Regularised patient-specific stopping power calibration for proton therapy planning based on proton radiographic images

Nils Krah[1,2], Jean Michel Létang[1], Ilaria Rinaldi[3], Simon Rit[1]

[1] University of Lyon, CNRS, Creatis lab, Lyon, France
[2] Institute of Nuclear Physics Lyon, France
[3] Maastro Clinic, Maastricht, The Netherlands

Proton radiography (2D)

Range accuracy

X-ray planning CT

Treatment planning

CT number to RSP conversion

Physics in Medicine & Biology

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PAPER

Regularised patient-specific stopping power calibration for proton therapy planning based on proton radiographic images

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Treatment planning software needs accurate knowledge about the **proton stopping power** in the patient:

$$S(x) = -\frac{\mathrm{d}E}{\mathrm{d}x}(E(x))$$

depends on proton energy

Integration yields the protons' penetration depth, called **range**:

$$\mathrm{Range} = \int_{E_{\mathrm{final}}}^{E_{\mathrm{in}}} \frac{\mathrm{d}E}{\rho S(E)}$$

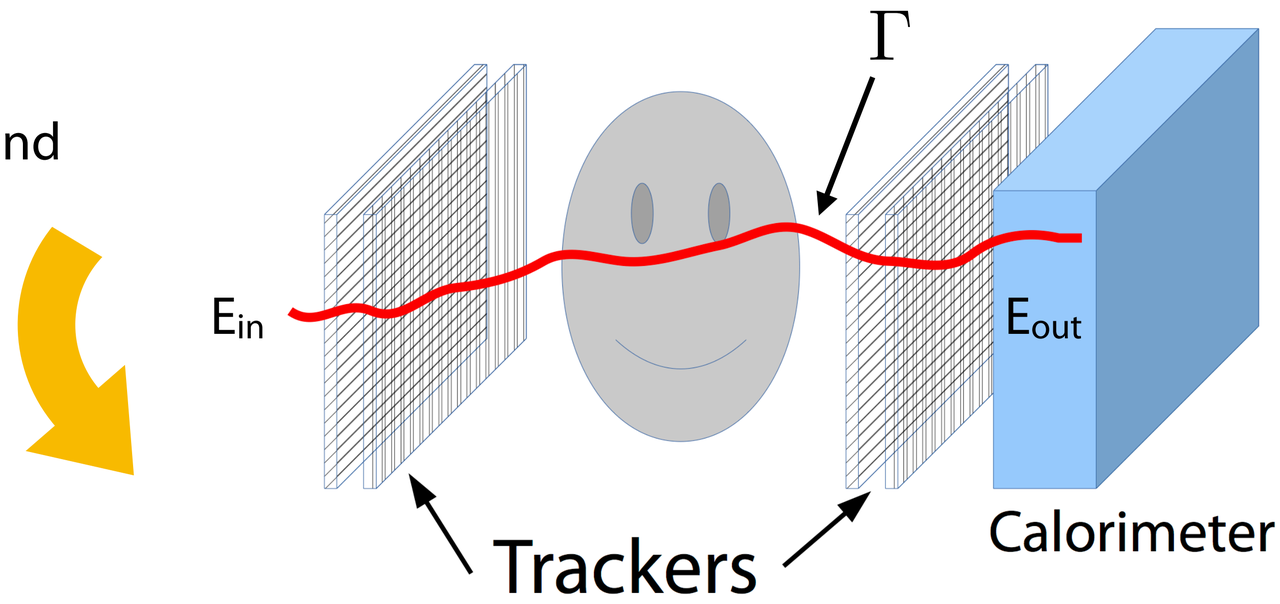
Convenient to define **Relative Stopping Power (RSP)** in reference to water:

$$RSP \equiv \frac{S(x)}{S_w(x)}$$

approximately energy independent

Option 1: Get Stopping Power from proton CT

Rotate around patient



Generates list mode data:
Trajectory estimate and WET for each proton.

Reconstruction formula for proton CT:

$$WET = \int_{\Gamma} RSP(x)\mathrm{d}l = \int_{E_{\mathrm{out}}}^{E_{\mathrm{in}}} \frac{\mathrm{d}E}{S_w(E)}$$

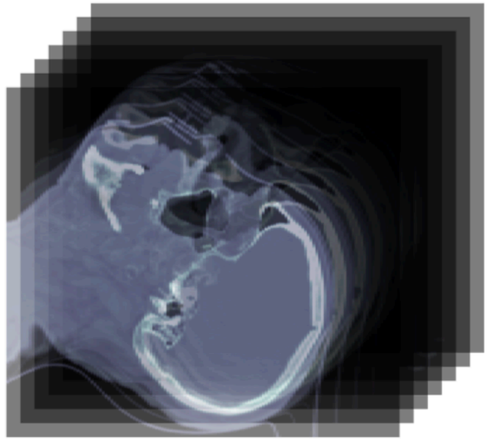
Not used clinically.
Only prototypes!

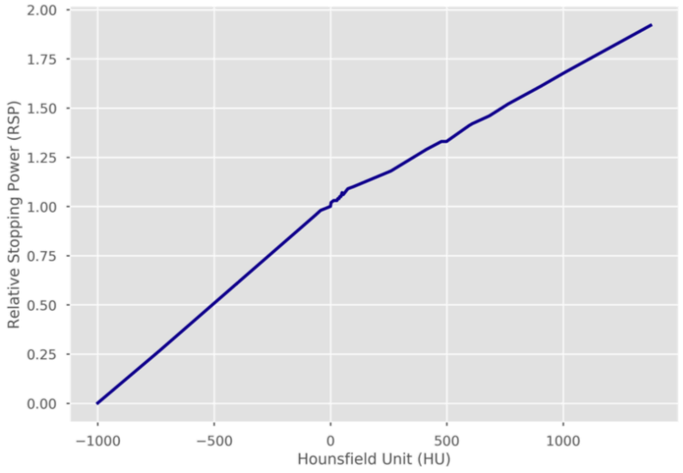
WET: water equivalent thickness

Johnson, R. P. (2018). Review of medical radiography and tomography with proton beams. Reports on Progress in Physics, 81(1), 016701. https://doi.org/10.1088/1361-6633/aa8b1d

Option 2: Use X-ray CT plus conversion (clinically used)

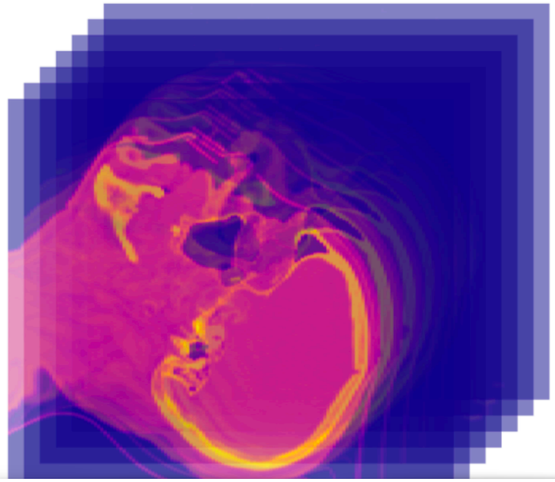
Planning CT





Conversion

Relative Stopping Power (RSP)



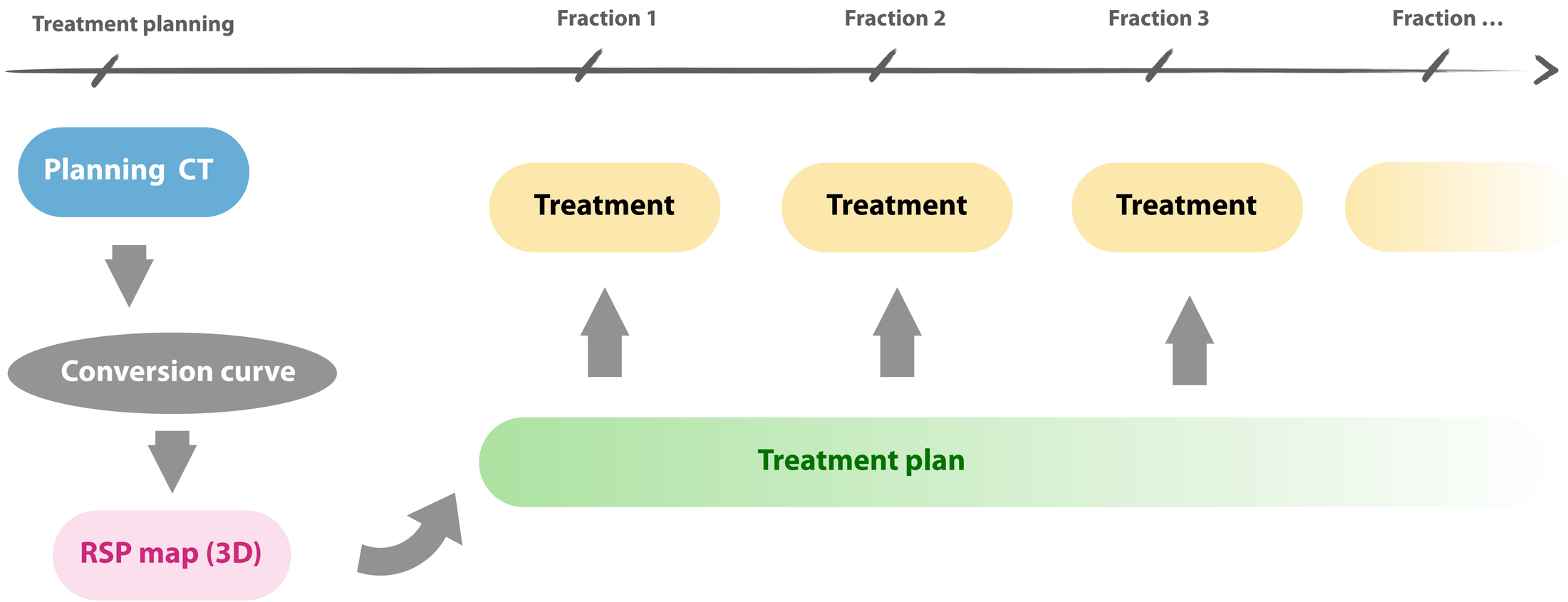
Conversion depends on chemical tissue composition
-> inter/intra patient variation

Uncertainties in

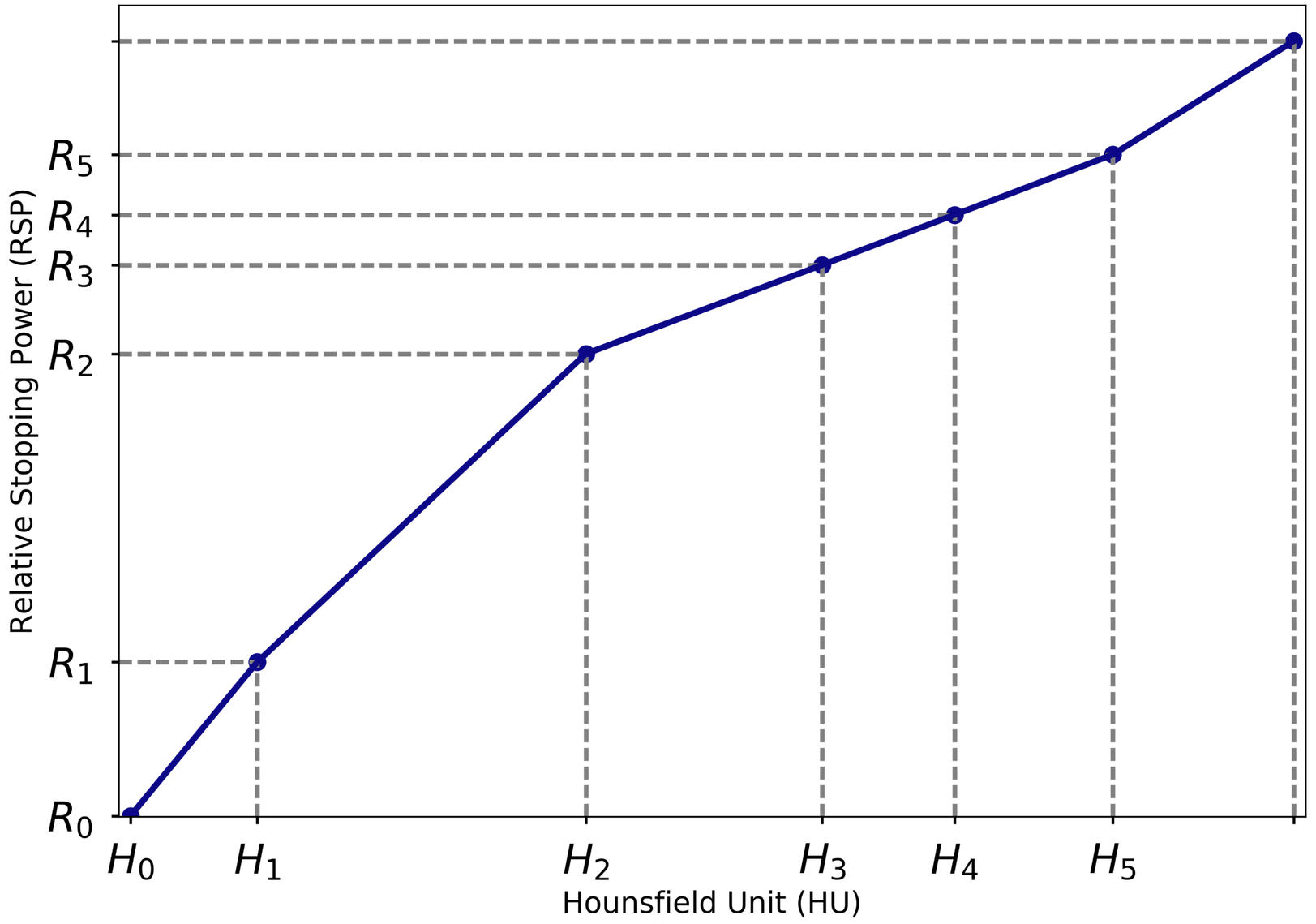
- Hounsfield Units (HU)
- Conversion curve

Range uncertainties

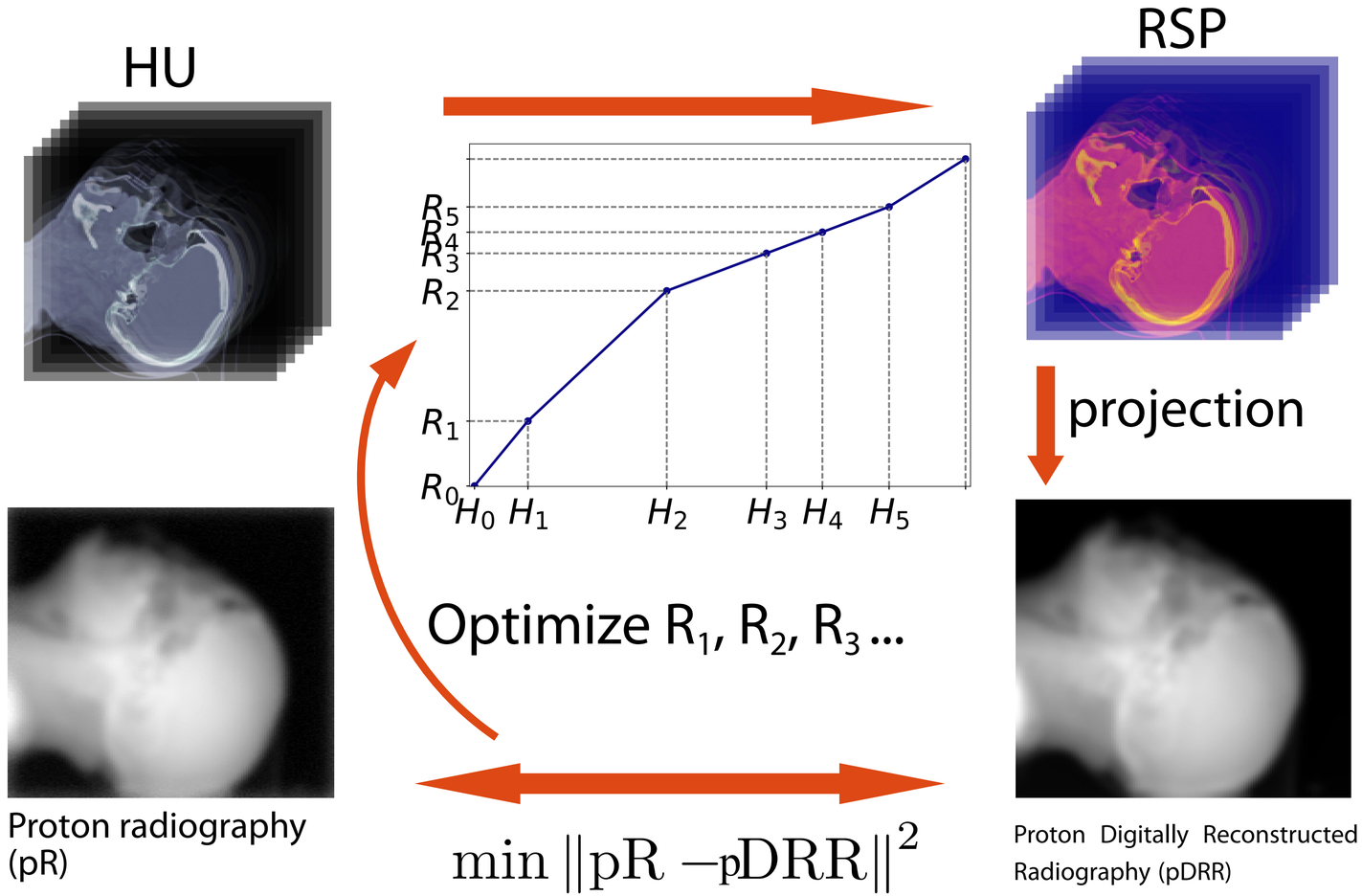
Typical clinical workflow in proton therapy



Goal: Find patient specific optimal conversion curve



Patient specific CT-RSP calibration using proton radiography

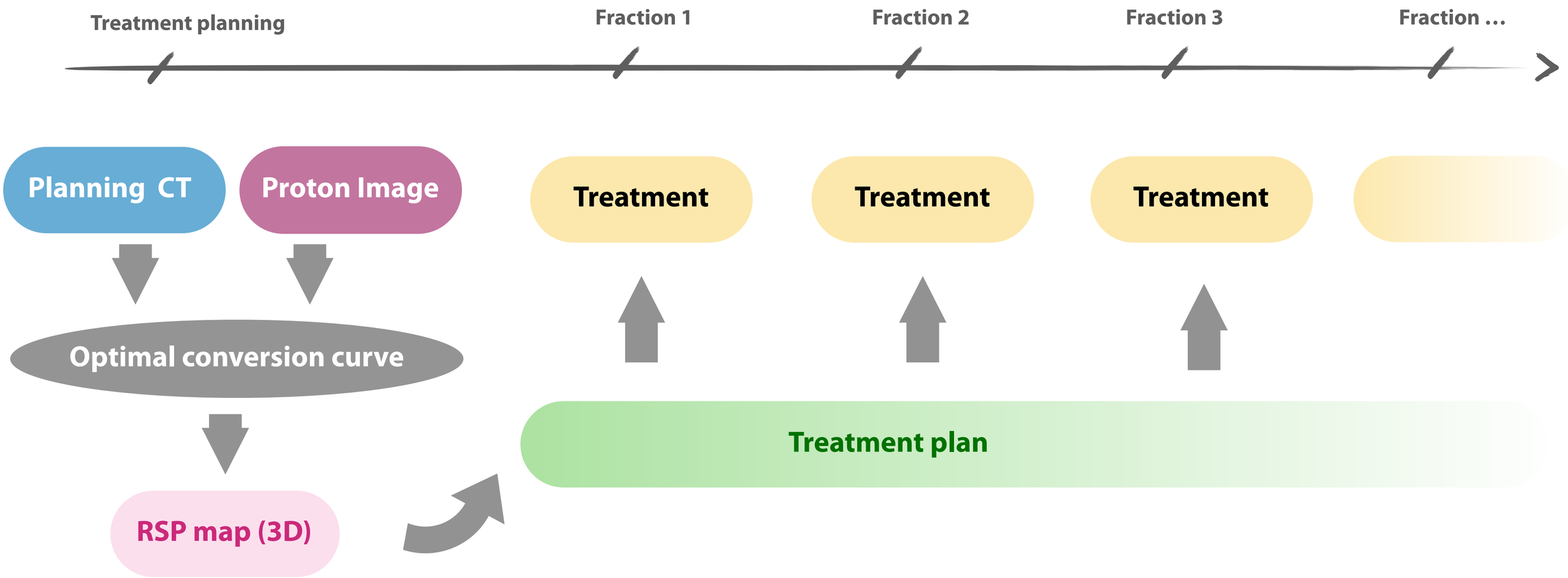


[1] Schneider, U. et al. (2004). First proton radiography of an animal patient. Medical Physics, 31(5)

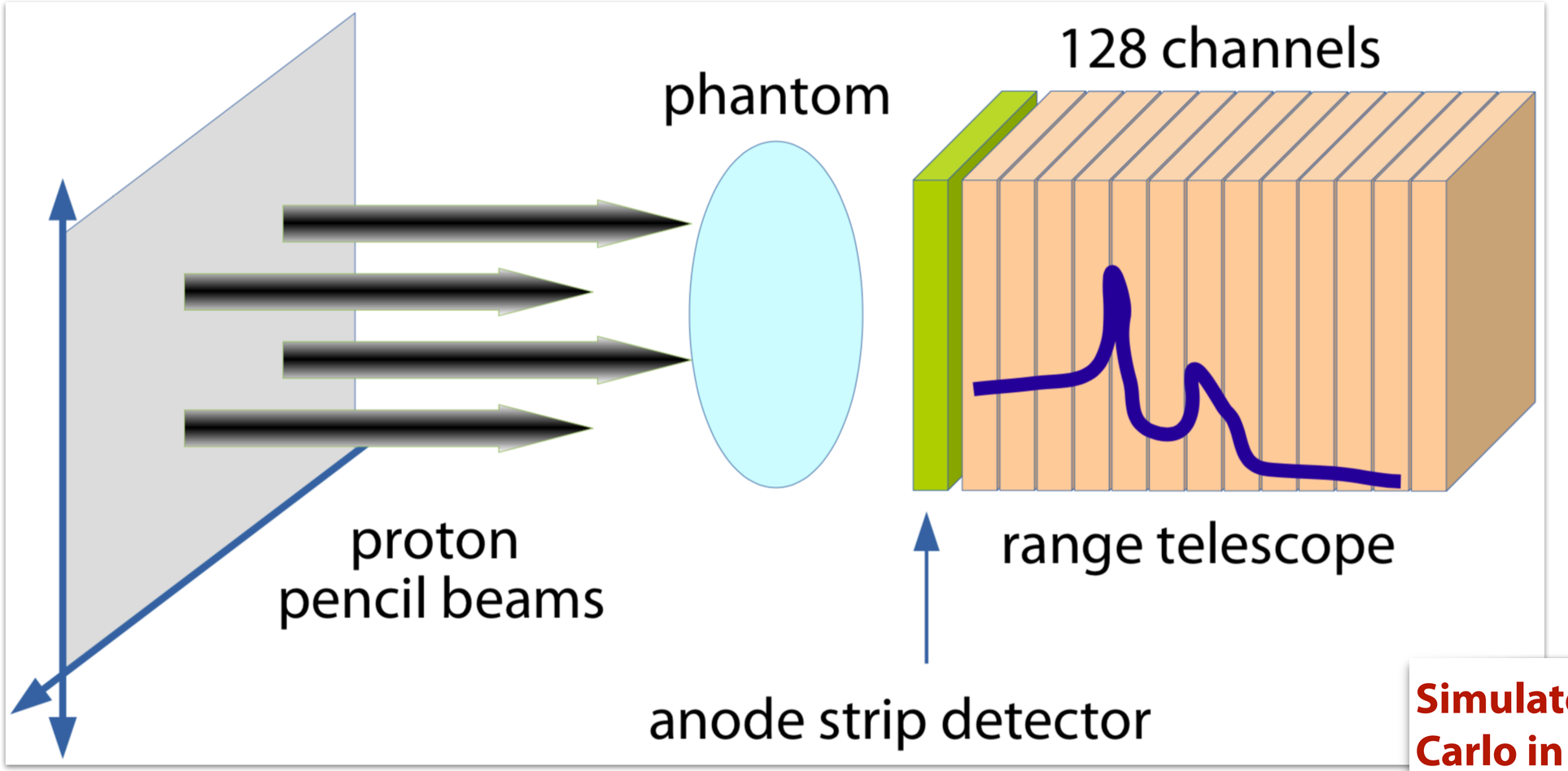
[2] Doolan, P. J. et al. (2015). Patient-specific stopping power calibration for proton therapy planning based on single-detector proton radiography. PMB 60(5)

[3] Collins-Fekete, C.-A. et al. (2017). Pre-treatment patient-specific stopping power by combining list-mode proton radiography and x-ray CT. PMB 62(17)

Modified clinical workflow



Proton imaging system

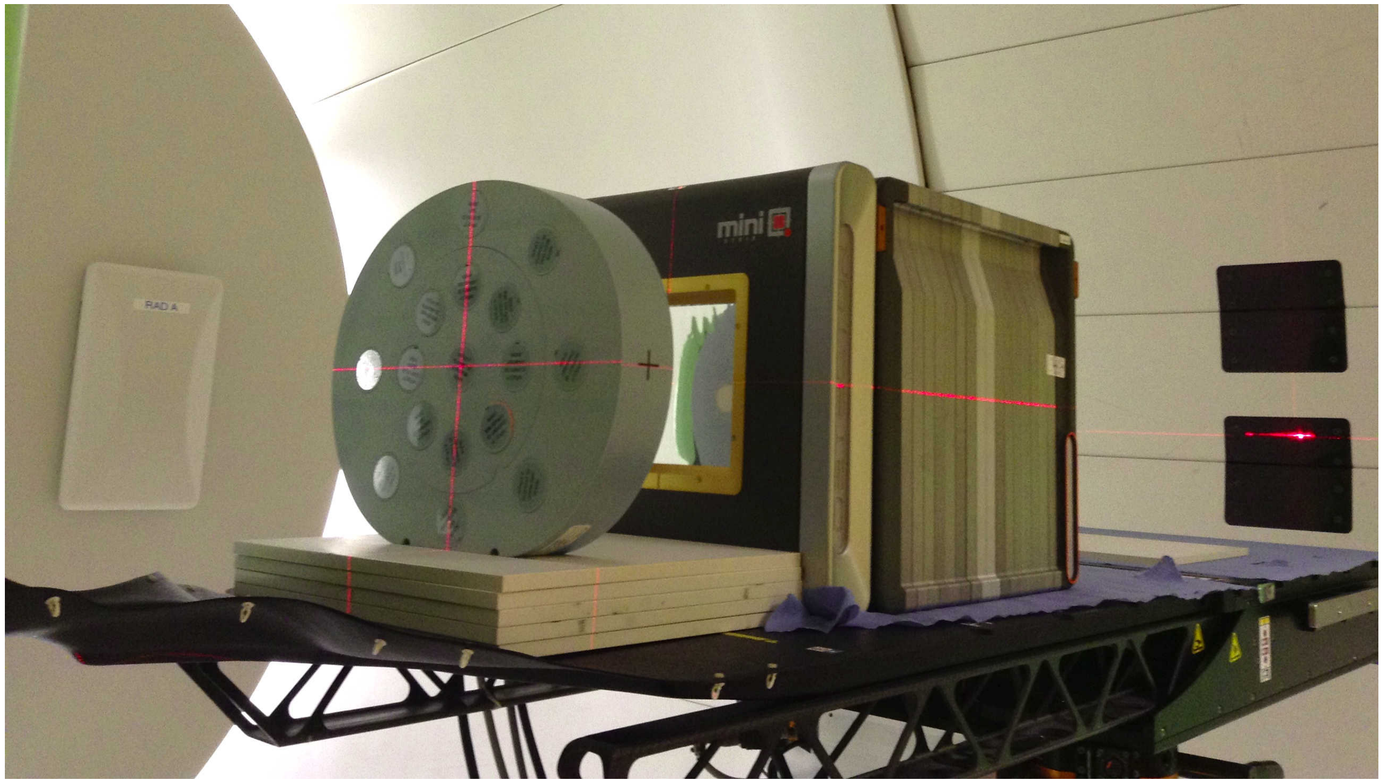


Simulated via Monte Carlo in this work

Krah, N. et al. (2018). Proton radiography with a commercial range telescope detector using dedicated post processing methods. PMB, 63(20), 205016

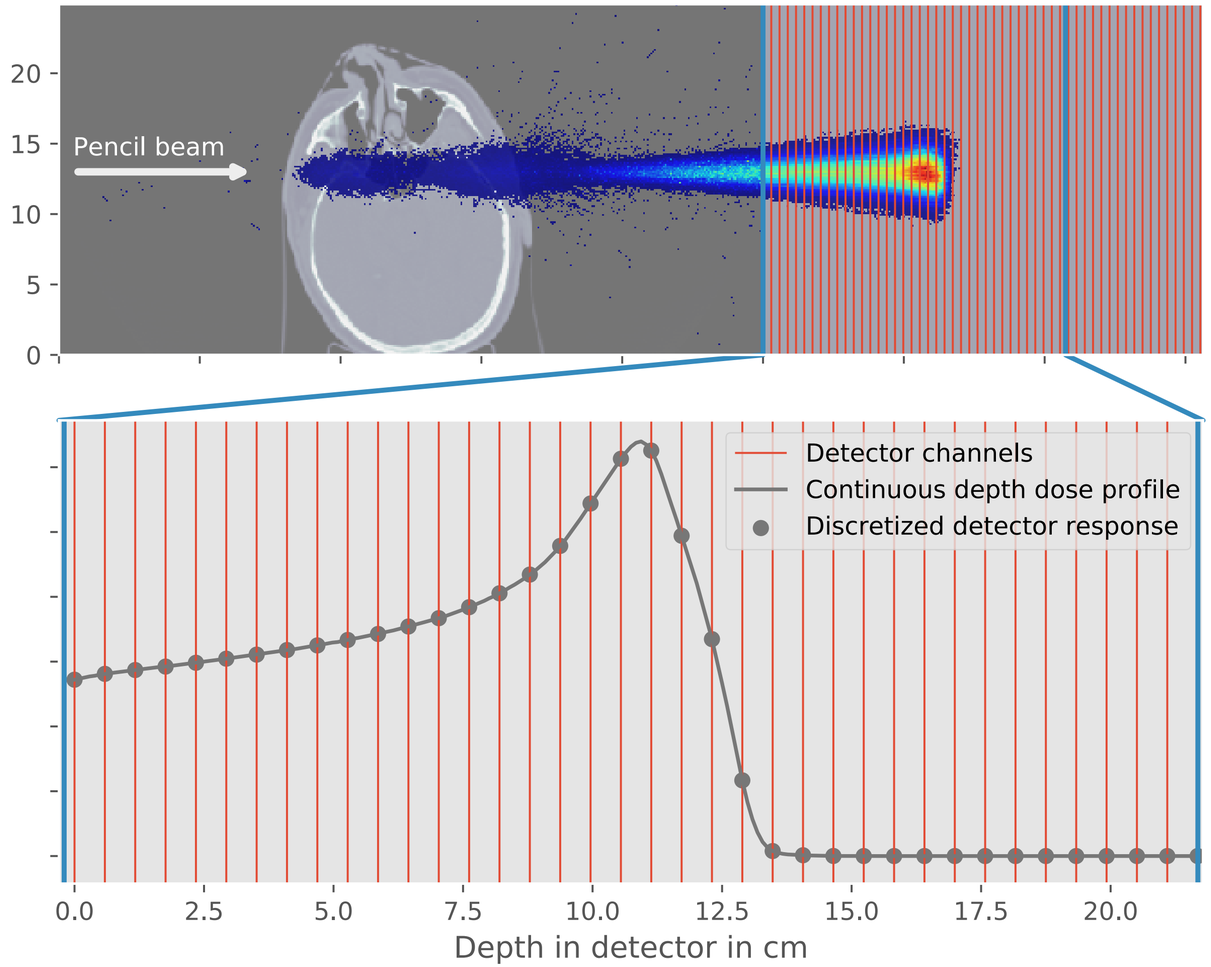
Example of a proton radiography system

… used at CPO, France



… and Maastro, Netherlands

Monte Carlo simulation of proton radiographies



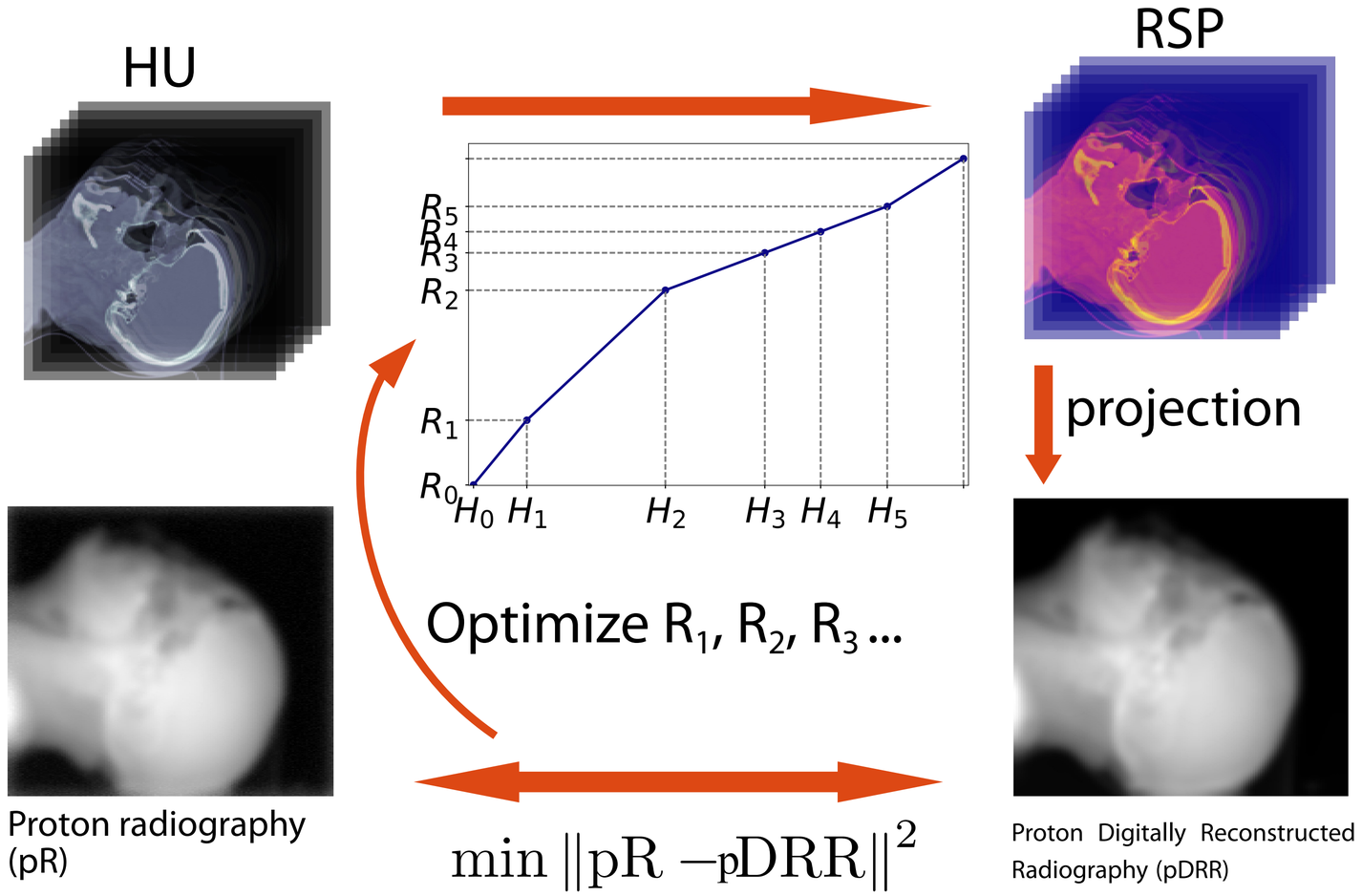
Used fast GPU-accelerated Monte Carlo code "Fred" developed at the University of Rome la Sapienza.

Takes 1-2 min per proton radiography.

Ground truth CT-RSP curve is the one used for the simulation.

Schiavi, A., Patera, V. et al. (2017). Fred: A GPU-accelerated fast-Monte Carlo code for rapid treatment plan recalculation in ion beam therapy. Physics in Medicine and Biology, 62(18)

Patient specific CT-RSP calibration using proton radiography



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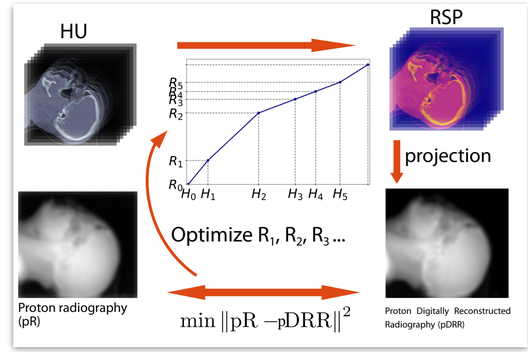
Efficient implementation of projection (1)



In each voxel, replaces CT number ***h*** by weight vector ***w***:

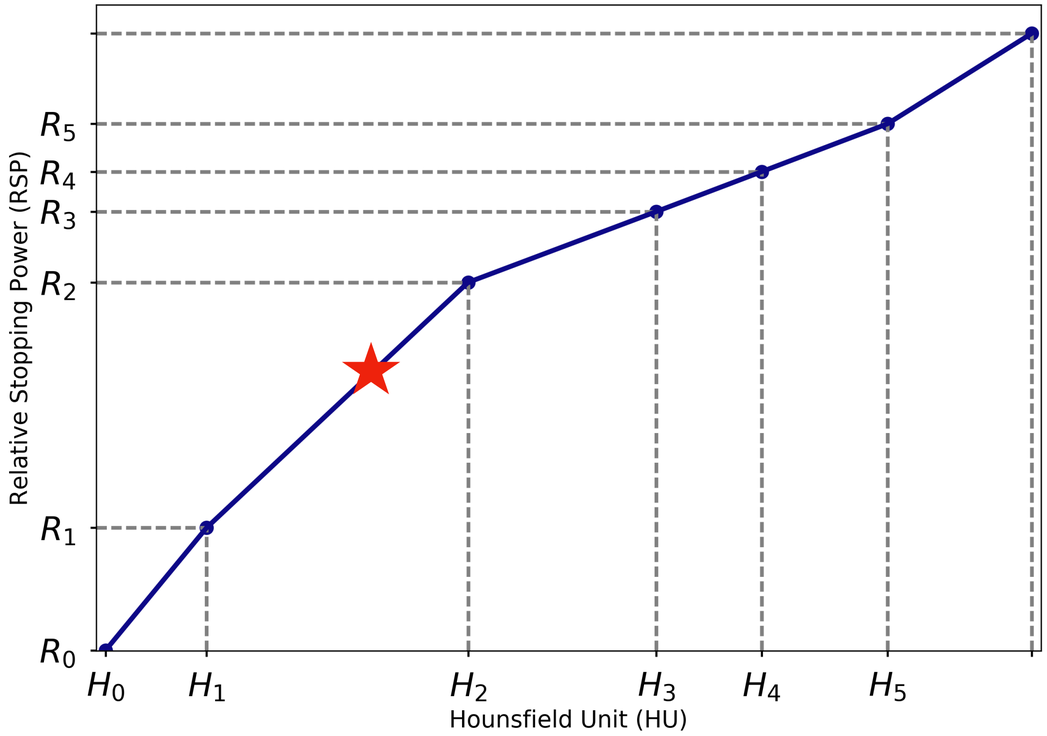
$$w_\alpha(h) \equiv \frac{h - H_{\alpha-1}}{H_\alpha - H_{\alpha-1}}\,\Omega_\alpha(h) + \frac{H_{\alpha+1} - h}{H_{\alpha+1} - H_\alpha}\,\Omega_{\alpha+1}(h)$$

$$w_0(h) = \frac{H_1 - h}{H_1 - H_0}\,\Omega_{\alpha=1}(h)$$

$$w_N(h) = \frac{h - H_{N-1}}{H_N - H_{N-1}}\,\Omega_{\alpha=N}(h)$$

with $$\Omega_\alpha(h) = \begin{cases} 1 & \text{for } H_{\alpha-1} \le h < H_\alpha \\ 0 & \text{otherwise.} \end{cases}$$

$$r = \sum_{\alpha=0}^{N} w_\alpha R_\alpha = \vec{w} \cdot \vec{R}$$

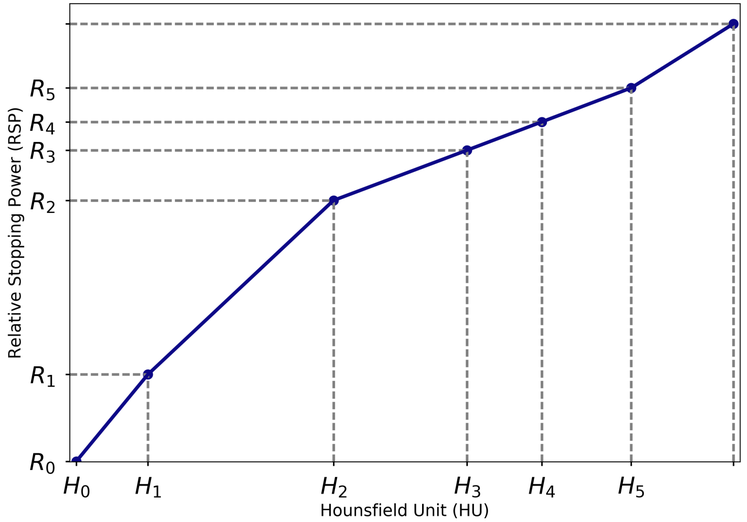


Krah, N., Rit, S. et al. (2019). Regularised patient-specific stopping power calibration for proton therapy planning based on proton radiographic images. PMB, 64(6)

Efficient implementation of projection (2)

3D RSP map is given by:

$$r_{ijk} = \sum_{\alpha=0}^{N} w_{ijk,\alpha}\, R_\alpha = \vec{w}_{ijk} \cdot \vec{R}$$



Proton digitally reconstructed radiography:

$$D_{i_p j_p} = \mathrm{proj}_{k,i_p j_p}\left(\sum_{\alpha=0}^{N} w_{ijk,\alpha}\, R_\alpha\right) = \sum_{\alpha=0}^{N} \mathrm{proj}_{k,i_p j_p}(w_{ijk,\alpha})\, R_\alpha = \sum_{\alpha=0}^{N} A_{i_p j_p,\alpha}\, R_\alpha$$

$$\text{with} \quad A_{i_p j_p,\alpha} = \mathrm{proj}_{k,i_p j_p}(w_{ijk,\alpha})$$

allows splitting projection from optimization

Krah, N., Rit, S. et al. (2019). Regularised patient-specific stopping power calibration for proton therapy planning based on proton radiographic images. PMB, 64(6)

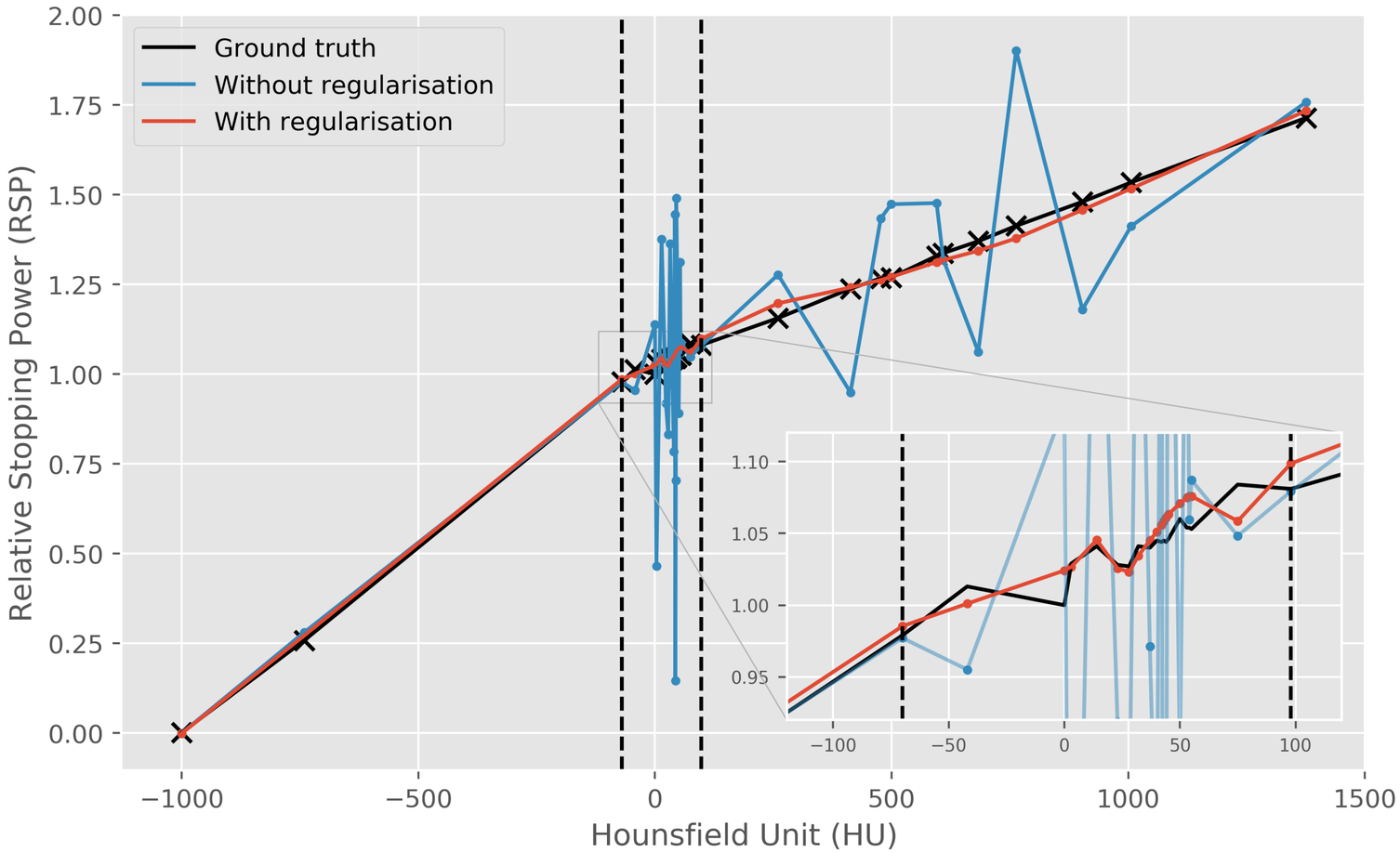
Naïve optimization

Cost function contains only data term:

$$E_{\text{data}}(\vec{R}) = \|\vec{P} - A\vec{R}\|^2$$

Find:

$$\hat{\vec{R}} = \text{argmin}\left\{E(\vec{R})\right\}$$



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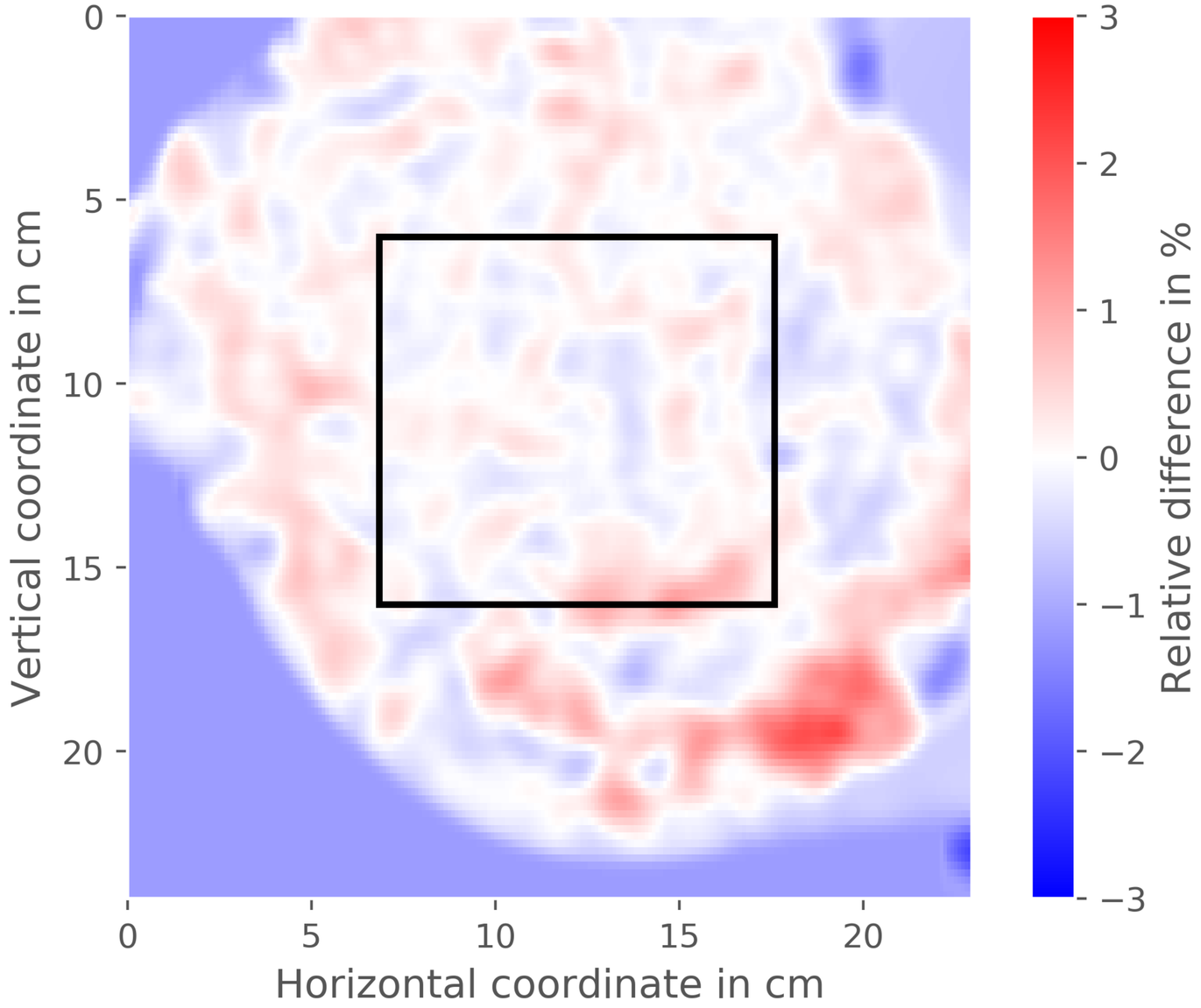
Residuals after optimization

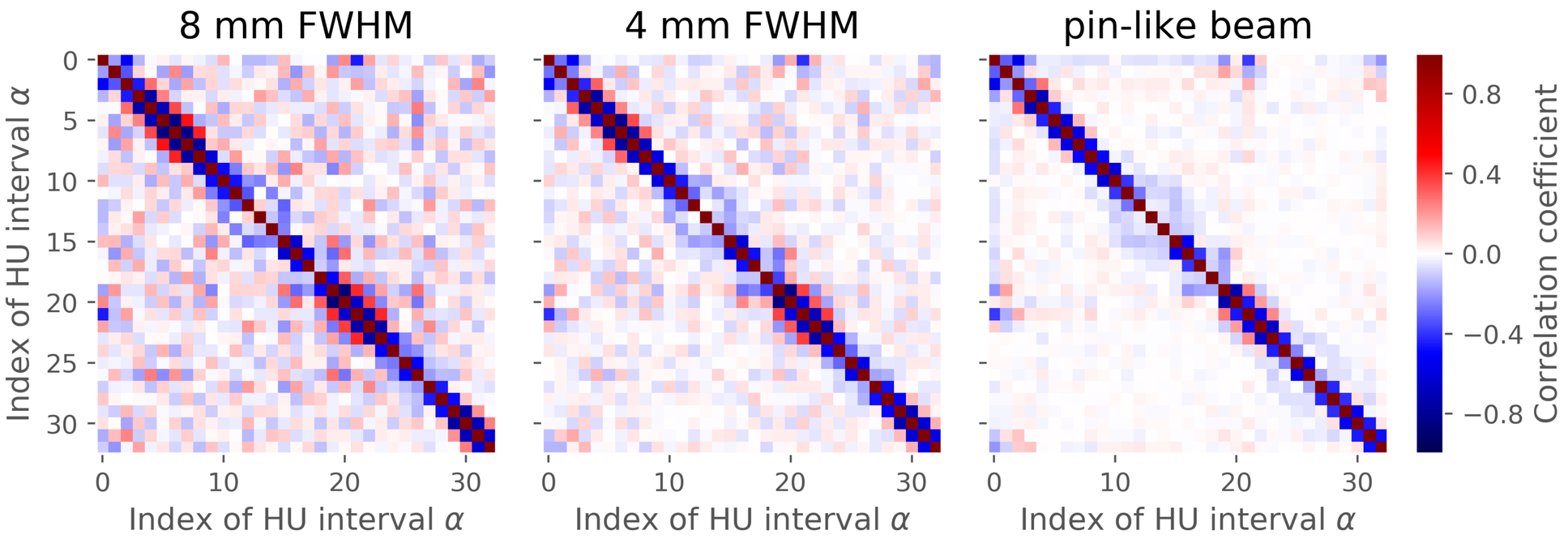


What goes wrong?

Parameter correlation

Correlation coefficient:

$$\rho_{\alpha\alpha'} = \frac{\mathrm{Cov}_{\alpha\alpha'}}{\sqrt{\mathrm{Cov}_{\alpha\alpha}\,\mathrm{Cov}_{\alpha'\alpha'}}} \quad \text{with} \quad \mathrm{Cov}_{\alpha\alpha'} = (A^T A)^{-1}{}_{\alpha\alpha'}$$



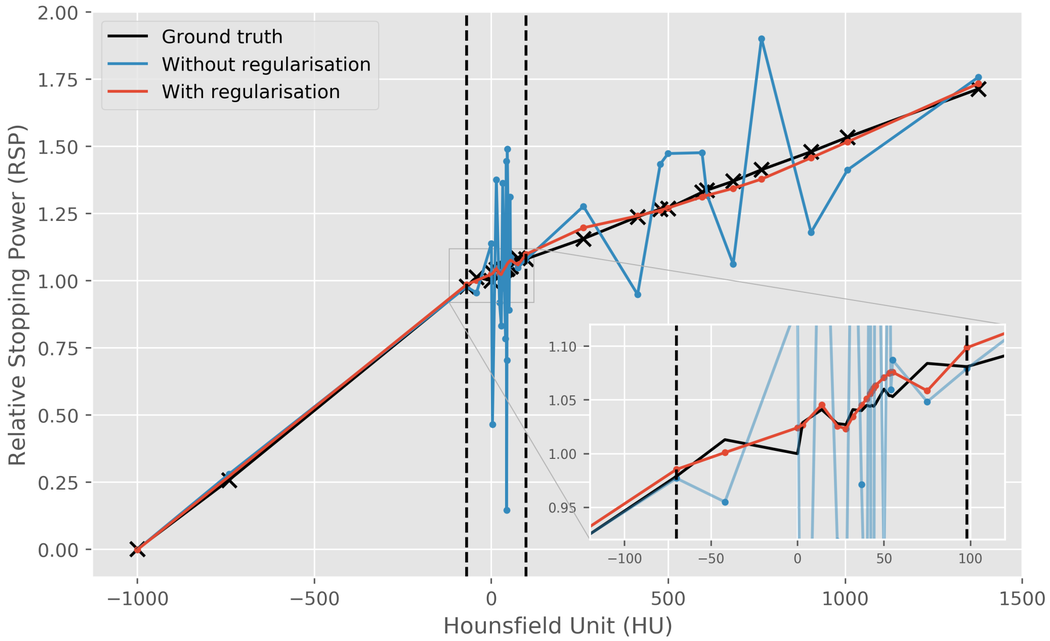
Size of proton beam is crucial

Regularization

Penalize variation of conversion curve:

$$E_{\mathrm{reg}} = \sum_{\alpha=\alpha_0}^{\alpha_M} \left(d_{\alpha+1} - d_\alpha\right)^2 \quad \text{with} \quad d_\alpha = \frac{R_\alpha - R_{\alpha-1}}{H_\alpha - H_{\alpha-1}}$$

$$E(\vec{R}) = E_{\mathrm{data}} + \gamma_{\mathrm{air}} E_{\mathrm{reg,air}} + \gamma_{\mathrm{soft}} E_{\mathrm{reg,soft}} + \gamma_{\mathrm{bone}} E_{\mathrm{reg,bone}}$$

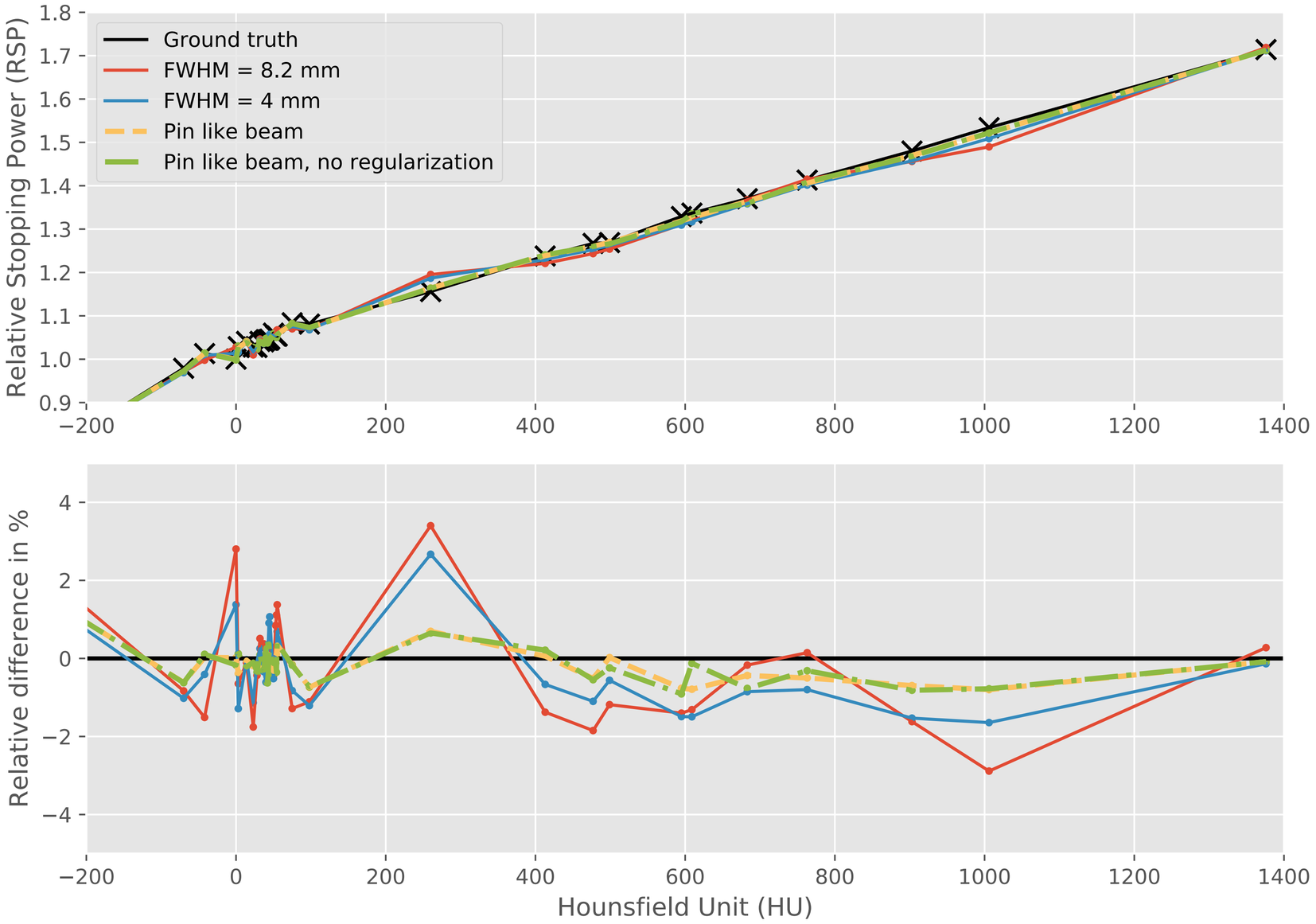


Note: E_{reg} can be written as matrix equation:

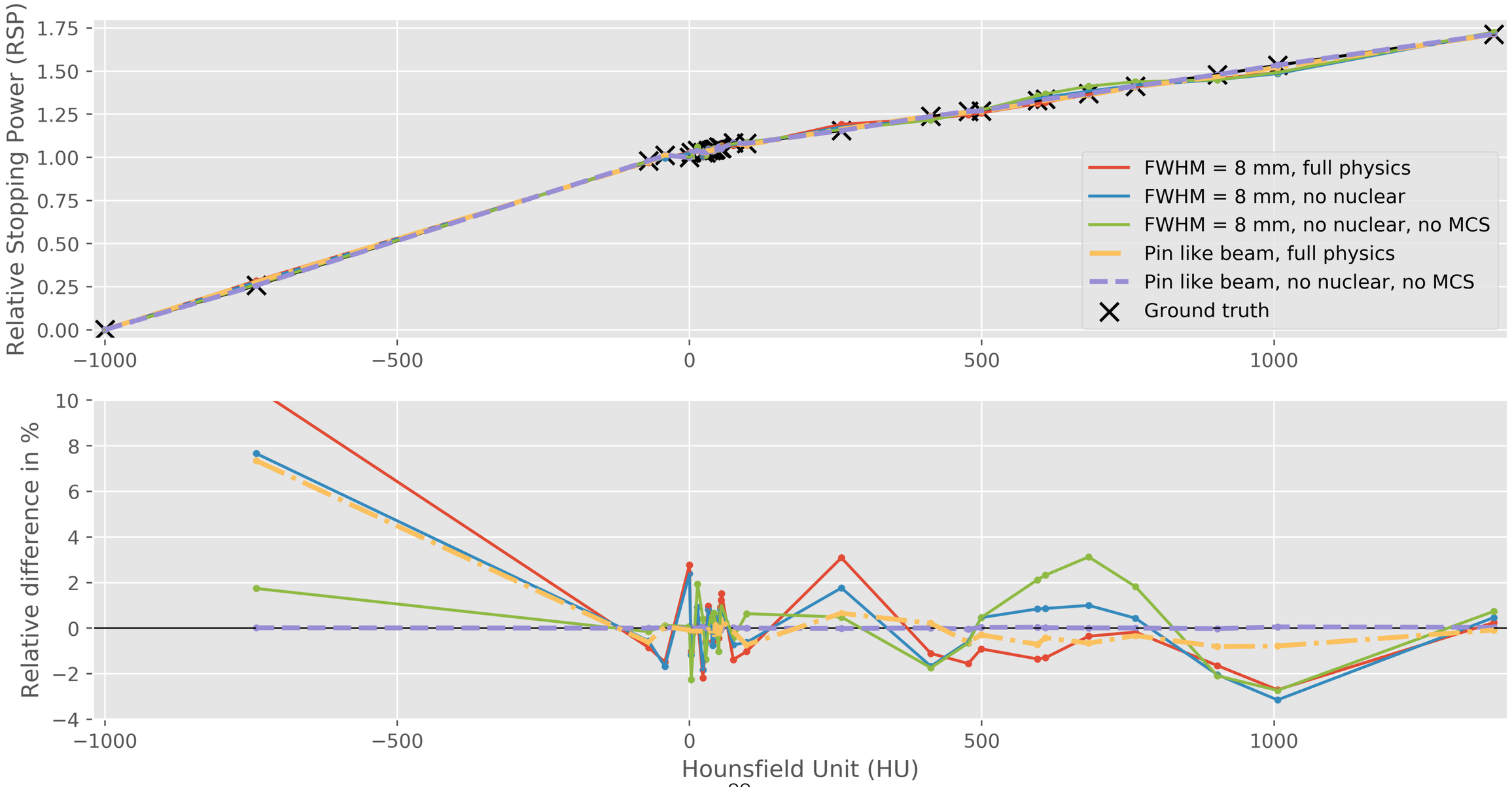
$$E_{\mathrm{reg}} = \sum_{\alpha=\alpha_0}^{\alpha_M} \left(A^{\mathrm{reg}}_{\alpha'\alpha} R_\alpha\right)^2 = \|A^{\mathrm{reg}} \vec{R}\|^2$$

with $$A^{\mathrm{reg}}_{\alpha'\alpha} = \frac{1}{H_{\alpha+1} - H_{\alpha-1}} \left(\delta_{\alpha',\alpha-1} - 2\delta_{\alpha',\alpha} + \delta_{\alpha',\alpha+1}\right), \quad \text{with} \quad \delta_{\alpha',\alpha} = \begin{cases} 1 & \text{for } \alpha' = \alpha \\ 0 & \text{otherwise.} \end{cases}$$

Regularization: proton beam size matters



Regularization: does physics matter?



How to choose the regularization weights?

$$E(\vec{R}) = E_{\text{data}} + \gamma_{\text{air}} E_{\text{reg,air}} + \gamma_{\text{soft}} E_{\text{reg,soft}} + \gamma_{\text{bone}} E_{\text{reg,bone}}$$

Less variation expected -> higher weight

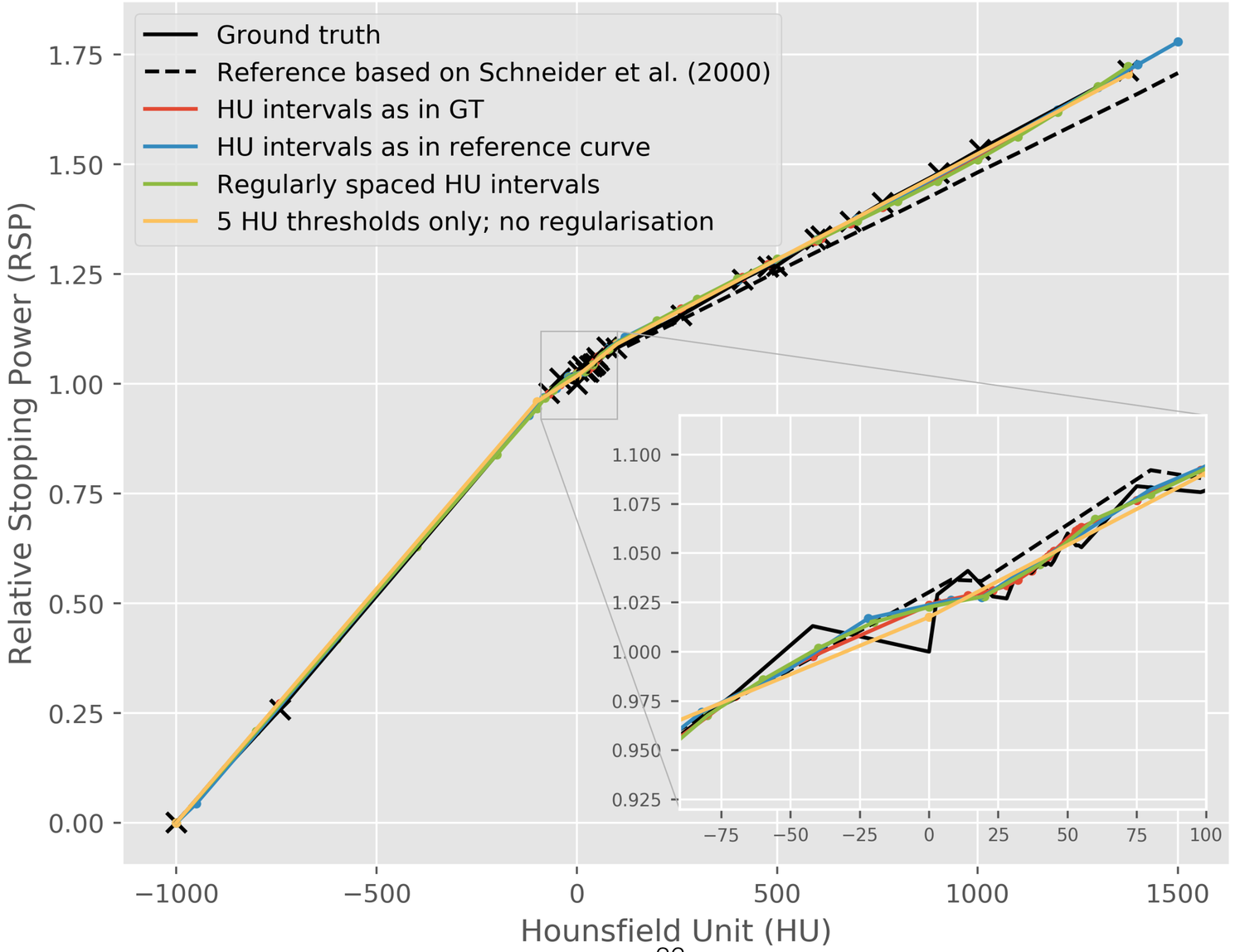
More variation expected -> lower weight

Choose the weighting factors so that the regularizer cost of the optimized curve is similar to that of a reference curve. (by iteration)

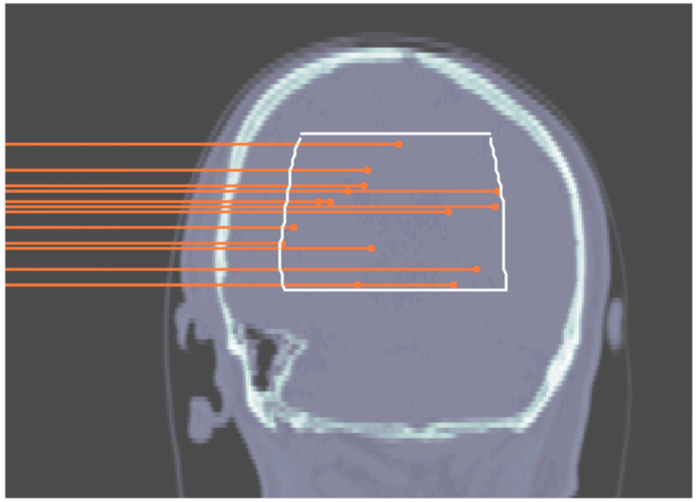
Choose regularizer weights based on reference curve

And what about the CT number intervals?

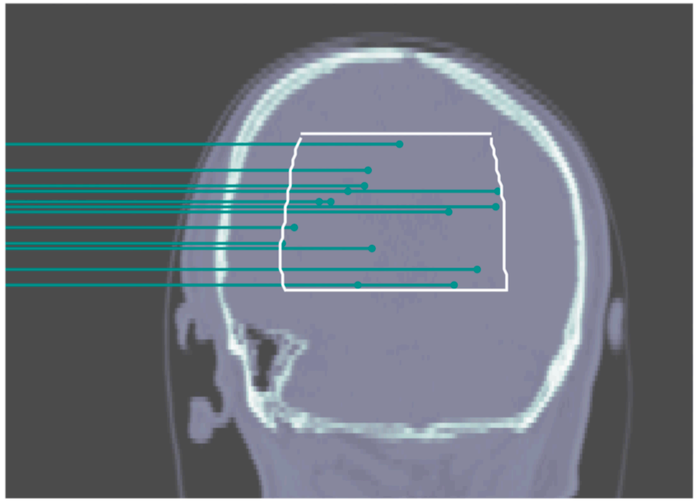
And what about the CT number intervals?



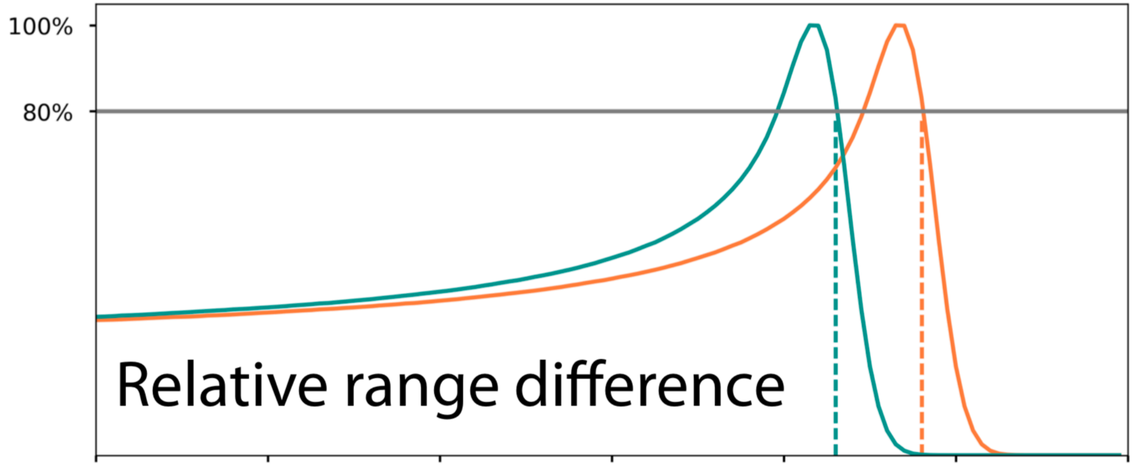
Test range accuracy in Monte Carlo simulation



with GT HU-RSP curve

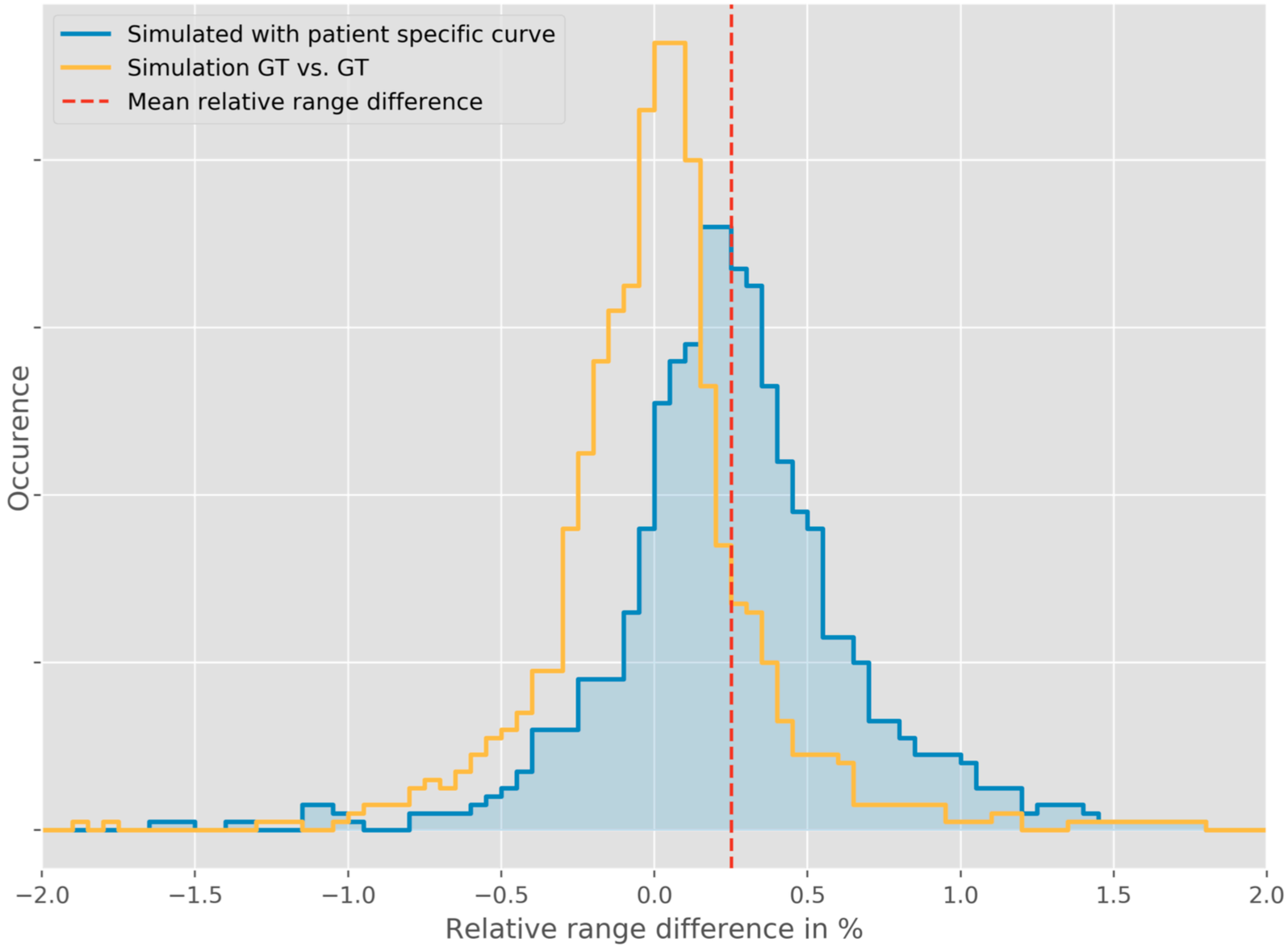


with re-calibrated curves



- 1000 PB
- Random position
- Random energy

Range accuracy with optimized CT-RSP curve



Does it matter of which region in the patient the proton radiography is acquired?

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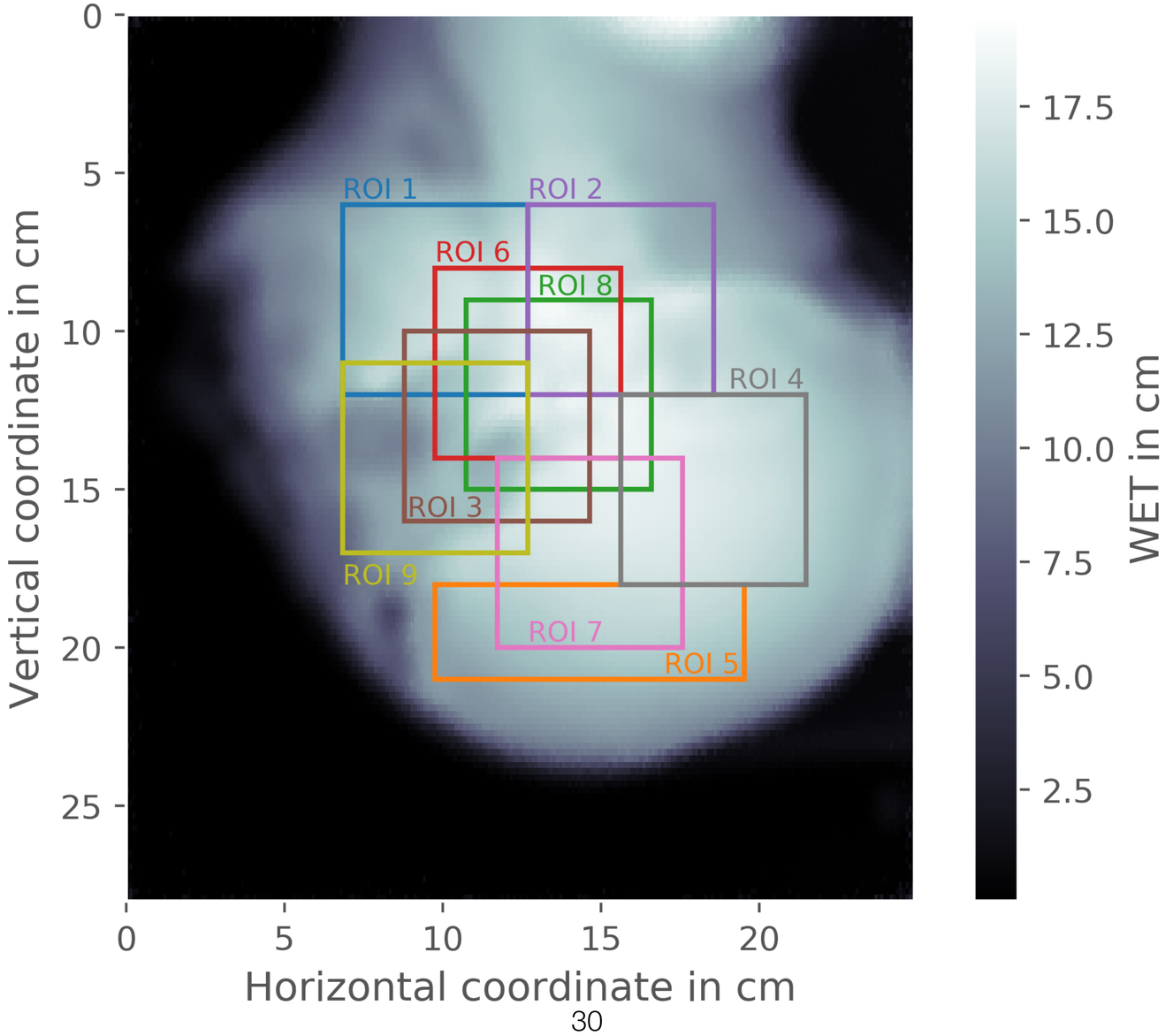

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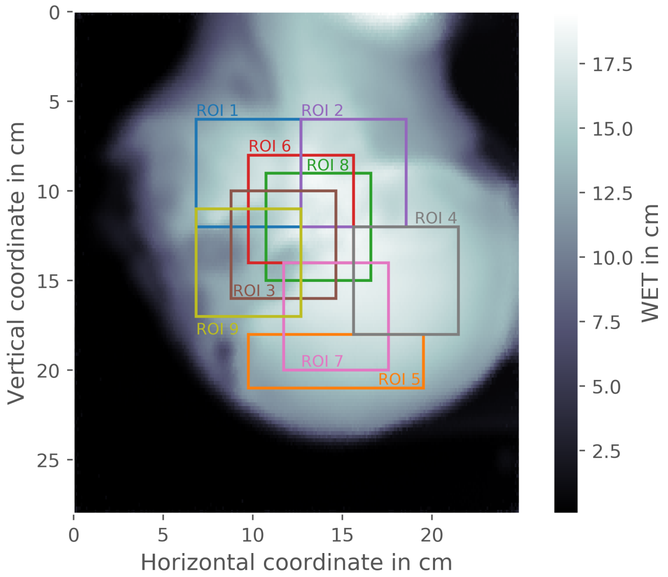

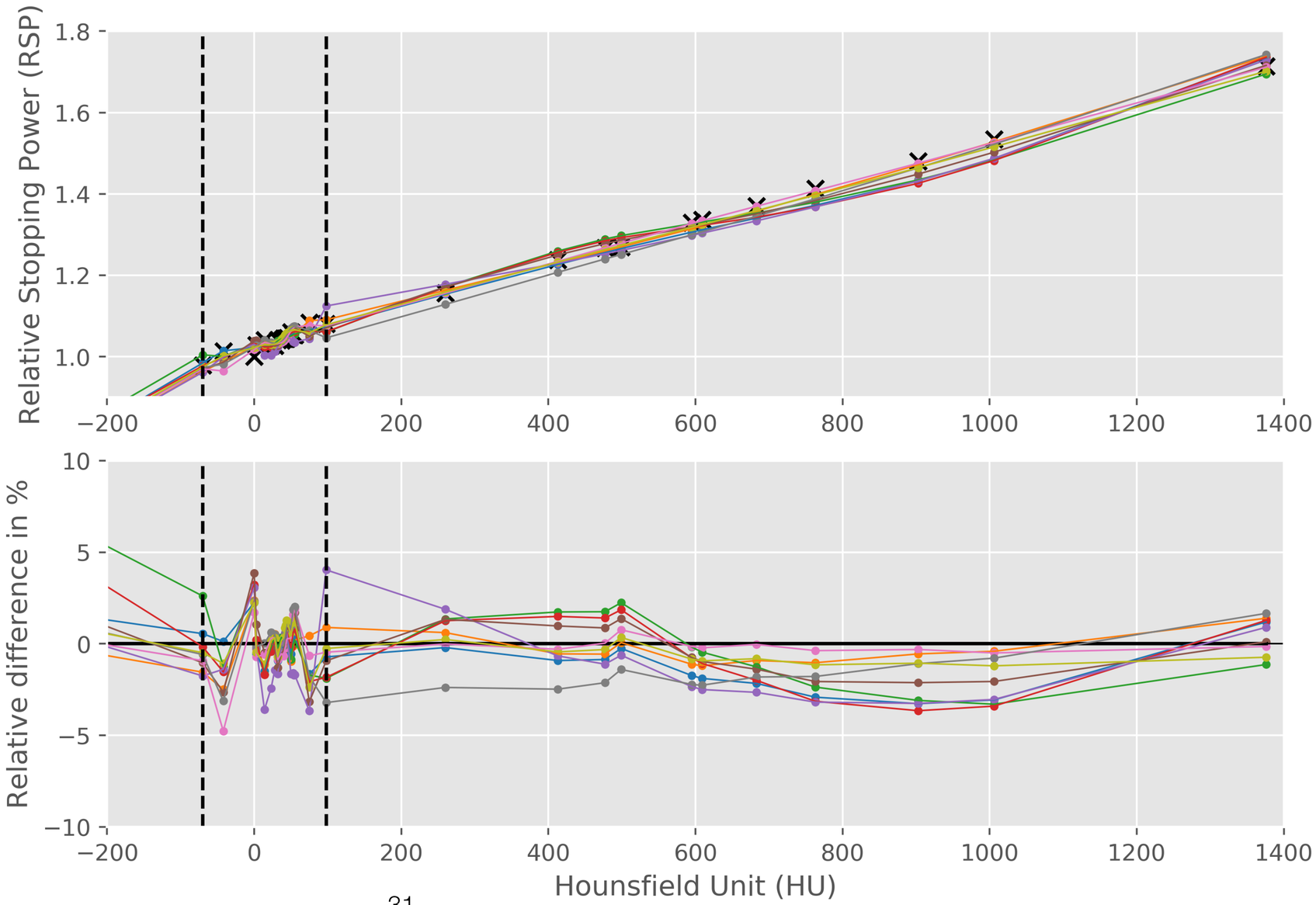

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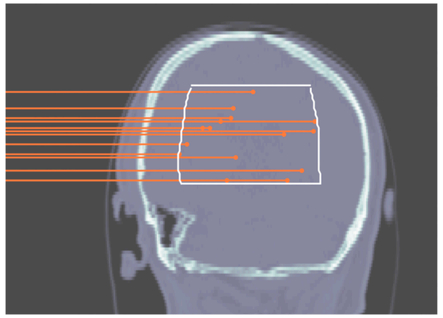
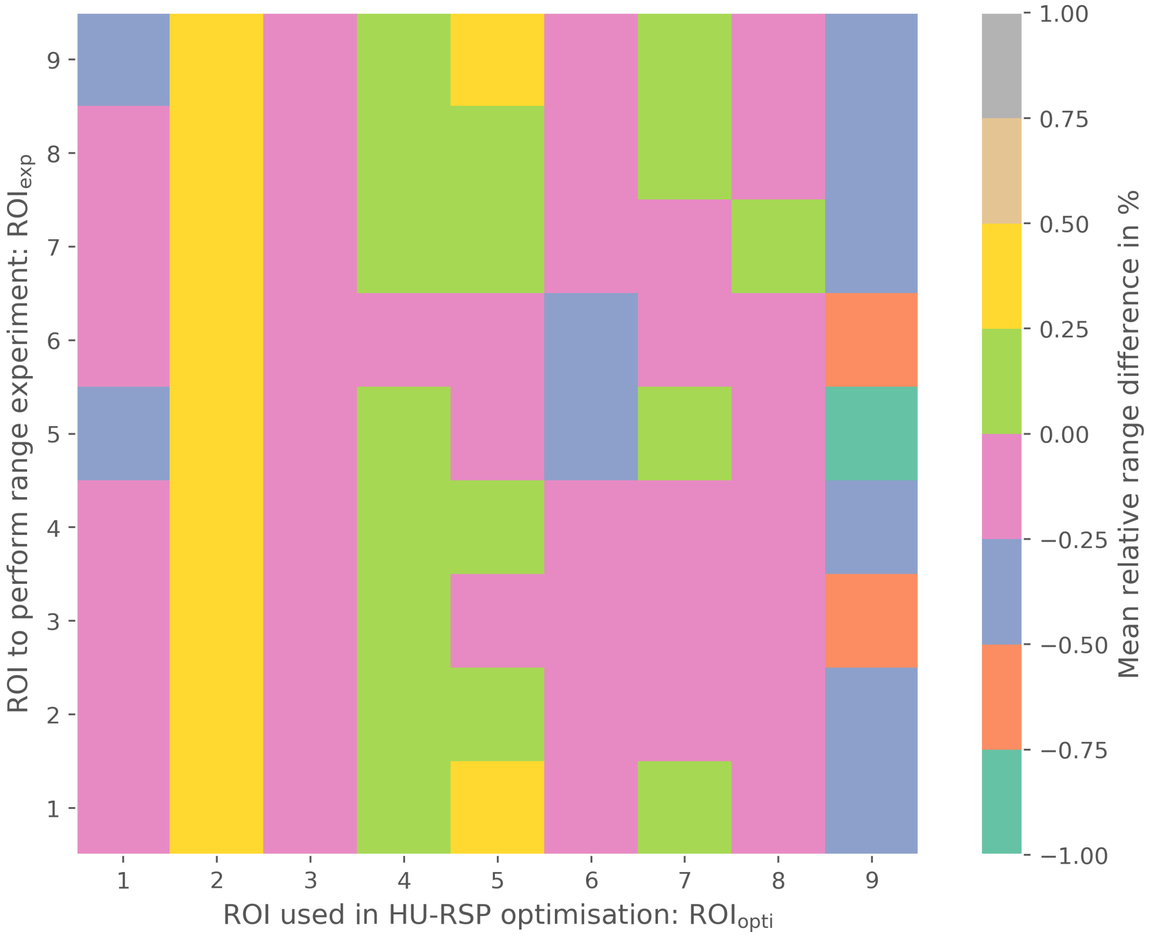
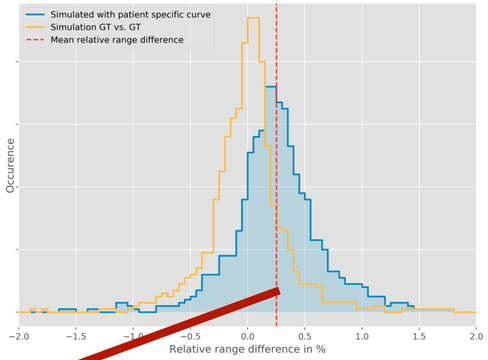
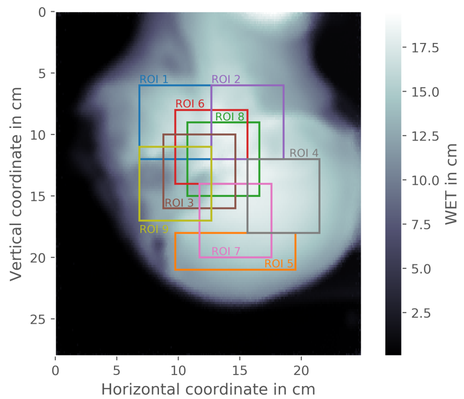


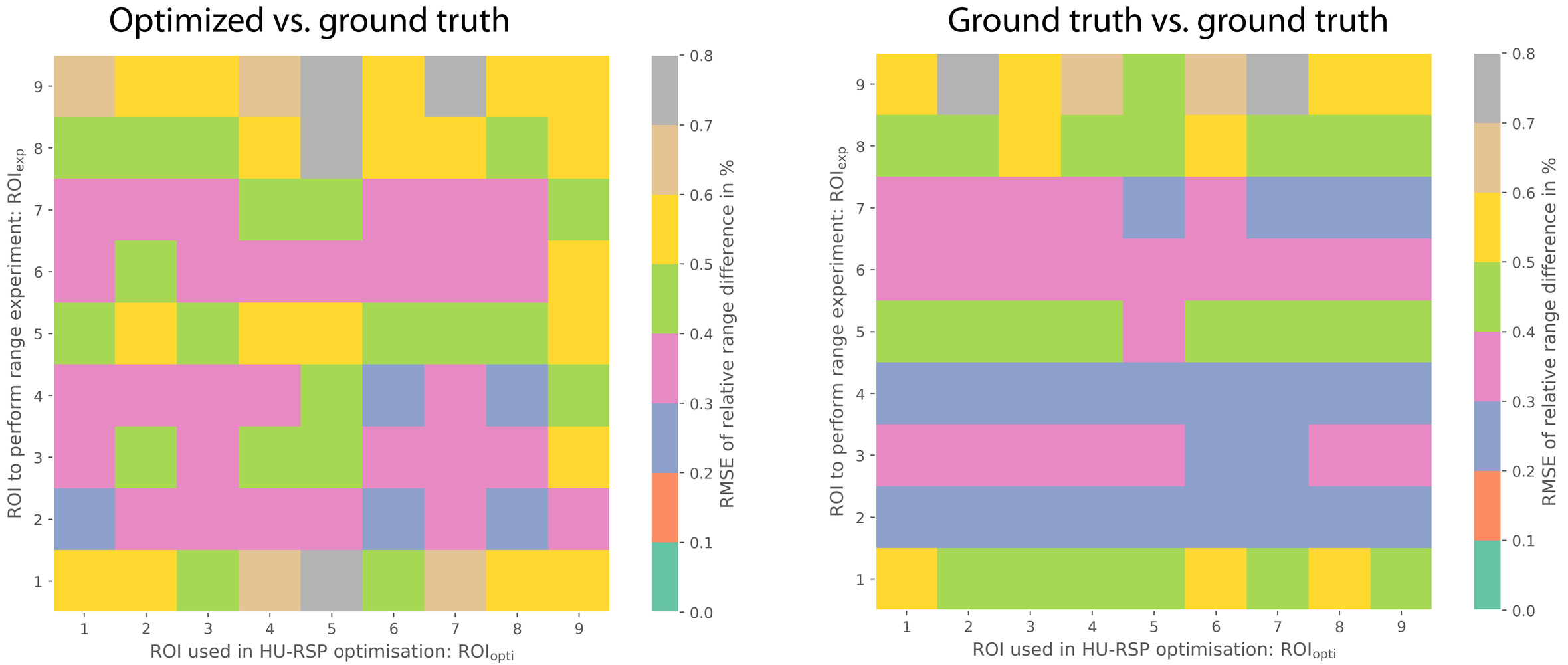






Does it matter of which region in the patient the proton radiography is acquired?

Standard deviation of range distribution



Summary

- **Patient specific calibration of CT-RSP curve feasible with relatively simple imaging system.**
- **Optimization needs to be regularized.**
- **Range accuracy with optimized curve better than 0.5%**
- **Region of which the proton radiography is acquired is not essential**
- **Intra-patient tissue variability not considered by this study**
- **Poor one-to-one correspondence between CT number & RSP cannot be resolved by patient specific conversion**


Thank you