The theory and practical aspects of proton imaging – proton radiography (pRad) and proton tomography (pCT)

Fritz DeJongh, ProtonVDA Inc

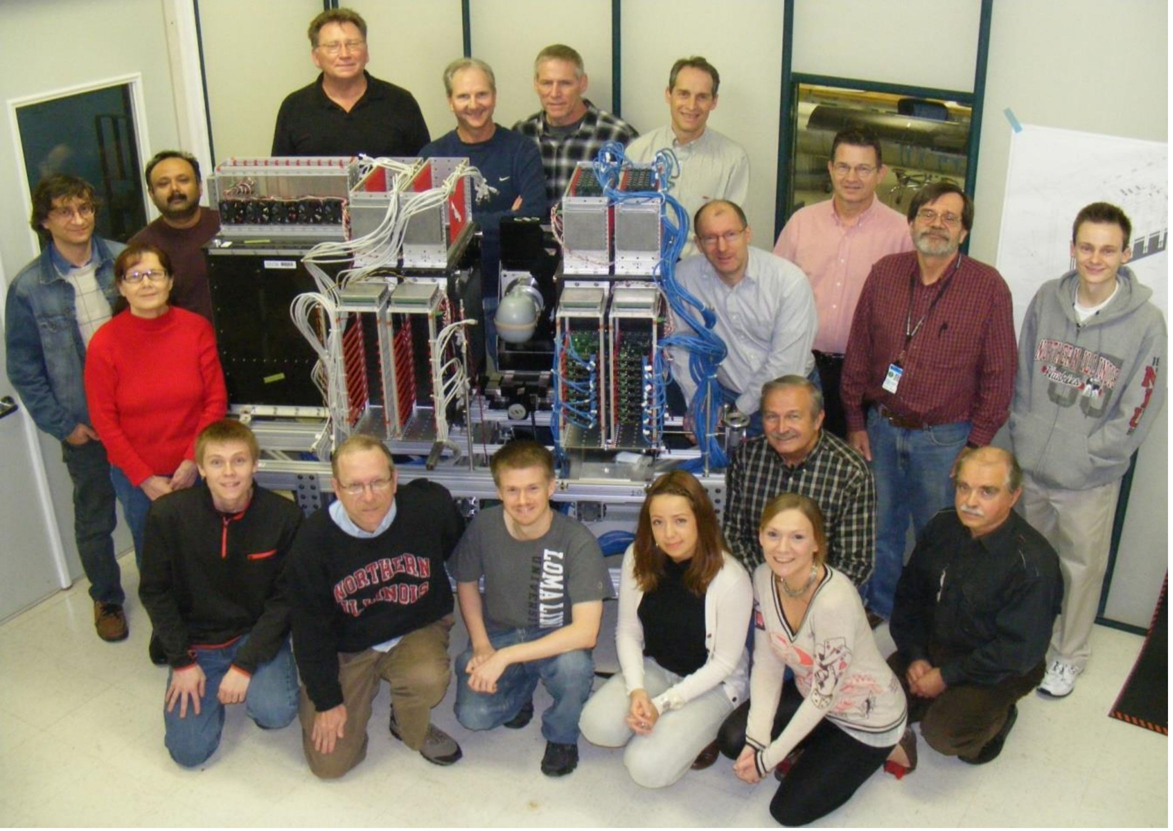
August 30 2018

"Stay away from negative people. They have a problem for every solution."

— Albert Einstein (As cited in Niek's e-mail signature)

"Everything should be made as simple as possible, but no simpler."

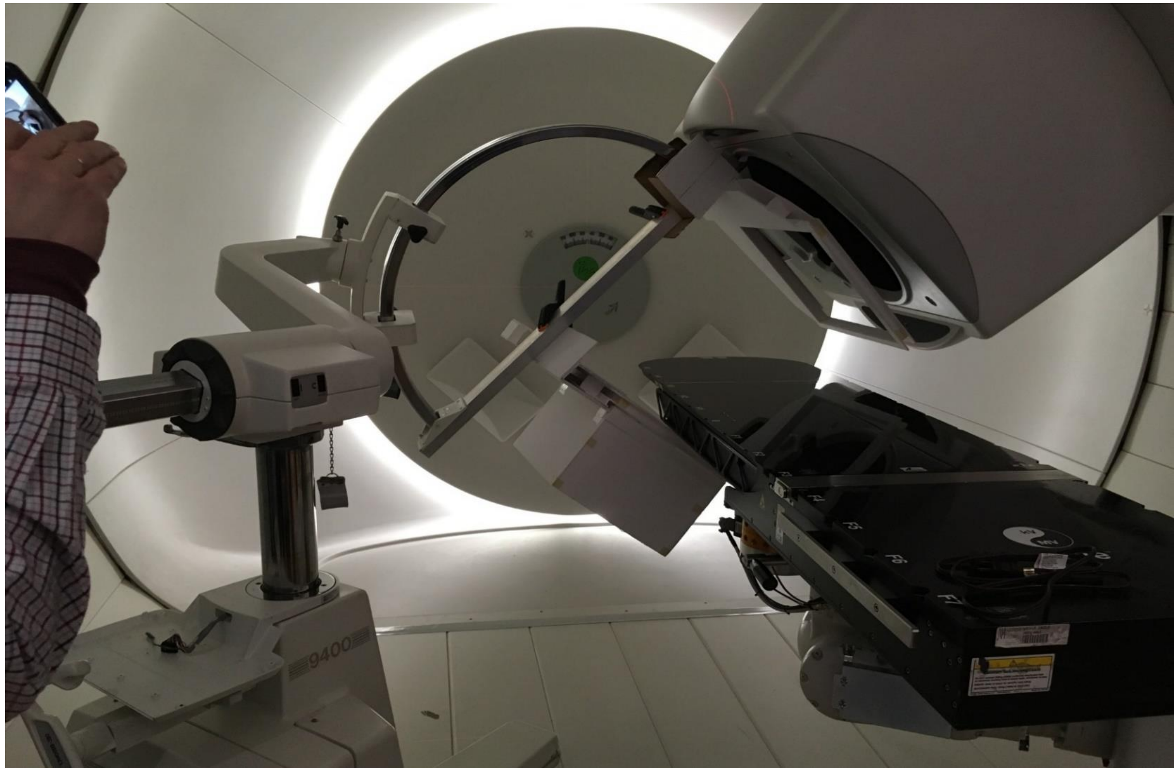
— Albert Einstein (at least, often attributed to him)



NIU – Fermilab project

Goal:
From this

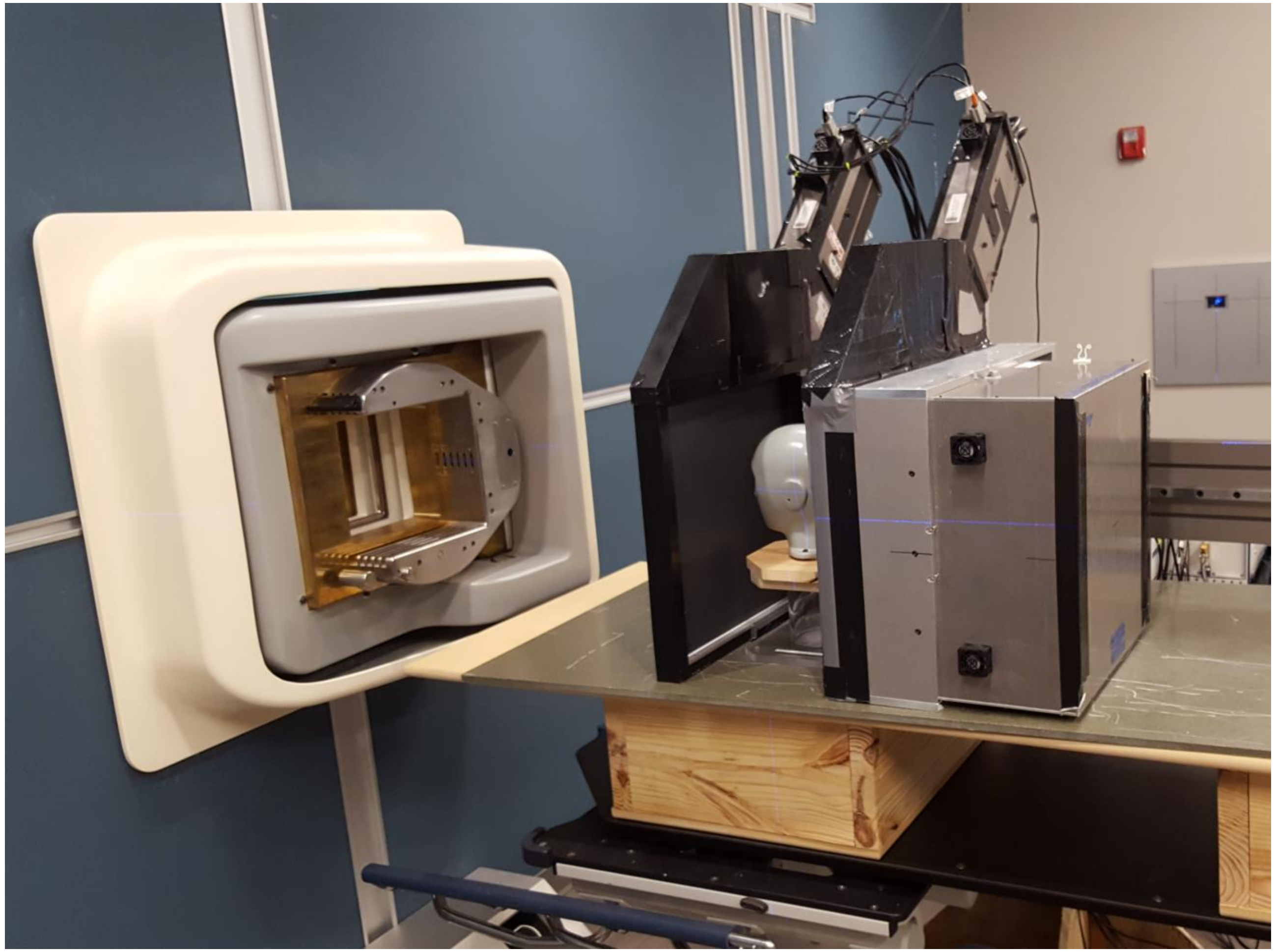
To this (mock up with gantry)

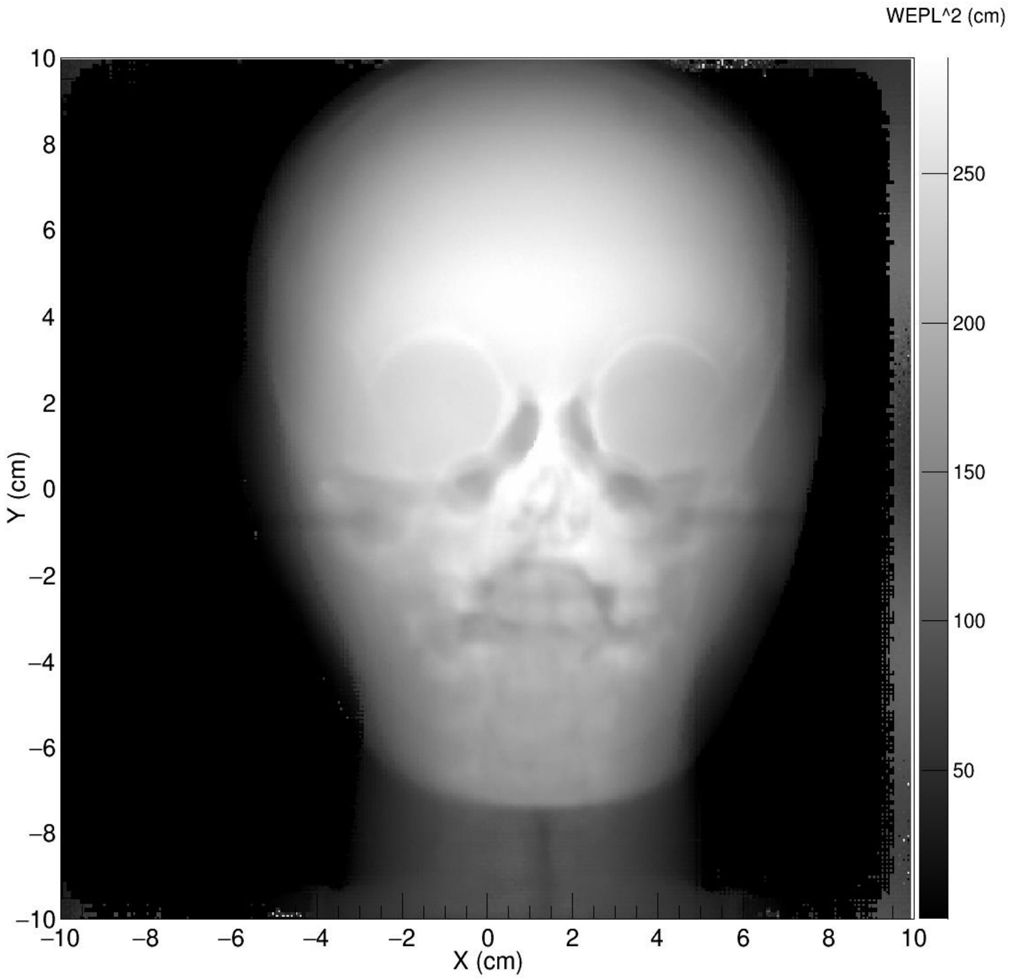


Test with ProtonVDA pRad system and ProNova Knoxville system July 26 and 27 2018

It works! See pRad of pediatric head phantom

Is simple as possible simple enough?





Disclosures

- I am a cofounder and co-owner of ProtonVDA Inc
- We hold intellectual property rights on our proton imaging innovations.
- I am the Principle Investigator on a Phase II SBIR grant from NCI which is funding this work.
- Our goal is to commercialize proton imaging technology and bring it into routine clinical use.

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

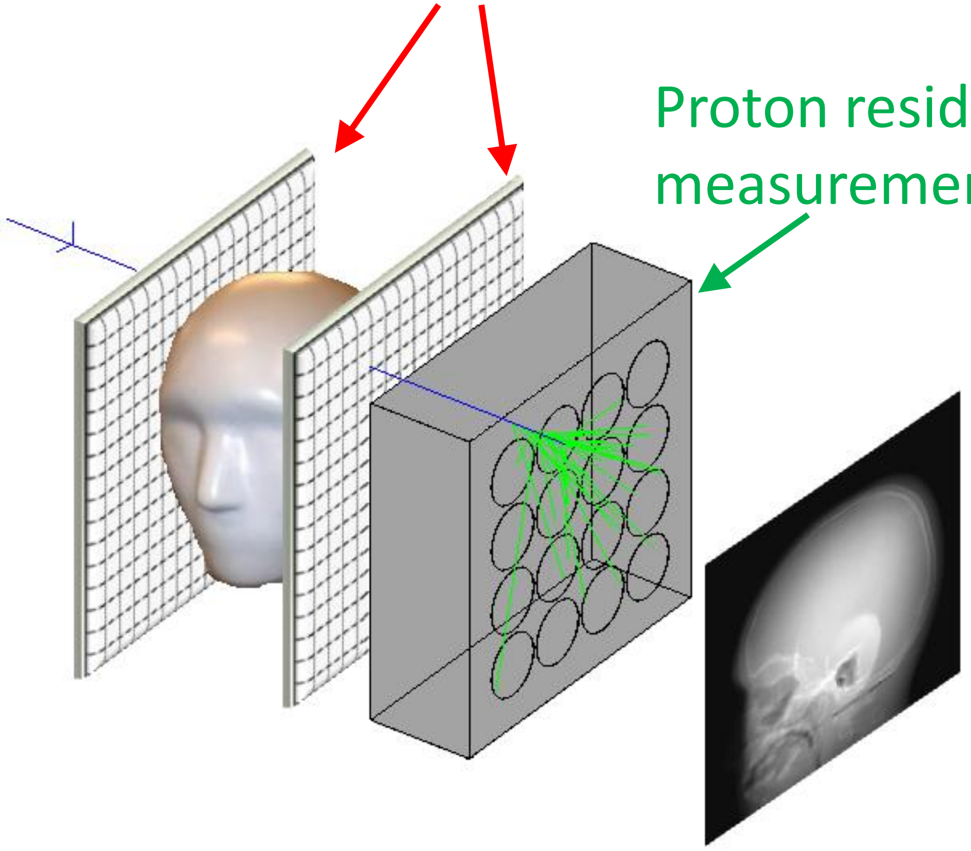
We aim to:

1. Develop a proton imaging system based on well-established fast scintillator technology.
   $\rightarrow$ 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

Principle of Proton Imaging (CT or radiography)

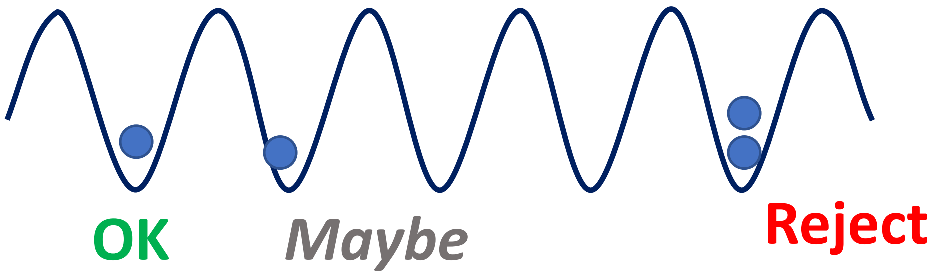


<u>Proton Imaging *immediately* before treatment:</u>
Use protons with enough energy to traverse patient.
Use ultra-low intensity beam (~0.01% of treatment intensity)
- Lower dose than equivalent x-ray image.

<u>Subsequent treatment beam uses:</u>
- Lower energy, protons stop in tumor
- Higher intensity, delivers prescribed dose

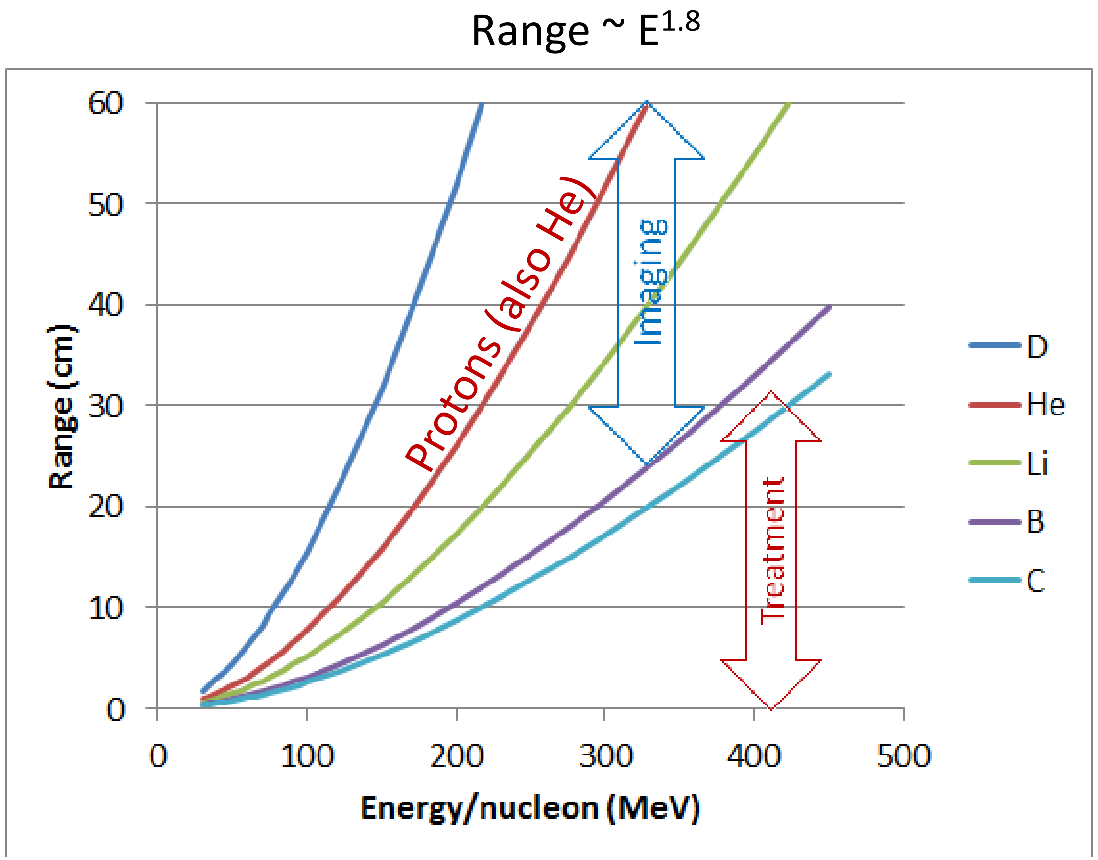
<u>Detector measures individual protons.</u>

Turn down beam intensity to obtain single-proton bunches:
Most bunches will be empty, ~10% will contain one proton.

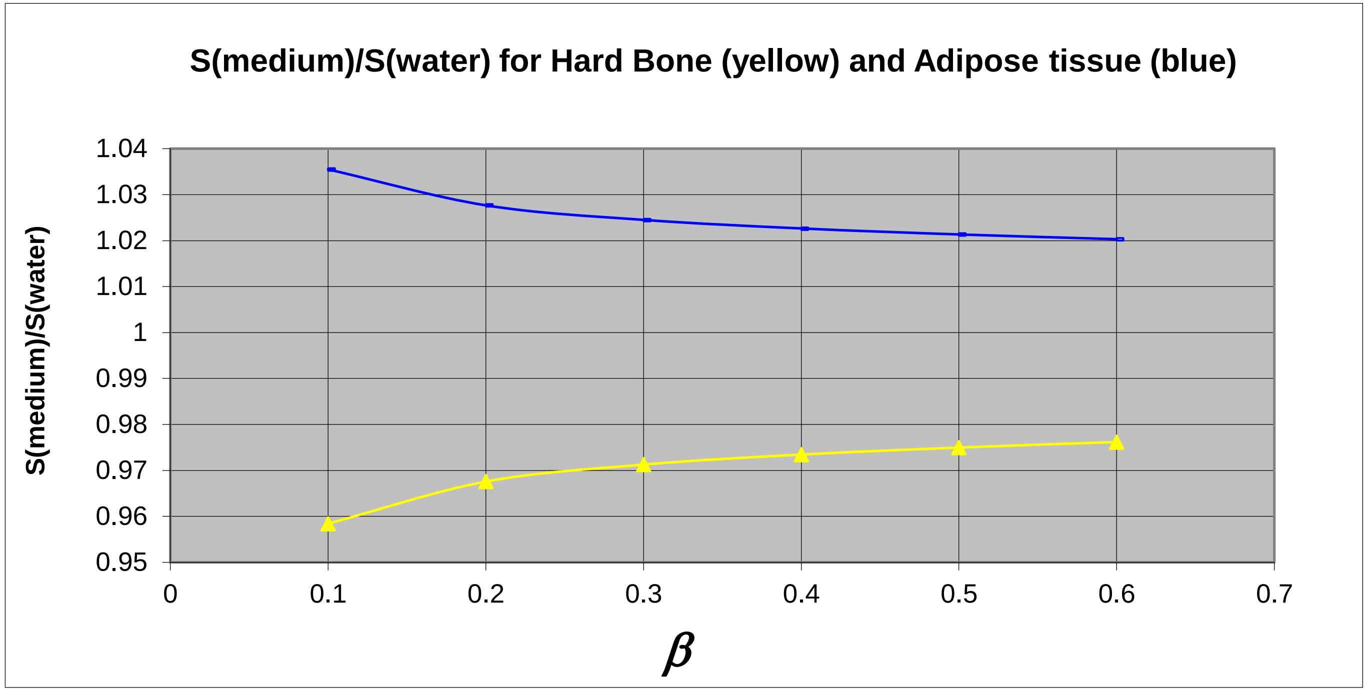


We bring the imager,
the proton radiation therapy center brings the protons

- What is provided by treatment system:
  - Protons with Kinetic Energy calibrated in terms of Range in water
  - Protons delivered in pencil beam scanning system calibrated to steer to given locations in isocenter plane
- What we need for patient treatment planning:
  - 3D map of Relative Stopping Power (RSP): dE/dx in each voxel relative to water to calculate range to tumor $\int(RSP)dx$
- What we need for patient setup:
  - Water Equivalent Thickness (WET) through patient to check for anatomical changes $\int(RSP)dx$
  - Position of patient in isocenter plane.



The Key: RSP has little β dependence



(George Coutrakon)

- Proton imaging measures RSP at higher β without stopping in patient.
- Proton treatment beam *stops* but has little range left where RSP deviates at low β
- $\rightarrow$ Overall range uncertainties < ½ %.

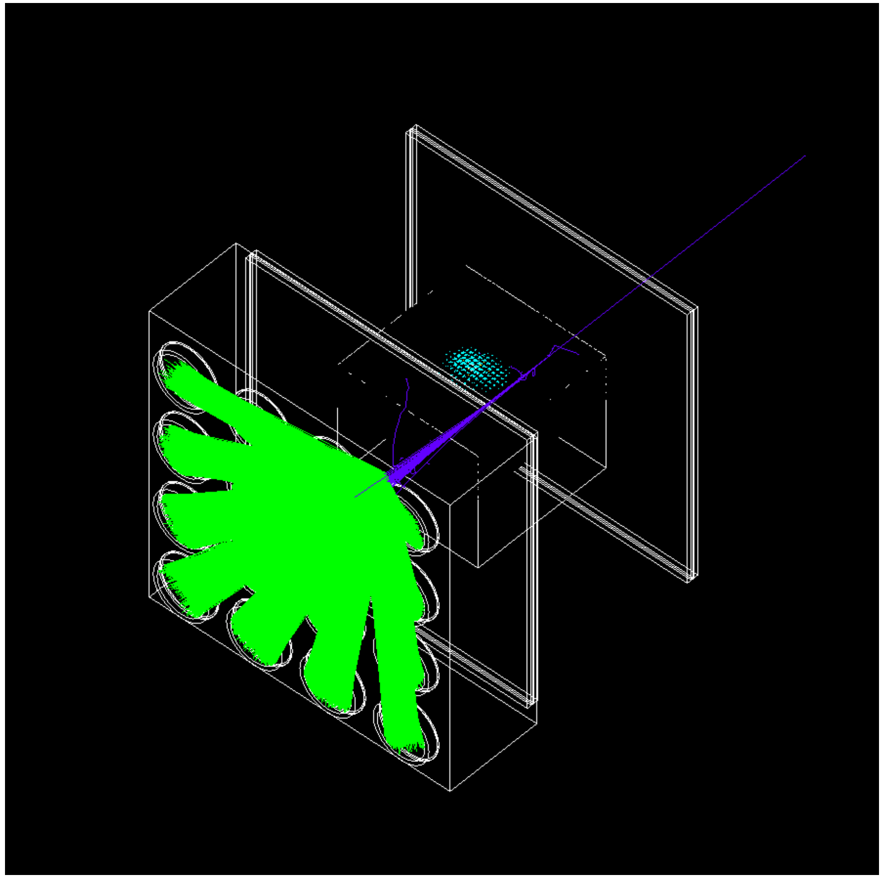
Approaching proton imaging as a fundamental physics measurement.

- Measure trajectory and residual range of protons
- Project onto 2D radiograph, or use tomography to infer 3D RSP distribution.
- Contend with
  - Range straggling
  - Multiple Coulomb scattering
  - Nuclear scattering

- What determines our RSP resolution?
  - How can we get the best resolution with the least dose to the patient?
  - Can we be quantum limited in some sense? Are we getting the most out of each proton?
- What determines our spatial resolution? Hit resolution, MCS, or size of pencil beam?
- Our approach: Measure individual protons as *simply as possible*
- Other approaches integrate ionization from treatment-intensity pencil beam. *Too simple?*

- How can we minimize the time for the measurement?
- How can we scale up the transverse field size to match the pencil beam scanning system?
- How can we fit within the space constraints of the treatment room?

Geant4 Simulation Tool



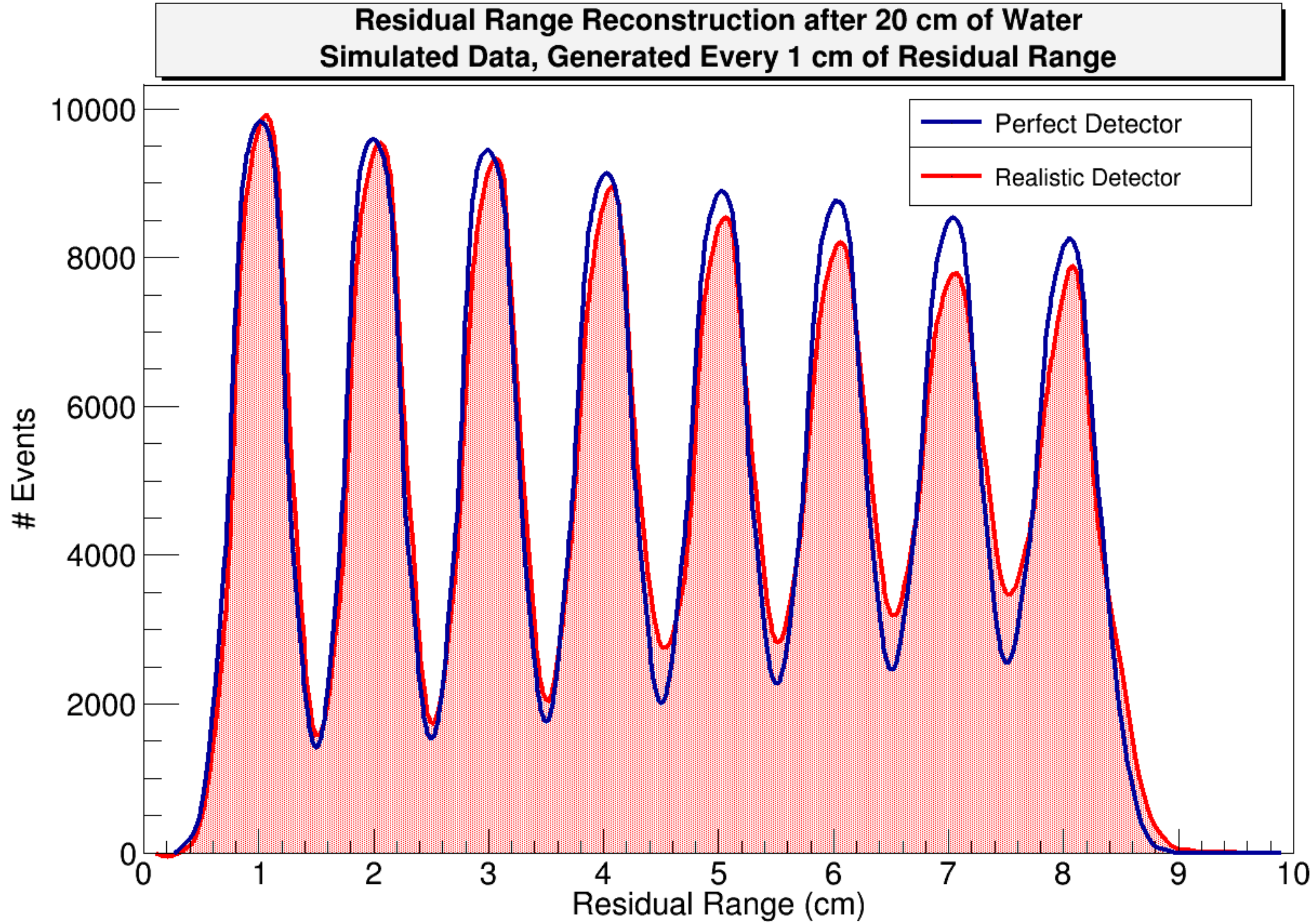
Adjustable Parameters:
- Tracking detector spacing
- Beam source point in x and y directions
- Beam width
- Phantom position and rotation
- Fast vs. slow simulation

- Choice of Phantom:
- Any set of DICOM files
- Water cube with/without material inserts
- Cylindrical phantom with inserts

- Toggle Physics Processes On/Off:
- Multiple Scattering
- Nuclear Interactions
- Range Straggling

- Accelerator Plan:
- Single target, random spread, or scanning pattern
- Single or multiple energies

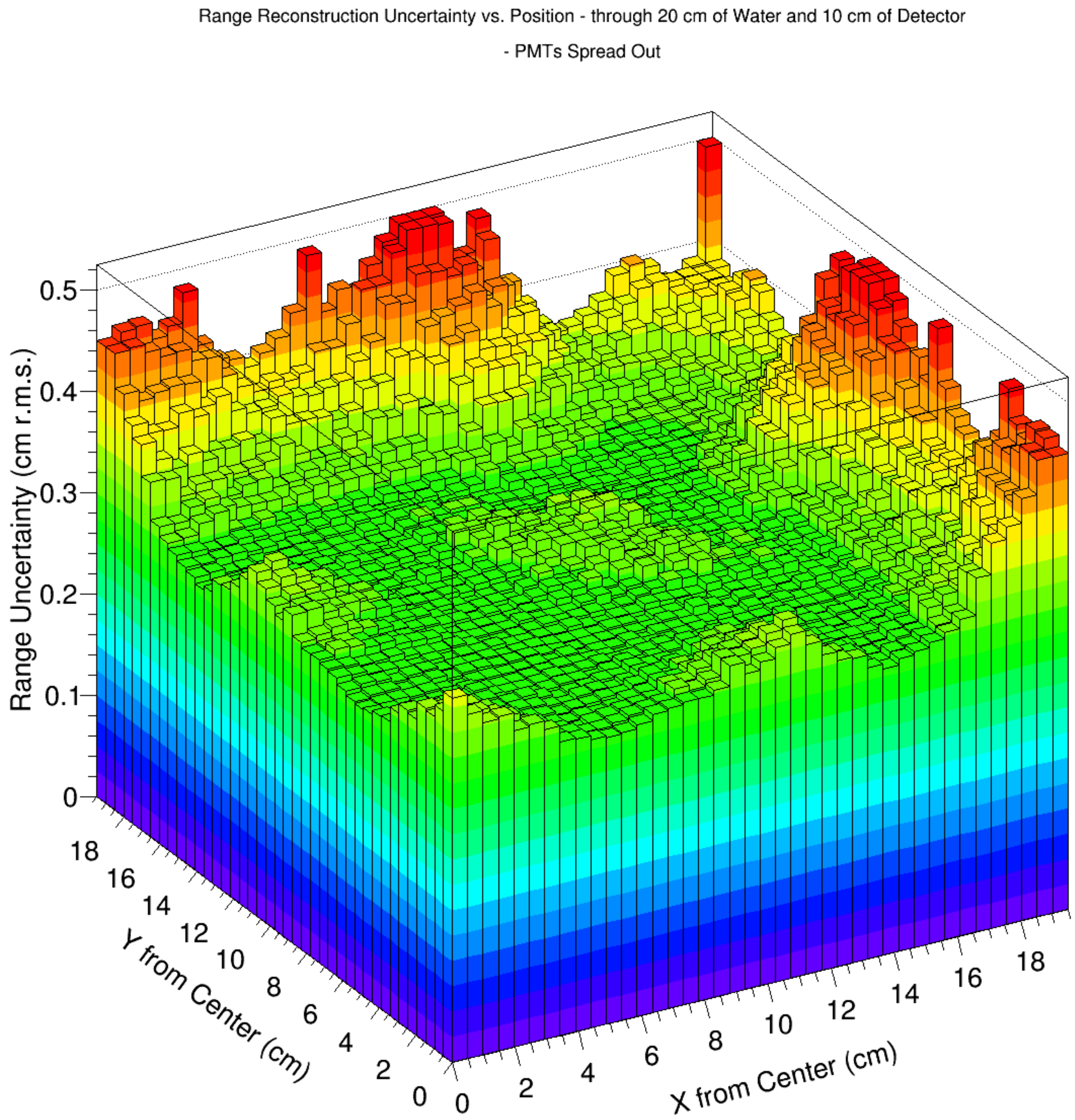
Residual Range resolution vs RR



Intrinsic range fluctuations (“range straggling”) ~3 mm

This sets the performance needs for the detector

Aim for resolution to be dominated by intrinsic fluctuations



Response of the range detector is position dependent.

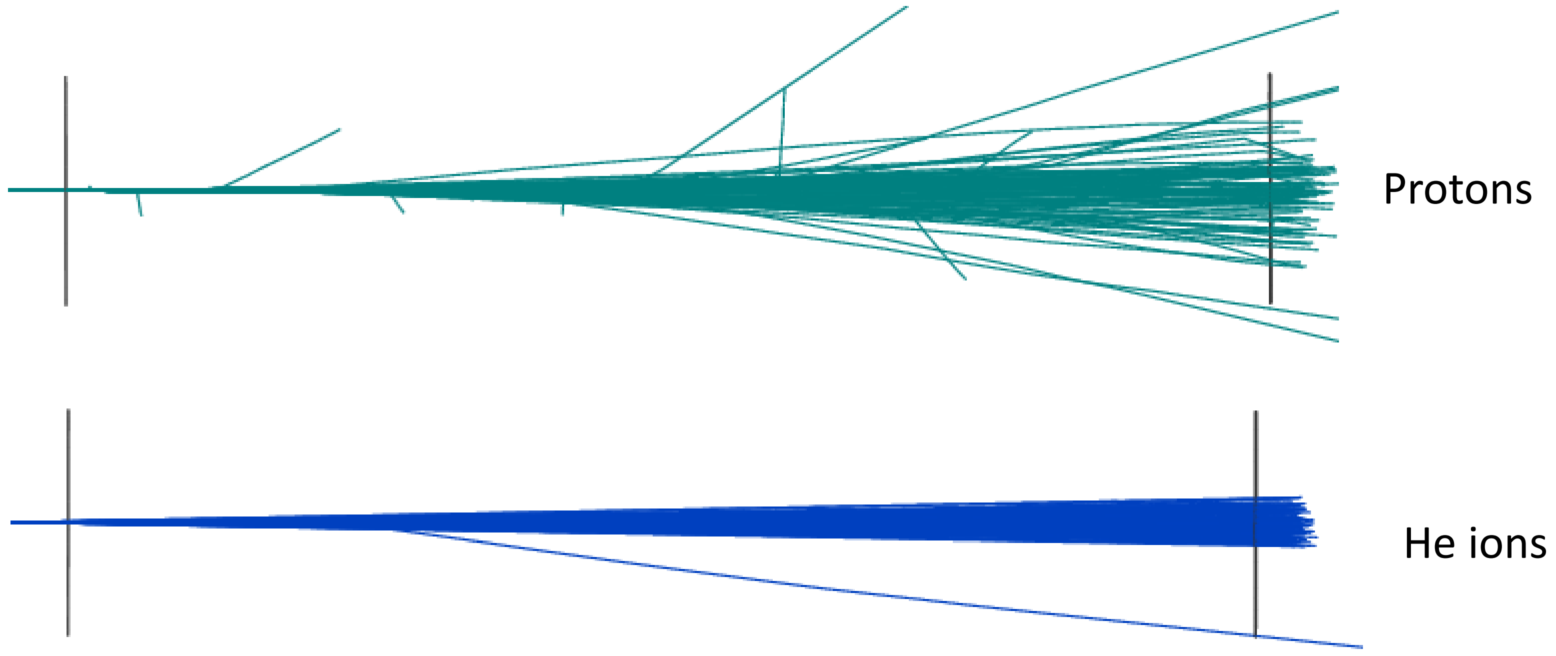
Need to correct for this to obtain Water Equivalent Path Length (WEPL) for each proton

WEPL = input range – residual range

A program call “Weplator” applies corrections from a calibration data set to convert range detector signals to WEPL

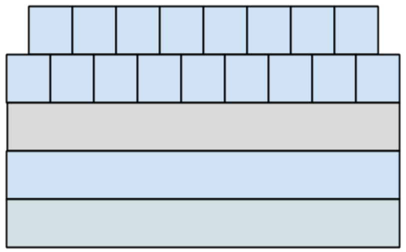
Multiple Coulomb Scattering spreads protons ~4mm after 20 cm water

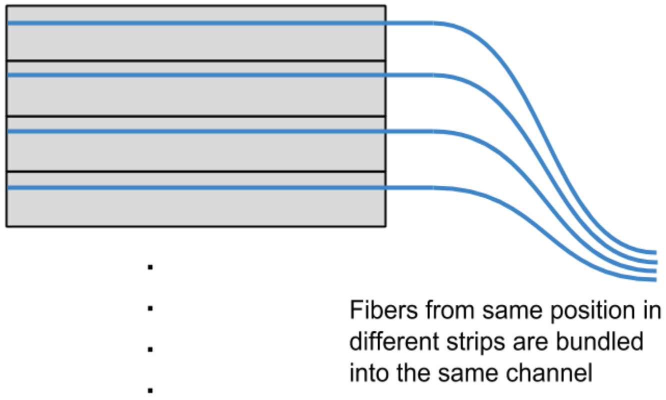
Input direction known from pencil beam scanning system



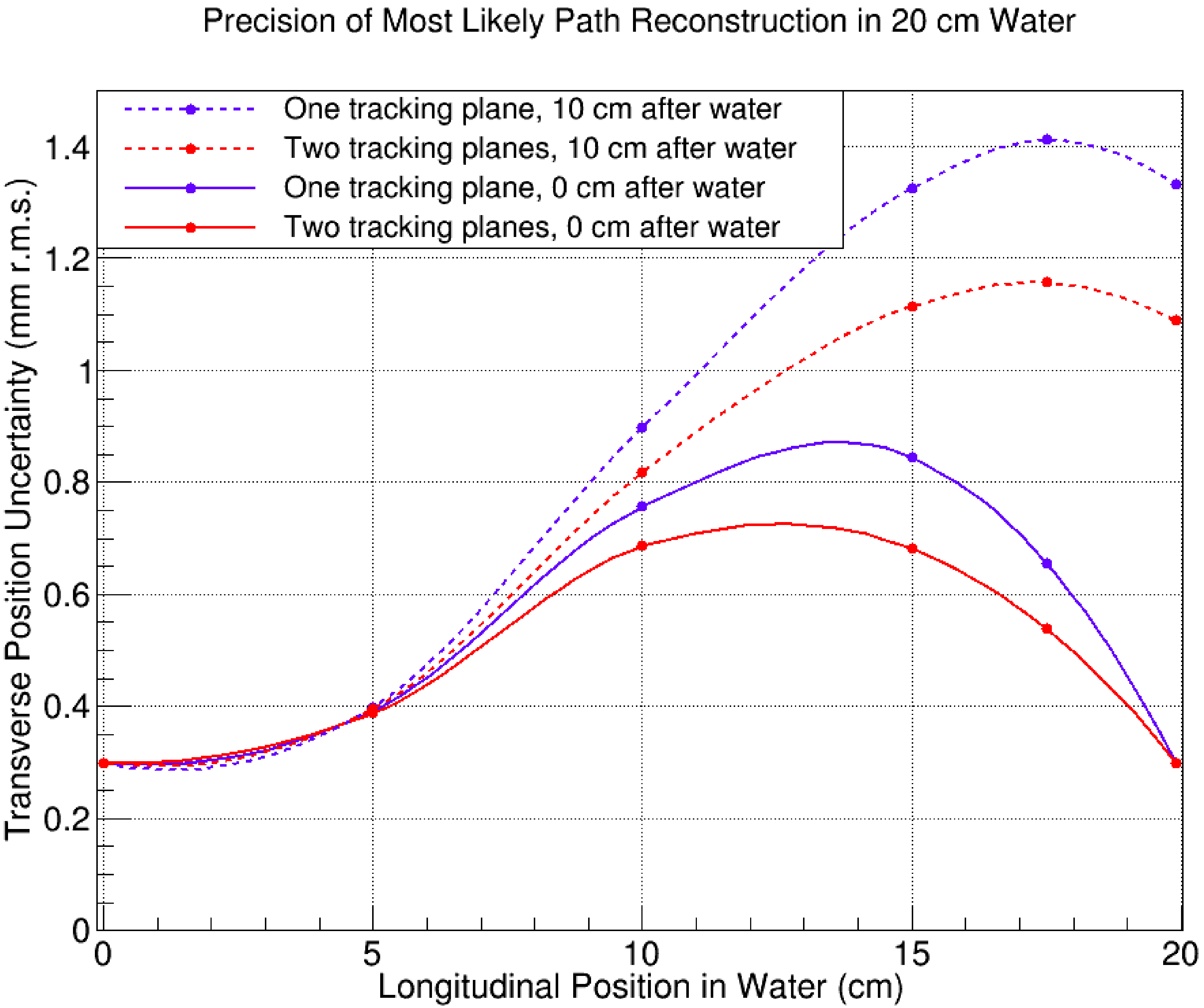
Tracking System Concept

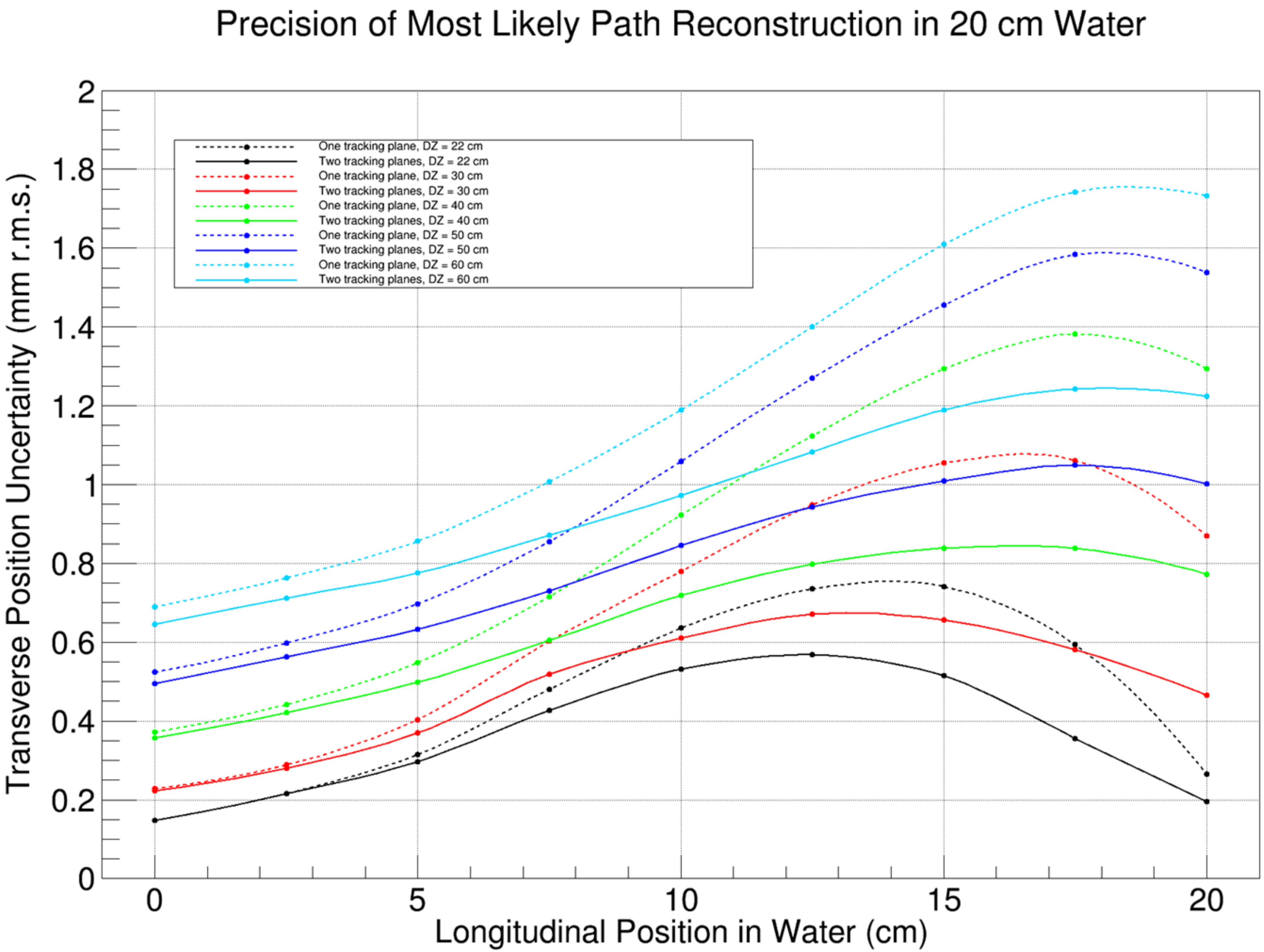
Scintillating fibers and SIPMs





Take advantage of pencil beam system to segment tracker and reduce channel count
Use knowledge of pencil beam to choose correct solution
One X-Y tracking plane can be read out with 64 SIPMs
With simple threshold electronics.


Precision of Most Likely Path Reconstruction in 20 cm Water
One tracking plane, 10 cm after water
Two tracking planes, 10 cm after water
One tracking plane, 0 cm after water
Two tracking planes, 0 cm after water
Transverse Position Uncertainty (mm r.m.s.)
Longitudinal Position in Water (cm)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
0
5
10
15
20



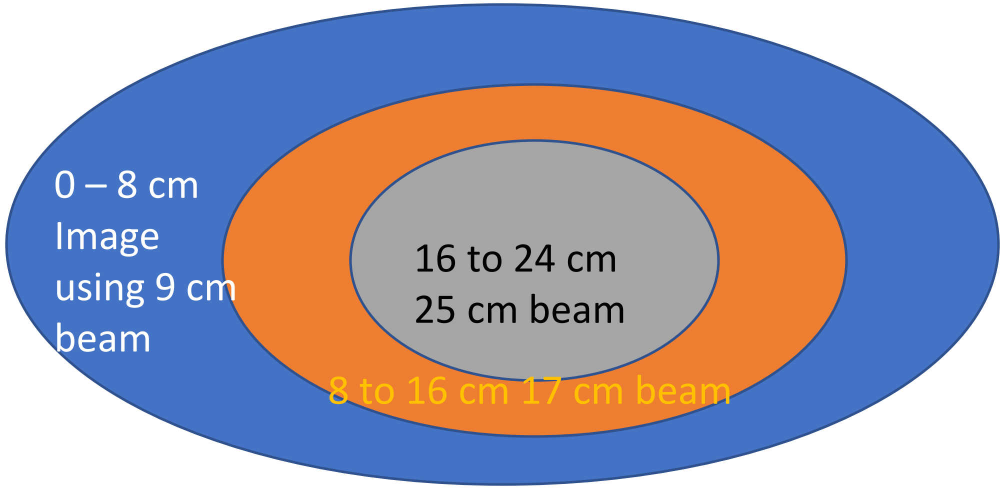
Precision of Most Likely Path Reconstruction in 20 cm Water
Transverse Position Uncertainty (mm r.m.s.)
Longitudinal Position in Water (cm)
One tracking plane, DZ = 22 cm
Two tracking planes, DZ = 22 cm
One tracking plane, DZ = 30 cm
Two tracking planes, DZ = 30 cm
One tracking plane, DZ = 40 cm
Two tracking planes, DZ = 40 cm
One tracking plane, DZ = 50 cm
Two tracking planes, DZ = 50 cm
One tracking plane, DZ = 60 cm
Two tracking planes, DZ = 60 cm
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
0
5
10
15
20

Establish Requirements

1. *Range resolution of 1 mm or better per pixel (1 x 1 mm^2)*
   a. Residual range resolution of 3 mm *per proton*. (An image averages many protons per pixel)
   b. $\rightarrow$ Resolution dominated by intrinsic fluctuations (For 20 cm WEPL).
   c. $\rightarrow$ Optimizes Dose / Resolution (< 0.01 cGy for an image)
2. Measure 10 million protons / second, resolving individual protons as close as 20 nsec.
3. Specialize for pencil beam scanning systems.
   a. Image and treat with same system.
   b. Challenge: Protons sequentially hit same region of detector. *Fast scintillator can handle it!*
4. Use pencil beam system to maintain low residual range across field of detector.
   a. More optimal for dose.
   b. Keeps range detector thin.
   c. Reduces cost and complexity of the detector.
5. Proton transverse position resolution (“hit” resolution) of 0.3 mm or better in the tracking detectors.
   a. Multiple scattering limits spatial resolution.
   b. *$\rightarrow$ Spatial resolution ~0.5 to 1 mm*

Requirements continued

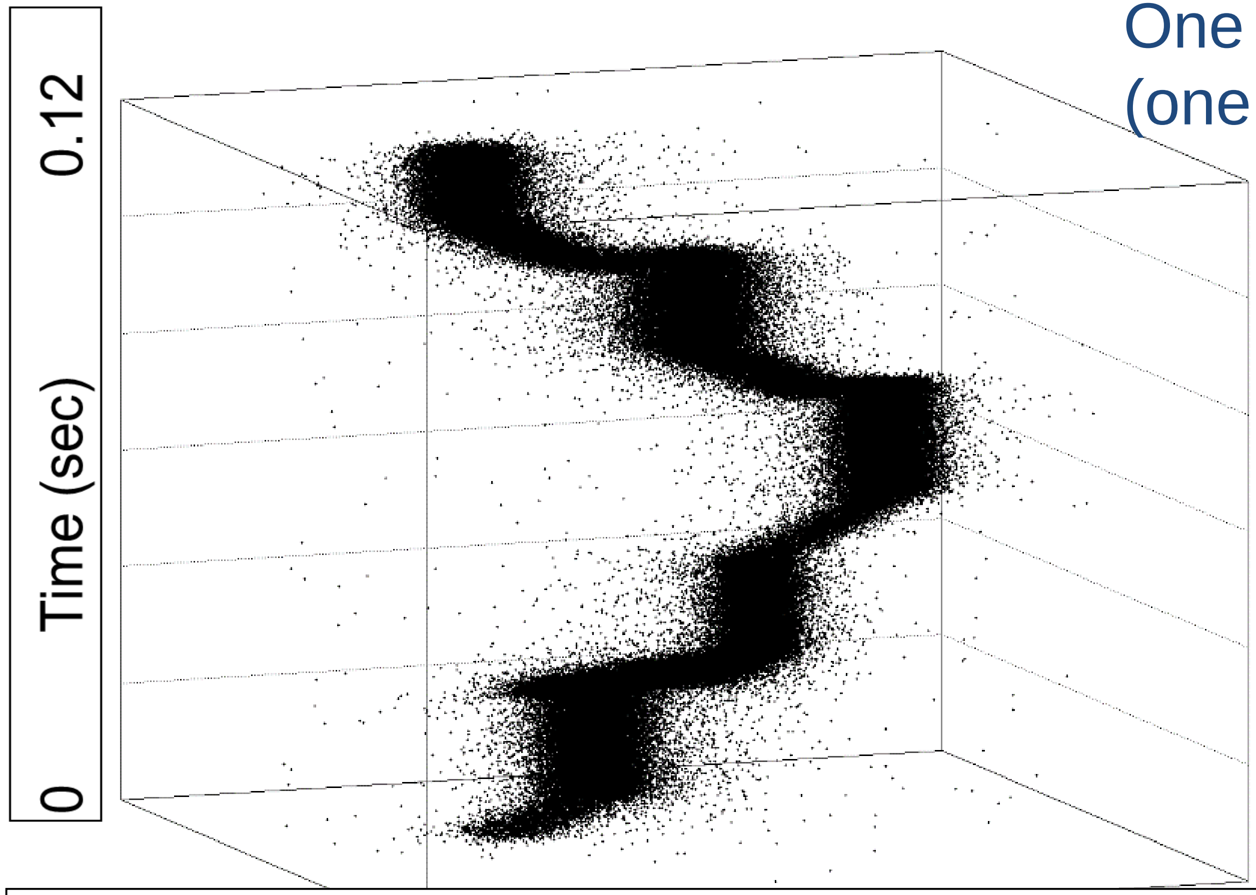
- Use pencil beam scanning system to divide the field for the proton radiograph into regions
  - different proton energy settings for each region based on the estimated range in that region (from a previous x-ray CT scan).
  - Set a low residual range for the protons in each region.
  - Benefits:
    - The residual range detector can be thinner, saving on weight and volume in the treatment area, and making the read-out easier.
      - **Our detector will have a depth of 10 cm.**
    - The lower total range for the protons is more optimal for range resolution relative to dose.
    - Lower range also results in fewer protons lost to nuclear interactions, which also results in lower dose for a given image quality.



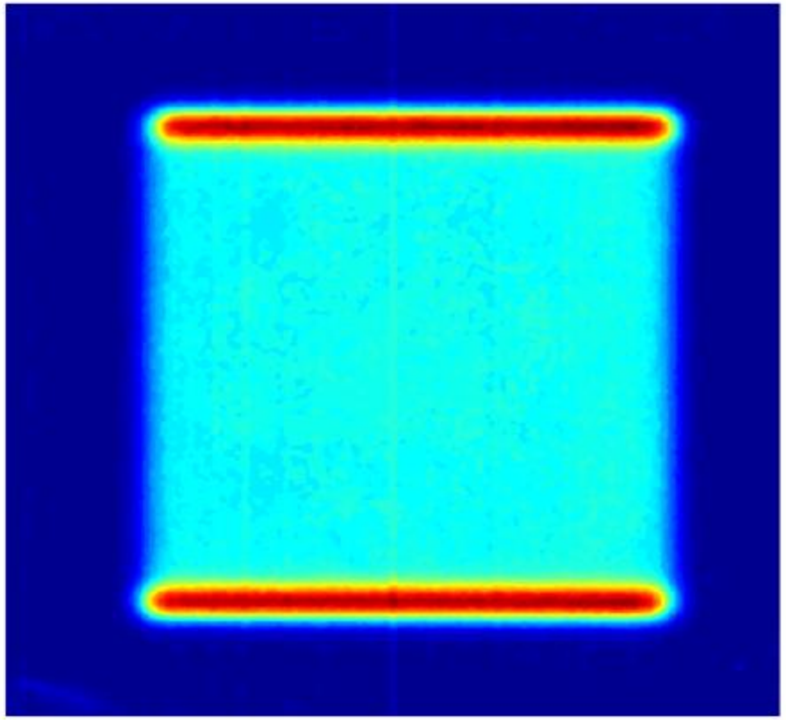
Test beam results

Northwestern Proton Center:
Scanning pencil beam at ultra-low intensity

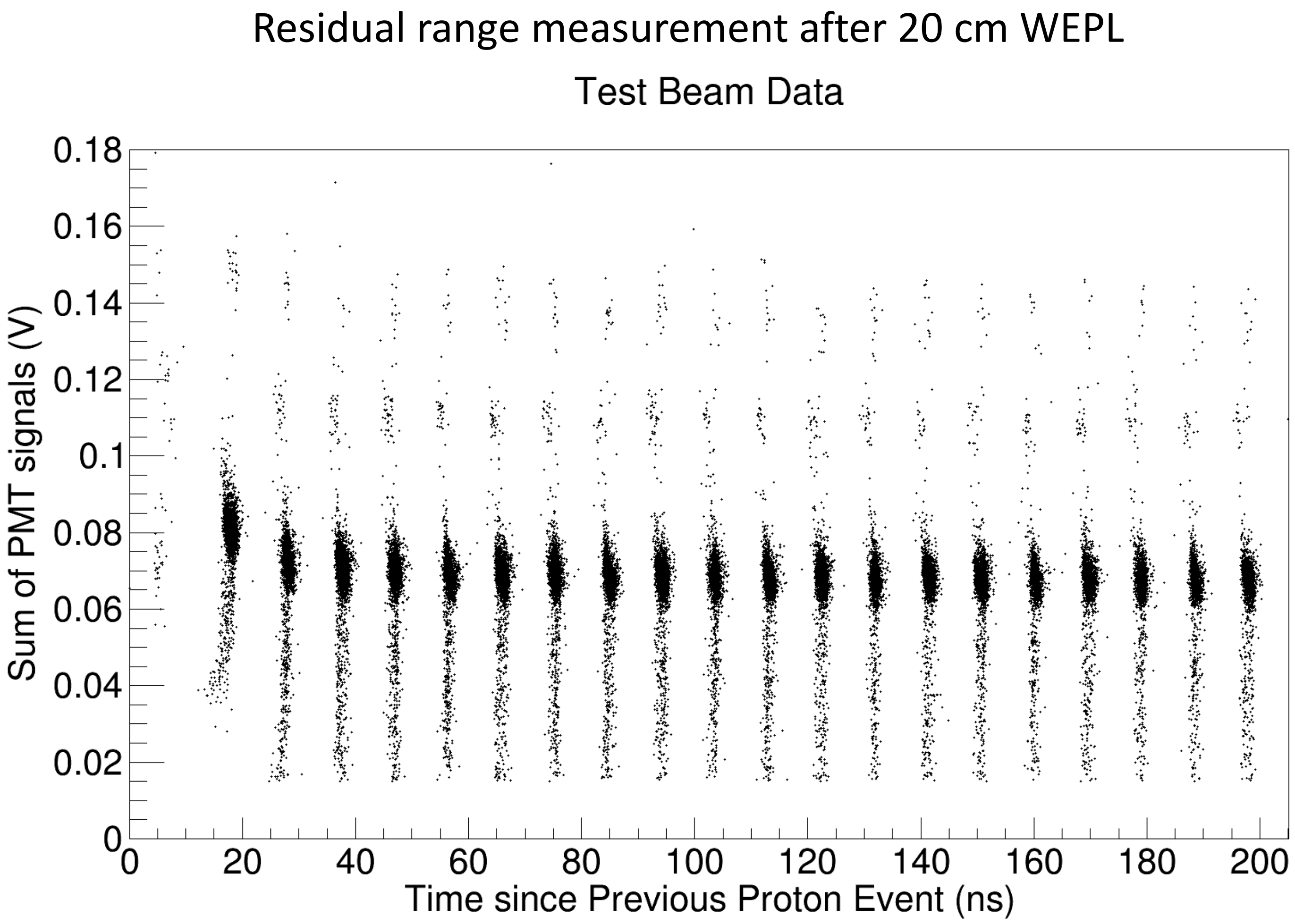
One dot = one proton
(one million total in image)



Transverse position from two position-weighted PMT outputs



Pencil beam scan pattern provides uniform coverage over 20 x 20 cm^2 in 0.3 sec

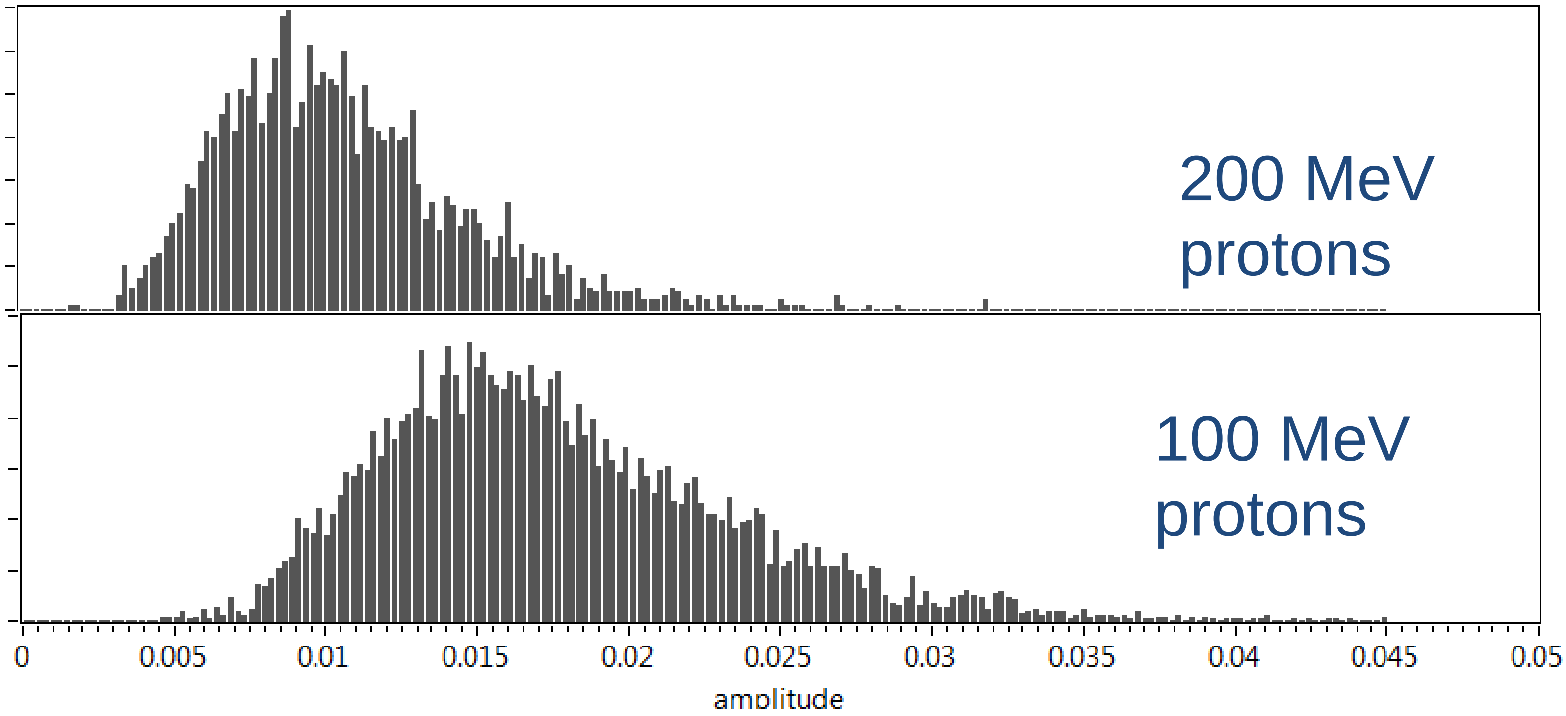


- One dot = One proton
- Time differences are quantized from RF accelerator system.
- Clusters around 0.07V are single proton events.
- Clusters at 0.14V are two-proton events.
- Clusters at 0.11V are from protons sitting on a tail of a proton 10 nsec earlier.
- Nuclear scatter events fall below 0.07V.

Windowing algorithms select events from main cluster and reject nuclear scatters

Scintillating fibers enable high tracking efficiency

Measured hit efficiency in Northwestern beam ~100%



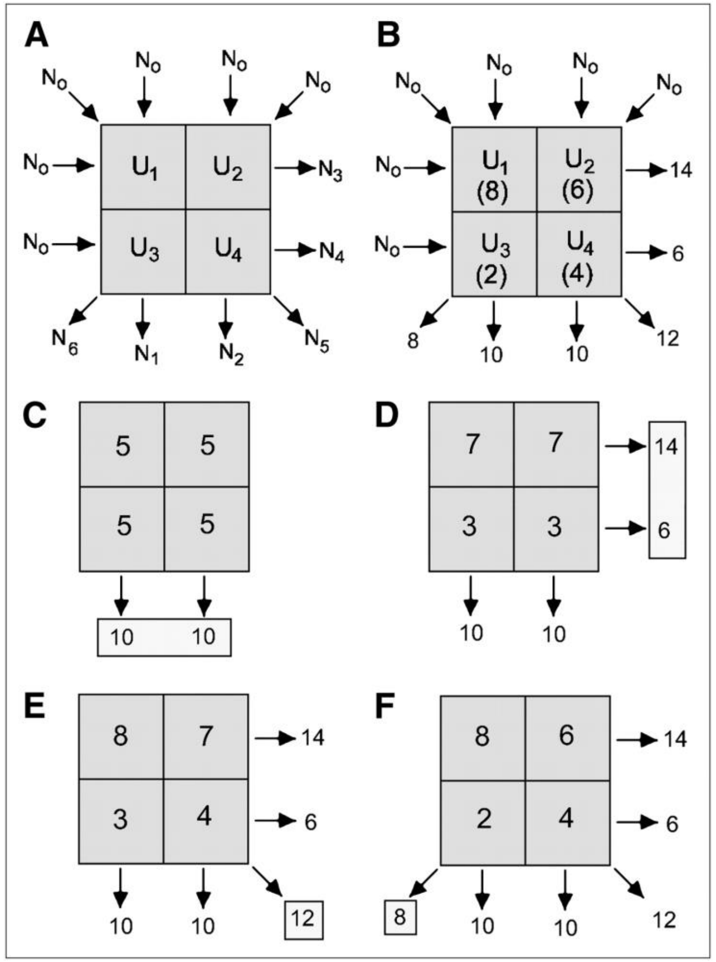
Histograms show pulse height spectrum

Our electronics and DAQ set a threshold and read out a bit per channel

Implementing pRad image reconstruction in CPU-GPU desktop computer using iterative algorithms

- Goal: Automatically acquire data and deliver imaging in < 1 minute. Program must:
  - Align detector to beam scanning system using "test pattern" of spots at start of scan.
    - Enables direct reconstruction of image in isocenter coordinates.
      Essential for pre-treatment verification of alignment
      Pixels in pRad represent projections along beam directions diverging from focal points.
  - Convert tracker hits to track positions in isocenter coordinates.
  - Convert range detector signals to residual range
  - Use Initial K.E. to obtain WEPL. Enables integrated range check through patient.
  - Choose an initial approximation to the image.
  - Find the path of each proton between the planes.
  - Iteratively adjust image to fit protons.

Illustration of Iterative Reconstruction



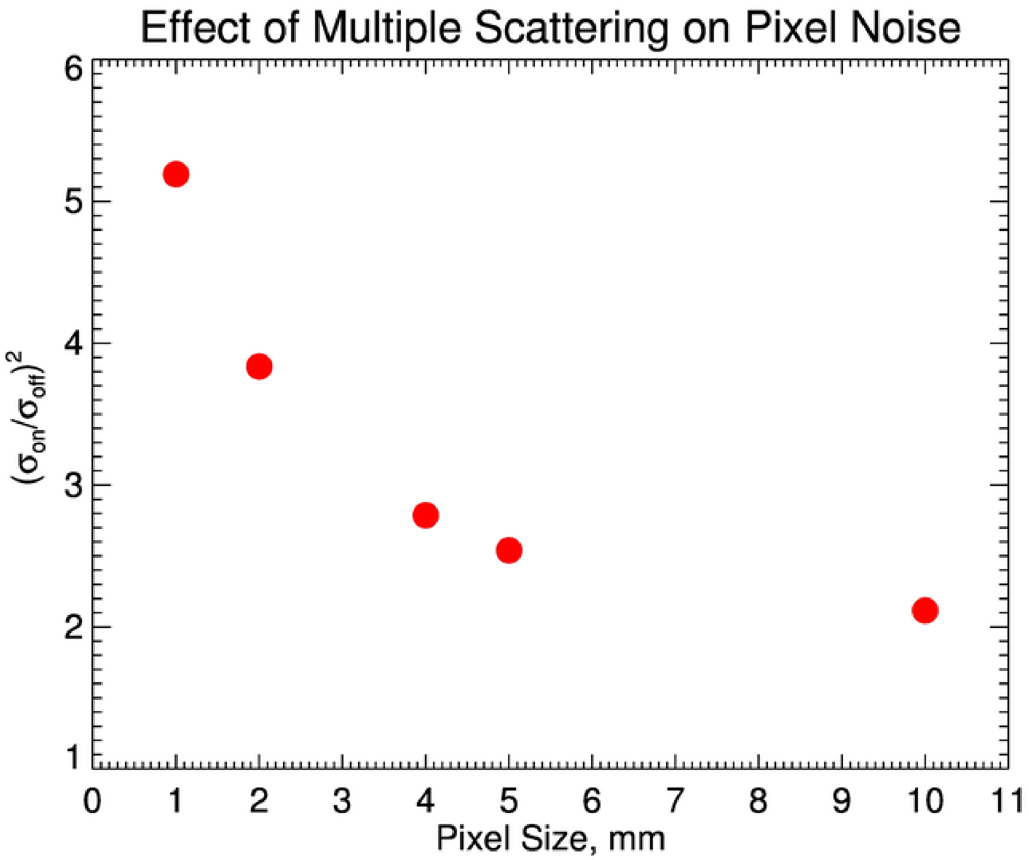
Algebraic Reconstruction Technique:

- Iterate through proton list. Adjust voxel densities sequentially for each proton.
- Can be parallelized

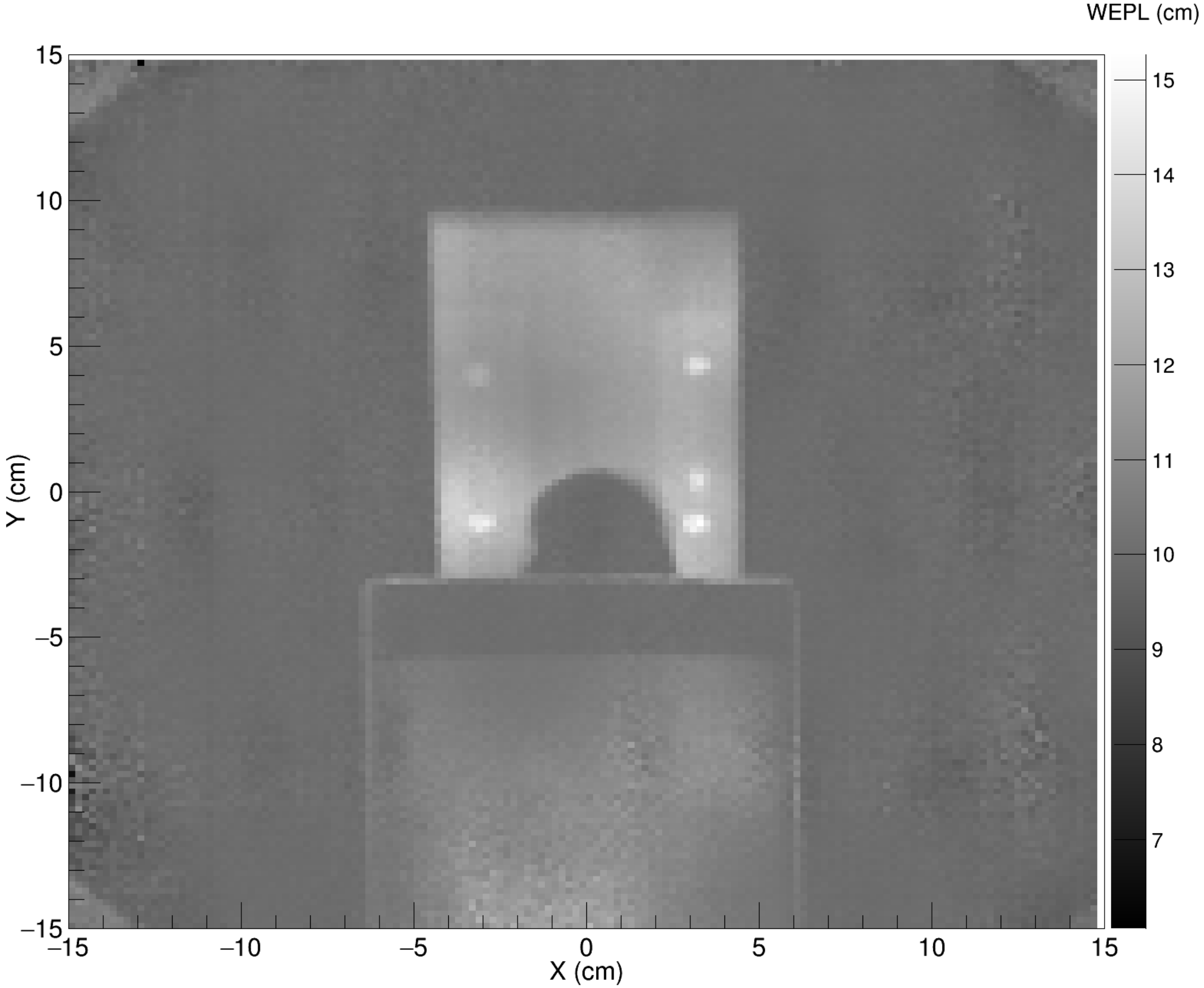
Simple 4-voxel illustration

Lee Goldman, J. Nucl. Med. Technol. **September 2007** vol. 35 no. 3 **115-128**

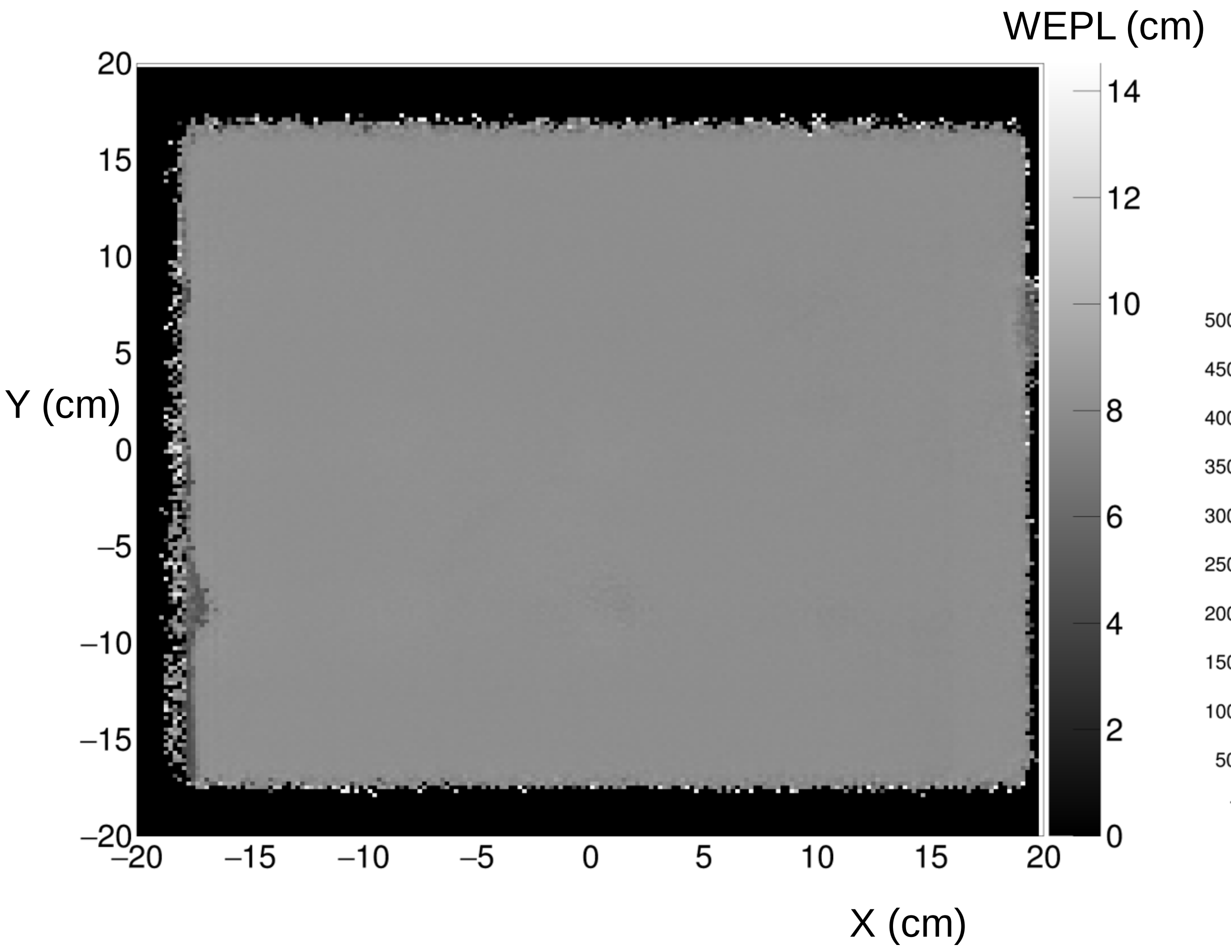
- pCT keeps 3D voxels (a few million voxels, a few hundred million protons)
- pRad sums voxels along proton direction to product 2D image – keeps 2D pixels
    - Iterative procedure improves image sharpness but adds noise



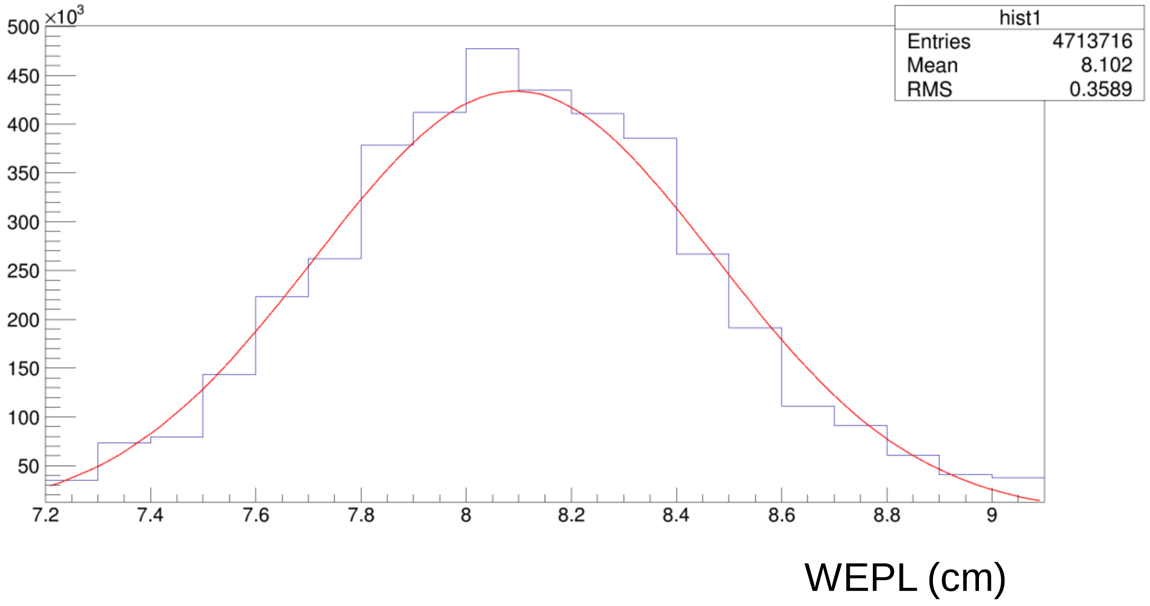
Our first real image – block of wood with screws

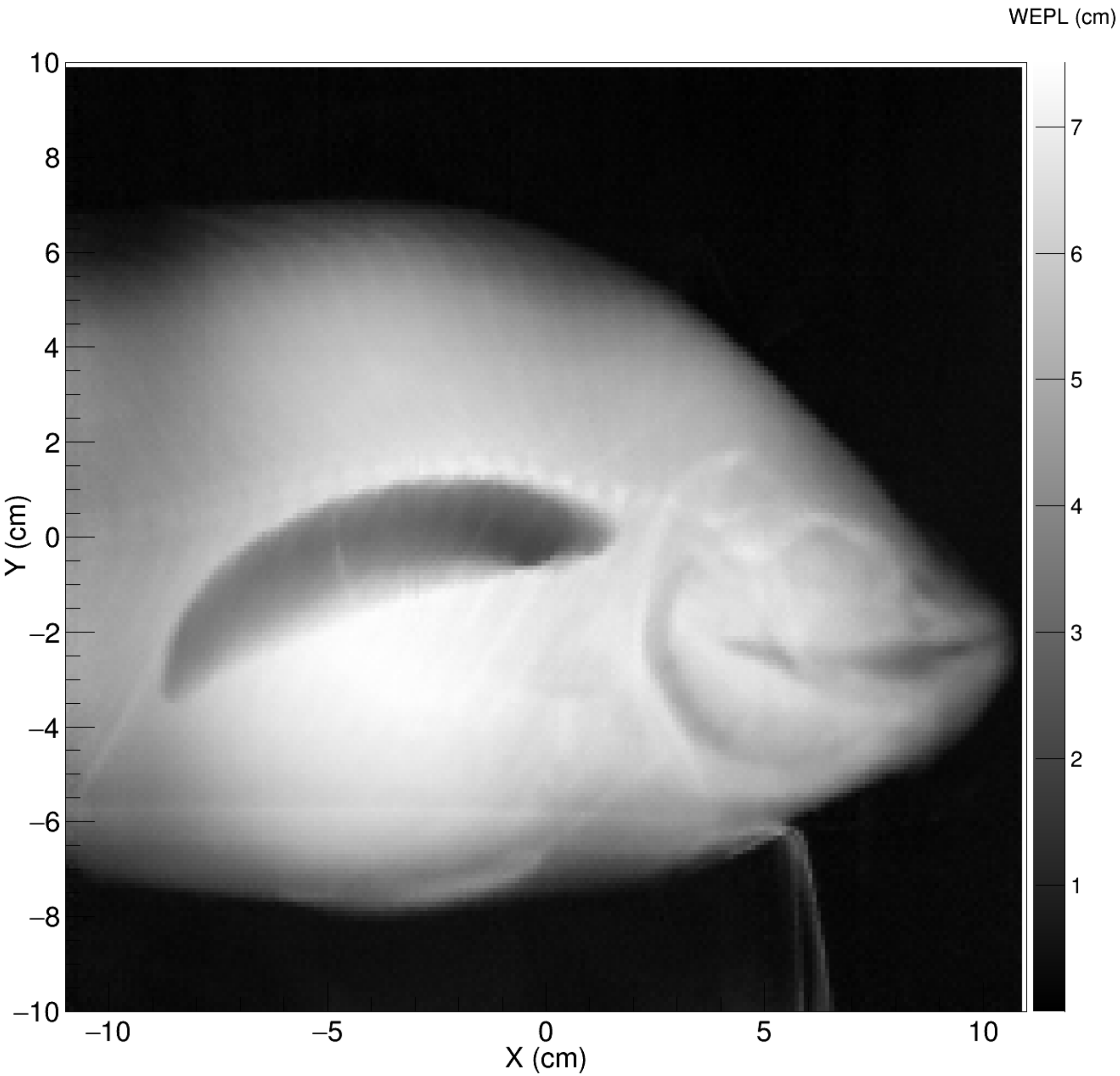


151 MeV scan through 8.1 cm block of water

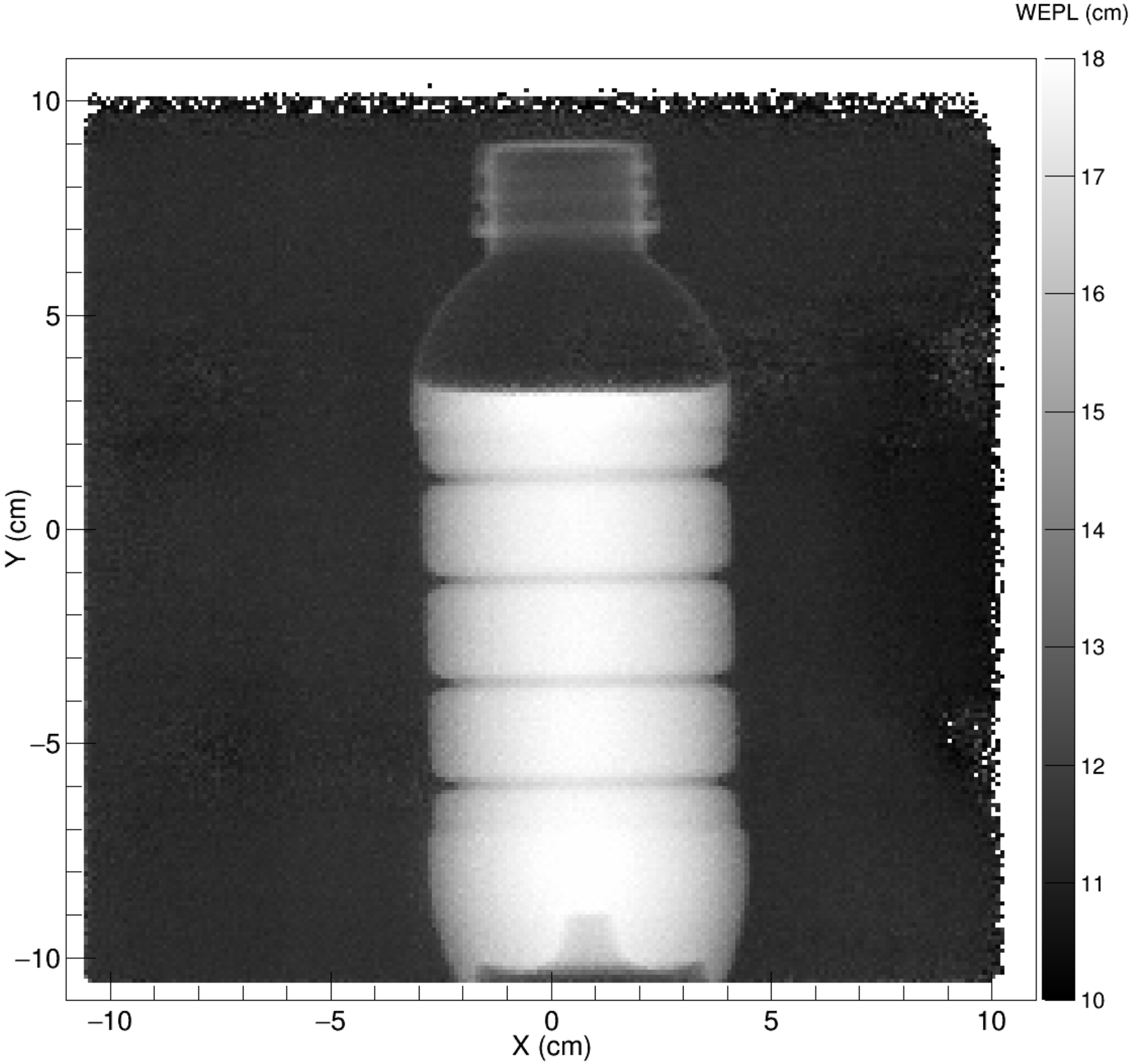


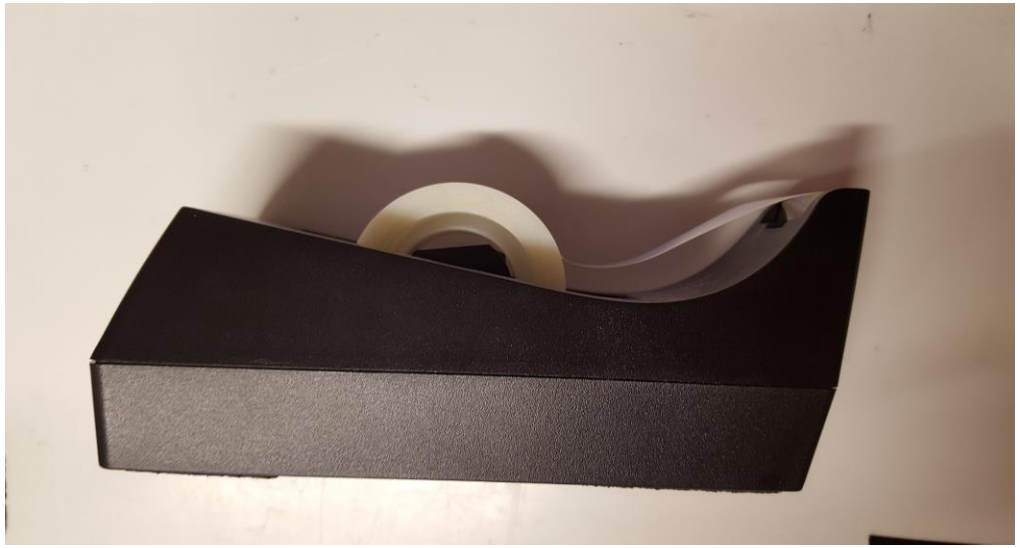
We are very close to our planned WEPL resolution / proton

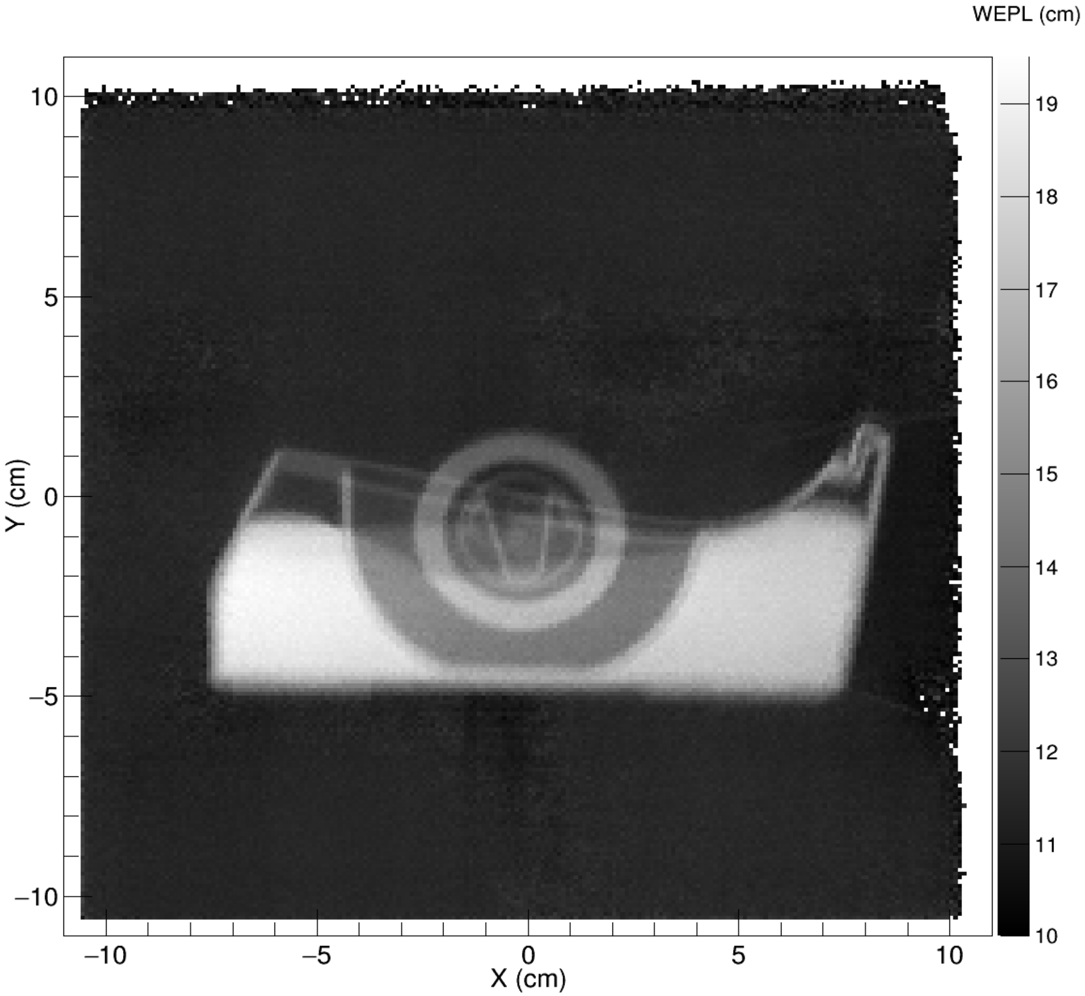



WEPL (cm)
10
8
6
4
2
0
−2
−4
−6
−8
−10
Y (cm)
−10
−5
0
5
10
X (cm)
7
6
5
4
3
2
1

Fast (~ 1 min) online image reconstruction

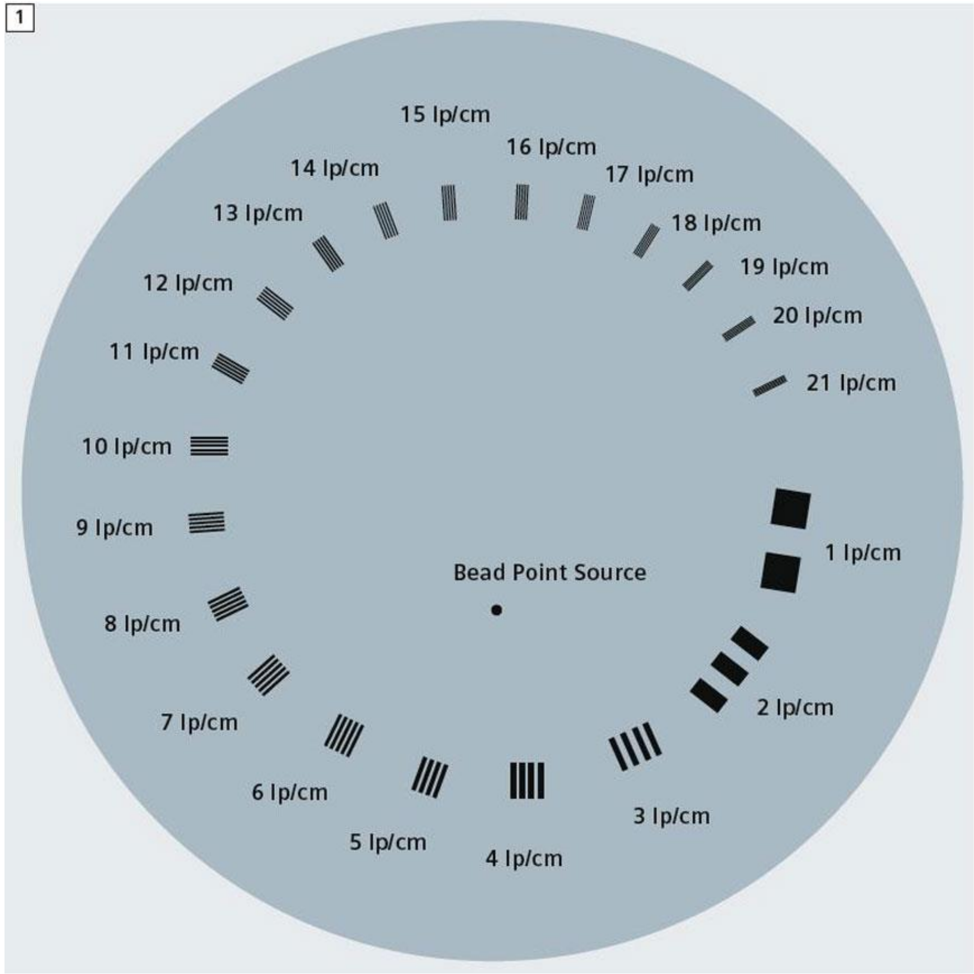






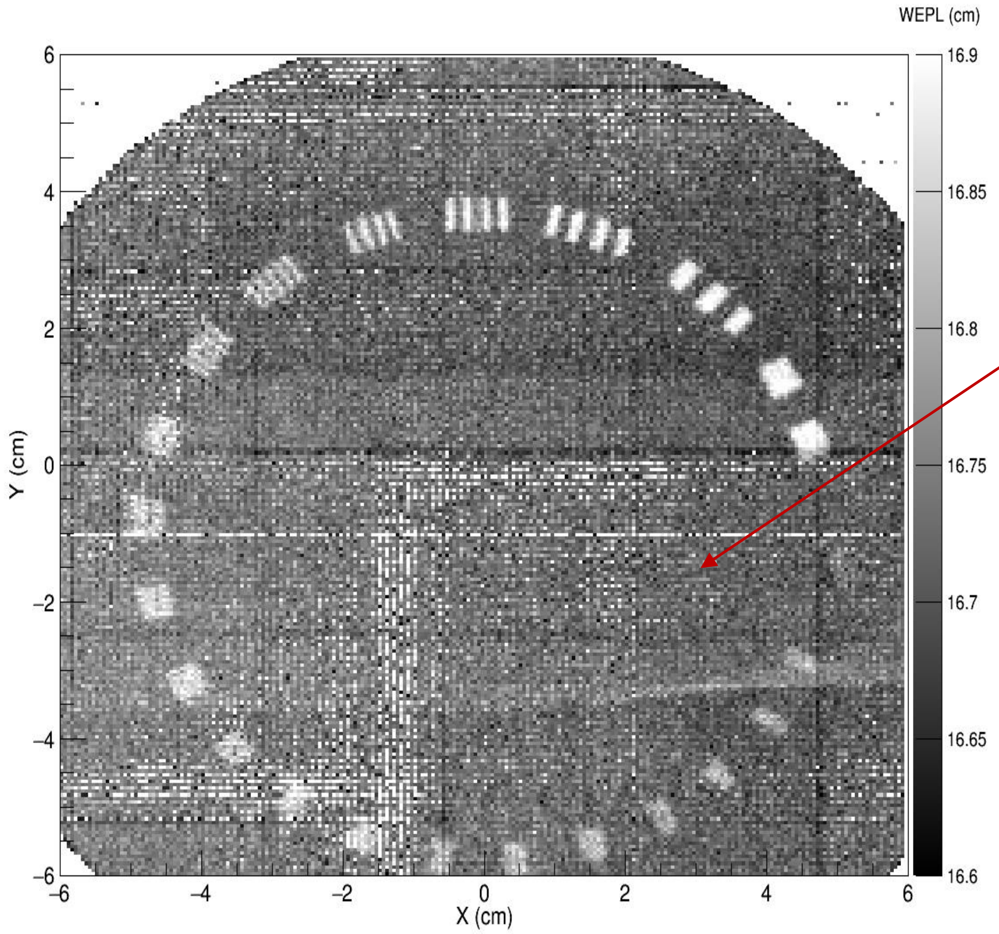
WEPL (cm)
10
5
0
−5
−10
Y (cm)
−10
−5
0
5
10
X (cm)
19
18
17
16
15
14
13
12
11
10

CATPHAN Line Pair Phantom

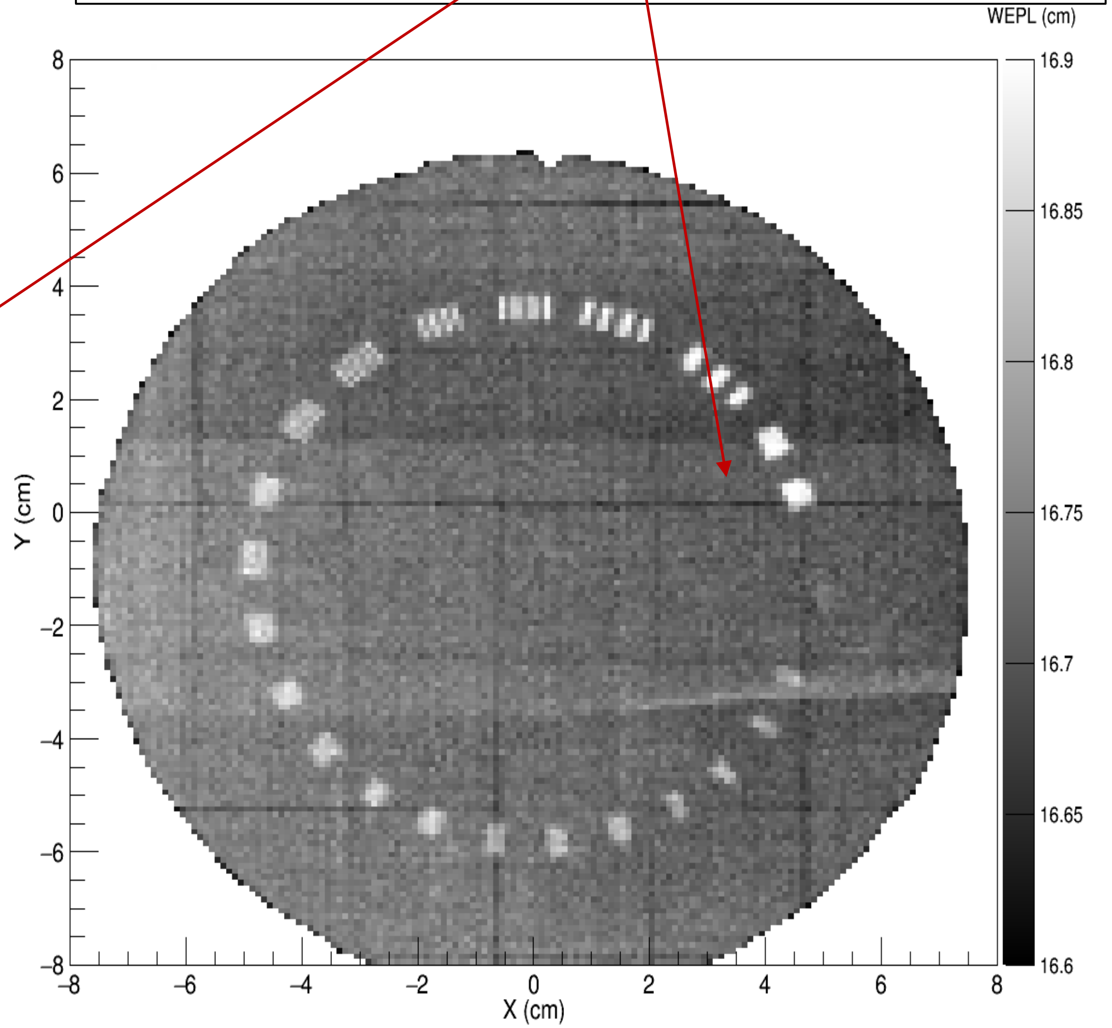


Offline reconstruction
Note: grey scale range only 3 mm!

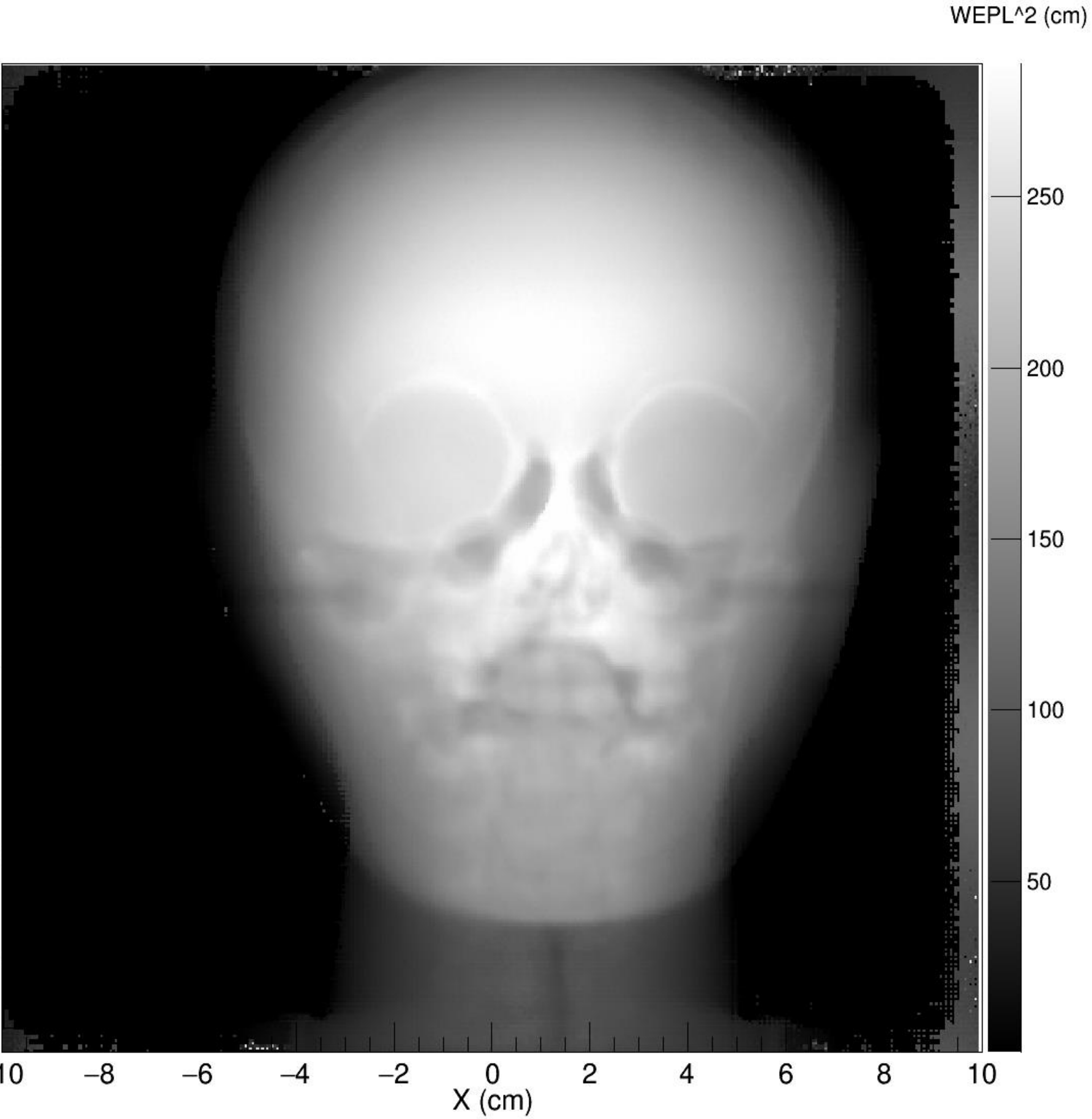
As to range sensitivity.. We clearly see the 0.2 mm tape supporting the phantom. The density of this tape is slightly above water density.

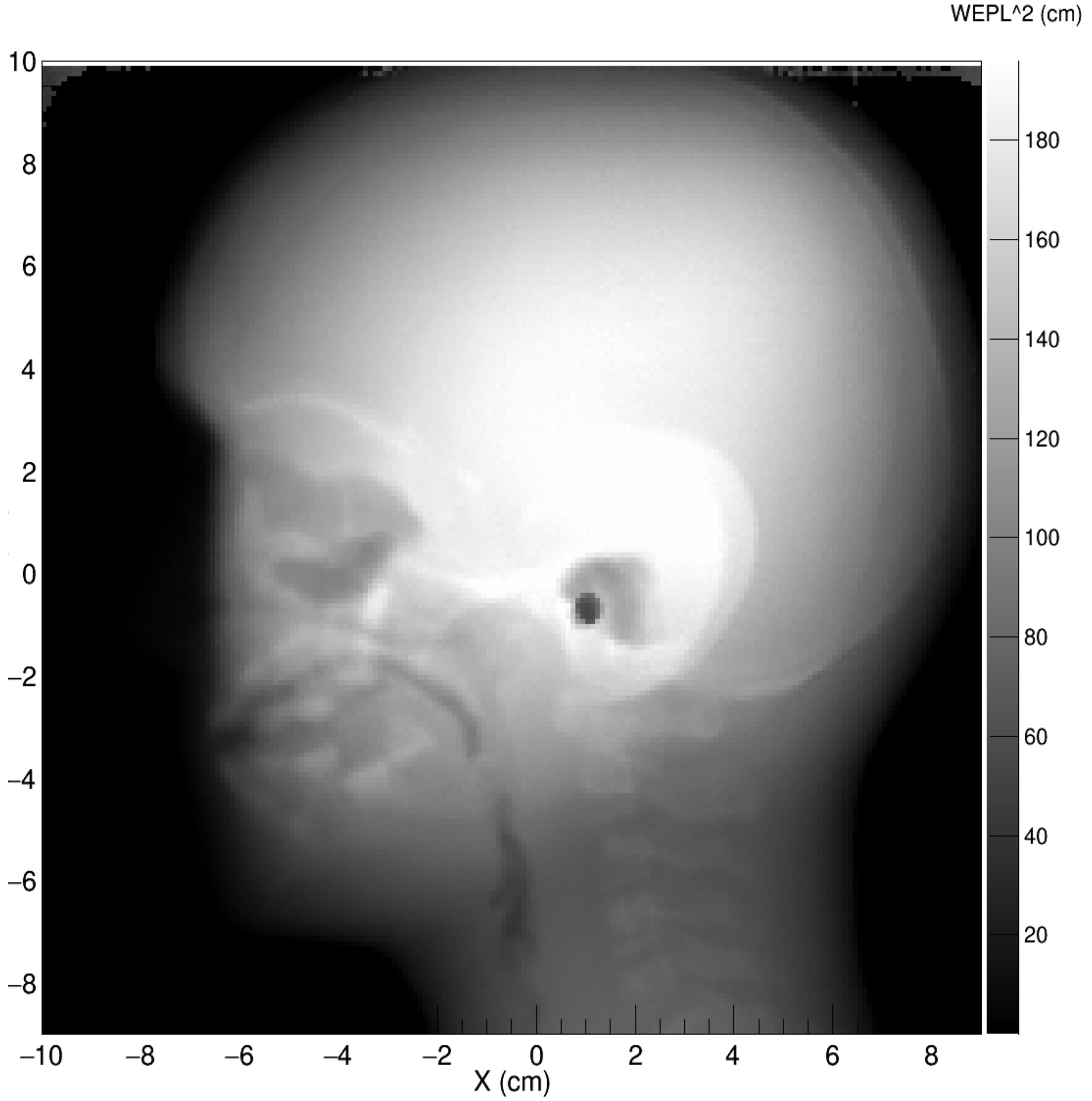


We see 7 line pairs/cm with 0.5 mm pixel size

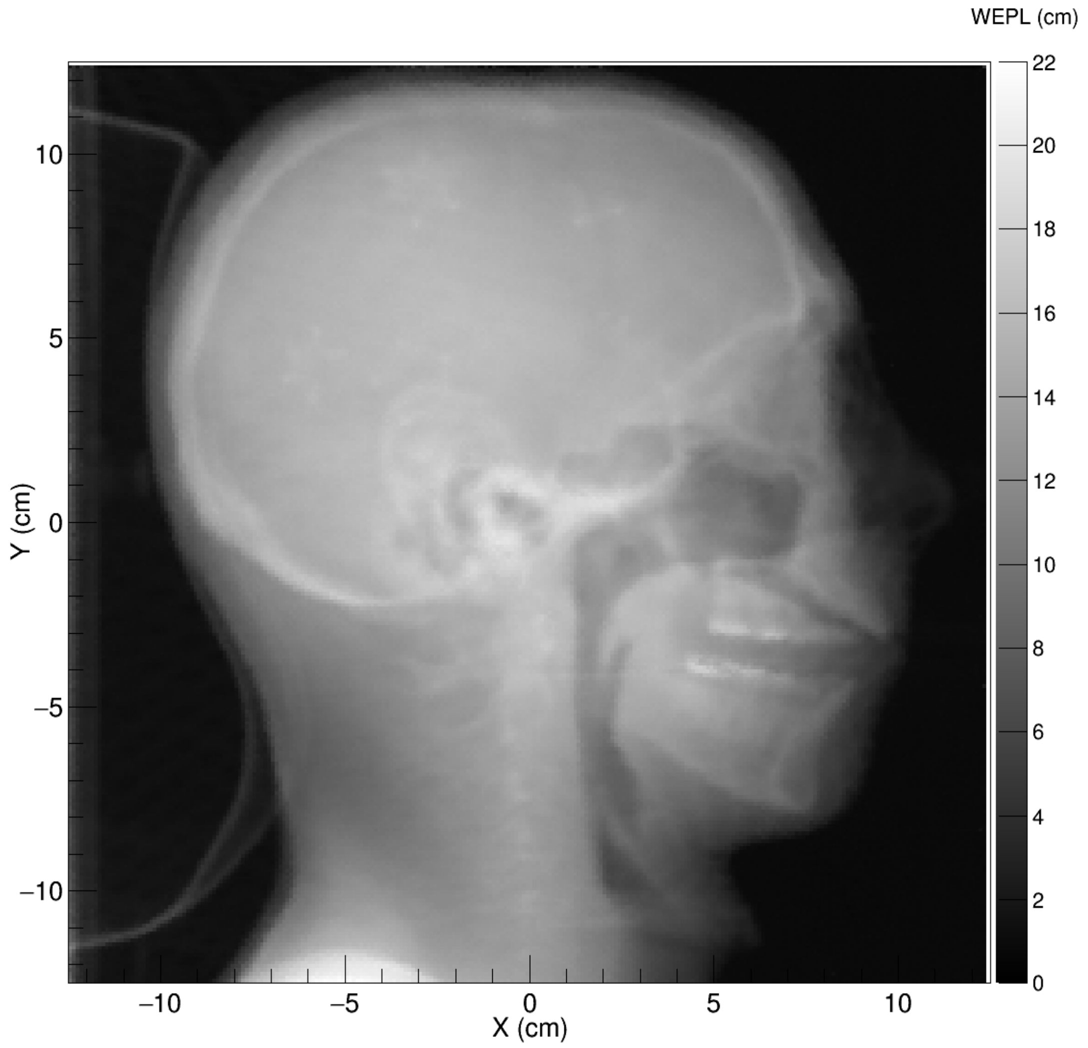


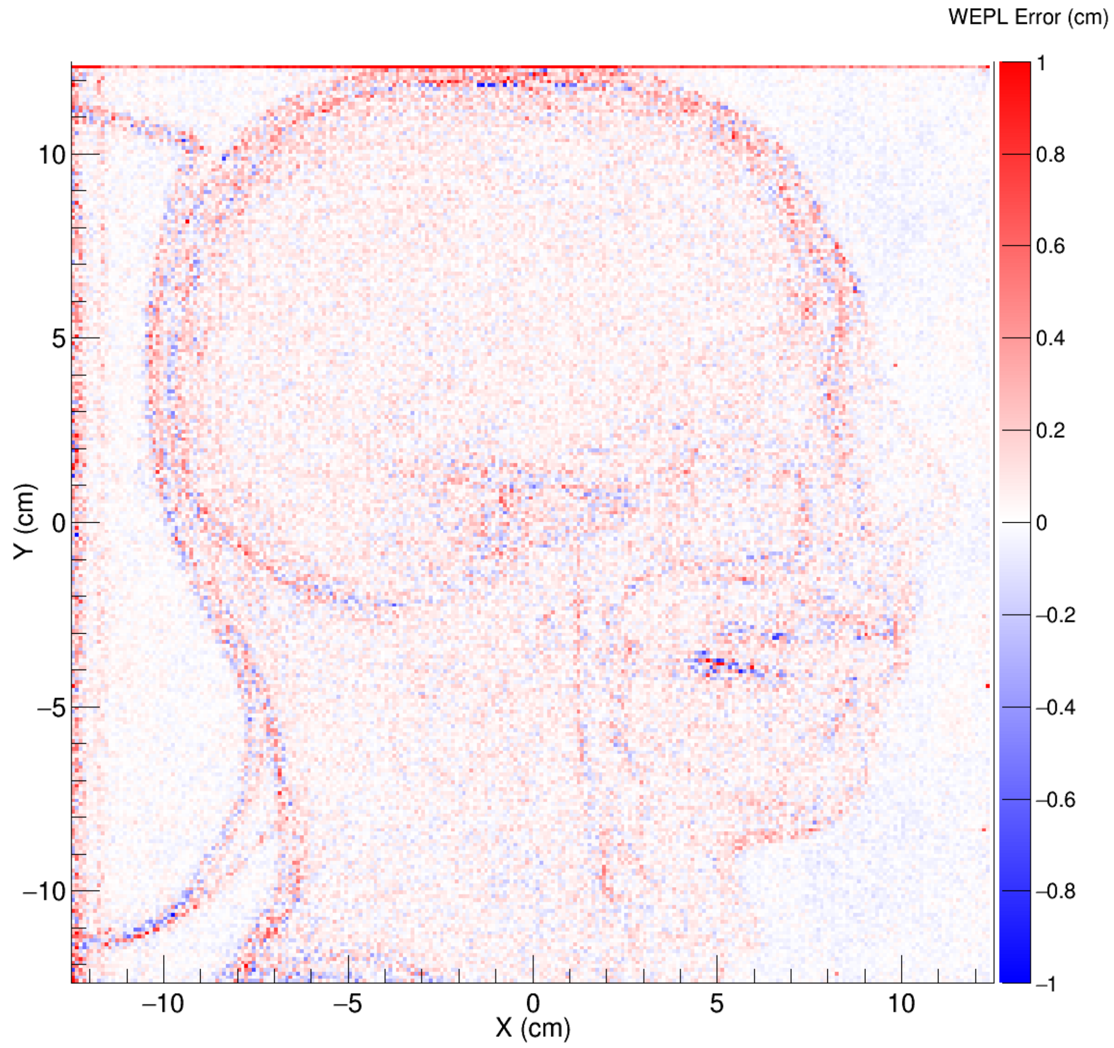
We see 6 line pairs/cm with 1 mm pixel size


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


WEPL^2 (cm)
10
8
6
4
2
0
−2
−4
−6
−8
−10
−8
−6
−4
−2
0
2
4
6
8
X (cm)
180
160
140
120
100
80
60
40
20

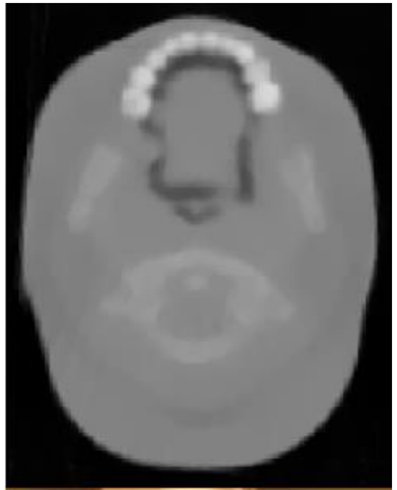
Simulation of a real human patient starting from X-ray CT scan
Image on right shows difference from an “ideal” image with no MCS

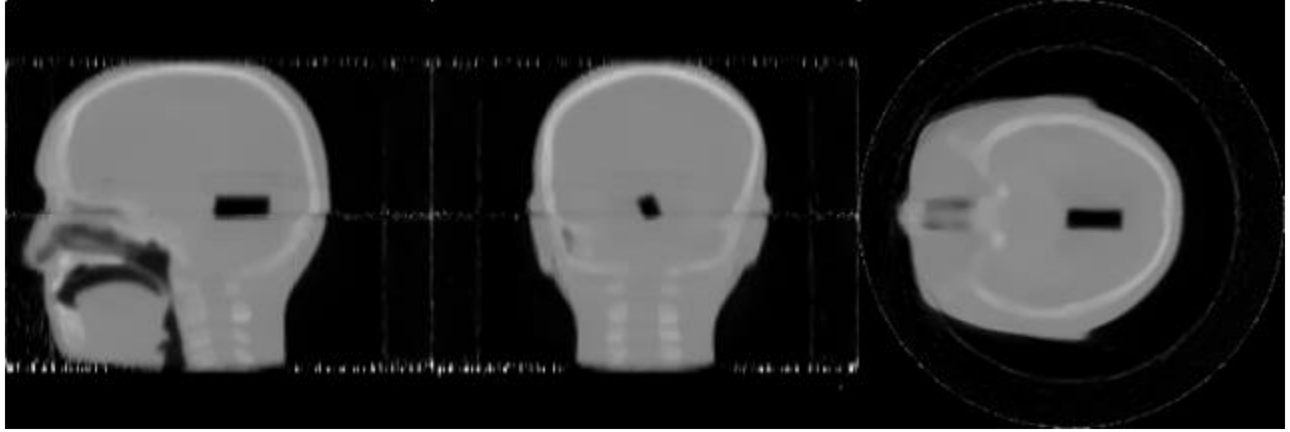


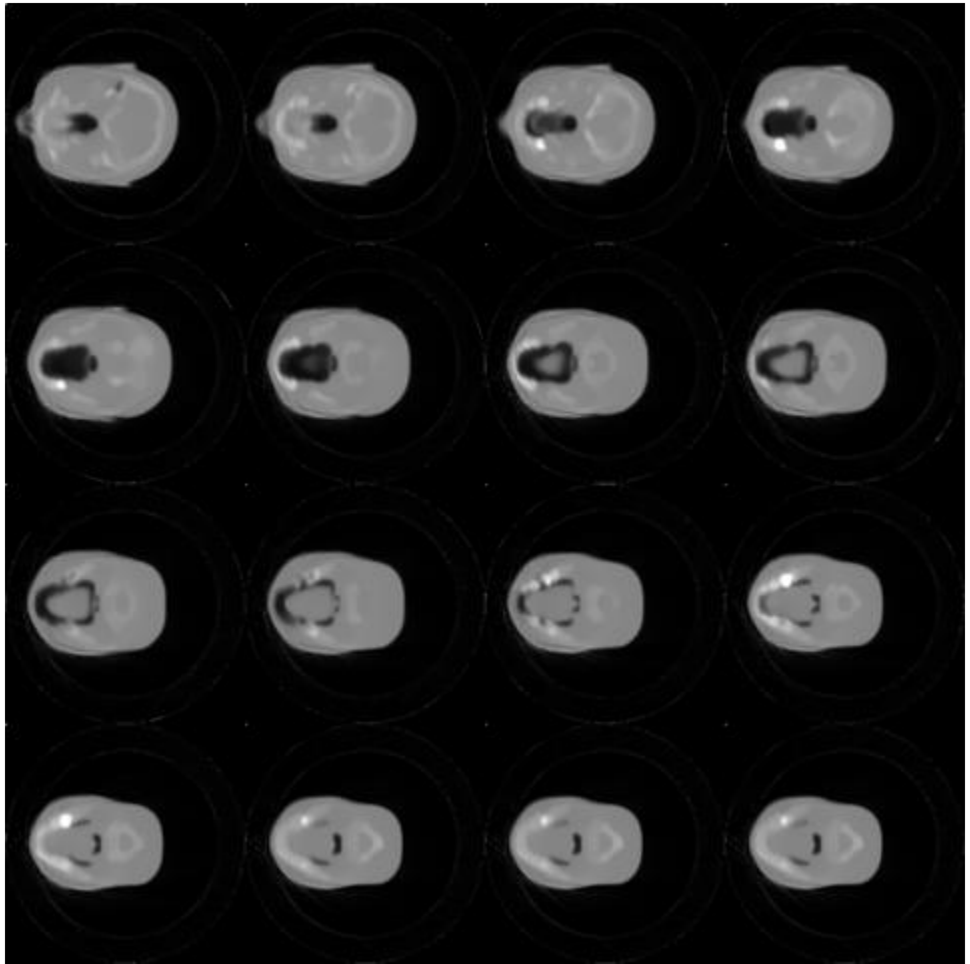


pCT has been demonstrated by a group from Loma Linda – UCSC “Phase II scanner”

- Pediatric (5 yr. old, CIRS) head phantom used for imaging
- Single reconstructed proton CT slice through lower mandible and teeth
- Data acquired at 1 million events per second using a 200 MeV proton beam and 90 beam entry angles (4 deg intervals)







Data from
LLUMC – USCS Phase 2 pCT detector
Led by Reinhard Schulte

Reconstruction from
Nick Karonis, NIU

3D reconstruction provides direct
determination of range to tumor.

Demonstrates another important
property of proton imaging:
No artifacts from high-Z materials.

Conclusions

<u>Demonstration of range detector concept:</u>

- High performance, optimize resolution vs. dose.
- Fast.
- Simple monolithic design, easily scaled to large field sizes.
- Thin and lightweight.
- Low electronics channel count.

<u>Demonstration of tracking detector concept:</u>

- Near 100% tracking efficiency

- **<u>Phase II project in progress:</u>**
  2 Year program

- Construct a fully functional prototype of a clinical proton radiography system
- 40 x 40 cm^2 field size
- Mounted on a c-arm to accommodate a wide variety of patient and beam orientations
- ~1 sec of beam time for radiograph
- CPU-GPU workstation for prompt (< 1 minute) delivery of a reconstructed image
- Perform a series of tests culminating in the production of images of phantoms.