ProtonVDA

TRANSFORMING PROTON THERAPY

ProtonVDA pCT Update: Algorithms and Images

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

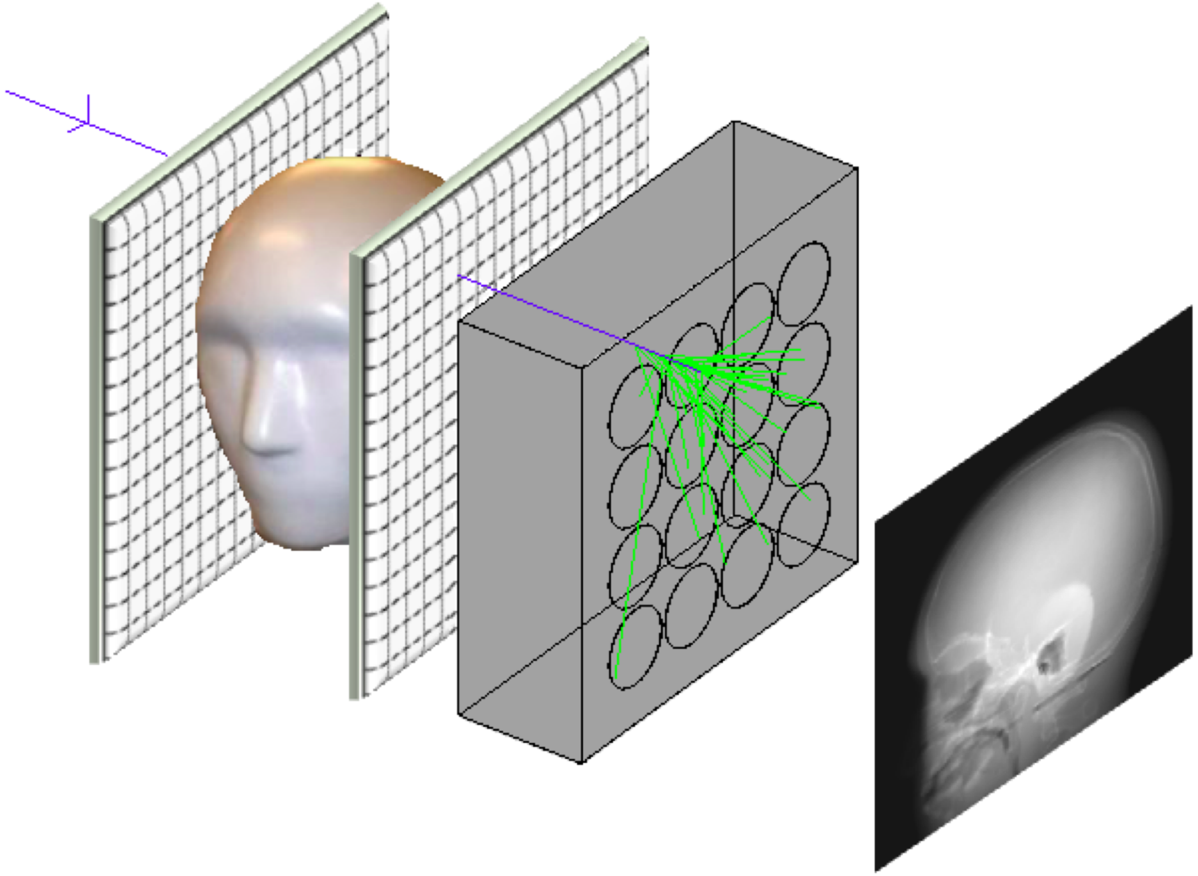
We aim to:

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

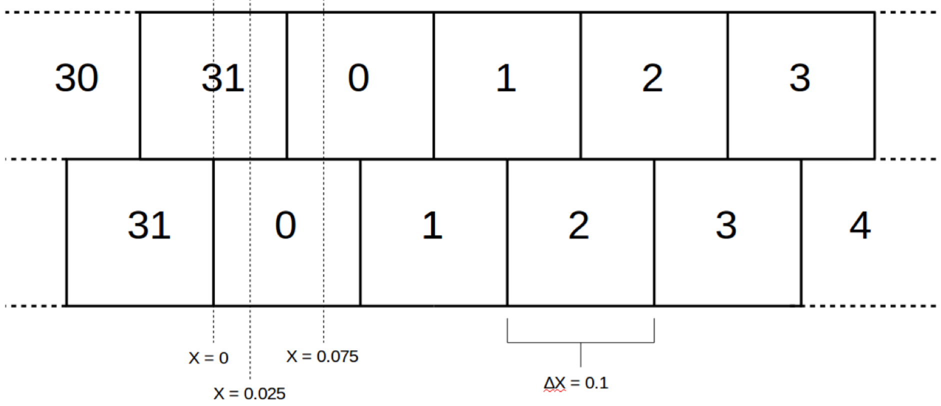
1. → High-performance, low-cost measurements of proton range.
2. Achieve lower dose to the patient relative to equivalent x-ray images.
3. Produce spatially sharp images.
4. Images free of artifacts from high-Z implants.

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

- ProtonVDA: Fritz DeJongh, Ethan DeJongh, Victor Rykalin, Igor Polnyi
- Loyola Stritch School of Medicine: James Welsh
- Northwestern Medicine Chicago Proton Center: Mark Pankuch
- 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



Fiber layout cross-section for one tracking plane:

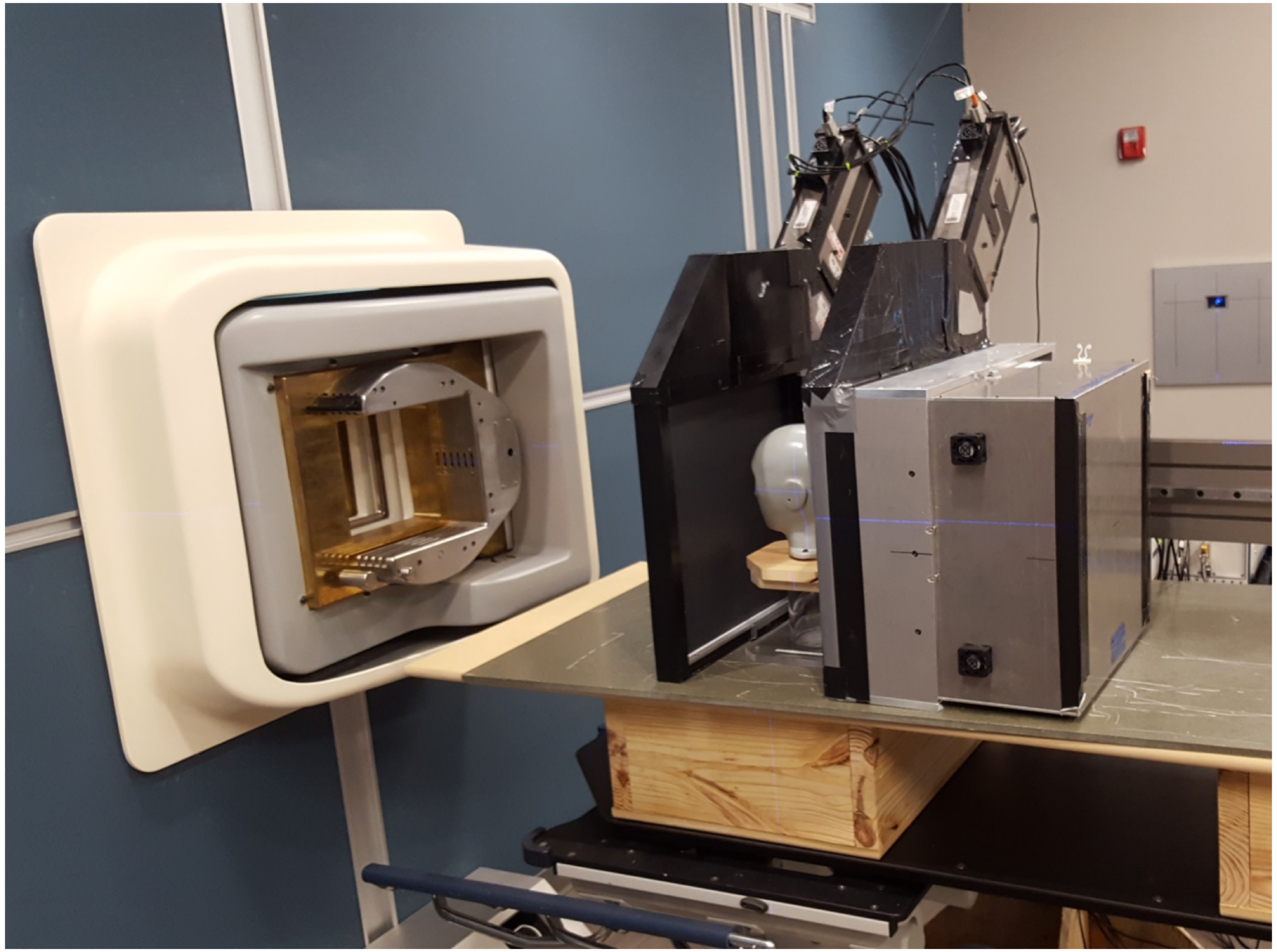


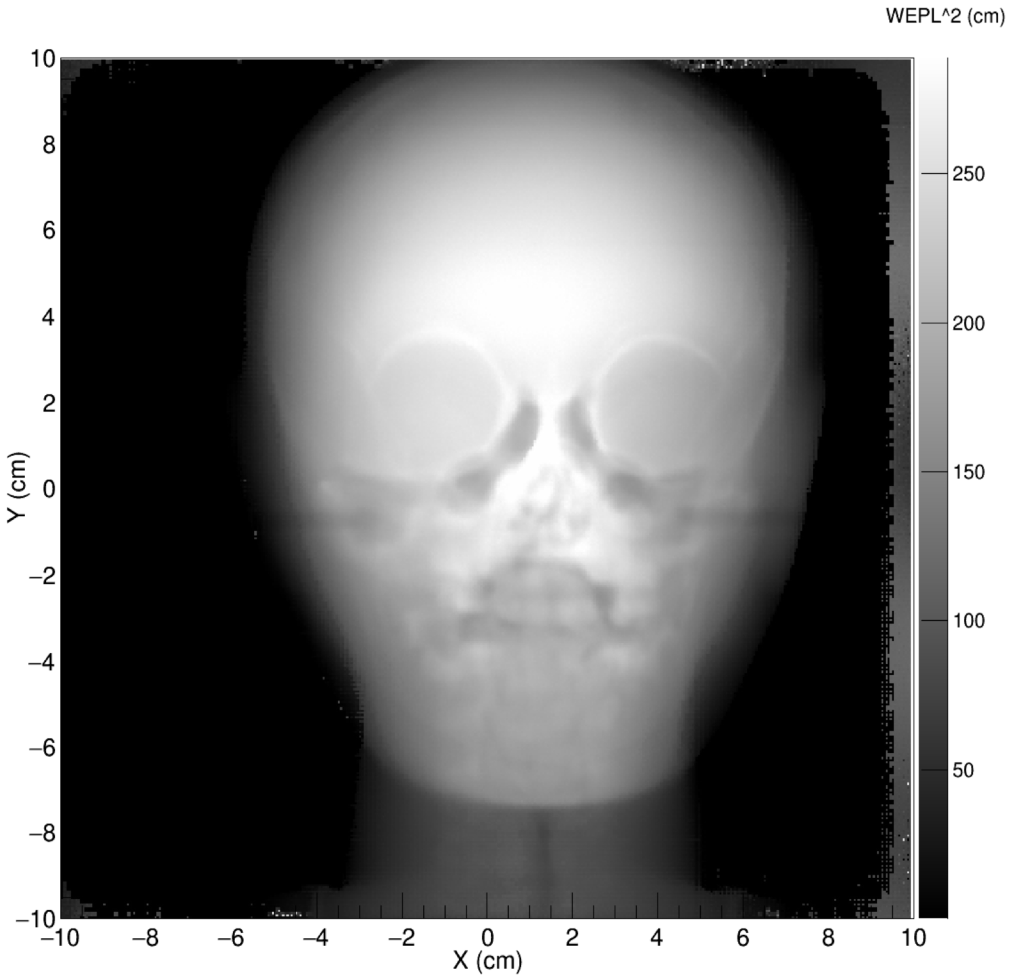
- X-Y tracking planes upstream and downstream

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

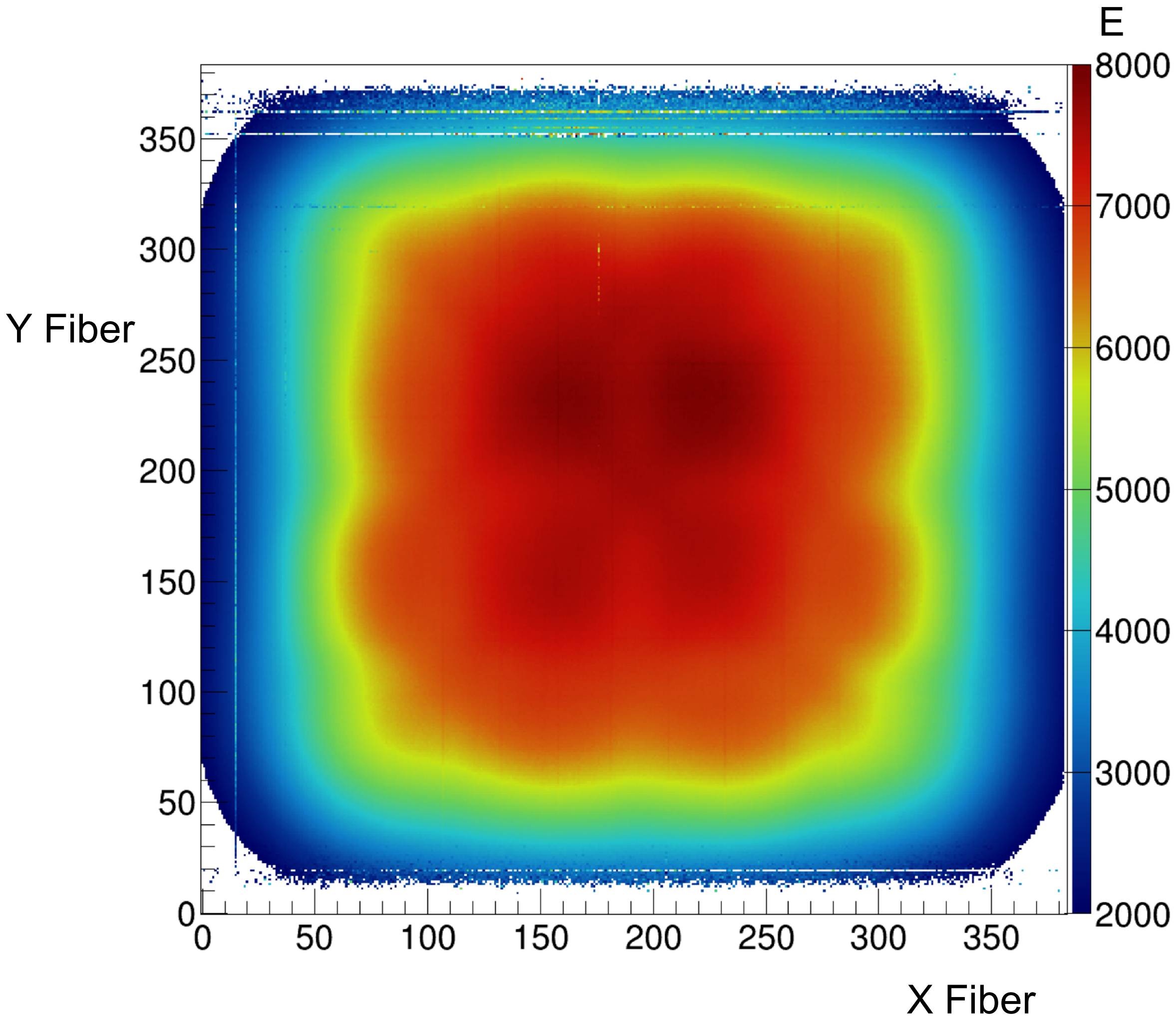
- 40 x 40 x 13 cm block of scintillator for range detector
  - 4 x 4 array of PMTs
  - Output digitized into four channels: E, U, V,C

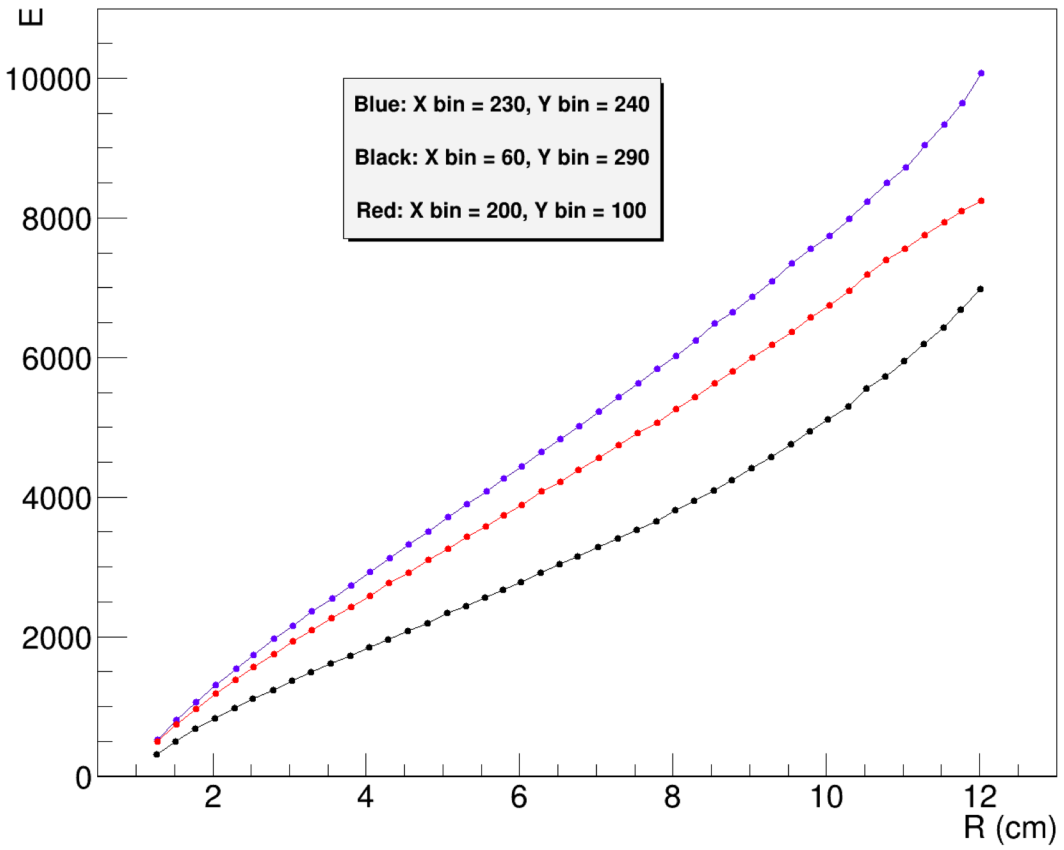
- Individual protons tracked at up 10 MHz
- > 99% tracking efficiency
- WEPL resolution ~ 3 mm per proton
- 40 x 40 cm image field size
- Fast (<1 min) image reconstruction for radiograph



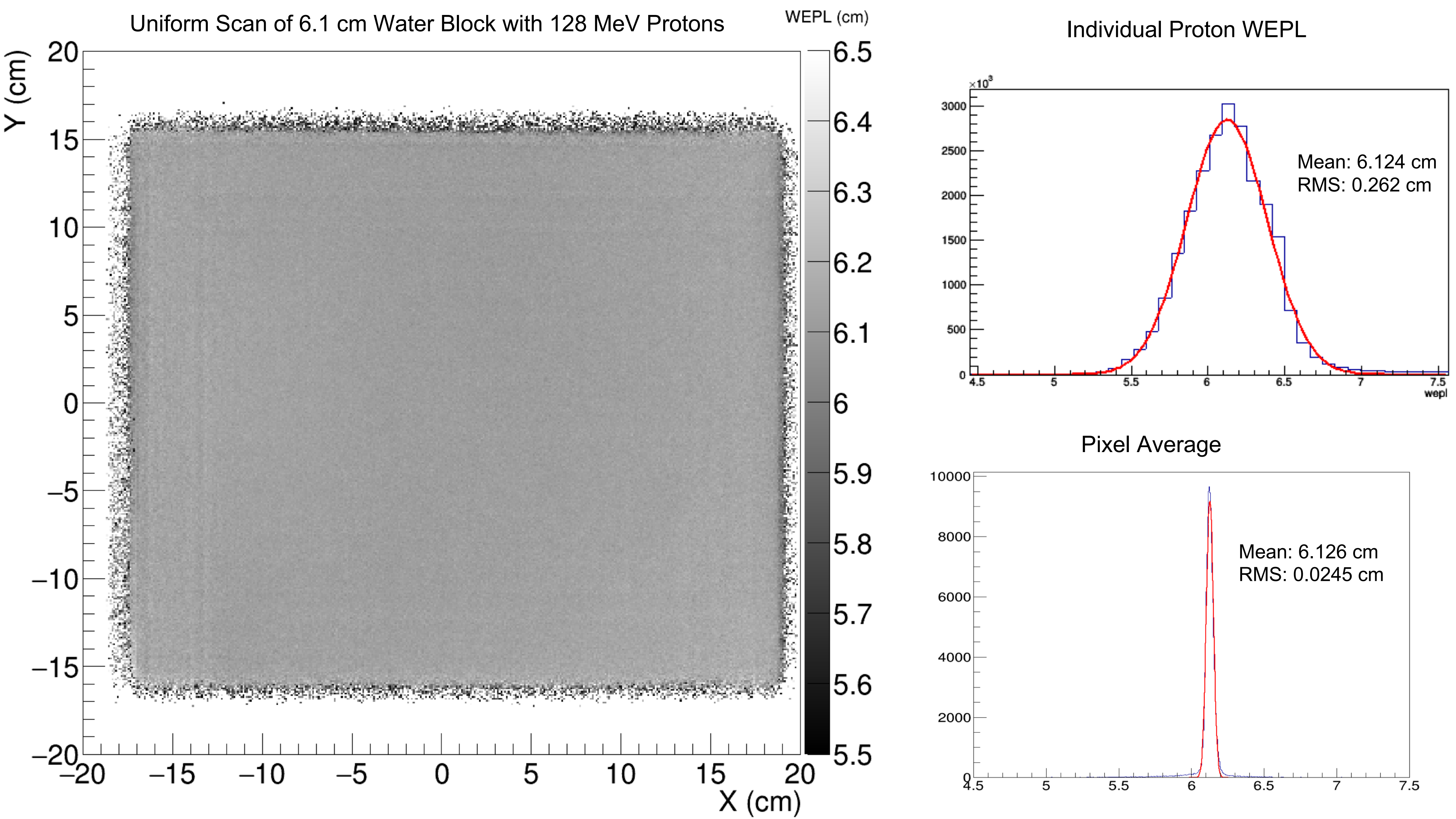


WEPL^2 (cm)
250
200
150
100
50
Y (cm)
10
8
6
4
2
0
−2
−4
−6
−8
−10
−10
−8
−6
−4
−2
0
2
4
6
8
10
X (cm)



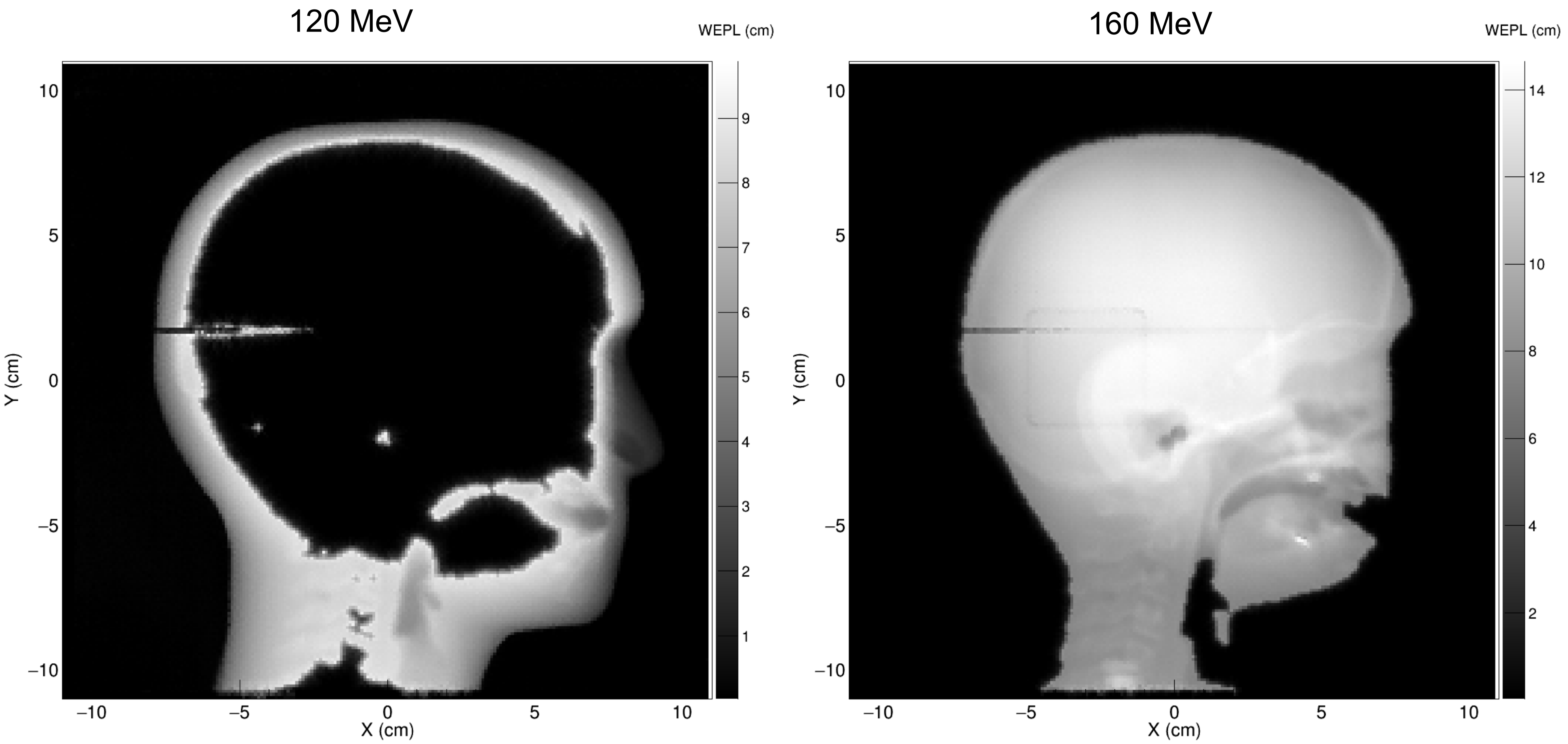


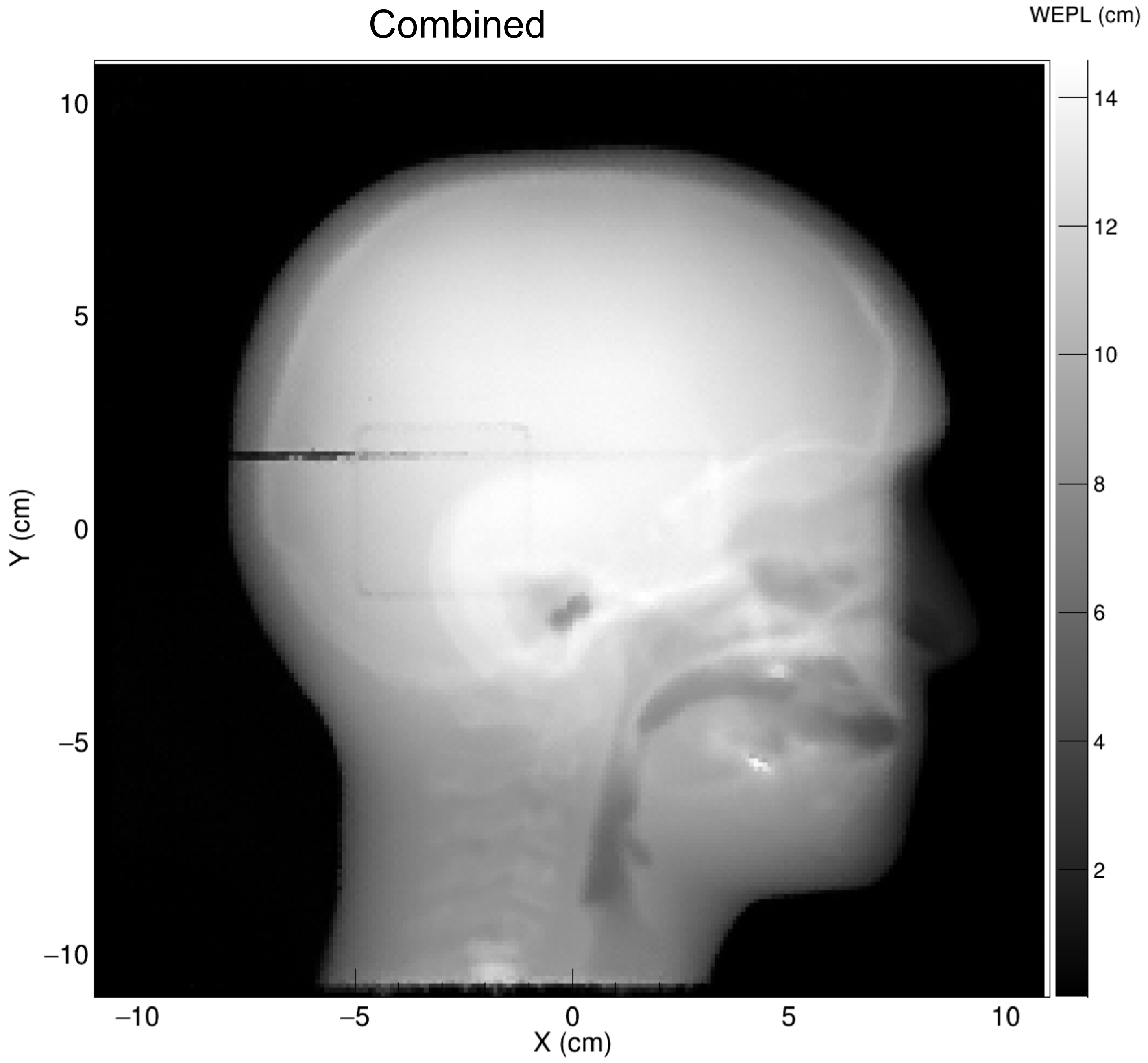
- Linear detector response vs. range gives very good range sensitivity



Uniform Scan of 6.1 cm Water Block with 128 MeV Protons
WEPL (cm)
Y (cm)
X (cm)
Individual Proton WEPL
$\times10^3$
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

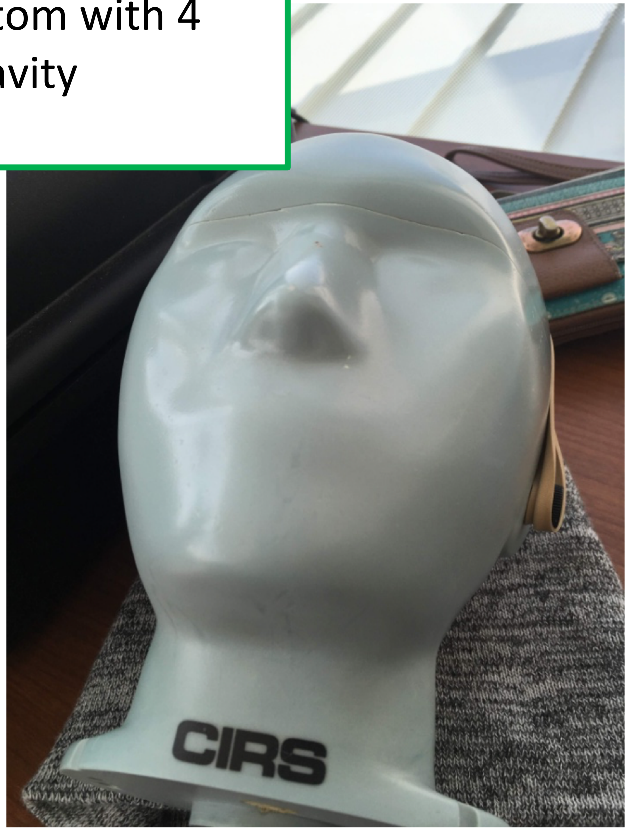


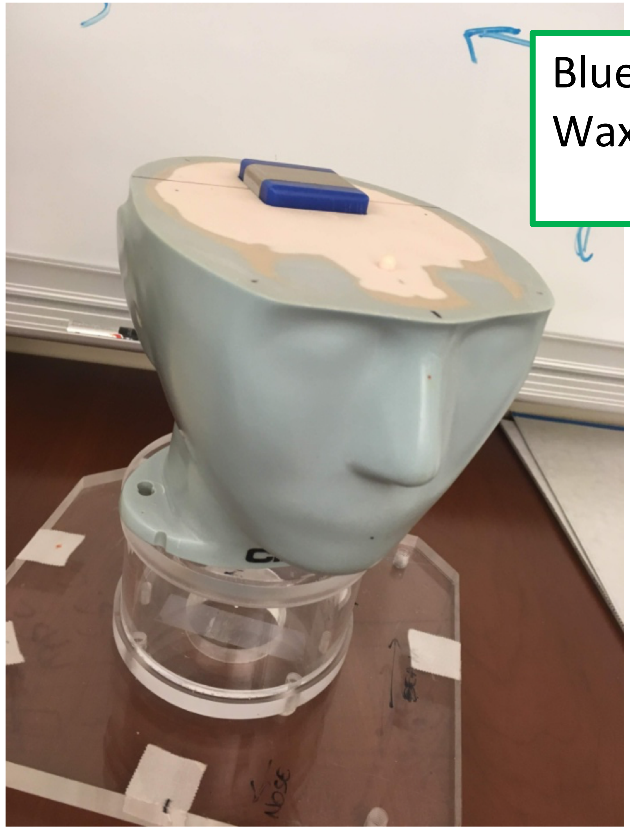


Combined
WEPL (cm)
14
12
10
8
6
4
2
10
5
0
−5
−10
Y (cm)
−10
−5
0
5
10
X (cm)

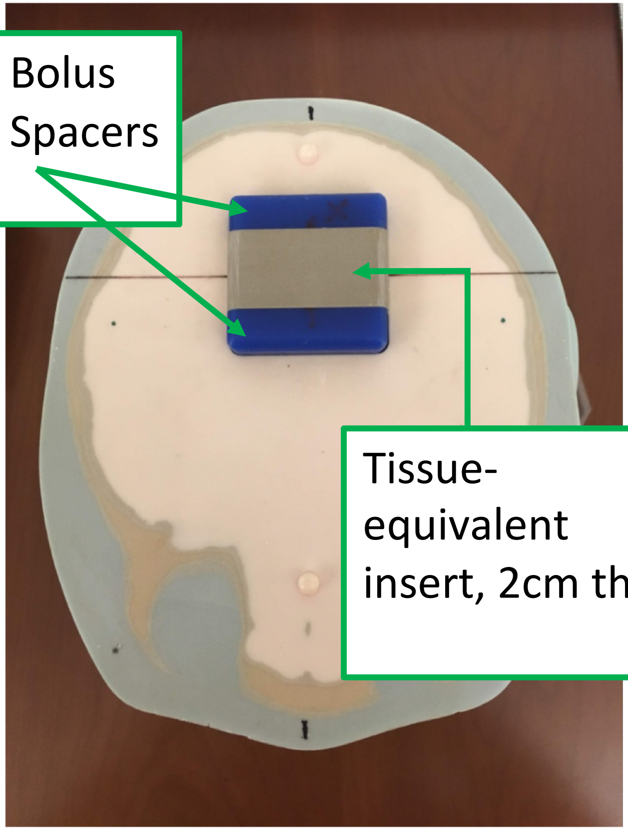
Pediatric Head Phantom with CIRS Inserts

Customized pediatric head phantom with 4 cm cubic cavity

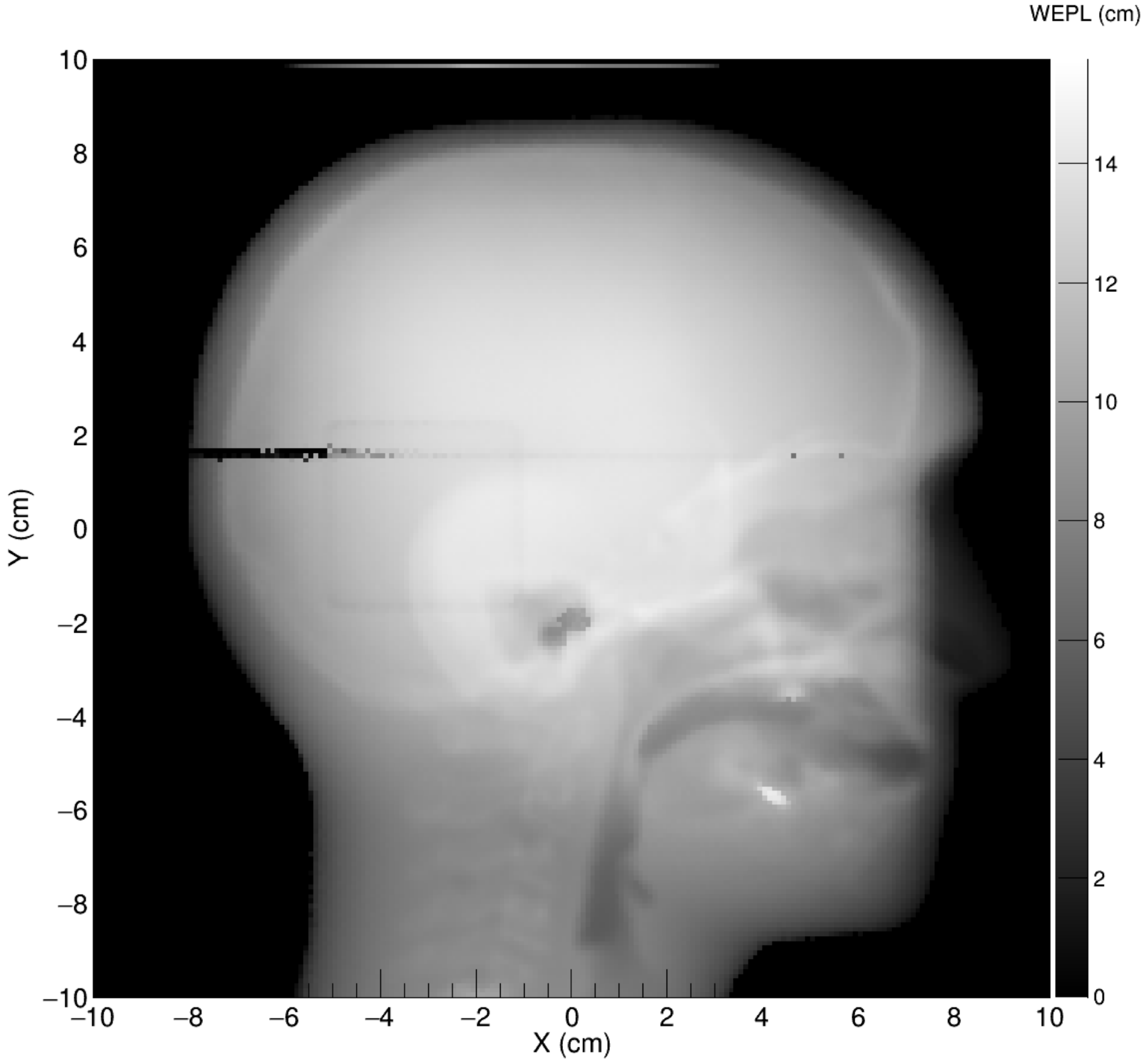




Blue Bolus Wax Spacers

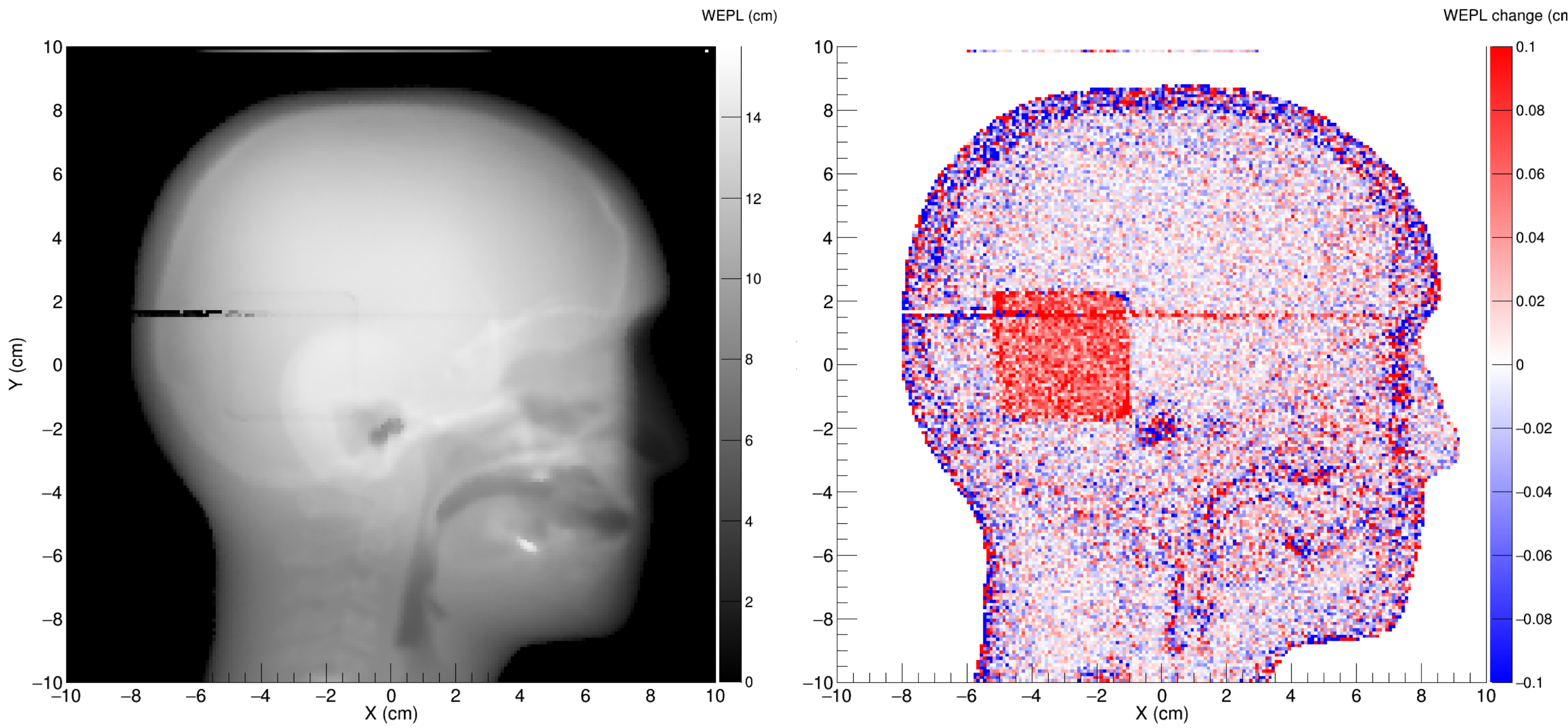


Tissue-equivalent insert, 2cm thick



Insert: spinal cord

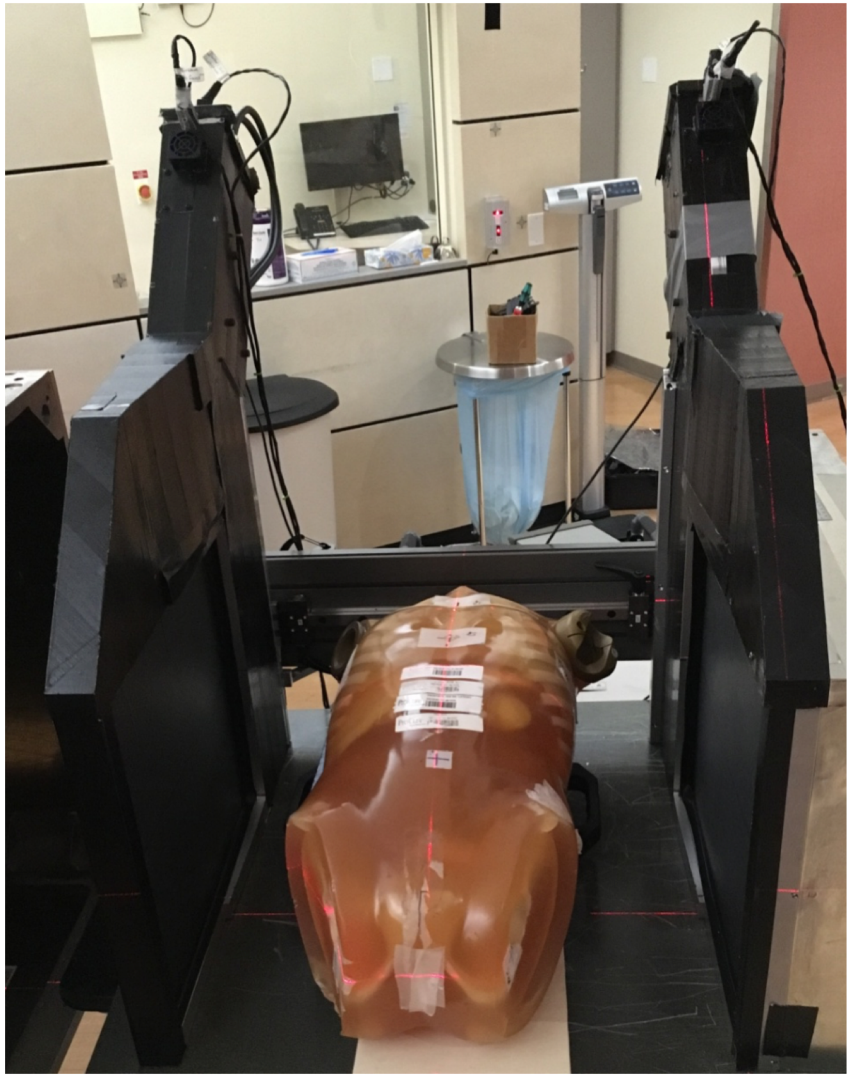
RSP: 1.04



Insert: spinal disc

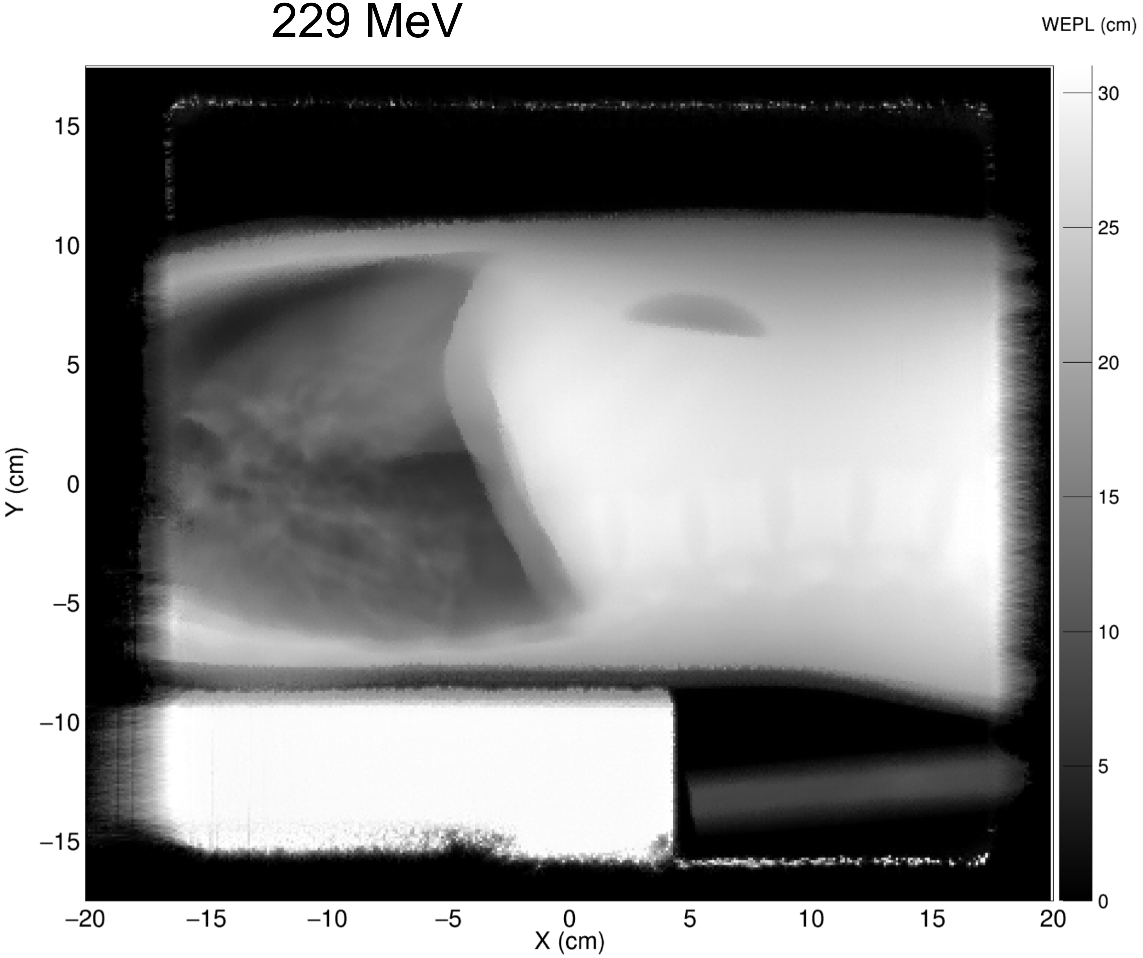
RSP: 1.07

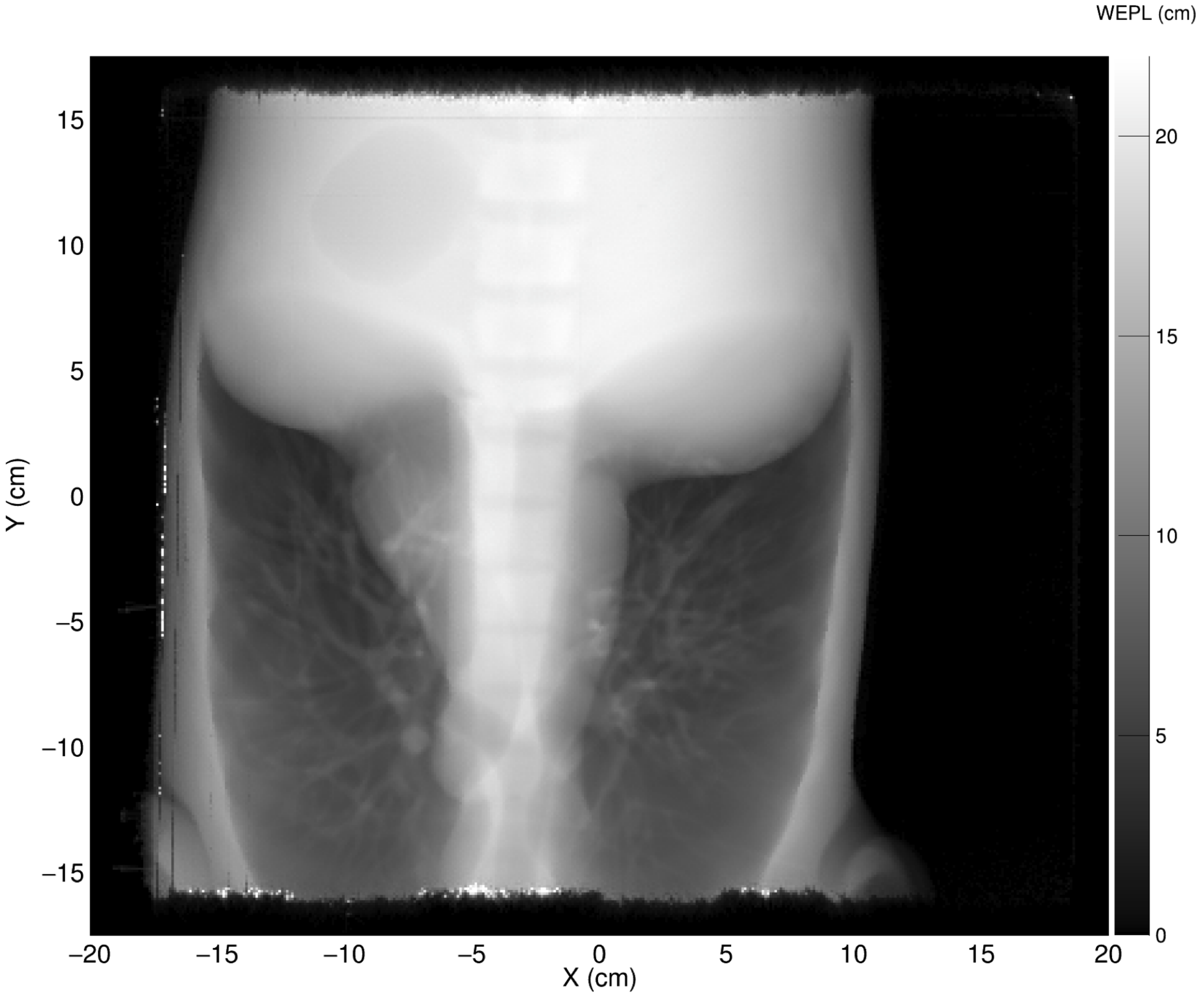
Expected difference: +0.6 mm
Measured difference: +0.58 ± 0.01 mm



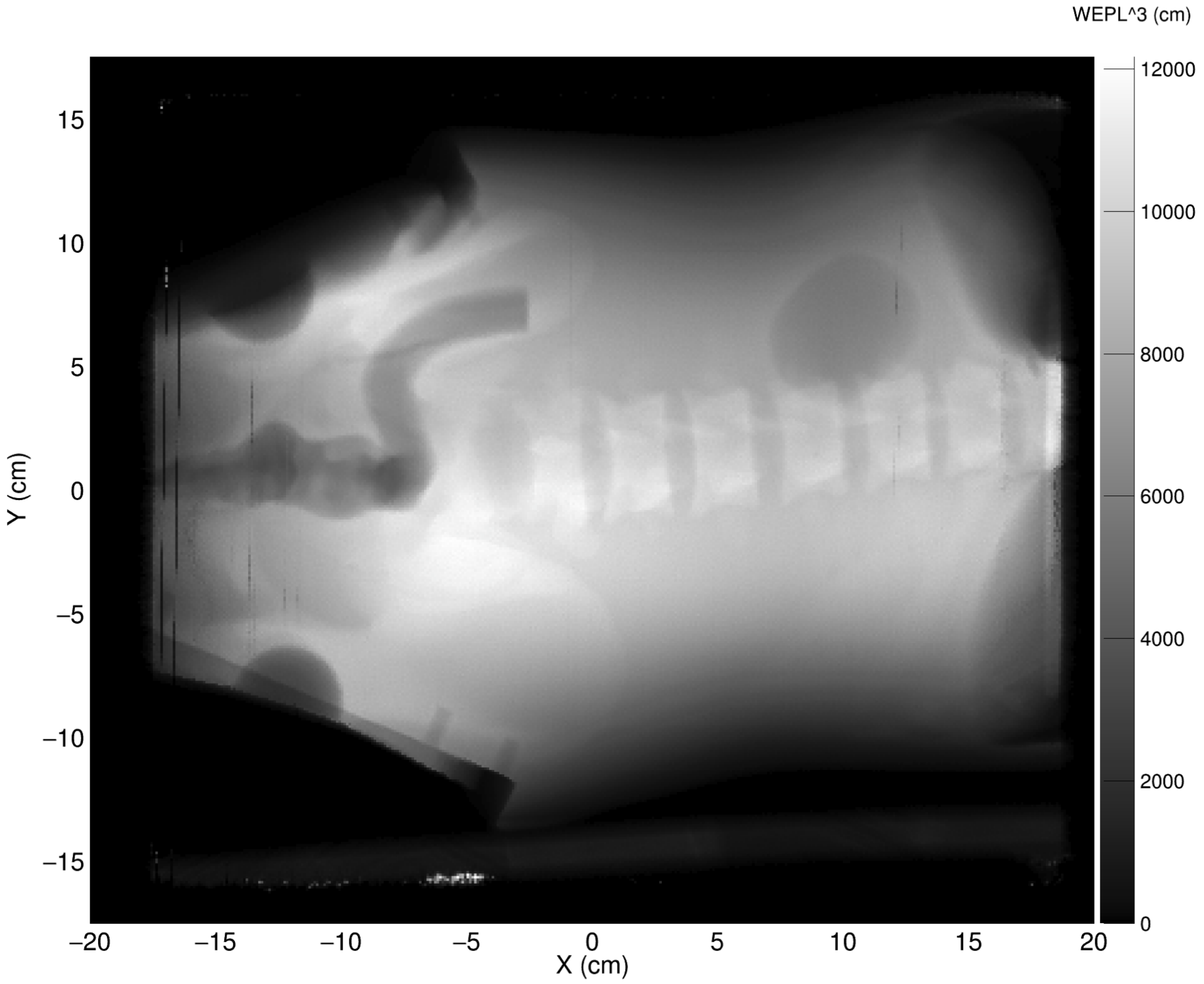
30 x 40 cm scan of torso phantom

- 4 energies: 120, 163, 200, 229 MeV

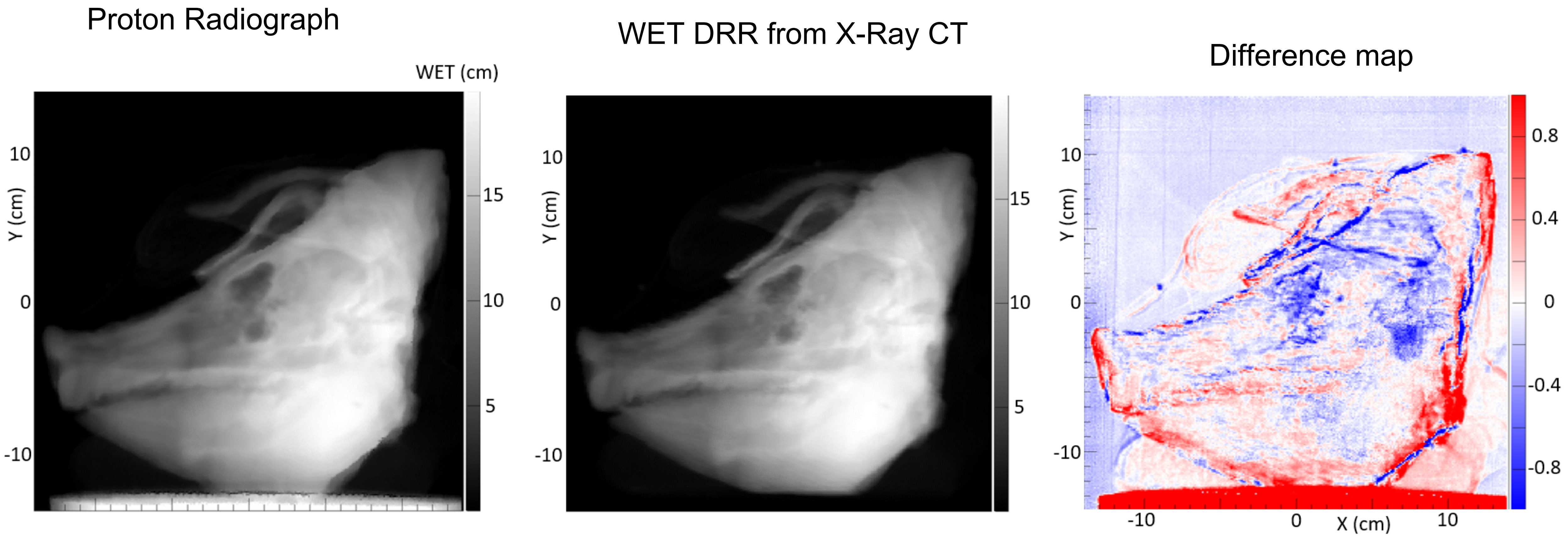




WEPL (cm)
Y (cm)
X (cm)



WEPL^3 (cm)
Y (cm)
X (cm)



Proton Radiograph
WET (cm)
Y (cm)
10
0
-10
15
10
5
WET DRR from X-Ray CT
Y (cm)
10
0
-10
15
10
5
Difference map
Y (cm)
10
0
-10
-10
0
X (cm)
10
0.8
0.4
0
-0.4
-0.8

What goes into an RSP measurement?

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- Acquisition of a large number of protons from a complete set of angles.
- Cuts, to select good events, reject nuclear scatters, etc.
- A well-calibrated WEPL for each proton.
- A well-aligned trajectory for each proton.
- A solver to find a 3D RSP map that explains the proton data.

For a given data set, image quality will be affected by:

- Accuracy of WEPL calibration
- Accuracy of tracker alignment
- Ability of solver to converge to an optimal solution to the proton data.

How can we check the elements of image quality?

$$A\,x = b$$

WEPL calibration

Straightforward checks with simple phantoms. Both

1. pRad
2. pCT: Using ROIs within uniform regions

Tracker alignment

Straightforward checks with phantoms with edges or line pairs. Both

1. pRad
2. pCT

Optimal solution

The missing ingredient!

In addition, in the short term at least, we will be looking at qualitative features, fixing problems, making improvements. We are still learning and have seen there are many details that are important.

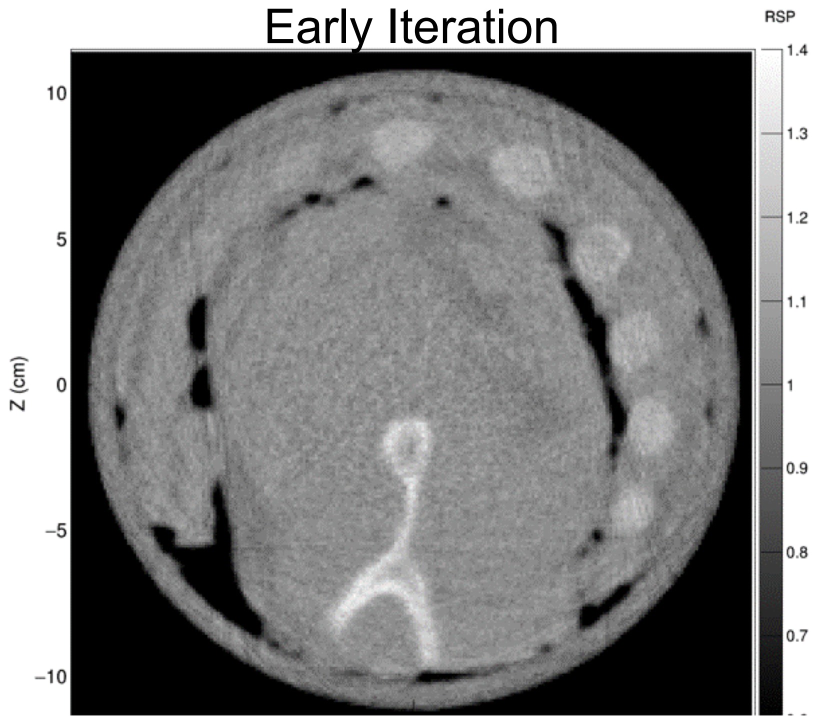
Our solution: the DV method

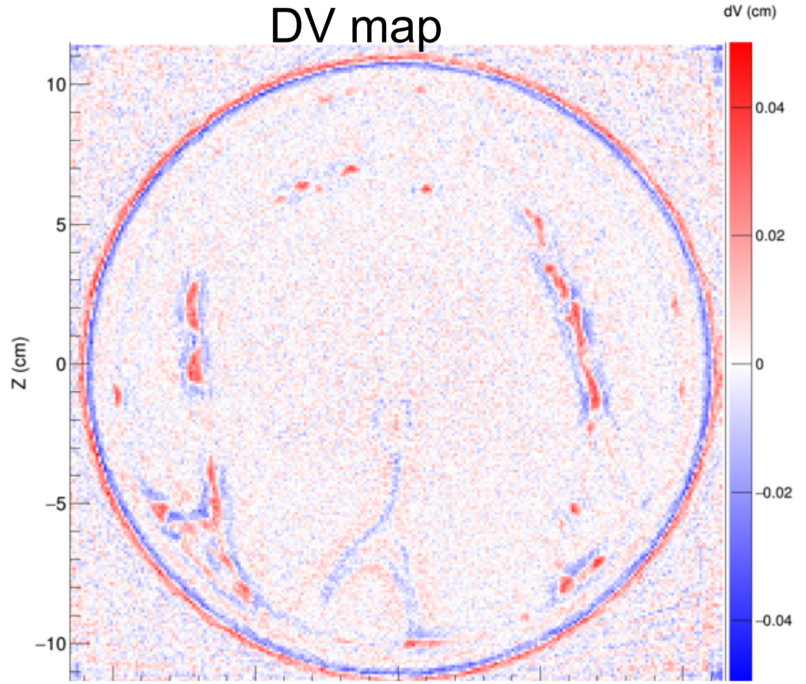
$$d_p = Ax - b$$

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

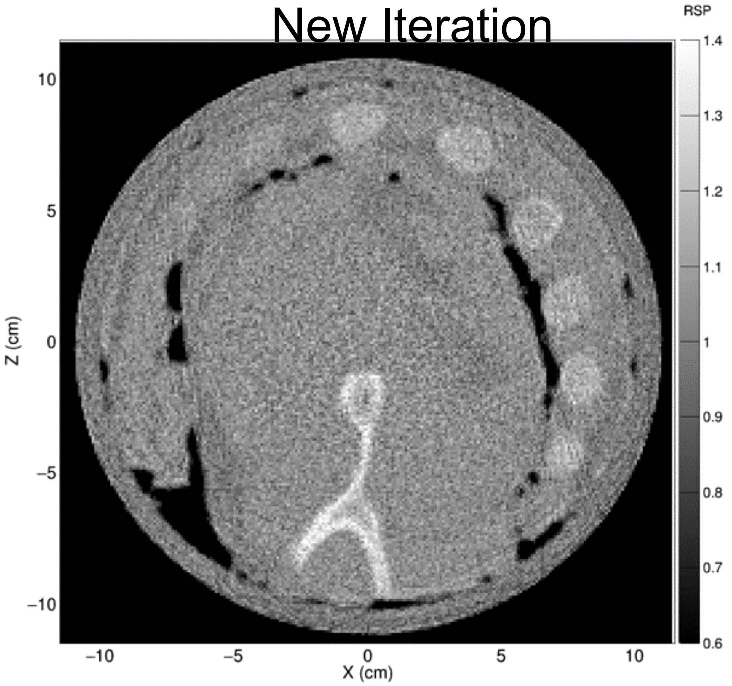
$$\bar{A}^T = V^{-1} A^T$$

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





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



Connection to least squares: Minimizing χ^2 corresponds to $d_v = 0$

- $\chi^2 = d_p \cdot d_p = (Ax - b) \cdot (Ax - b)$
- $d\chi^2/dx_i = 2\, a^T{}_i \cdot (Ax) - 2\, a^T{}_i \cdot b$ where a_i is the ith column of A

Least squares: Set $d\chi^2/dx_i = 0 \;\forall\, i$

(This is the gradient used in Landweber iteration)

- $a^T{}_i \cdot Ax - a^T{}_i \cdot b = 0$

Divide by $\Sigma_j\, \alpha^T{}_{ij}$ and go to matrix notation:

- $\bar{A}^T A\, x - \bar{A}^T b = 0$

The left side is d_v :

- $d_v = \bar{A}^T d_p = \bar{A}^T (Ax - b)$

Benefits of DV method

- Definition of a unique, optimal solution
- Image quality metric that does not depend on knowledge of a ground truth
- Ability to calculate optimal step size for each iteration
- Ability to optimize multiple iterations at a time
- Stopping criteria determined by distance from optimal solution
- Does not depend on starting point
- Suitable for noisy data: $Ax = b$ cannot be true for all protons, but $DV = 0$ can be true for all voxels

Optimization of λ_k

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

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

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

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

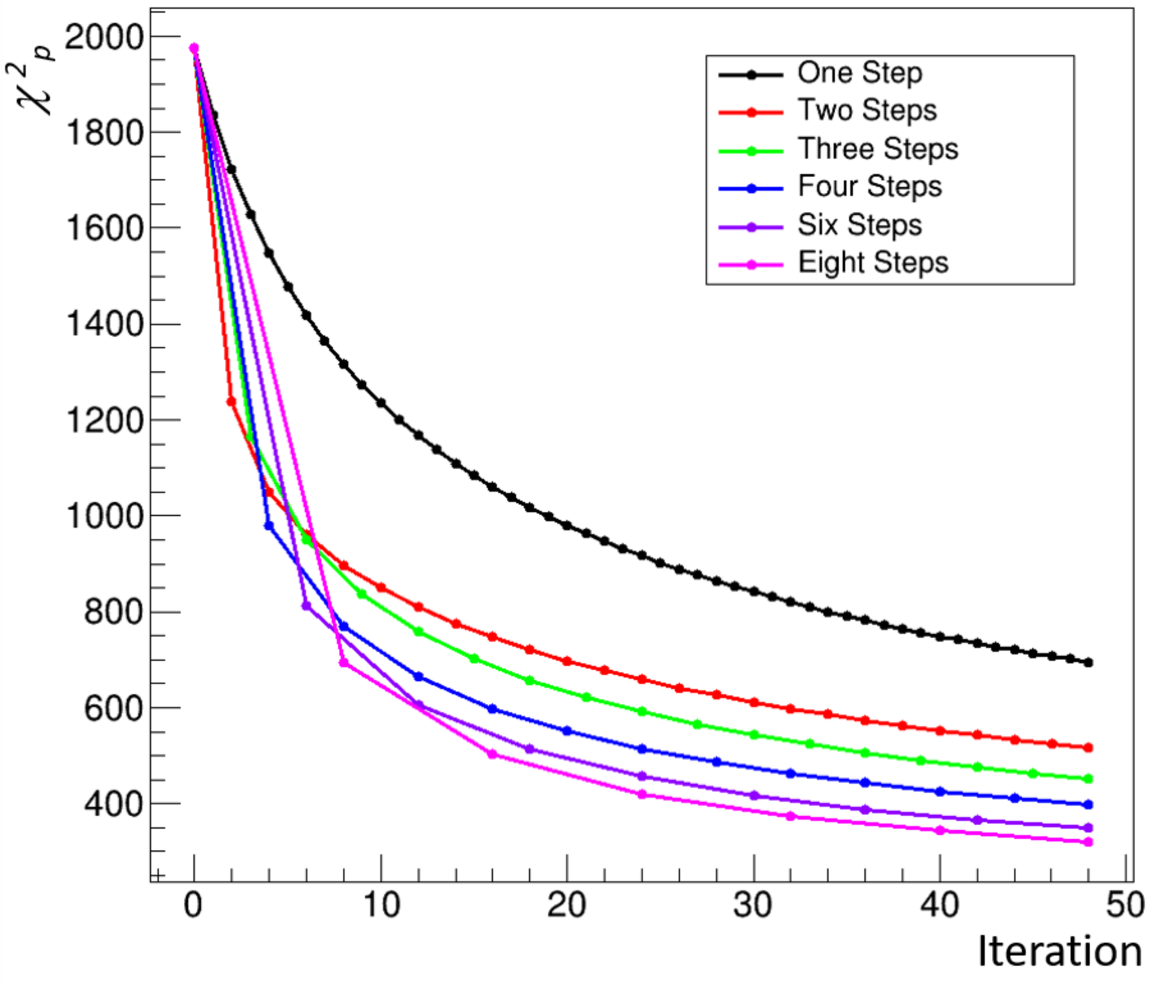
$$d\chi^2_{k+1} / d\lambda_k = -2 d_{pk} \cdot (A d_{vk}) + 2\lambda_k |A d_{vk}|^2 = 0$$

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

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

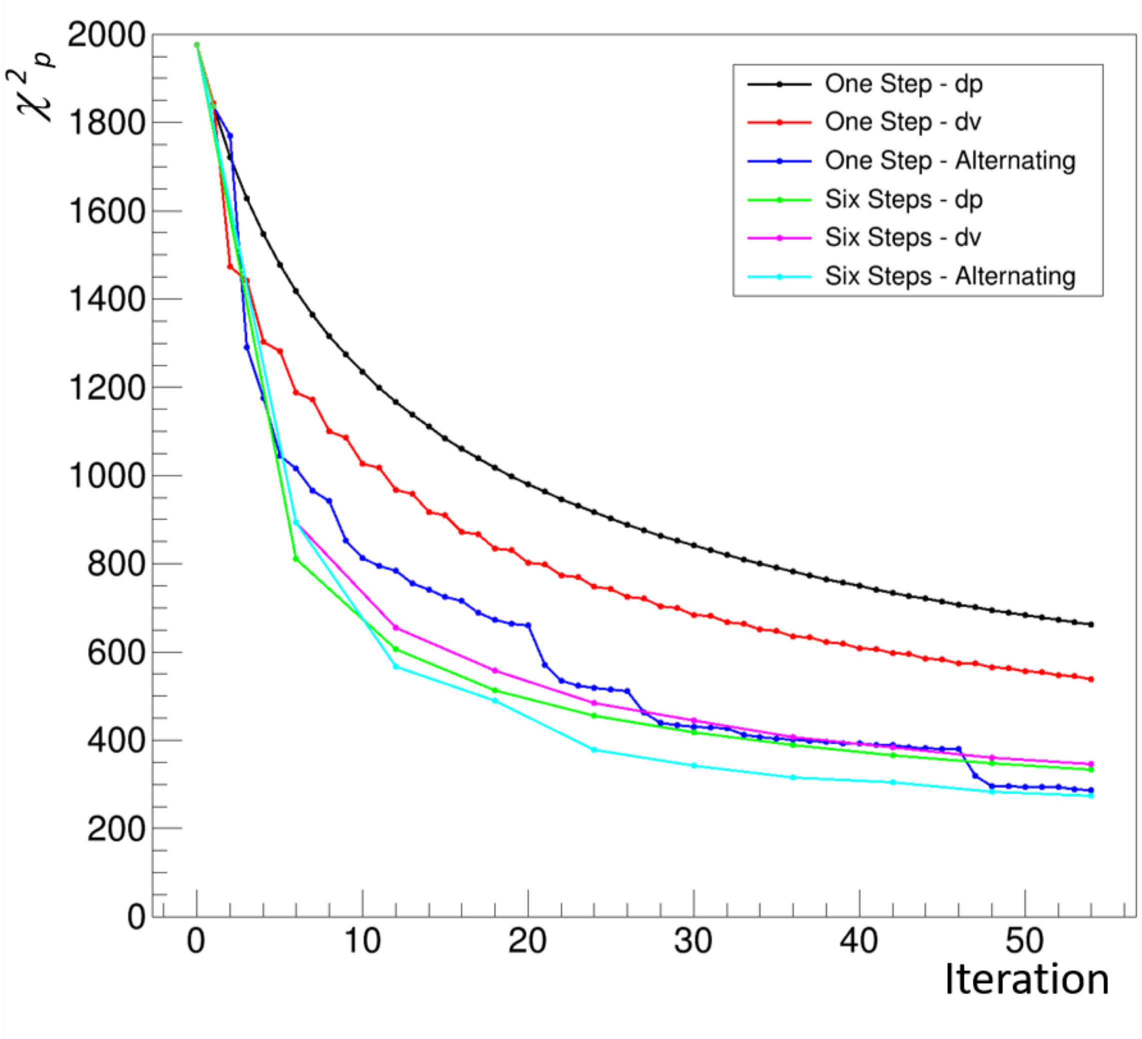
$$\lambda_k = d_{vk} \cdot (\bar{A}^T A d_{vk}) / |\bar{A}^T A d_{vk}|^2$$

Multi-step optimization



- Simulated pCT data for simple water phantom

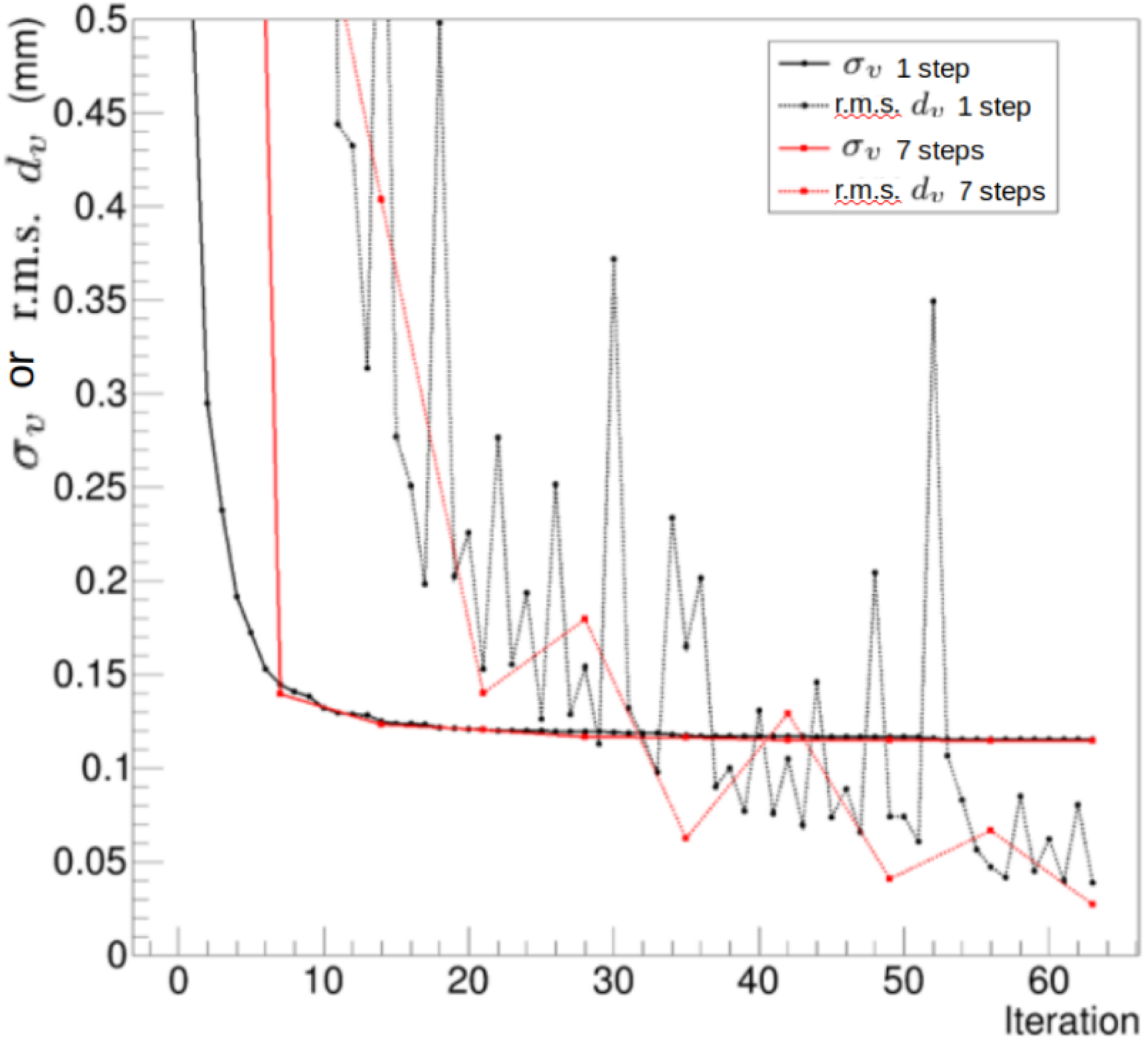
Alternating between chi2-p and chi2-v leads to faster convergence



Stopping Criteria

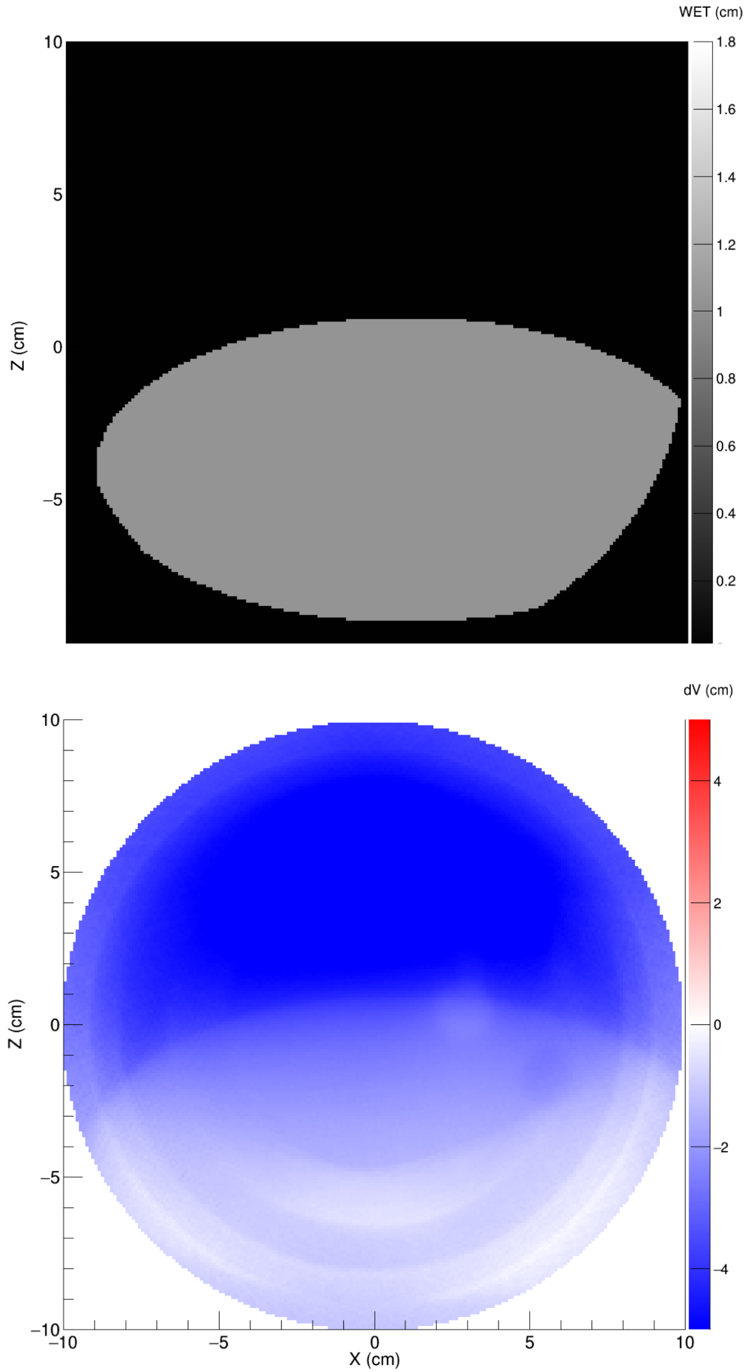
WEPL uncertainty per proton: $$\sigma_p = \sqrt{\frac{\chi_p^2}{N_p - N_v}}$$

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



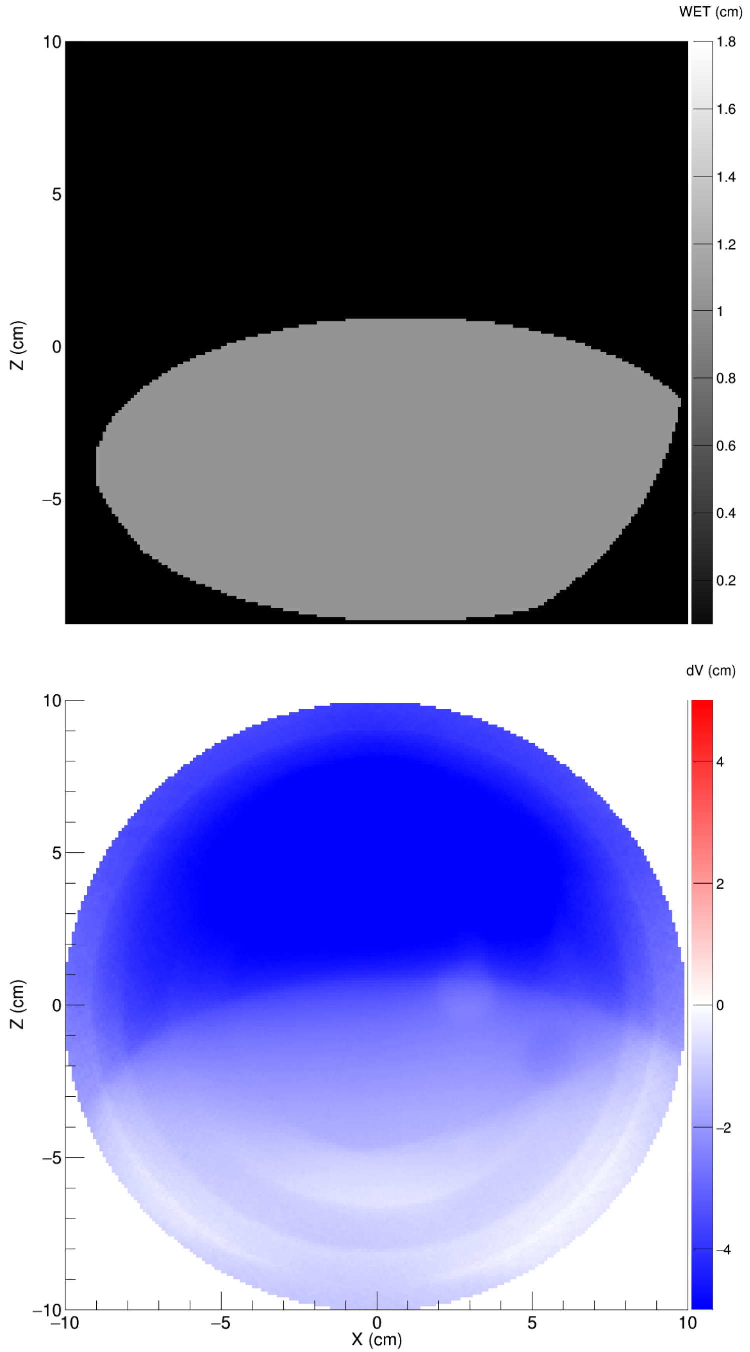
ART
Lambda = 0.002

Iteration 0



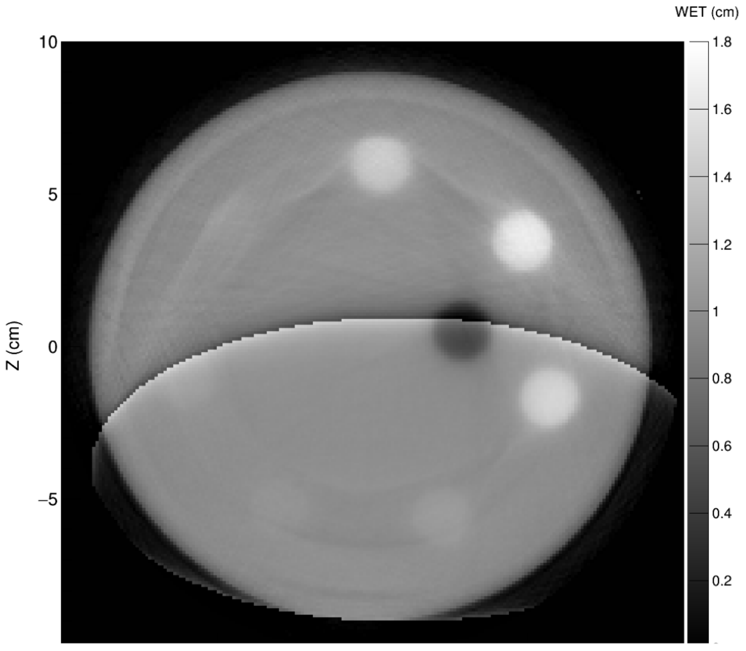
5-step DV
optimization

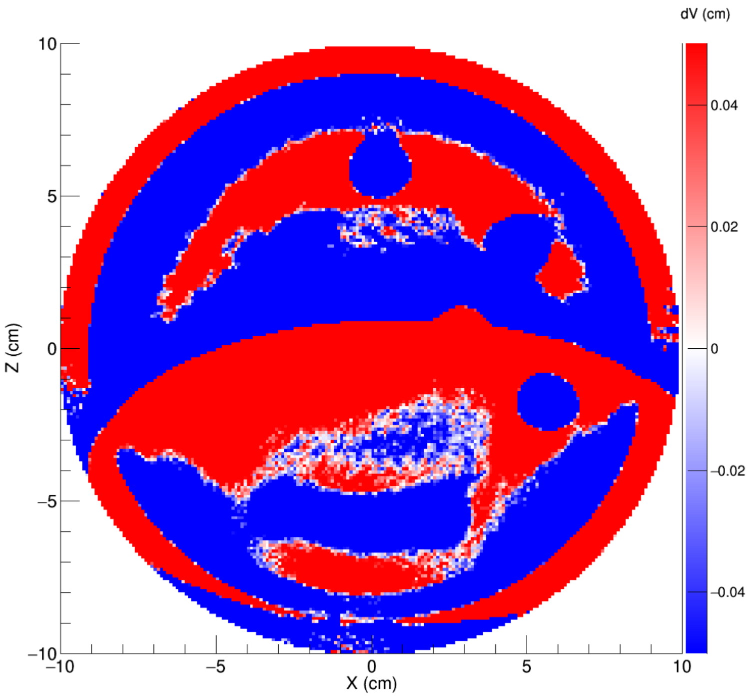
Iteration 0



ART
Lambda = 0.002

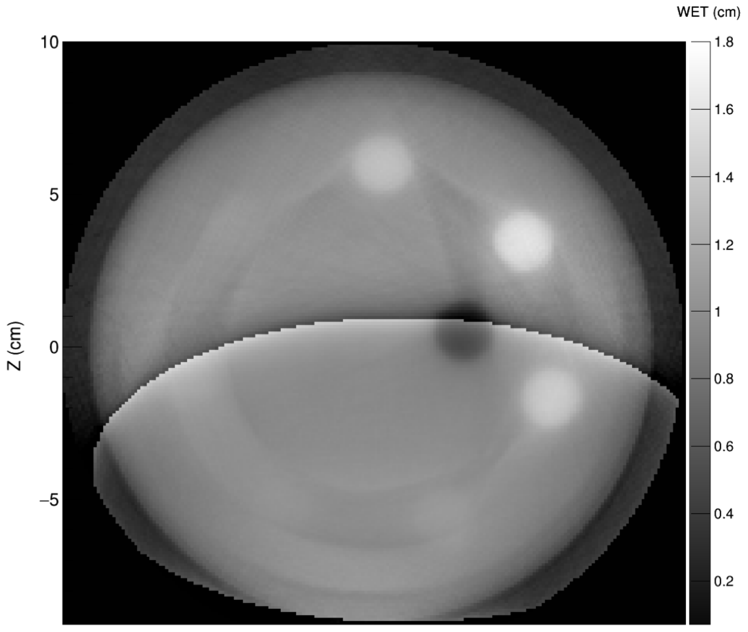
Iteration 5

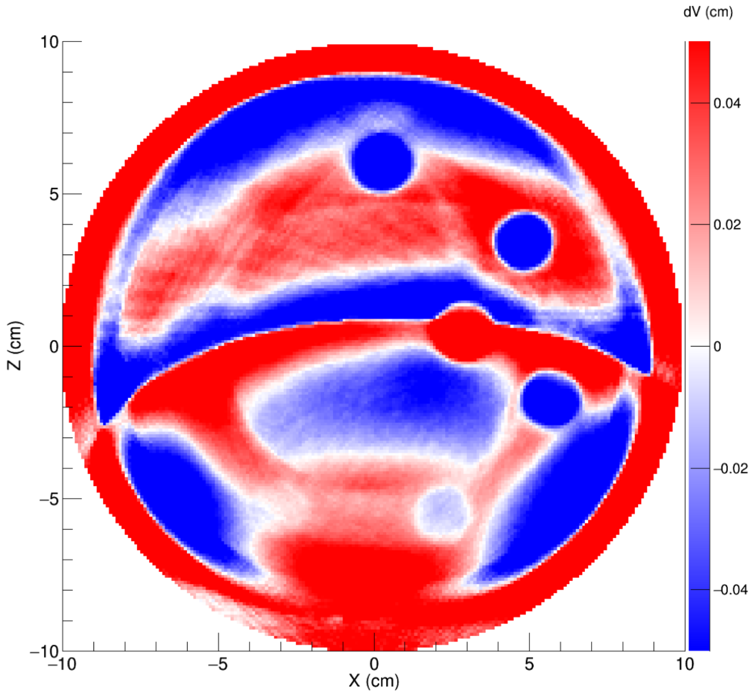




5-step DV
optimization

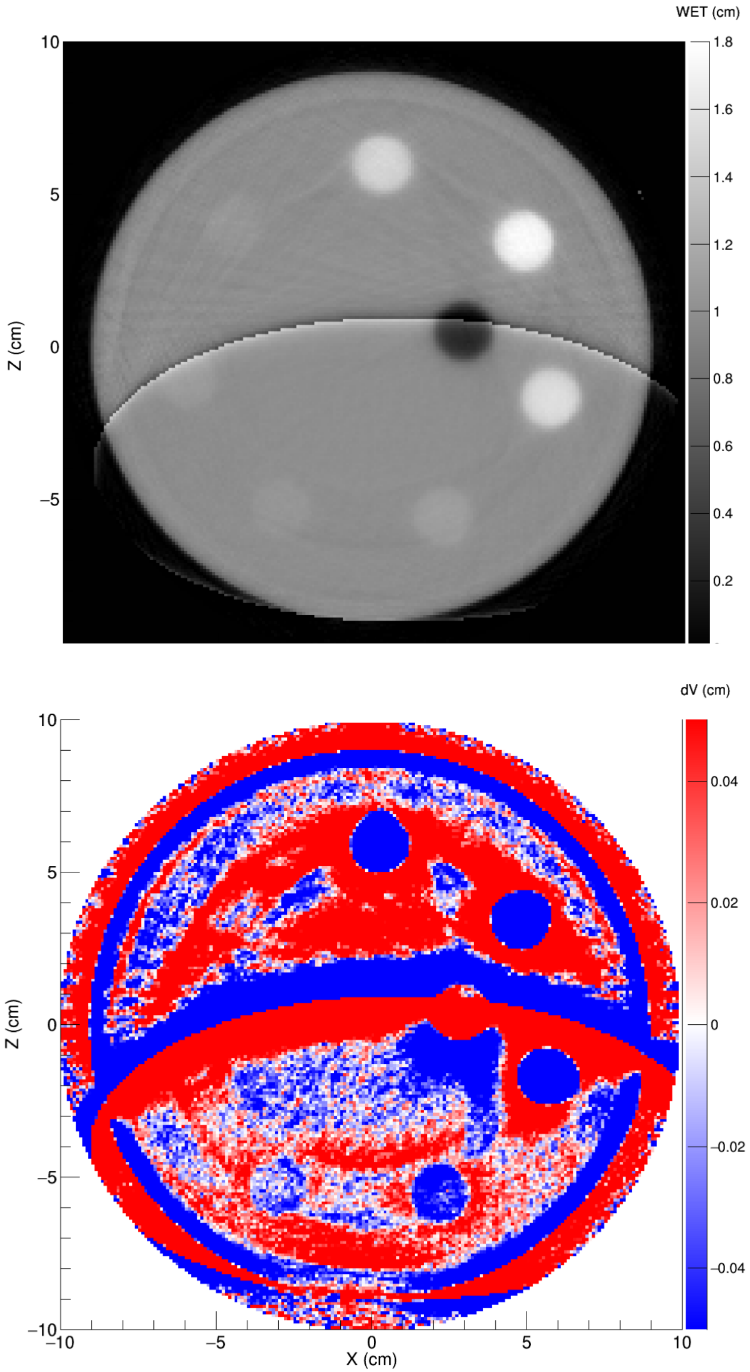
Iteration 1





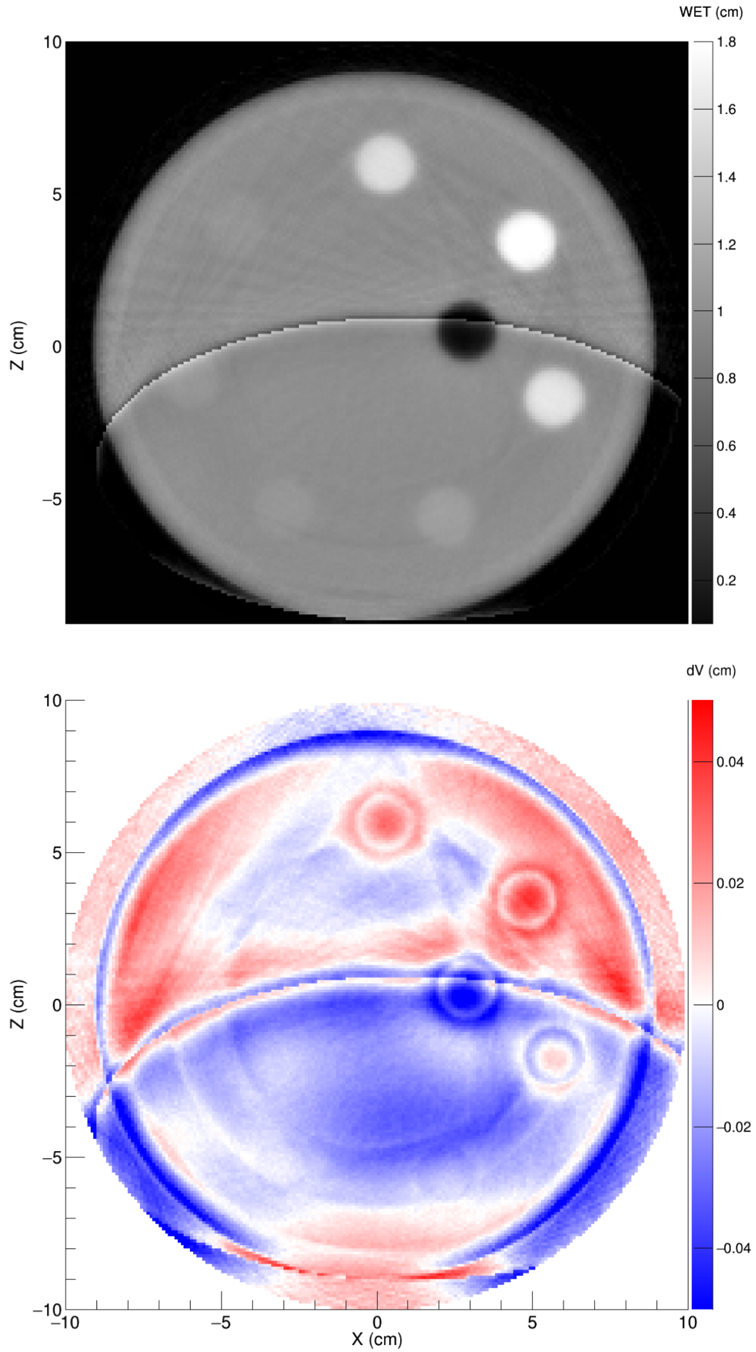
ART
Lambda = 0.002

Iteration 10



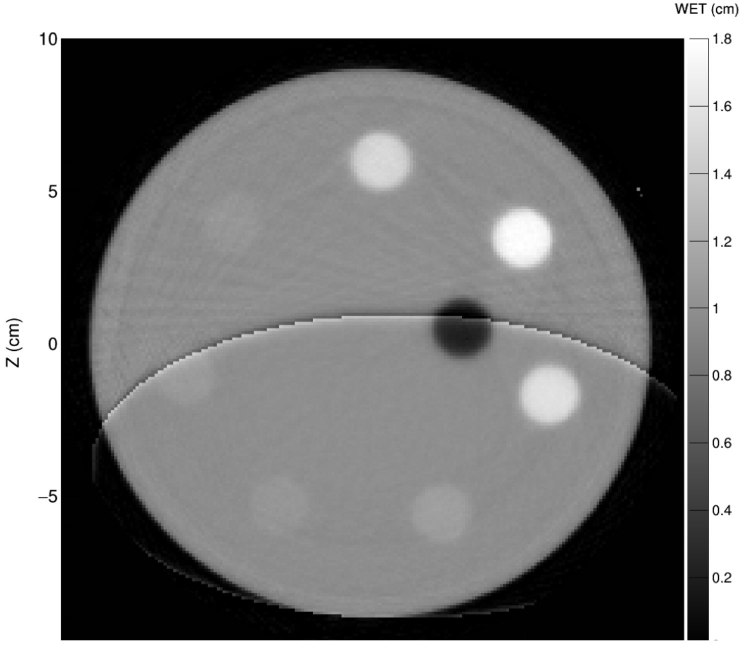
5-step DV
optimization

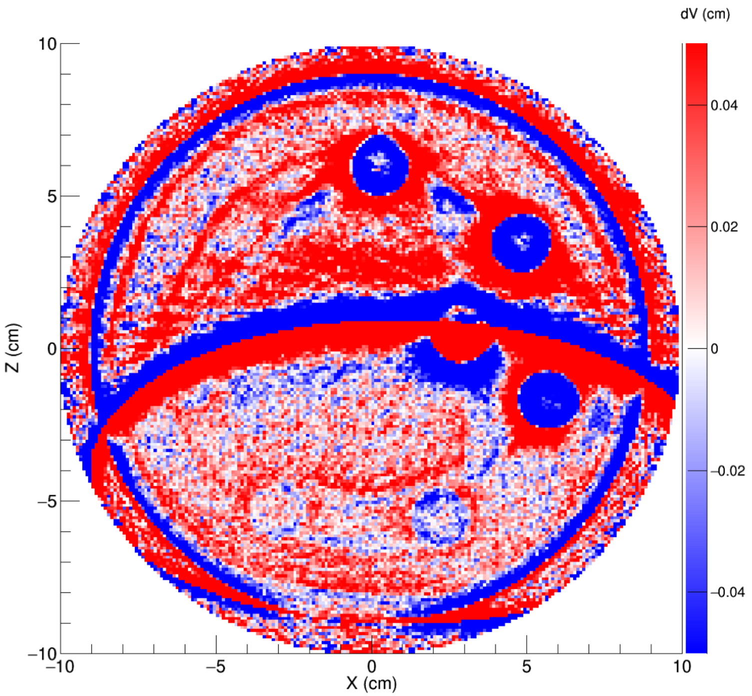
Iteration 2



ART
Lambda = 0.002

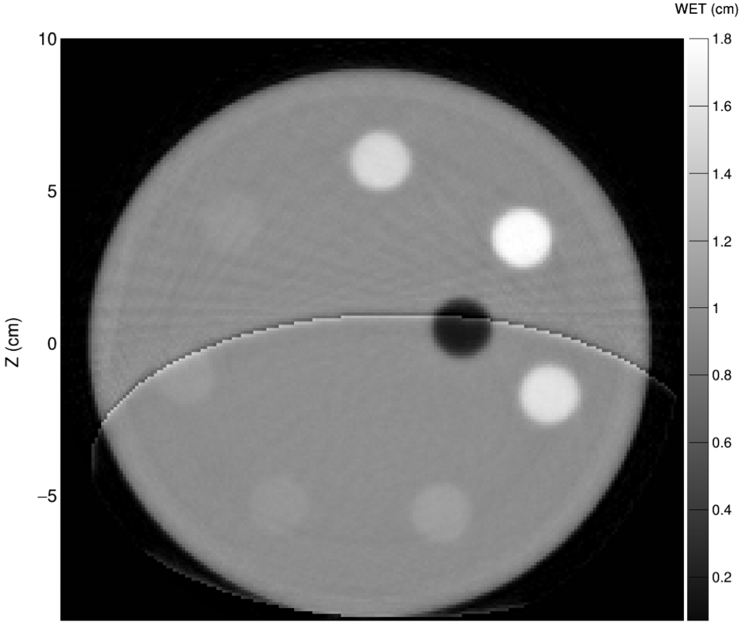
Iteration 15

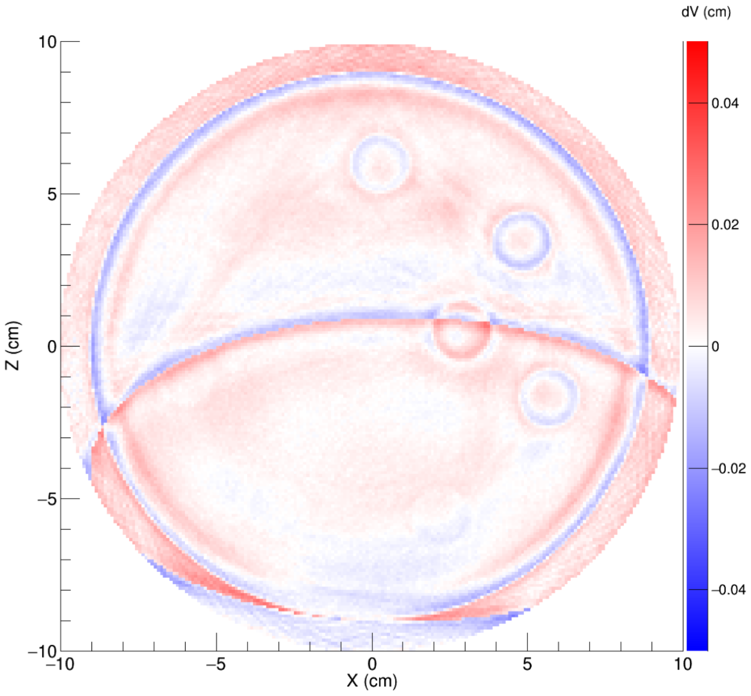




5-step DV
optimization

Iteration 3



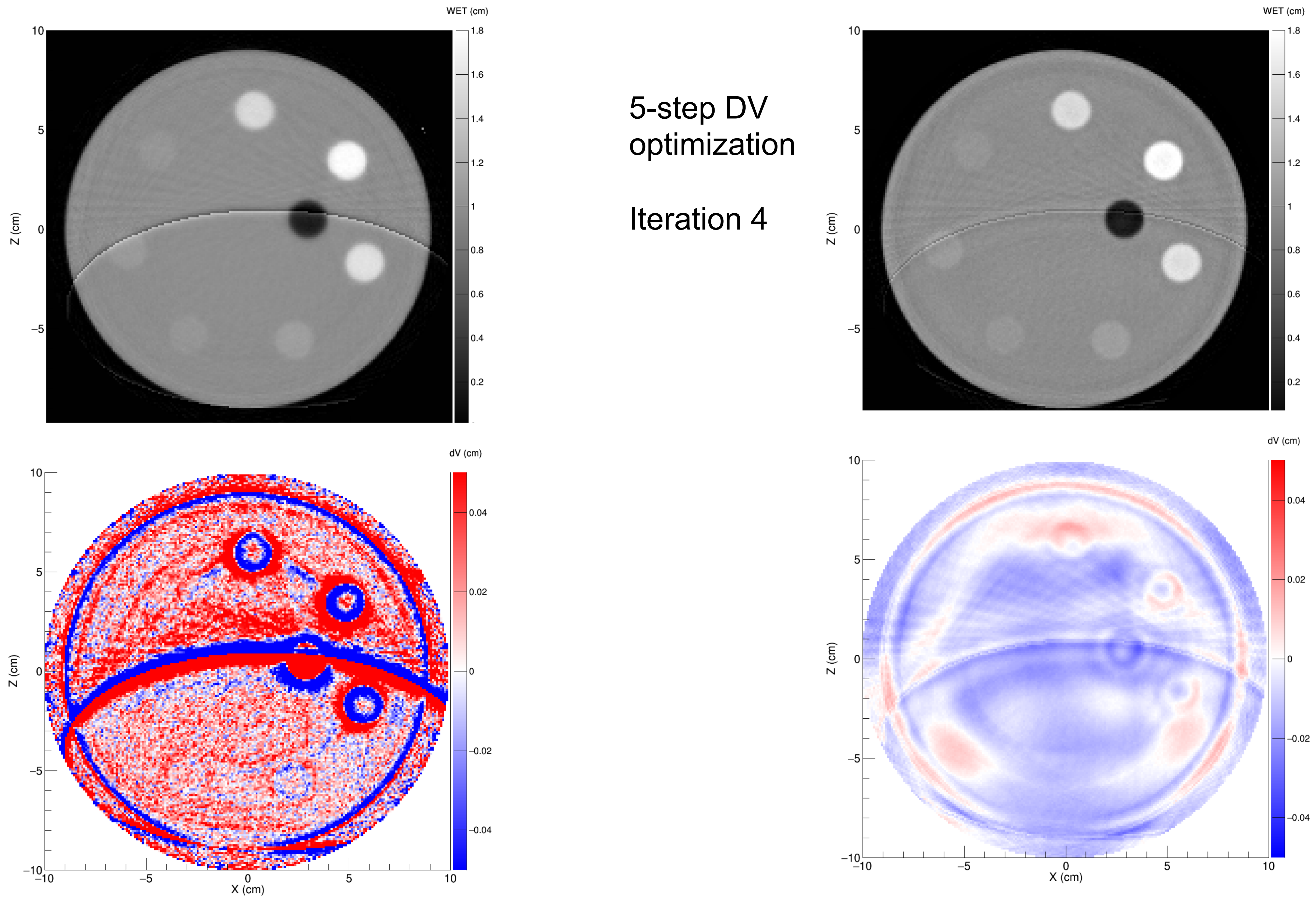


ART
Lambda = 0.002

Iteration 20

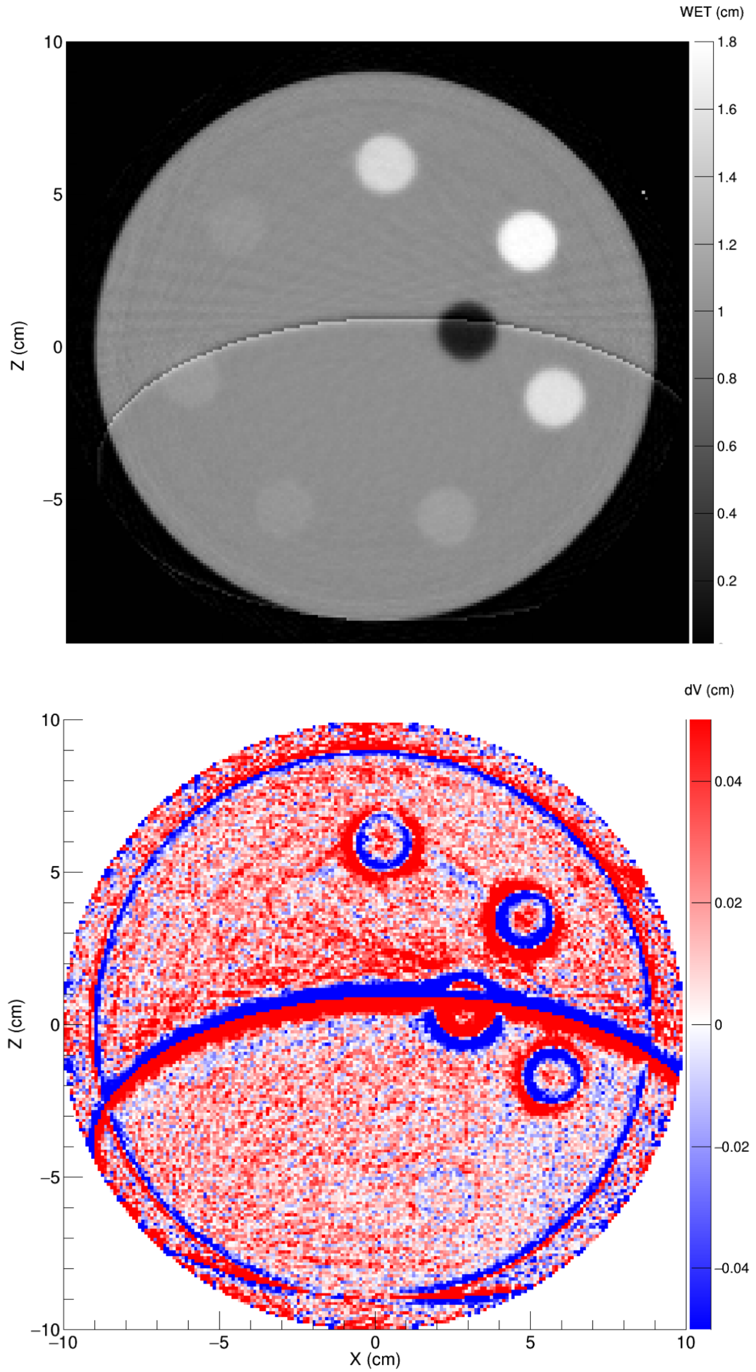
5-step DV
optimization

Iteration 4



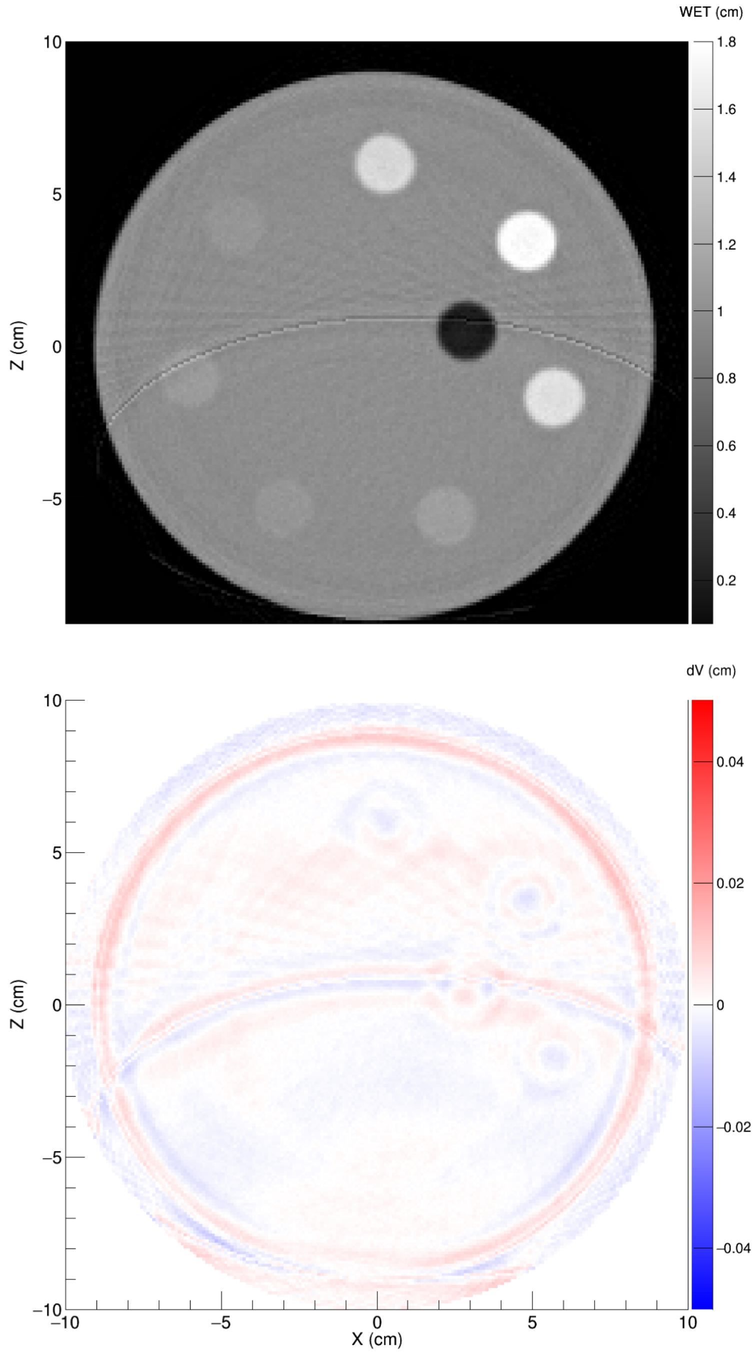
ART
Lambda = 0.002

Iteration 25



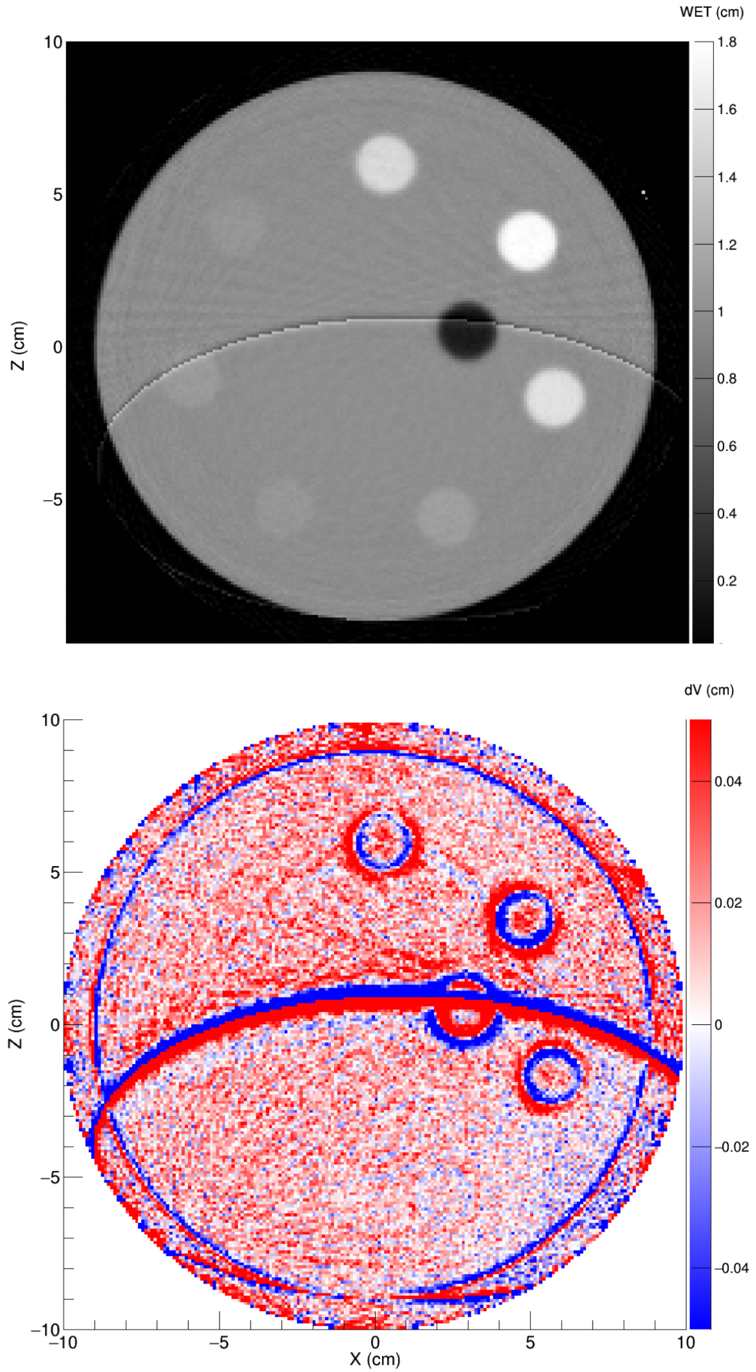
5-step DV
optimization

Iteration 5



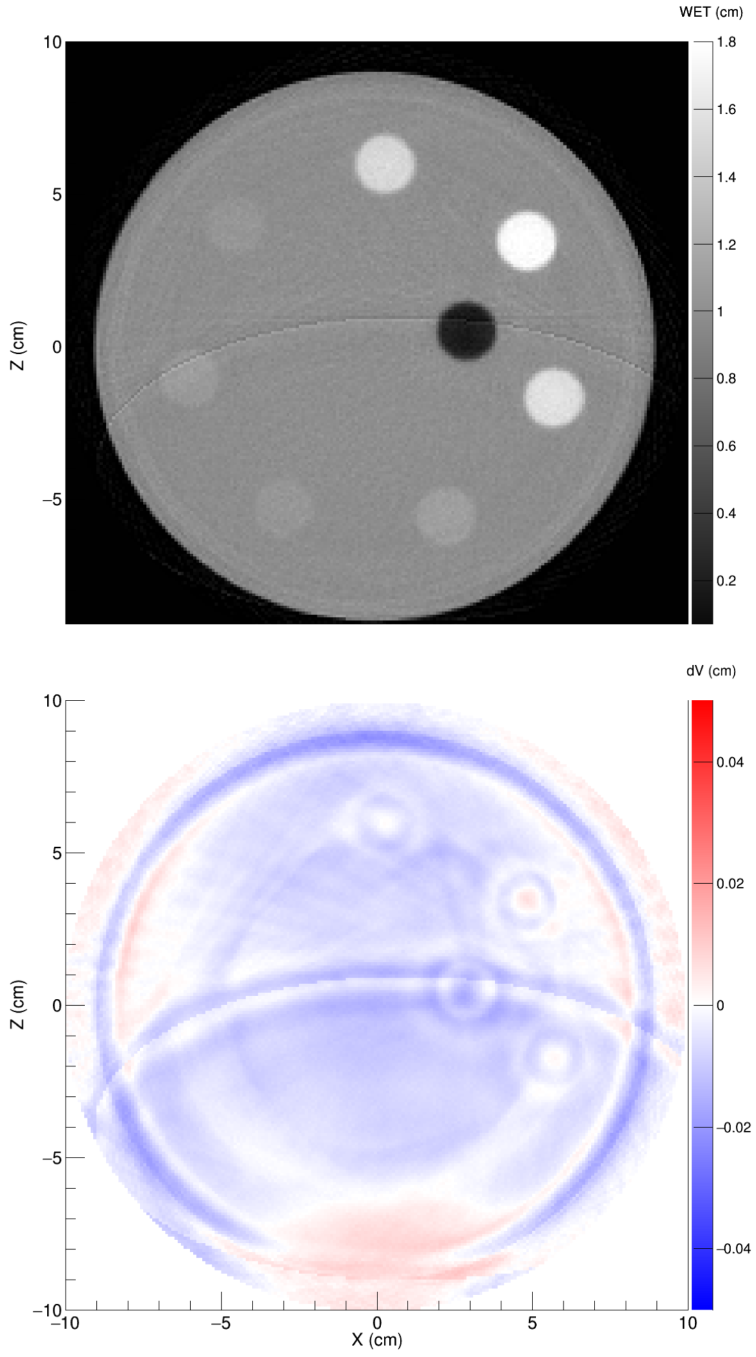
ART
Lambda = 0.002

Iteration 30



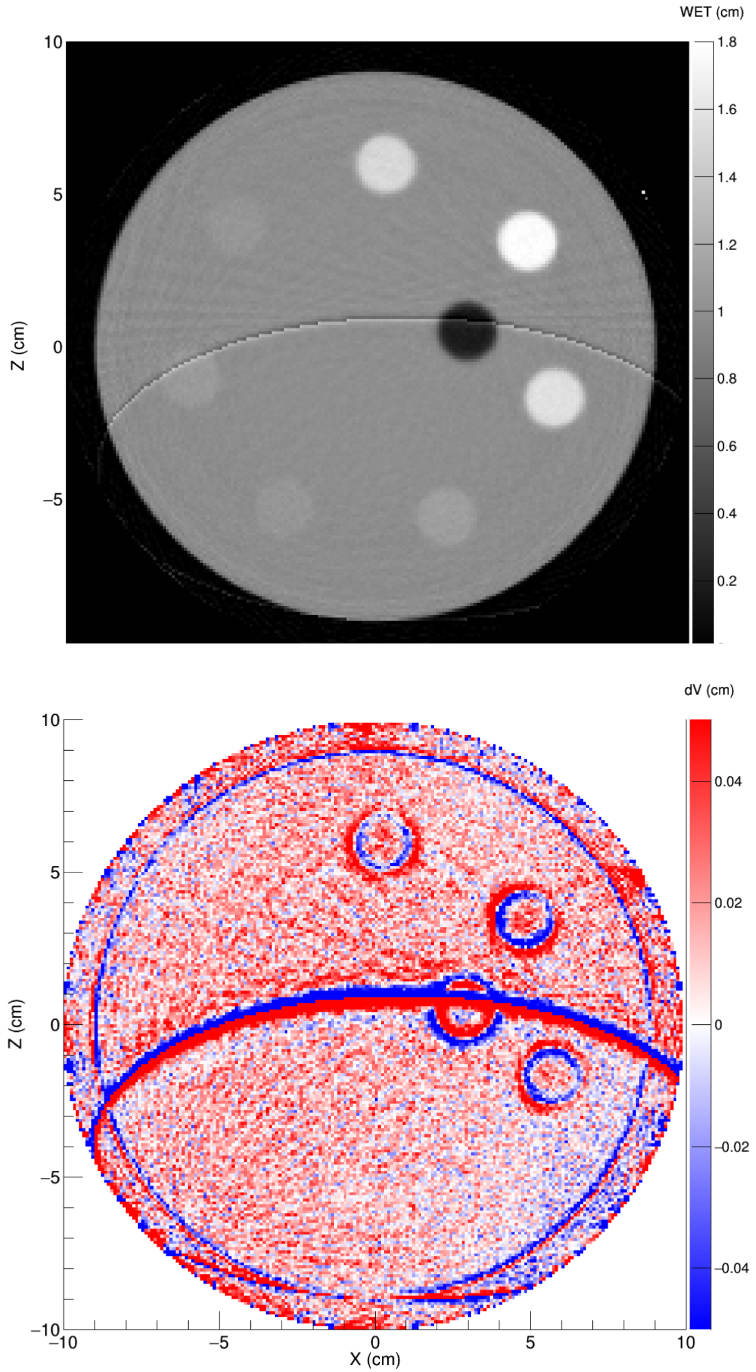
5-step DV optimization

Iteration 6



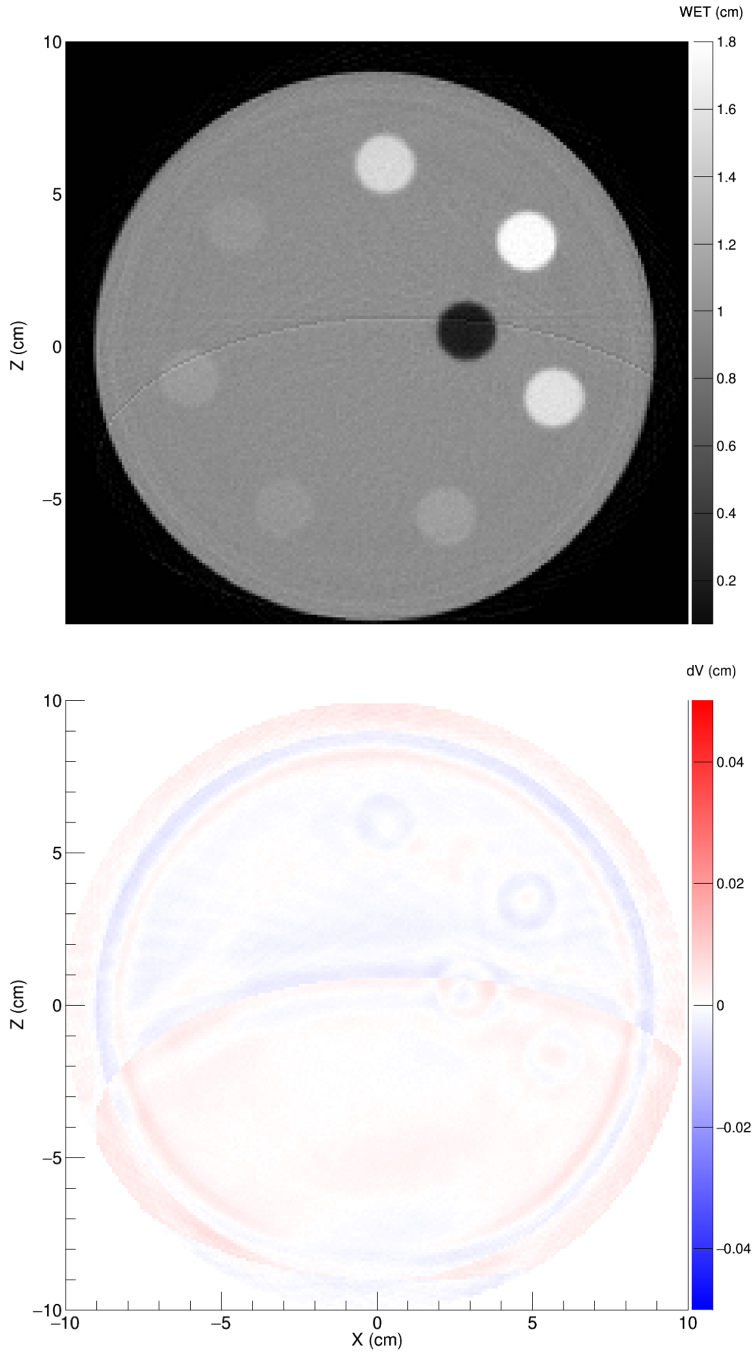
ART
Lambda = 0.002

Iteration 35



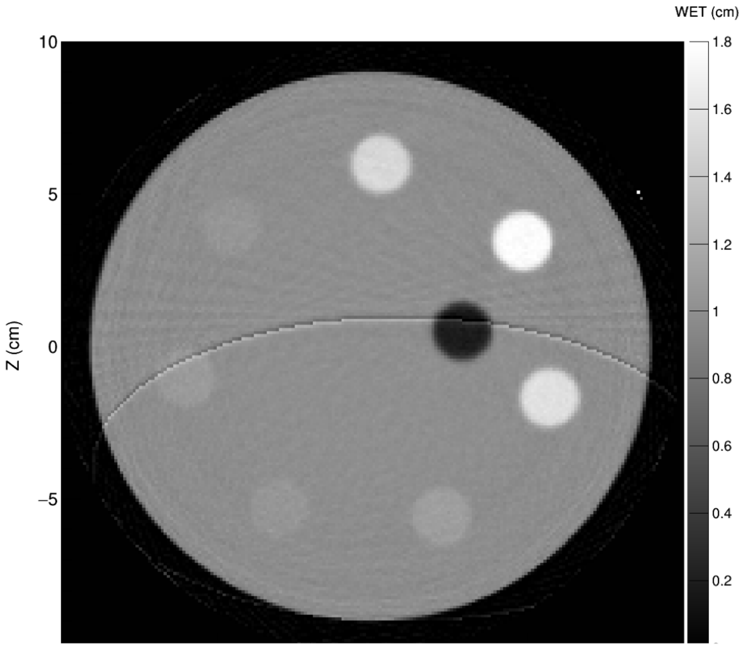
5-step DV
optimization

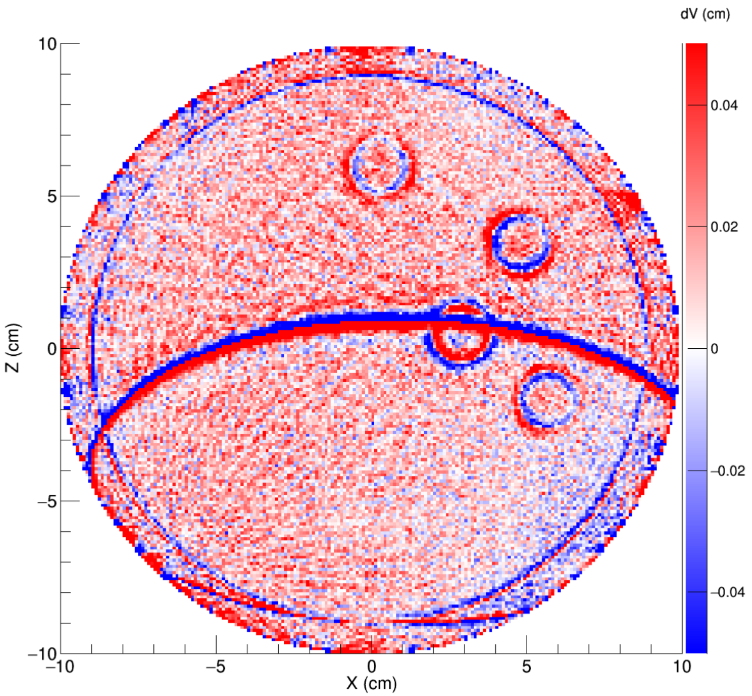
Iteration 7



ART
Lambda = 0.002

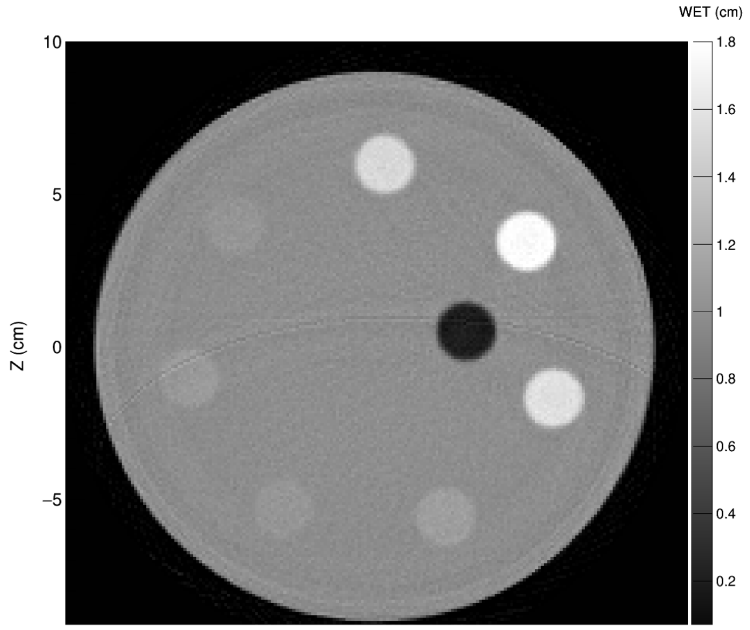
Iteration 40

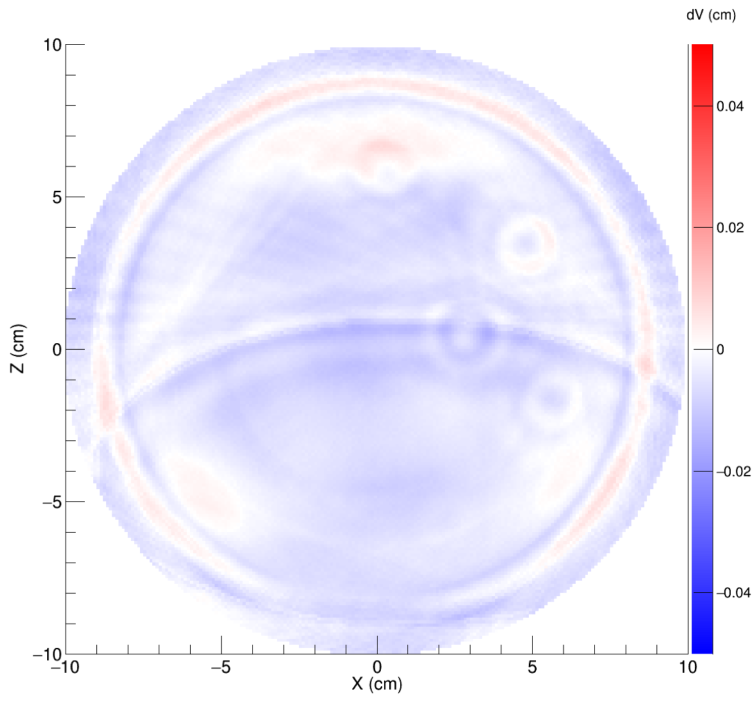




5-step DV
optimization

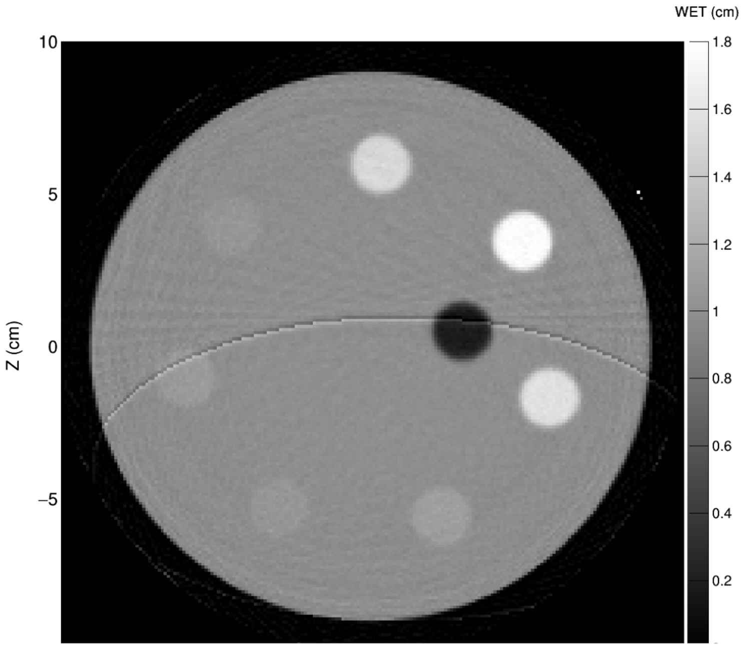
Iteration 8

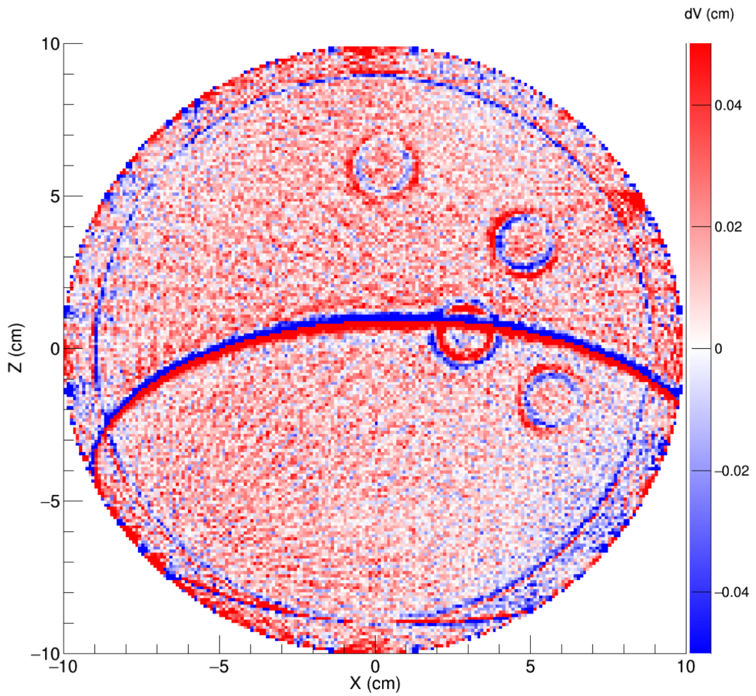




ART
Lambda = 0.002

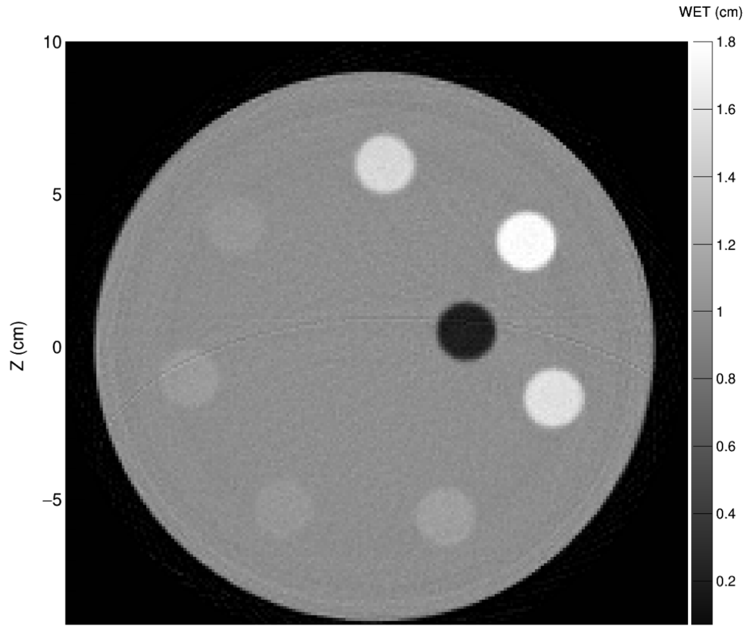
Iteration 45

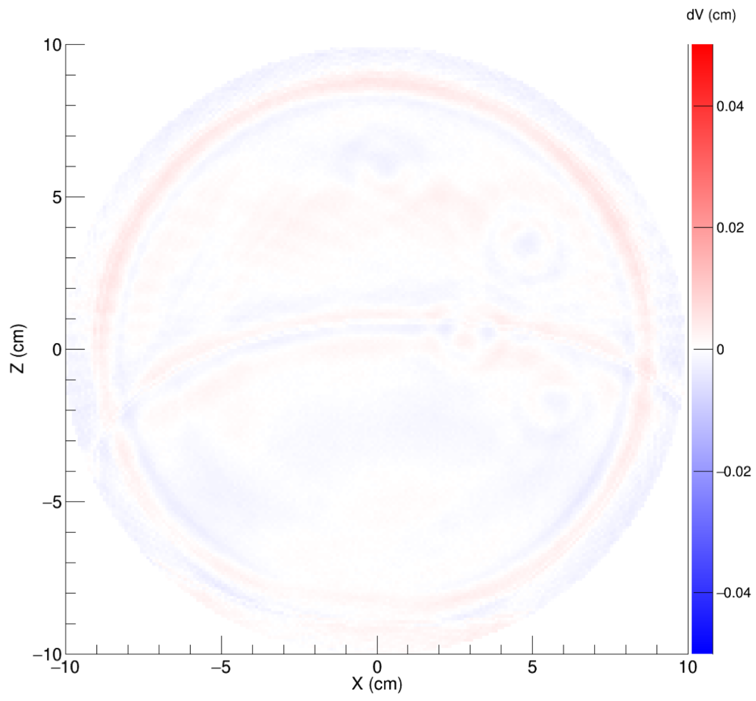




5-step DV
optimization

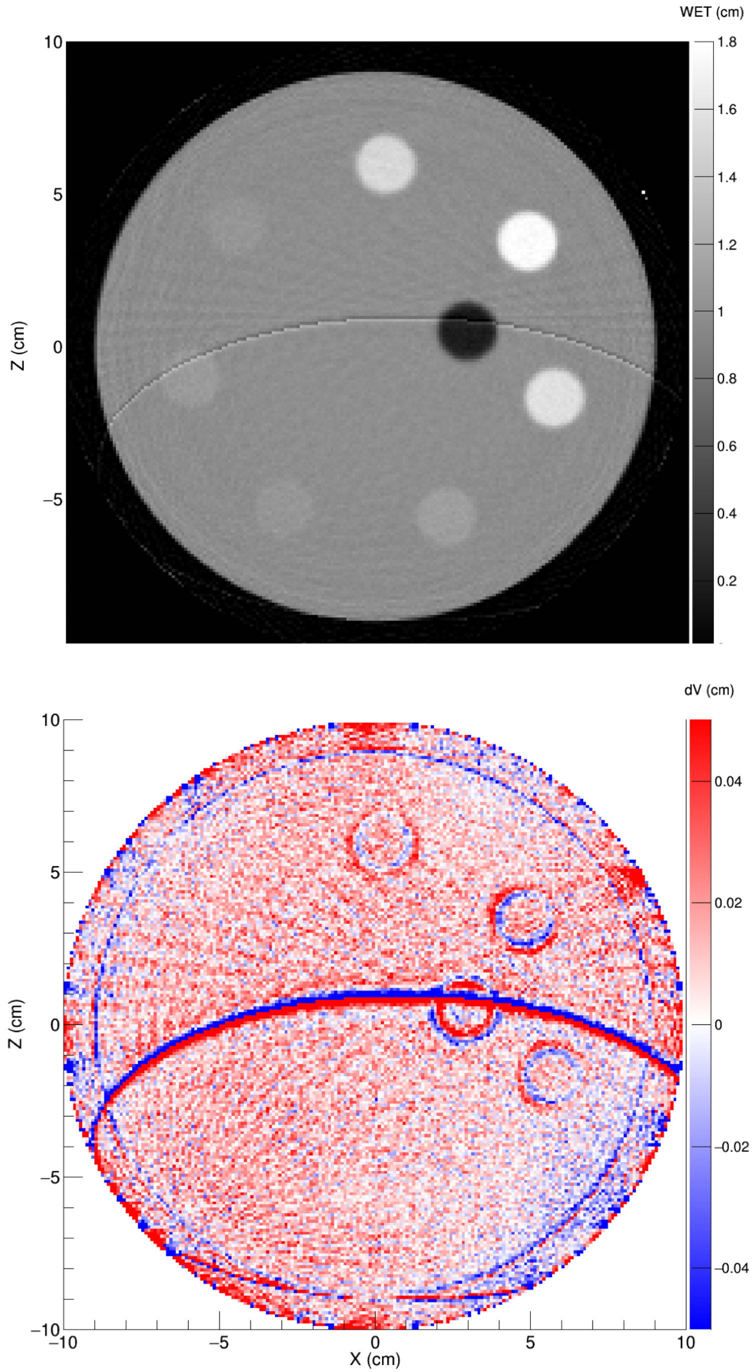
Iteration 9





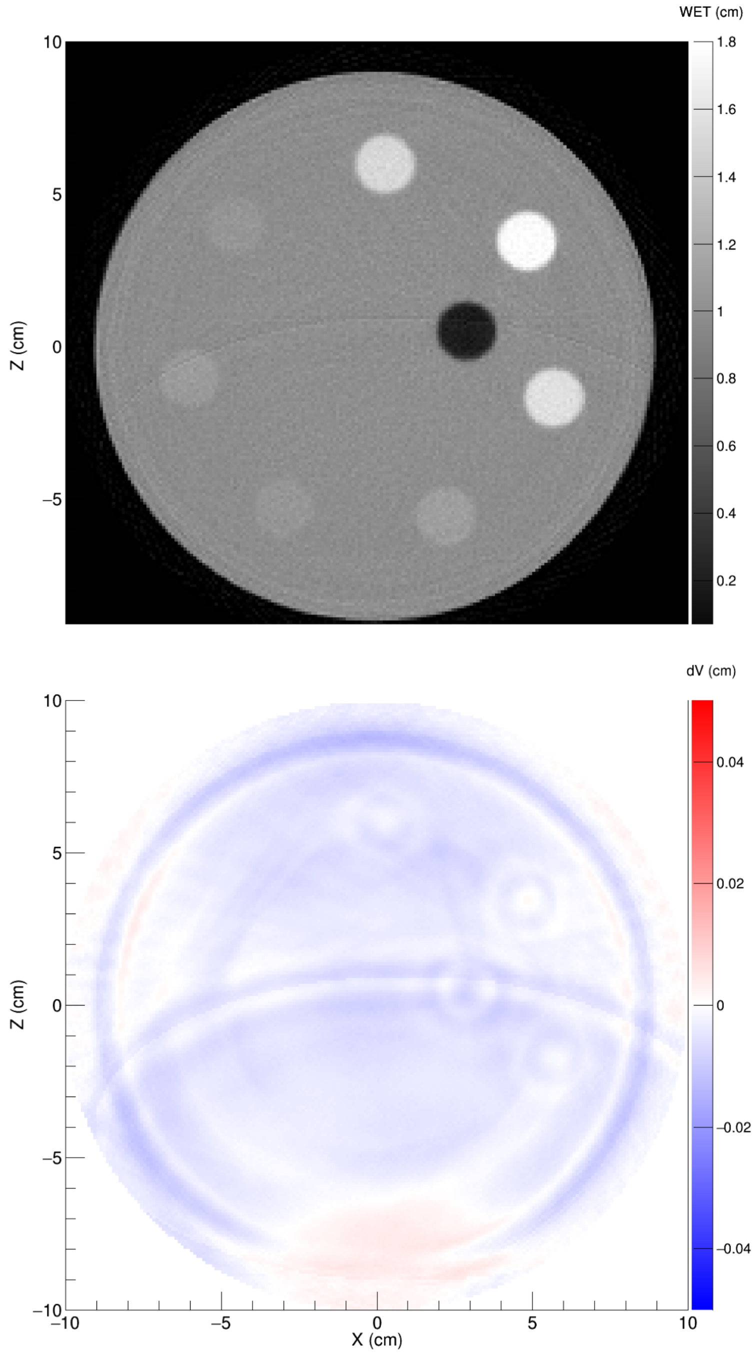
ART
Lambda = 0.002

Iteration 50



5-step DV
optimization

Iteration 10

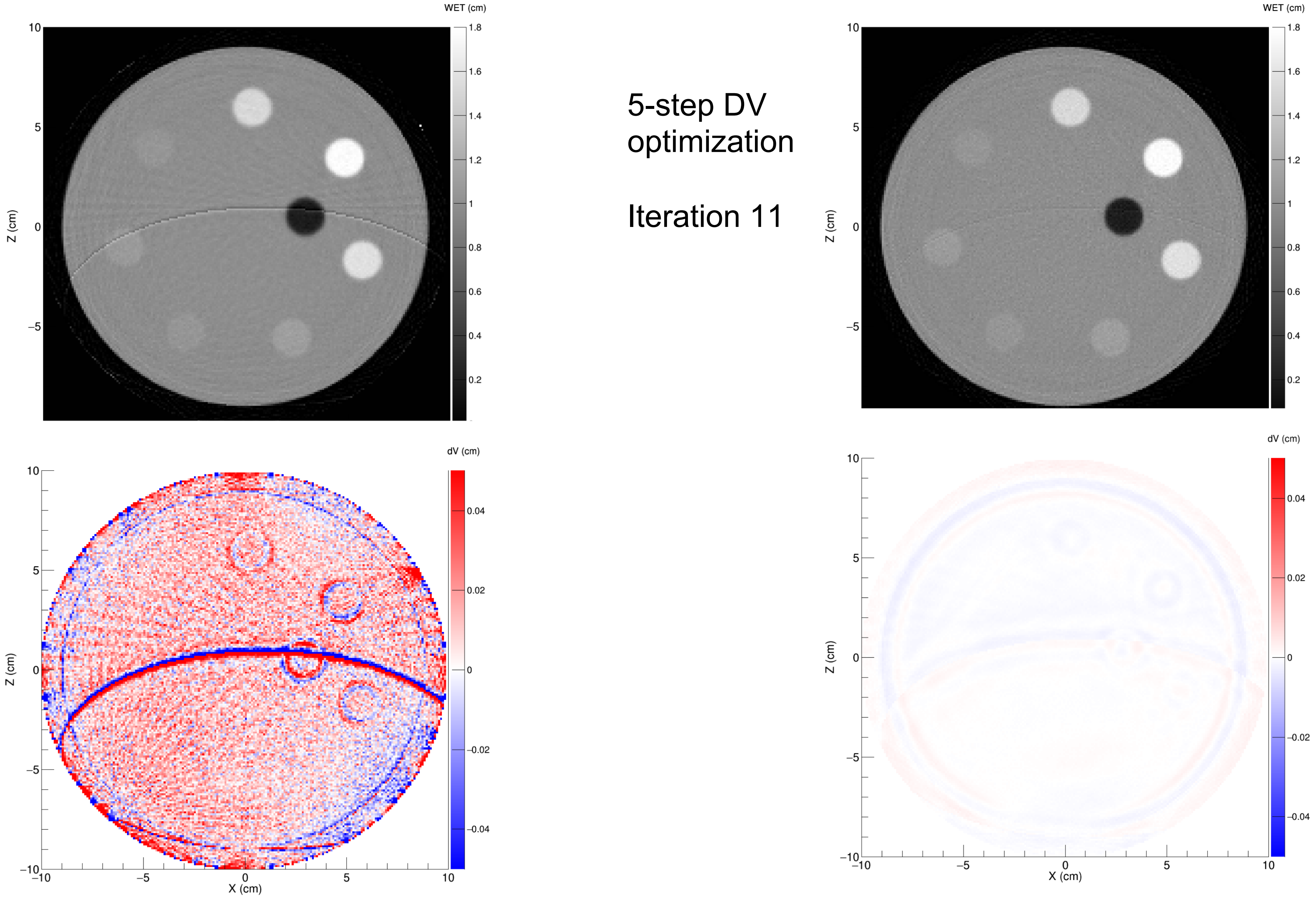


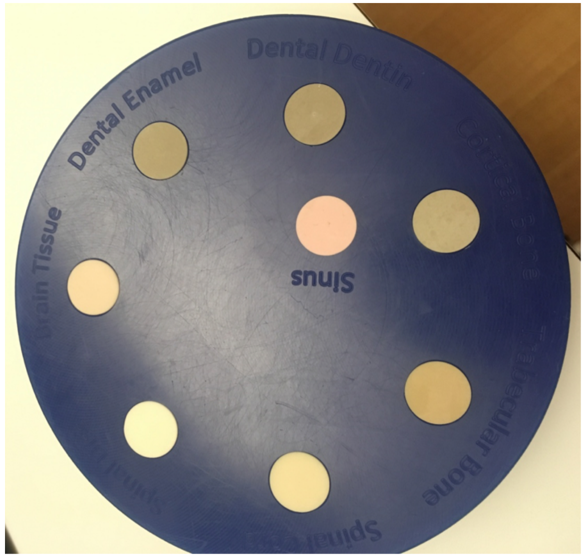
ART
Lambda = 0.002

Iteration 55

5-step DV
optimization

Iteration 11





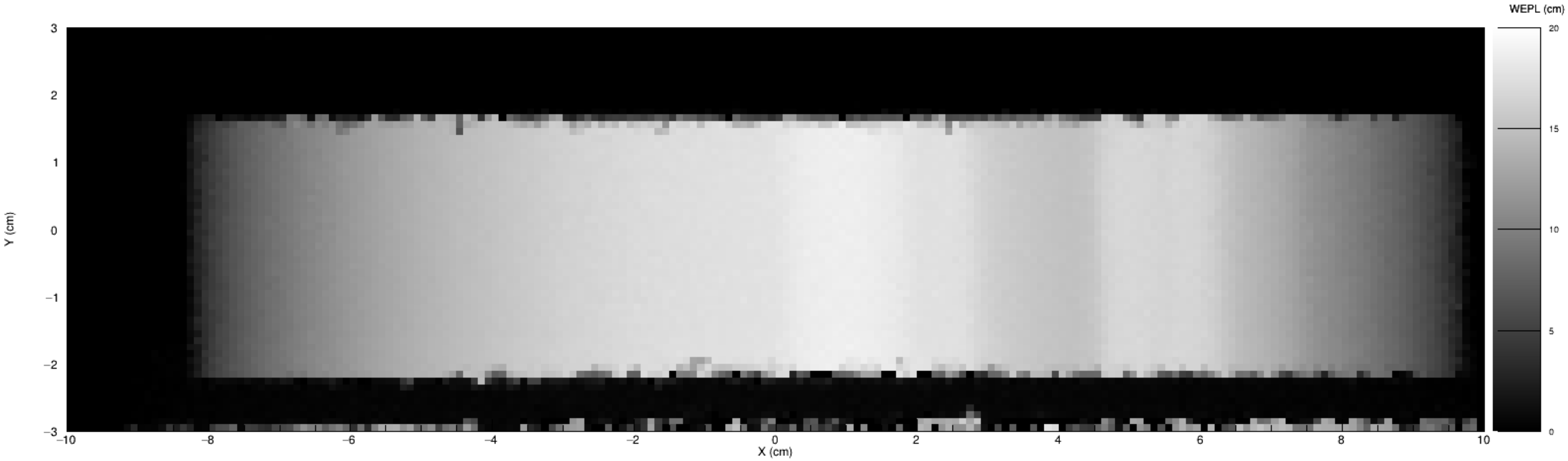
George Phantom pCT data (projections)

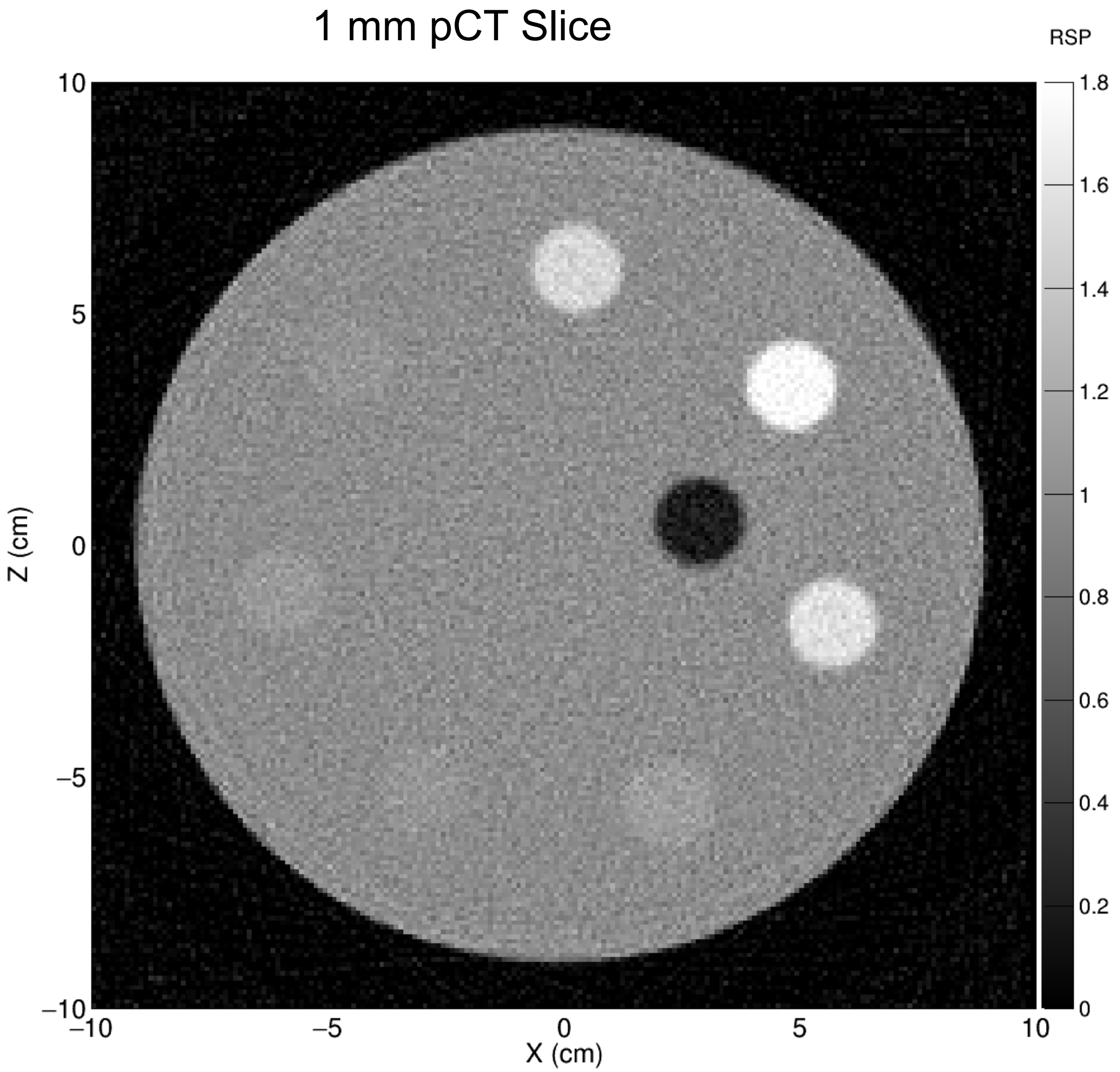
- Made with 3 energies: 195, 160, and 118 MeV

- Data taken every 4 degrees

- 1 mm^3 voxels

- ~20 million protons in final cut

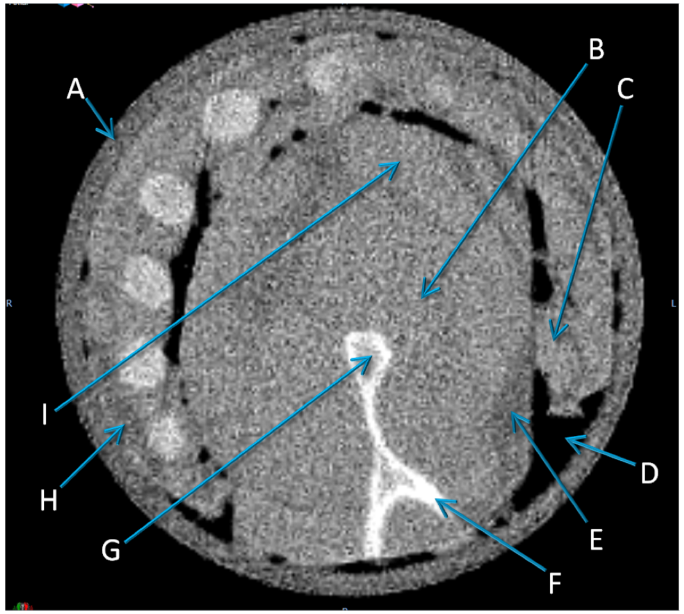




Insert	RSP	RSP from pCT image In ROI for each insert (Statistical uncertainty only)	Difference (pCT – Nominal)
Sinus	0.200	0.192 ± 0.002	-0.008
Enamel	1.755	1.768 ± 0.002	0.013
Dentin	1.495	1.504 ± 0.002	0.009
Brain	1.040	1.043 ± 0.002	0.003
Spinal Cord	1.040	1.046 ± 0.002	0.006
Spinal Disc	1.070	1.079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

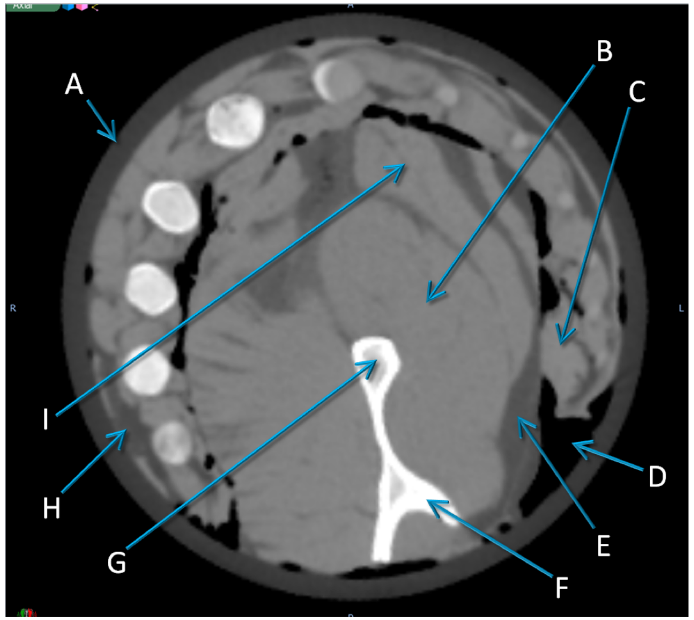
Pork shoulder and ribs
- 4 energies, data taken in 4 degree intervals
- Vertical CT taken for comparison

pCT Slice
(1 mm)



Region	Volume (cm^3)	pCT RSP Mean	SD	SE(%)	x-ray CT RSP	Diff. (%)
Air	3.7	0.017	0.150	15	0.006	64
Adipose (Shoulder)	6.6	0.983	0.086	0.1	0.977	0.6
Adipose (Rib)	1.2	0.965	0.054	0.2	0.967	-0.2
Muscle (Shoulder-Med)	17.5	1.044	0.112	0.1	1.046	-0.2
Muscle (Shoulder-Lat)	25.6	1.043	0.114	0.1	1.043	0.0
Muscle (Rib)	5.8	1.051	0.091	0.1	1.046	0.5
Trabecular Bone (Rib)	1.1	1.120	0.062	0.2	1.141	-1.9
Trabecular (Shoulder)	1.1	1.116	0.082	0.2	1.114	0.2
Compact Bone	0.4	1.467	0.127	0.4	1.568	-6.9
Blue Wax	6.2	0.972	0.114	0.1	0.932	4.1

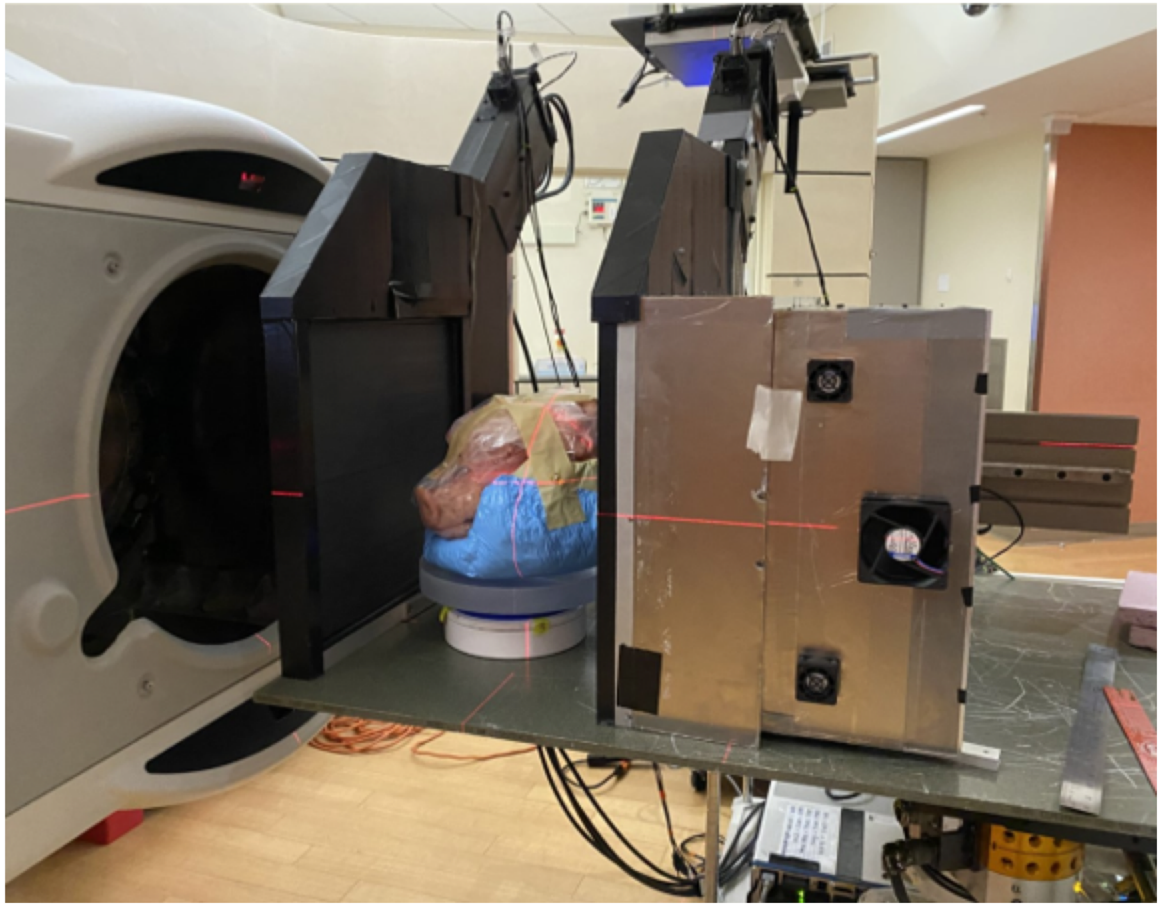
RSP derived
from xCT

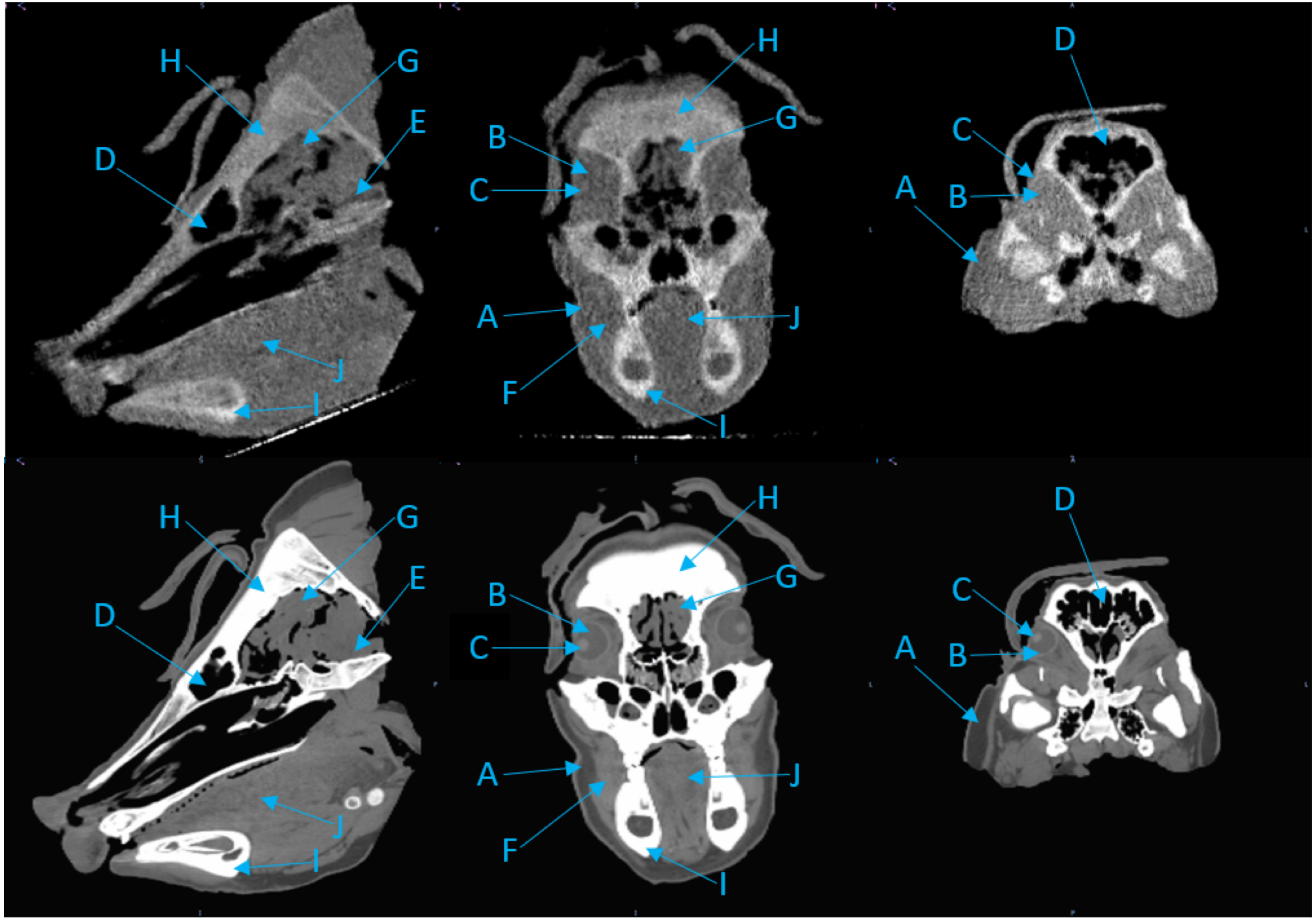


A: Blue Wax
B: Muscle (Shoulder-Med)
C: Muscle (Ribs)
D: Air
E: Adipose (Shoulder)
F: Compact Bone
G: Trabecular Bone (Shoulder)
H: Adipose (Ribs)
I: Muscle (Shoulder-Lat)

pCT of fresh pig's head

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

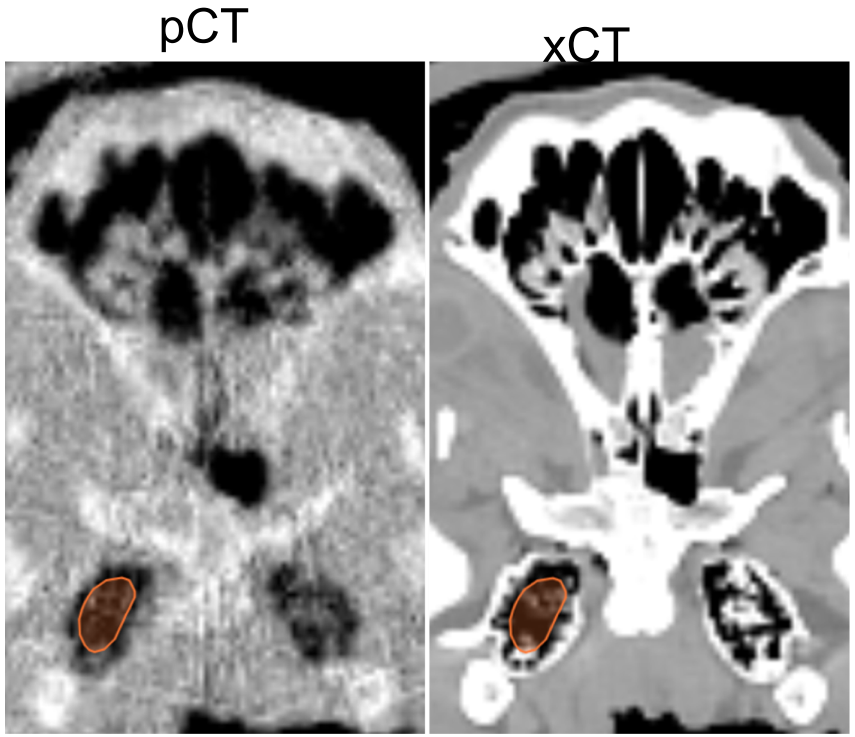




Comparison of tissues between pCT and xCT using 3-D contours

A: Adipose
B: Eye
C: Lens
D: Sinus
E: Brain Stem
F: Muscle
G: Brain
H: Skull
I: Mandible
J: Tongue

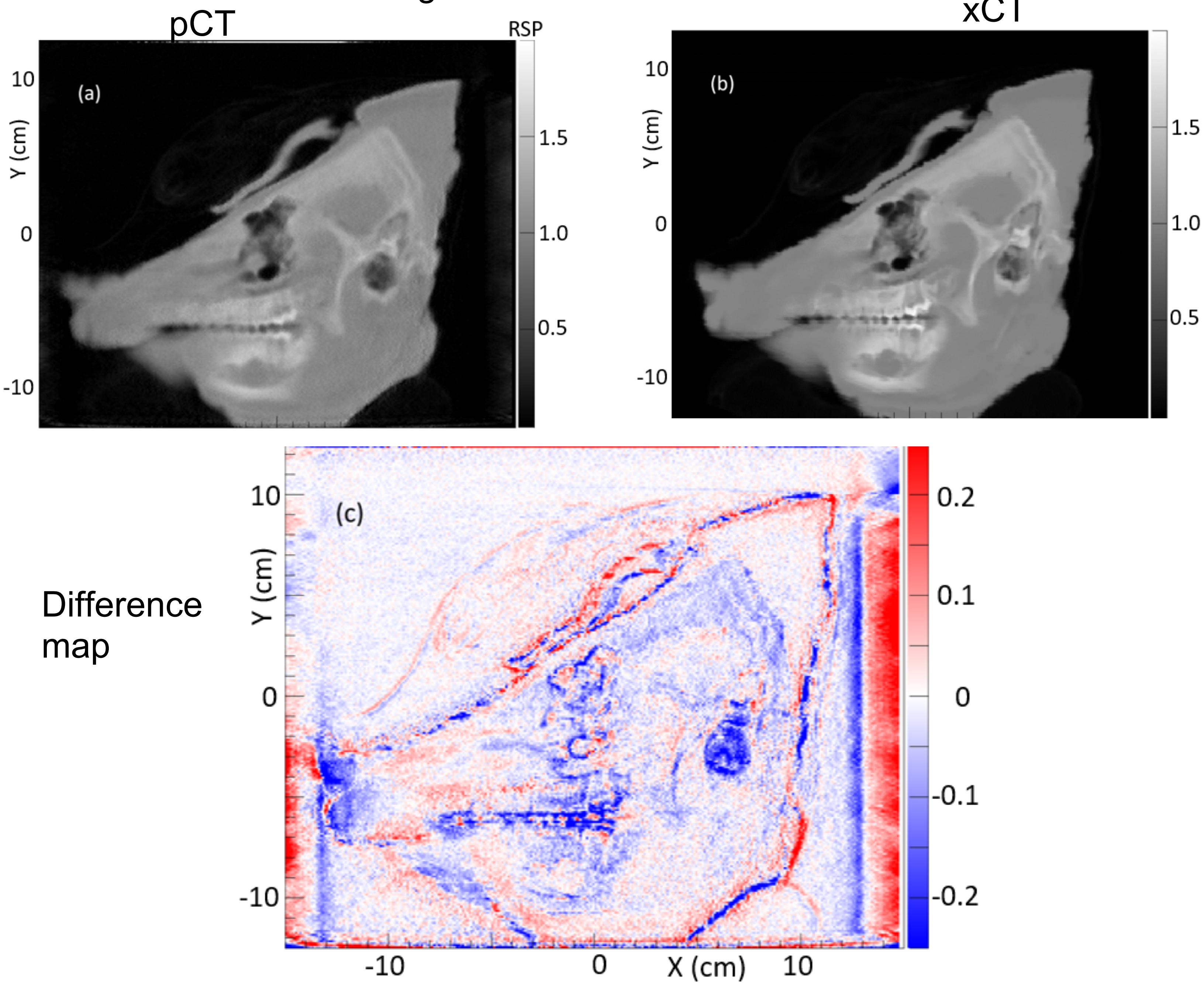
Contours: tympanic bullae

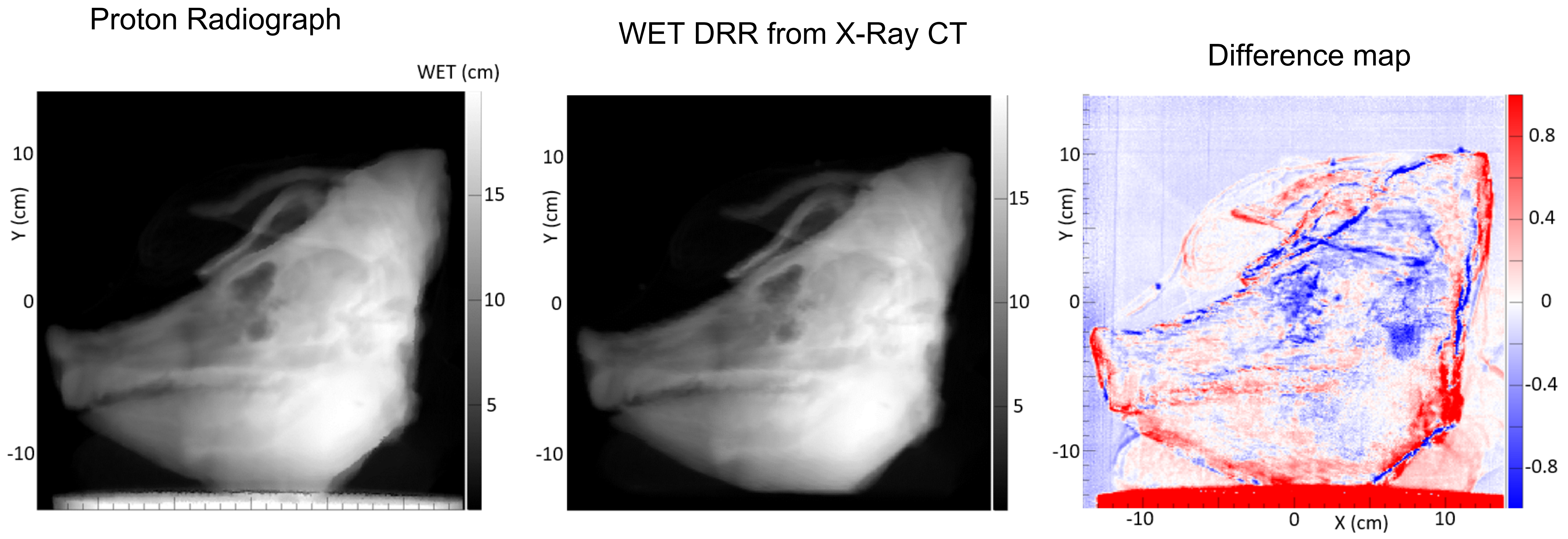


Region	Volume (cm^3)	pCT RSP Mean	SD	SE(%)	Hor CT[a] RSP	Diff (%)	Hor CT[b] RSP	Diff (%)	Vert CT RSP	Diff (%)
Bullae	0.8	0.491	0.24	1.7	0.684	-39.3	0.690	-40.5	0.634	-29.1
Adipose	3.7	0.950	0.14	0.2	0.961	-1.2	0.962	-1.3	0.954	-0.4
Muscle	2.0	1.033	0.16	0.3	1.058	-2.4	1.059	-2.5	1.052	-1.8
Tongue	9.4	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

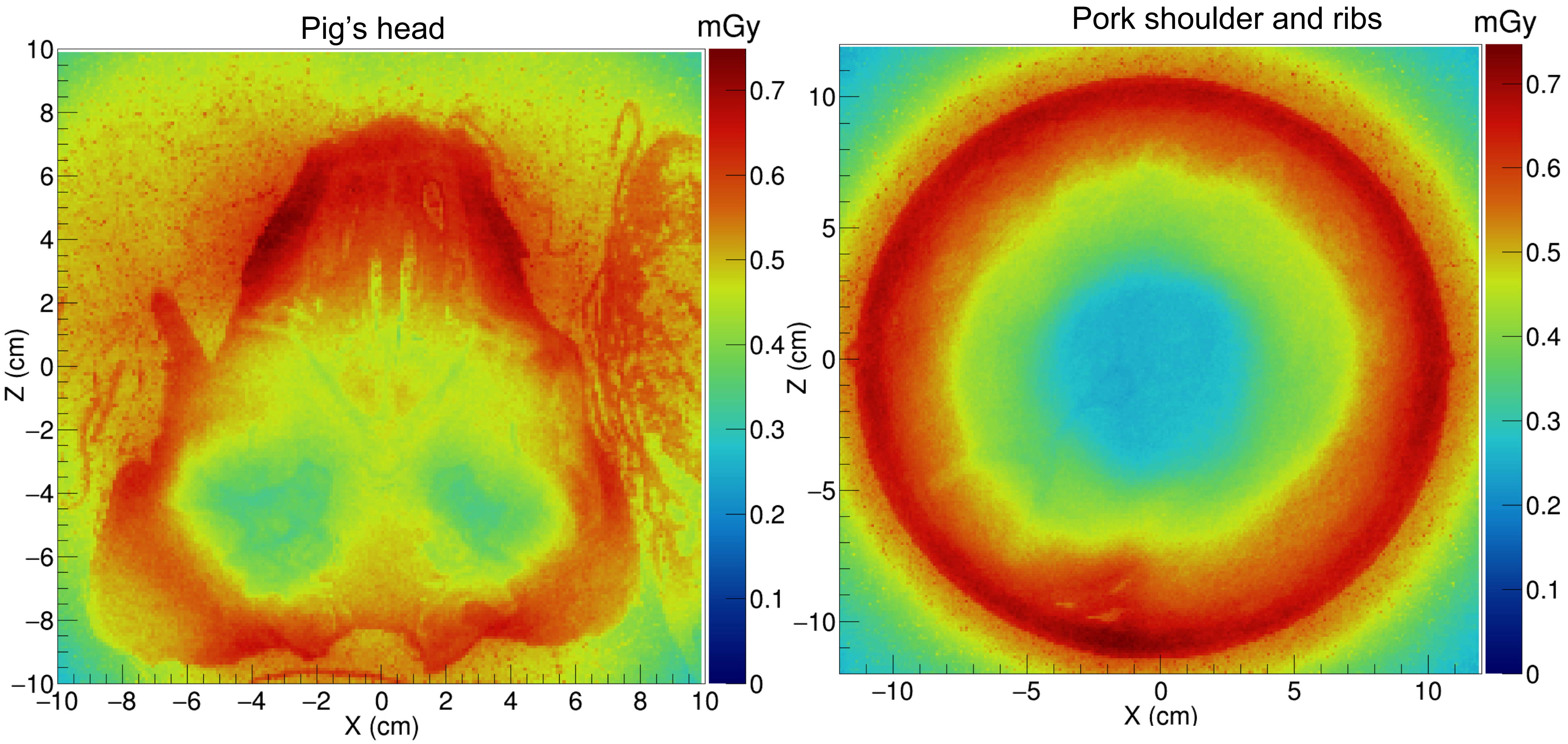
[a] Low dose protocol
[b] High dose protocol

Average of 10 1-mm lateral slices




Proton Radiograph
WET DRR from X-Ray CT
Difference map
WET (cm)
Y (cm)
X (cm)
10
0
-10
15
5
0.8
0.4
-0.4
-0.8

Dose estimation – simulated in TOPAS



Next Steps

- Demonstrate use of pCT with gantry
- Implement fast, automatic pCT reconstruction
- Incorporate optical tracking data to improve spatial resolution
- Perform range measurements in phantoms using film stacks
- Study NTCP benefits of proton imaging (see talk by Andrew Best)