Proton radiography in proton therapy treatment

Aleksandra K. Biegun

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a.k.biegun@rug.nl

university of groningen

kvi - center for advanced radiation technology

A.K. Biegun
E.R. van der Graaf
S. Brandenburg

Graduate School of Medicine
OSAKA UNIVERSITY

J. Takatsu
T. Nakaji

umcg

M-J. van Goethem

Nikhef

J. Visser
M. van Beuzekom
E.N. Koffeman

Photons vs. protons

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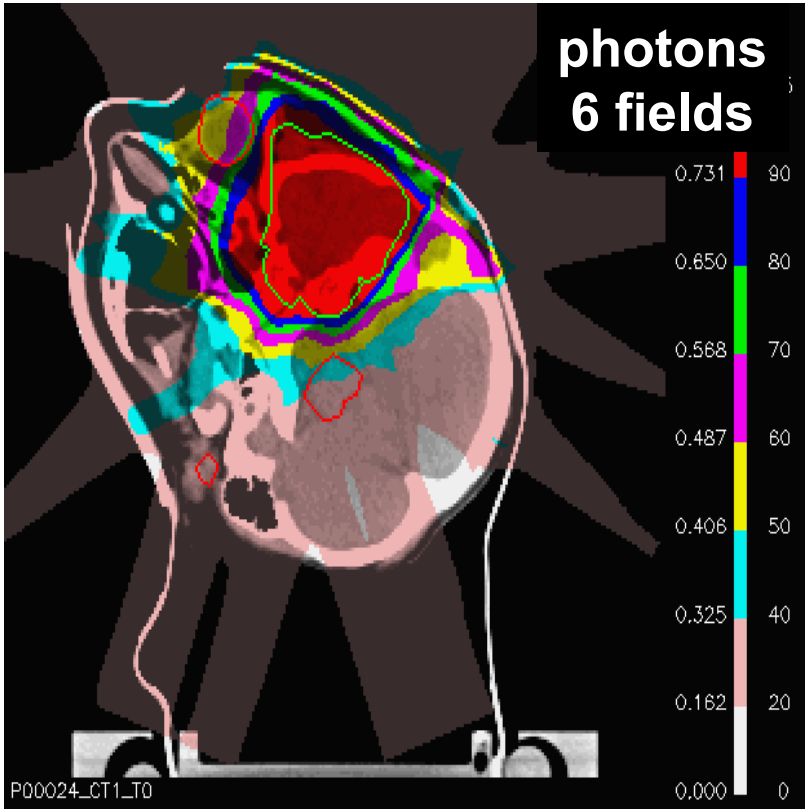

source: Tony Lomax, PSI

Photons vs. protons

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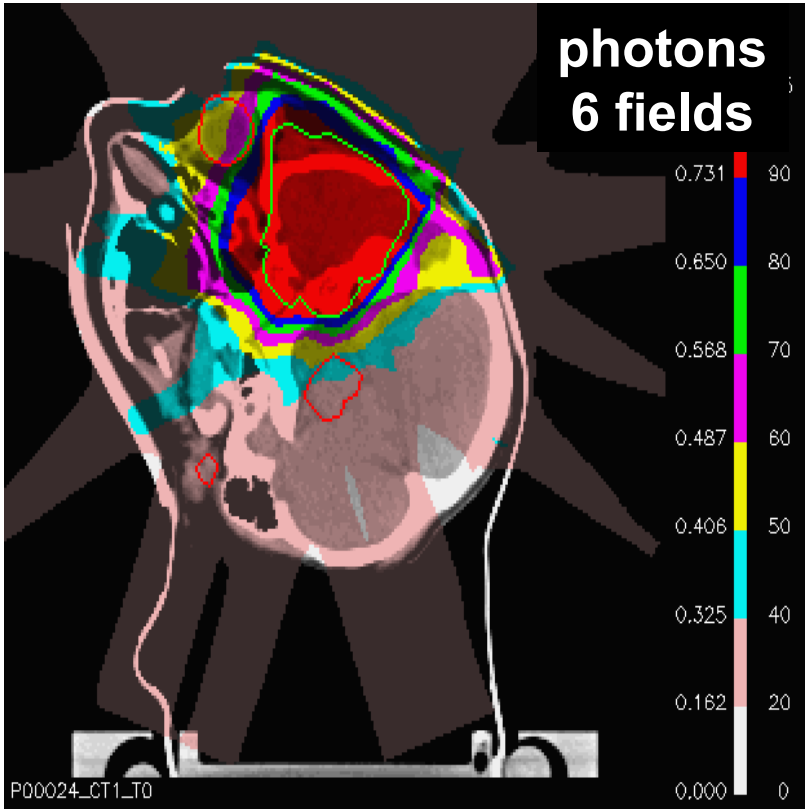

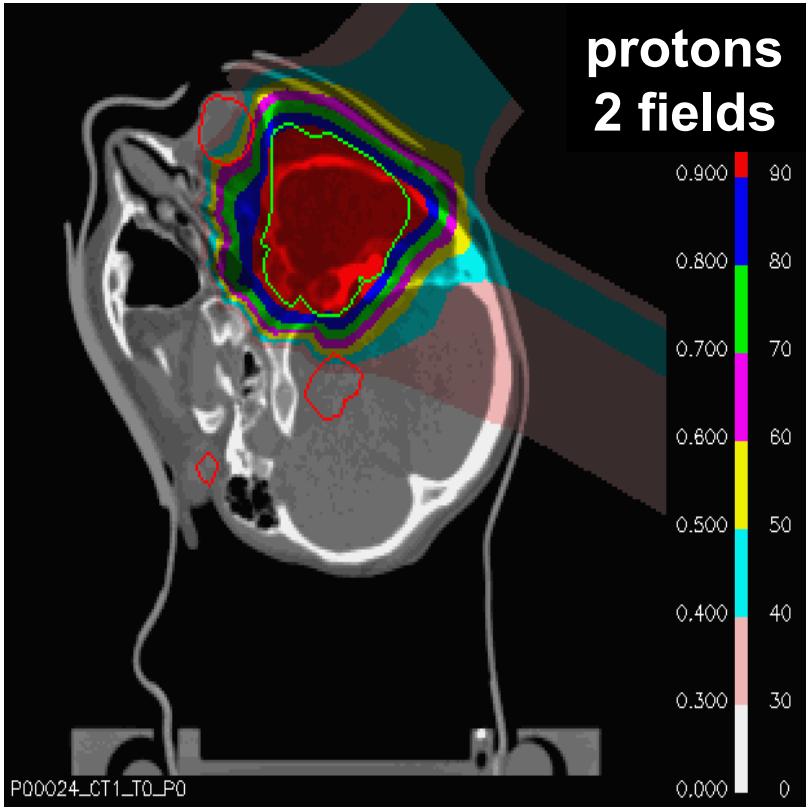

source: Tony Lomax, PSI

Integral dose to healthy tissue for protons is 6 times lower!

Proton therapy work flow

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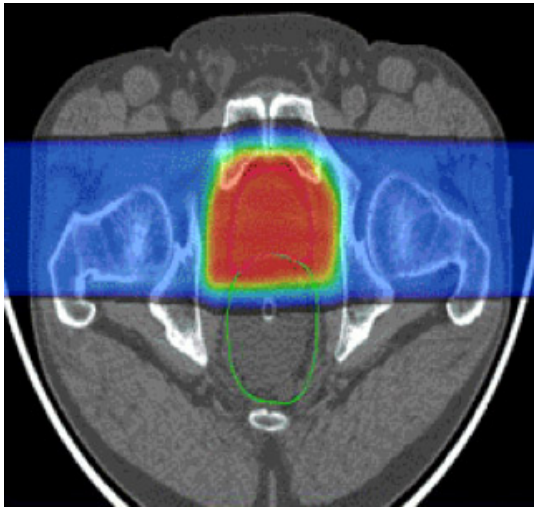
CT scan

$$HU = 1000\,\frac{\mu - \mu_{water}}{\mu_{water}}$$

Translation

3D map of proton stopping powers (PSP)

Treatment planning



Treatment

Treatment verification

Proton therapy work flow

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$$HU = 1000\,\frac{\mu - \mu_{water}}{\mu_{water}}$$

Knowledge of patient

Translation

3D map of proton stopping powers (PSP)

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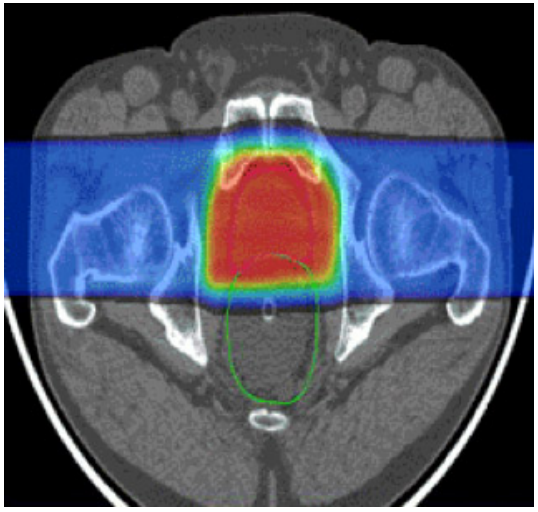

Treatment

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Knowledge of patient in proton therapy treatment

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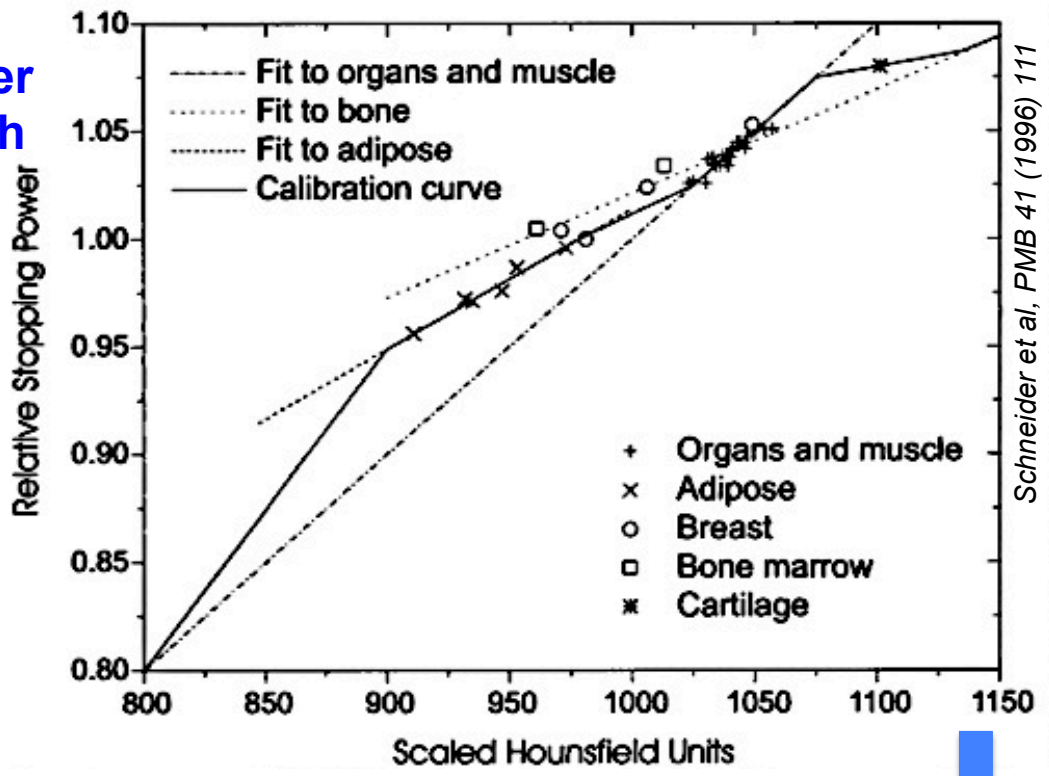
Schneider approach



3D map of Proton Stopping Powers (PSP)

- Conversion HU to stopping power is NOT unique
- Systematic uncertainties of 3-4% or more require larger than necessary irradiation safety margins around the tumor

… And the consequence…

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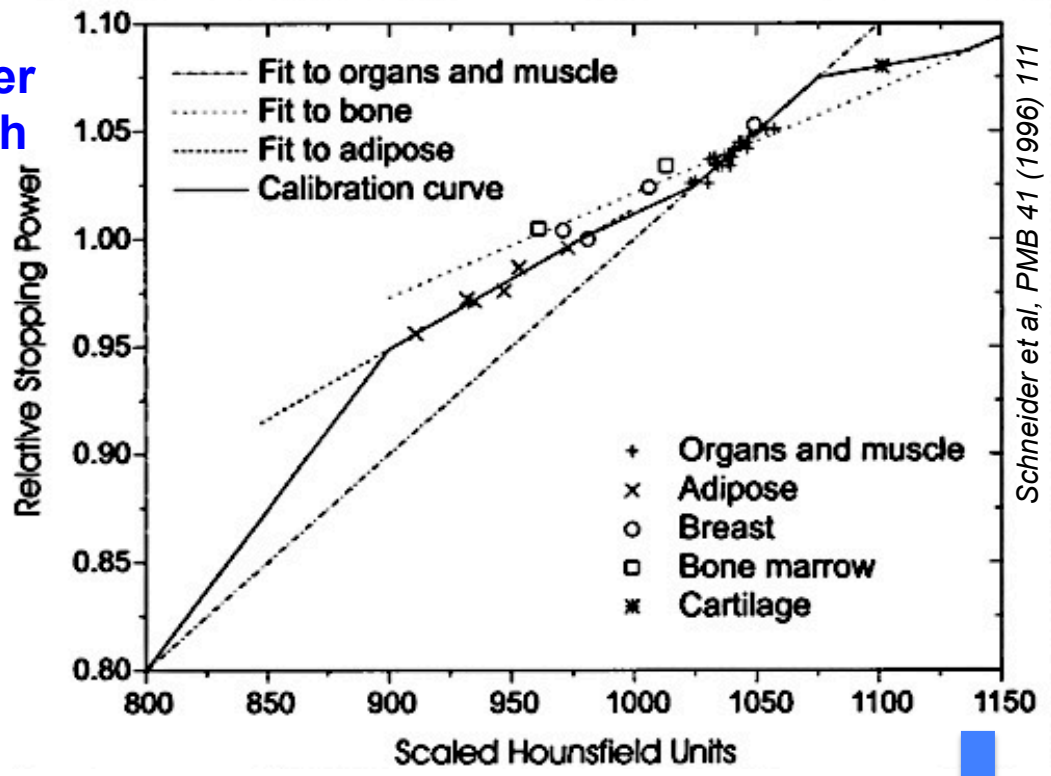
CT scan

$$HU = 1000\,\frac{\mu - \mu_{water}}{\mu_{water}}$$

Schneider approach



3D map of Proton Stopping Powers (PSP)

- Conversion HU to stopping power is NOT unique
- Systematic uncertainties of 3-4% or more require larger than necessary irradiation safety margins around the tumor

Leads to increased dose in healthy tissues

Why proton radiography?

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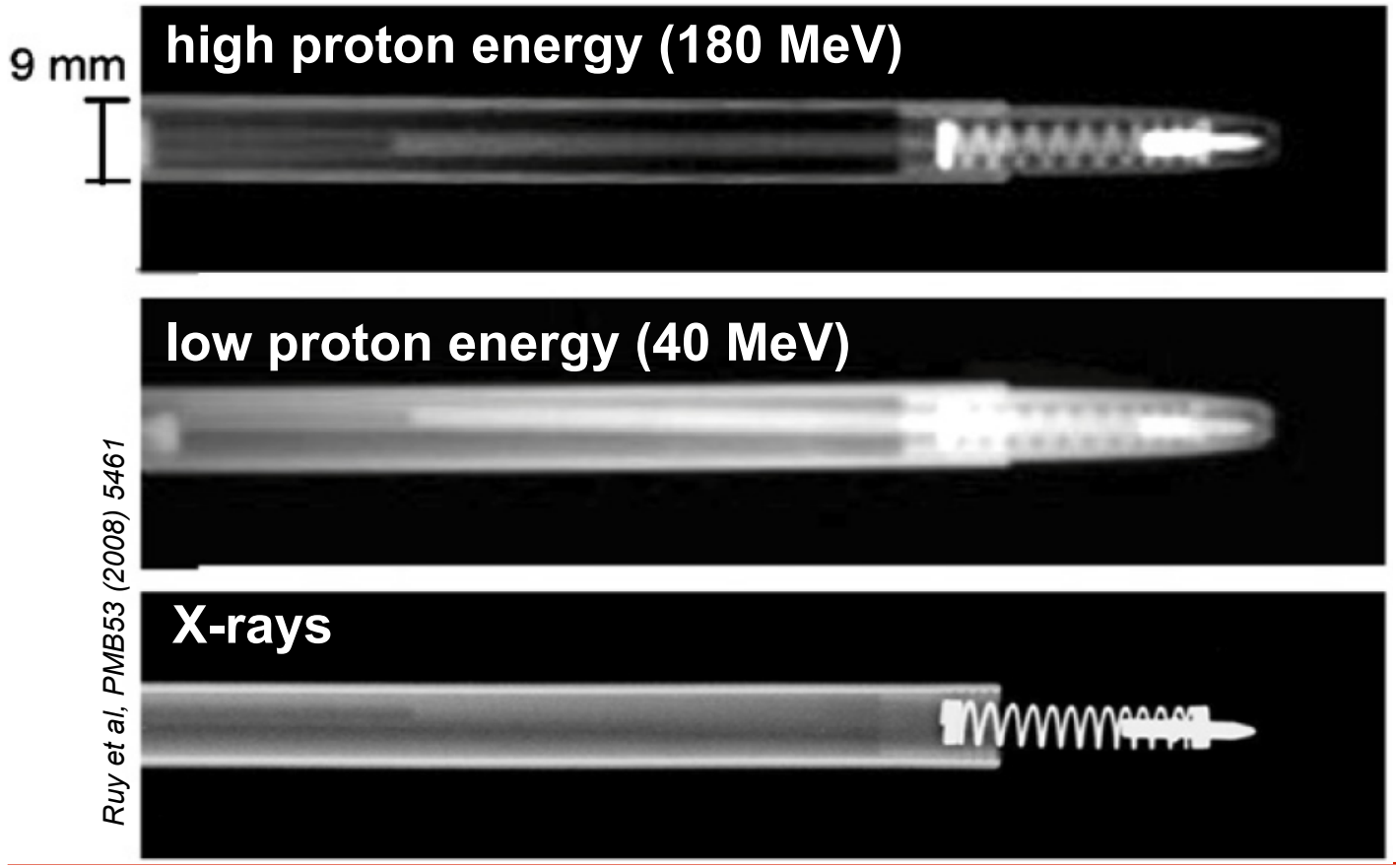
- High resolving power for proton beam (centerpiece of the pen visible)
- X-ray produces a clearer image of the spring,
  but density resolution for the centerpiece is not high



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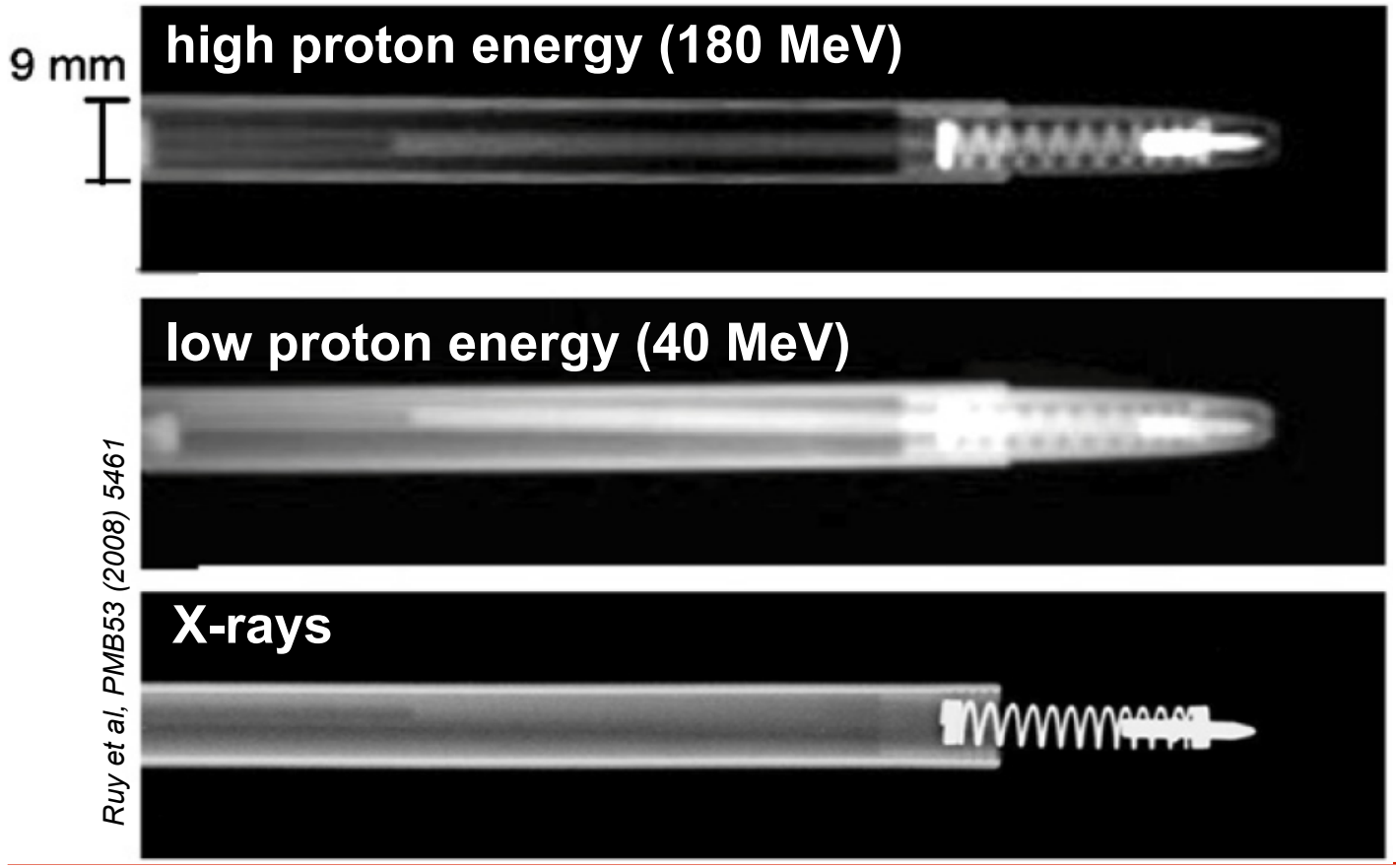

Protons
help
to improve
determination
of energy losses
in “soft material”

What is proton radiography?

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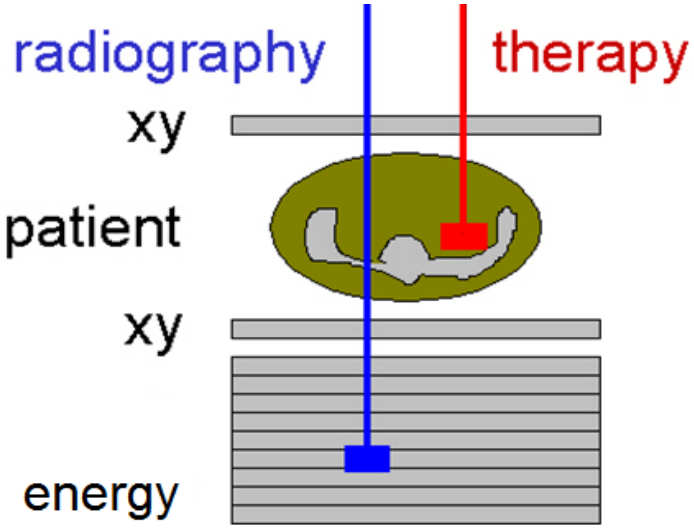
- Proton beam energy higher than the therapeutic energies, i.e. protons pass through the patient

- Position detectors: before and after the patient
- Range / residual energy detector: after the patient



Proton radiography: Geant4 MC simulations

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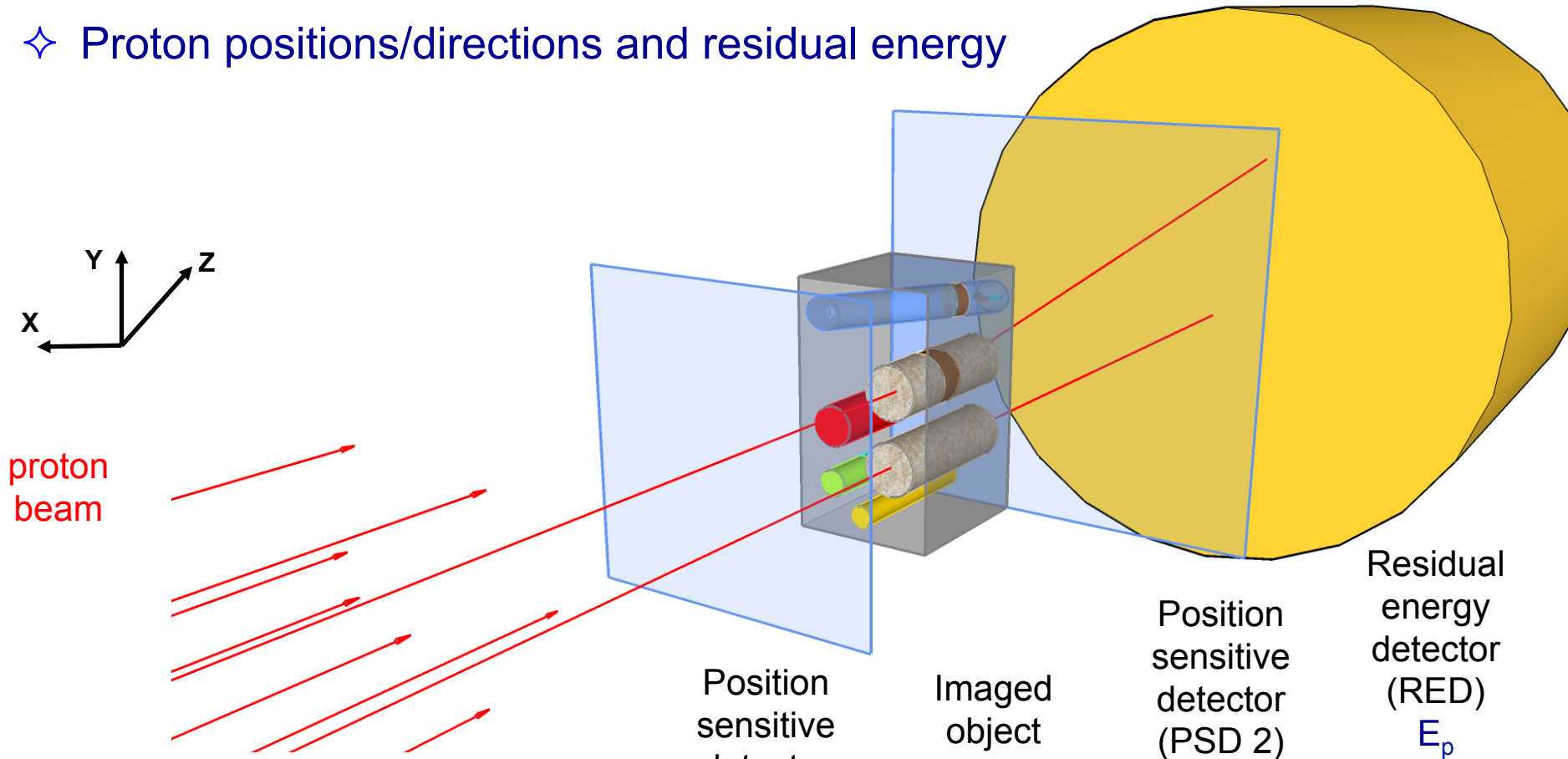
- $50*10^6$ protons generated, scattered beam, E_p=150 MeV
- Proton positions/directions and residual energy



Complex phantom (54 x 94 x 60 mm^3)

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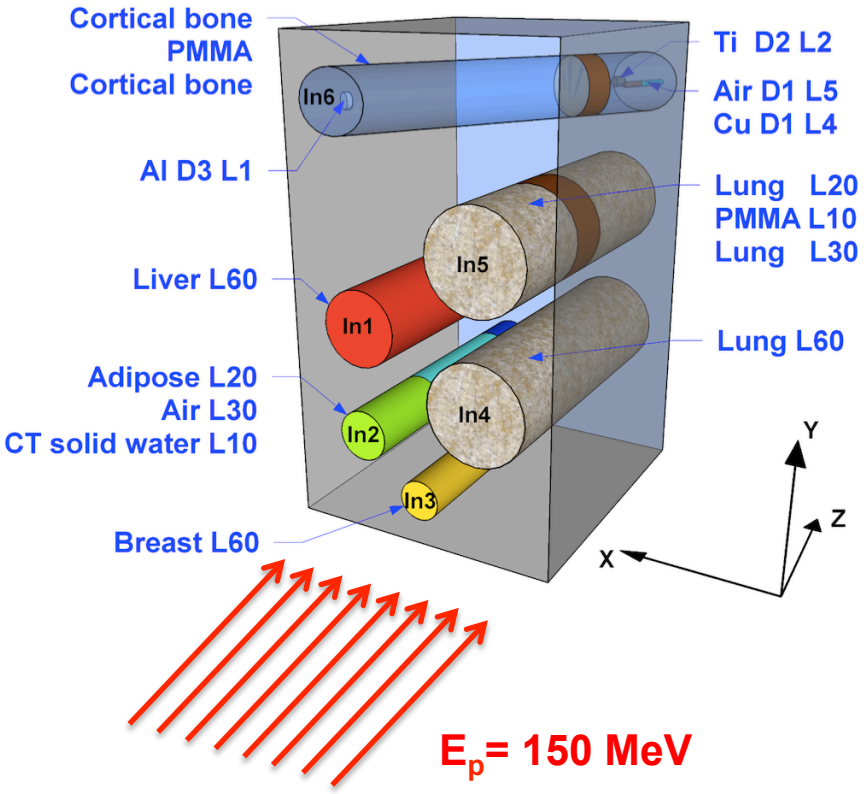
- Few materials on proton beam
- 11 various materials, including 5 tissue surrogates



Phantom material	Physical density (g/cm^3)	Phantom material	Physical density (g/cm^3)
Cortical bone*	1.820	Breast*	0.981
PMMA	1.180	Lung*	0.428
Liver*	1.095	Al	2.702
Adipose (fat)*	0.946	Ti	4.519
Air	0.0012	Cu	8.920
CT solid water	1.045	* Tissue-equivalent materials	

https://www.sunnuclear.com/documents/datasheets/gammex/ct_electron_density_phantom.pdf

Proton scattering angle, θ

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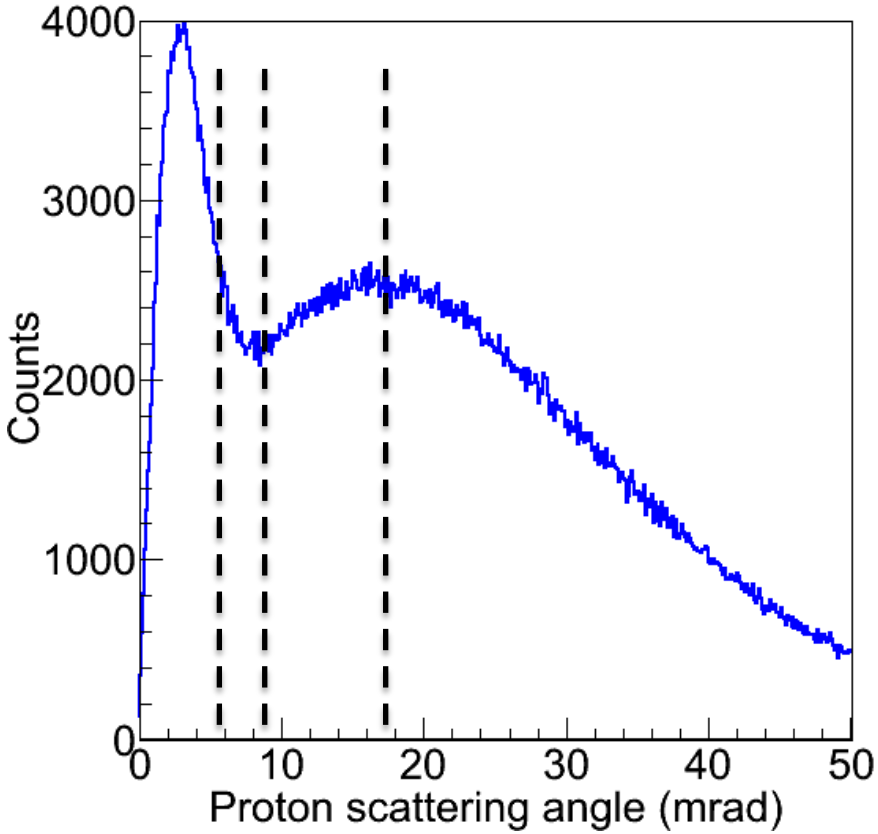

$$\theta(rad) = \cos^{-1}\left(\frac{\vec{p}_0\,\vec{p}_3}{\left|\vec{p}_0\right|\left|\vec{p}_3\right|}\right)$$

$\vec{p}_0, \vec{p}_3$ – proton momenta in the source and energy detector, respectively

Geant4 simulations

Energy loss radiographs: $\Delta E = E_{beam} - E_{residual}$

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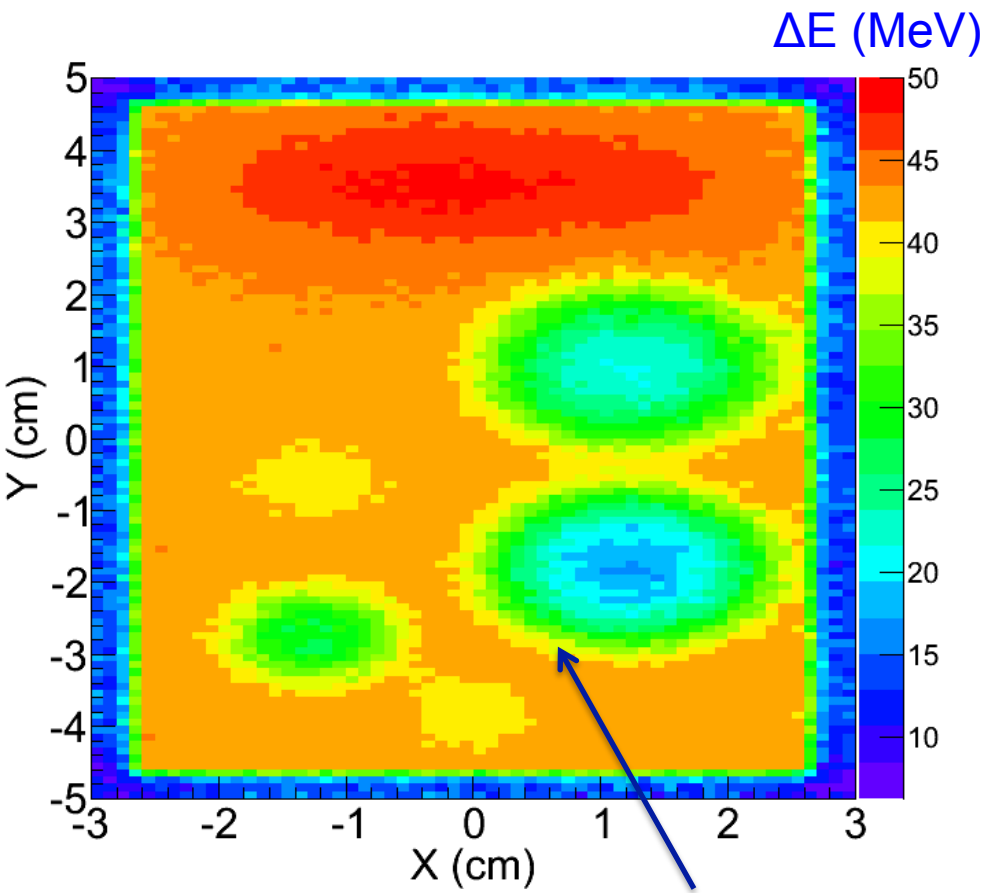
- Protons that passed through all 3 detectors are considered



A.K. Biegun et al, JINST 11 (2016) C12015

Geant4 simulations

Energy loss radiographs: $\Delta E = E_{beam} - E_{residual}$

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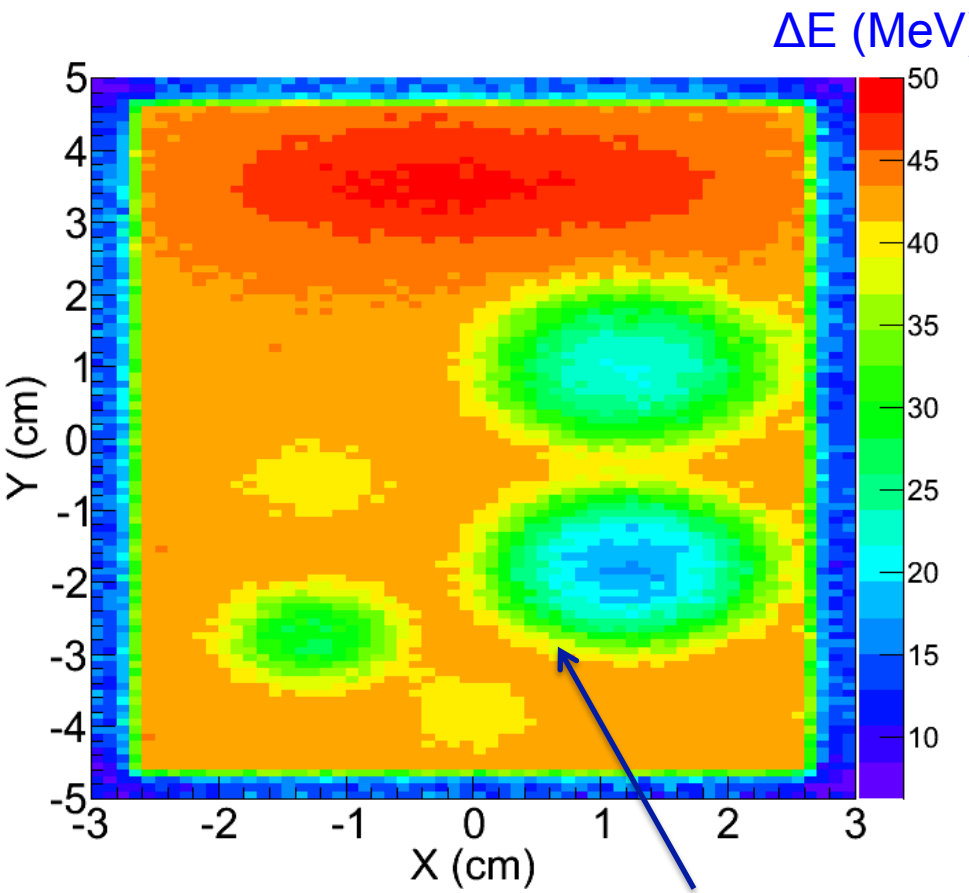
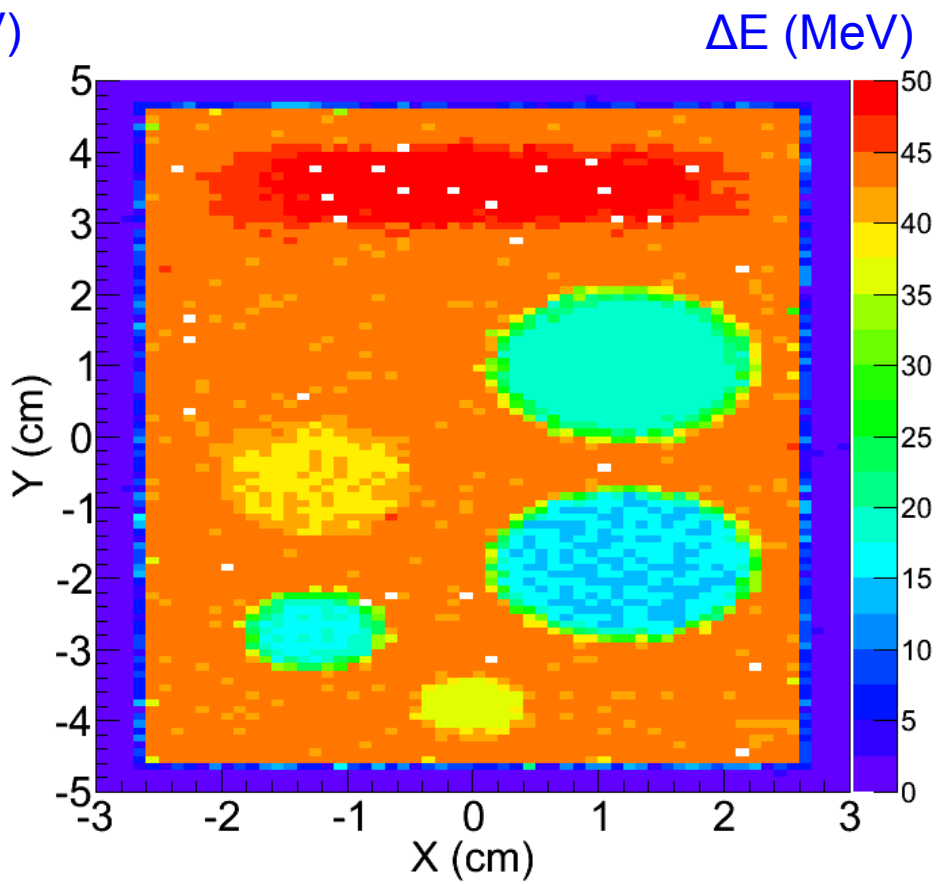
- Protons that passed through all 3 detectors are considered
- Protons with maximum scattering angle $\theta < 5.2$ mrad





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Statistics @ E_p = 150 MeV

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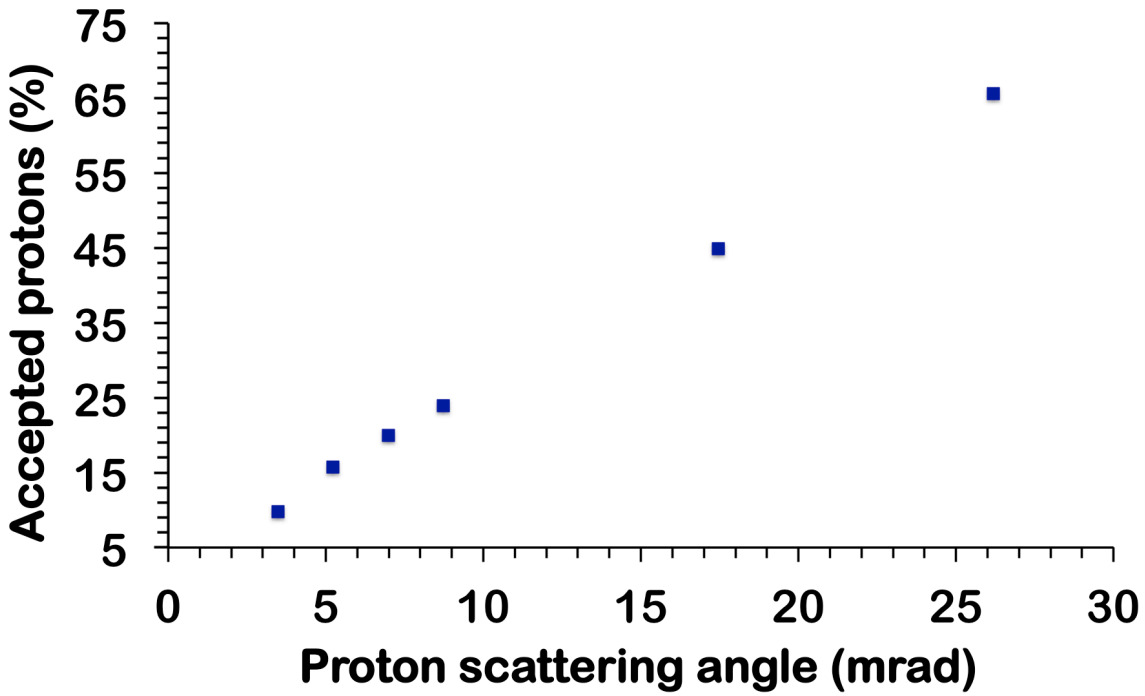

θ (mrad)	Accepted protons (%)
26.2	65.6
17.4	44.9
8.7	23.9
6.7	20.0
5.2	15.7
3.5	9.8

A.K. Biegun et al, JINST 11 (2016) C12015

Geant4 simulations

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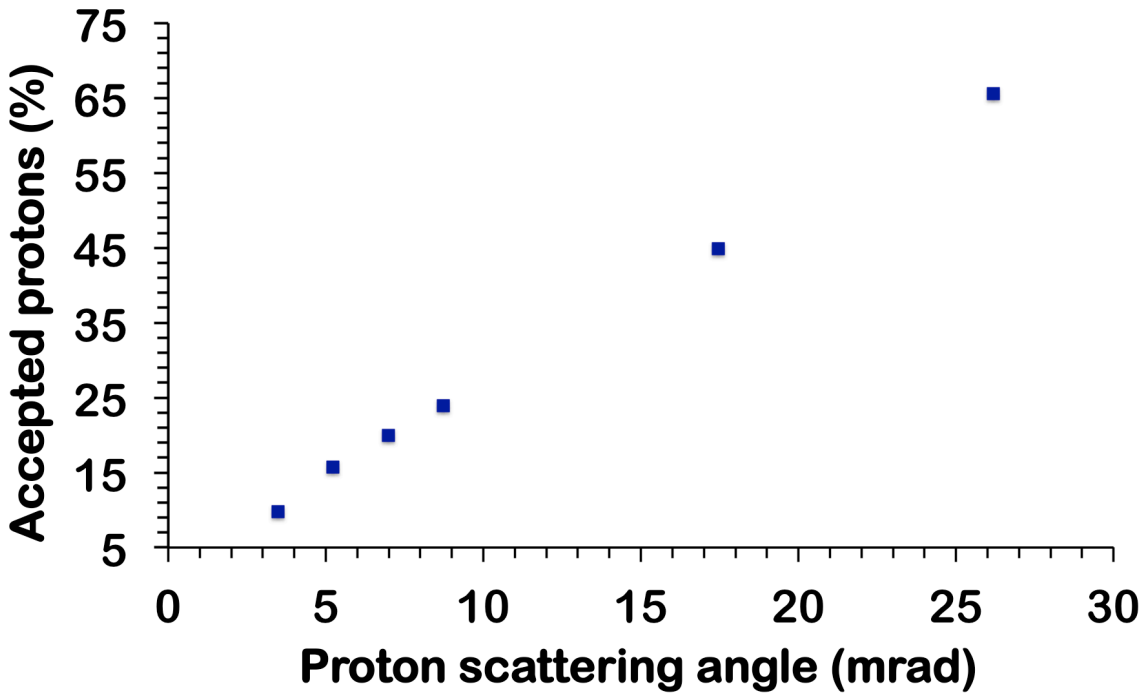

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Significant number of protons (>70%) simulated at E_p=150 MeV is eliminated at θ < 8.7 mrad

A.K. Biegun et al, JINST 11 (2016) C12015

Geant4 simulations

Proton radiography @KVI–CART: Exp setup'15

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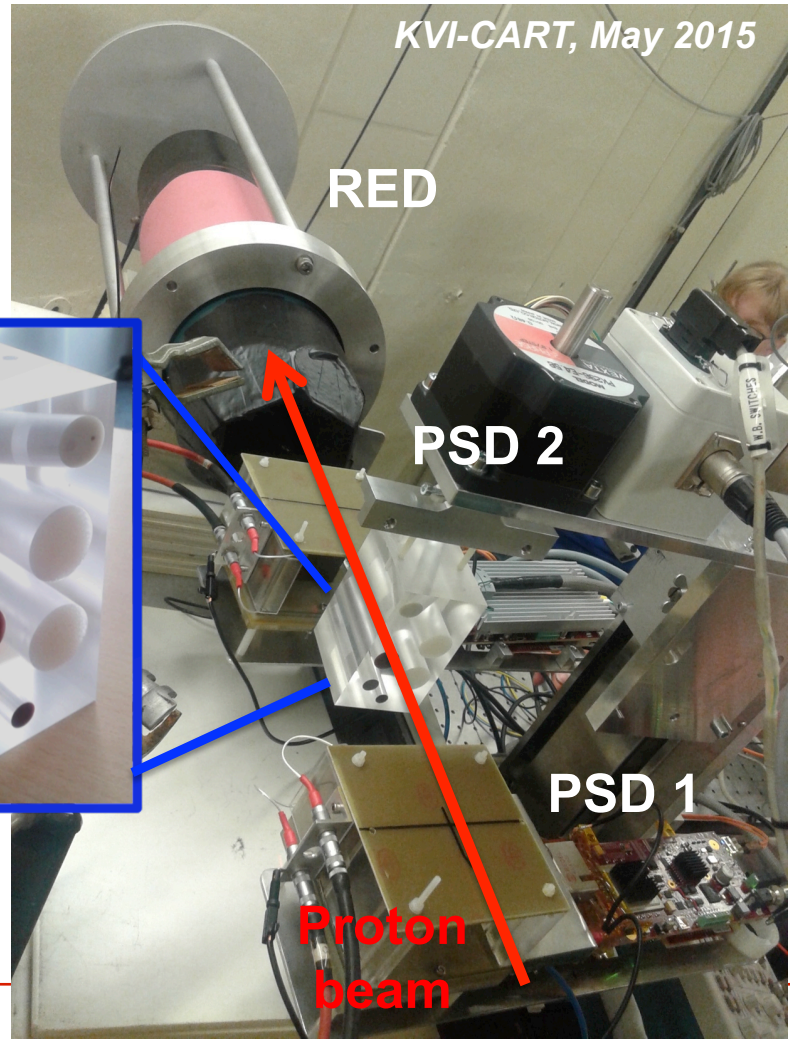
Collaboration with J. Visser, M. van Beuzekom, E.N. Koffeman

Nikhef

- **Tracking detectors**:
  - Timepix3-based TPC
  - Count rate ~20 kHz
- **Energy**: BaF_2 scintillator
- **Proton beam energy**:
  - E_p = 150 MeV

  AGOR @KVI-CART
  Groningen (NL)

Count rate not high enough as required in clinics



Energy loss reconstruction: Sims vs. Exp'2015

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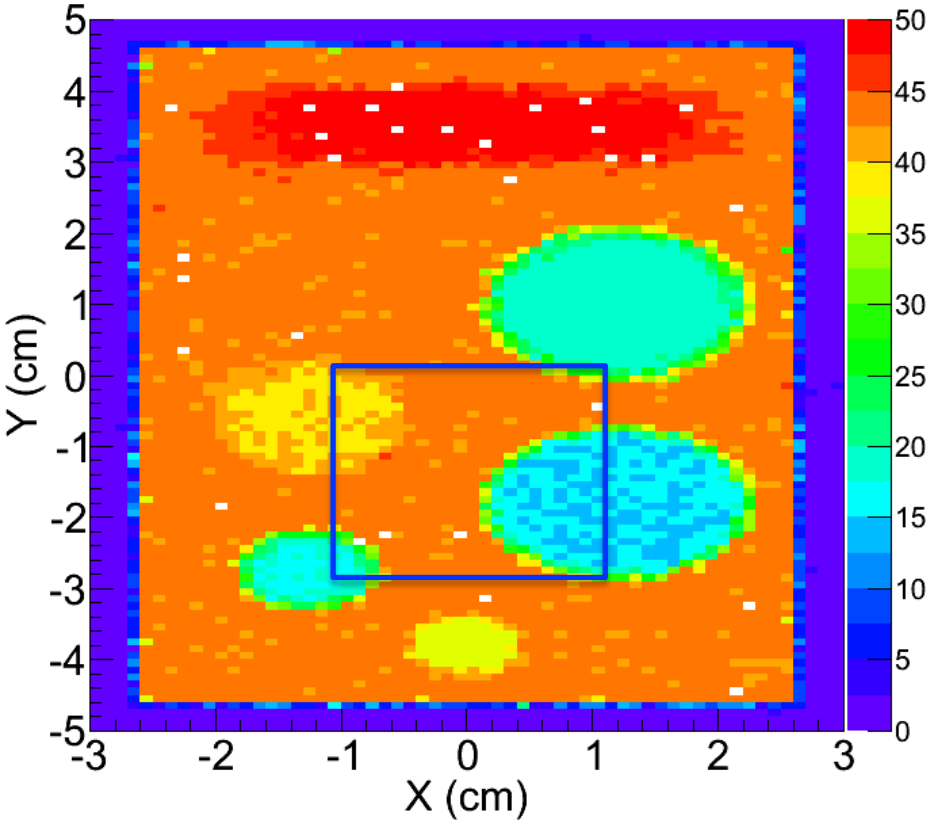
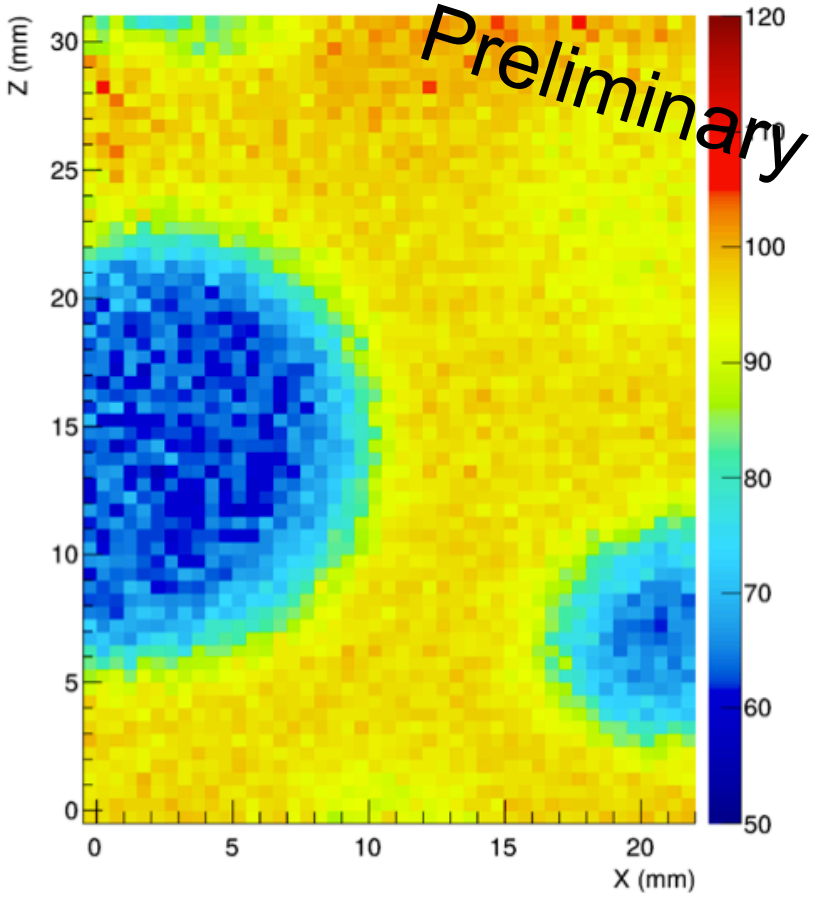
✧ θ < 5.2 mrad



ΔE (arb. unit)



Master thesis: M. Dietze with J. Visser, M. van Beuzekom, E. Koffeman (Nikhef June 2016)

✧ Phantom only partially covered by Timepix3-based TPCs (3.0 x 3.0 cm^2)

Energy loss reconstruction: Sims vs. Exp'2015

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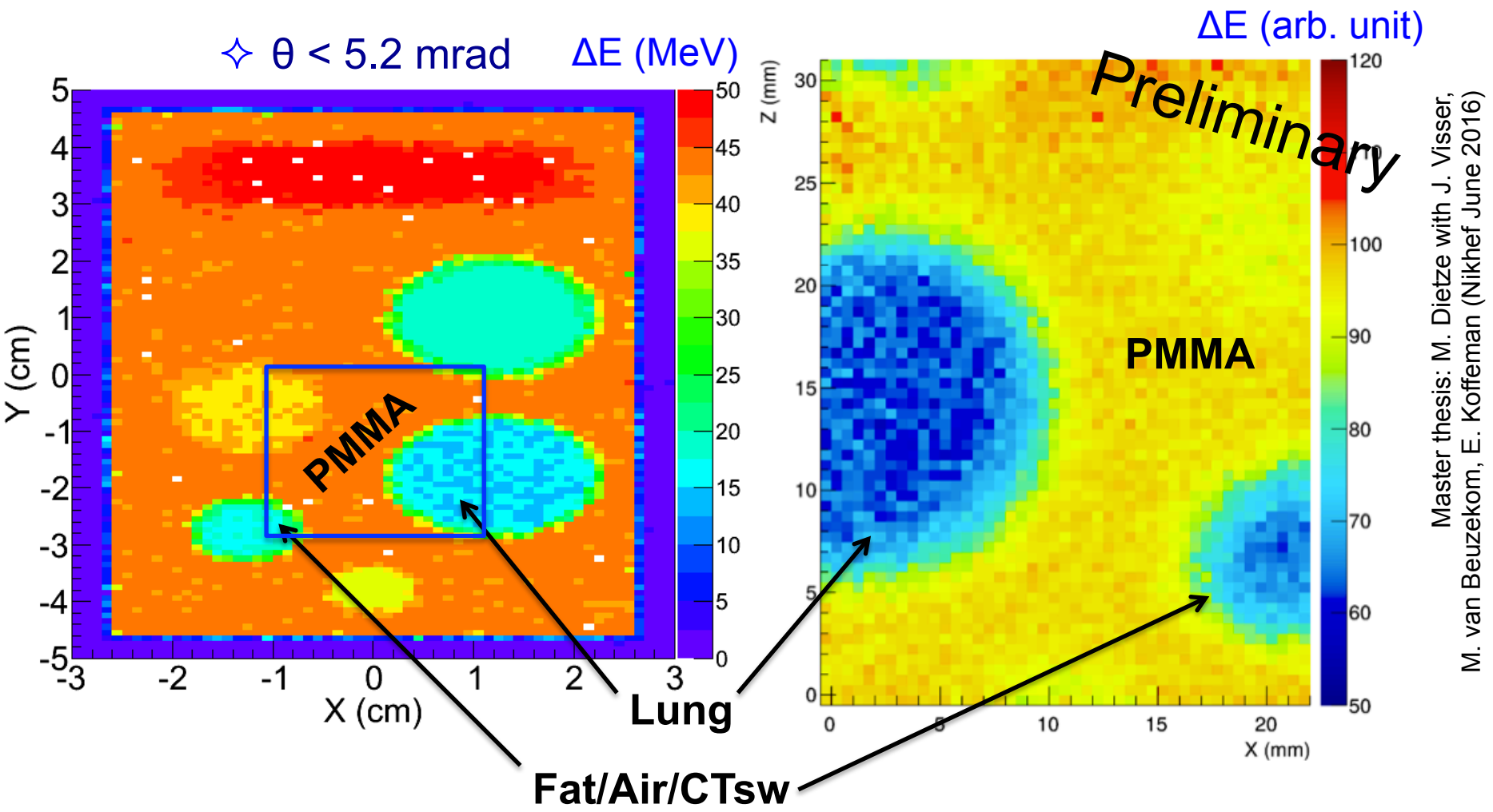

Simulations and experimental results comparable

Scattering angle reconstruction: Exp'2015

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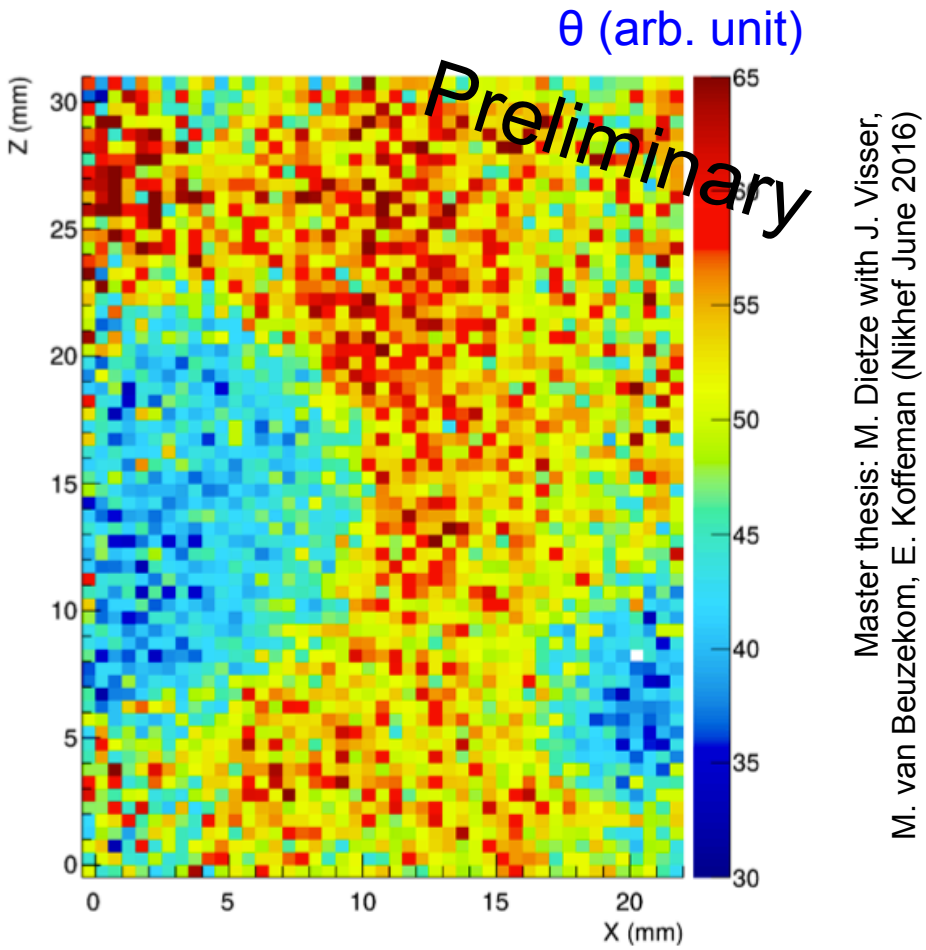

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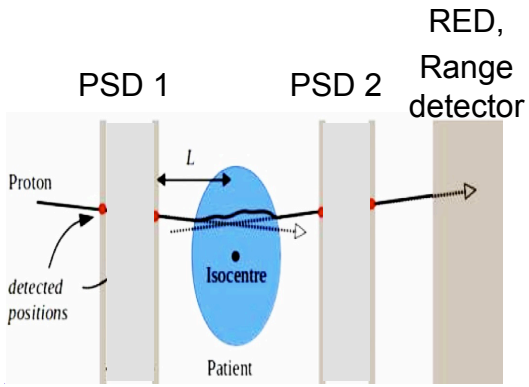
Scattering angle well reconstructed, but more statistics needed

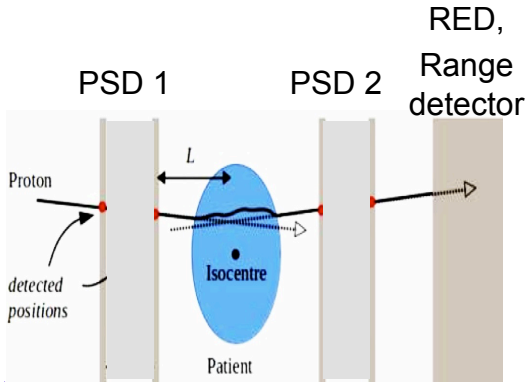
Current systems



Group	Year	PSDs (# of units)	RED/Range Detector	Rate (Hz)	Imaging device
PSI	2005	x-y Sci-Fi (2+2)	Plastic scintillator telescope	1 M	pRad
LLU/UCSC/ NIU	2013	x-y SiSDs (2+2)	CsI (Tl)	15 k	pCT
LLU/UCSC/ CSUSB	2014	x-y SiSDs (2+2)	Plastic scintillator telescope	2 M	pCT
AQUA	2013	x-y GEMs (1+1)	Plastic scintillator telescope	1 M	pRad
PRIMA I	2014	x-y SiSDs (2+2)	YAG:Ce calorimeter	10 k	pCT
PRIMA II	2014	x-y SiSDs (2+2)	YAG:Ce calorimeter	1 M	pCT
INFN	2014	x-y Sci-Fi (2+2)	x-y Sci-Fi	1 M	pCT
NIU/FNAL	2014	x-y Sci-Fi (2+2)	Plastic scintillator telescope	2 M	pCT
Niigata University	2014	x-y SiSDs (2+2)	NaI (Tl) calorimeter	5 k	pCT
PRaVDA	2015	X-u-v SiSDs (6+6)	CMOS APS telescope	1 M	pCT

G. Poludniowski et al., Br J Radiol (2015) ***88****:20150134*

Current systems



- Trend towards Si tracking detectors → very fast
- Different approaches for energy/range detectors
- Count rate close to what is required

G. Poludniowski et al., Br J Radiol (2015) ***88****:20150134*

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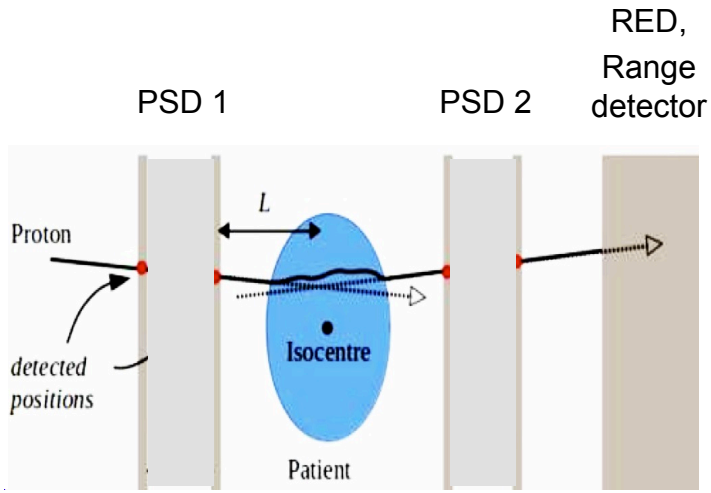
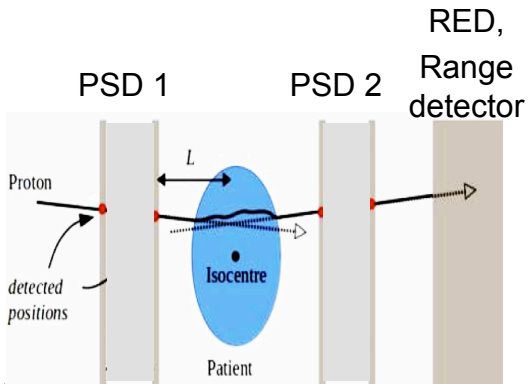
But…



- Si (Z=14, ρ=2.33 g/cm^3)
  → Multiple Coulomb Scattering already in the detector material

- Range detector does not give yet accurate enough residual energy important for proton stopping powers determination of an object

Simulations for:



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G. Poludniowski et al., Br J Radiol (2015) ***88****:20150134*

Various PSDs in proton radiography setup

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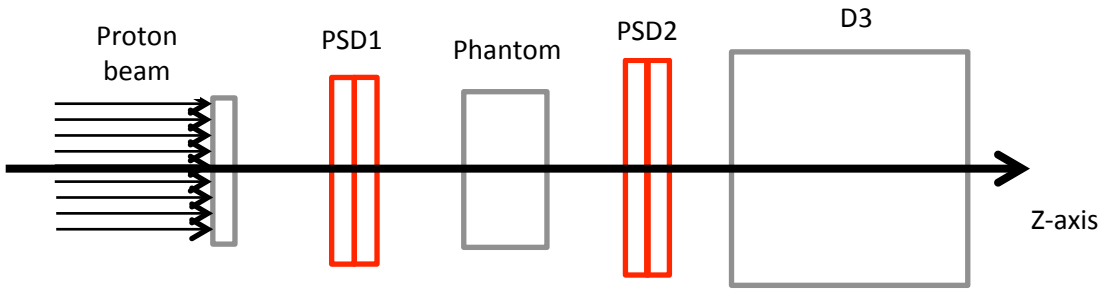
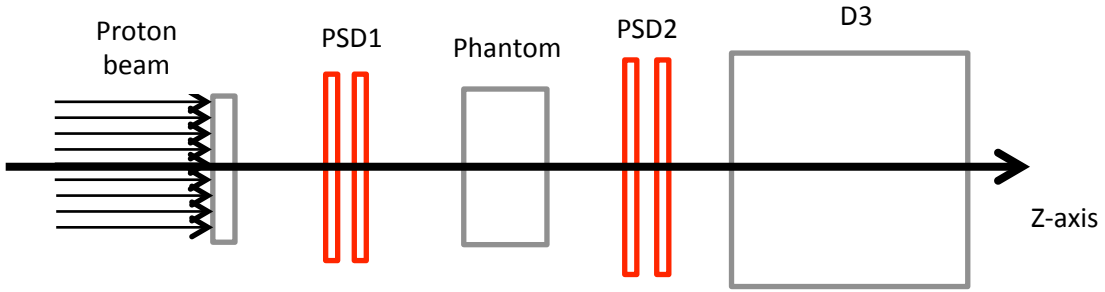
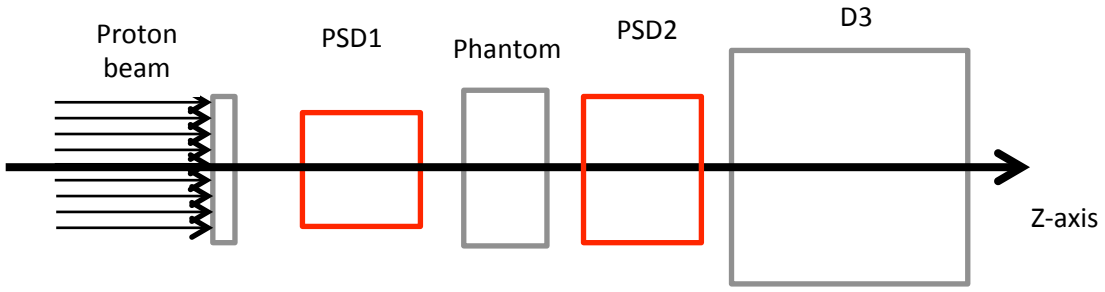


- Two plane fiber scintillating hodoscope (PSI)



- Two plane silicon strip detectors (PRIMA I)



- Time Projection Chamber (Nikhef)

Geant4 simulations

PSD = Position Sensitive Detector

PSDs parameters

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PSD detector type	Number of PSDs	Material	Material thickness (mm)	Material density (g/cm^3)	WET (mm)
Ideal	1	Air	0.001	0.0012	-
Plastic scintillator Fiber [1]	2	Bicron BCF12	4.0	1.032	4.106
Silicon strip detector [2]	2	Silicon	0.4	2.33	0.752
Gaseous TPC [3]	1	Isobutene C_4H_{10}	30	0.0025	0.394

[1] U.Schneider et al., *First proton radiography of an animal patient*, Med Phys 2014, 31 (5), 1046-1051
[2] M. Scaringella et al., *A proton computed tomography based medical imaging system*, JINS 2014, 9:C12009
[3] A.K. Biegun et al., *Proton Radiography with Timepix3-based Time Projection Chambers: Towards clinical application*, in preparation

Scattering angle θ_{12} of protons

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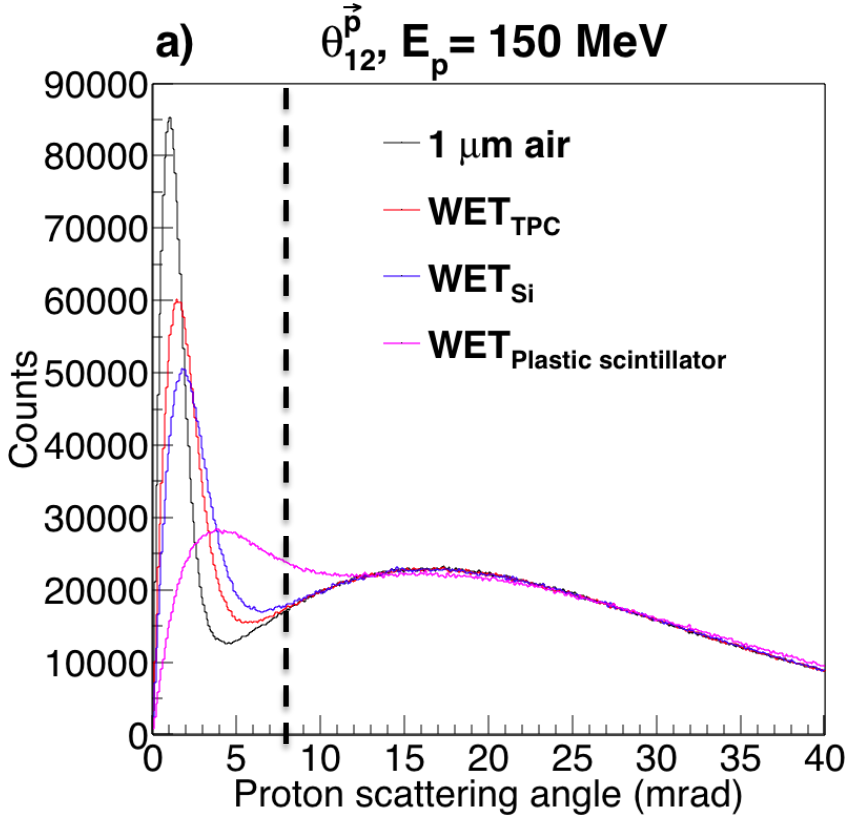
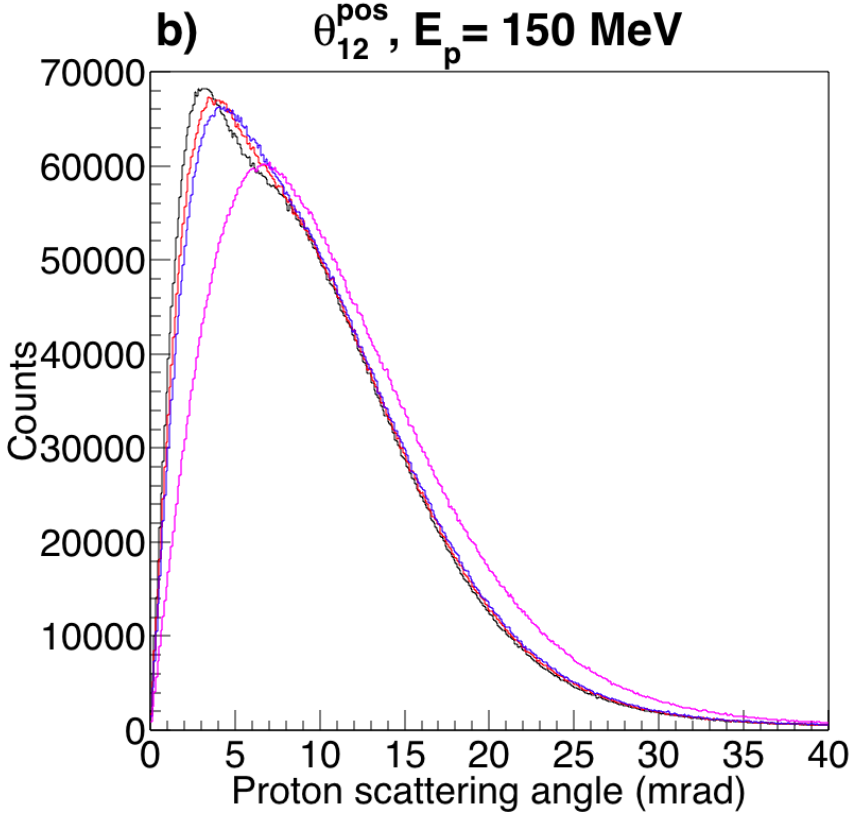
$$\phi_{12}^{\vec{p}}(rad) = \cos^{-1}\frac{\vec{p}_1\,\vec{p}_2}{\left|\vec{p}_1\right|\left|\vec{p}_2\right|}$$

$$\phi_{12}^{pos}(rad) = \tan^{-1}\frac{\sqrt{(x_2-x_1)^2+(y_2-y_1)^2}}{(z_2-z_1)}$$





A.K. Biegun al., under review at Physica Medica: EJMP

Geant4 simulations

Statistics @ E_p = 150, 190 and 230 MeV

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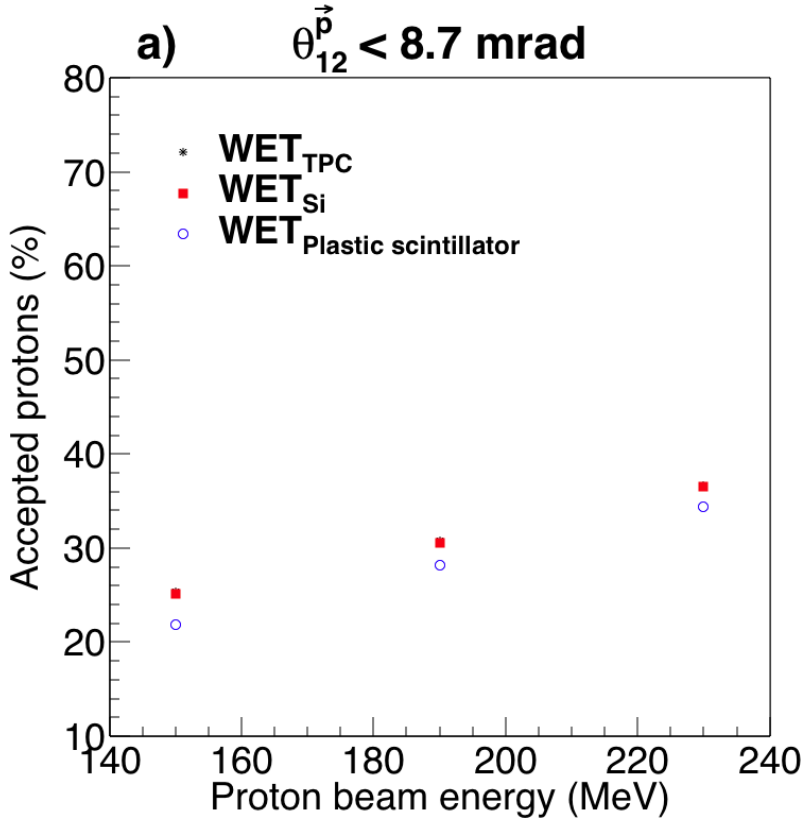

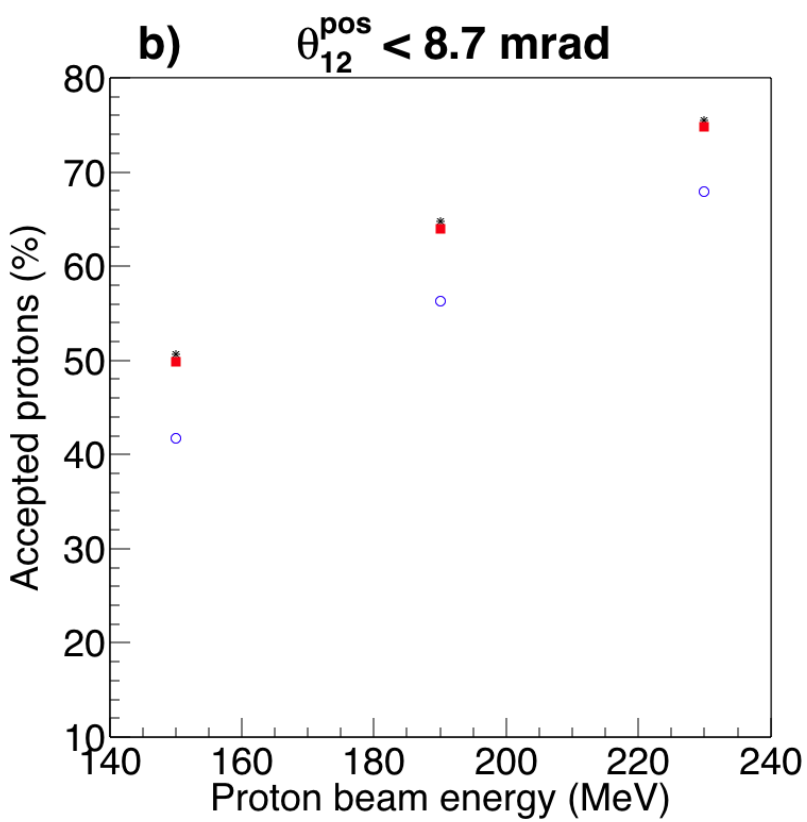

Using *position* of protons to calculate θ_{12} more protons, by factor of 2, are accepted to build the radiographic image

Geant4 simulations

A.K. Biegun al., under review at Physica Medica: EJMP

Energy loss radiographs for various PSDs

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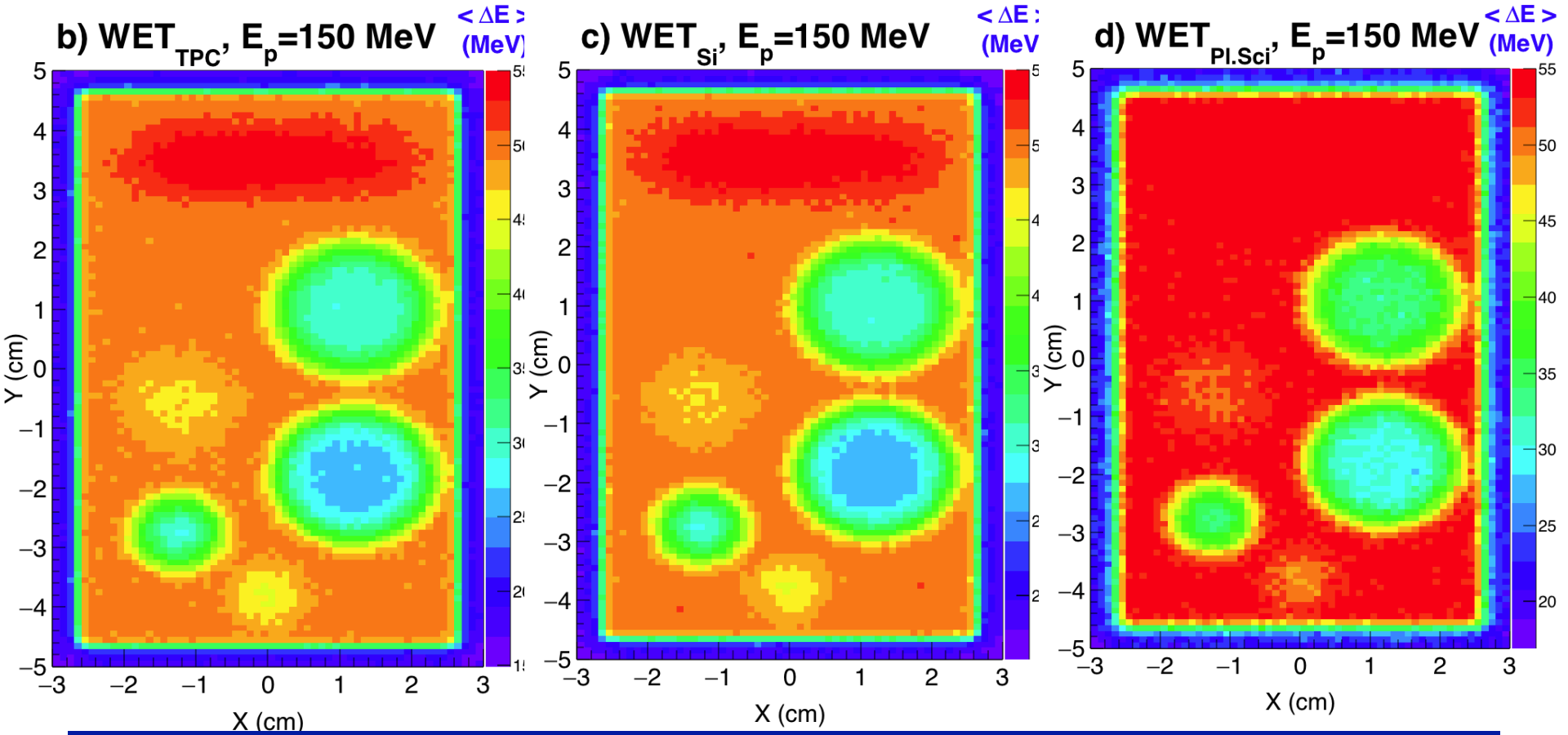

WET$_{TPC}$ allows to reconstruct the best radiographic image

A.K. Biegun al., under review at Physica Medica: EJMP

Ideal system with tracking detectors

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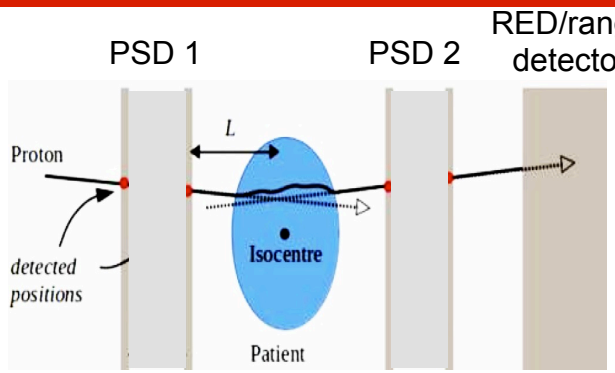

*G. Poludniowski et al., Br J Radiol (2015) **88**:20150134*

✓Tracking detectors

- **Low Z and WET** → minimum MCS in a detector
- **Fast** → high count rate (> MHz), based on Timepix3/Timepix4,

  time resolution ~ns
- **Spatial resolution** → 50 μm
- **Full proton track** determination
- **Modular** → ultimate size 30x30 cm^2

✓Residual energy detector

- **Fast** scintillator (YAG:Ce, $LaBr_3$)
- **Good energy resolution** (up to 1%)
- High count rate (> MHz)

Ideal system with tracking detectors

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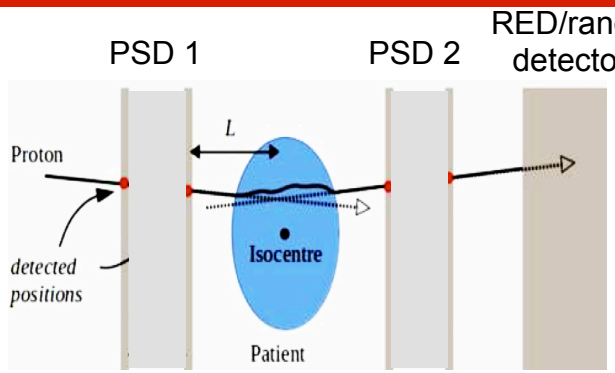

*G. Poludniowski et al., Br J Radiol (2015) **88**:20150134*

✓**Easy to mount on a gantry in proton therapy centers**

✓**Scan time + reconstruction in a clinic of up to 10 s**

Needs to be clinically acceptable!

✓**Tracking detectors**

- **Low Z and WET** → minimum MCS in a detector
- **Fast** → high count rate (> MHz), based on Timepix3/Timepix4,

  time resolution ~ns
- **Spatial resolution** → 50 μm
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✓**Residual energy detector**

- **Fast** scintillator (YAG:Ce, $LaBr_3$)
- **Good energy resolution** (up to 1%)
- High count rate (> MHz)

Calibration of Relative Proton Stopping Powers

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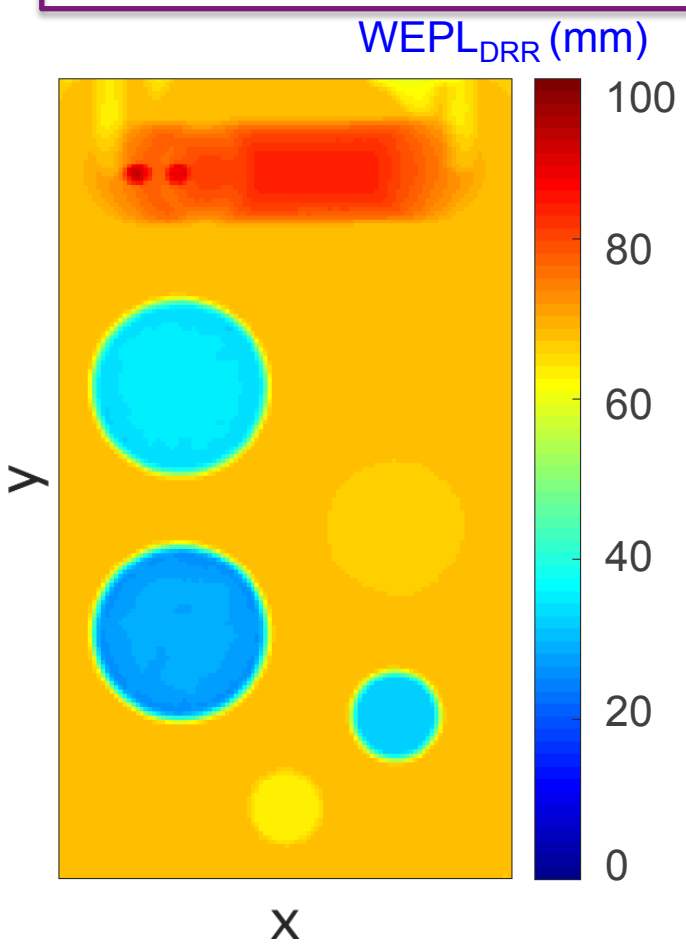
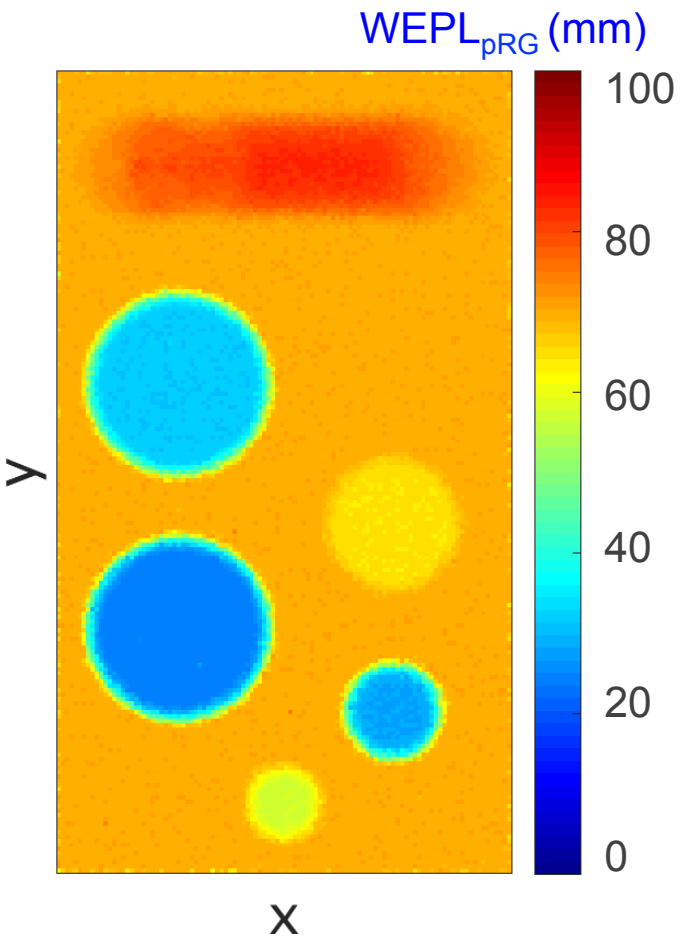
- X-ray CT @120 kVp

$$WEPL_{DRR(x,y)} = \sum_z \rho_s(HU_{SC}(x,y,z))\Delta z$$

- Proton radiography: protons scattered < 5.2 mrad





WEPL = Water Equivalent Path Length DRR = Digitally Reconstructed Radiograph pRG = proton RadioGraphy

Optimization of the clinical calibration curve

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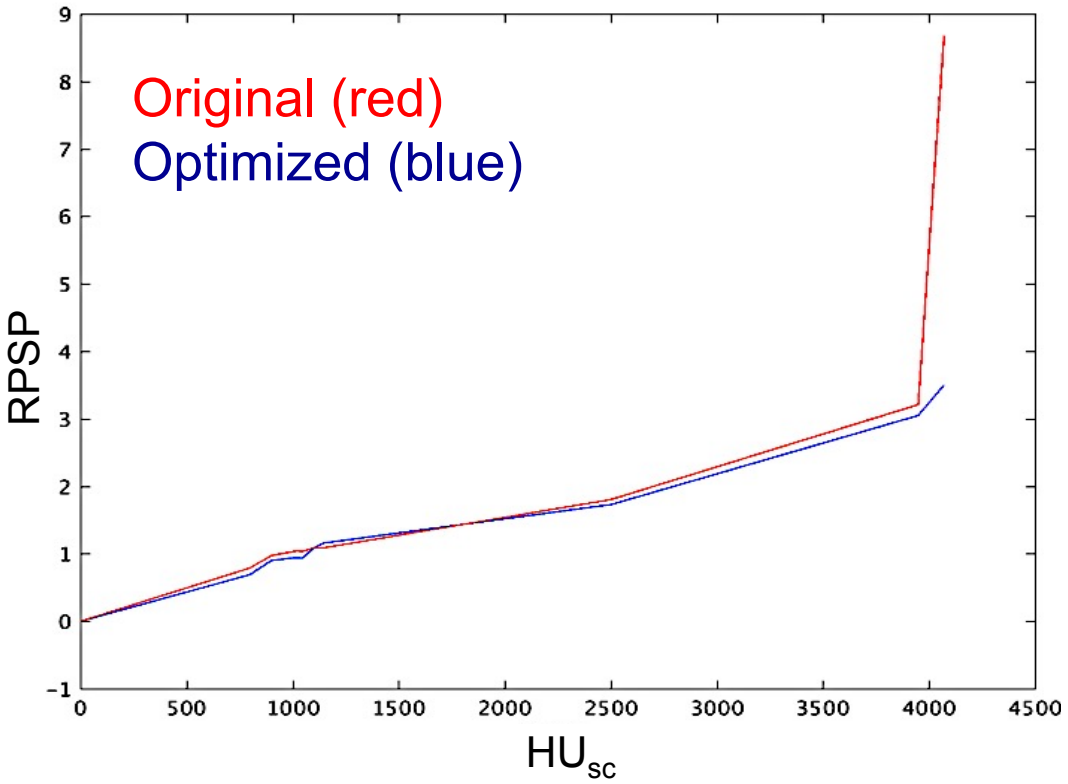
$$\mathrm{RMSE} = \sqrt{\frac{\sum_{x,y}(\mathrm{WEPL}_{DRR}(x,y) - \mathrm{WEPL}_{pRG}(x,y))^2}{N}}$$

$$\chi^2 = \sum_{x,y} \frac{(\mathrm{WEPL}_{DRR}(x,y) - \mathrm{WEPL}_{pRG}(x,y))^2}{\mathrm{WEPL}_{pRG}(x,y)}$$



RPSP = Relative Proton Stopping Power

Optimization of the clinical calibration curve

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$$\mathrm{RMSE} = \sqrt{\frac{\sum_{x,y}(\mathrm{WEPL}_{DRR}(x,y) - \mathrm{WEPL}_{pRG}(x,y))^2}{N}}$$

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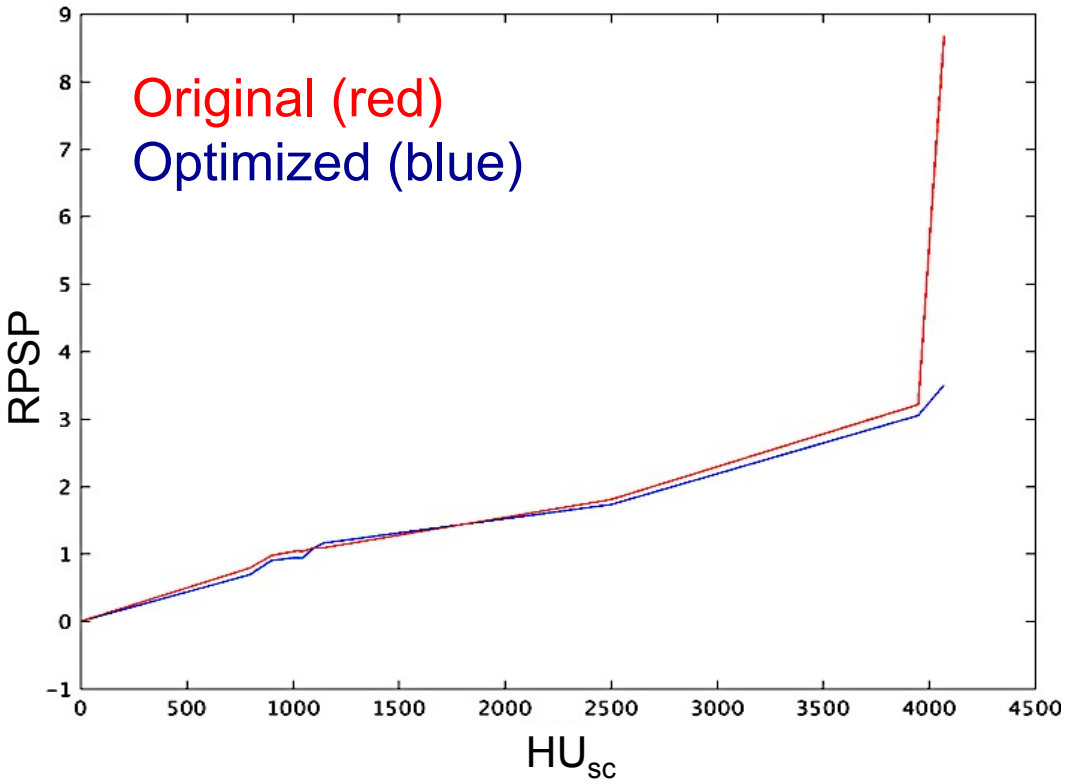

Before optimization

Metric	With PMMA
RMSE	3.59 mm
χ^2	5083.80

After optimization

Metric	With PMMA
RMSE	2.36 mm (**-34.33%**)
χ^2	2287.10 (**-55.01%**)

RPSP = Relative Proton Stopping Power

Future proton therapy work flow

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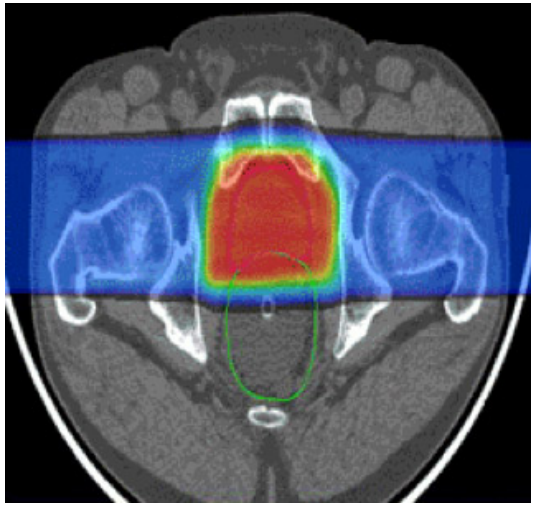
Proton Treatment Plan



1) X-ray CT scan (DECT, SCT)

Calculated PSP

2) Proton radiography

Directly measured PSP

Future proton therapy work flow

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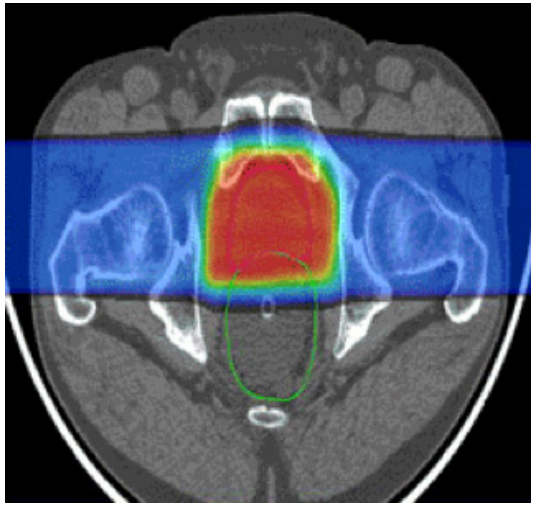
Proton Treatment Plan



1) X-ray CT scan (DECT, SCT)

Calculated PSP

2) Proton radiography

Directly measured PSP

- **RPSP calibration**
- **Online treatment plan adaptation**

Fast (1-10 sec)

Future proton therapy work flow

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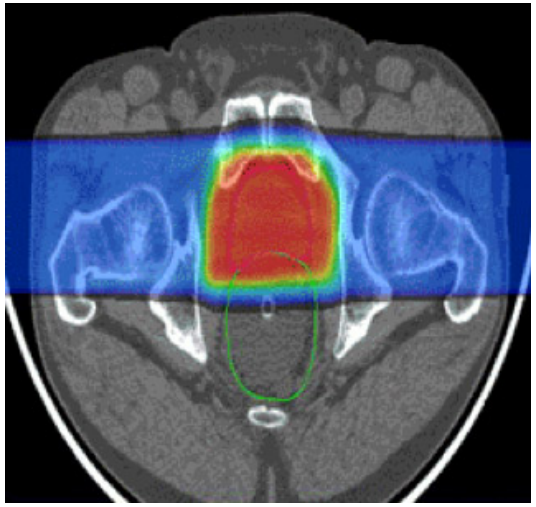
Proton Treatment Plan



1) X-ray CT scan (DECT, SCT)

Calculated PSP

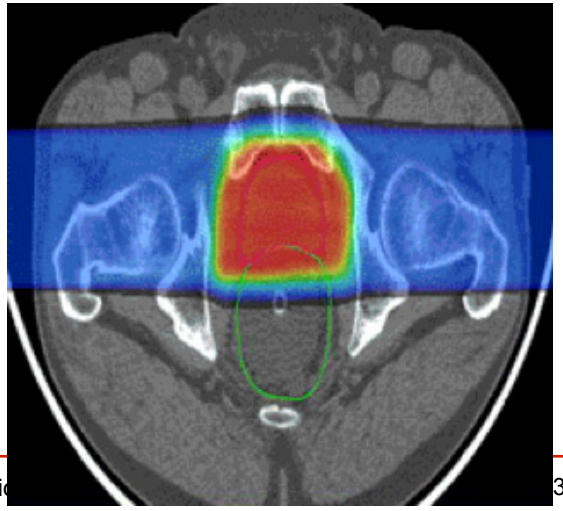
2) Proton radiography

Directly measured PSP

- RPSP calibration
- Online treatment plan adaptation

Fast (1-10 sec)

Updated Proton Treatment Plan



Treatment

Treatment verification

Future proton therapy work flow

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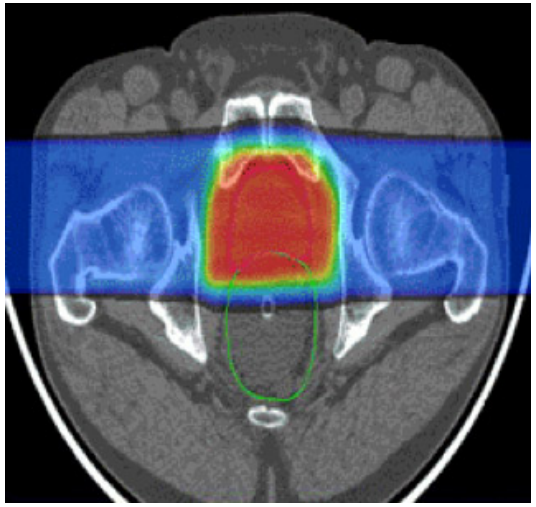
Proton Treatment Plan



1) X-ray CT scan (DECT, SCT)

Calculated PSP

2) Proton radiography

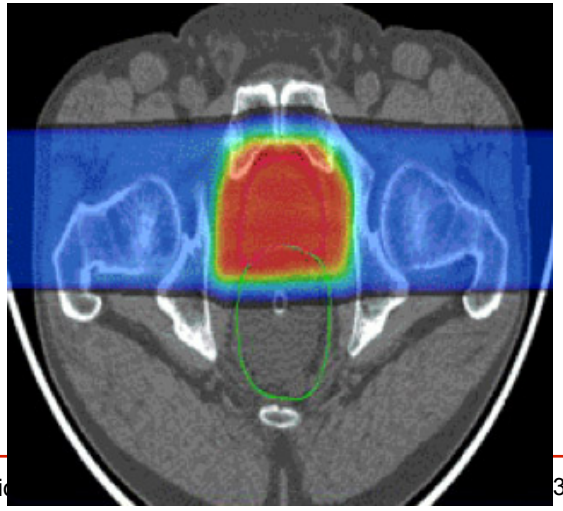
Direct[illegible] PSP

Nikhef

- RPSP calibration
- Online treatment plan adaptation

Fast (1-10 sec)

Updated Proton Treatment Plan



Treatment

Treatment verification

Backup slides

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Energy loss radiographs: Projections

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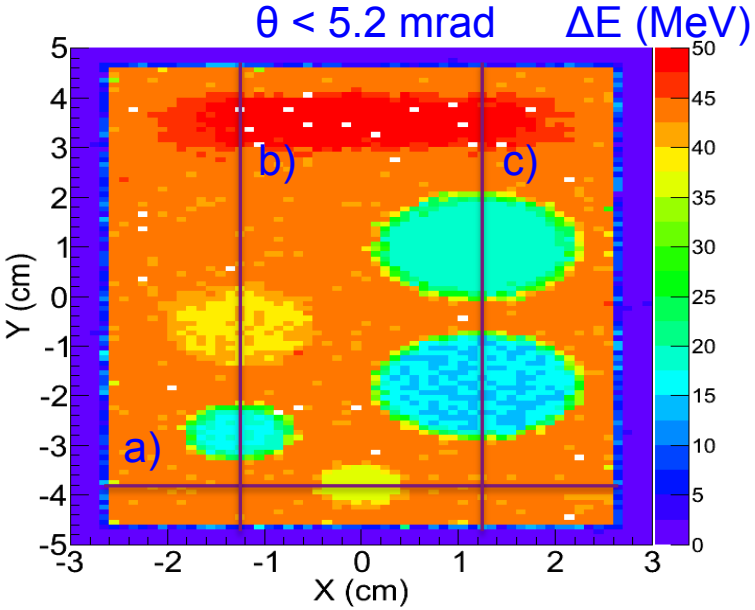
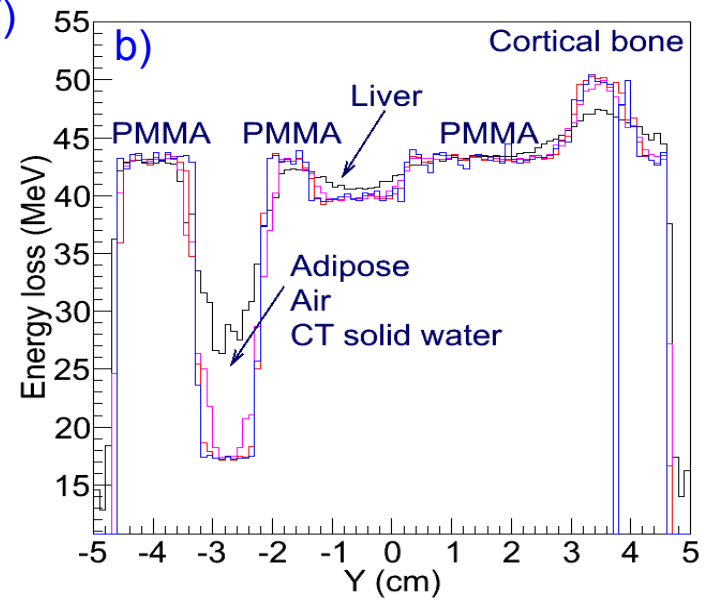
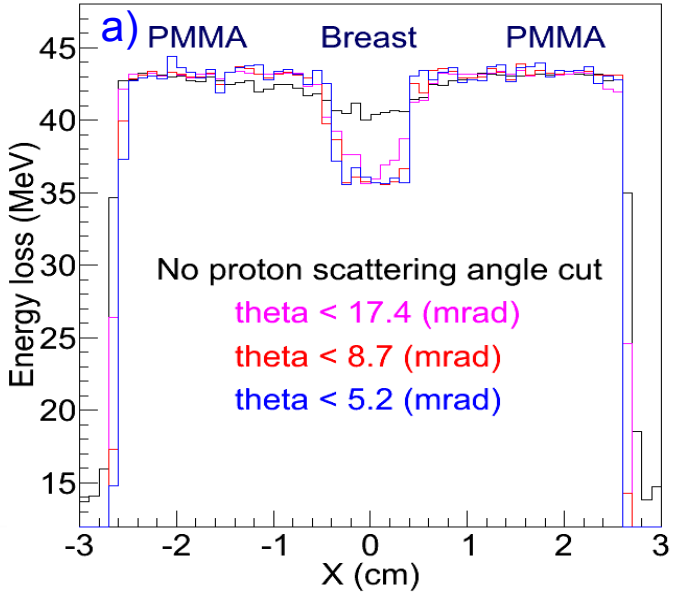
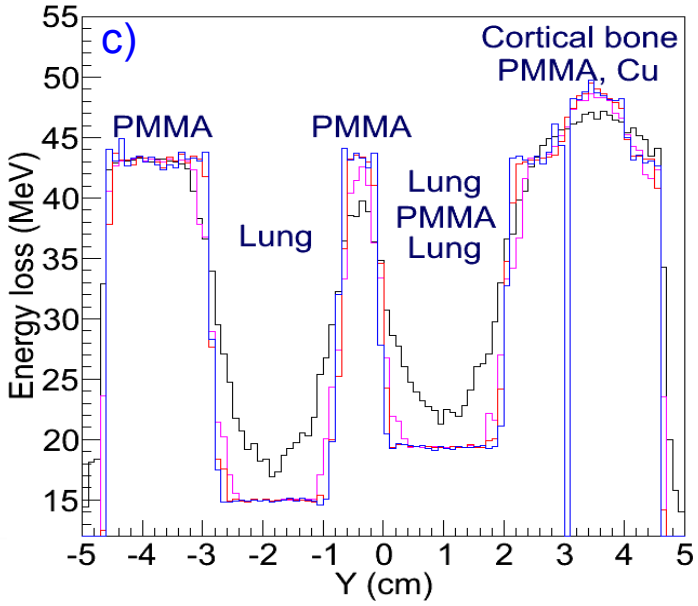




A.K. Biegun et al, JINST 11 (2016) C12015





Bin size: 1 mm

Geant4 simulations

Energy loss radiographs: Projections

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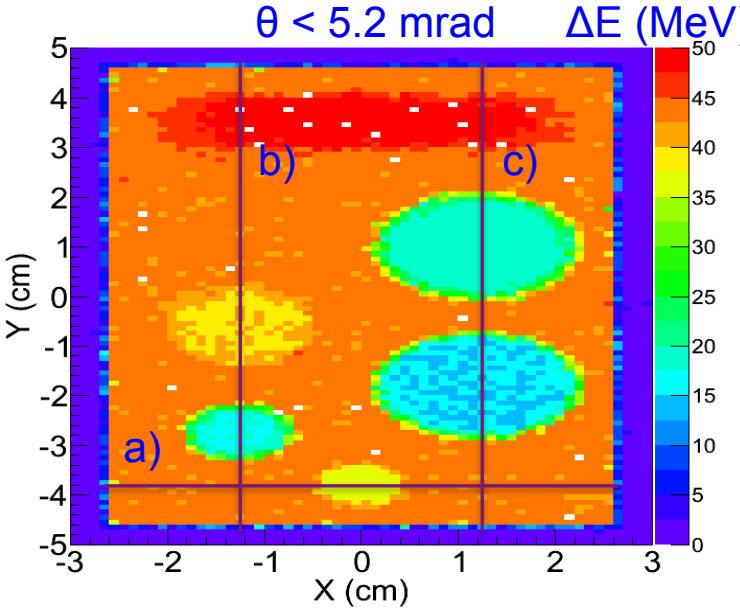
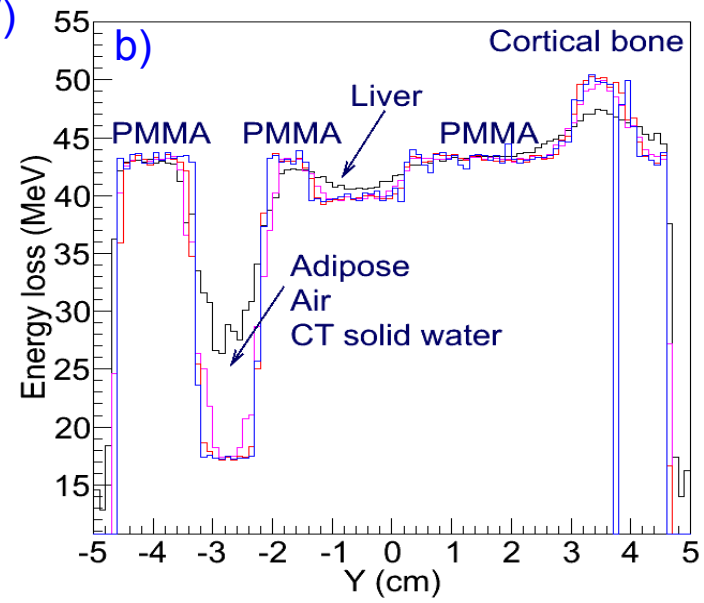
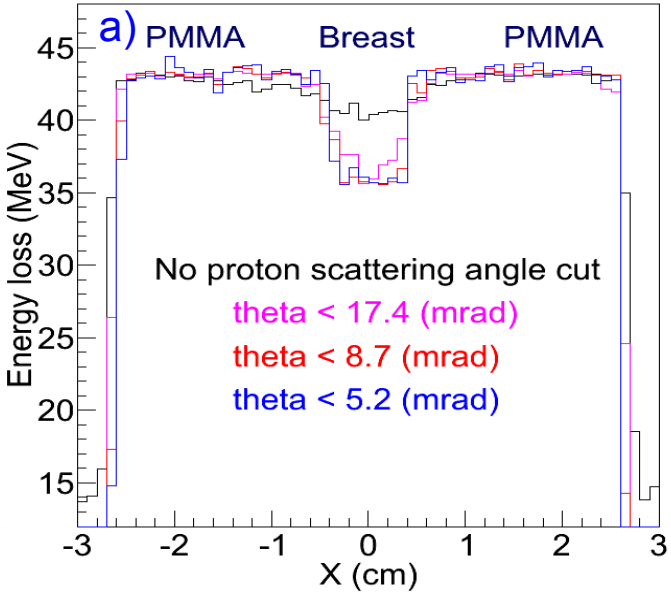
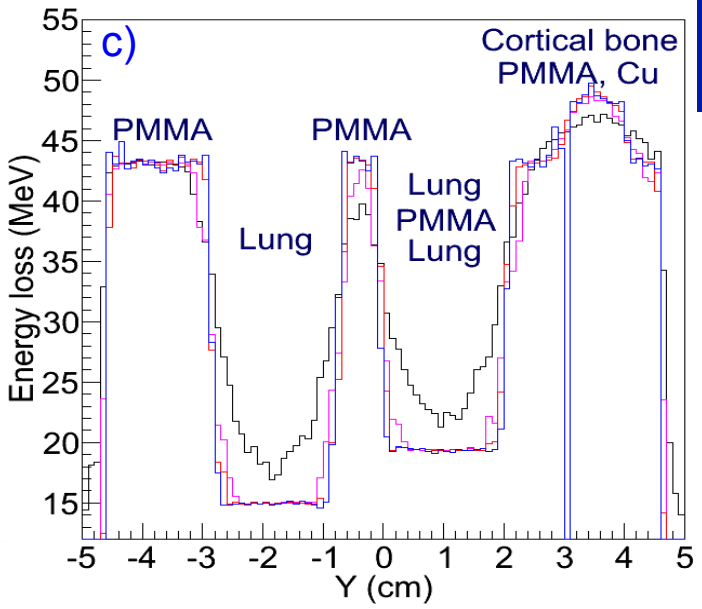




A.K. Biegun et al, JINST 11 (2016) C12015





Sharper edges between materials for smaller scattering angles of protons

Bin size: 1 mm

Geant4 simulations

Goal…

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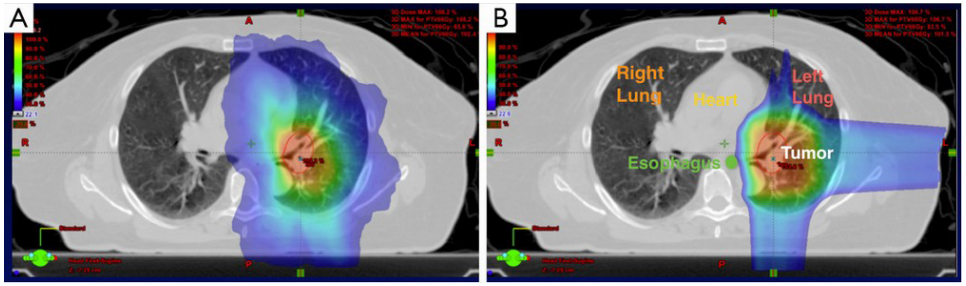
Fast and compact detection system with:

- Spatial and angular resolutions
- Energy resolutions
- Compatible with reconstruction algorithms

to deliver an accurate map of proton stopping powers of the patient

to fully benefit from proton therapy



http://tcr.amegroups.com/article/view/5403/html

Ongoing and future work

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Simulations

- Further analysis of the alternative approach for **θ** is necessary, also for more realistic phantoms and real patient CT data
- Realistic tracking detectors need to be implemented in simulations

Experimental work

- Development of Timepix-based TPC is needed to achieve clinically relevant count rates (> MHz)
- Fast energy detector with energy resolution <1% should be consider

Both simulations and experimental work are necessary to have a proton radiography system relevant and accepted in hospitals!

Proton radiography: The ultimate aim

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Detection system:

Position detectors:

(1) Improved data acquisition for Timepix3 (fast & compact) → **MHz rate**

(3) Increase the size of the detectors (sufficient in clinics) → **100 x 100 mm^2**

(4) 3D information of the proton tract with a good position resolution (good angle reconstruction) → **50 µm**

Energy:

(1) Fast energy detector → **MHz rate**

(2) Energy resolution → **≤ 1%**

Pros and Cons

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- Advantage:

  Proton stopping powers measured directly

  → Decrease uncertainty of Relative PSP (RPSP)

  derived from stoichiometric calibration with X-ray CT

  → Optimize treatment plan for the patient

- Challenge:

  Proton undergoes multiple Coulomb scattering causing image blurring

Why proton radiography?

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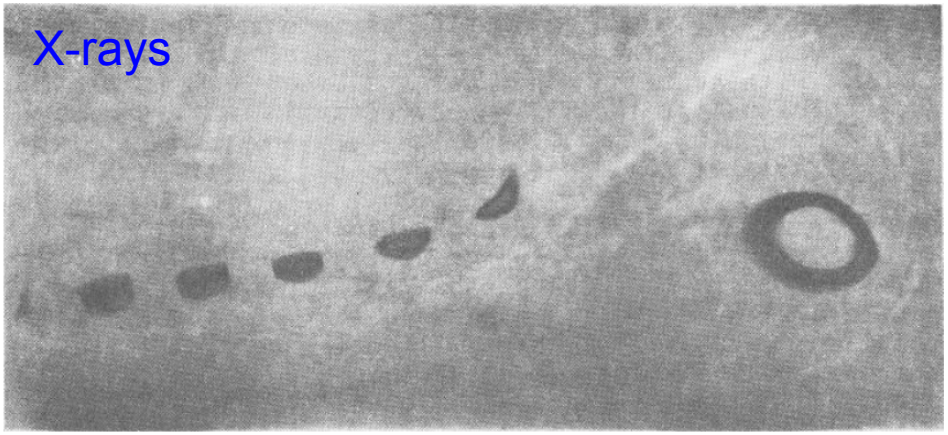
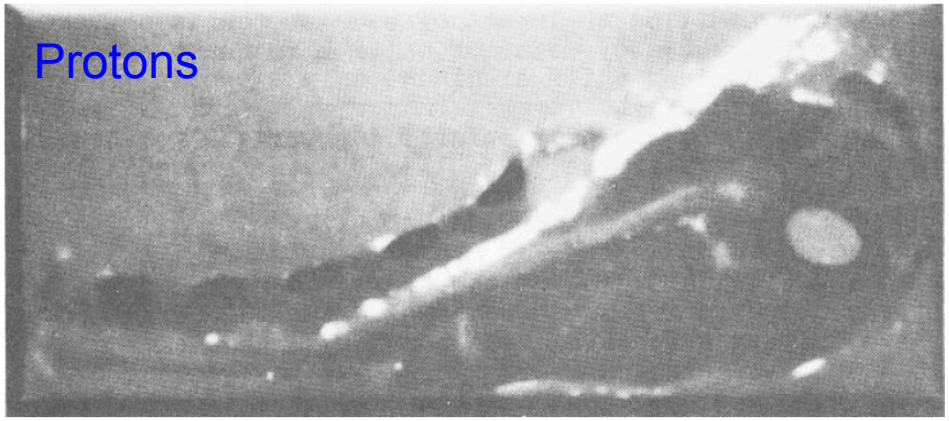
- A lamb chop 1 cm thick immersed in 12.5 cm thick water phantom
- $E_{X\text{-rays}}$ = 30 kVp
- E_p = 160 MeV



(-) much less contrast for fat
(-) no contrast for lean meat (muscle)

(+) much better spatial resolution



(-) poor spatial resolution

(+) high contrast for soft tissues

A.M. Koehler. AIP Conf Proc (1972) 586-562

Reconstruction of imaged object: trapezoid

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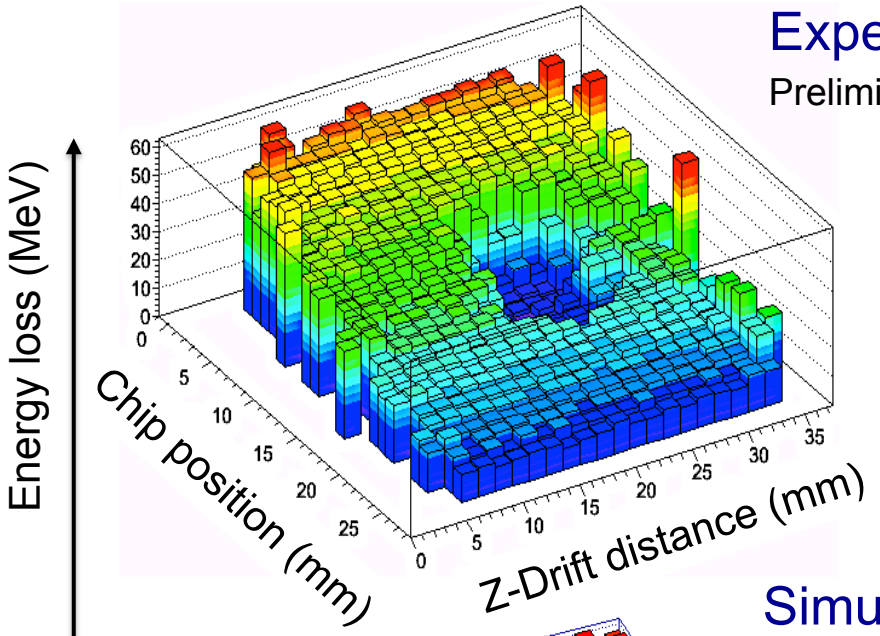
Scattered proton beam
of 30 x 30 mm^2 size

Brass trapezoid ρ = 8.55 g/cm^3
Polymer ρ = 1.18 g/cm^3

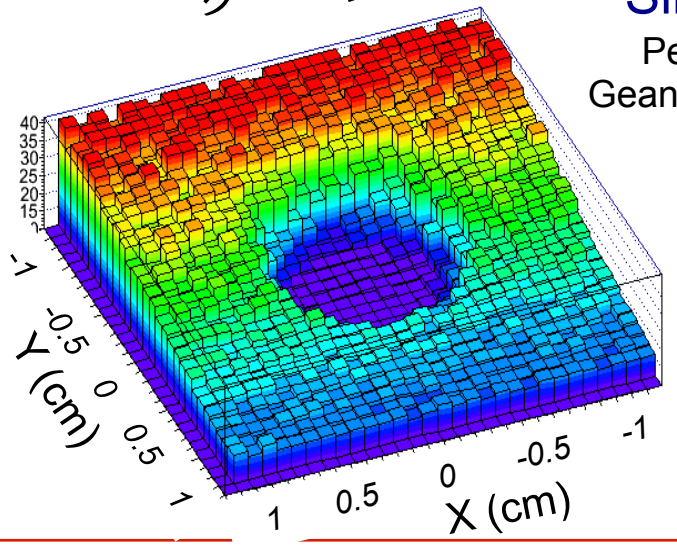
Experiment

Preliminary data



Simulations

Performed with
Geant4-based MC



Reconstruction of object with tissue-like inserts

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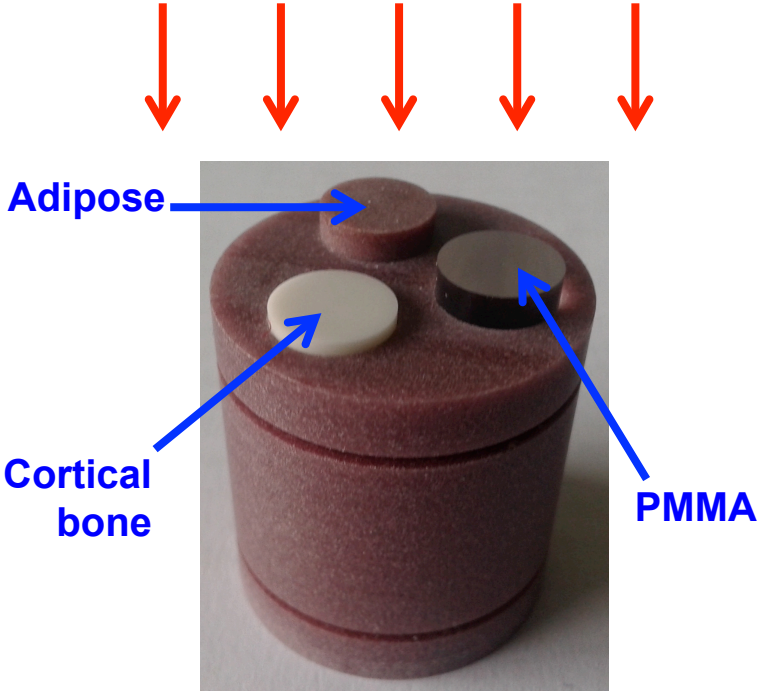
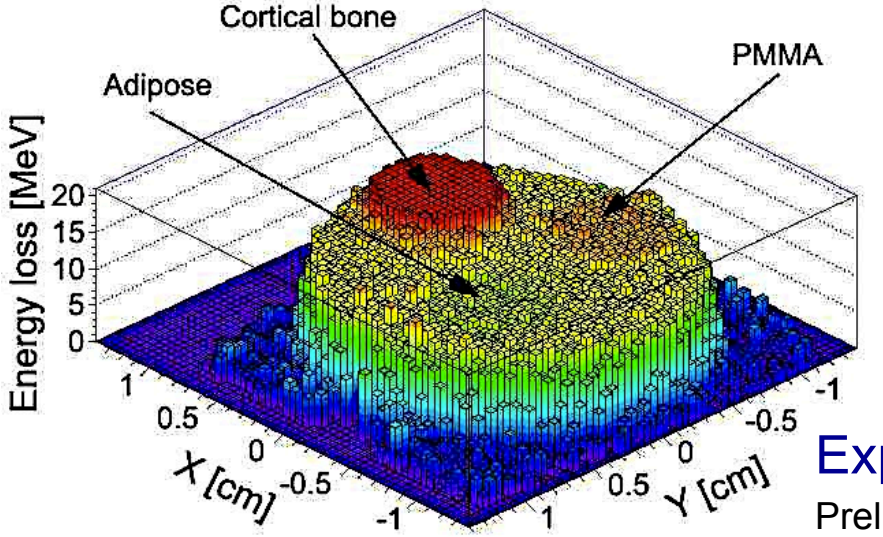
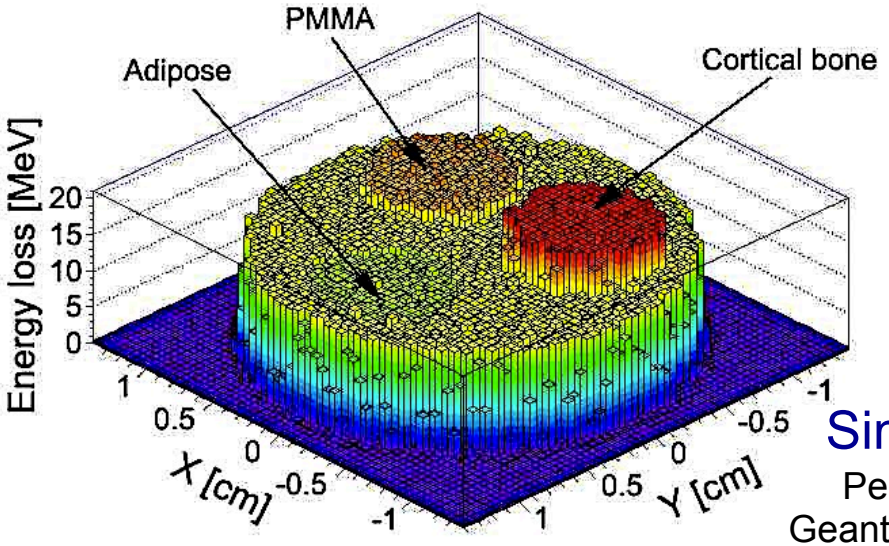
Scattered proton beam
of 30 x 30 mm^2 size





Experiment
Preliminary data



Simulations
Performed with
Geant4-based MC

Adipose (fat)	ρ = 0.92 g/cm^3
PMMA	ρ = 1.19 g/cm^3
Cortical bone	ρ = 1.82 g/cm^3
CT solid water	ρ = 1.015 g/cm^3

Reconstruction of object with air and liquid inserts

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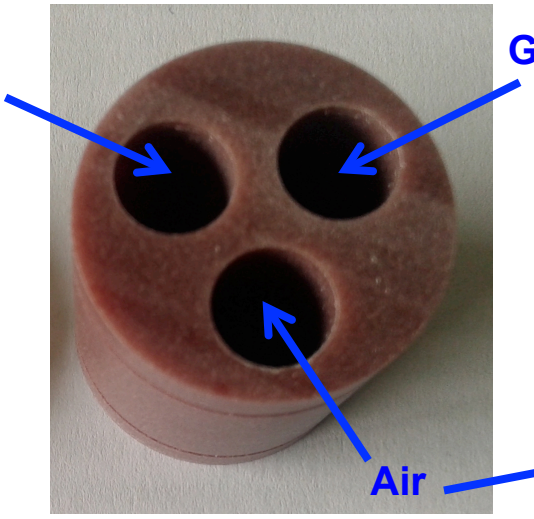
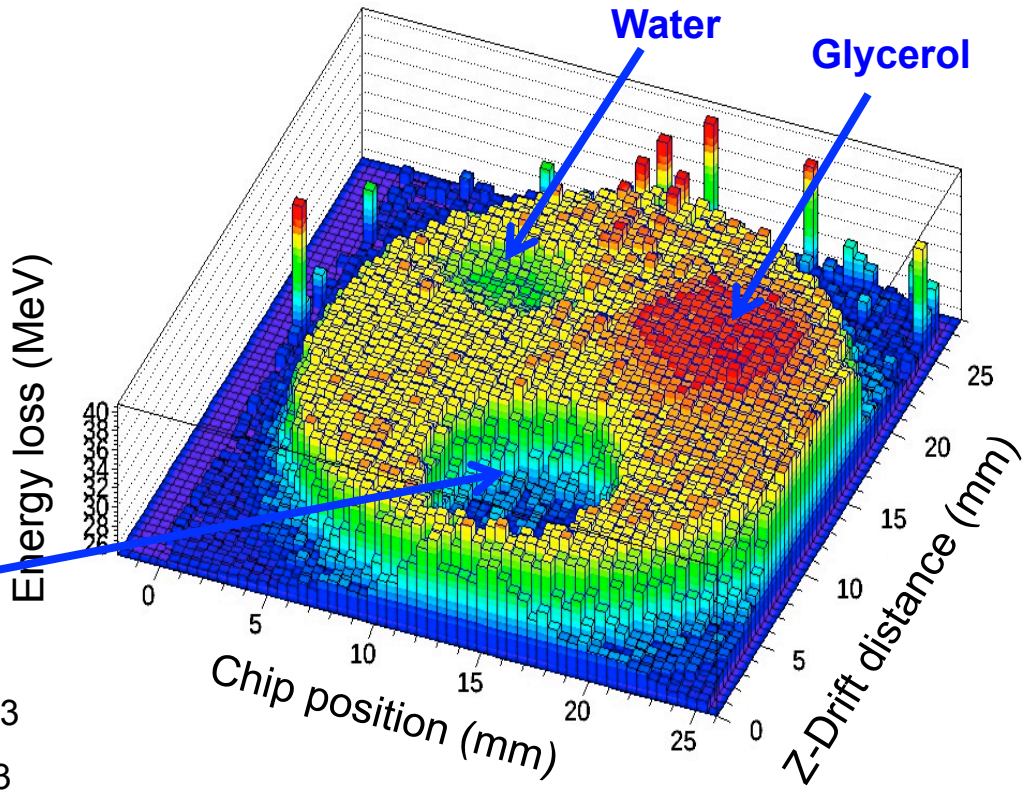
Scattered proton beam
of 30 x 30 mm^2 size



Experiment

Preliminary data



Air	ρ = 1.29*10^{-3}	g/cm^3
Water	ρ = 1.00	g/cm^3
Glycerol	ρ = 1.26	g/cm^3
CT solid water	ρ = 1.015	g/cm^3

The AGOR cyclotron

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- Superconducting magnet (up to 4.1 T)
- **Protons up to 190 MeV**
- Alpha particles, **^{12}C up to 90 MeV/u**
- Heavy ions: 600 $(q/A)^2$ MeV/u

Tumor modification during treatment: an example

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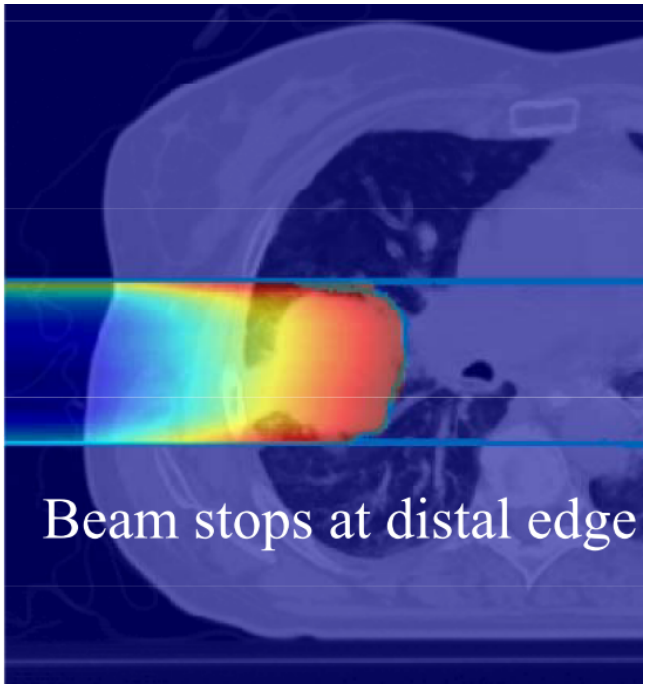
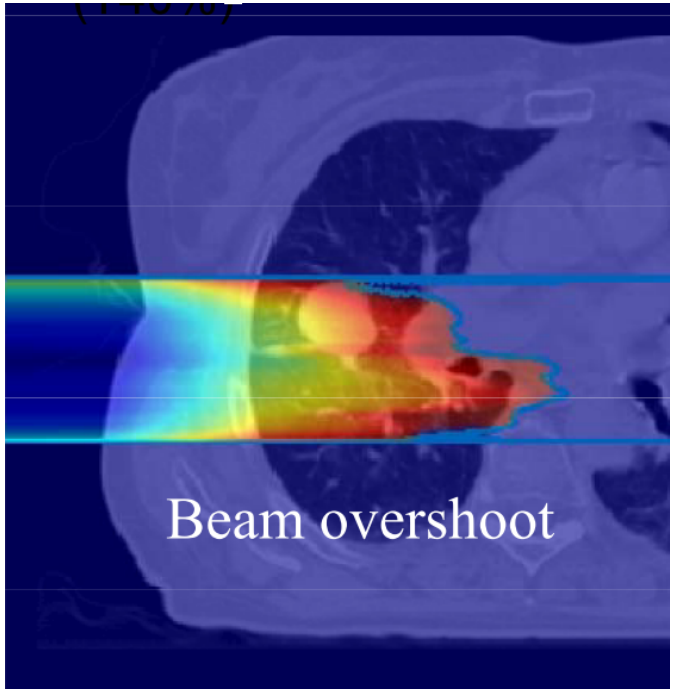
source: S. Mori en G.T.Y Chen, MGH



before treatment



after 5 weeks