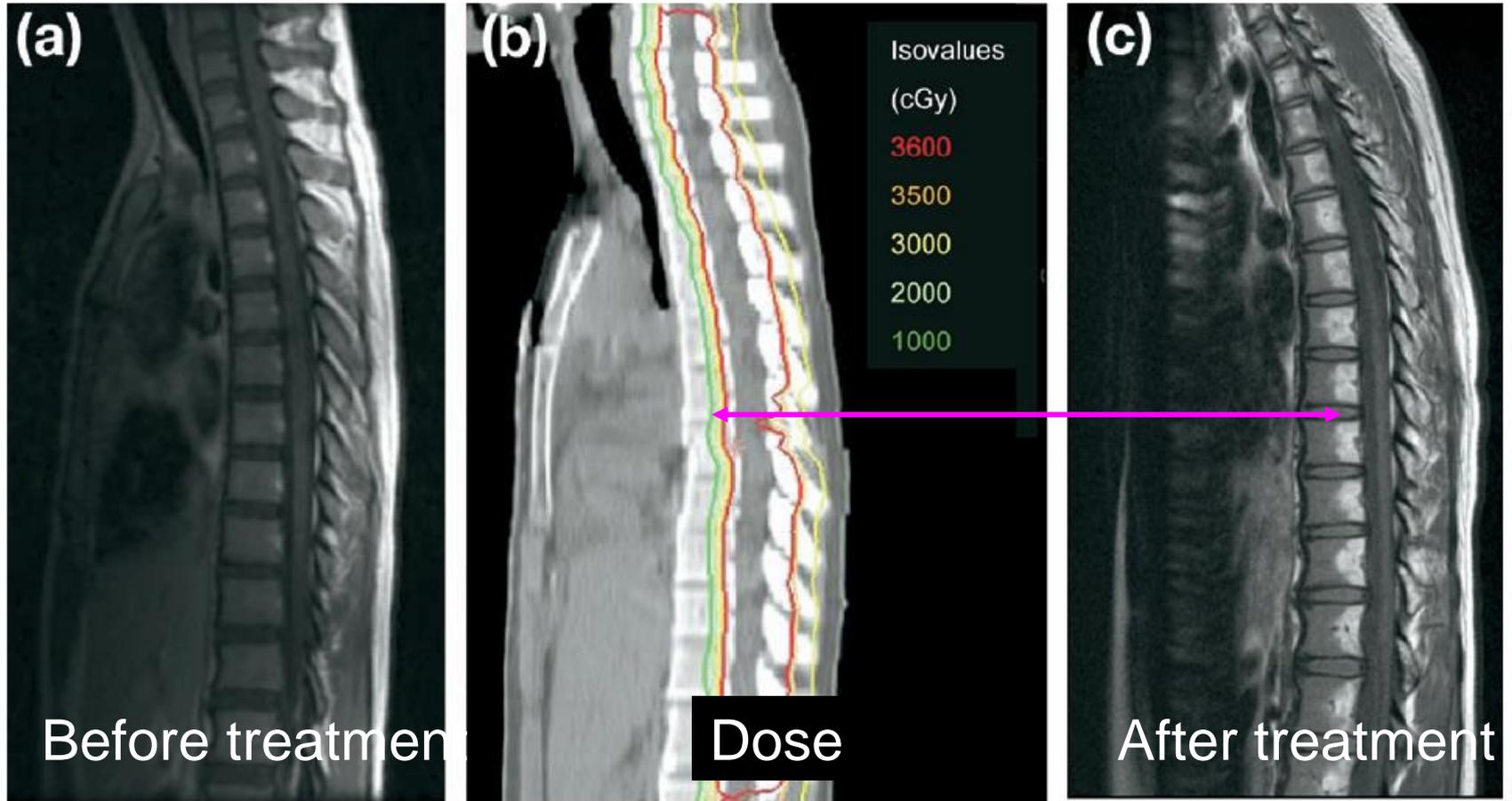- Low dose (< 1 Gy)

- In the patient

- Relative to patient anatomy

Comparison of techniques

	PET	Prompt γ	Acoustic	MRI
1 mm accuracy	(✓)	(✓)	(✗)	✓
Response time	minutes	pico seconds	milli seconds	days
Low dose	1 Gy	1 Gy	1 Gy	5-20 Gy
In vivo	✓	(✓)	(✗) one in 1995	(✓) bone, liver
Patient anatomy	(✓) (PET/CT)	✗	✗	✓

Imaging for online control of particle therapy:
A control loop approach

Measure
proton range
in the patient

Fine-tune
treatment
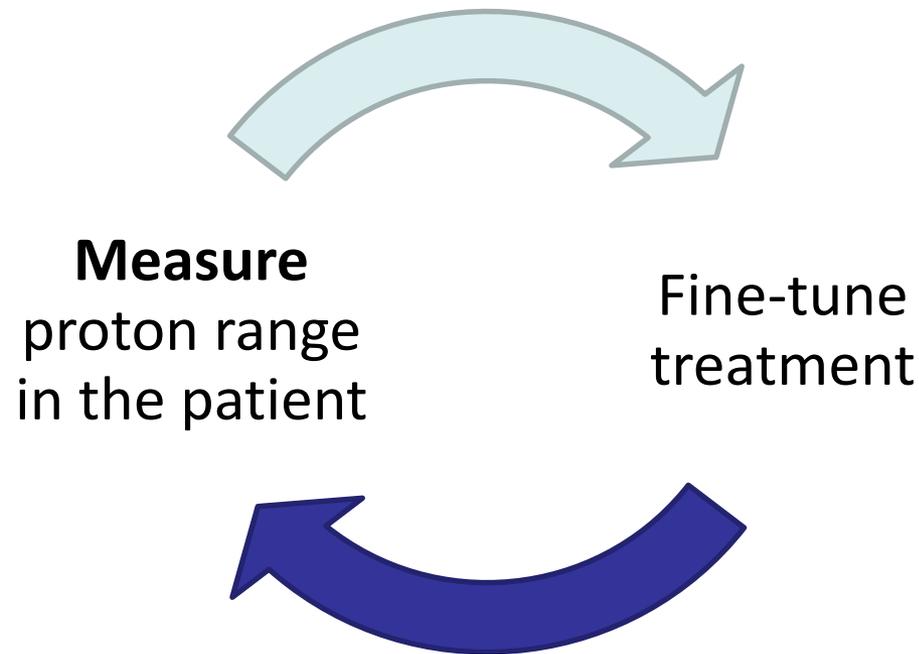
MRI scan before and after treatment

Before treatment

Dose

Isovalues
(cGy)
3600
3500
3000
2000
1000
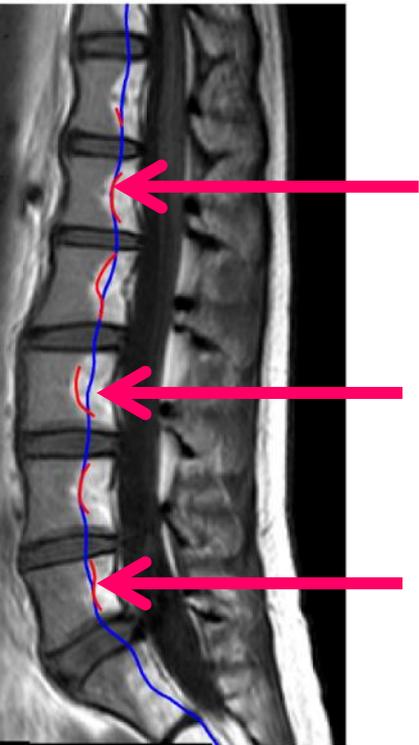
After treatment

Krejcarek, Yock, et al.
IJROBP 2007;68(3):646-649

Biology: Bone marrow changes Visible in MRI

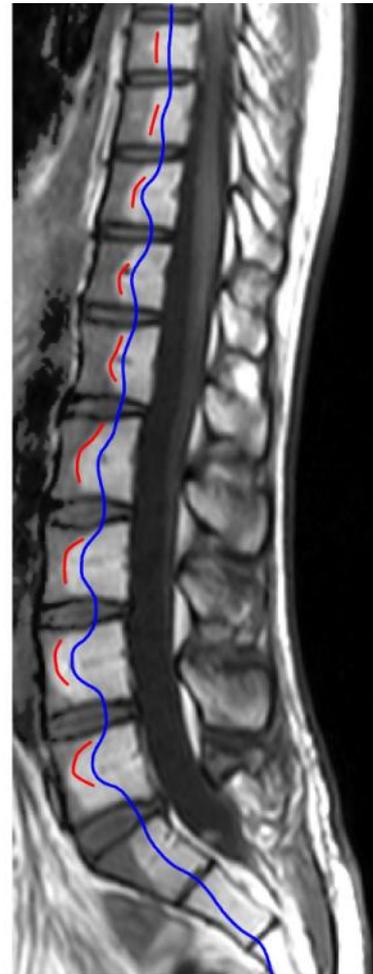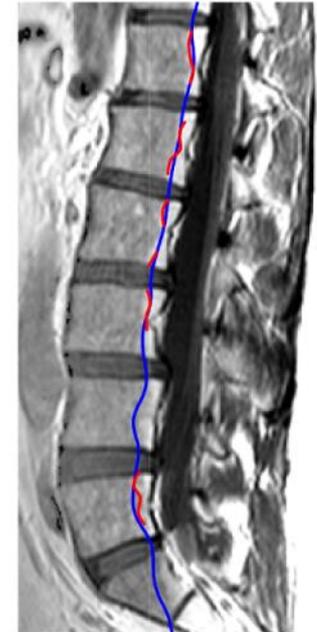planned 50% isodose
MRI 50% isodose

0 1 2 3cm
Pt. 1, 36 Gy (RBE)

0 1 2 3cm
Pt. 5, 50.4 Gy (RBE)
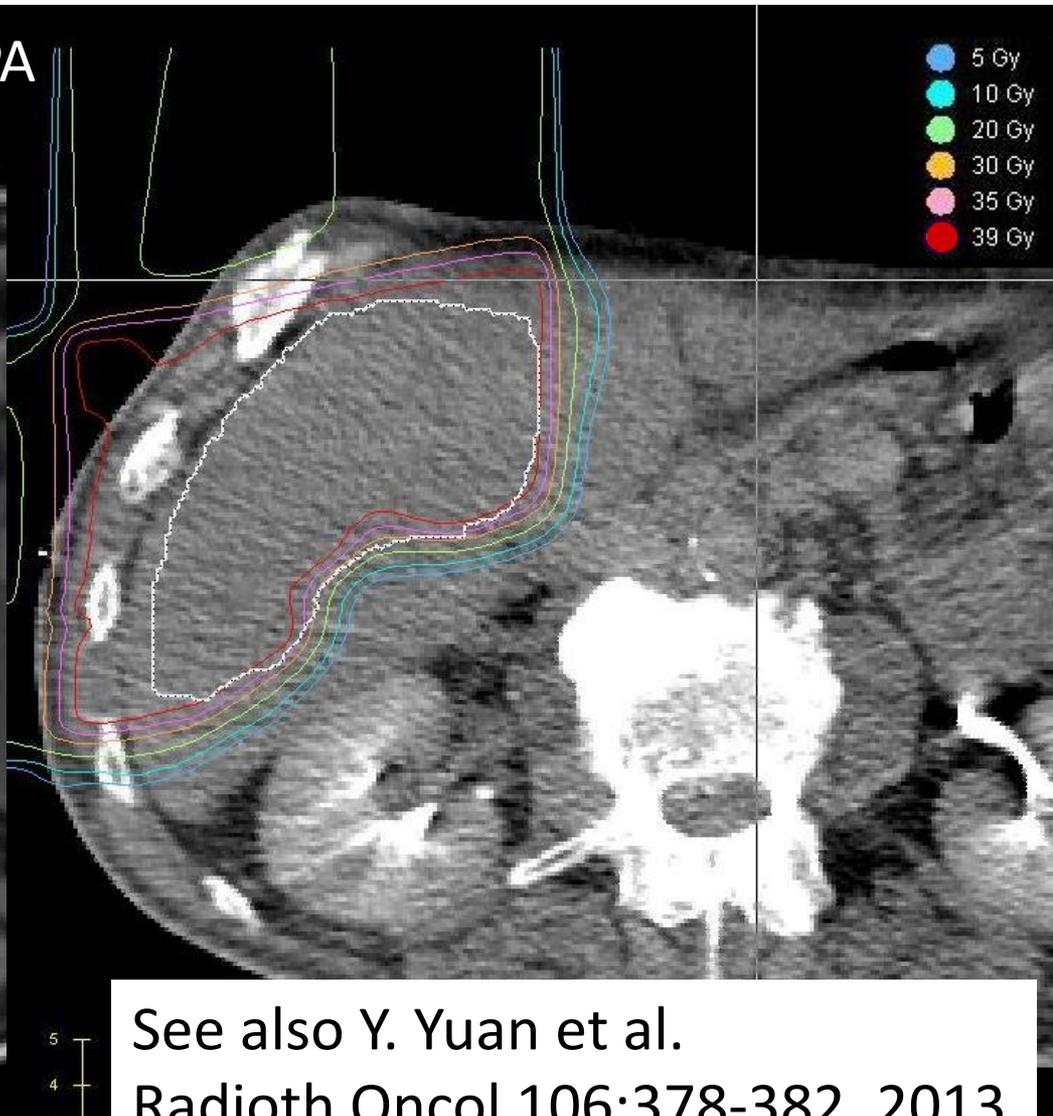
0 1 2 3cm
Pt. 6, 36 Gy (RBE)

0 1 2 3cm
Pt. 10, 36 Gy (RBE)

Gensheimer et al., Red Journal 78(1):268-275, 2010
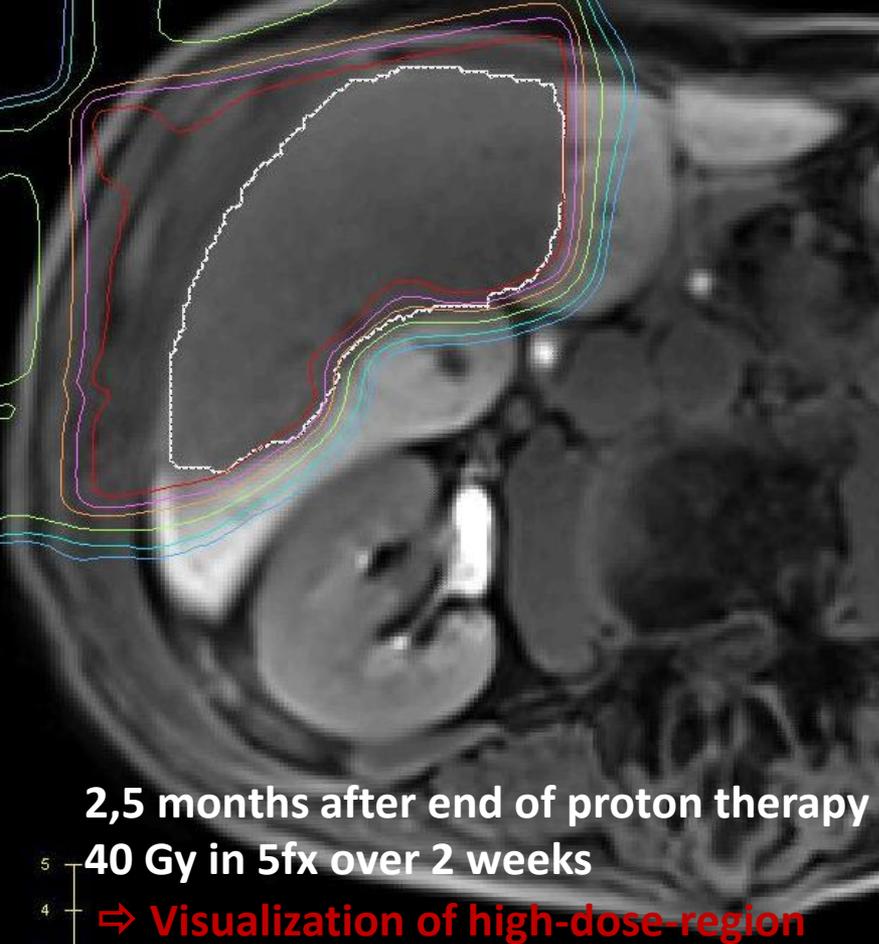
Biology: Focal liver reaction
Visible in contrast enhanced MRI

MRI contrast agent : Gd-EOB-DTPA
("Eovist", "Primovist")

5 Gy
10 Gy
20 Gy
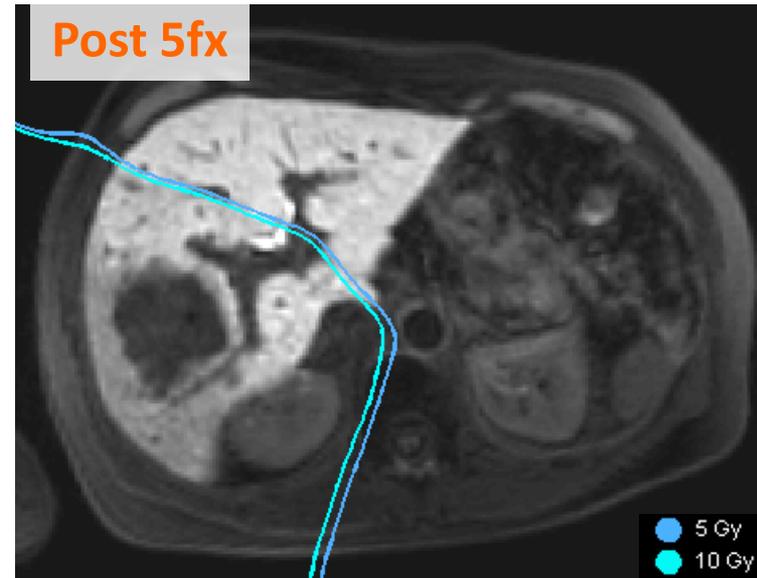30 Gy
35 Gy
39 Gy

**2,5 months after end of proton therapy
40 Gy in 5fx over 2 weeks
⇨ Visualization of high-dose-region**

See also Y. Yuan et al.
Radioth Oncol 106:378-382, 2013

Patient #5

Post 3fx

Post 5fx

5 Gy
10 Gy
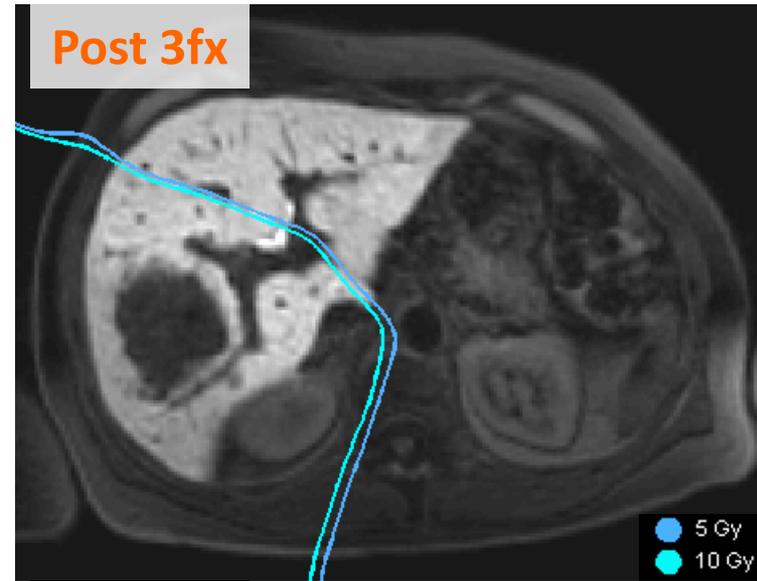
Difference Image (Post 5fx - Post 3fx)

Dose-correlated changes visible about 10-12 days after start of treatment!

5 Gy
10 Gy