Proton radiography in proton therapy treatment

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4-9 June 2017, Cracow, Poland

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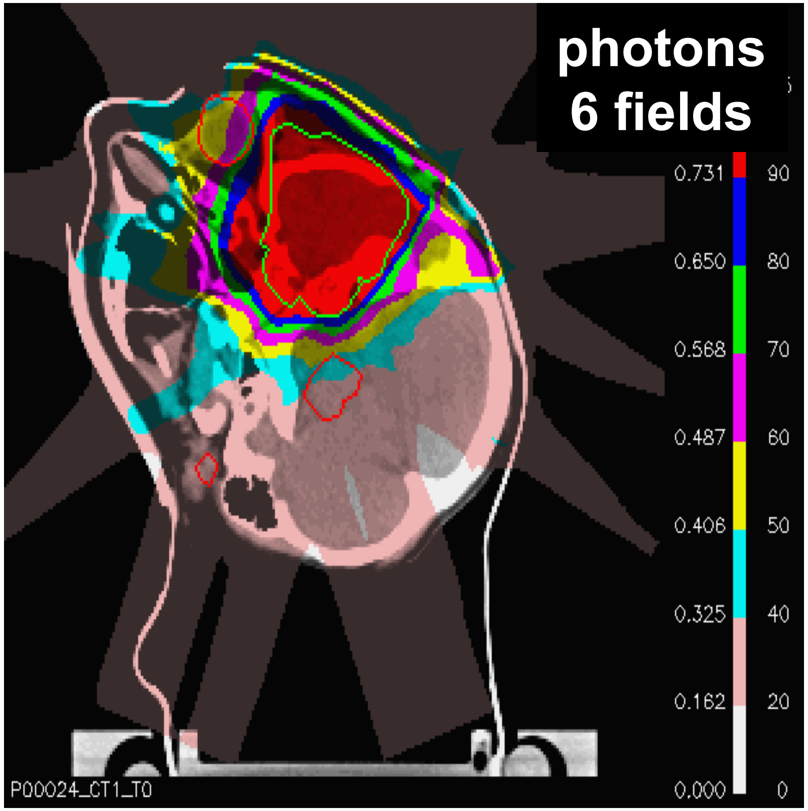
Photons vs. protons

source: T. Lomax, PSI



Photons vs. protons

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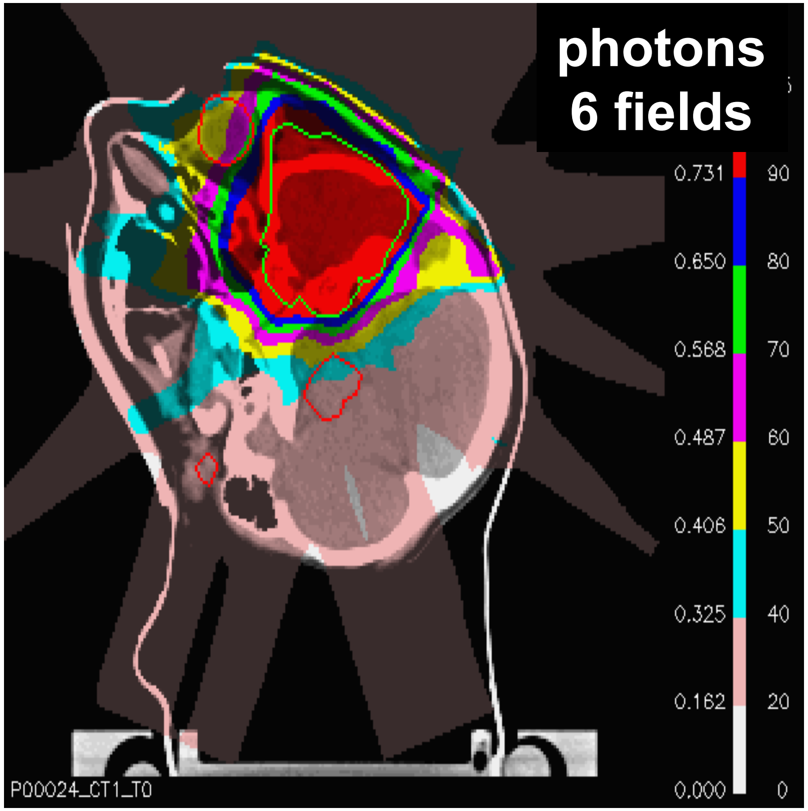
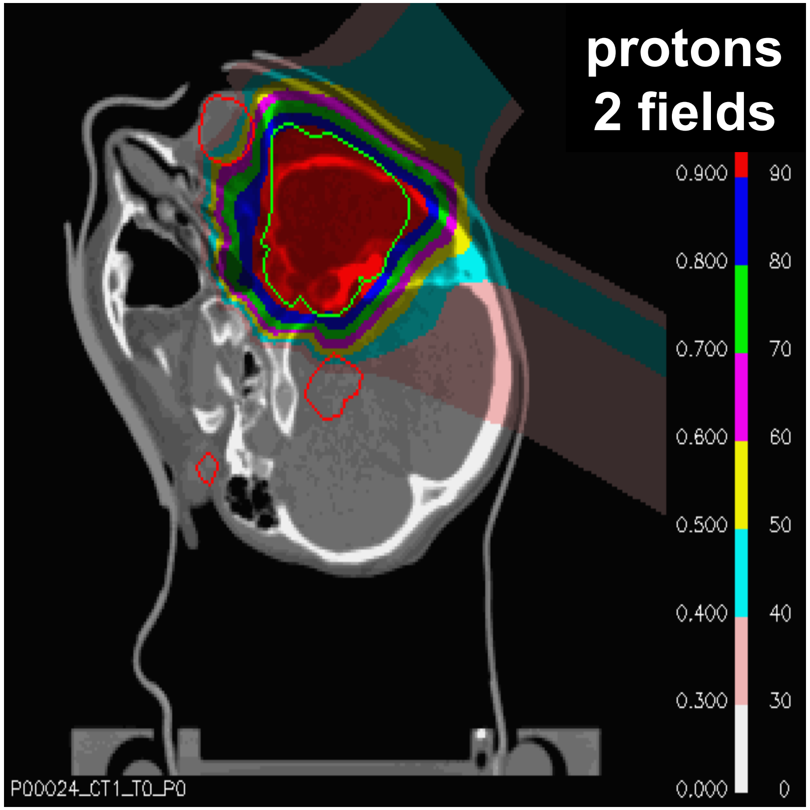




source: T. Lomax, PSI

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

Proton therapy work flow

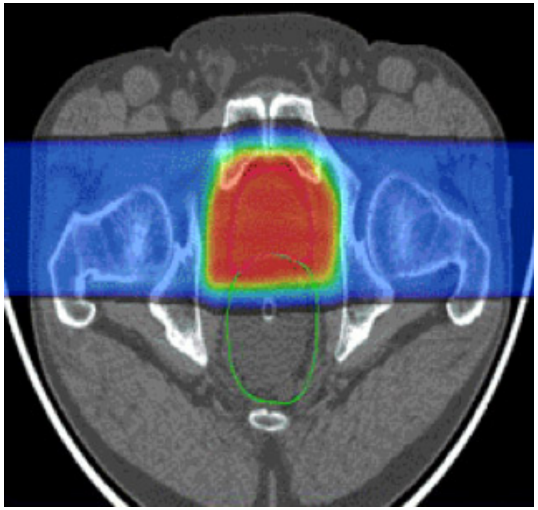
CT scan

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

Translation →

3D map of proton stopping powers (PSP)

↓ **Treatment planning**



← **Treatment** ←

Treatment verification

Proton therapy work flow

CT scan

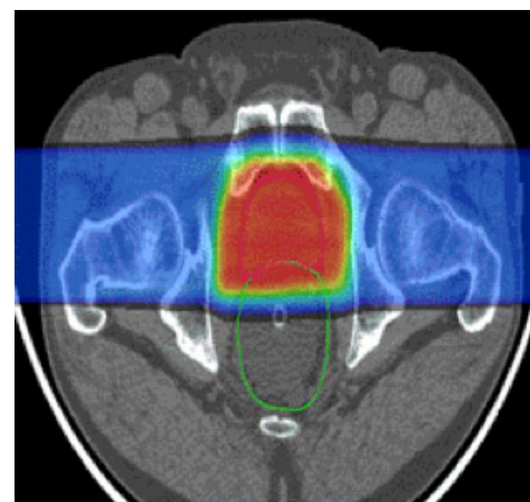
$$HU = 1000\,\frac{\mu - \mu_{water}}{\mu_{water}}$$

Knowledge of patient

Translation

3D map of proton stopping powers (PSP)

Treatment planning



Treatment

Treatment verification

Knowledge of patient in proton therapy treatment

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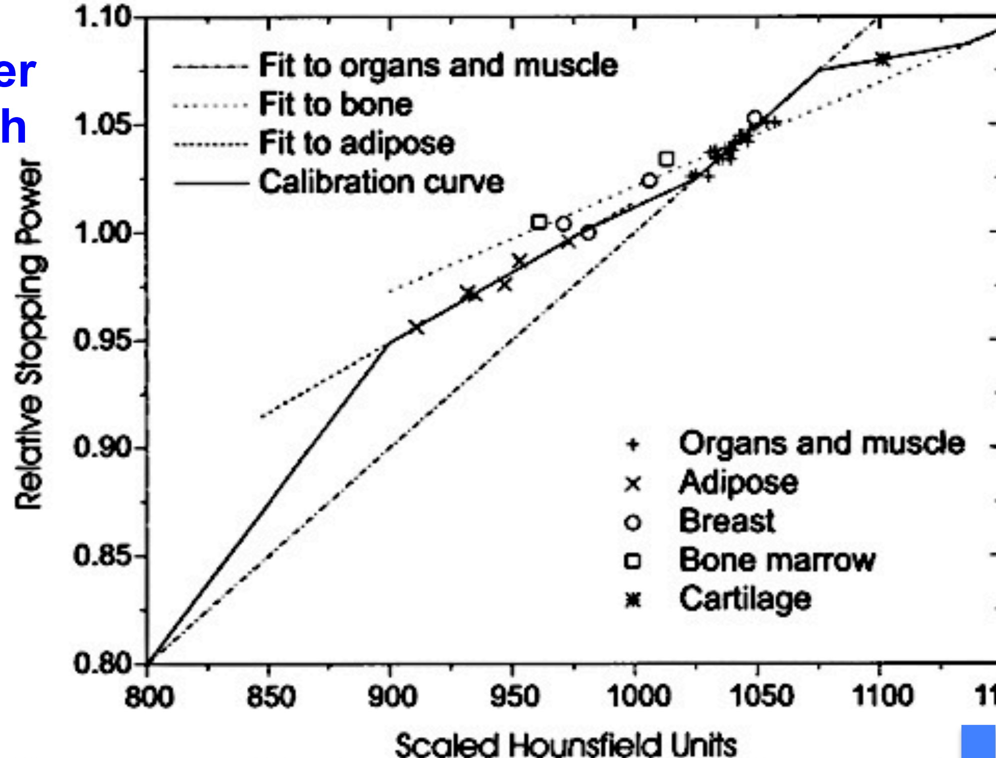
CT scan

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

Schneider approach



U. Schneider et al, PMB 41 (1996) 111

3D map of proton stopping powers

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

… And the consequence…

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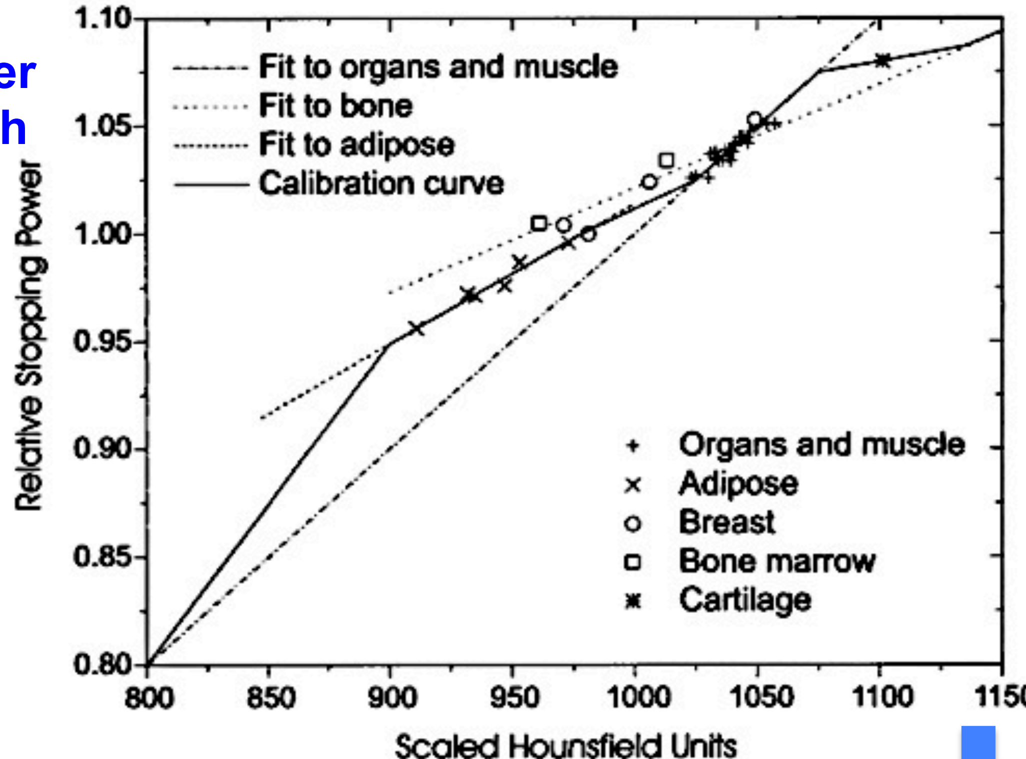
CT scan

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

Schneider approach



U. Schneider et al, PMB 41 (1996) 111

3D map of proton stopping powers

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

Leads to increased dose in healthy tissues

Why proton radiography?

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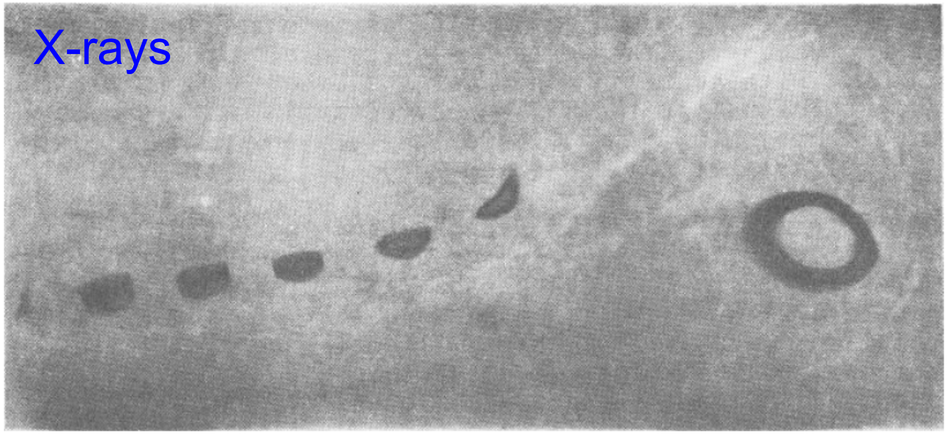
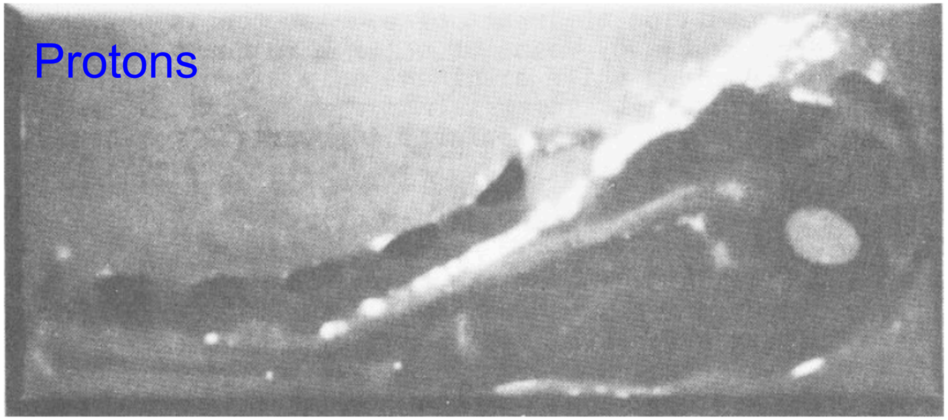
- A lamb chop 1 cm thick immersed in 12.5 cm thick water phantom
- $E_{X\text{-rays}}$ = 30 kVp
- E_p = 160 MeV



(-) 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

Why proton radiography?

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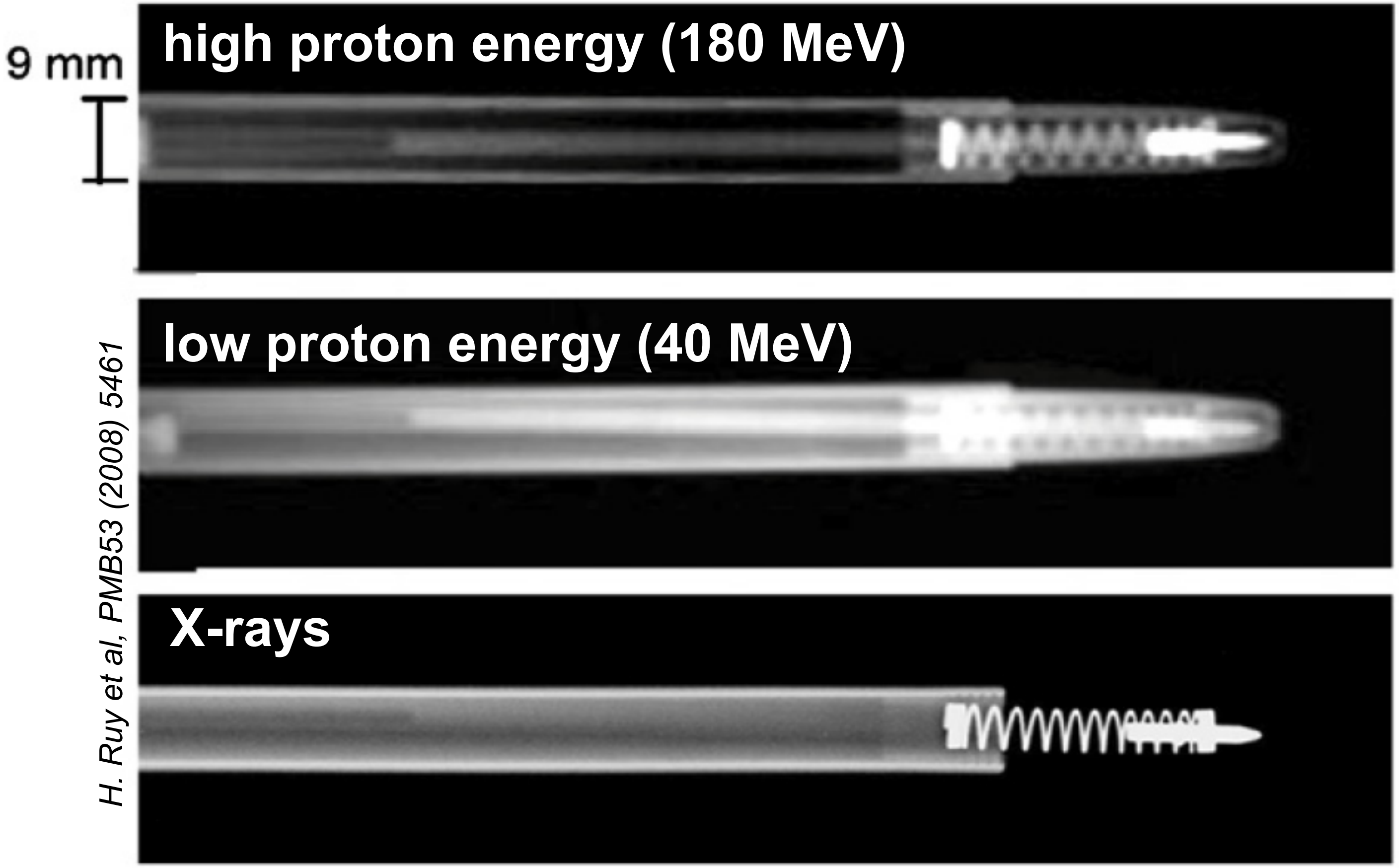
- High resolving power for proton beam (centerpiece of the pen visible)
- X-ray produces a clearer image of the spring,
  but density resolution for the centerpiece is not high



H. Ruy et al, PMB53 (2008) 5461

Why proton radiography?

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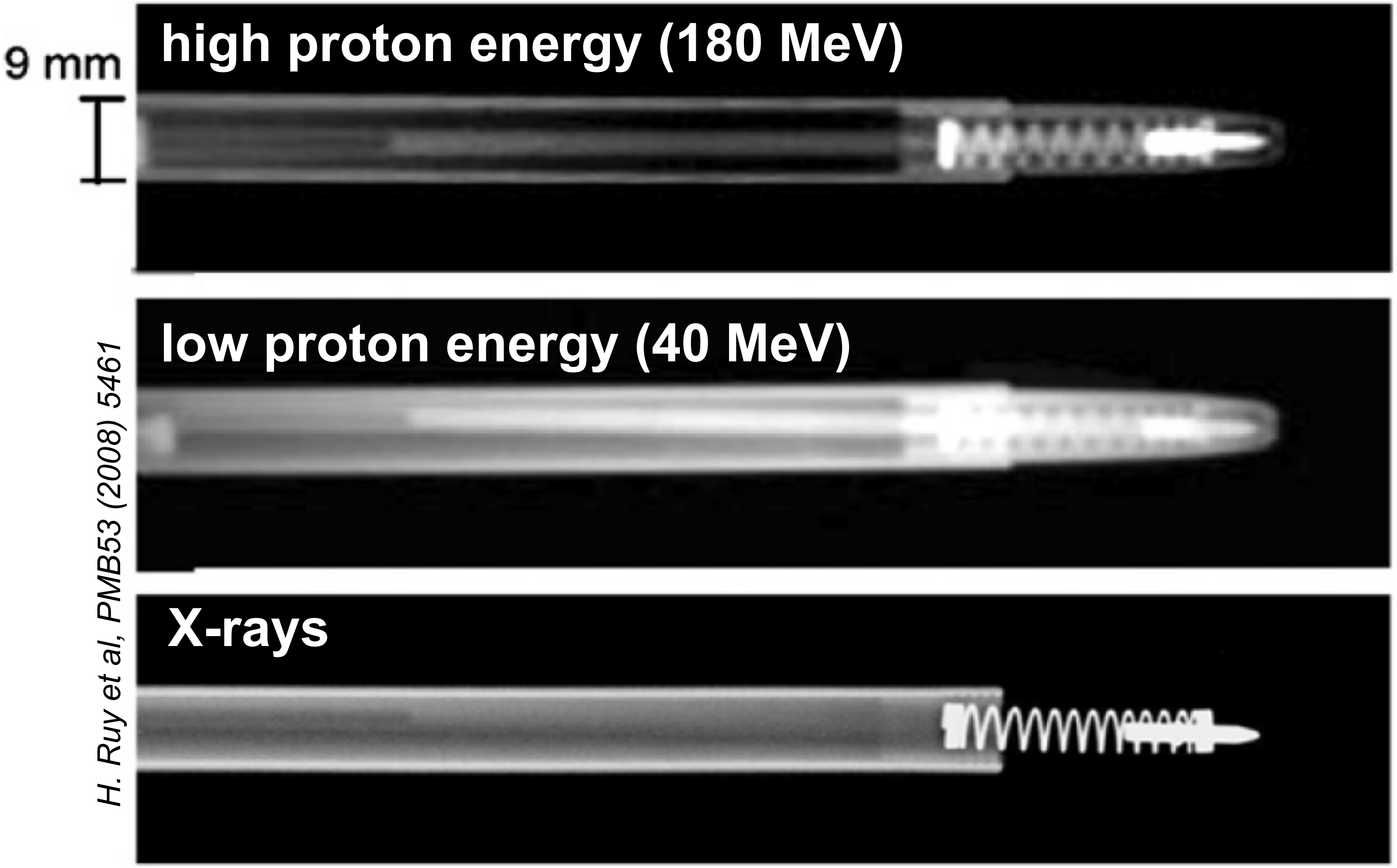

H. Ruy et al, PMB53 (2008) 5461

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

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

What is proton radiography?

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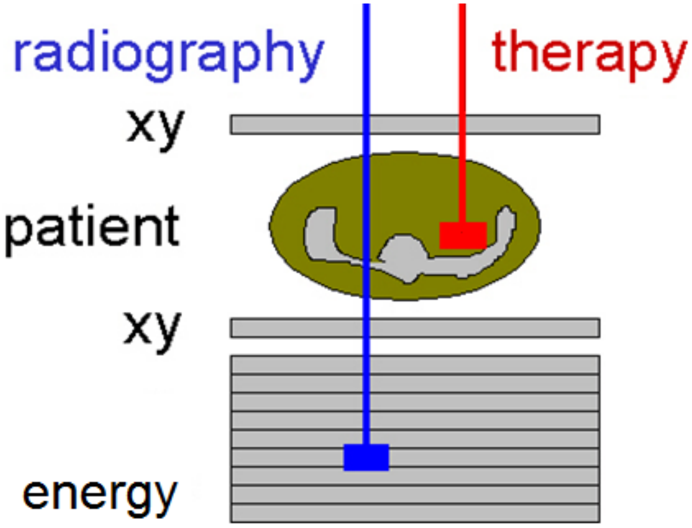
- Proton beam energy higher than the therapeutic energies, i.e. protons pass through the patient



What is proton radiography?

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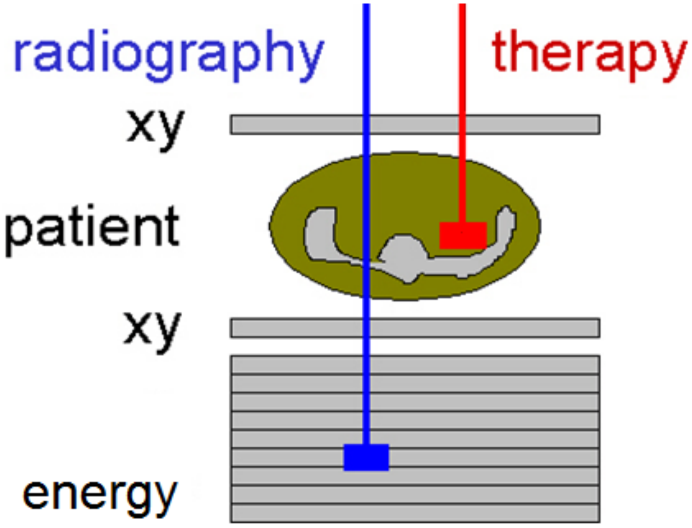
- ✧ Proton beam energy higher than the therapeutic energies, i.e. protons pass through the patient

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



Proton radiography: Geant4 MC simulations

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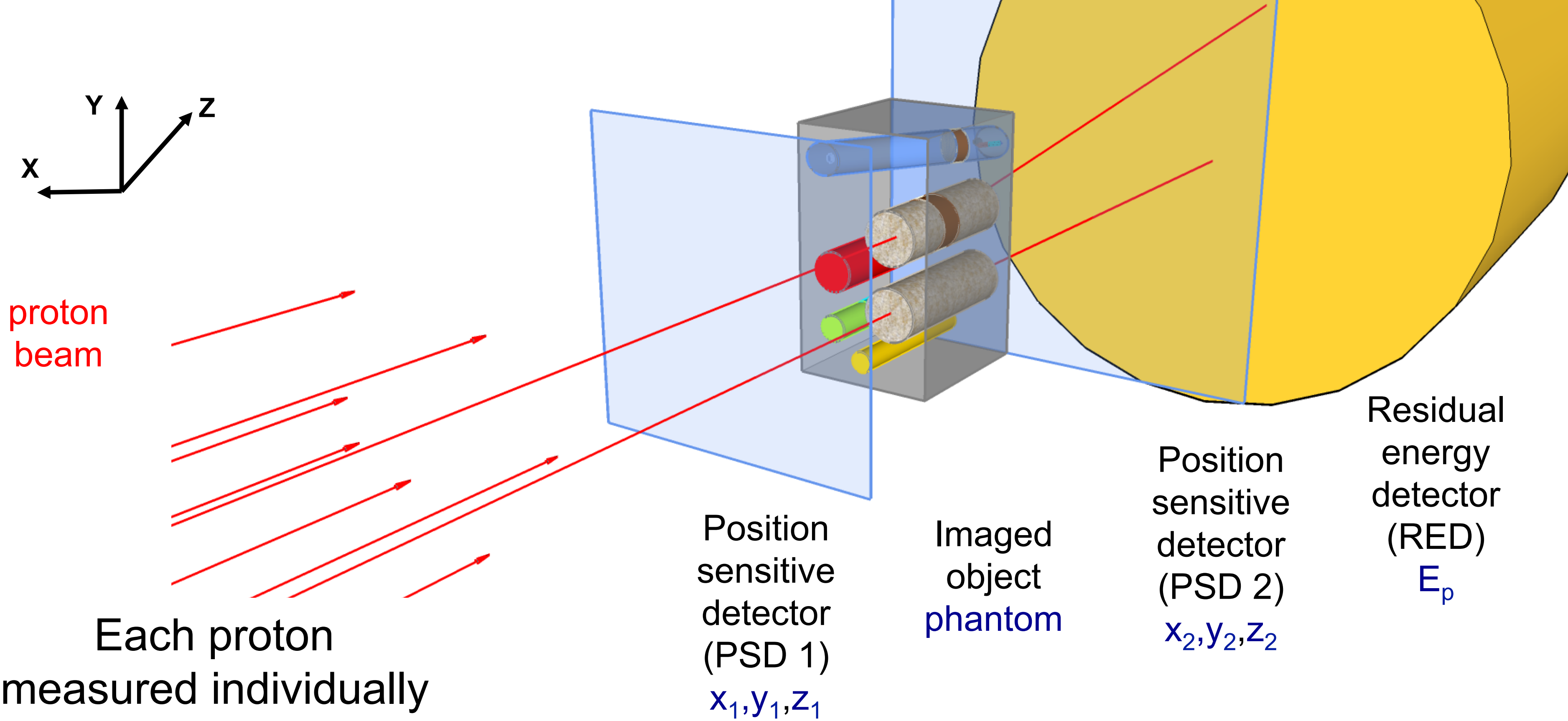
- $50*10^6$ protons generated, scattered beam, E_p=150 MeV
- Proton positions/directions detected
- Proton residual energy measured



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

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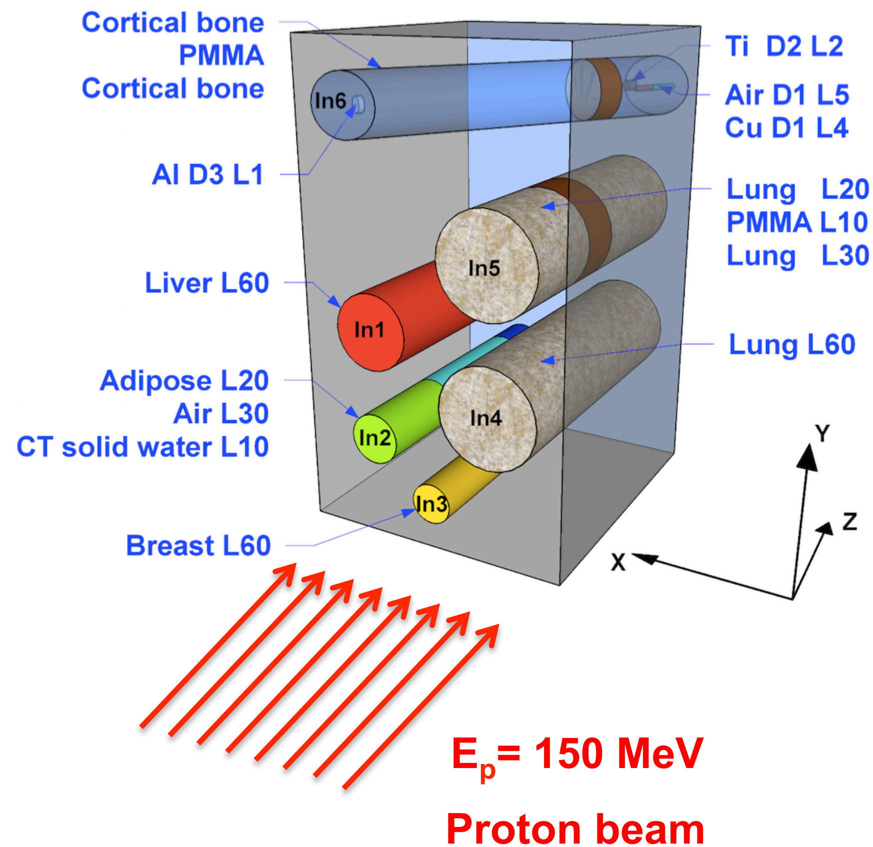
- ✧ Few materials on proton beam
- ✧ 11 various materials, including 5 tissue surrogates



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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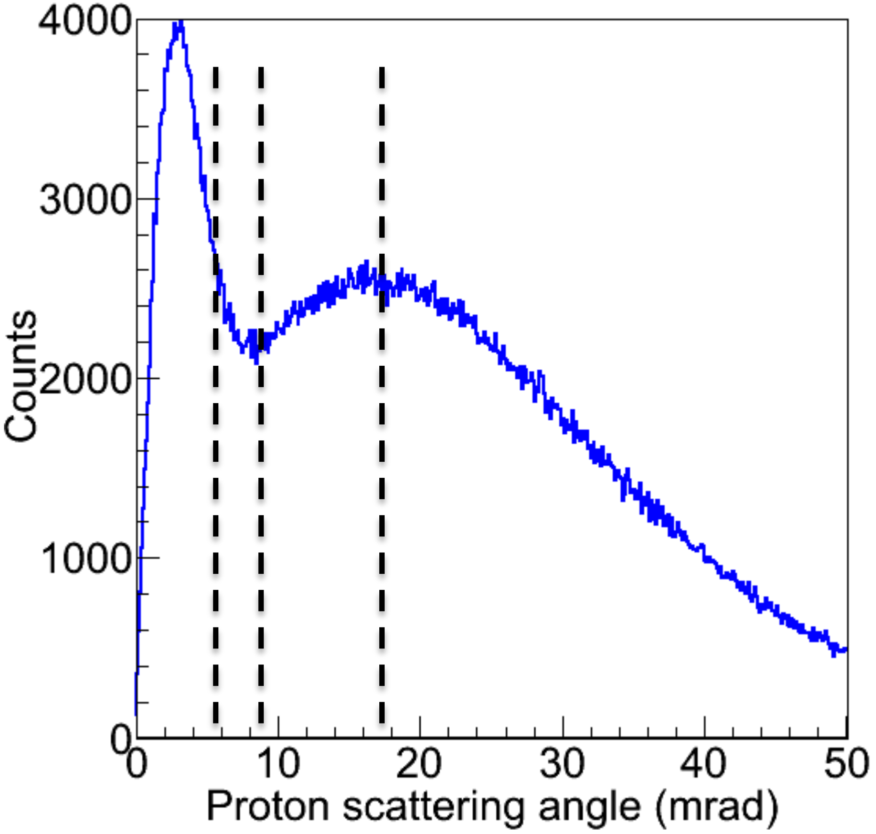

$$\theta(rad) = \cos^{-1}\left(\frac{\vec{p}_0\,\vec{p}_3}{\left|\vec{p}_0\right|\left|\vec{p}_3\right|}\right)$$

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

Geant4 simulations

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

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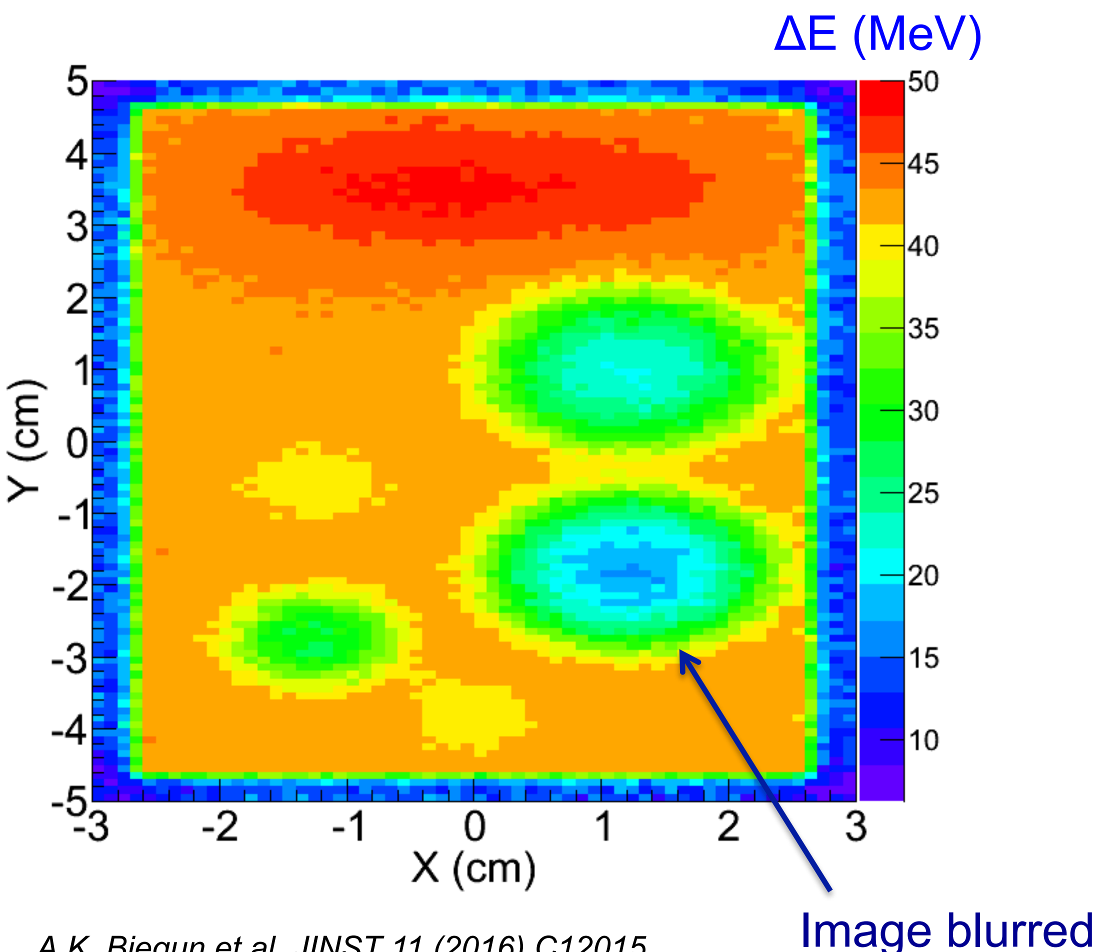
- Protons that passed through all 3 detectors are considered



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

Geant4 simulations

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

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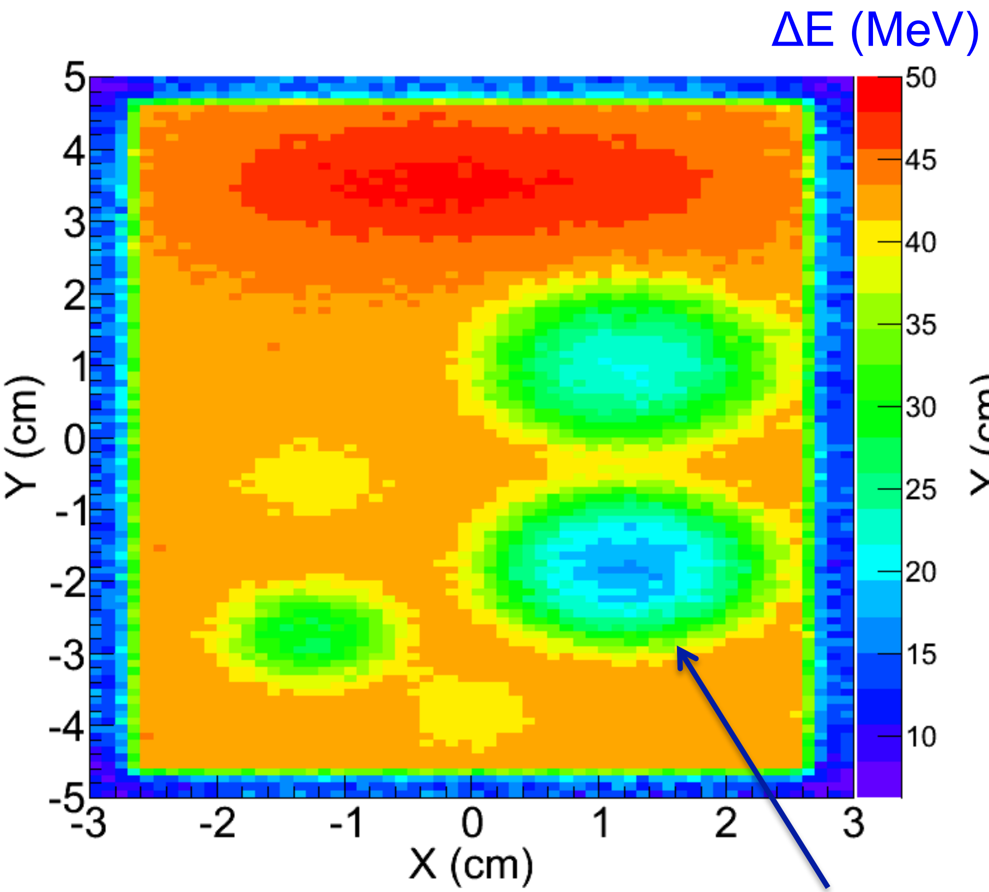
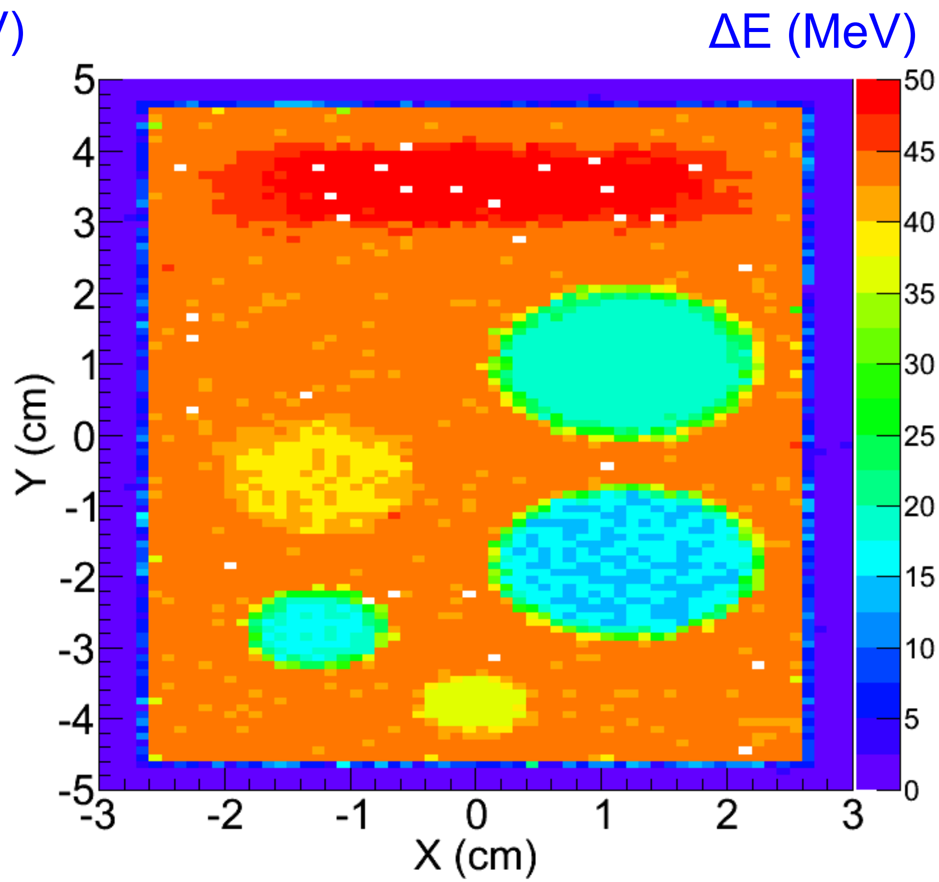
- ✧ Protons that passed through all 3 detectors are considered
- ✧ Protons with maximum scattering angle θ < 5.2 mrad

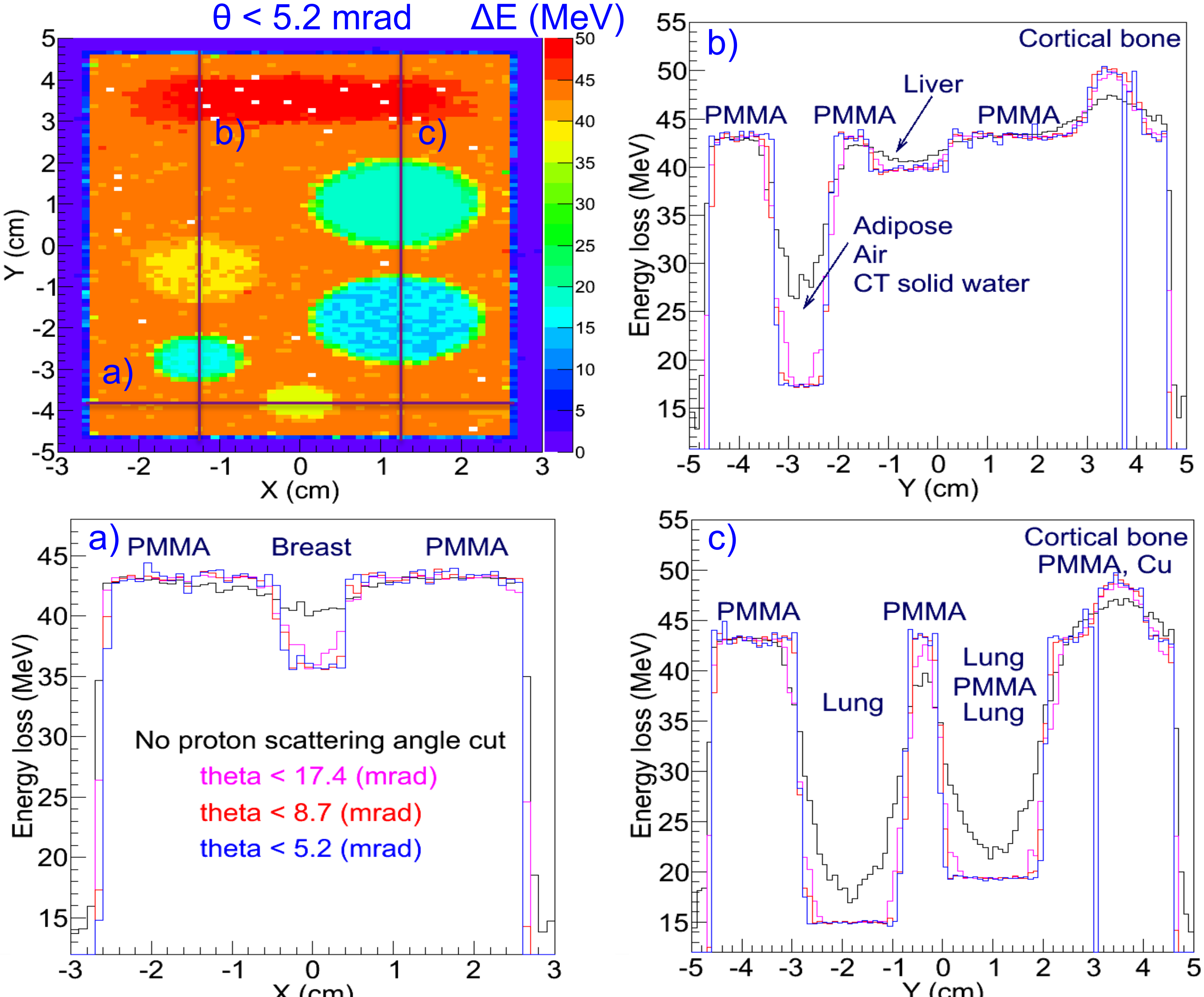




A.K. Biegun et al, JINST 11 (2016) C12015

Geant4 simulations

Energy loss radiographs: Projections



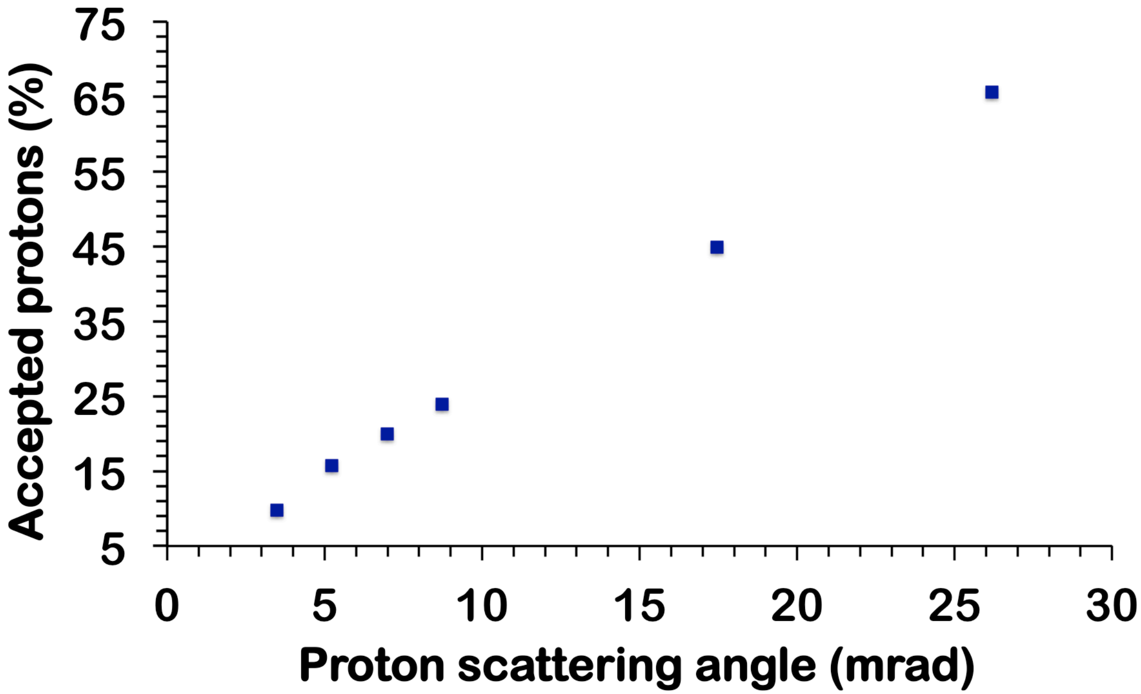
A.K. Biegun et al, JINST 11 (2016) C12015

Sharper edges between materials for smaller scattering angles of protons

Bin size: 1 mm

Geant4 simulations

Statistics @ E_p = 150 MeV



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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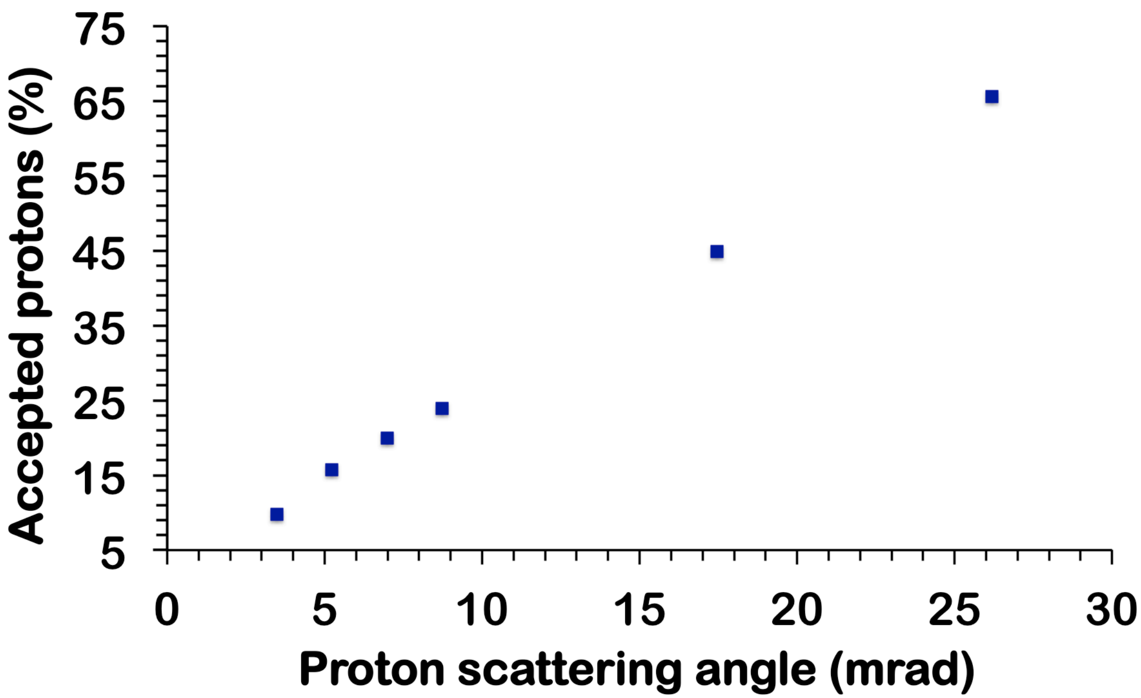

θ (mrad)	Accepted protons (%)
26.2	65.6
17.4	44.9
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5.2	15.7
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Significant number of protons (>70%) simulated at E_p=150 MeV is eliminated at θ < 8.7 mrad

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

Geant4 simulations

Statistics @ E_p = 150, 190 and 230 MeV

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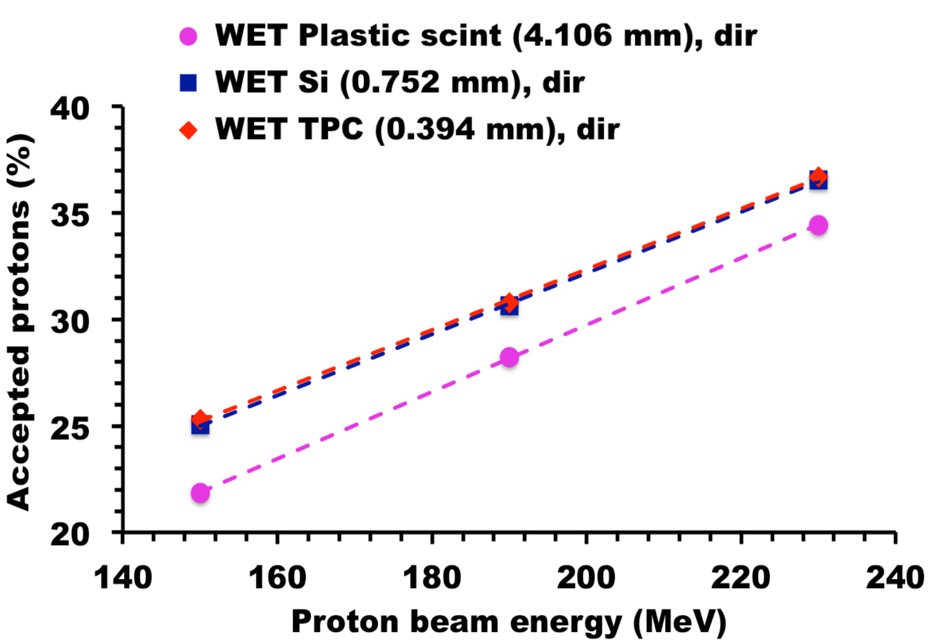
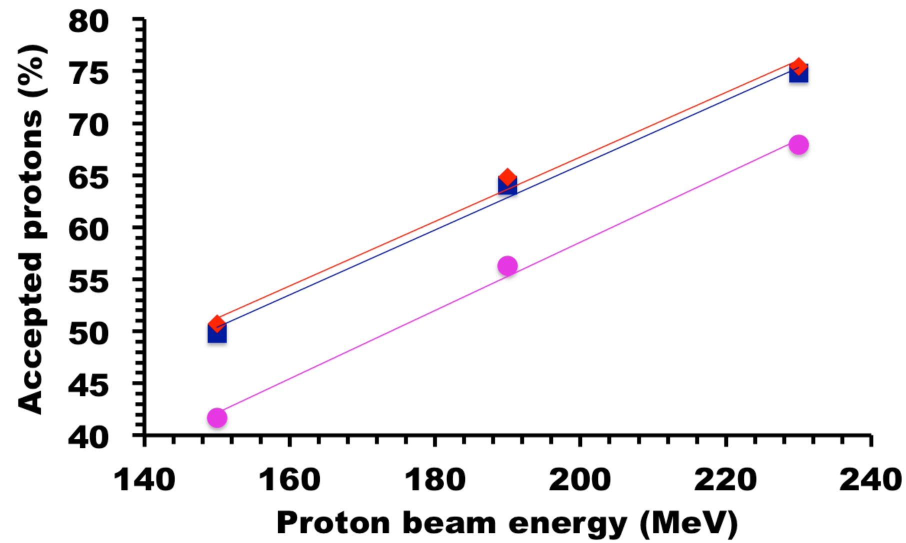
✧ $\theta_{12}^{\vec{p}} < 8.7$ mrad

✧ $\theta_{12}^{pos} < 8.7$ mrad





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

Proton radiography @KVI–CART: Exp setup’15

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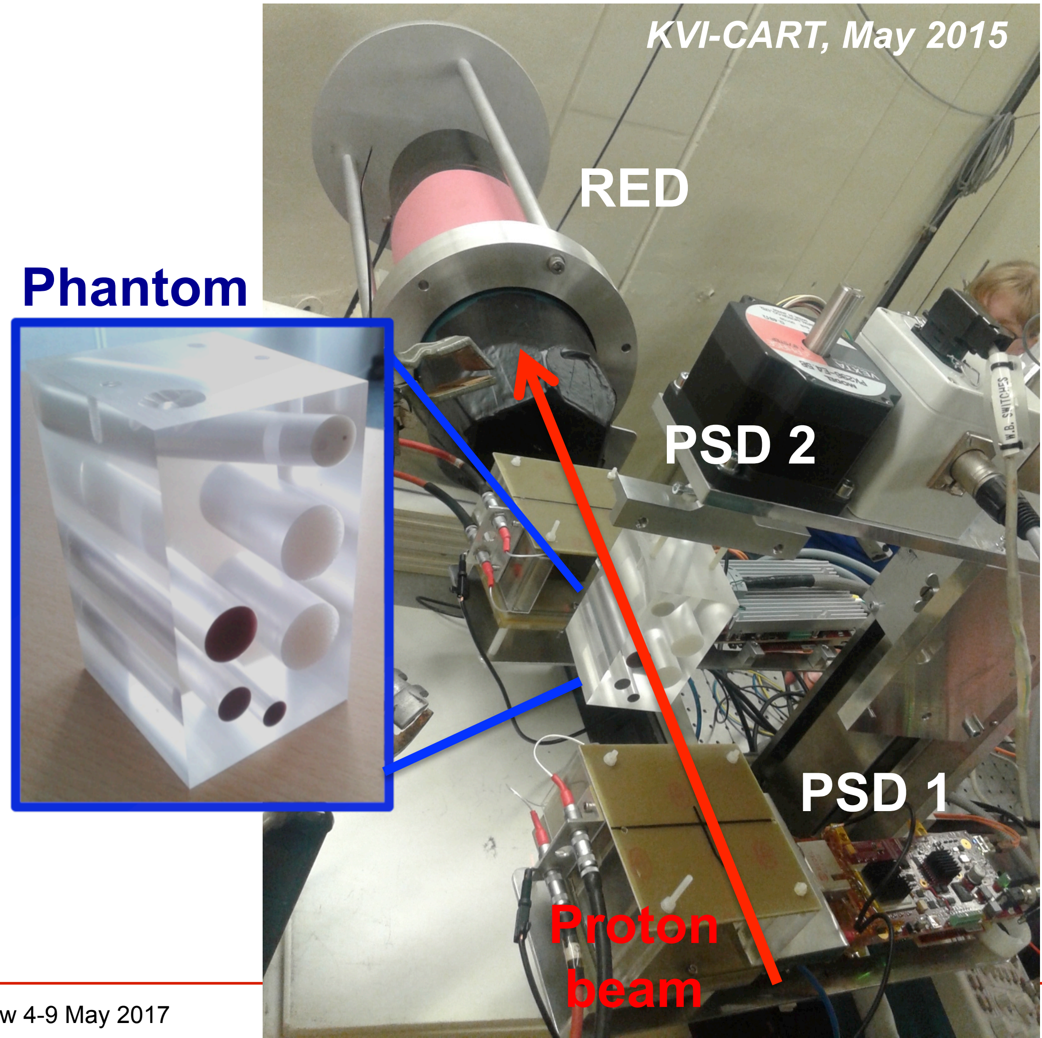
Collaboration with J. Visser, M. van Beuzekom, E.N. Koffeman

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 yet high enough as required in clinics



Energy loss reconstruction: Sims vs. Exp'2015

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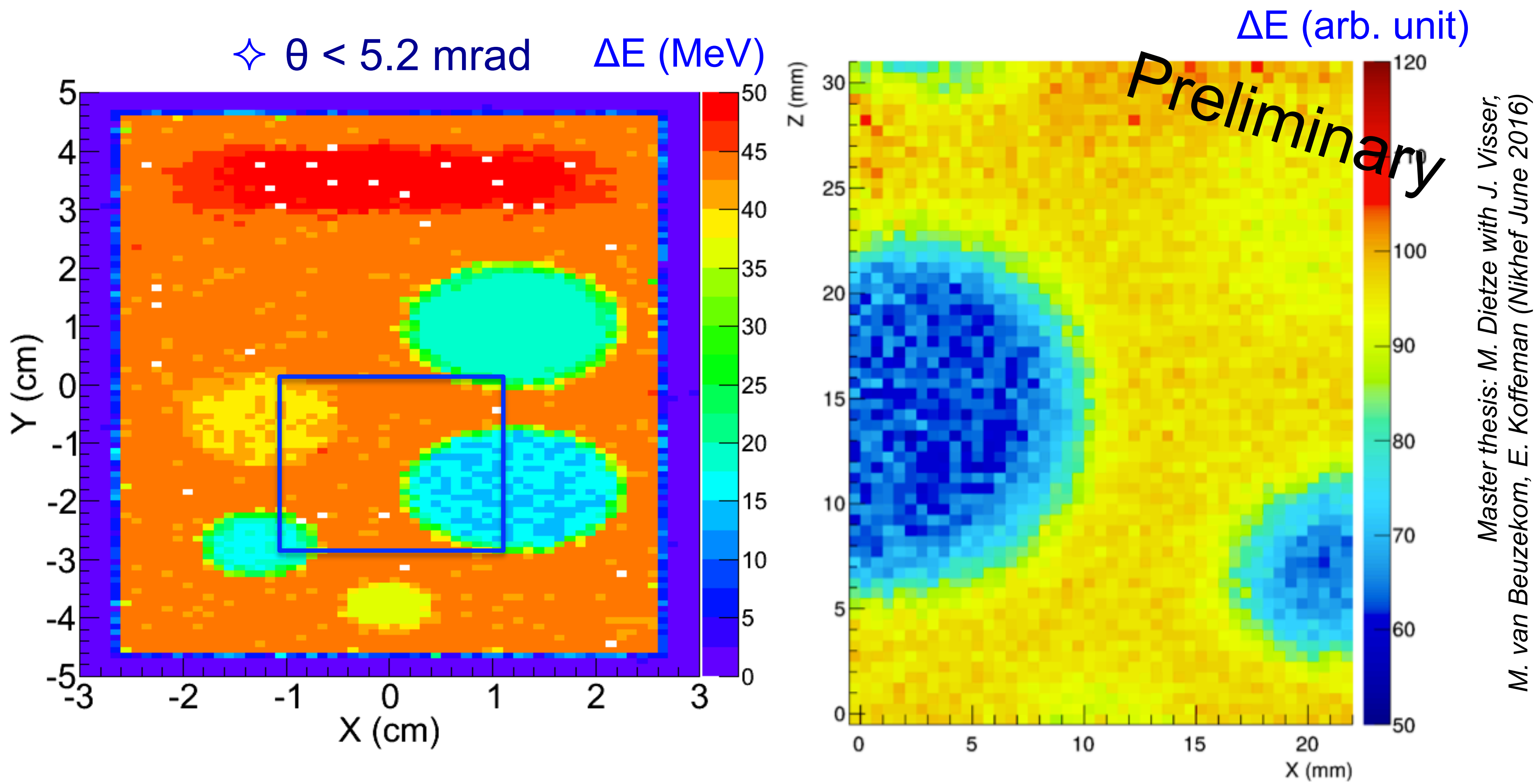

✧ Phantom only partially covered by Timepix3-based TPCs (3.0 x 3.0 cm^2)

Energy loss reconstruction: Sims vs. Exp'2015

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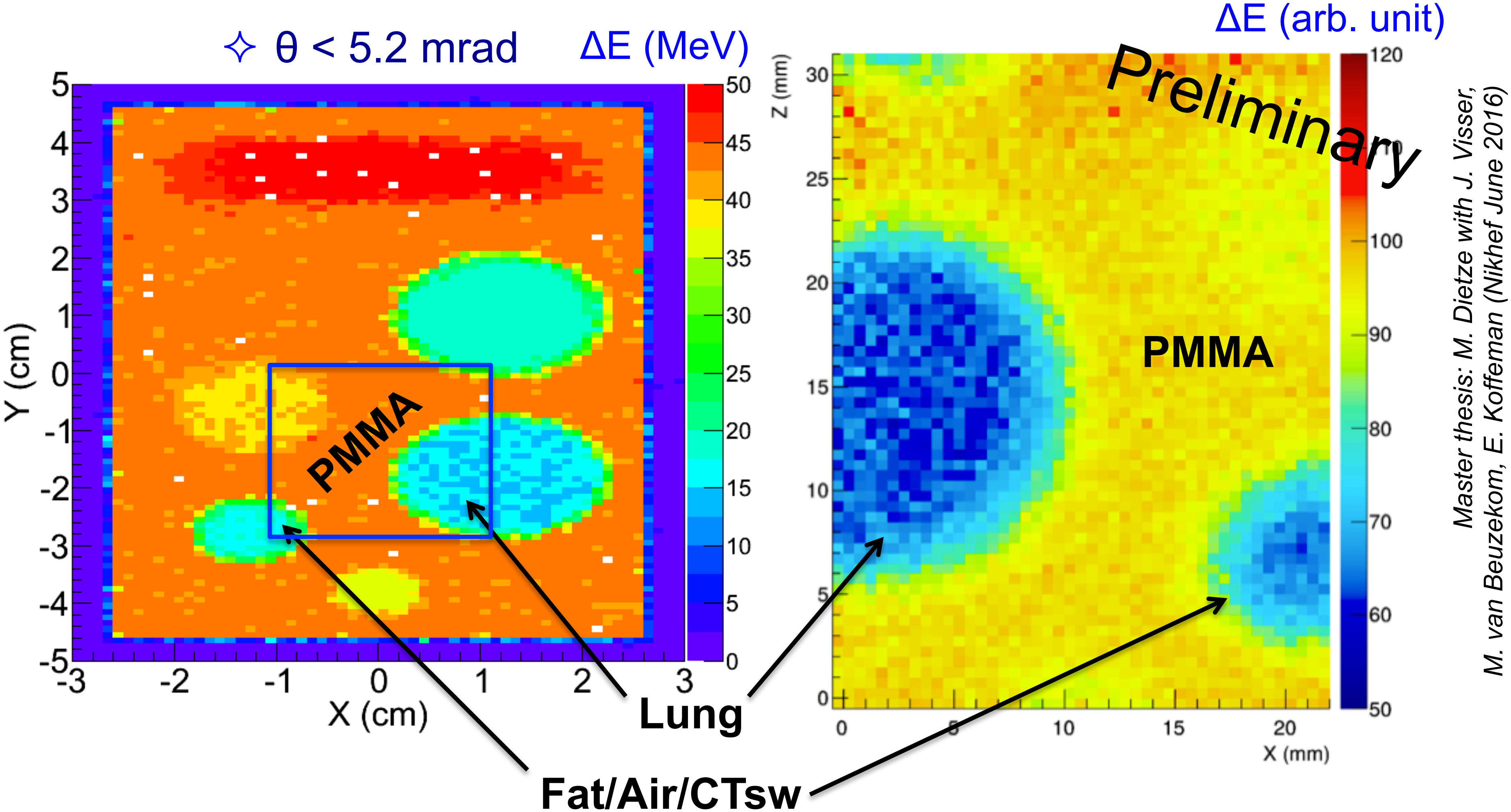

Simulations and experimental results comparable!

Clinical calibration curve (120 kVp)

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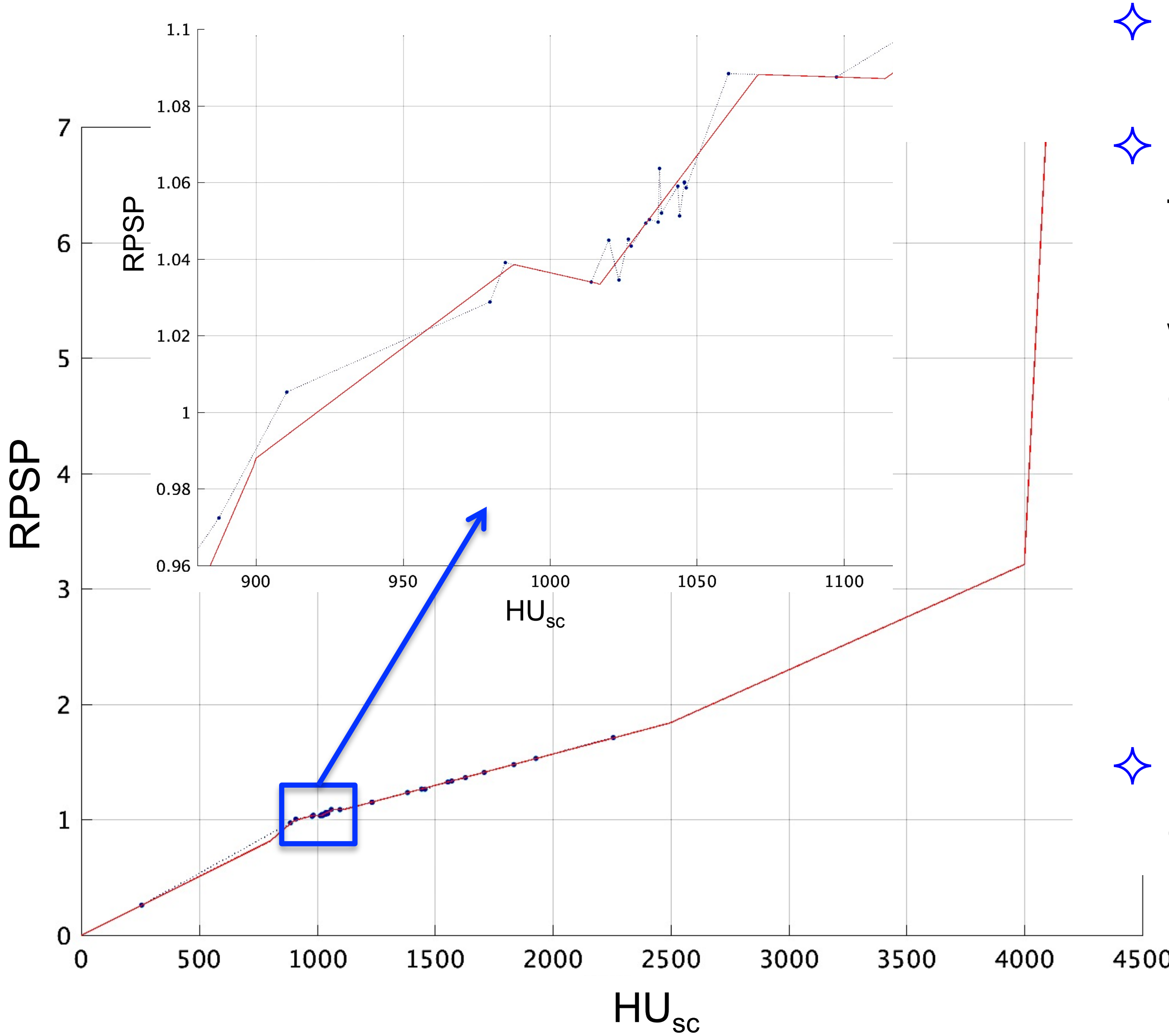
Master thesis: K. Ortega Marin with A.K. Biegun (KVI-CART/RuG July 2016)



- ✧ Specific for the scanner
- ✧ Stoichiometric method for biological tissues (35 standard human tissues) was used to obtain clinical calibration curve

  W. Snyder et al, Report of the Task Group on Reference Man, ICRP publication (1975)

  *U. Schneider, E. Pedroni, A. Lomax, PMB **41** (1996) 111*

- ✧ 9 linear segments in the calibration curve

$HU_{sc} = 1000 * \mu / \mu_{water}$
$HU_{sc} = HU + 1000$

Gammex and Complex phantoms in CT scanner

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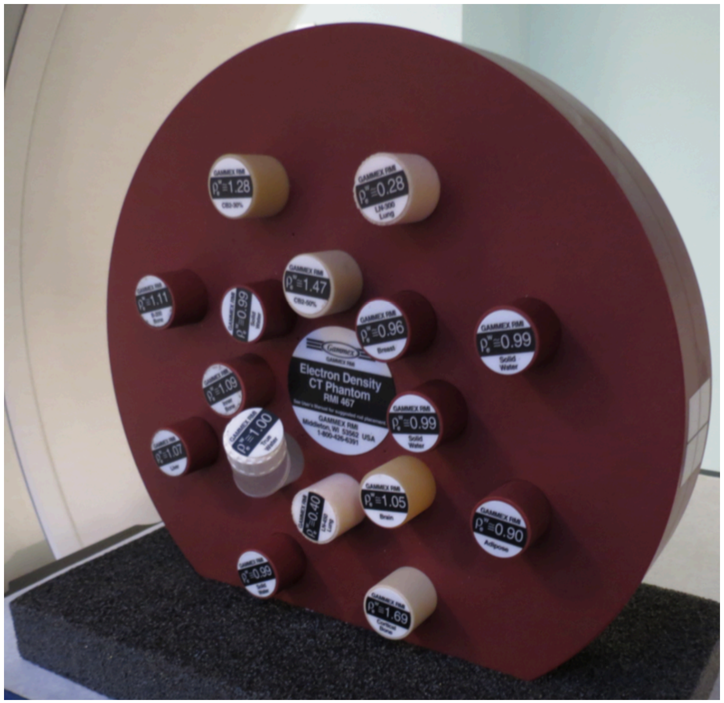
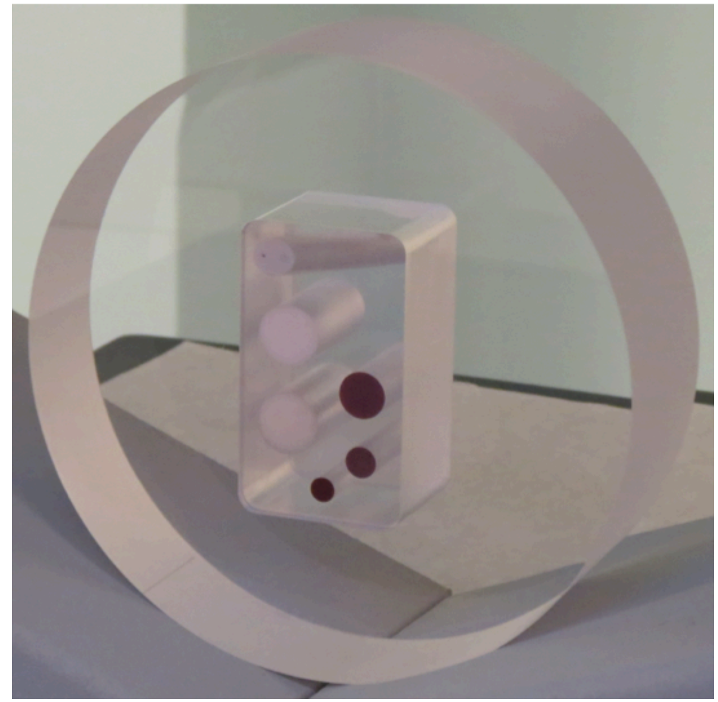
- *Siemens Somatom Definition AS* (Radiotherapy department, UMCG)





December 2015. Acknowledgment to Arjen van der Schaaf, UMCG

Master thesis: K. Ortega Marin with A.K. Biegun (KVI-CART/RuG July 2016)

- X-ray CT tube voltage:
  - Gammex (*calibration*) phantom: **120 kVp**
  - Complex (*patient*) phantom: 70, 80, 100, **120** and 140 **kVp**

- CT scan of Gammex phantom to create a clinical calibration curve with tissue materials

Water Equivalent Path Length (WEPL)

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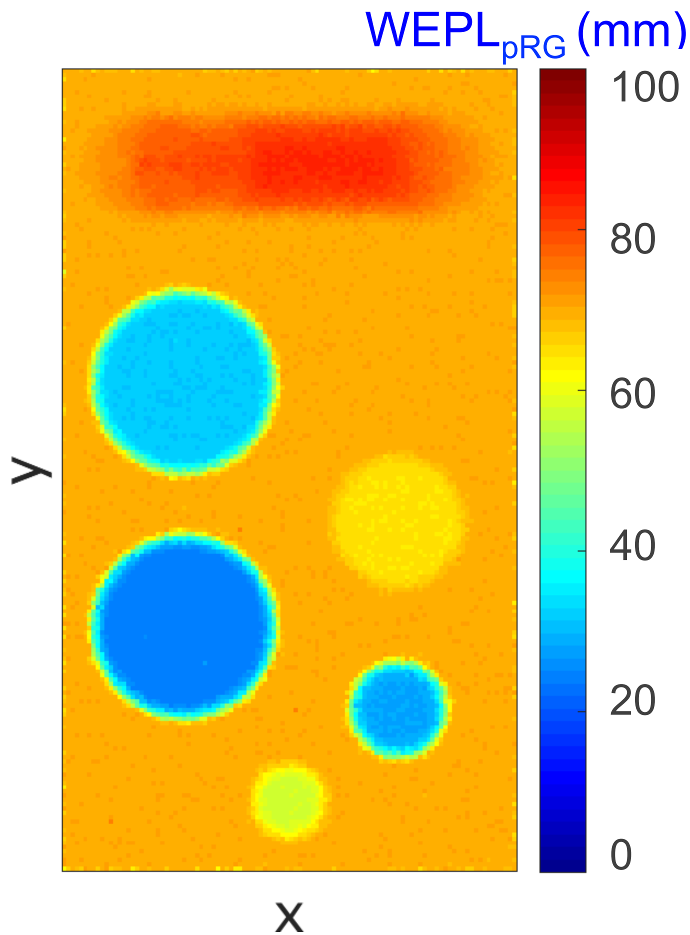
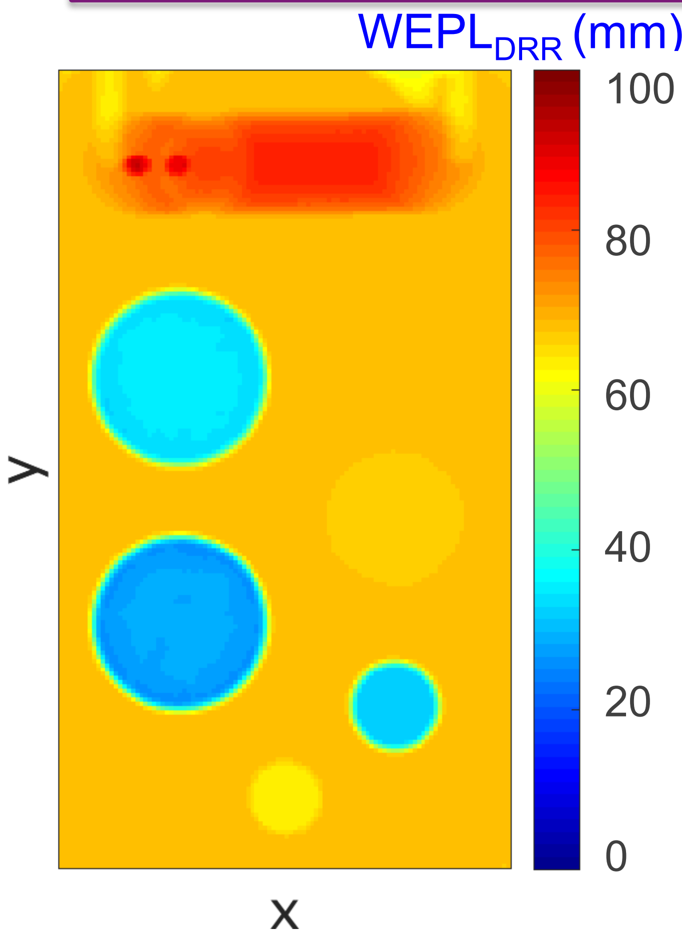
- Proton radiography: protons scattered < 5.2 mrad
- X-ray CT @120 kVp

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





Difference between $WEPL_{DRR}$ and $WEPL_{pRG}$

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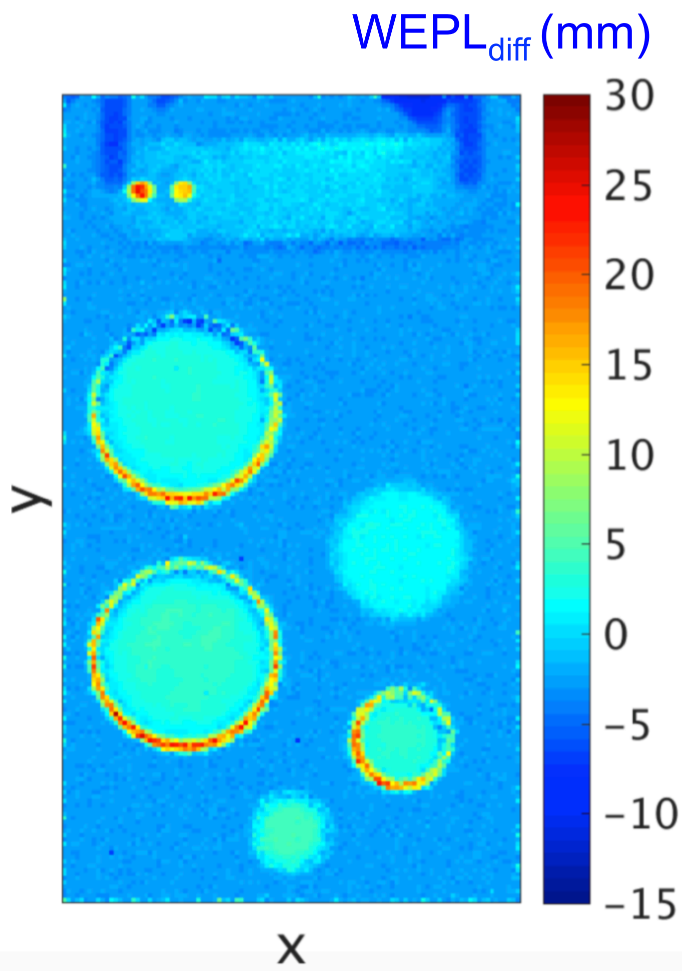

- ✧ Large overestimation in WEPL at high density materials (Cu, Ti)
- ✧ $WEPL_{DRR} > WEPL_{pRG}$ in all inserts
- ✧ $WEPL_{DRR} < WEPL_{pRG}$ in surrounding PMMA

  → PMMA not included in the clinical calibration curve

Metrics to optimize the clinical calibration curve

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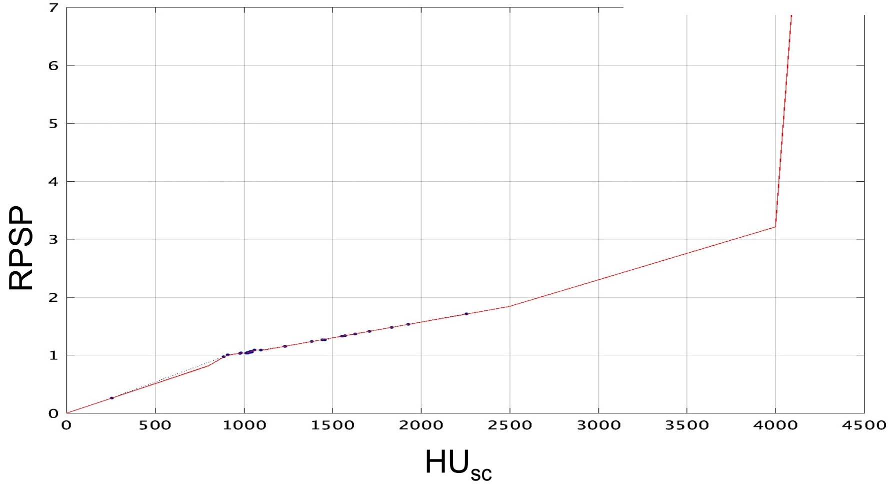
$$\mathrm{RMSE} = \sqrt{\frac{\sum_{x,y}(\mathrm{WEPL}_{DRR}(x,y) - \mathrm{WEPL}_{pRG}(x,y))^2}{N}}$$

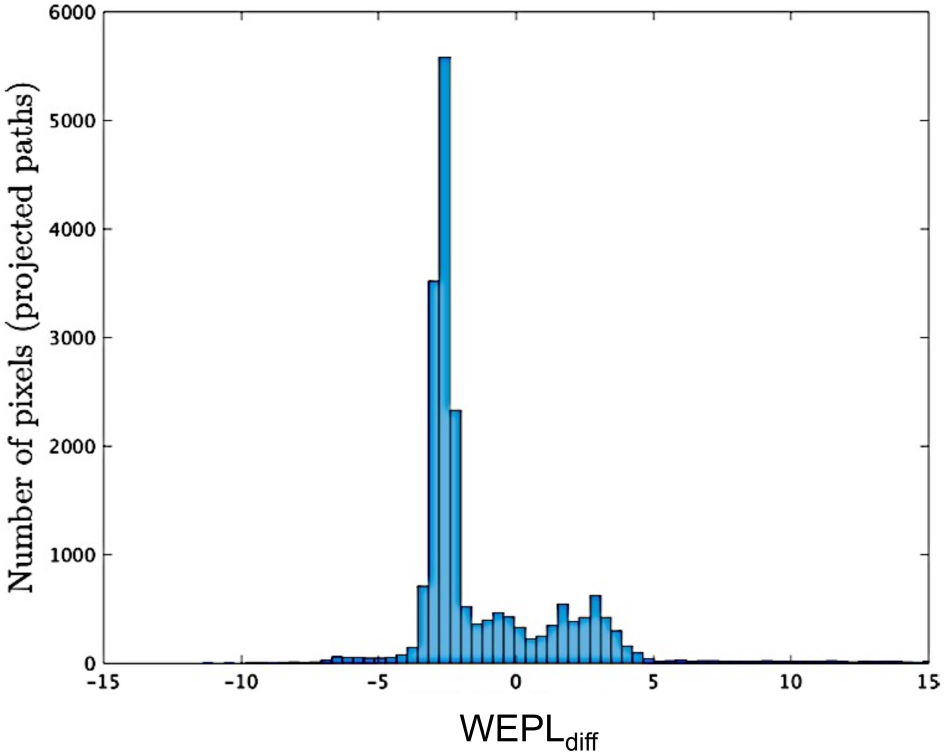
$$\chi^2 = \sum_{x,y} \frac{(\mathrm{WEPL}_{DRR}(x,y) - \mathrm{WEPL}_{pRG}(x,y))^2}{\mathrm{WEPL}_{pRG}(x,y)}$$

- Modifications of RPSP splitting point for 9 segments were done after either RMSE or χ^2 was minimized

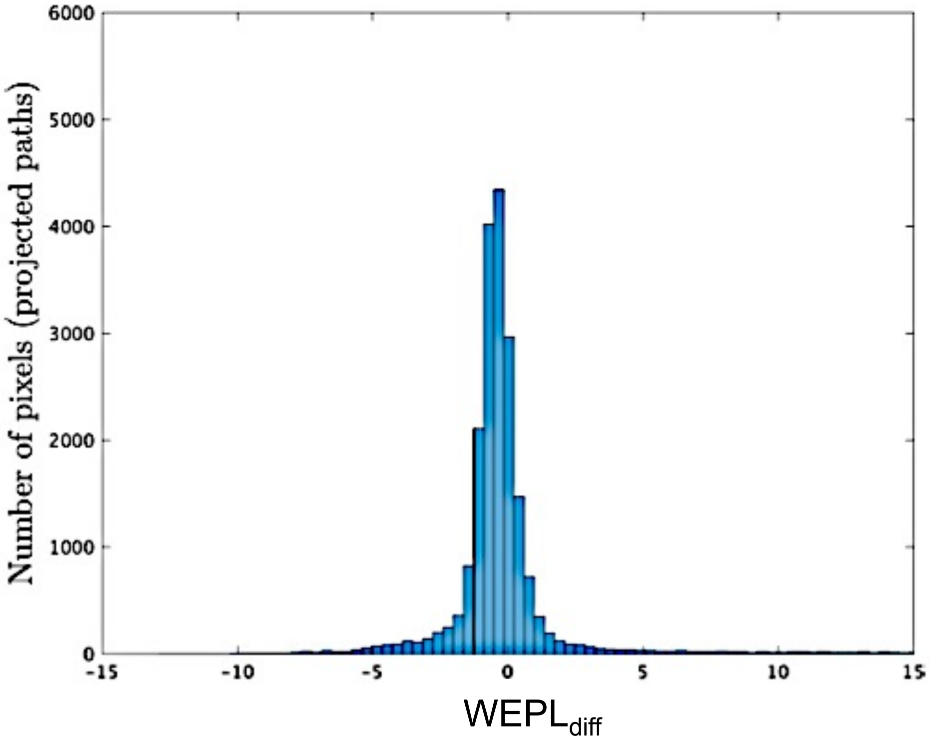


Number of pixels with certain WEPL

✧ Difference **before** optimization



✧ Difference **after** optimization



✧ Large fraction of pixels have a difference in WEPL between -2.5 mm and -3.5 mm (PMMA)

Original & optimized clinical calibration curves

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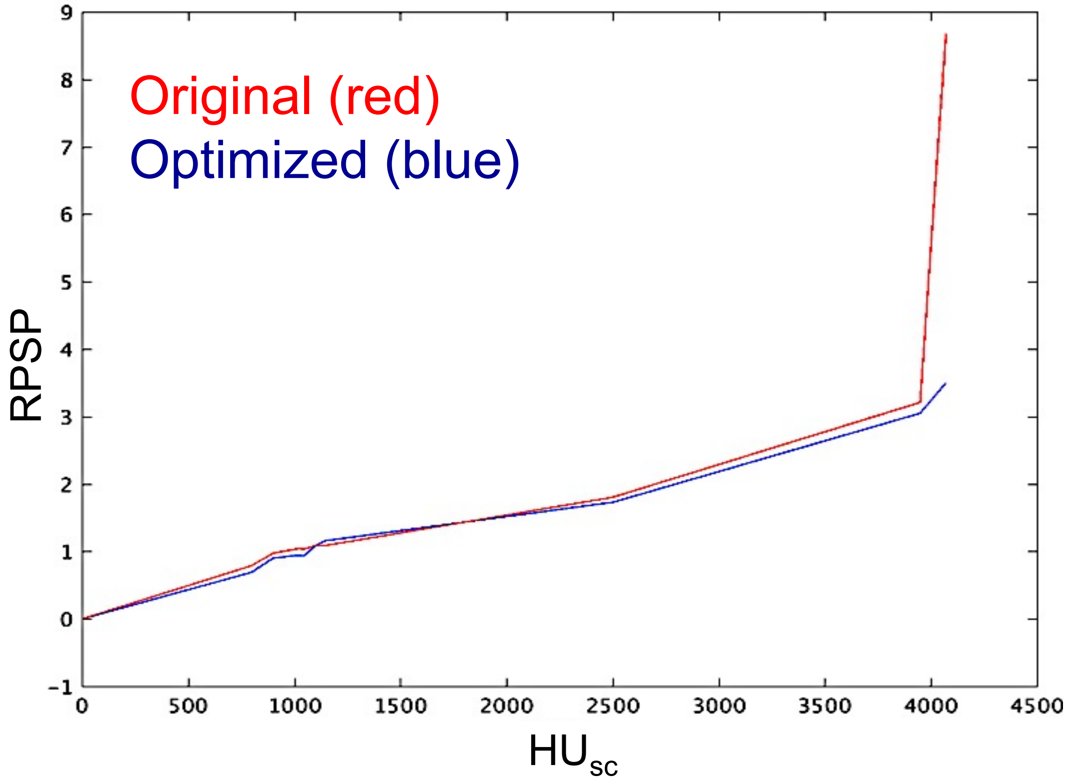

Before optimization

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%**)

Summary

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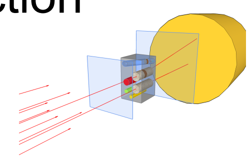
pRG

- ✧ Delivers proton stopping powers directly
- ✧ MCS decreases image quality, but angular selection improves it
- ✧ Experiments and simulations with the Complex (patient) phantom have been done

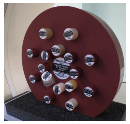
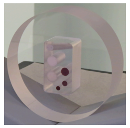


→ Experimental results of ΔE are comparable with simulations

→ $WEPL_{pRG}$

X-ray CT

- ✧ CT scans of Gammex (calibration) and Complex (patient) phantoms


+


→ $WEPL_{DRR}$

pRG + X-ray CT

- ✧ $WEPL_{DRR} – WEPL_{pRG}$
- ✧ Optimization of the “patient-specific” calibration curve for Complex (patient) phantom

→ $WEPL_{diff}$

→ Optimized RPSP for treatment planning

Future work

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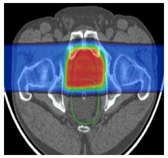
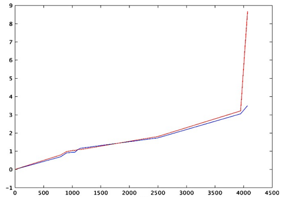
- Compare proton treatment plan before / after optimization

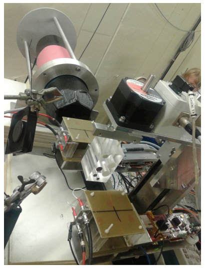


- Further optimization of the clinical calibration curve:
  spit of each segments into smaller segments
  to account for larger heterogeneities in human tissue



- Include CT/DECT patient data in Geant4 MC pRG simulations

- Development of detectors (tracking and energy) for pRG
  to achieve clinically relevant count rates (> MHz)



- Validate Geant4 MC simulations with the pRG experimental data

Backup slides

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☺

Scattering angle reconstruction: Exp'2015

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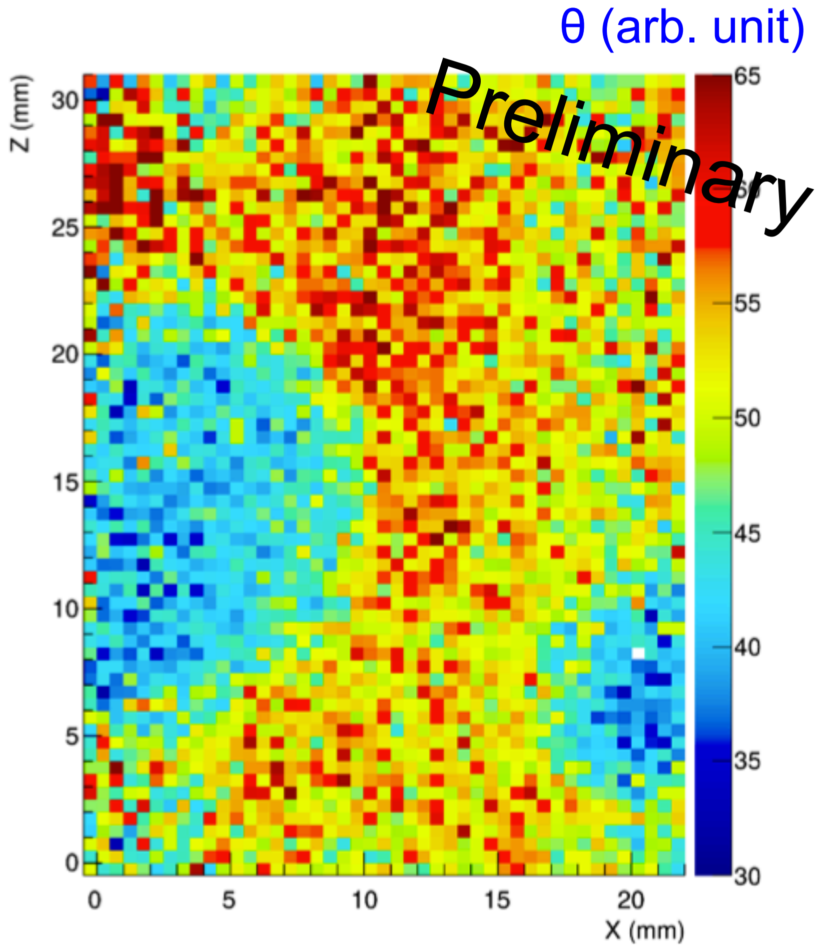
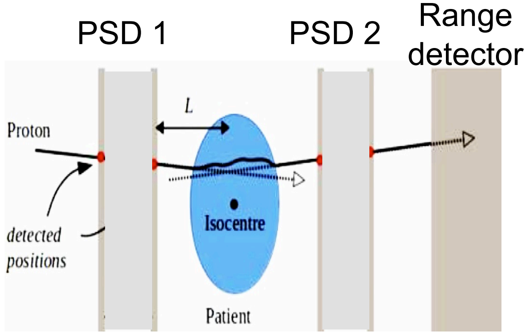


Master thesis: M. Dietze with J. Visser, M. van Beuzekom, E. Koffeman (Nikhef June 2016)

Scattering angle well reconstructed, but more statistics needed

Current systems

RED, Range detector

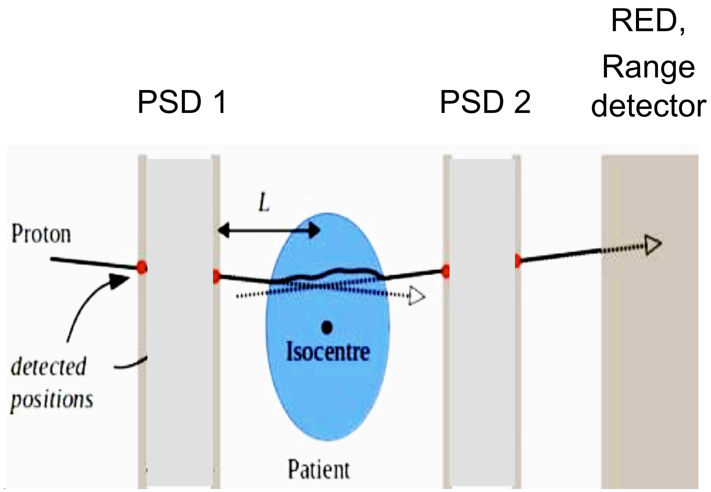


- ✧ Trend towards Si tracking detectors → very fast
- ✧ Different approaches for energy/range detectors
- ✧ Count rate close to what is required

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

Group	Year	PSDs (# of units)	RED/Range Detector	Rate (Hz)	Imaging device
PSI	2005	x-y Sci-Fi (4)	Plastic scintillator telescope	1 M	pRad
LLU/UCSC/ NIU	2013	x-y SiSDs (4)	CsI (Tl)	15 k	pCT
LLU/UCSC/ CSUSB	2014	x-y SiSDs (4)	Plastic scintillator hybrid telescope	2 M	pCT
AQUA	2013	x-y GEMs (2)	Plastic scintillator telescope	1 M	pRad
PRIMA I	2014	x-y SiSDs (4)	YAG:Ce calorimeter	10 k	pCT
PRIMA II	2014	x-y SiSDs (4)	YAG:Ce calorimeter	1 M	pCT
INFN	2014	x-y Sci-Fi (4)	x-y Sci-Fi	1 M	pCT
NIU/FNAL	2014	x-y Sci-Fi (4)	Plastic scintillator telescope	2 M	pCT
Niigata University	2014	x-y SiSDs (4)	NaI (Tl) calorimeter	5 k	pCT
PRaVDA	2015	X-u-v SiSDs	CMOS APS telescope	1 M	pCT

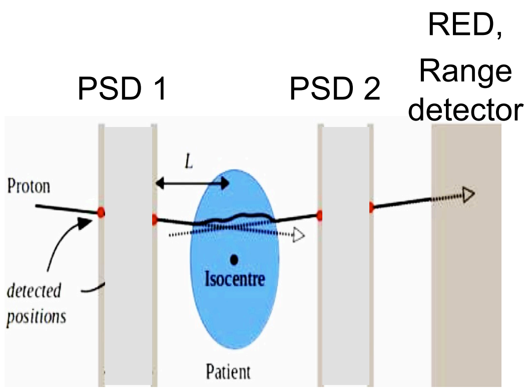
But…



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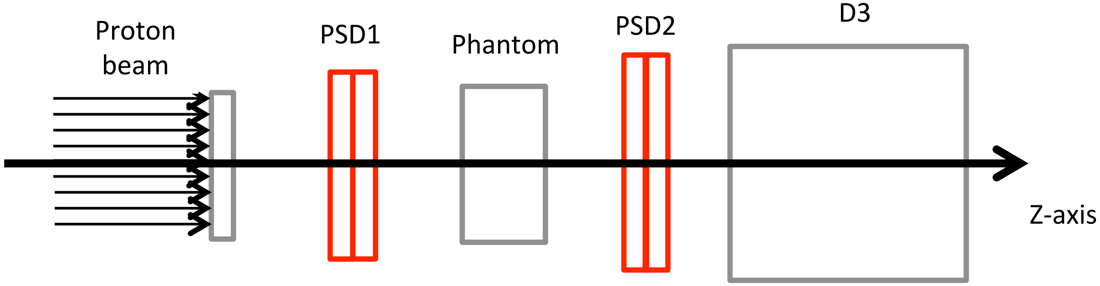
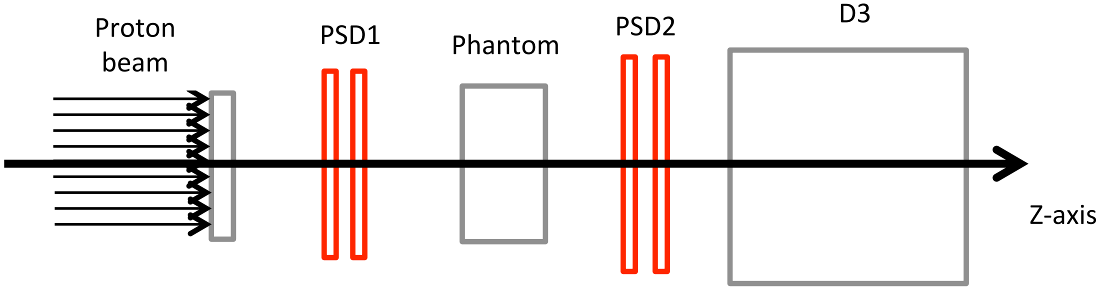
G. Poludniowski et al., Br J Radiol (2015) ***88****:20150134*

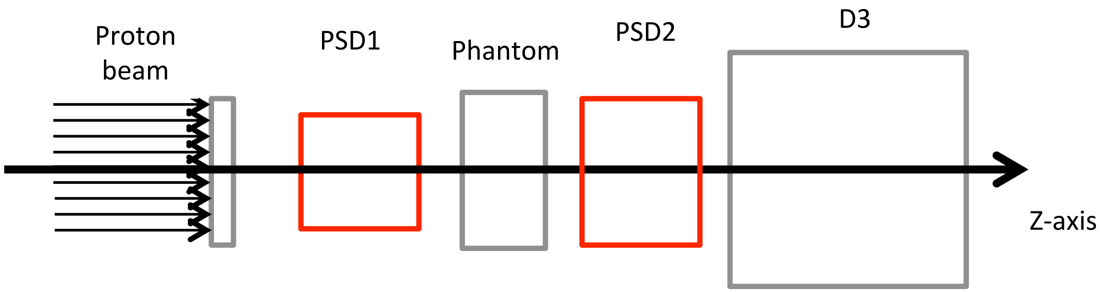
Various PSDs in proton radiography setup



- Two plane
  fiber scintillating hodoscope
  (PSI)



- Two plane
  silicon strip detectors
  (PRIMA I)



- Time Projection Chamber
  (Nikhef)

Geant4 simulations

PSDs parameters

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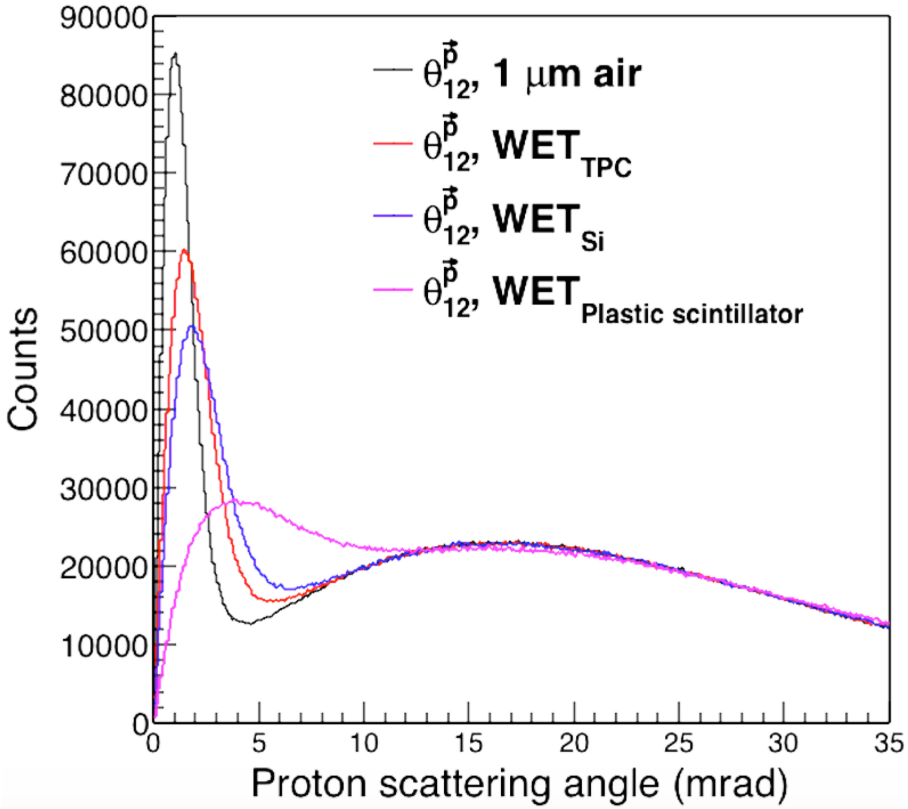
PSD detector type	Number of PSDs	Material	Material thickness (mm)	Material density (g/cm^3)	WET (mm)
Ideal	1	Air	0.001	0.0012	-
Plastic scintillator Fiber *[1]*	2	Bicron BCF12	4.0	1.032	4.106
Silicon strip detector *[2]*	2	Silicon	0.4	2.33	0.752
Gaseous TPC *[3]*	1	Isobutene C_4H_{10}	30	0.0025	0.394

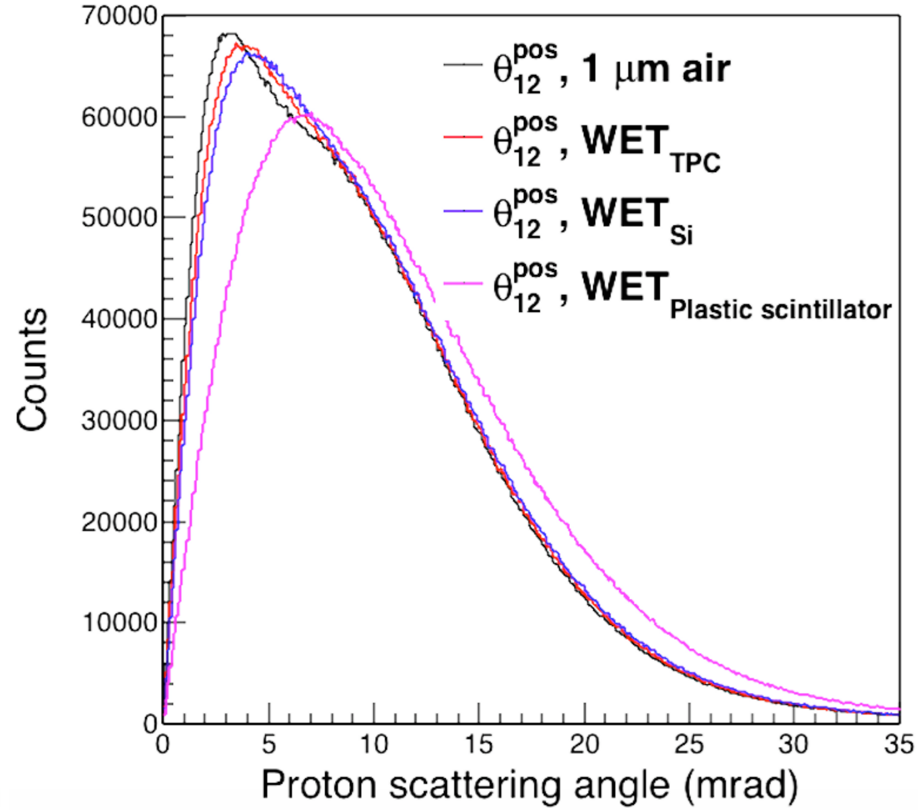
[1] U. Schneider et al., Med Phys 31:5 (2014) 1046-1051
[2] M. Scaringella et al., JINST 9 (2014) C12009
[3] A.K. Biegun et al., JINST 11 (2016) C12015

Statistics @ E_p = 150, 190 and 230 MeV

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

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





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

Geant4 simulations

Statistics @ E_p = 150, 190 and 230 MeV

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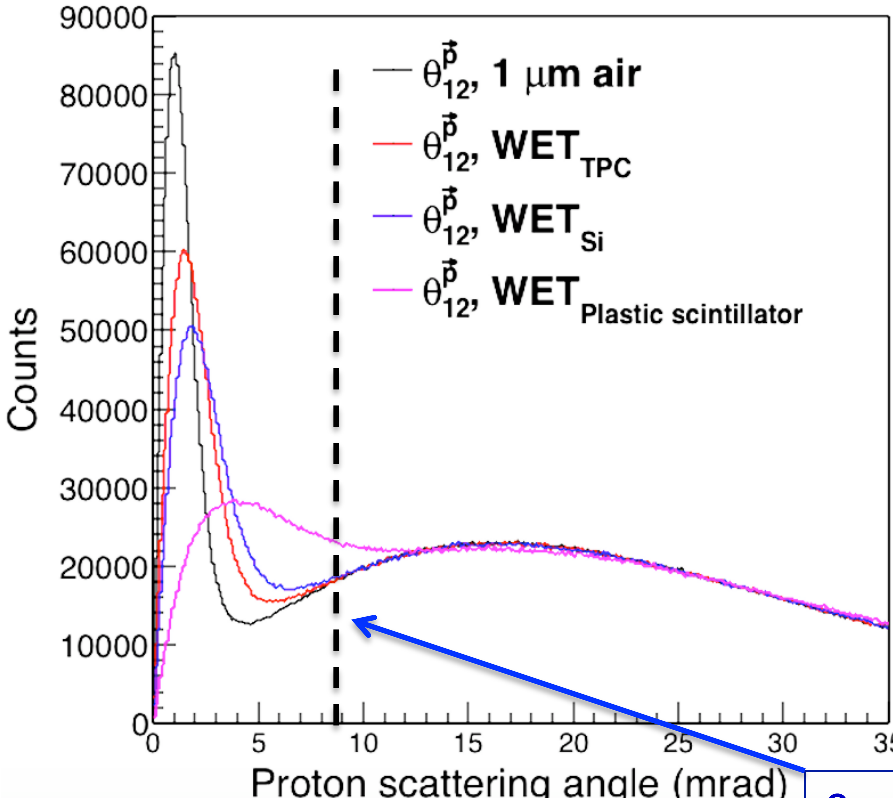
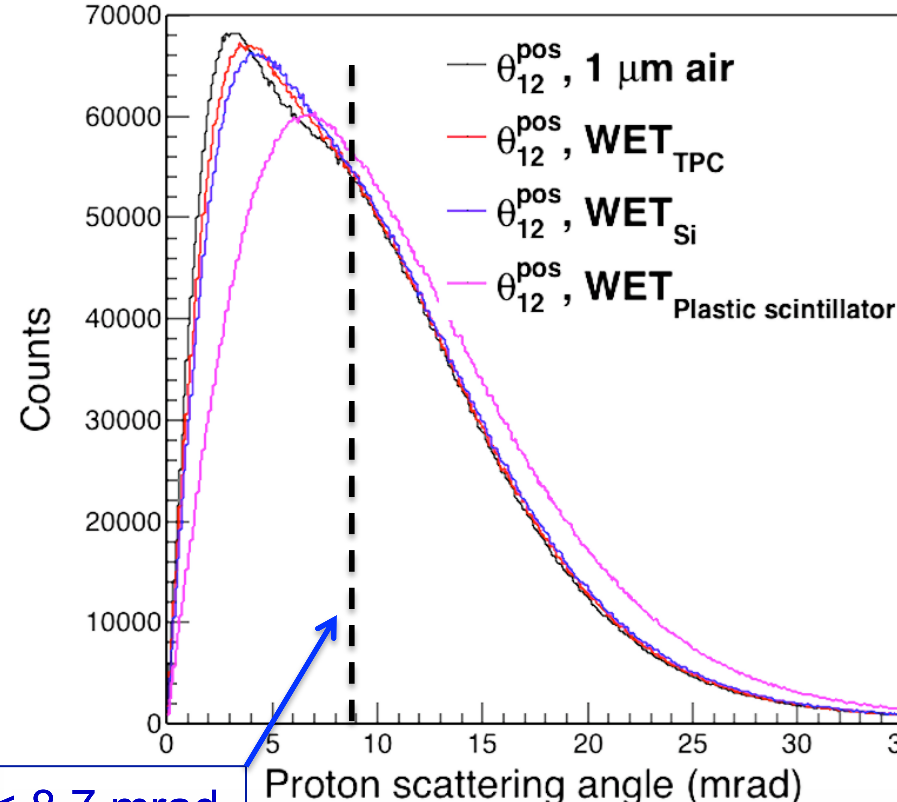
$$\phi_{12}^{\vec{p}}(rad) = \cos^{-1}\frac{\vec{p}_1\,\vec{p}_2}{|\vec{p}_1||\vec{p}_2|}$$

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





θ_{12} < 8.7 mrad

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

Geant4 simulations

Statistics @ E_p = 150, 190 and 230 MeV

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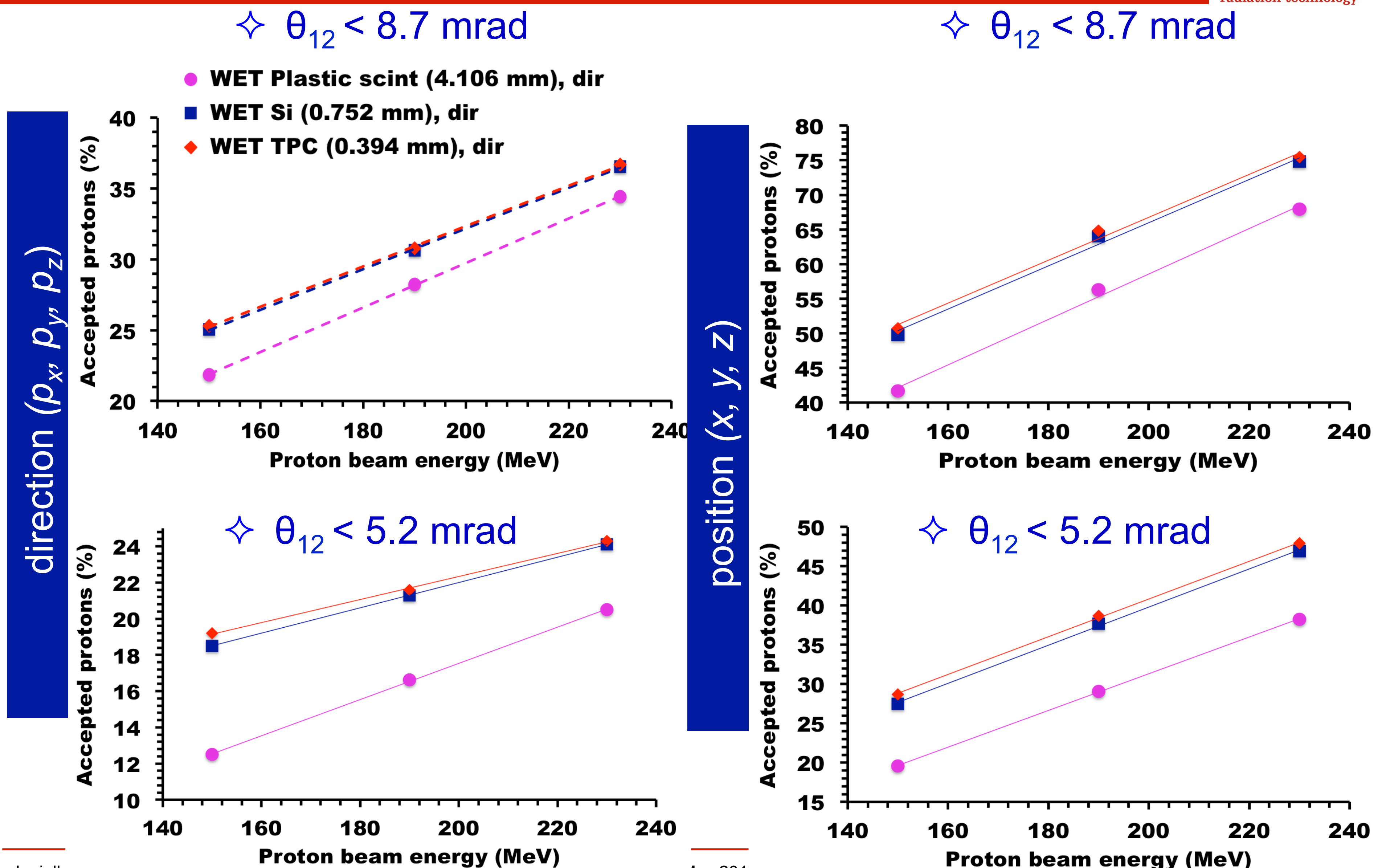

Work flow diagram

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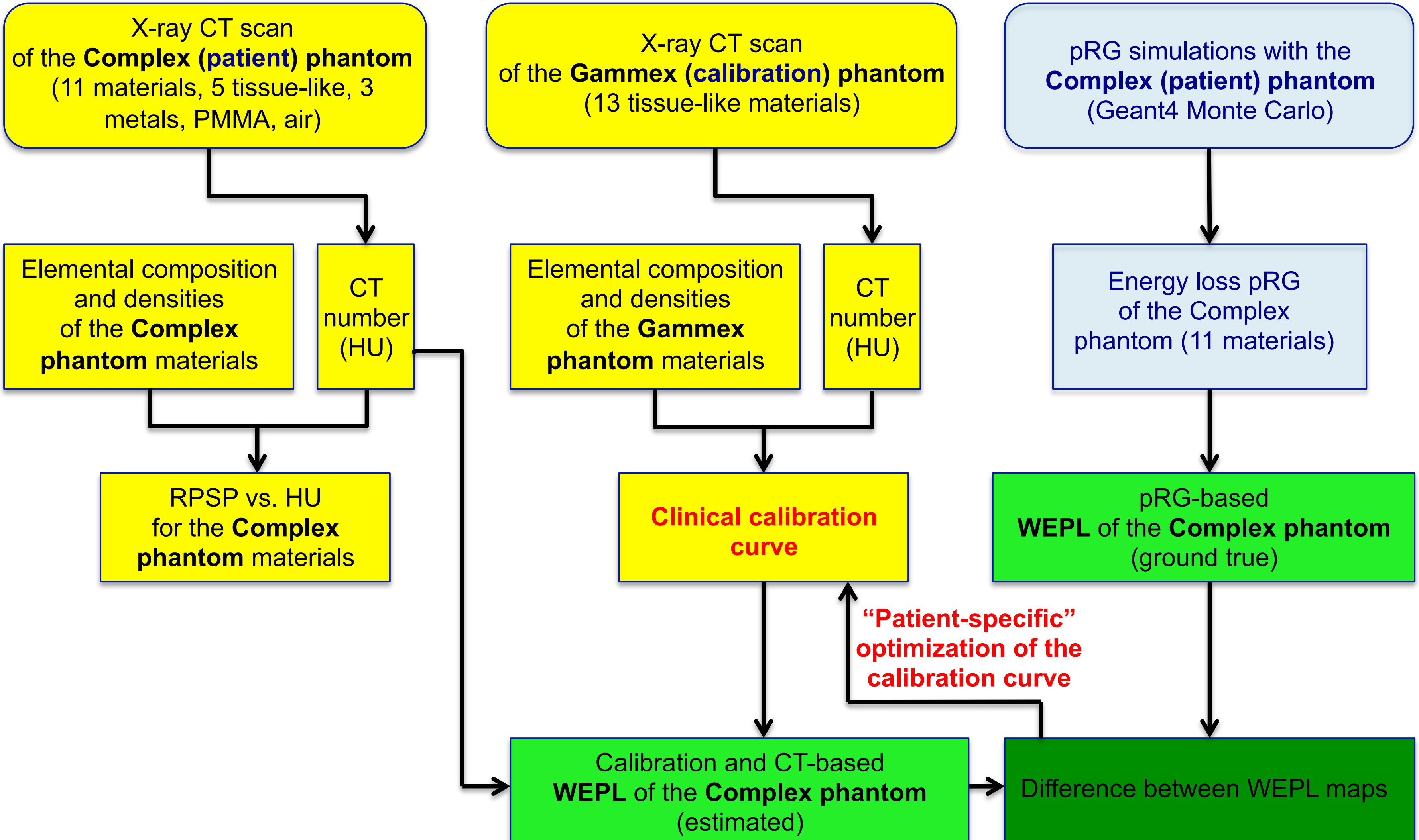

K. Ortega Marin, MSc thesis, KVI-CART/RuG (2016)

Clinical calibration curve (120 kVp)

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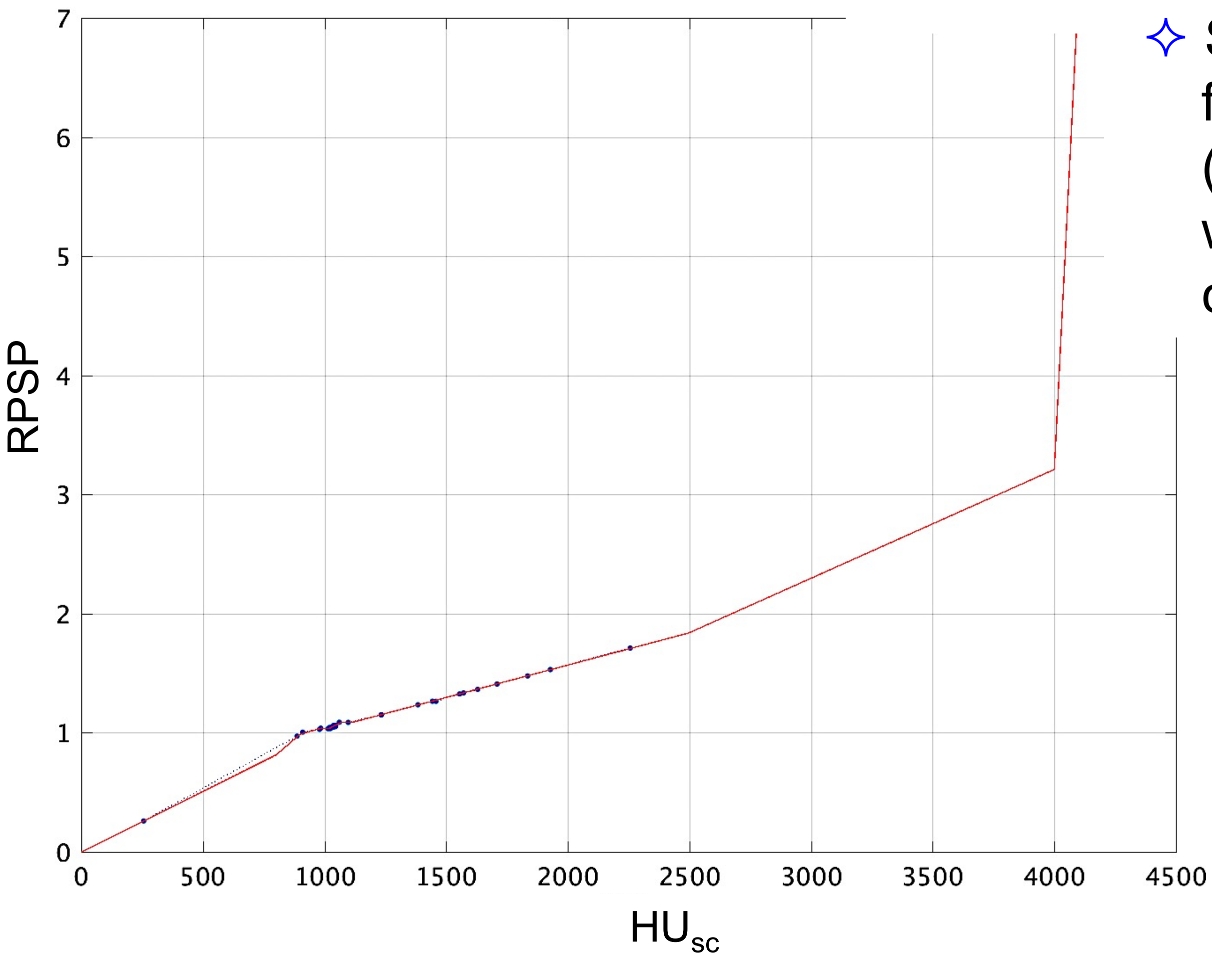
Master thesis: K. Ortega Marin with A.K. Biegun (KVI-CART/RuG July 2016)



- ✧ Specific for the scanner
- ✧ Stoichiometric method for biological tissues (35 standard human tissues) was used to obtain clinical calibration curve

W. Snyder et al, Report of the Task Group on Reference Man, ICRP publication (1975)

*U. Schneider, E. Pedroni, A. Lomax, PMB **41** (1996) 111*

$HU_{sc} = 1000 * \mu / \mu_{water}$

$HU_{sc} = HU + 1000$

Water Equivalent Path Length (WEPL)

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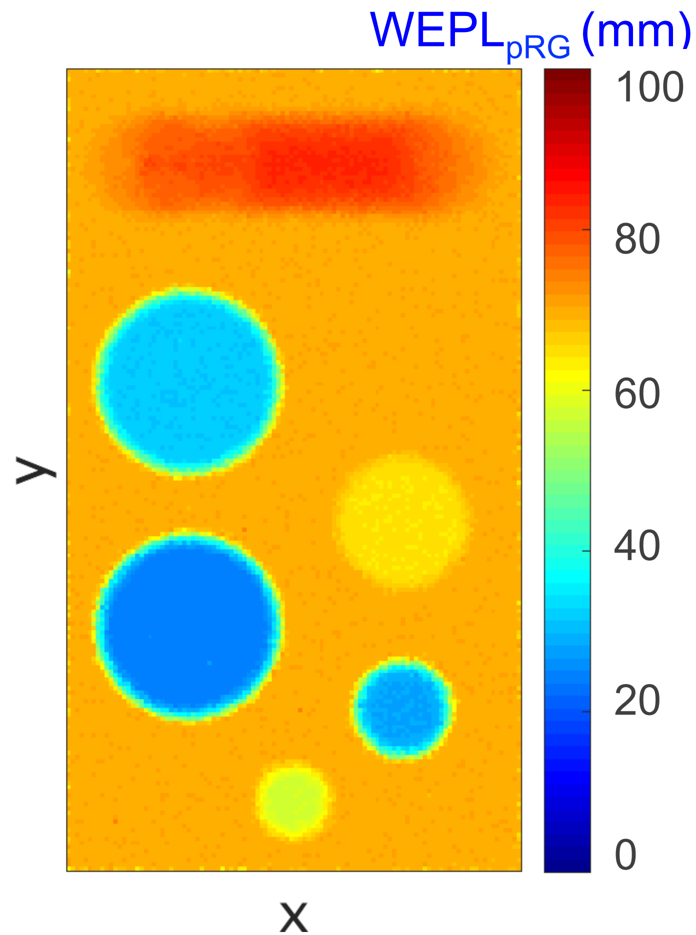
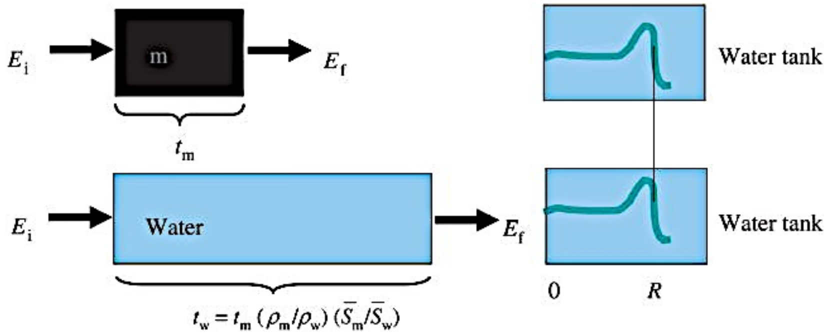
✧ Proton radiography:
protons scattered < 5.2 mrad

Voxel size: 1 x 1 x 6 mm^3

$$WEPL_{pRG} = t_m \times \rho_s = t_m \frac{\rho_m}{\rho_w} \frac{\overline{S}_m}{\overline{S}_w}$$



WEPL of material – thickness t_w of water, in which a proton with an energy E_i will stop at the same range as after passing a thickness t_m of the material



Original & optimized clinical calibration curves

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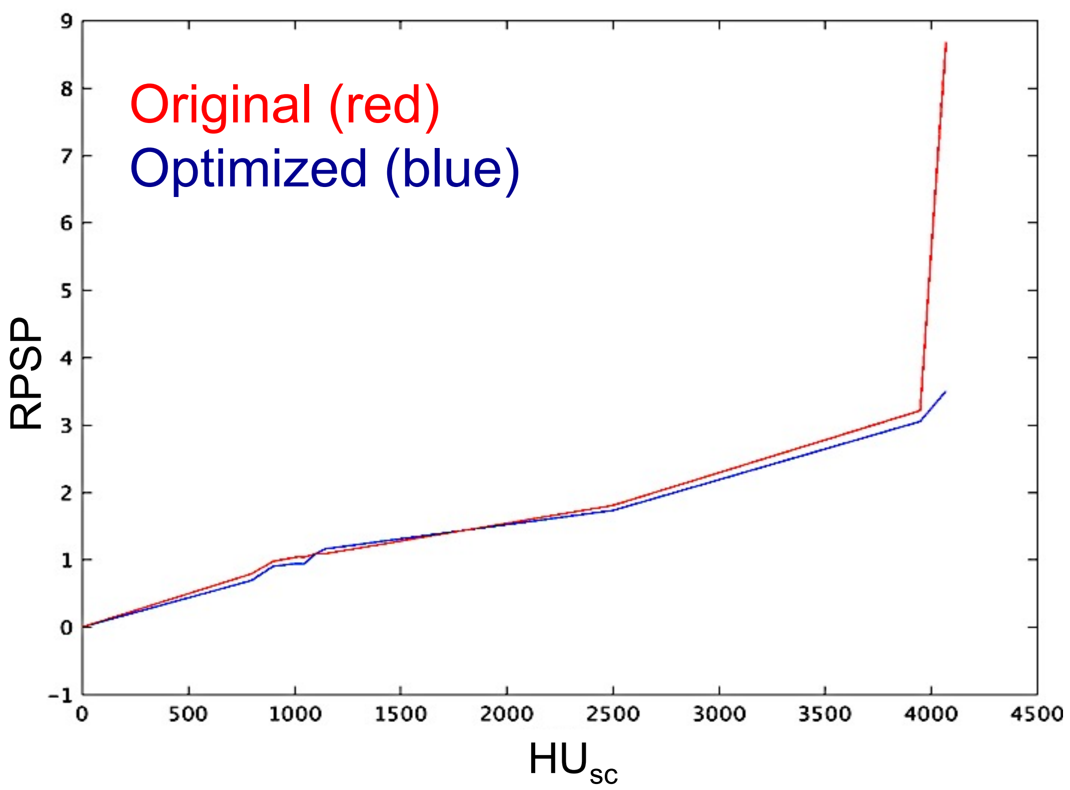


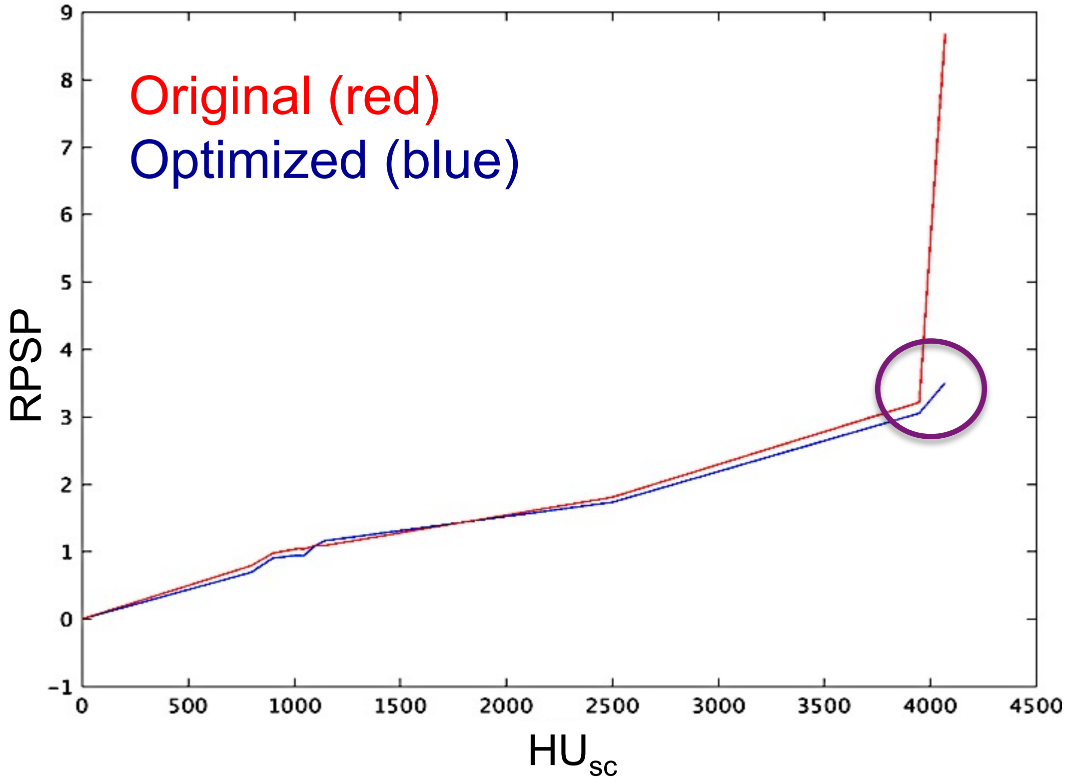
Before optimization

Metric	With PMMA	Without PMMA
RMSE	3.59 mm	2.65 mm
χ^2	5083.80	970.65

After optimization

Metric	With PMMA	Without PMMA
RMSE	2.36 mm (**-34.33%**)	1.38 mm (**-48.34%**)
χ^2	2287.10 (**-55.01%**)	260.28 (**-73.18**)

Original & optimized clinical calibration curves



Before optimization

- ✧ HU saturates for to ~4000 for metals

After optimization

- ✧ No saturation for metals

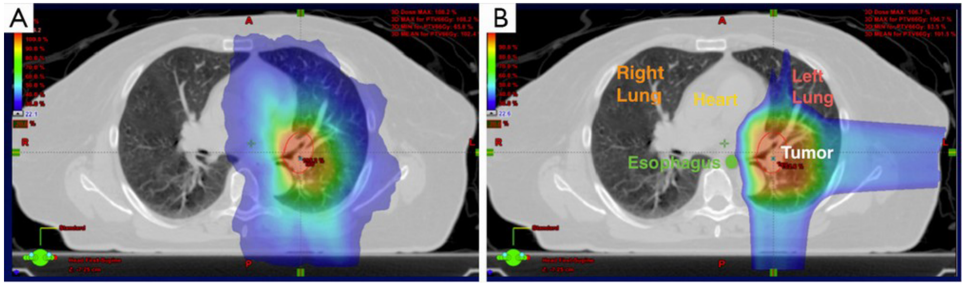
Goal…

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

Future work

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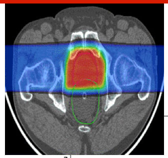
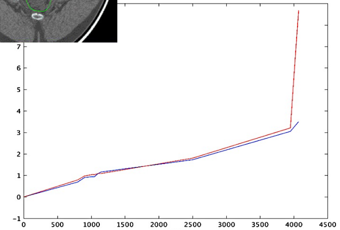
- Compare proton treatment plan before / after optimization

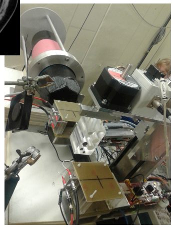


- Optimization of the clinical calibration curve:
  - further spit of each segments into smaller segments
    → to account for larger heterogeneities in human tissue

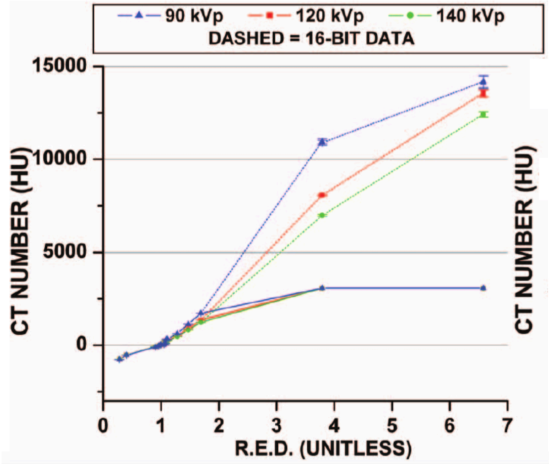


- Include CT/DECT patient data in Geant4 MC pRG simulations

- Validate Geant4 MC simulations with the pRG experimental data

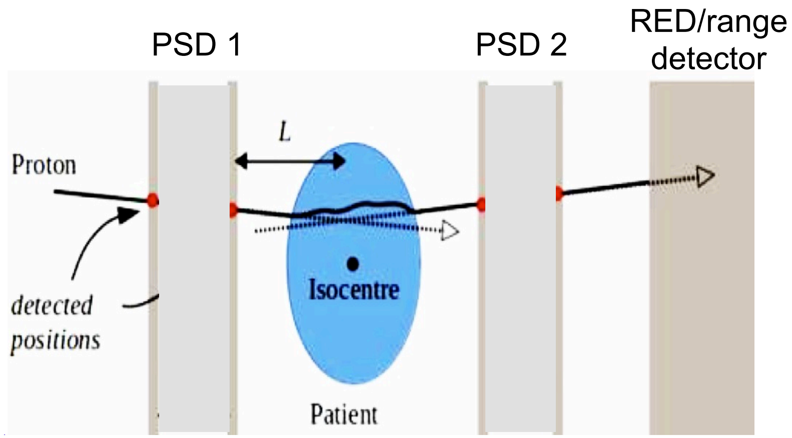


- Using 16 bit CT scanner
  → to improve HU determinations for metals



Glide-Hurst et al, Med Phys 40(6) (2013) 061711

Ideal system with tracking detectors



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**

All to be clinically acceptable!

✓**Tracking detectors**

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

  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** of up to 1%
- **Fast** → high count rate (> MHz)

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%**

Reconstruction of imaged object: trapezoid

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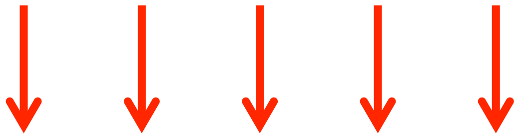
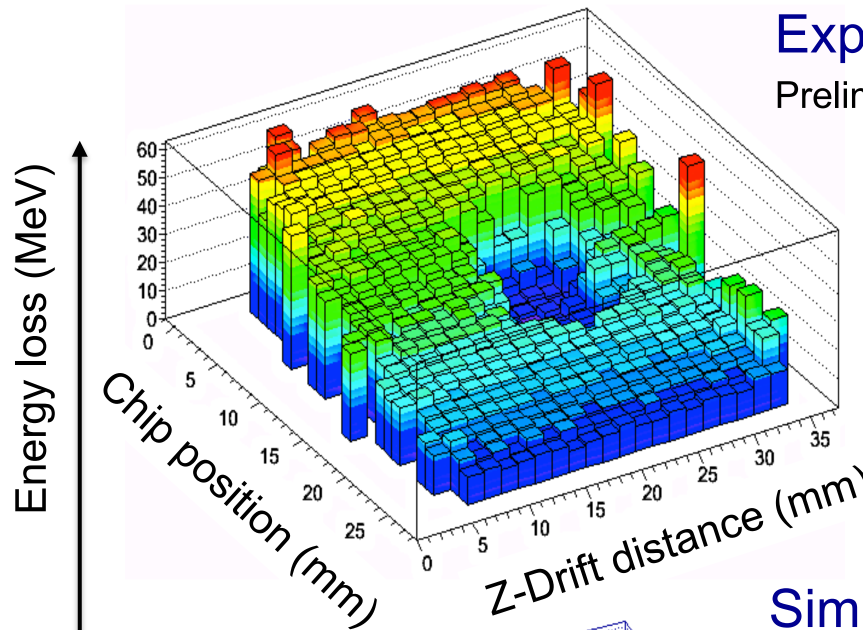
Scattered proton beam of 30 x 30 mm^2 size



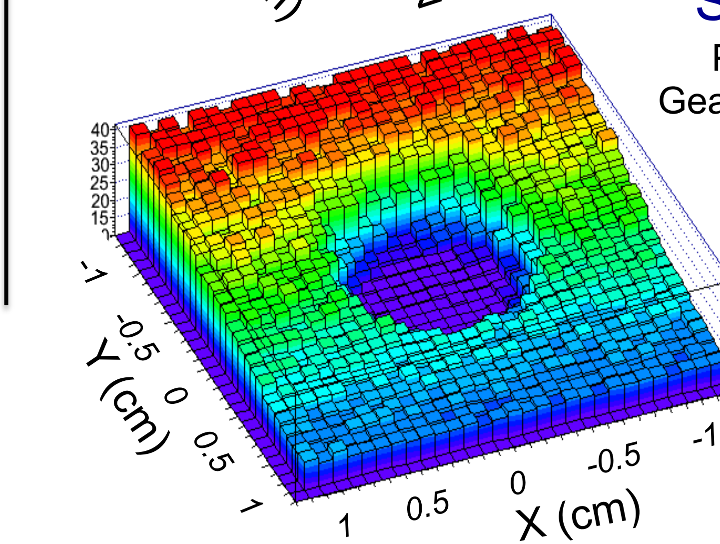
Experiment

Preliminary data



Simulations

Performed with Geant4-based MC



Brass trapezoid $\rho = 8.55$ g/cm^3
Polymer $\rho = 1.18$ g/cm^3

Reconstruction of object with tissue-like inserts

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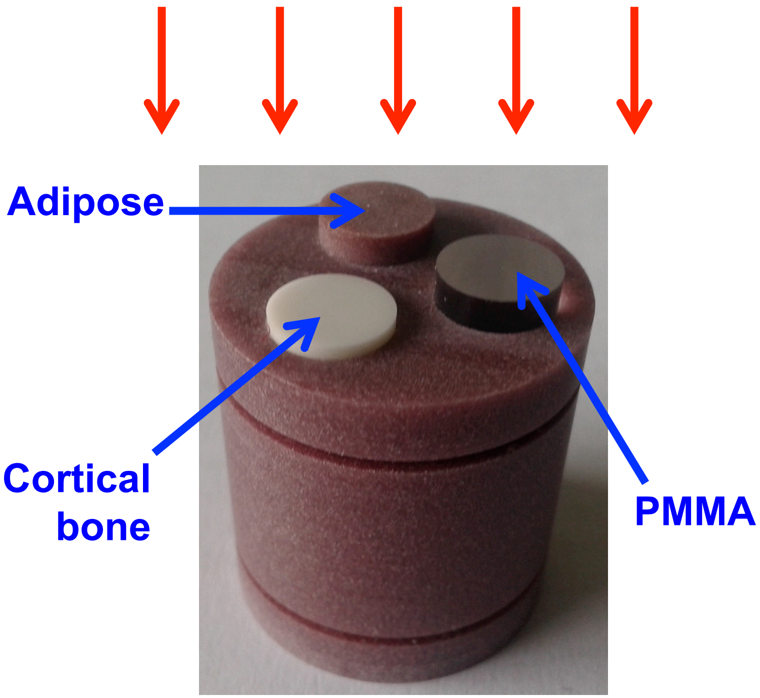
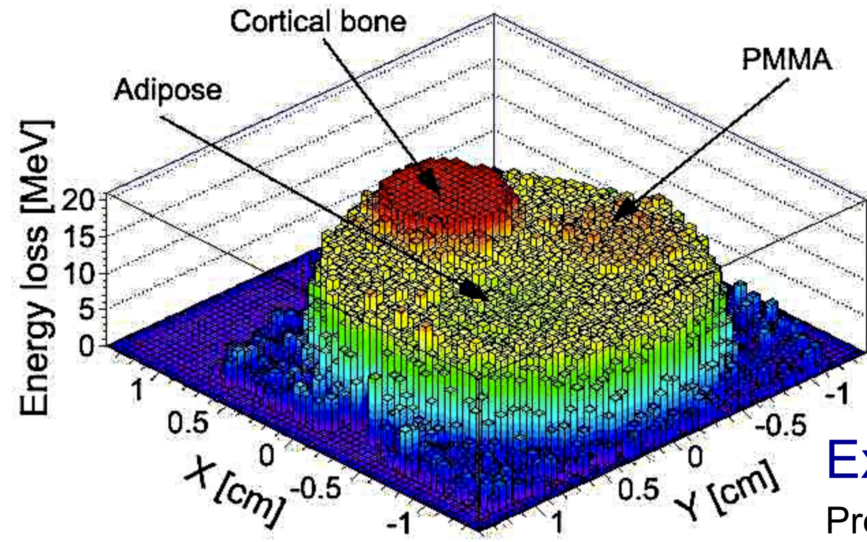
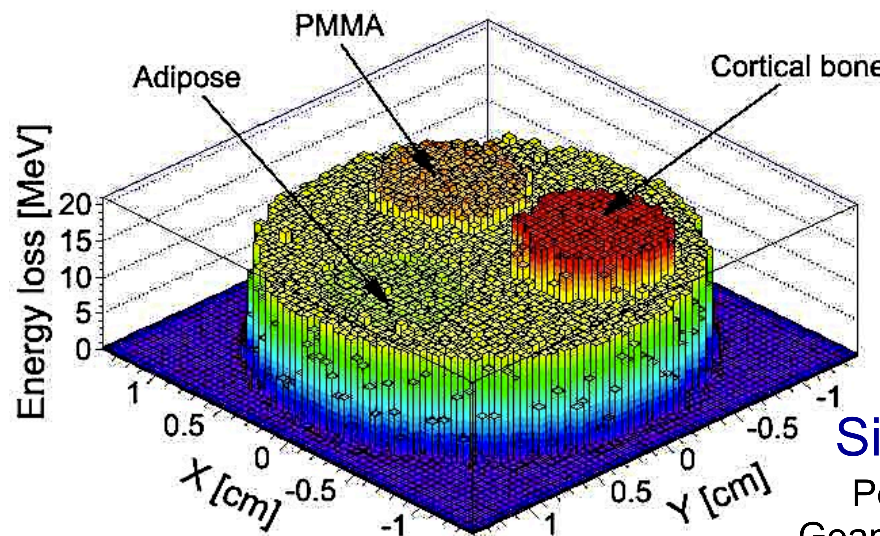
Scattered proton beam
of 30 x 30 mm^2 size



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



Experiment
Preliminary data



Simulations
Performed with
Geant4-based MC

Reconstruction of object with air and liquid inserts

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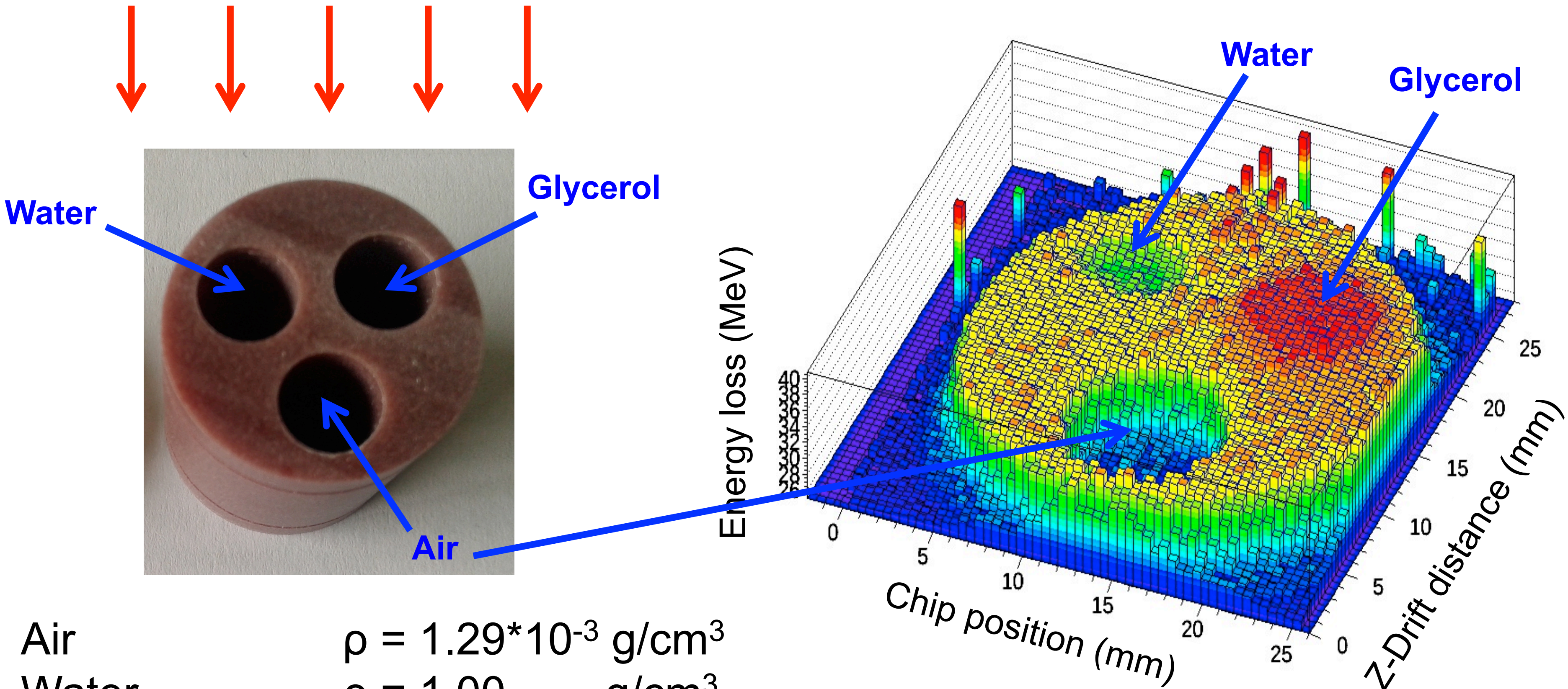
Scattered proton beam
of 30 x 30 mm^2 size

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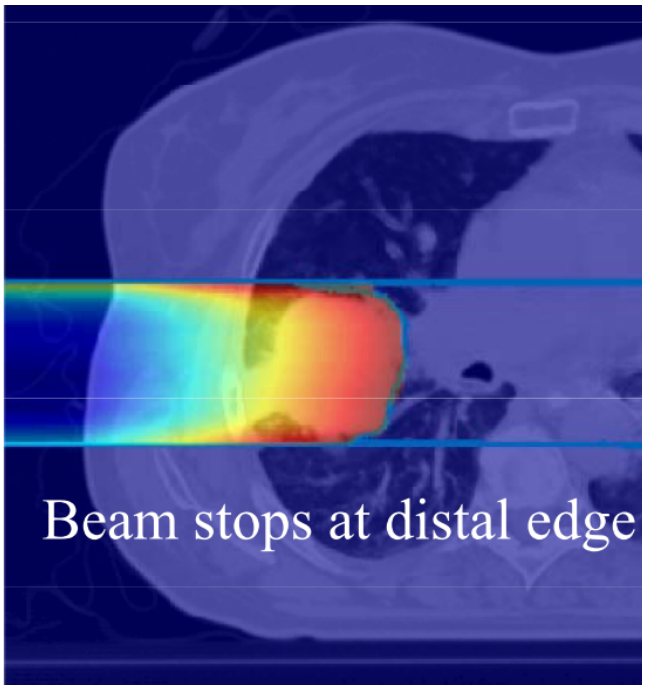
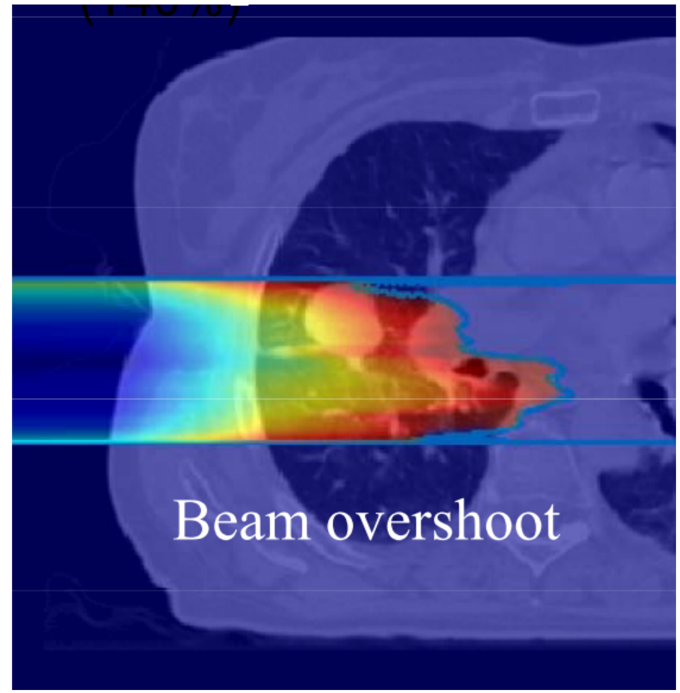
- Superconducting magnet (up to 4.1 T)
- **Protons up to 190 MeV**
- Alpha particles, **^{12}C up to 90 MeV/u**
- Heavy ions: 600 $(q/A)^2$ MeV/u

Tumor modification during treatment: an example

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



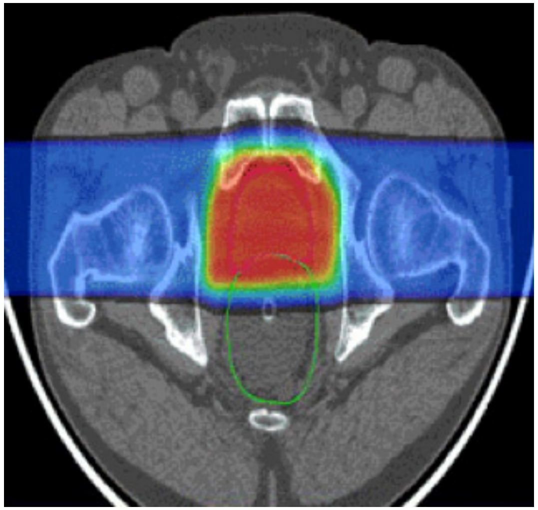
before treatment



after 5 weeks

Future proton therapy work flow

Proton Treatment Plan



Scan of a patient immediately before treatment

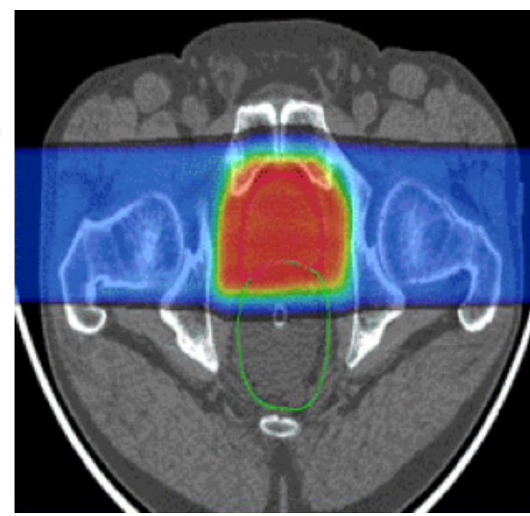
* **Proton radiography/CT**

Directly measured 3D map of proton stopping powers

Online treatment plan adaptation

* **Accurate (< 1%)**
* **Fast (1-10 sec)**

Updated Proton Treatment Plan



Treatment

Treatment verification