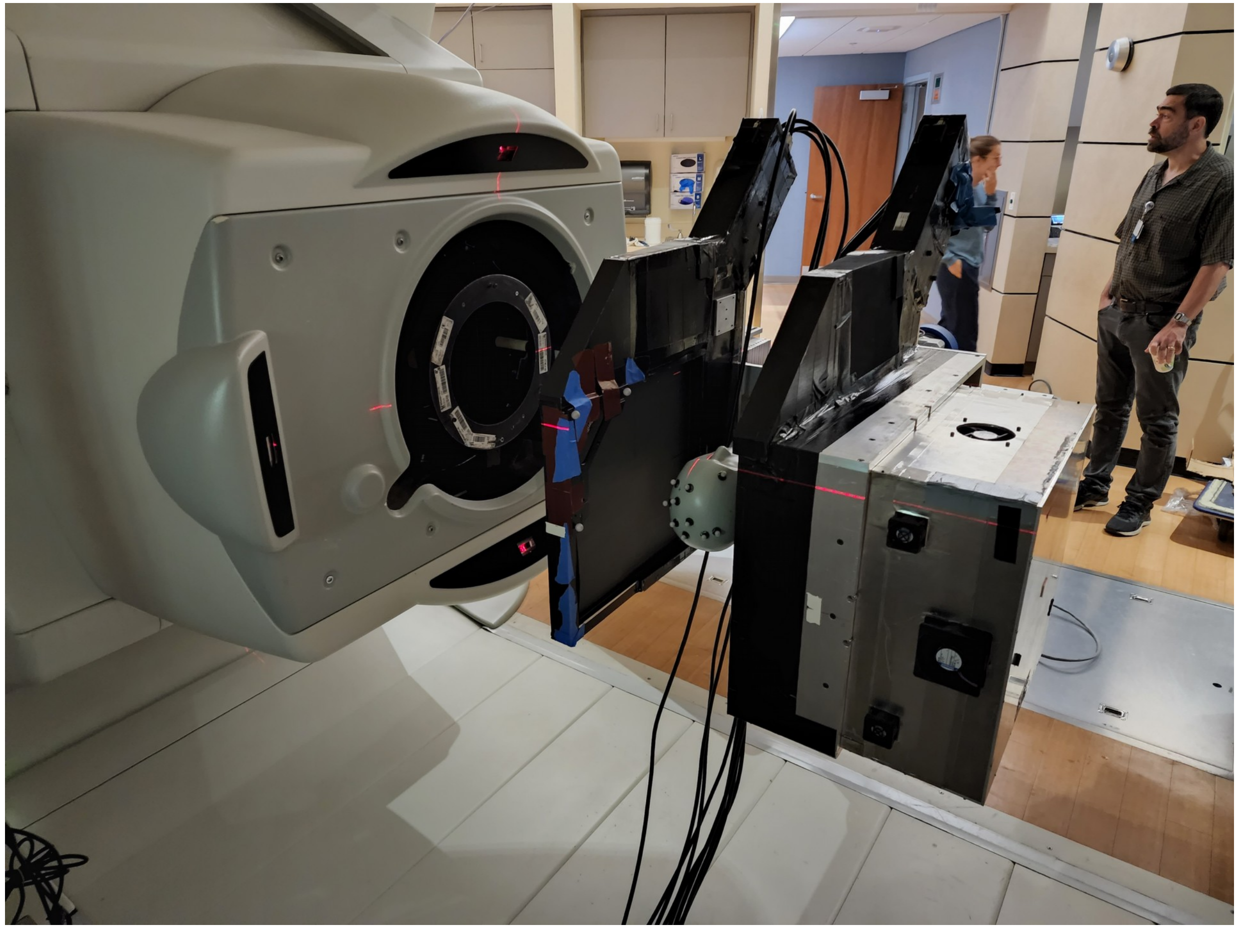
ProtonVDA

TRANSFORMING PROTON THERAPY

ProtonVDA pCT Update: Images and Algorithms



Ethan DeJongh
ProtonVDA LLC
October 14, 2022

Proton Imaging can help reduce range uncertainties by directly measuring proton stopping power

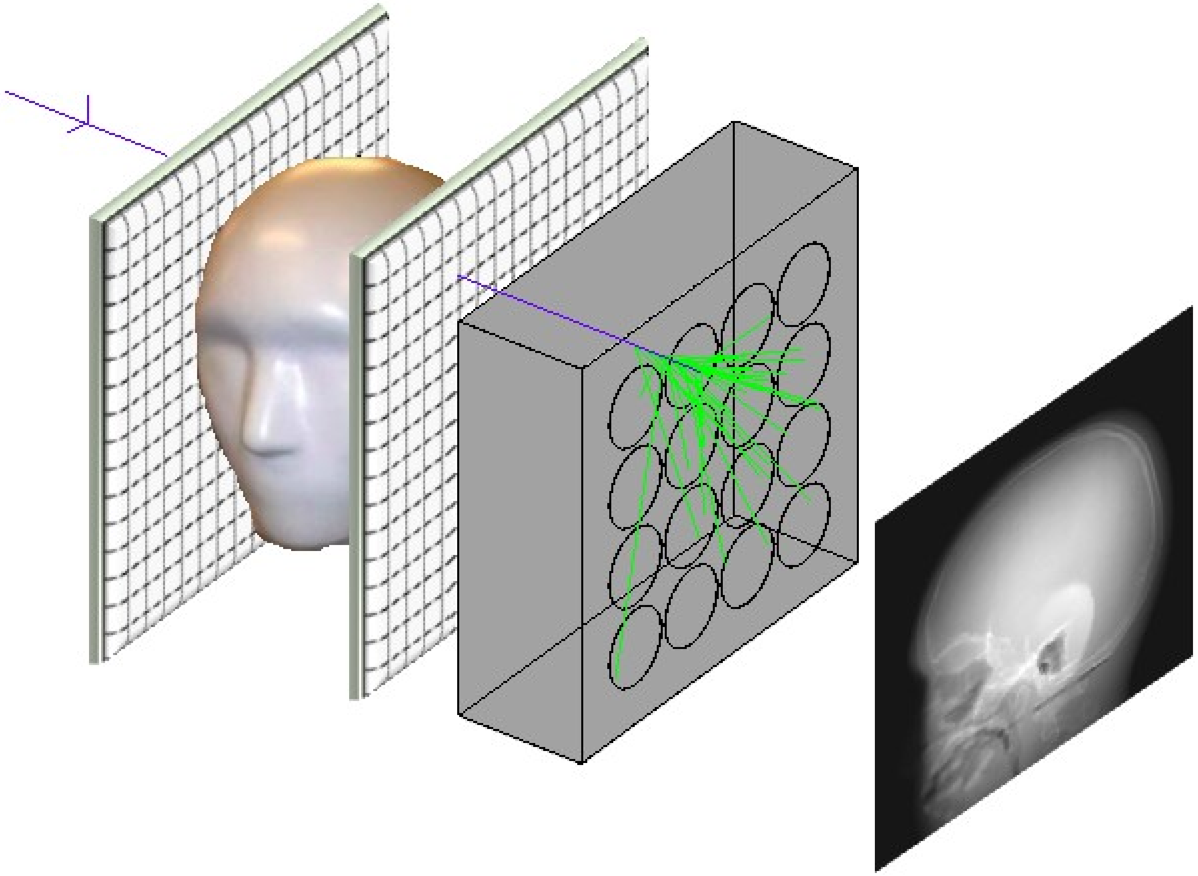
We aim to:

Develop a proton imaging system based on well-established fast scintillator technology.

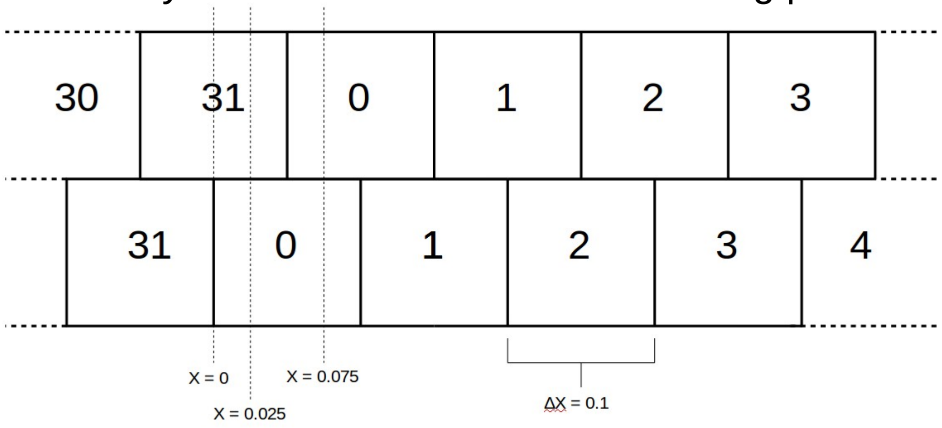
1. → High-performance, low-cost measurements of proton range.
2. Achieve lower dose to the patient relative to equivalent x-ray images.
3. Produce spatially sharp images.
4. Images free of artifacts from high-Z implants.

Multidisciplinary team of detector physicists, medical physicists, computer scientists, and radiation oncologists:

- ProtonVDA: Fritz DeJongh, Ethan DeJongh, Victor Rykalin
- Loyola Stritch School of Medicine: James Welsh
- Northwestern Medicine Chicago Proton Center: Mark Pankuch, Brad Kreydick
- Northern Illinois University, Dept. of Computer Science: Nick Karonis, Cesar Ordonez, John Winans, Kirk Duffin. Dept. of Physics: George Coutrakon, Christina Sarosiek
- Loma Linda University: Reinhard Schulte
- Cosylab – product development team



Fiber layout cross-section for one tracking plane:

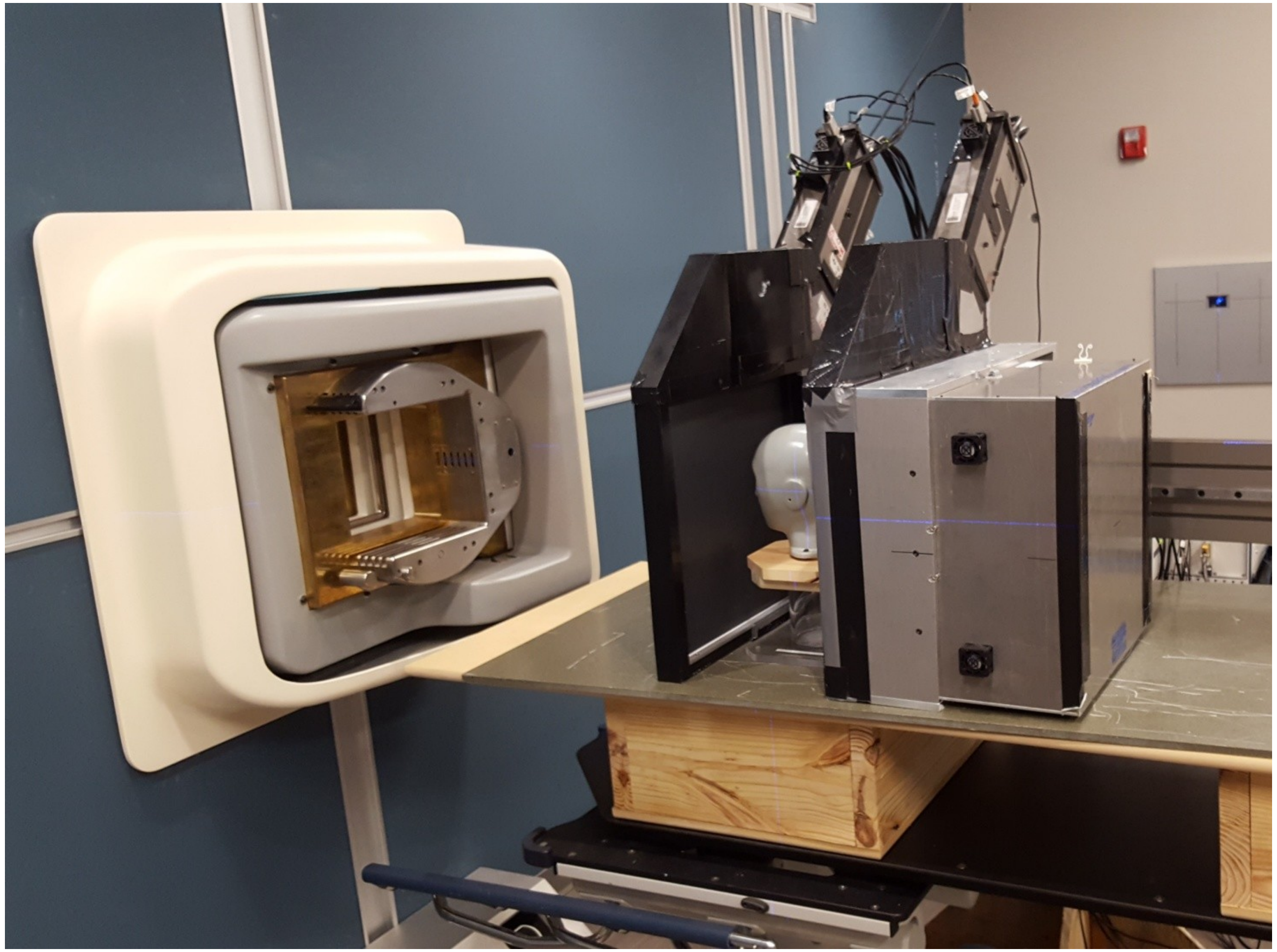


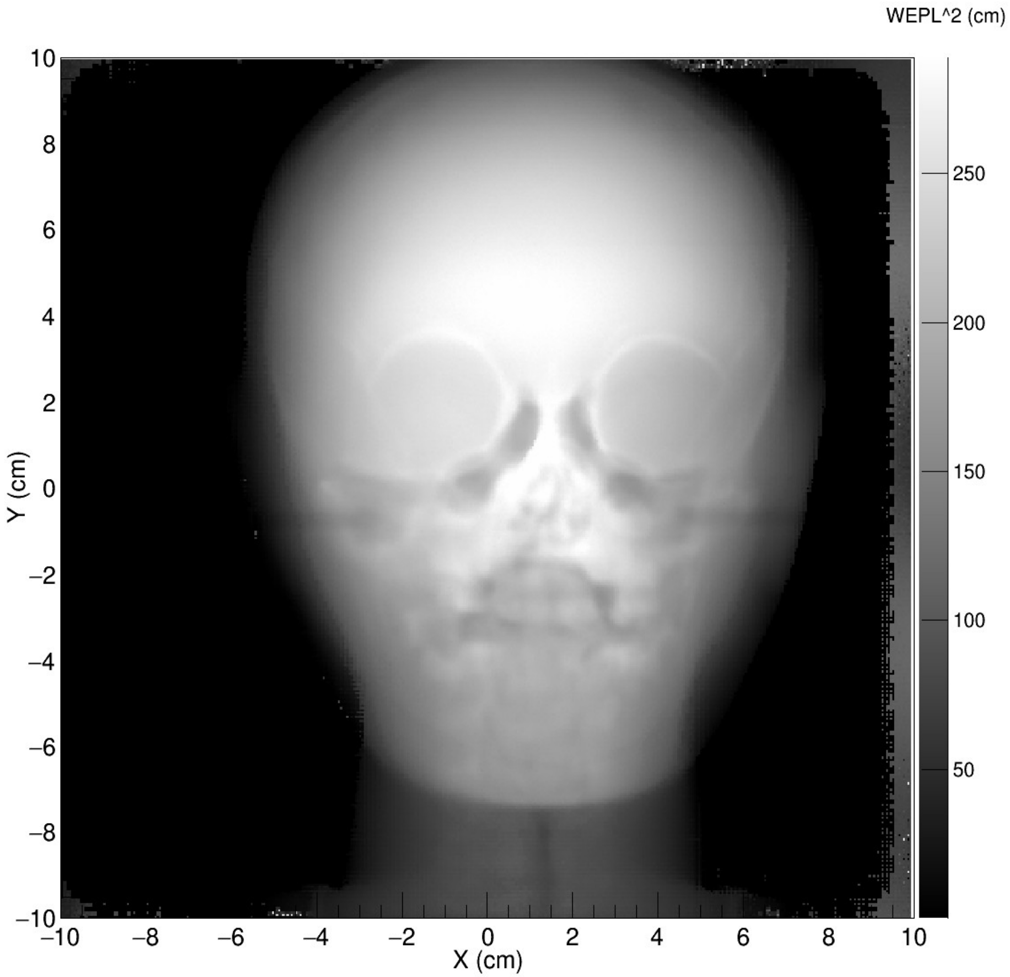
- X-Y tracking planes upstream and downstream

- Multiplexed fiber readout
  - 32 digitized channels per tracking plane
  - position ambiguities resolved using pencil beam targeting information
  - reduces amount of electronics needed

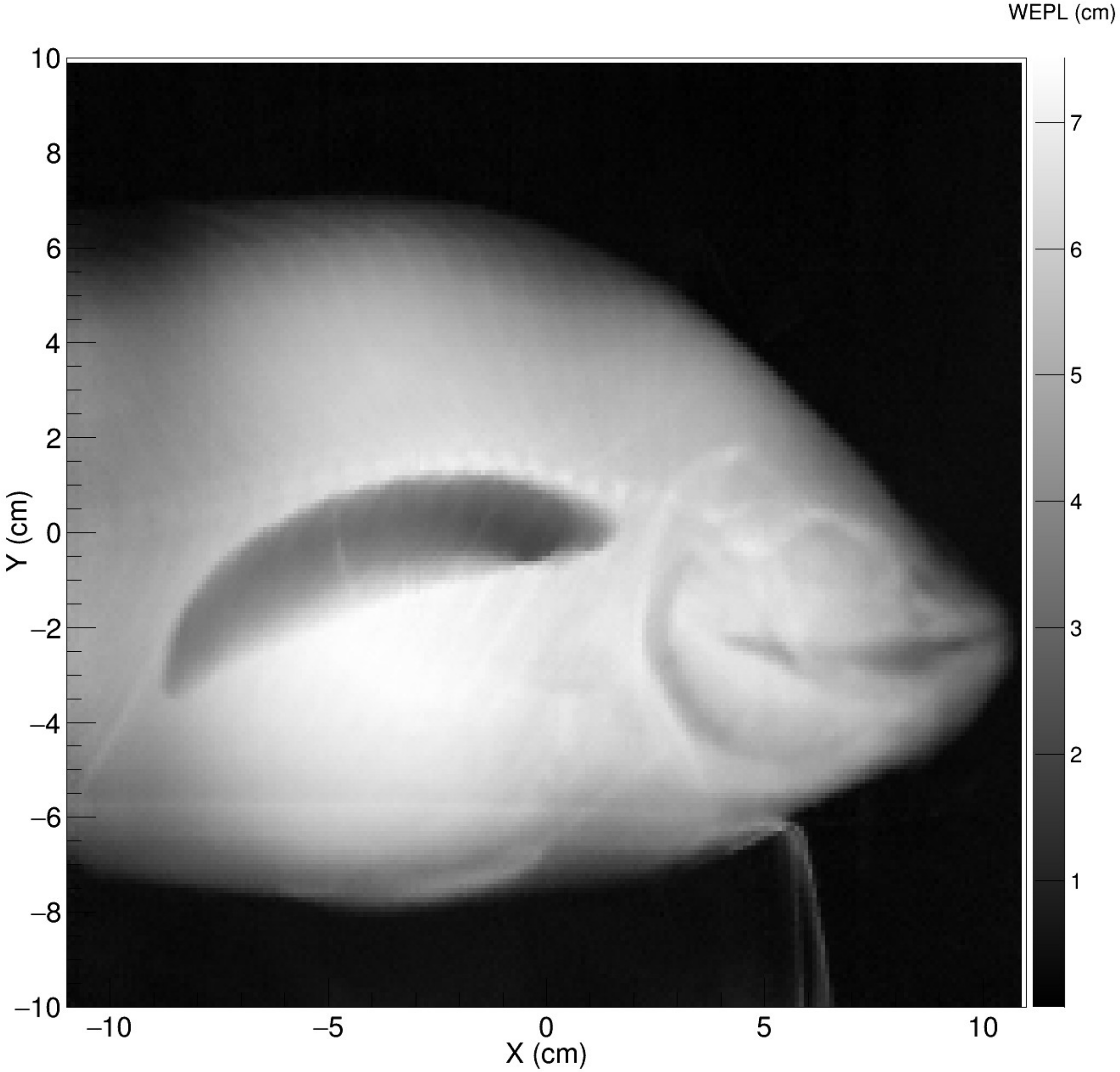
- 40 x 40 x 13 cm block of scintillator for range detector
  - 4 x 4 array of PMTs
  - Output digitized into four channels: E, U, V,C

- Individual protons tracked at up to 3 MHz
- > 99% tracking efficiency
- WEPL resolution ~ 3 mm per proton
- 40 x 40 cm image field size
- Fast (<1 min) image reconstruction for radiograph



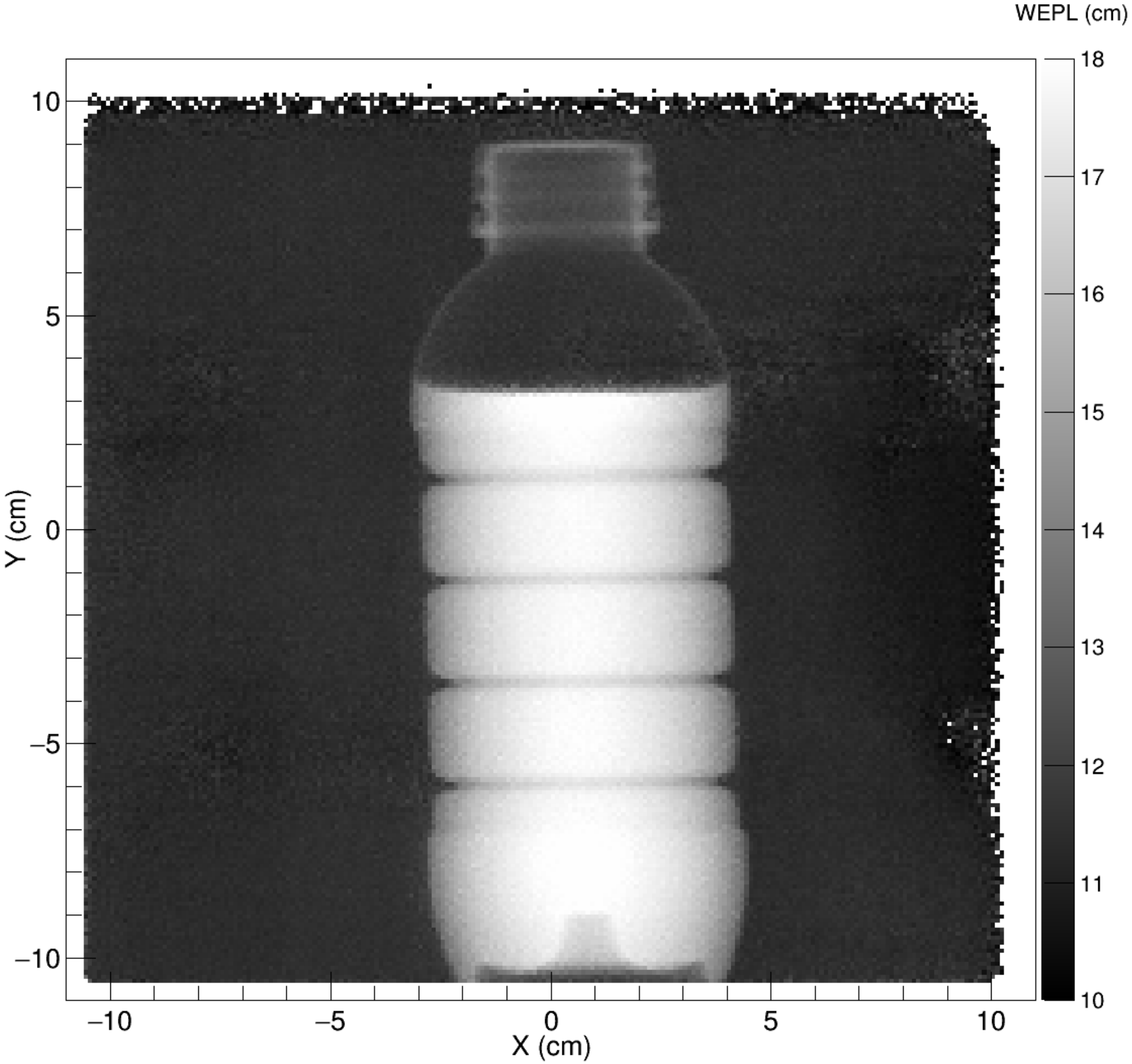

WEPL^2 (cm)
250
200
150
100
50
Y (cm)
10
8
6
4
2
0
−2
−4
−6
−8
−10
X (cm)
−10
−8
−6
−4
−2
0
2
4
6
8
10

First pRad images – Spring 2018

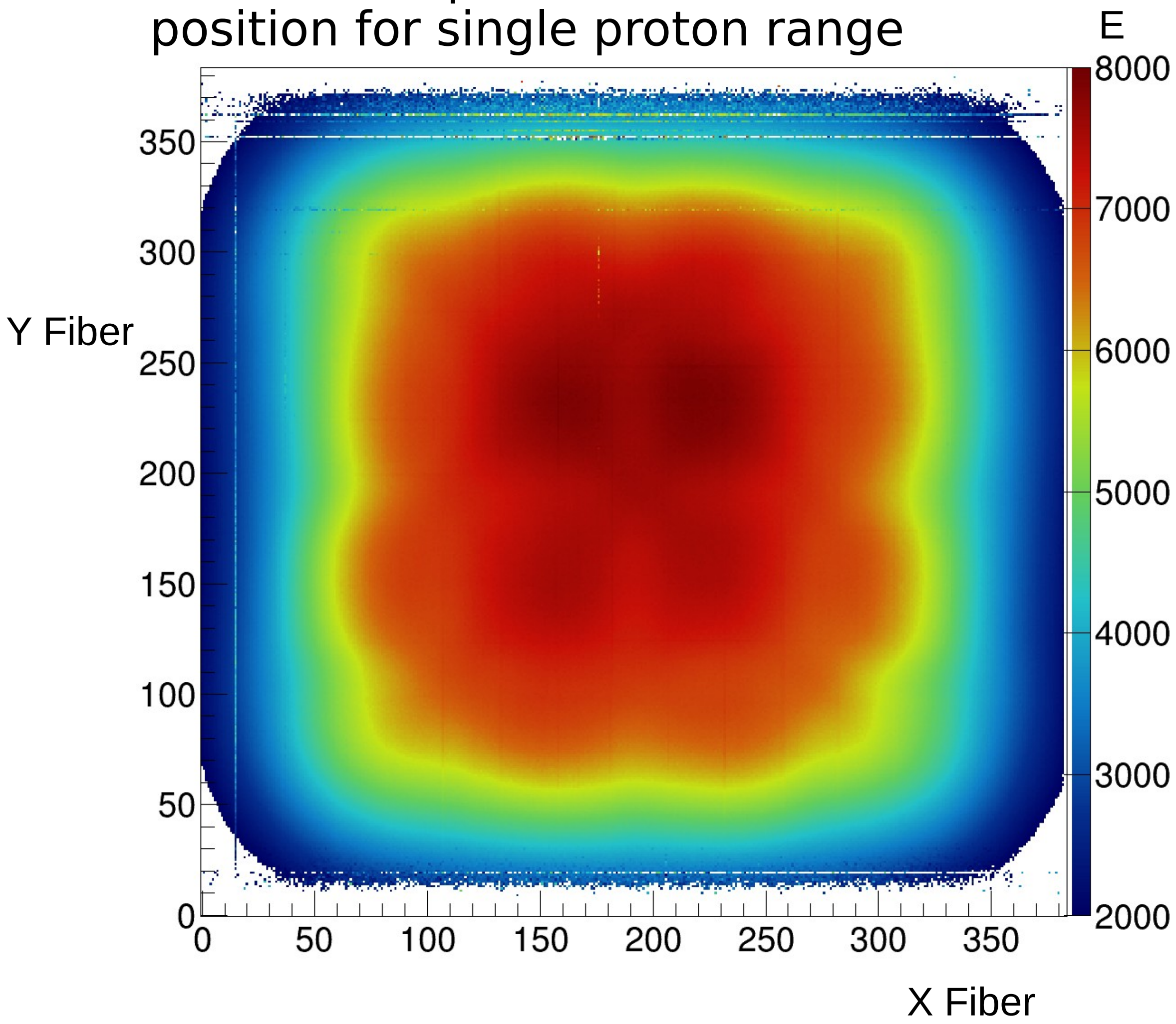


Fast (< 1 min) online image reconstruction

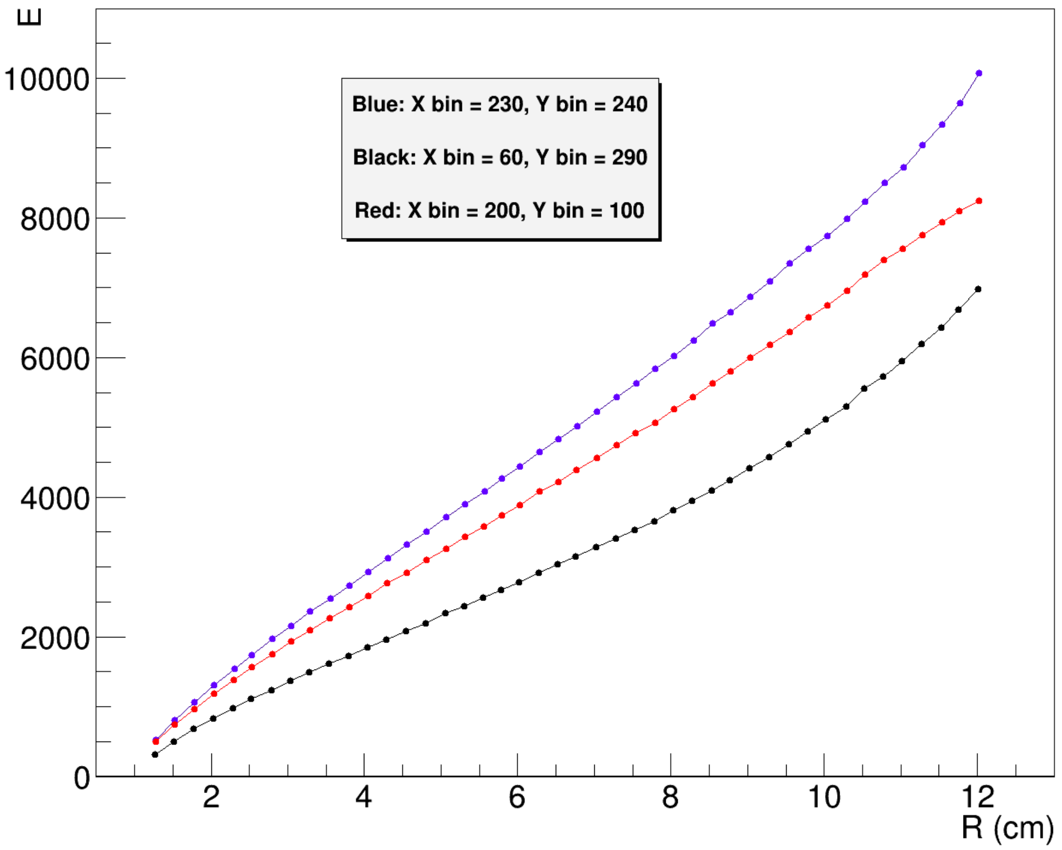
Water bottle plus solid water – 180 MeV



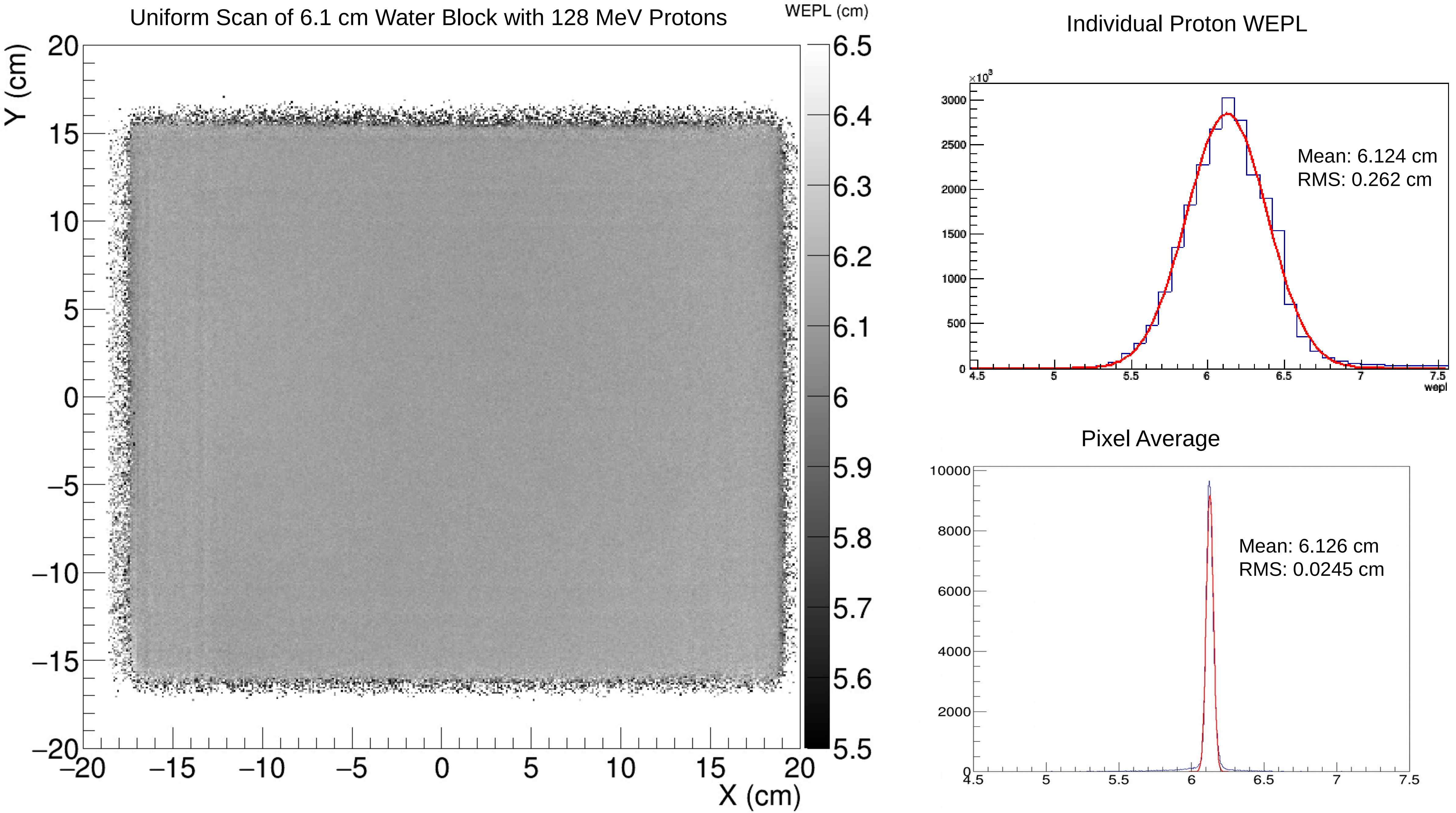
Detector response vs downstream tracker position for single proton range



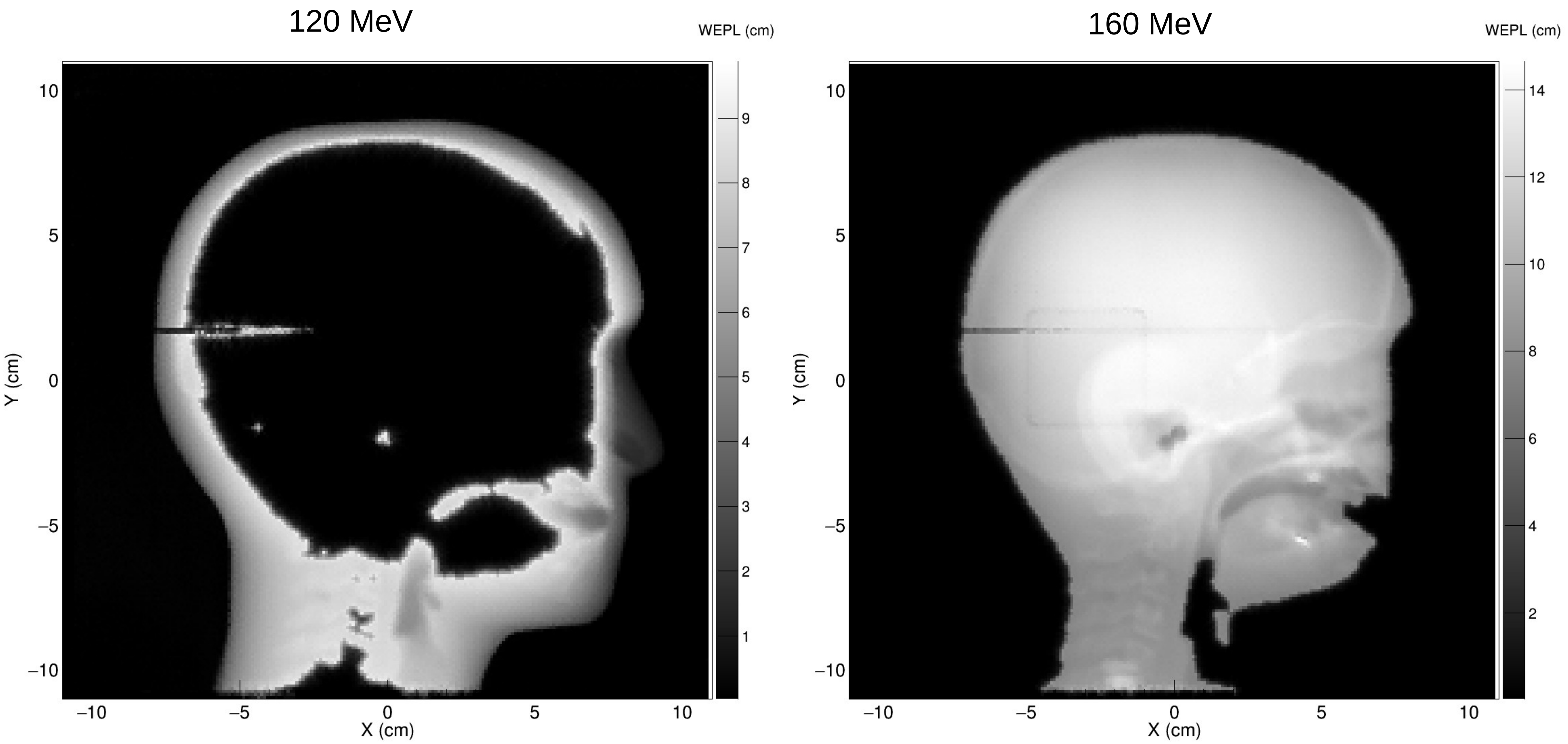
Detector response vs proton range for single positions

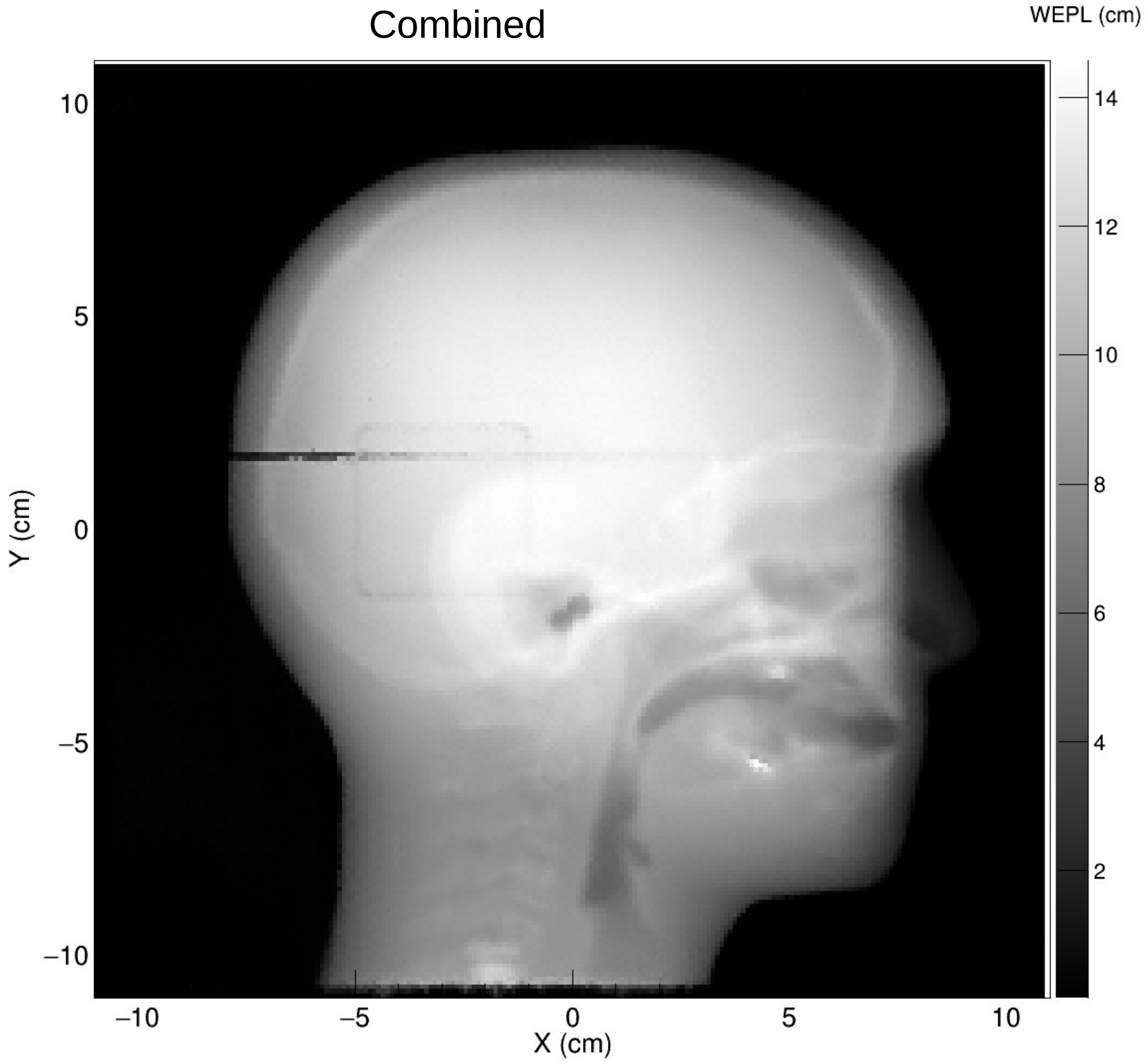


- Linear detector response vs. range gives very good range sensitivity


Uniform Scan of 6.1 cm Water Block with 128 MeV Protons
WEPL (cm)
Y (cm)
X (cm)
Individual Proton WEPL
×10³
wepl
Mean: 6.124 cm
RMS: 0.262 cm
Pixel Average
Mean: 6.126 cm
RMS: 0.0245 cm

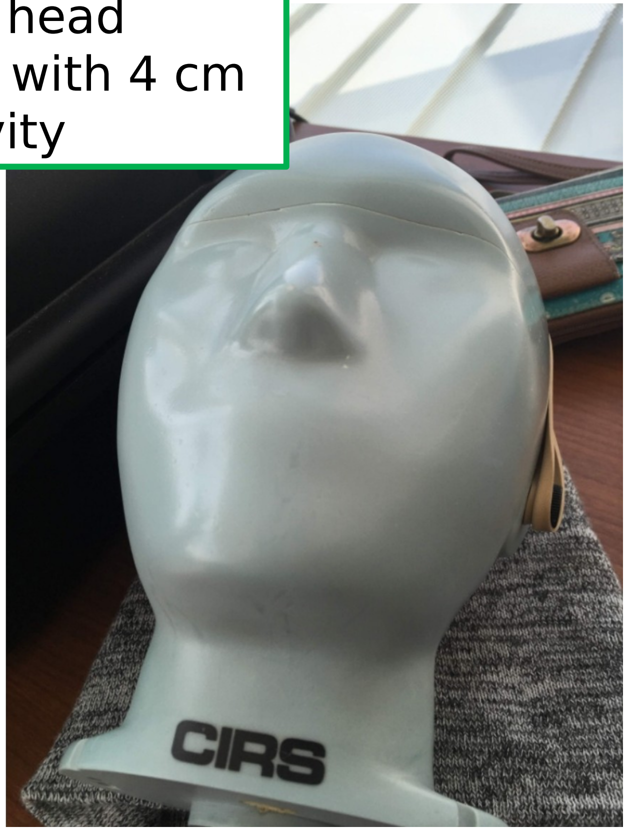
Imaging with Multiple Proton Energies – Pediatric Head Phantom



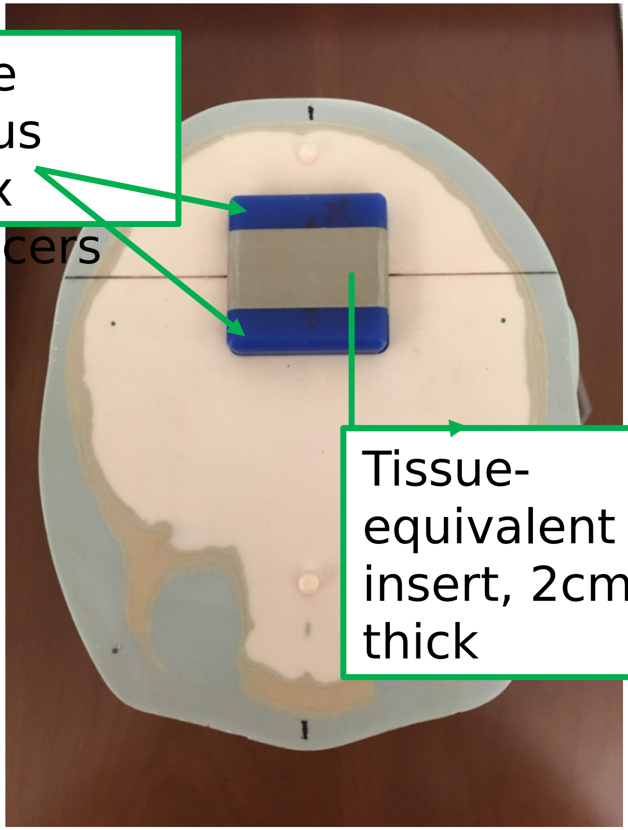

Combined
WEPL (cm)
14
12
10
8
6
4
2
10
5
0
−5
−10
Y (cm)
−10
−5
0
5
10
X (cm)

Pediatric Head Phantom with CIRS Inserts

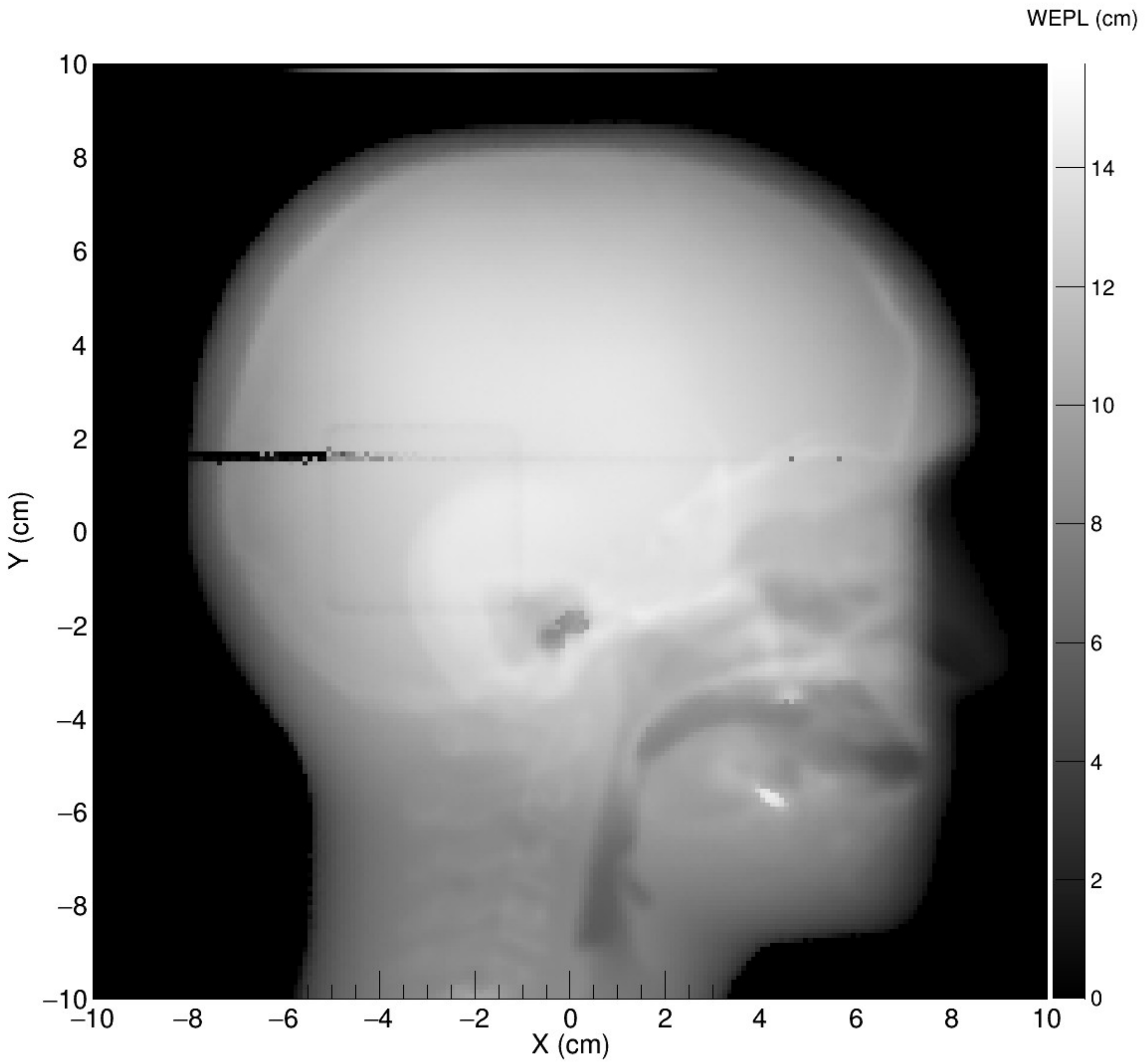
Customized pediatric head phantom with 4 cm cubic cavity



Blue Bolus Wax Spacers

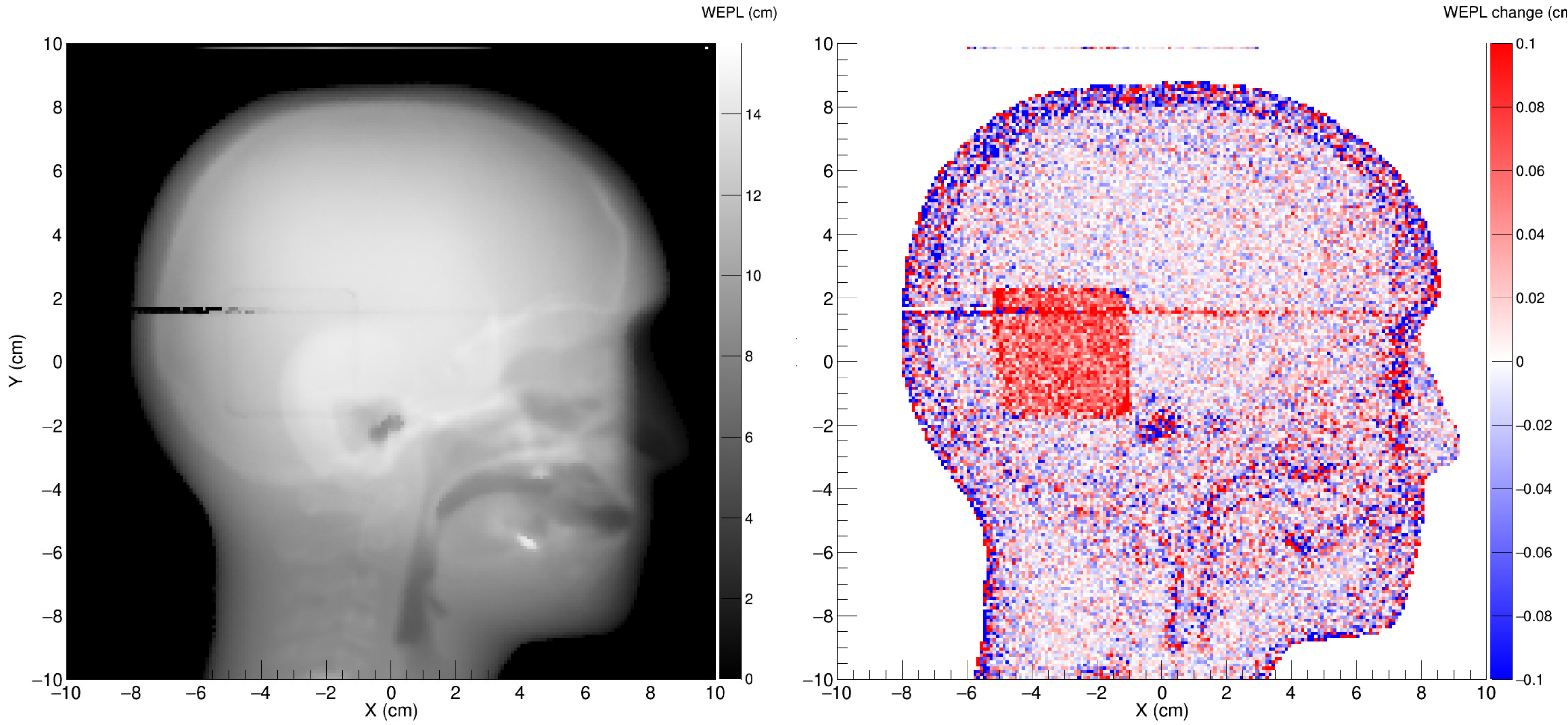


Tissue-equivalent insert, 2cm thick



Insert: spinal cord

RSP: 1.04

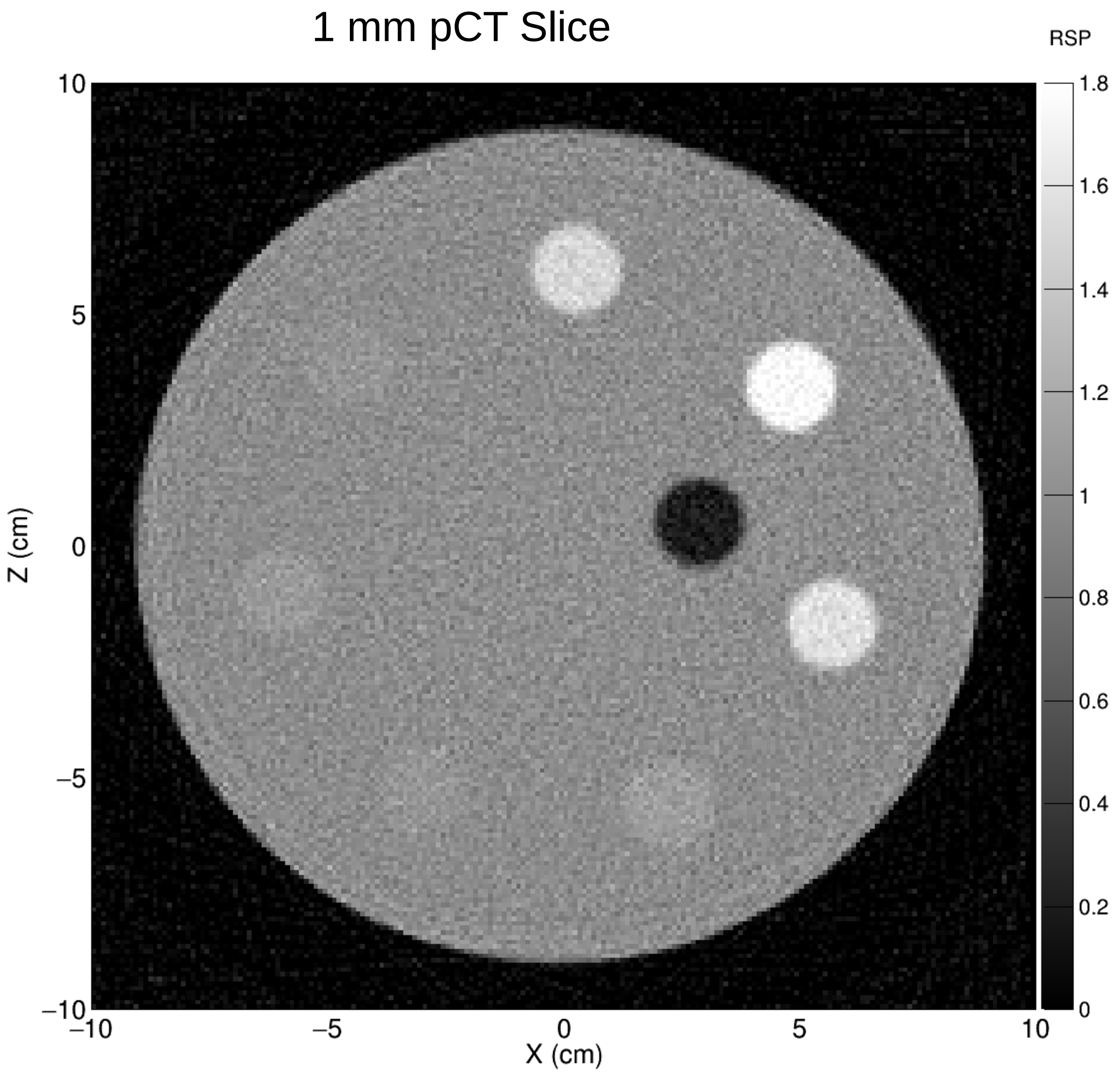


Insert: spinal disc

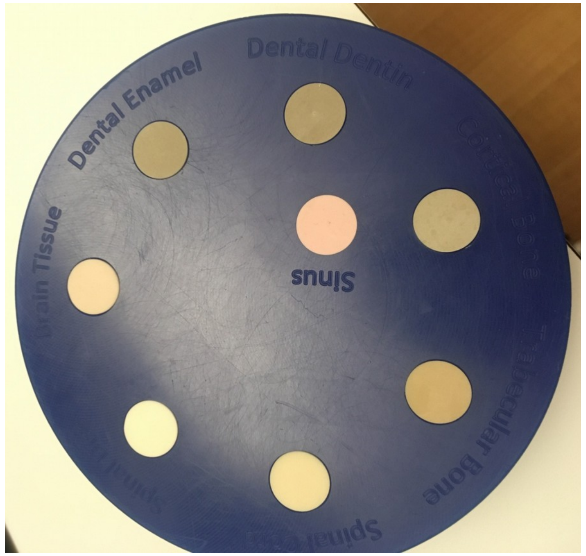
RSP: 1.07

Expected difference: +0.6 mm
Measured difference: +0.58 ± 0.01 mm

First pCT images – Summer 2019



Insert	RSP	RSP from pCT image In ROI for each insert (Statistical uncertainty only)	Difference (pCT – Nominal)
Sinus	0.200	0.192 ± 0.002	-0.008
Enamel	1.755	1.768 ± 0.002	0.013
Dentin	1.495	1.504 ± 0.002	0.009
Brain	1.040	1.043 ± 0.002	0.003
Spinal Cord	1.040	1.046 ± 0.002	0.006
Spinal Disc	1.070	1.079 ± 0.002	0.009
Trabecular Bone	1.100	1.106 ± 0.002	0.006
Cortical Bone	1.555	1.570 ± 0.002	0.015

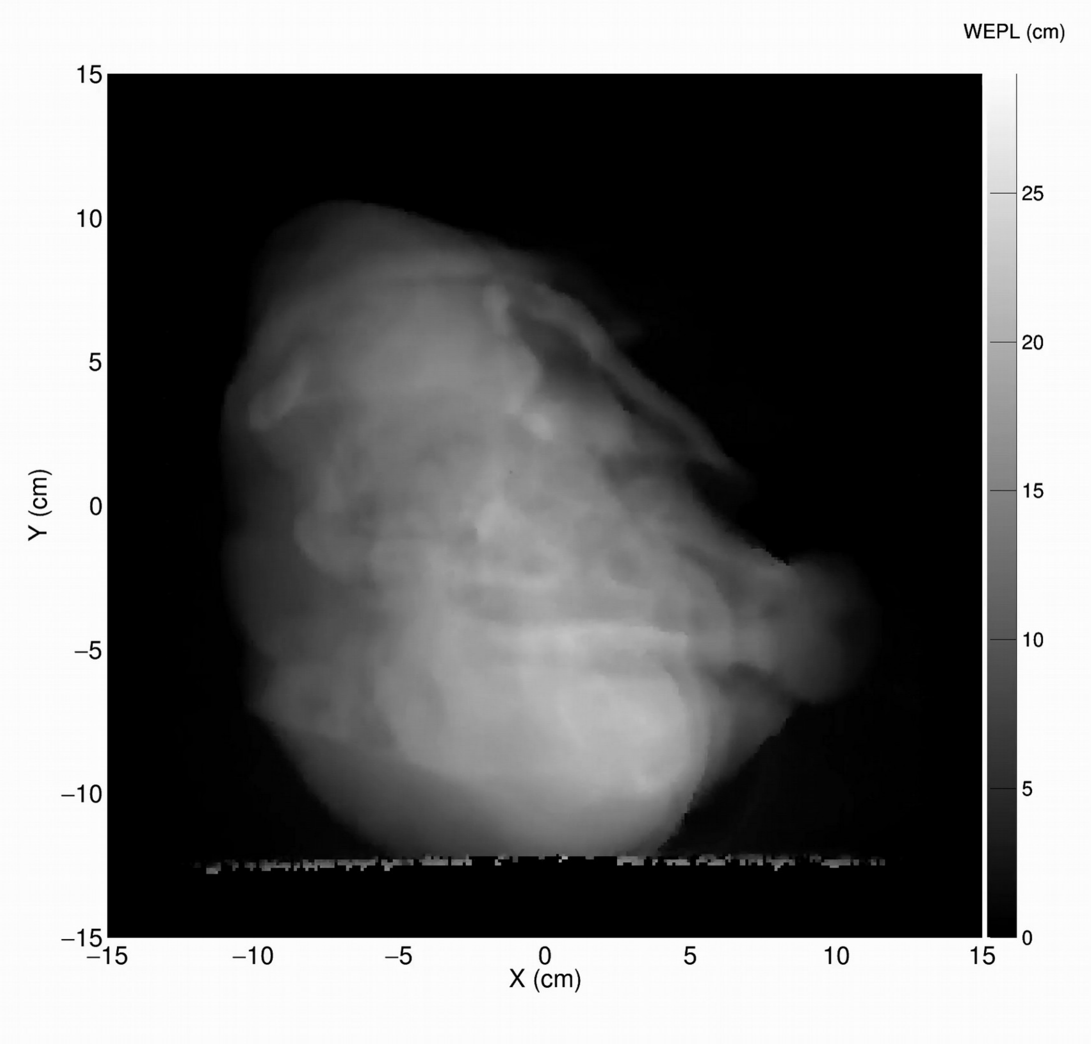


* <1% RSP errors

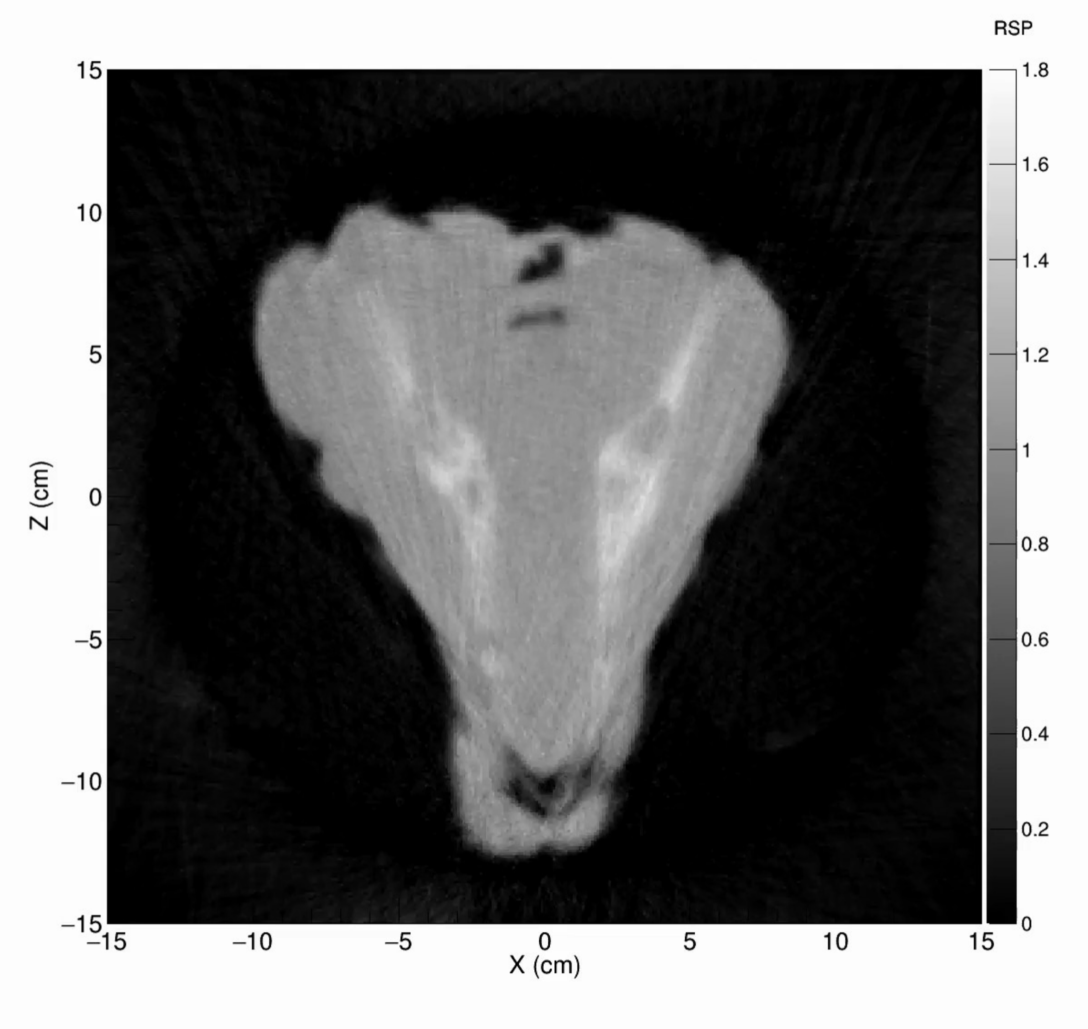
pCT of fresh pig's head – January 2020

- 4 energies, data taken in 4 degree intervals
- Vertical CT taken for comparison

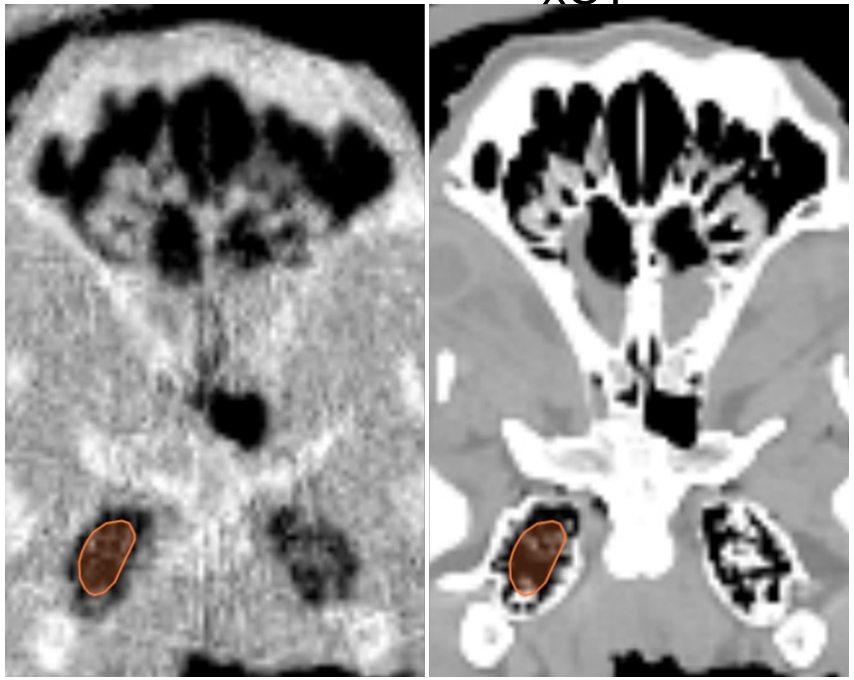
Proton radiographs taken every 4 degrees



Horizontal pCT slices – 1 mm



Contours: tympanic bullae



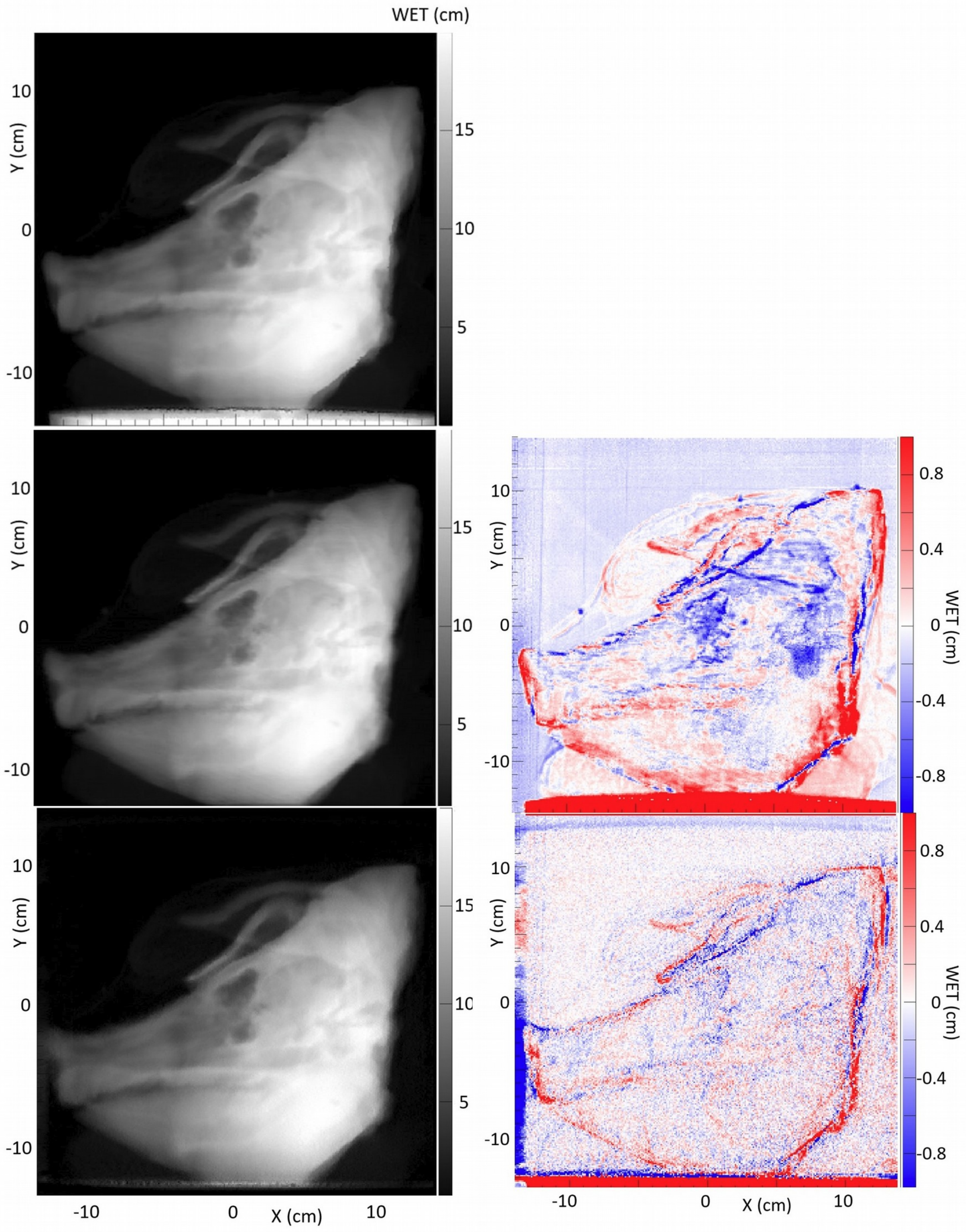
Region	Volume (cm^3)	pCT RSP Mean	pCT RSP SD	pCT RSP SE(%)	Hor CT[a] RSP	Diff (%)	Hor CT[b] RSP	Diff (%)	Vert CT RSP	Diff (%)
Bullae	0.8	0.491	0.24	1.7	0.684	-39.3	0.690	-40.5	0.634	-29.1
Adipose	3.7	0.950	0.14	0.2	0.961	-1.2	0.962	-1.3	0.954	-0.4
Muscle	2.0	1.033	0.16	0.3	1.058	-2.4	1.059	-2.5	1.052	-1.8
Tongue	9.4	1.047	0.23	0.2	1.035	1.1	1.036	1.1	1.031	1.5
Brain Stem	0.7	0.994	0.16	0.6	1.038	-4.4	1.038	-4.4	1.016	-2.2
Brain	2.5	1.025	0.16	0.3	1.037	-1.2	1.039	-1.4	1.031	-0.6
Lens	0.1	1.099	0.12	1.6	1.078	1.9	1.080	1.7	1.076	2.1
Eye Left	0.5	1.015	0.13	0.5	1.015	0.0	1.017	-0.2	1.018	-0.3
Eye Right	0.8	1.011	0.15	0.5	1.021	-1.0	1.021	-1.0	1.014	-0.3
Skull	0.5	1.266	0.12	0.4	1.297	-2.4	1.303	-2.9	1.320	-4.3
Mandible	0.5	1.540	0.16	0.5	1.559	-1.2	1.565	-1.6	1.562	-1.4
Sinus Air	0.1	0.067	0.12	17	0.057	15	0.058	13	0.039	42

[a] Low dose protocol
[b] High dose protocol

Proton Radiograph

X-Ray CT DRR – converted to WET

pCT DRR

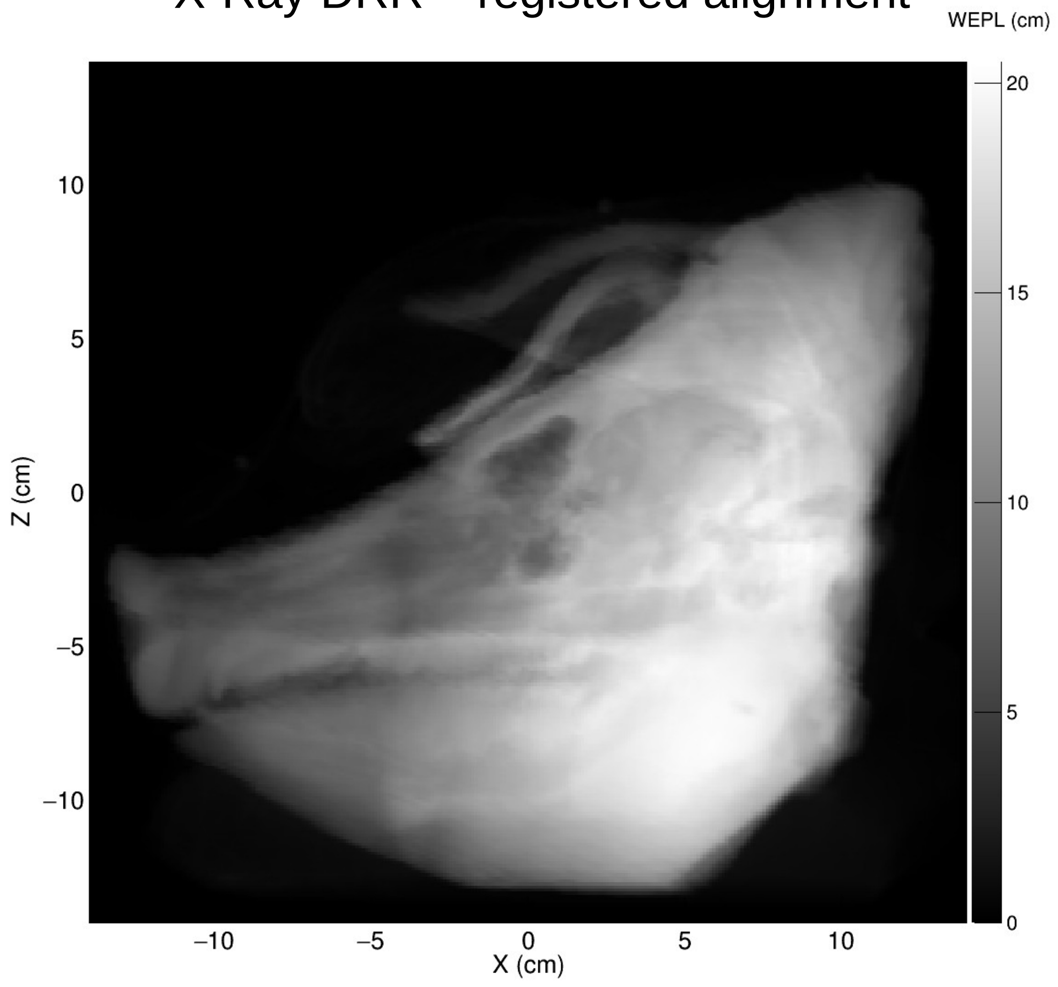


Difference – pRad vs. xCT

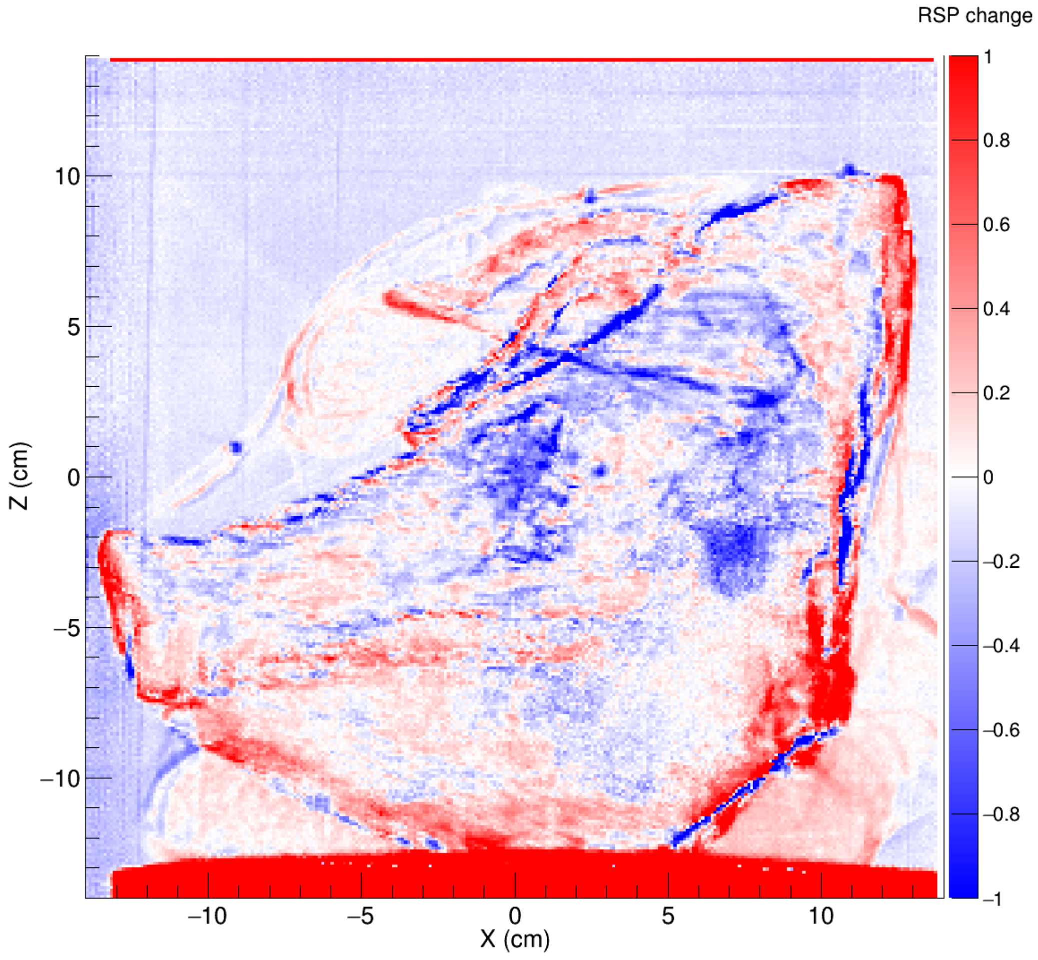
Difference – pRad vs. pCT

Using pRad to align the patient

X-Ray DRR – registered alignment

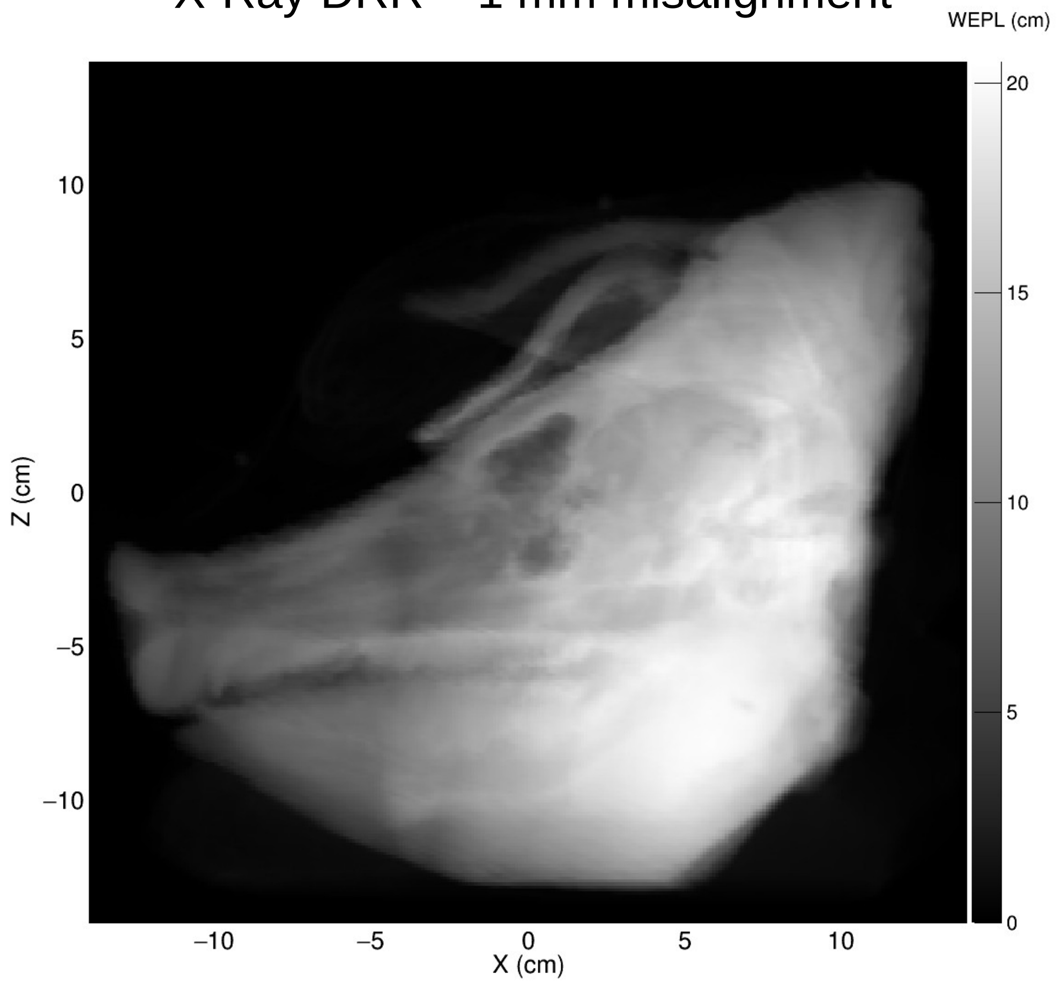


Difference – pRad vs DRR

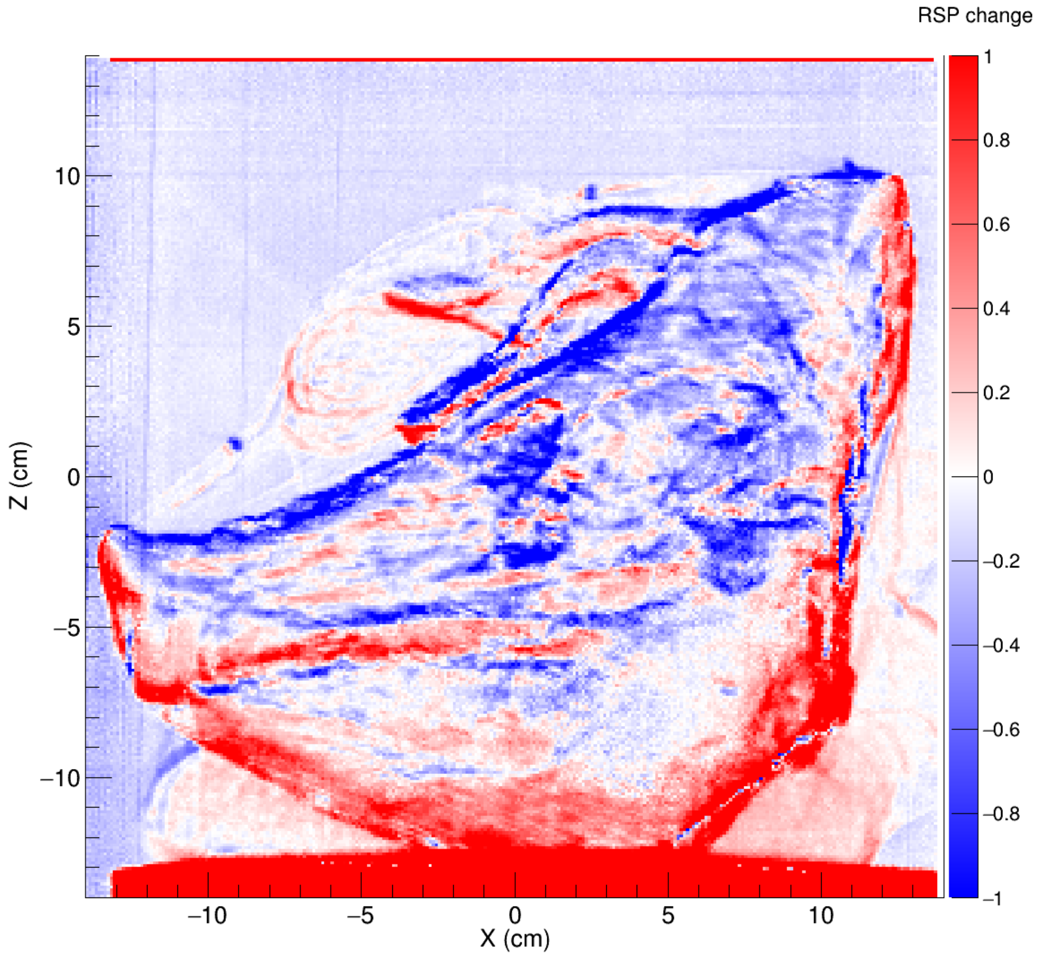


Using pRad to align the patient

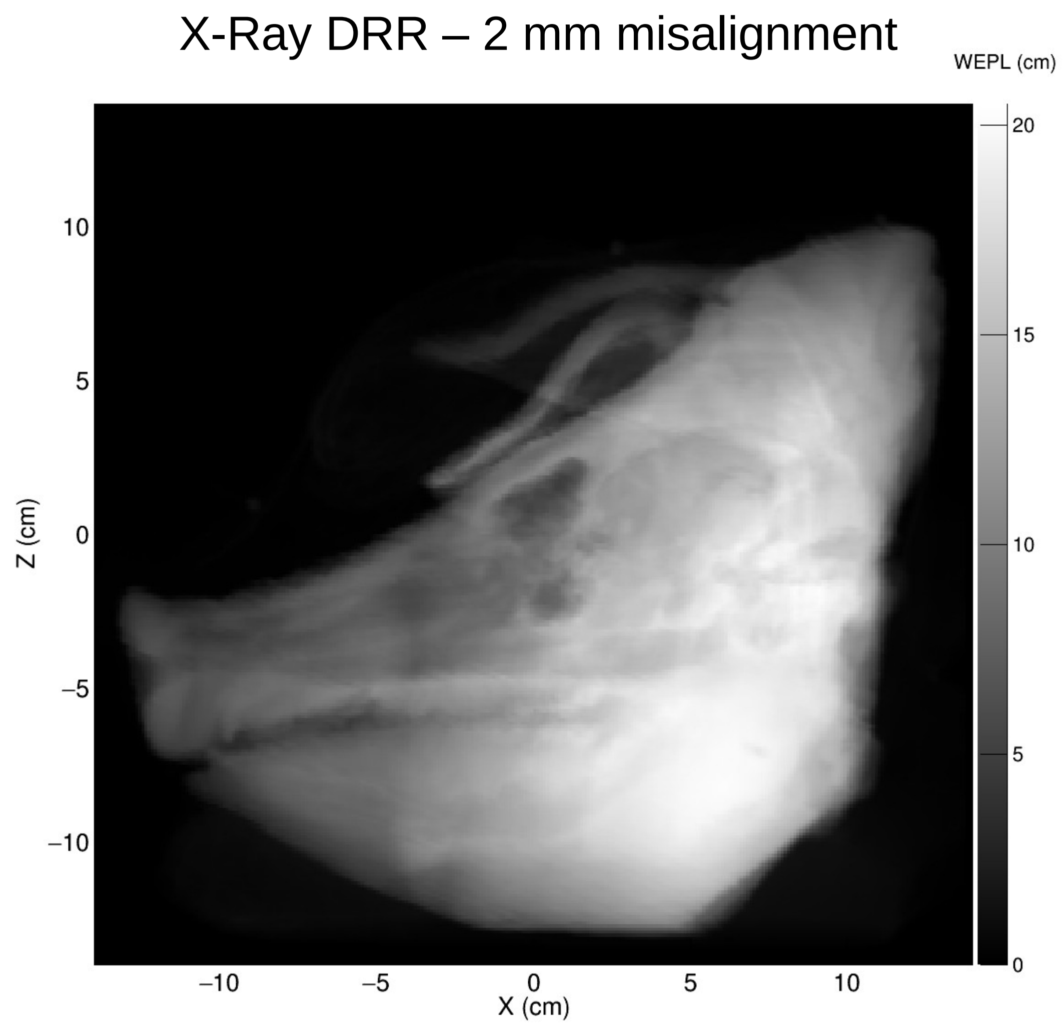
X-Ray DRR – 1 mm misalignment

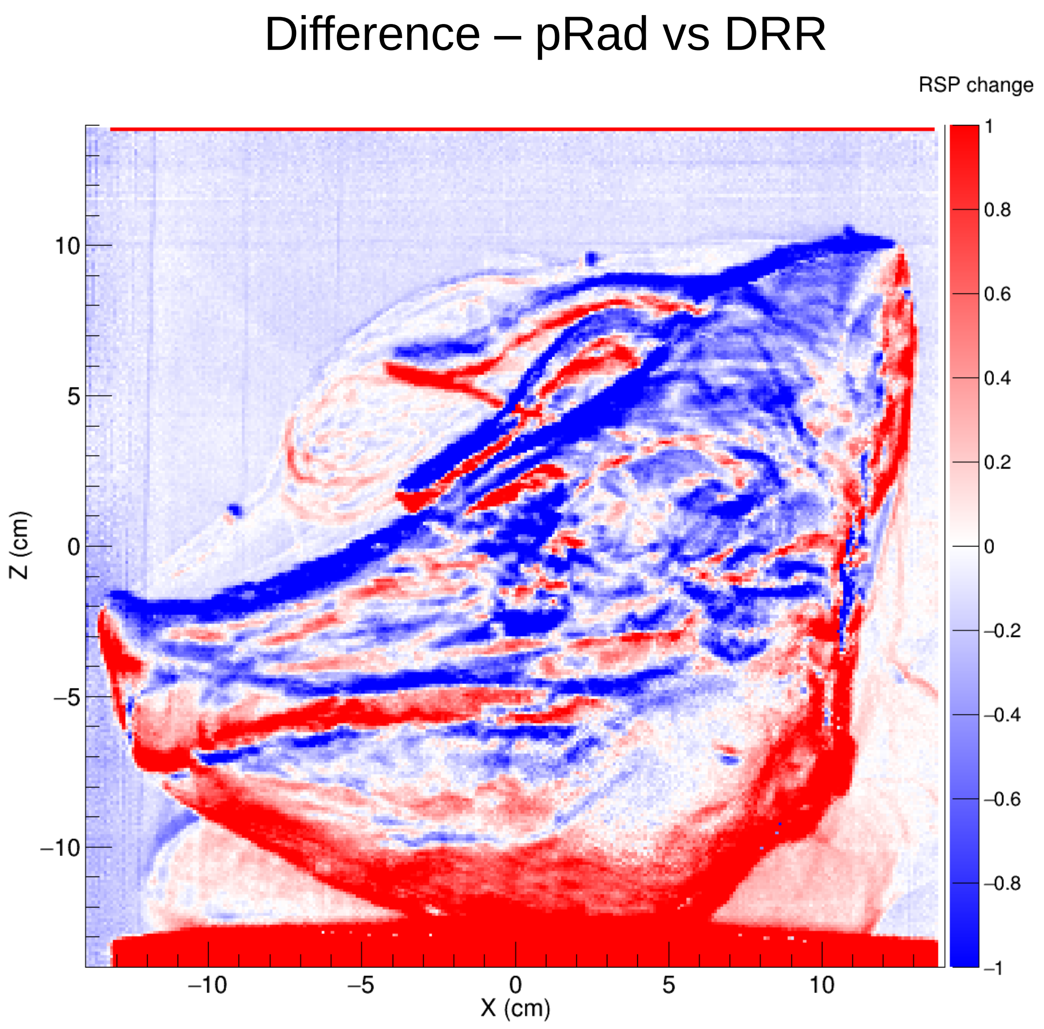


Difference – pRad vs DRR



Using pRad to align the patient

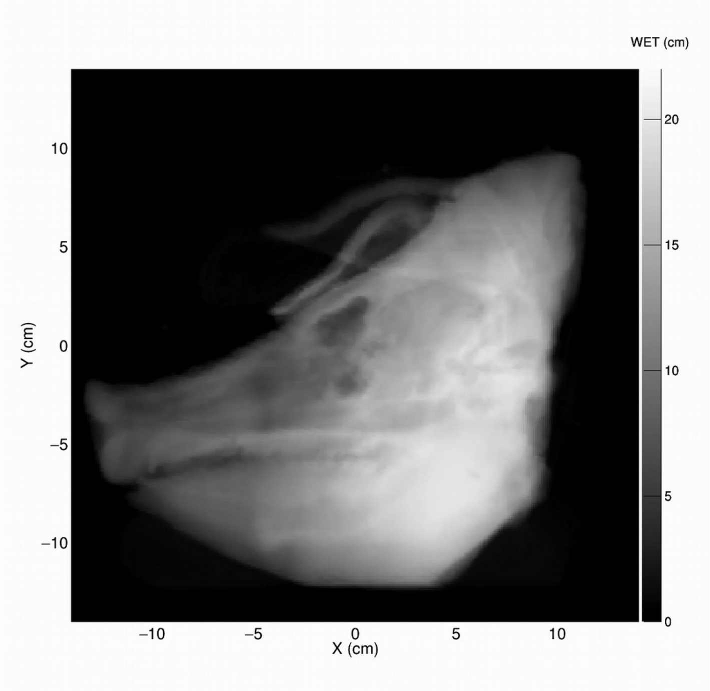




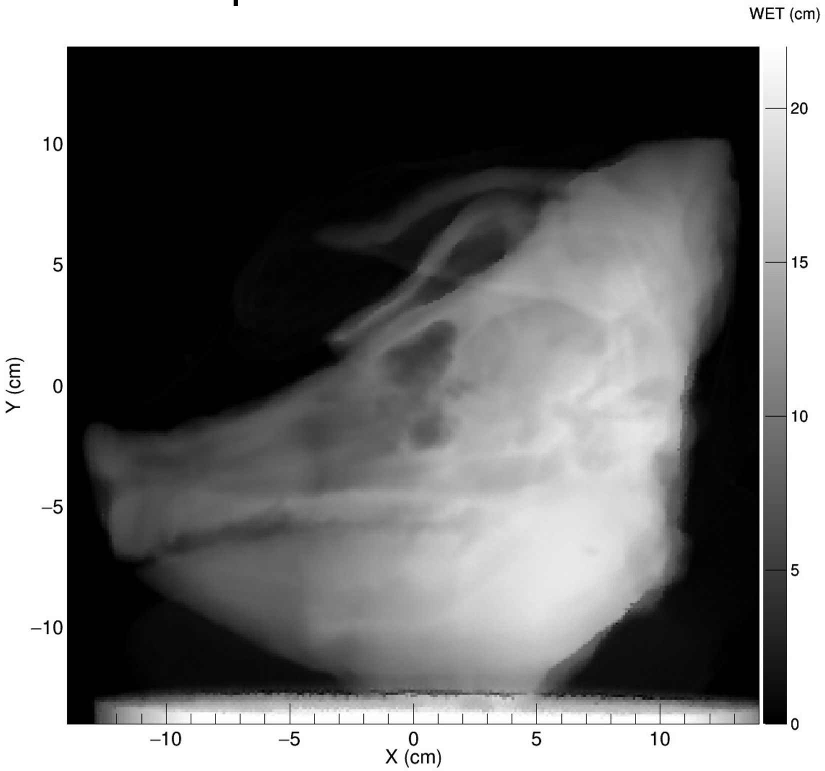
A single pRad can be used for 3-D alignment

- Automated alignment of X-Ray DRR using TOPAS
- Iterative adjustment of one parameter at a time (6 parameters – 3 rotations, 3 translations)

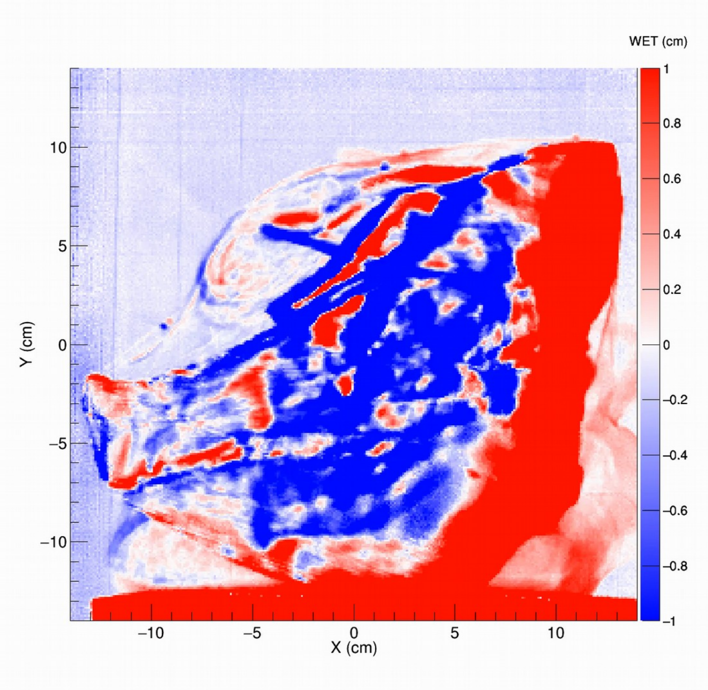
X-Ray DRR



pRad



Difference



Our Reconstruction Algorithm: the DV method

$$d_p = Ax - b$$

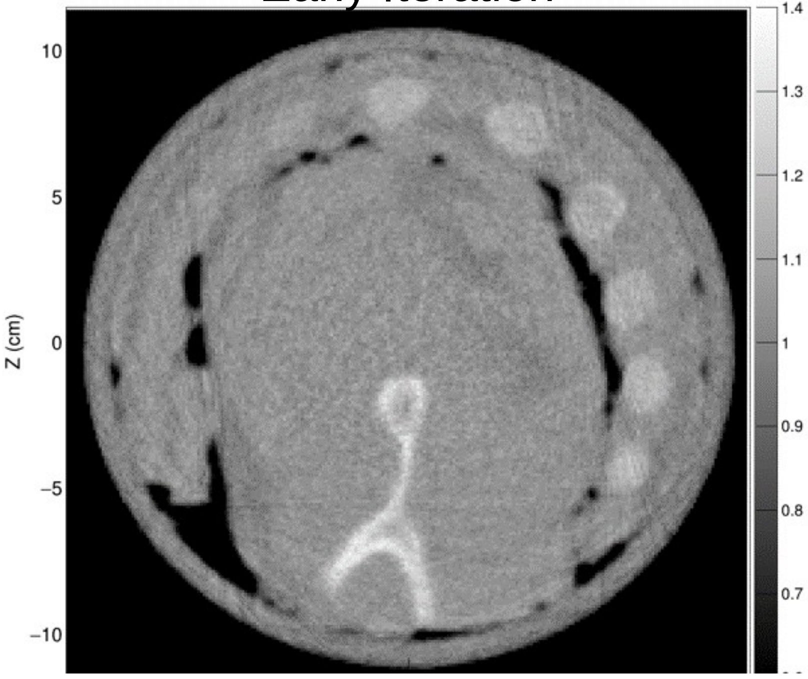
$$d_v = \bar{A}^T d_p$$

$$\bar{A}^T = V^{-1} A^T$$

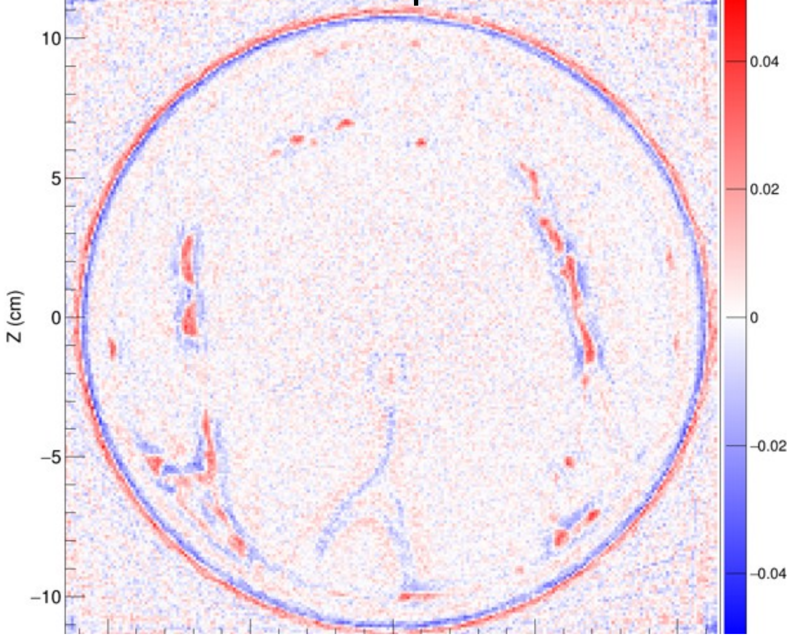
$$V^{-1} = diag\left(\frac{1}{\sum_j \alpha_{ij}^T}\right)$$

$$x_{k+1} = x_k - \lambda_k\, d_{vk}$$

Early Iteration

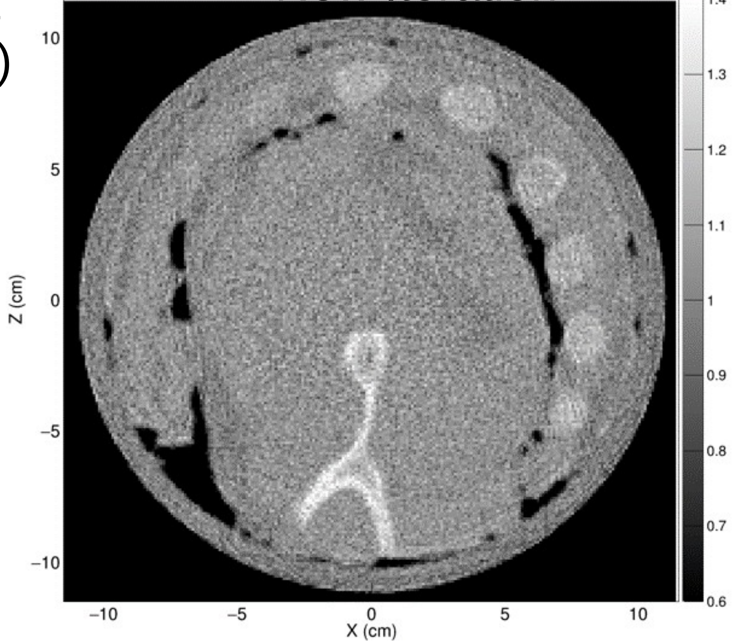


DV map



*Real pCT of fresh meat sample (no ground truth)

New Iteration



Optimization of λ_k

$$d_{pk} = Ax_k - b$$
$$d_{vk} = \bar{A}^T d_{pk}$$
$$x_{k+1} = x_k - \lambda_k\, d_{vk}$$
$$d_{p(k+1)} = Ax_{k+1} - b$$
$$= d_{pk} - \lambda_k\, Ad_{vk}$$

$$d_{v(k+1)} = \bar{A}^T d_{p(k+1)}$$
$$= d_{vk} - \lambda_k\, \bar{A}^T(Ad_{vk})$$

- One possible choice for λ_k: Minimize χ^2_{k+1}

$$\chi^2_{k+1} = d_{p(k+1)} \cdot d_{p(k+1)}$$
$$= d_{pk} \cdot d_{pk} - 2\lambda_k\, d_{pk} \cdot (Ad_{vk}) + \lambda^2_k\, |Ad_{vk}|^2$$
$$= \chi^2_k - 2\lambda_k\, d_{pk} \cdot (Ad_{vk}) + \lambda^2_k\, |Ad_{vk}|^2$$

$$d\chi^2_{k+1} / d\lambda_k = -2\, d_{pk} \cdot (Ad_{vk}) + 2\lambda_k\, |Ad_{vk}|^2 = 0$$

$$\lambda_k = d_{pk} \cdot (Ad_{vk}) \,/\, |Ad_{vk}|^2$$

- Another choice for λ_k: Minimize $d_{v(k+1)} \cdot d_{v(k+1)}$

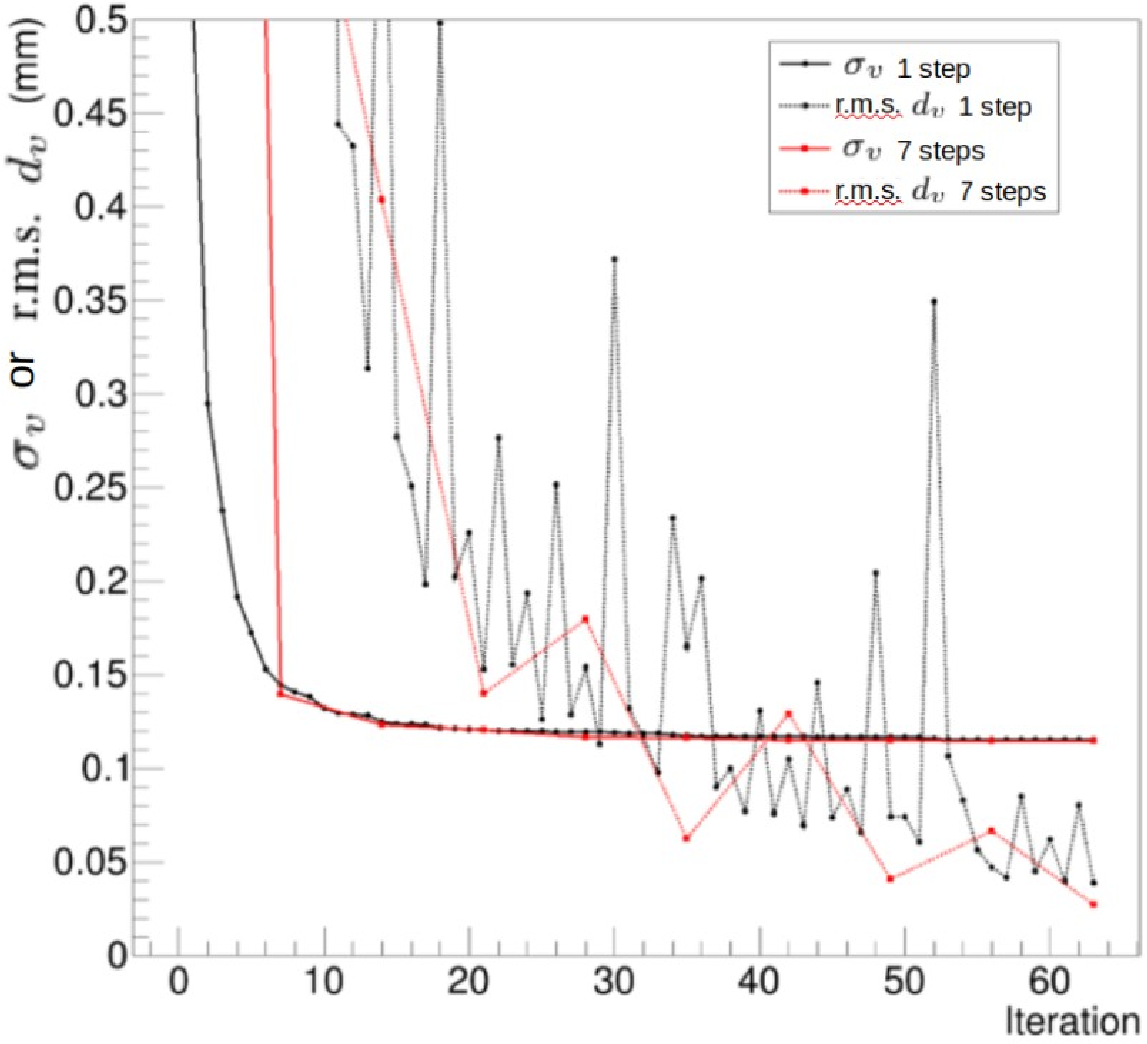
$$\lambda_k = d_{vk} \cdot (\bar{A}^T Ad_{vk}) \,/\, |\bar{A}^T Ad_{vk}|^2$$

Stopping Criteria

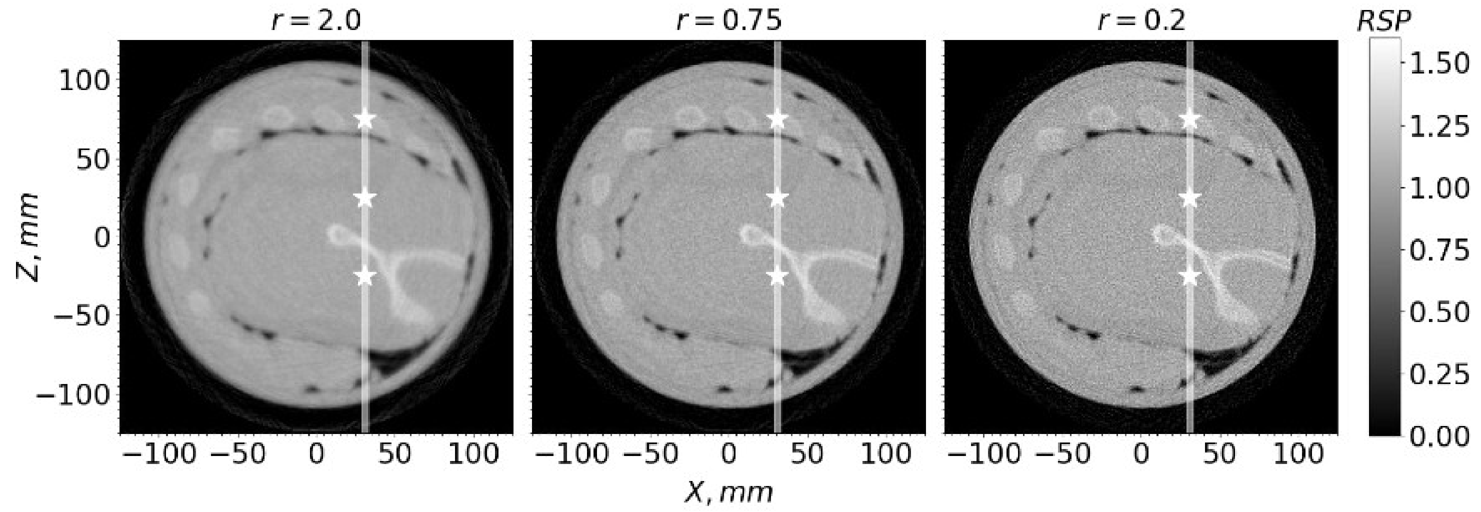
WEPL uncertainty per proton: $$\sigma_p = \sqrt{\frac{\chi_p^2}{N_p - N_v}}$$

Estimated RSP uncertainty per voxel: $$\sigma_v = \frac{\sigma_p}{\bar{\alpha}\sqrt{N_{pv}}}$$

Define Parameter: $$r = \frac{\text{r.m.s. } d_v}{\sigma_v}$$



Analysis of autocorrelation function shows minimal correlations between voxels in a uniform region when 0.5 < r < 1



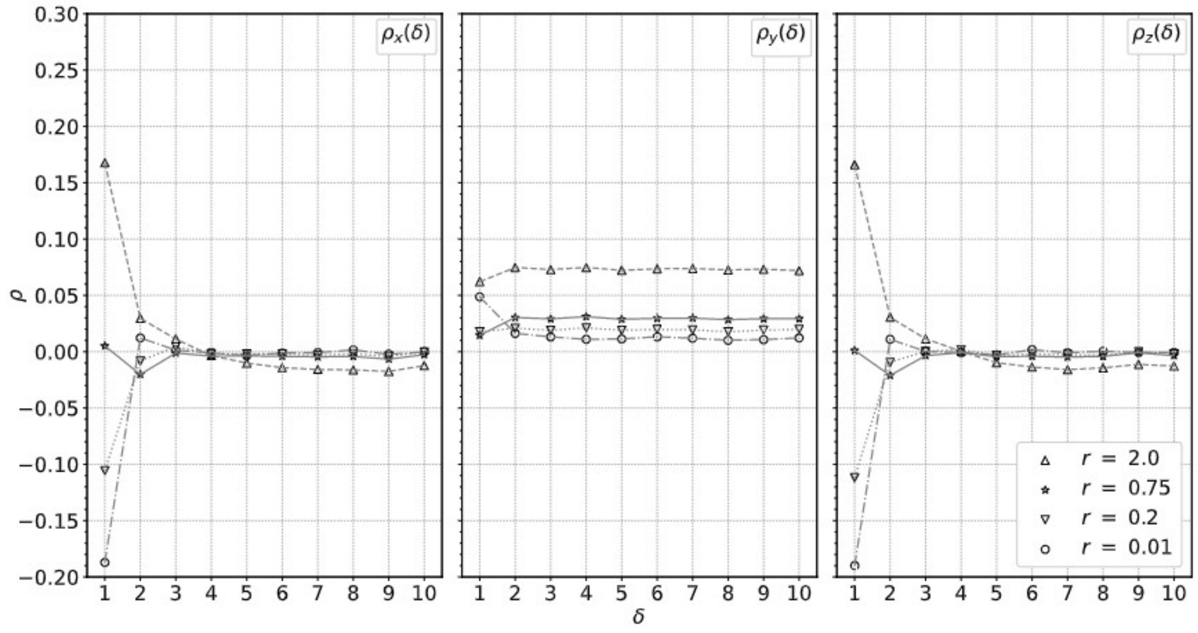


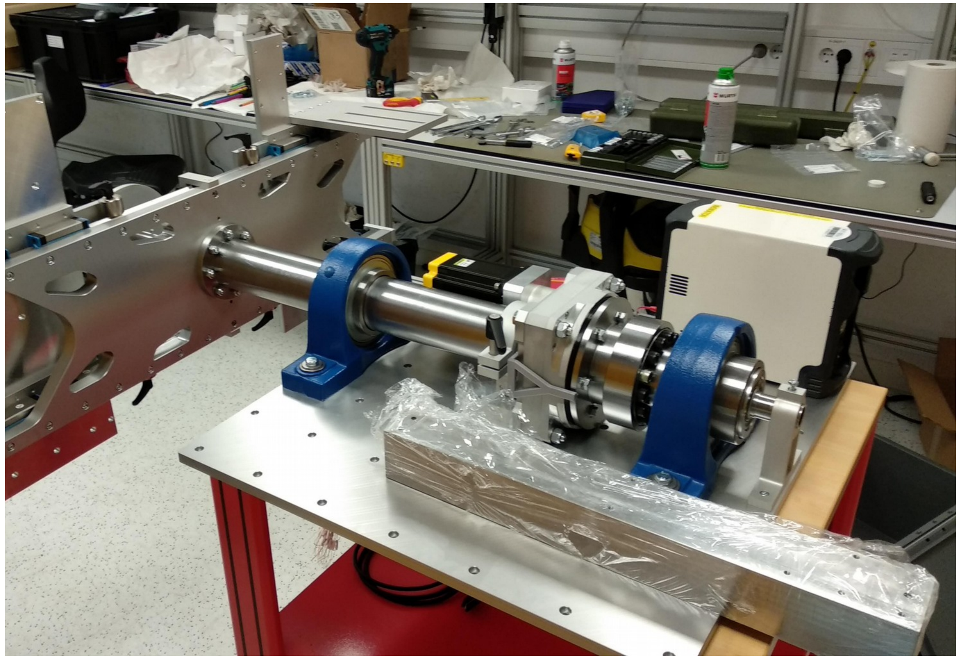
Figure 10: Autocorrelation functions ρ_x (left) ρ_y (middle) ρ_z (right) versus the separation δ between voxels within a ROI of the simulated cylindrical water phantom for the r values in the legend.

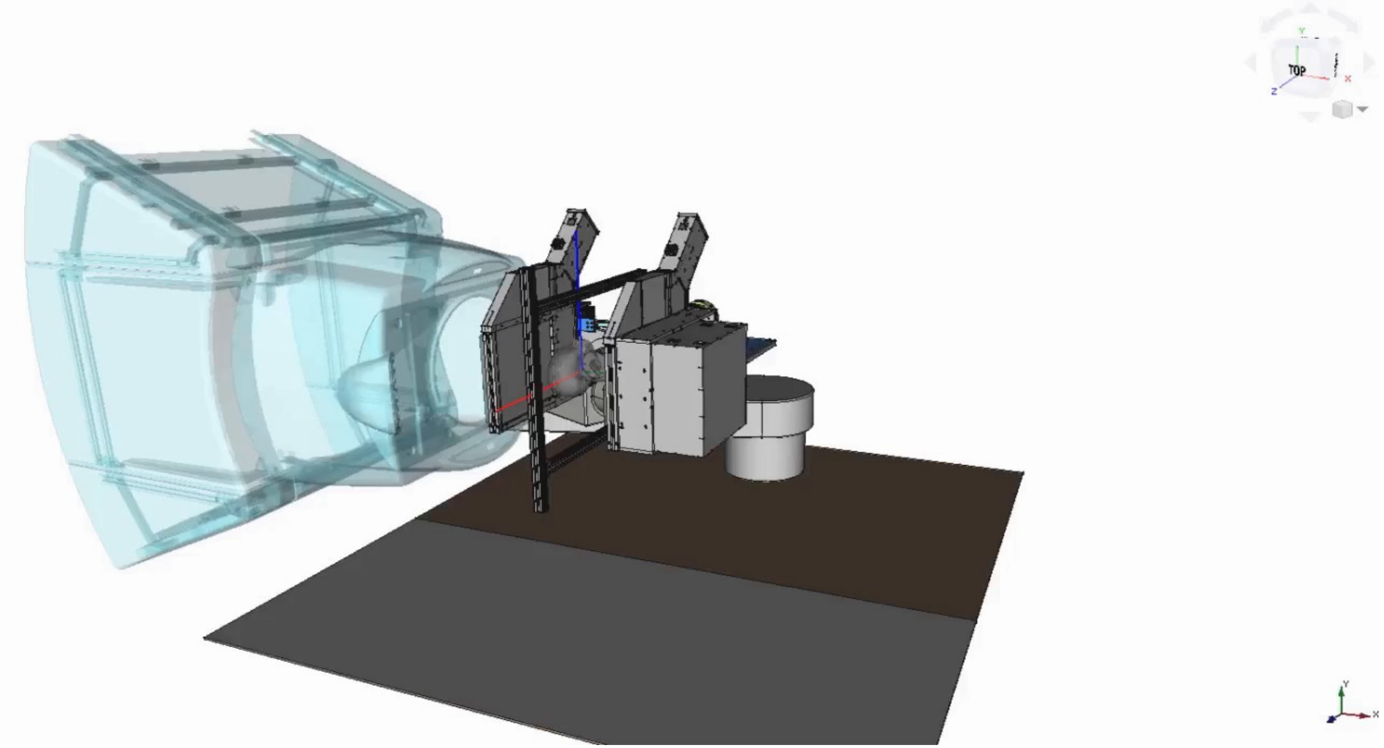
First ever pCT test in a gantry system!
June 25, 2022

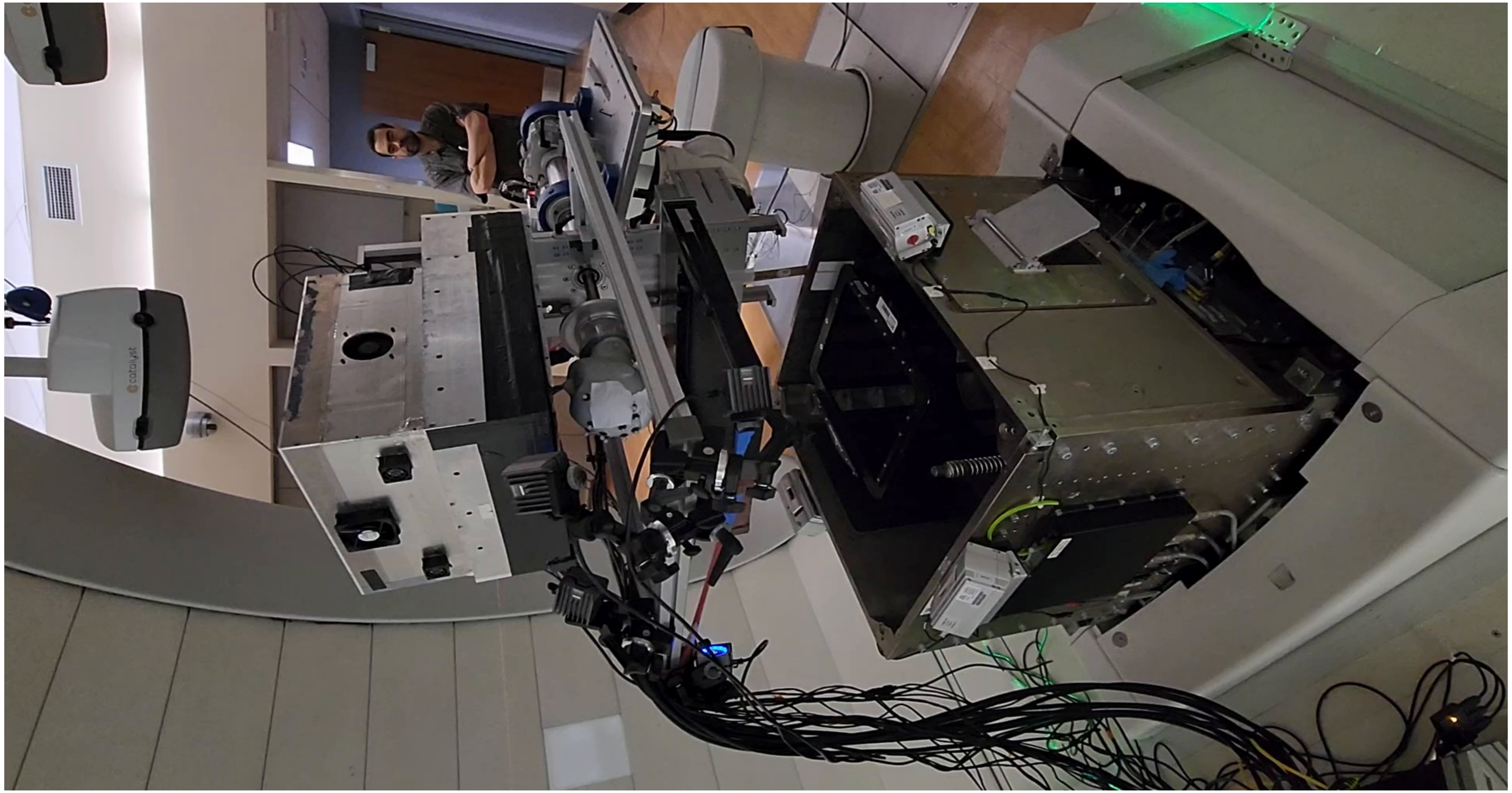
We acquired proton imaging data from 45 angles for a pediatric head phantom using 3 proton energies – 120, 162, and 198 MeV.

The test took over 6 hours to complete.

Mounting system designed and built by Cosylab

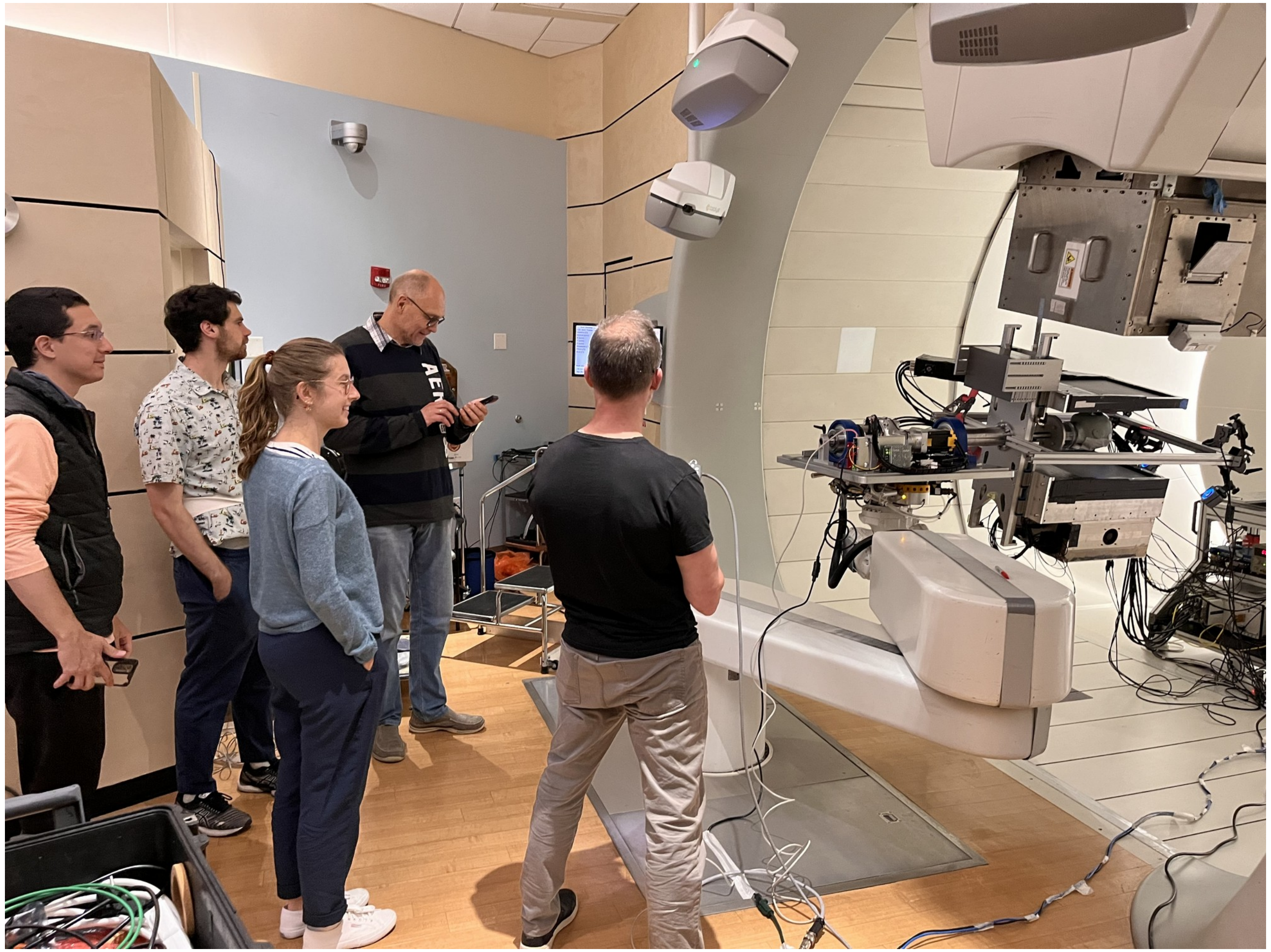





catalyst

Issues affecting image reconstruction:

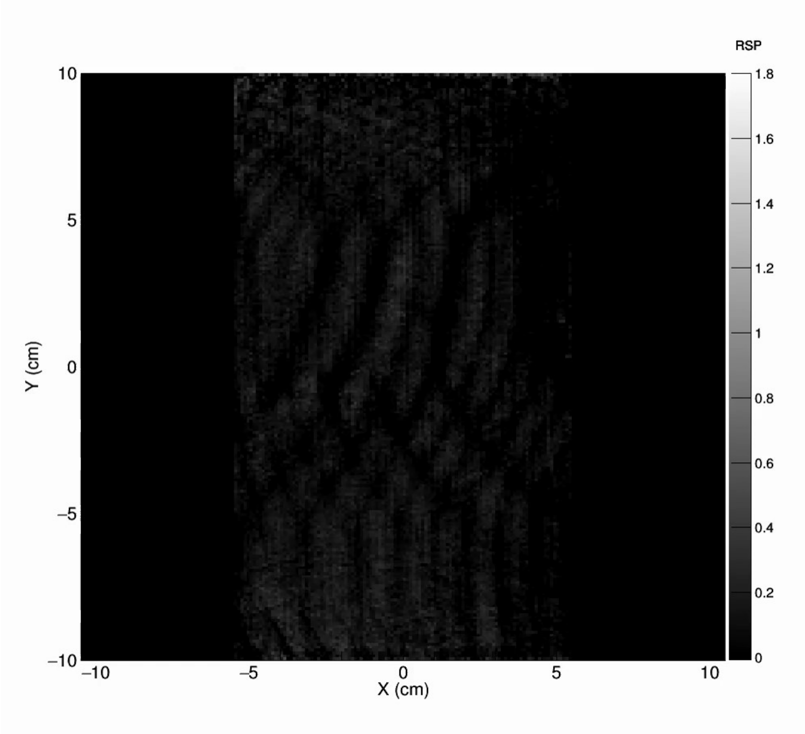
- Separate rotational axes for imaging system and gantry
- Shifting of detector geometry vs. angle
- Sagging of gantry vs. angle
- Change in PMT gains vs. angle
- Beam steering not well calibrated at low intensity

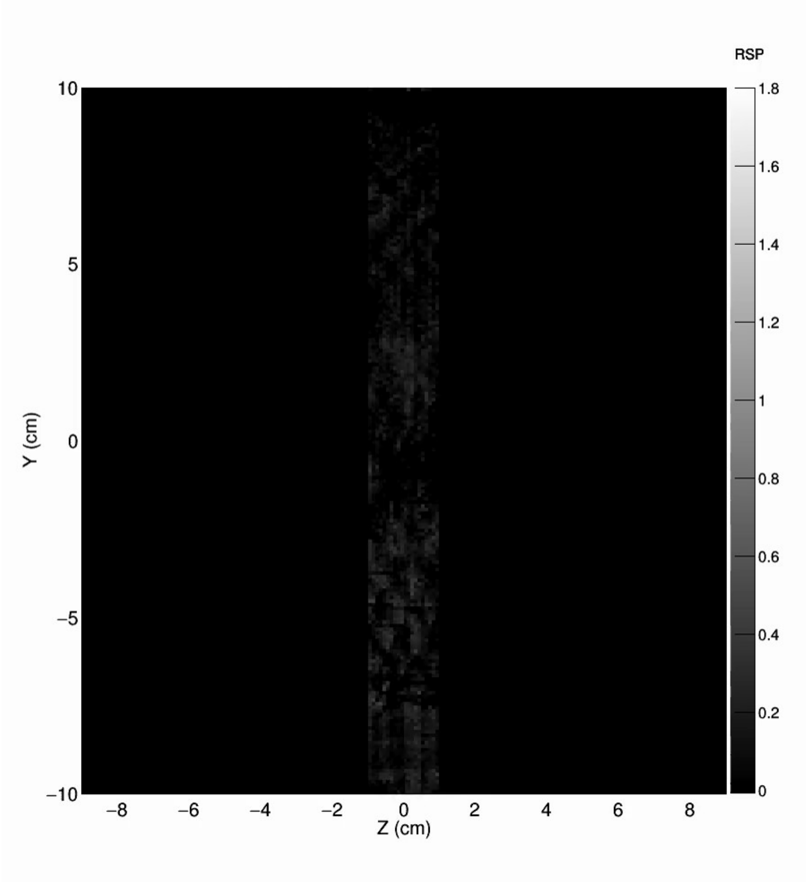


1 mm pCT slices from gantry data

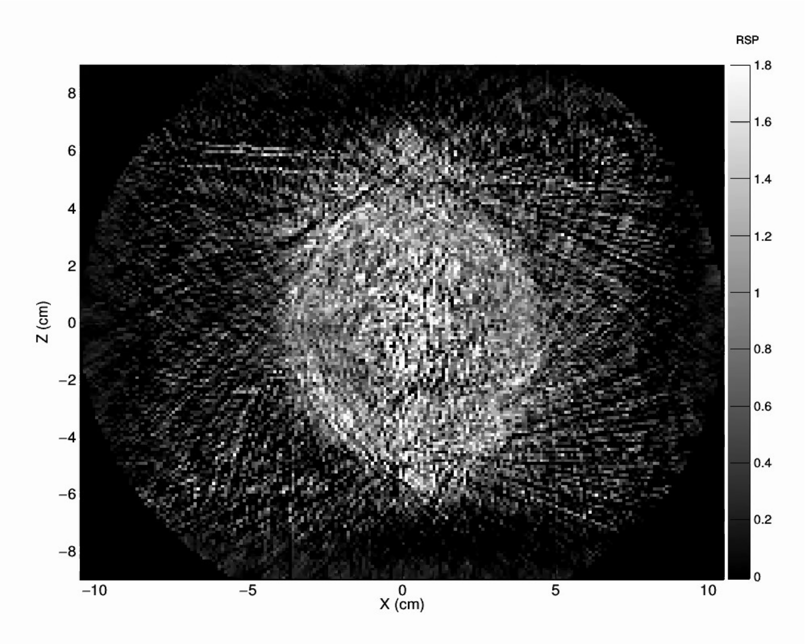
Vertical – from front of head

Vertical – from side of head

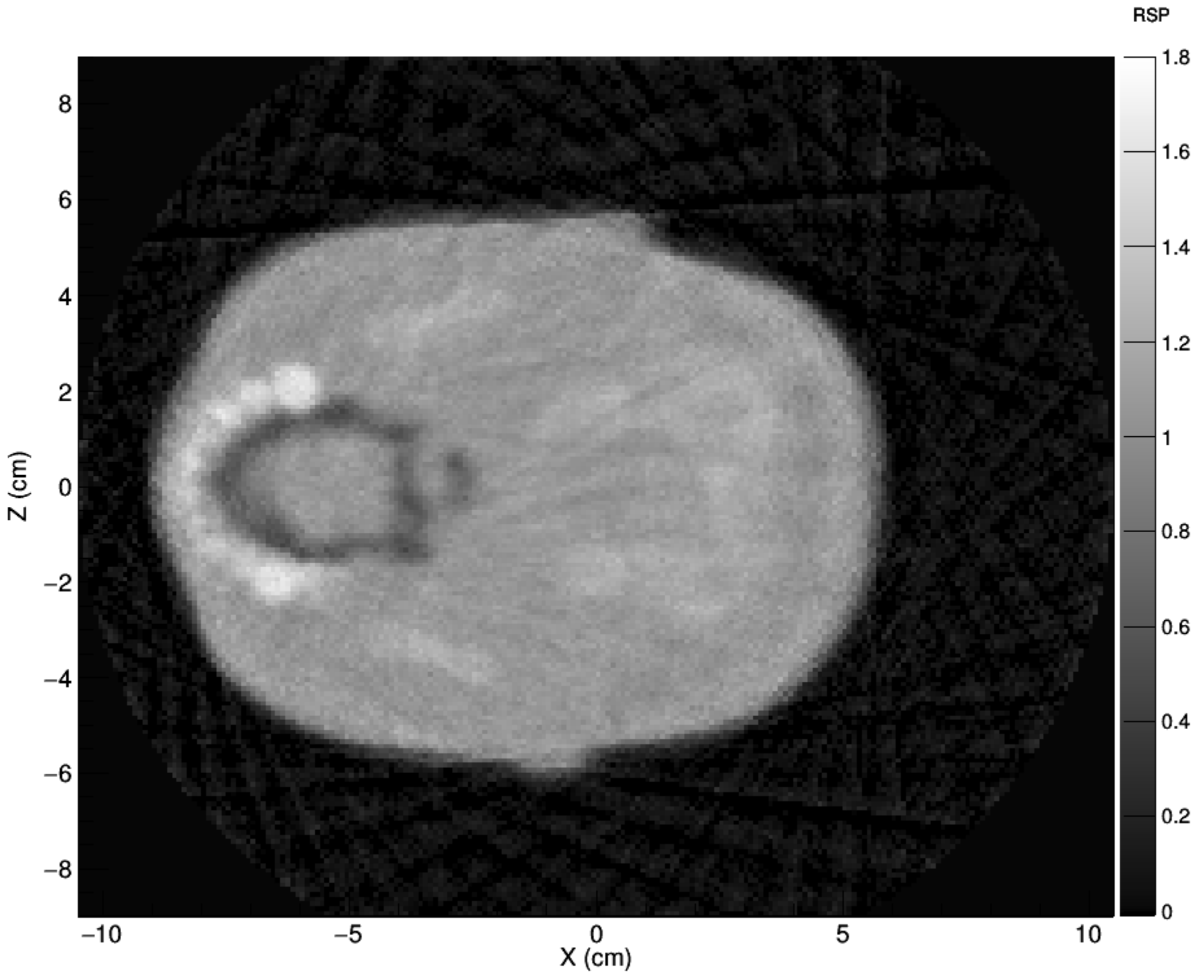




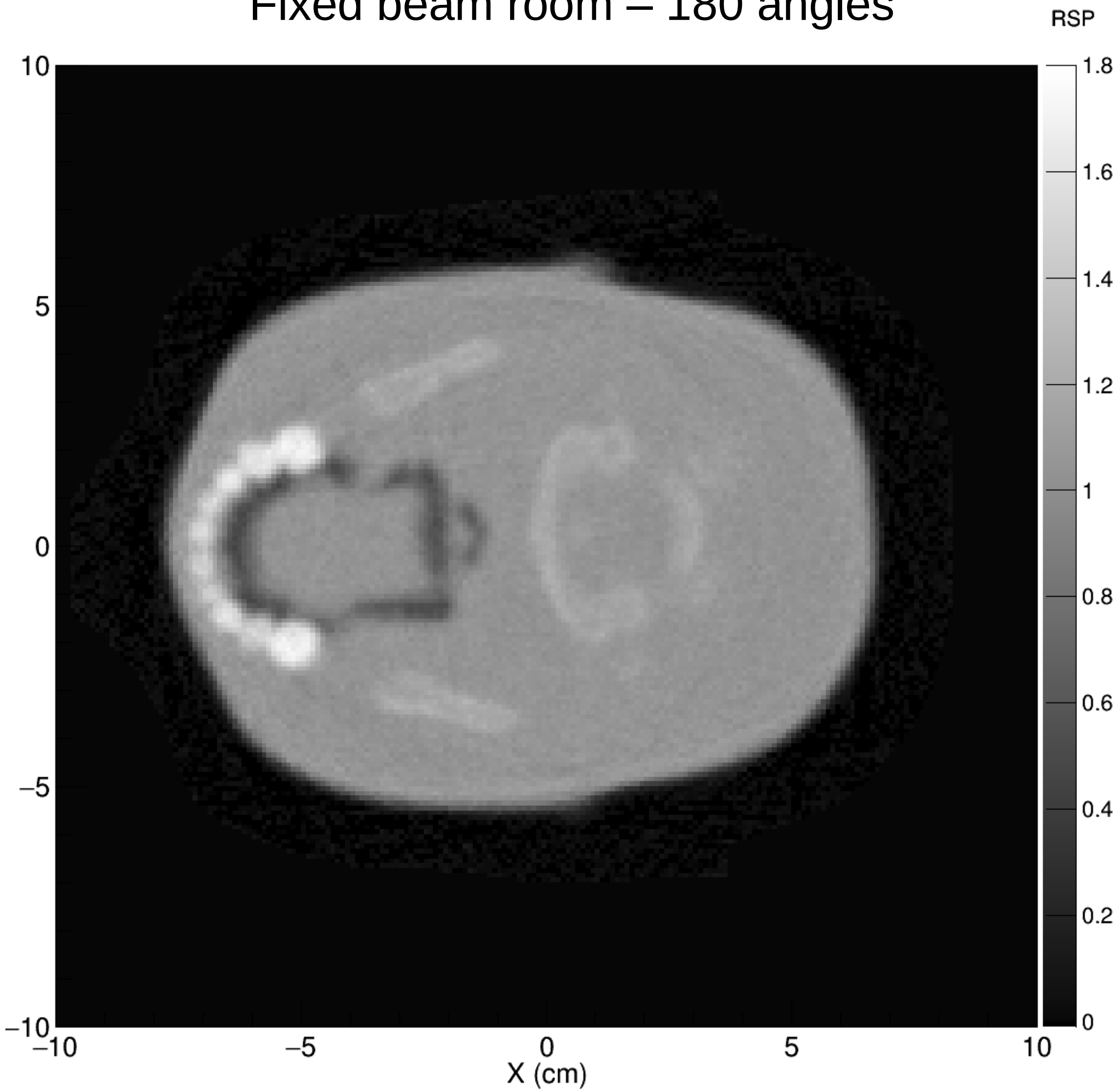
Horizontal



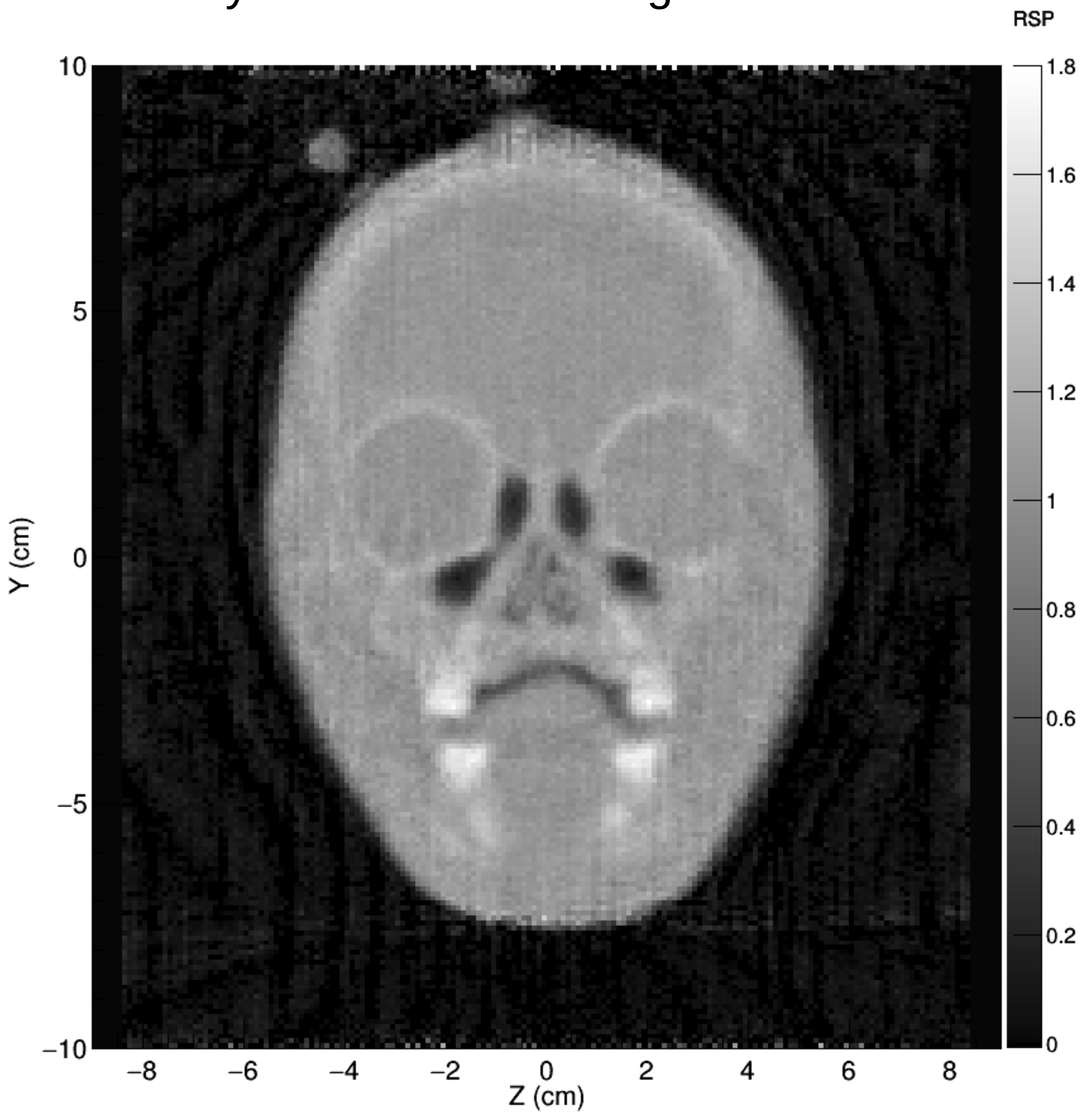
Gantry room data – 45 angles



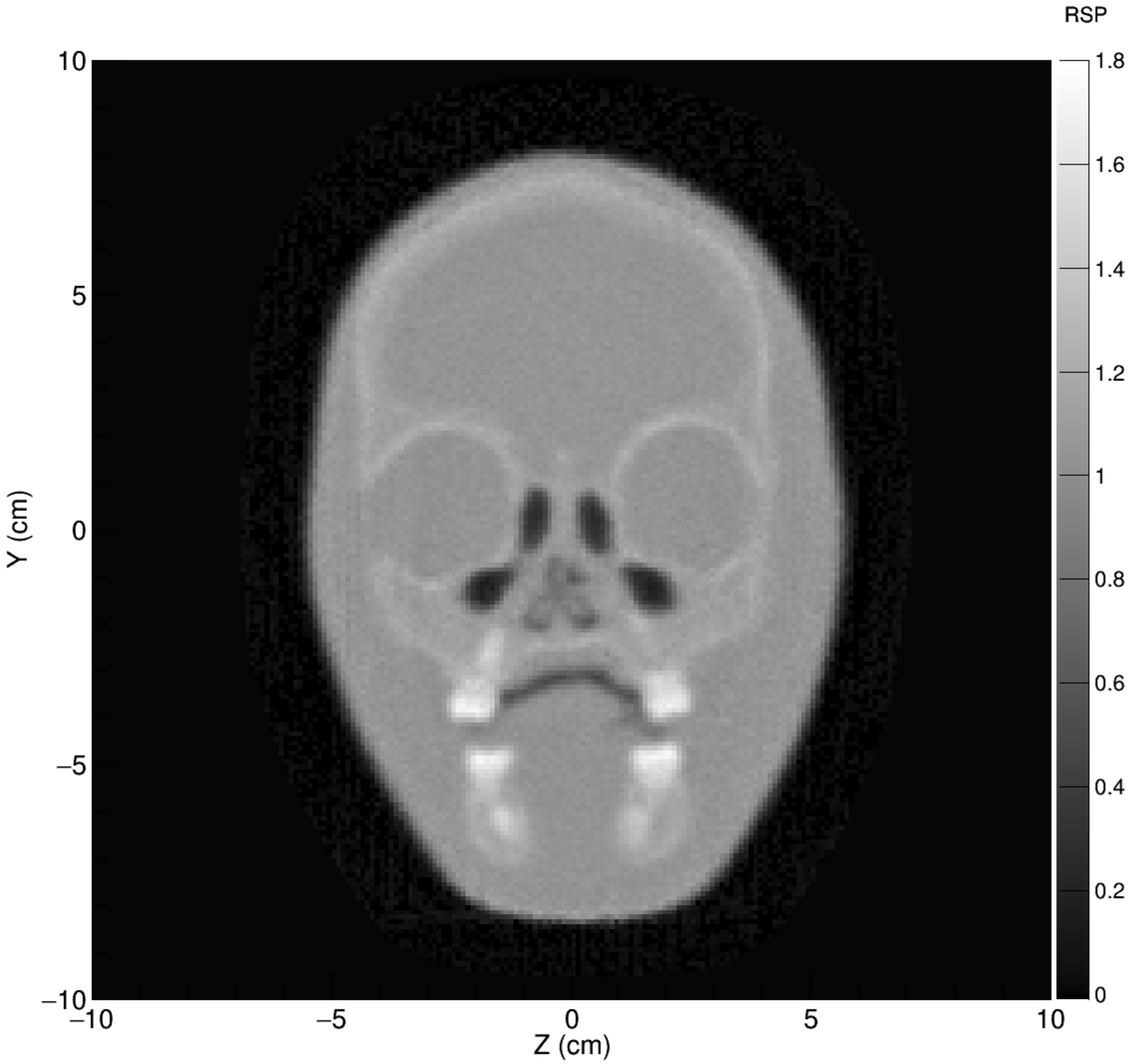
Fixed beam room – 180 angles



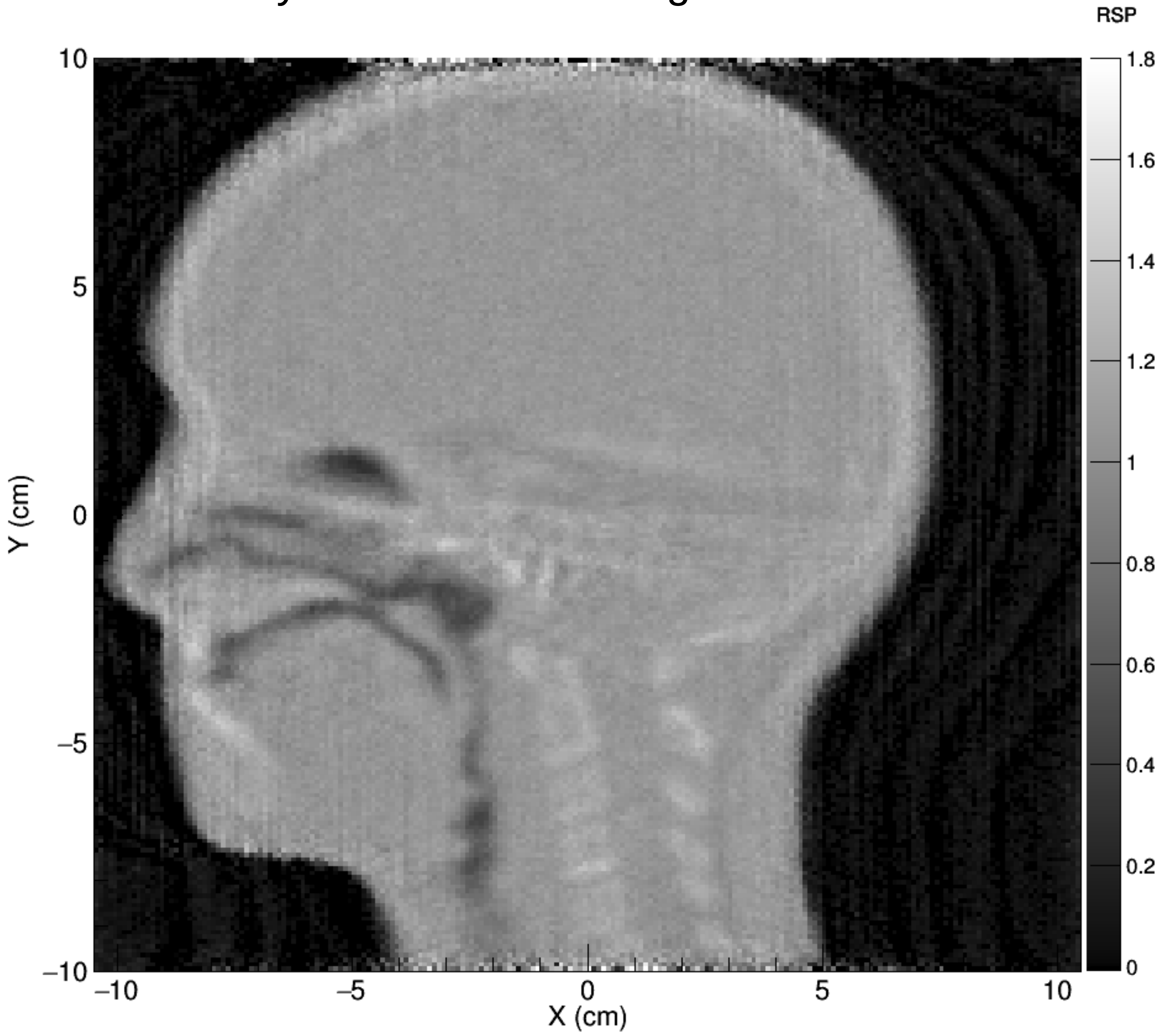
Gantry room data – 45 angles



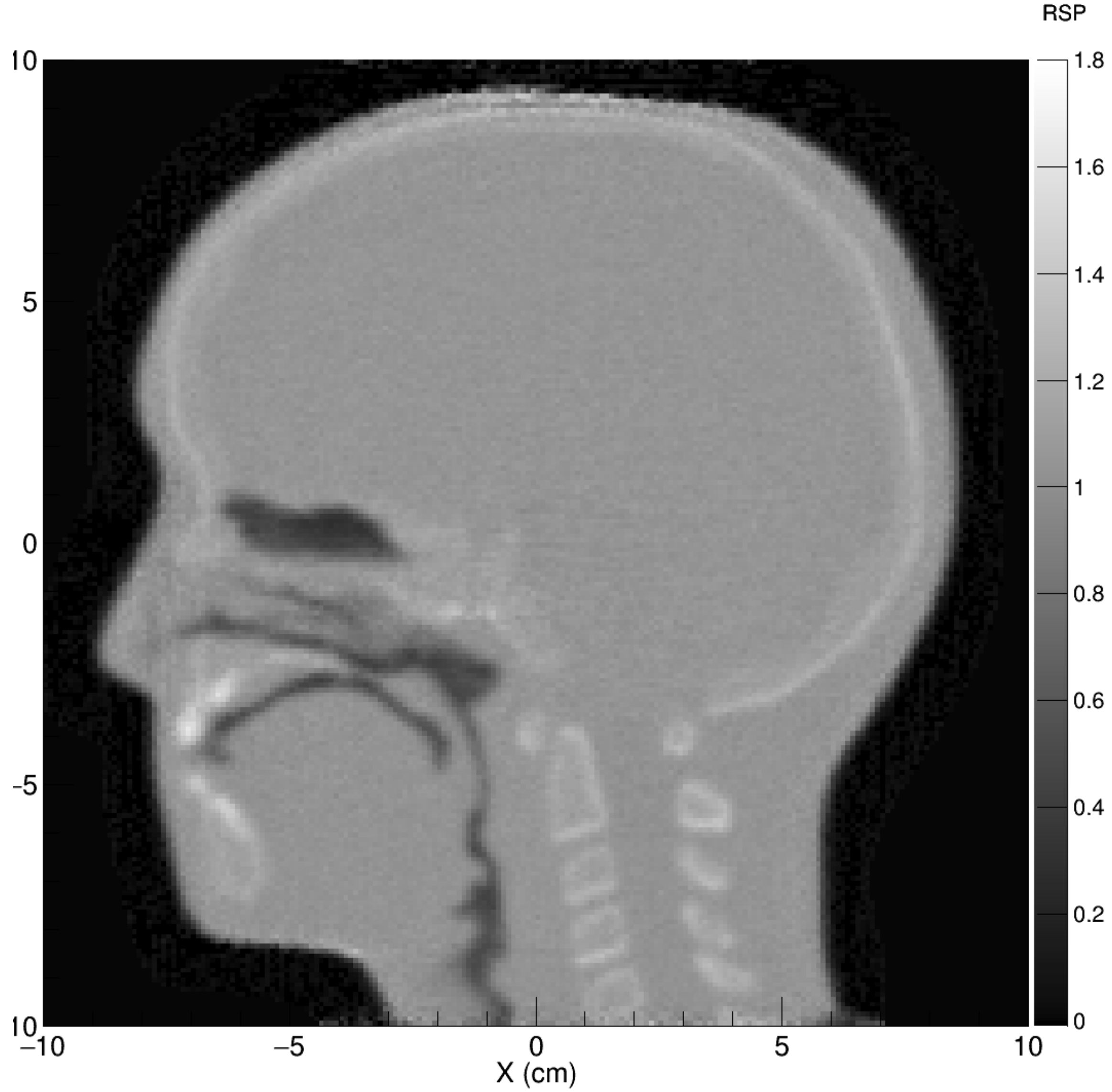
Fixed beam room – 180 angles



Gantry room data – 45 angles

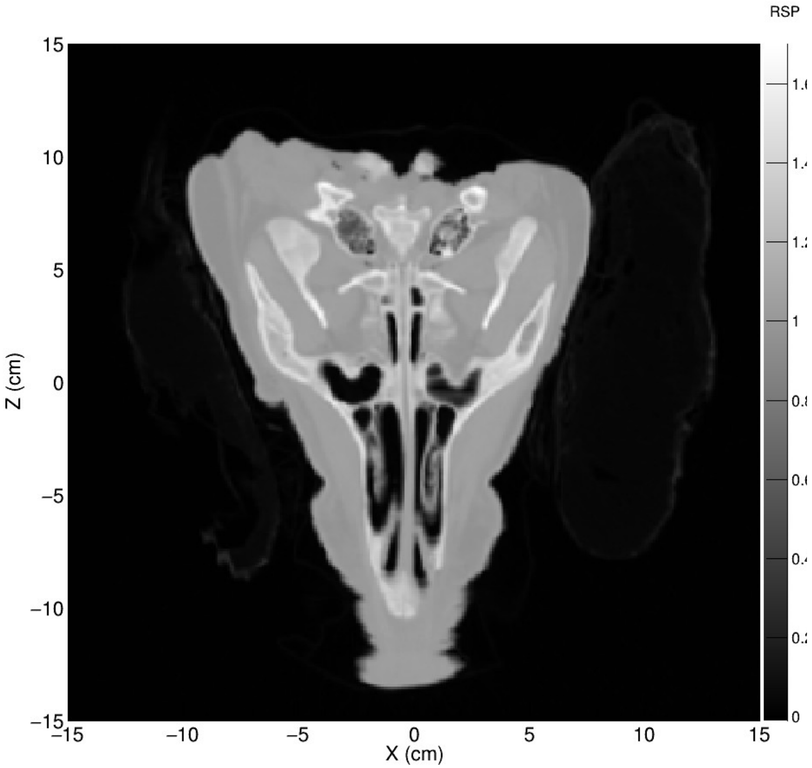


Fixed beam room – 180 angles

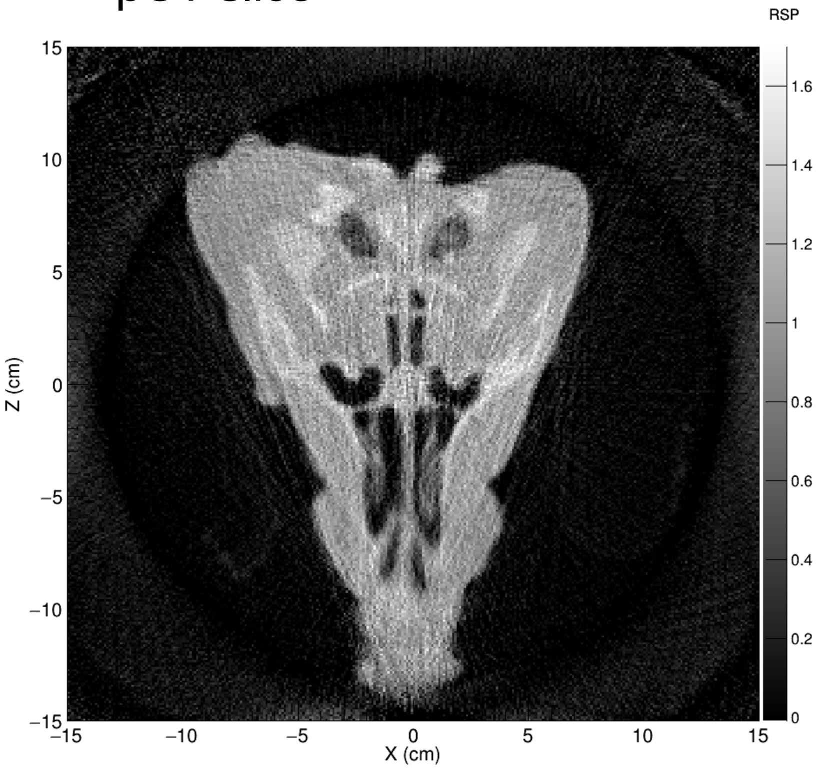


Using protons to update RSP maps from xCT

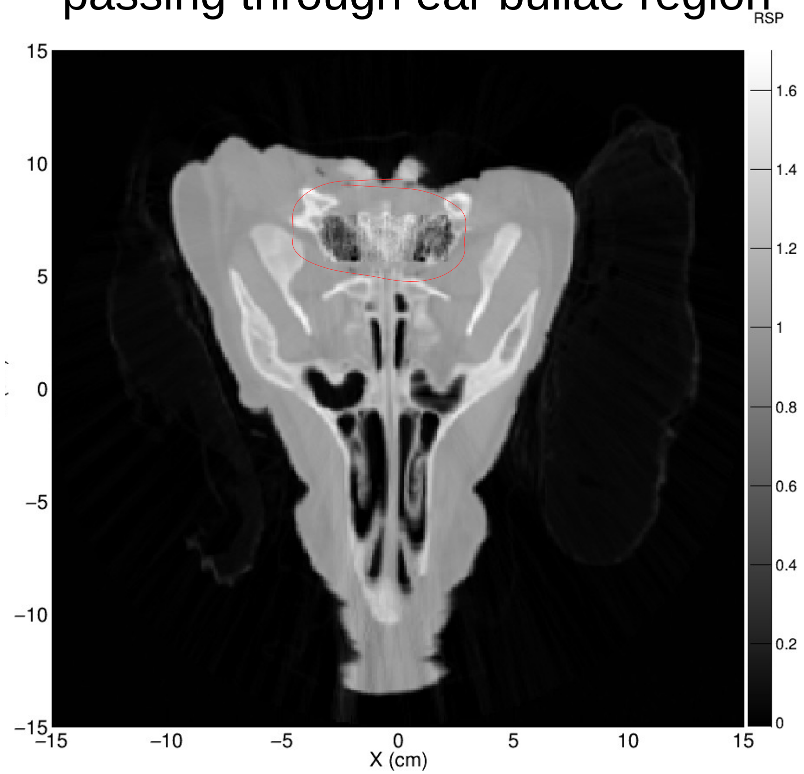
xCT slice (converted to RSP)



pCT slice



xCT slice updated with protons
passing through ear bullae region



RSP map can be updated using
any set of list-mode protons

Combined fit using Lagrange multipliers

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Proton Imaging Algorithms

Optimize χ^2 for X-Ray CT image (x_x) subject to constraint of $d_v = 0$ for protons

Optimize χ^2 for X-Ray CT image (x_x) subject to constraint of $d_v = 0$ for protons

$$\mathcal{L}(x, y) = (x - x_x)^T W (x - x_x) + y^T d_v$$

$$g_x = \partial\mathcal{L}/\partial x = 2W(x - x_x) + y^T \bar{A}^T A = 0 \quad \text{where } W = diag(1/\sigma_i^2)$$
$$g_y = \partial\mathcal{L}/\partial y = d_v = \bar{A}^T (Ax - b) = 0$$

Uzawa's method (from Yousef Saad's book):

- solve for x, update y
- λ_k can be optimized as in the DV algorithm

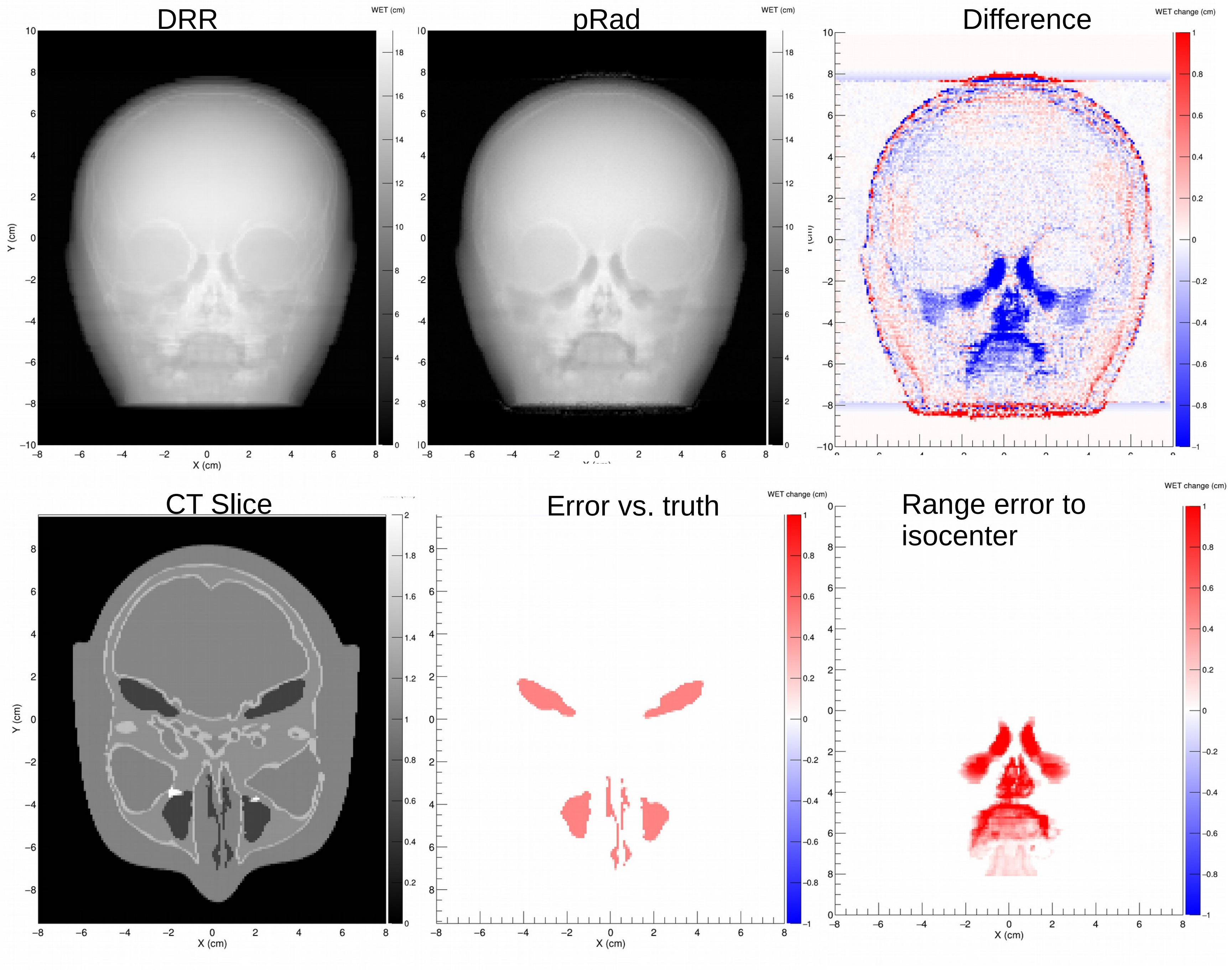
$$y_0 = 0$$
$$x_k = x_x - \frac{1}{2} V A^T \bar{A} y_k$$
$$d_{pk} = A x_k - b = d_{px} - \frac{1}{2} A V A^T \bar{A} y_k$$
$$d_{vk} = \bar{A}^T d_{pk} = d_{vx} - \frac{1}{2} \bar{A}^T A V A^T \bar{A} y_k$$
$$y_{k+1} = y_k + \lambda_k d_{vk}$$

Updating RSP maps with a single pRad

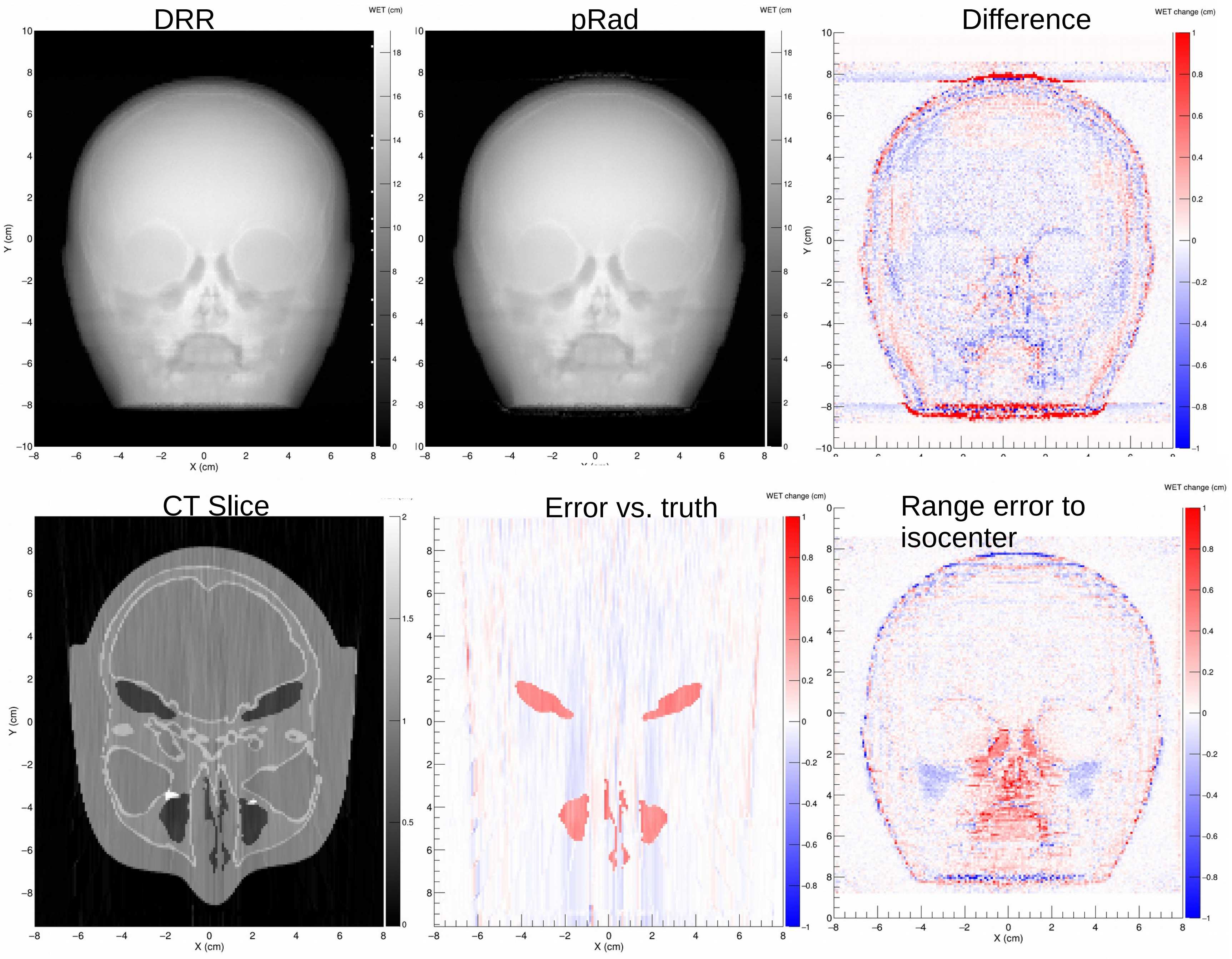
Simulated head phantom:

Filled sinuses in X-Ray image

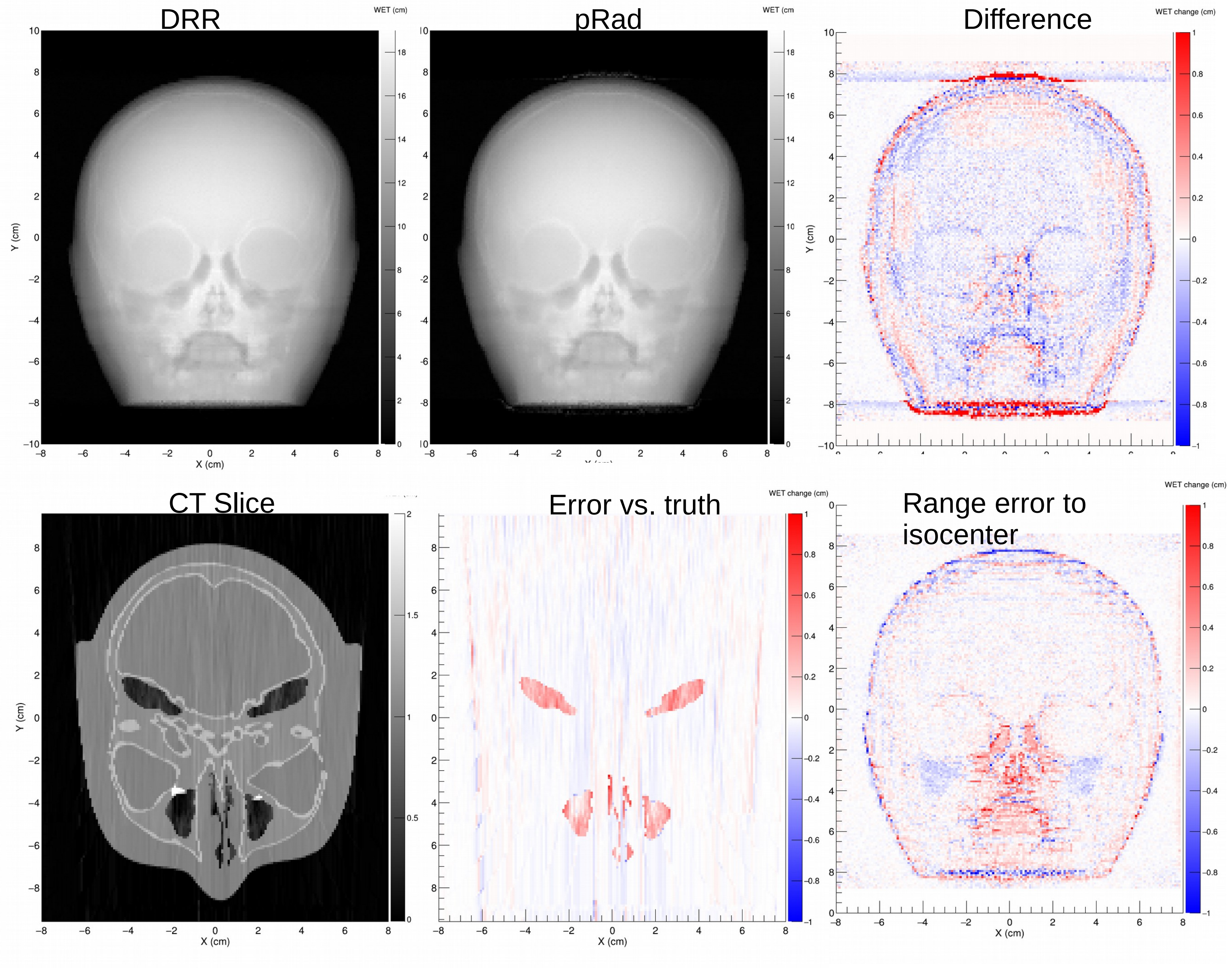
Empty sinuses in pRad



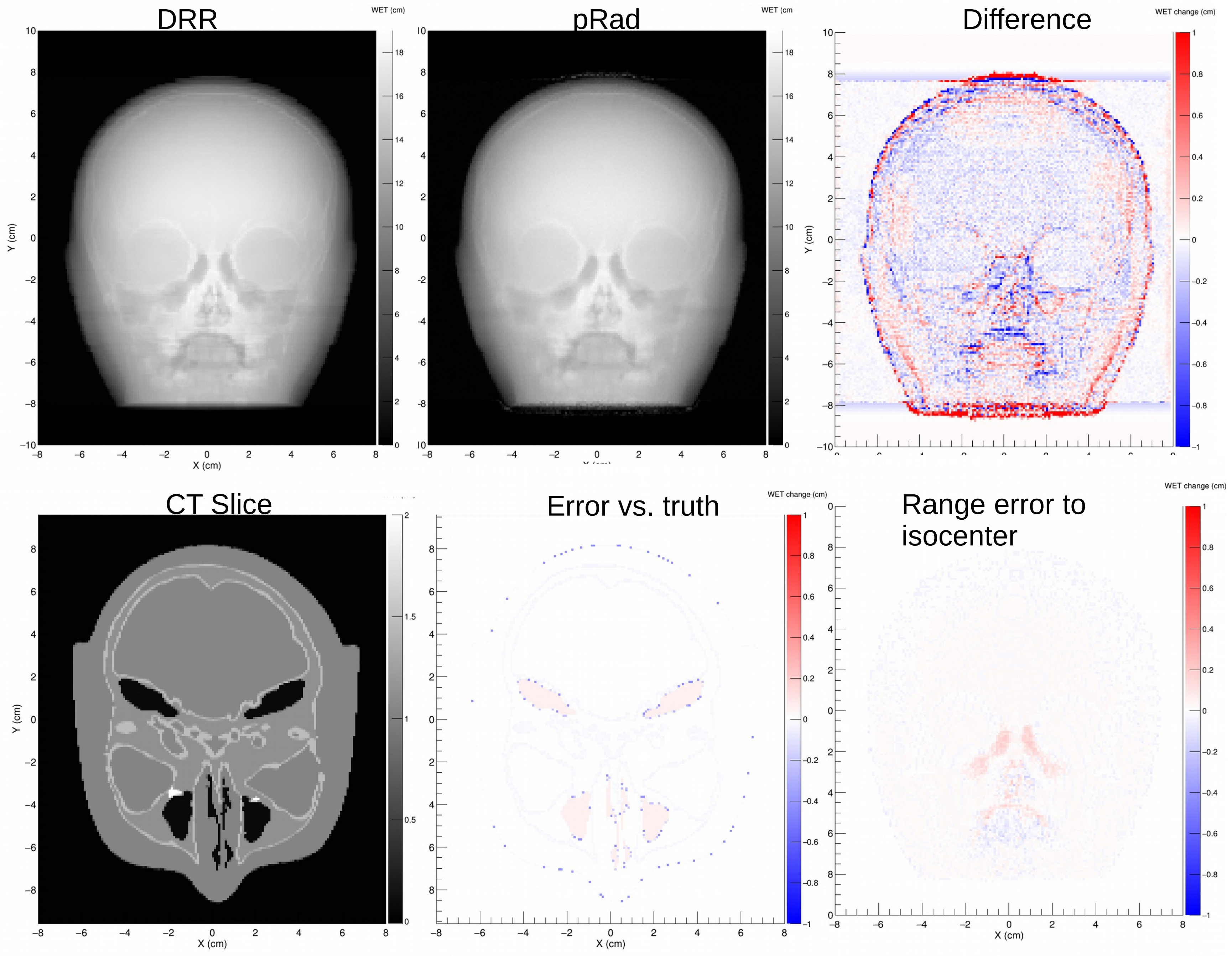
Updated RSP map from a single pRad



Updated RSP map from a single pRad – with knowledge of additional uncertainty in sinus voxels

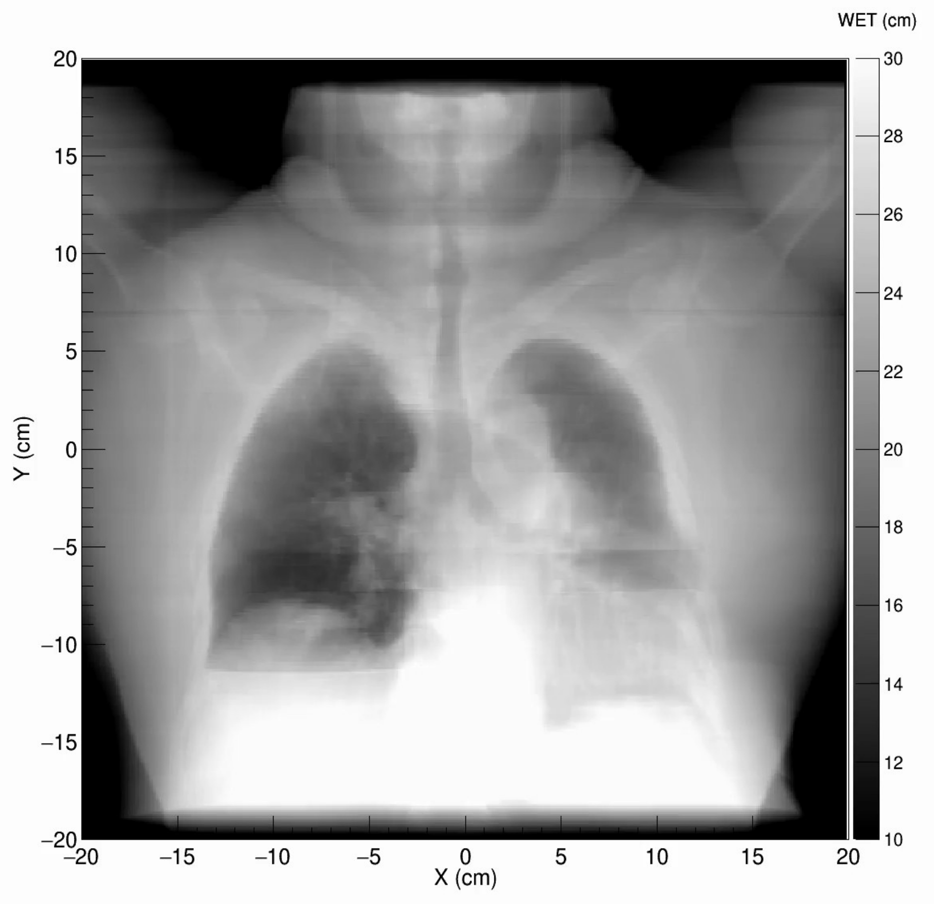


Updated RSP map from a single pRad – using correlated voxels based on RSP

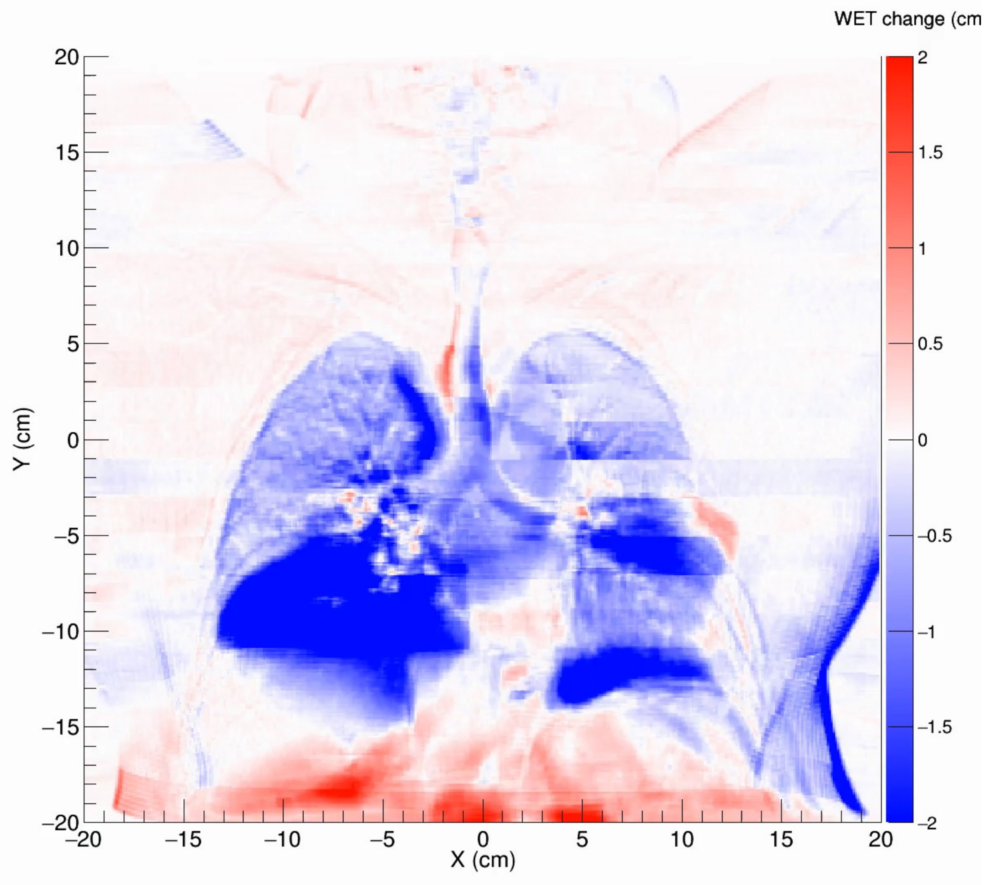


Another potential use for pRad – motion monitoring
- pencil beams can scan 10 x 10 cm2 area in 0.1 s (10 frames/second)

Simulated pRads from 4DCT (TOPAS)



Difference from average



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Summary

Milestones Acheived:
- Demonstration of WET and RSP accuracy for pRad and pCT with phantoms
- Fast, automatic image reconstruction
- pCT images of fresh meat samples, detection of x-ray RSP errors
- Automated 3-d alignment with pRad
- Development of iterative algorithm with objective stopping criteria
- pCT from gantry-mounted system

Next Steps:
- Continue developing x-ray update method for rapid adaptive planning
- Deformable image registration with list-mode protons
- Live animal imaging, motion studies
- Clinical trials, images of human patients

*see our publications at protonvda.com