Design, optimization, and characterization of a Multilayer Strip Ionization Chamber (MLSIC) device for proton FLASH-RT QA in a synchrocyclotron and an isochronous cyclotron

Shuang Zhou[4] Arash Darafsheh[1] Zhiyan Xiao[2] Anthony Mascia[2]

Yongbing Zhang[2] Jun Zhou[3] Liyong Lin[3] David Zhang[4] Liuxing Shen[4]

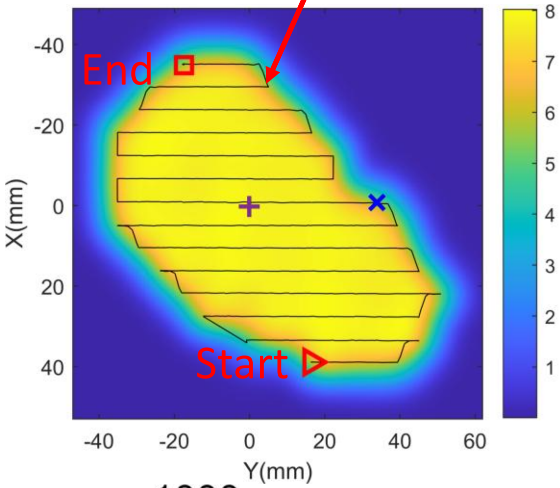
Hao Jiang[4] Qinghao Chen[1] Tianyu Zhao[1] Stephanie Perkins[1]

Tiezhi Zhang[4,5]

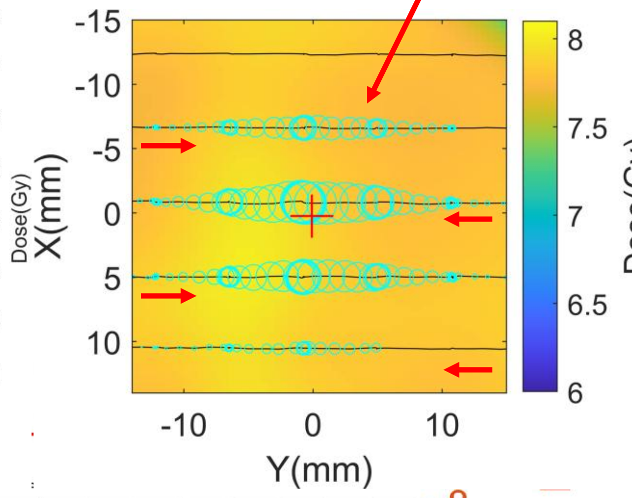
1 Department of Radiation Oncology, WashU Medicine, St. Louis, Missouri, USA
2 Department of Radiation Oncology, University of Cincinnati College of Medicine, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, USA
3 Department of Radiation Oncology, Emory University, Emory Proton Therapy Center, Atlanta, Georgia, USA
4 TetraImaging LLC, Stony Brook, New York, USA
5 Department of Radiation Oncology, Stony Brook University, Stony Brook, New York, USA

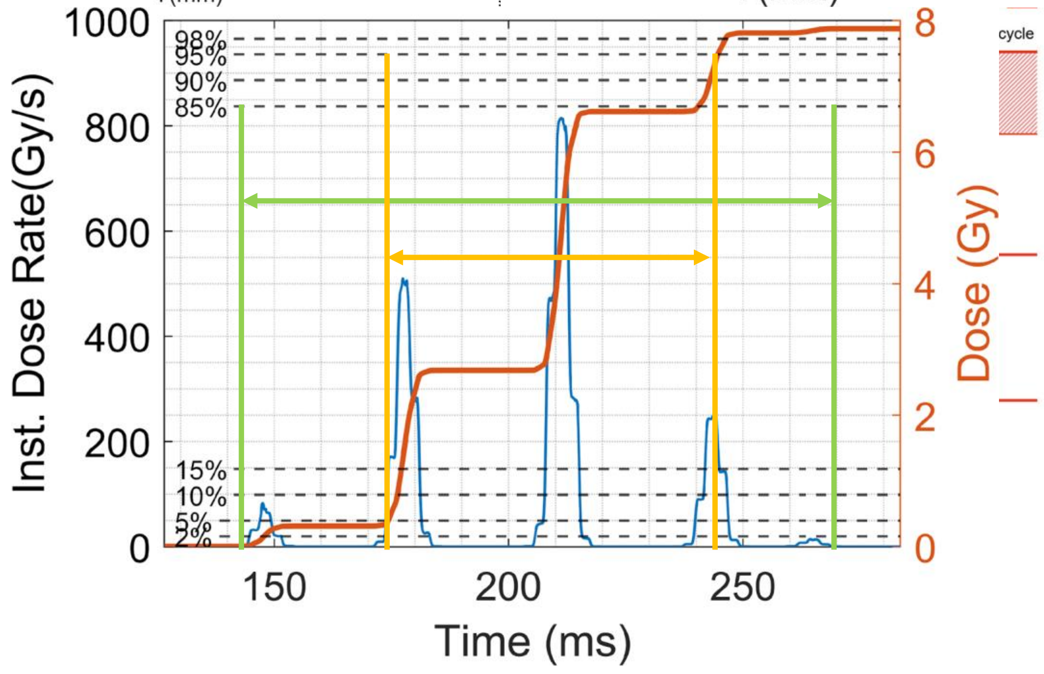
FLASH Dose rate Review

Proton trajectory



Proton spot dose contribution to voxel "+"





Percentile dose rate

Deffet, Sylvain, Valentin Hamaide, and Edmond Sterpin. *Medical Physics* 50.9 (2023): 5784-5792.

Dose at Voxel i

$$\dot{D}_i^{PERC} = \frac{D_i - 2pD_i}{t_{1,i} - t_{0,i}} = \frac{(1-2p)D_i}{t_{1,i} - t_{0,i}} \qquad t_{1,i} = t_i((1-p)D_i) \qquad t_{0,i} = t_i(pD_i).$$

Average dose rate(ADR)

Folkerts, Michael M., et al. *Medical physics* 47.12 (2020): 6396-6404.

$$\dot{D}_i^{ADR} = \frac{D_i}{t_{1,i} - t_{0,i}} \qquad t_{1,i} = t_i(D_i - d),\ t_{0,i} = t_i(d).$$

Dose average dose rate(DADR)

Van De Water, Steven, et al. *Acta oncologica* 58.10 (2019): 1463-1469.

$$\dot{D}_i^{DADR} = \frac{1}{D_i}\sum_s D_{i,s}\frac{D_{i,s}}{T_s}$$

Dose weighted dose rate

Folkerts, Michael M., et al. *Medical physics* 47.12 (2020): 6396-6404.

PBS dose rate

$$\dot{D}_i^{PBS} = \frac{D_i - 2pD_{th}}{t_{1,i} - t_{0,i}}$$

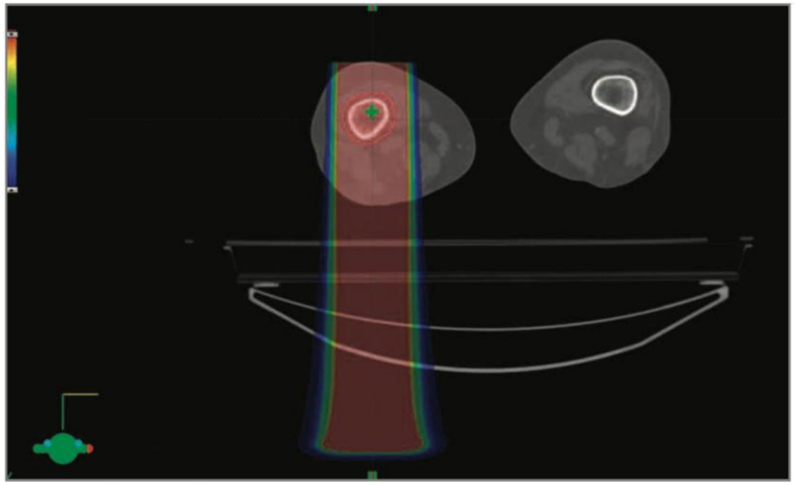
Global dose threshold

Instantaneous dose rate

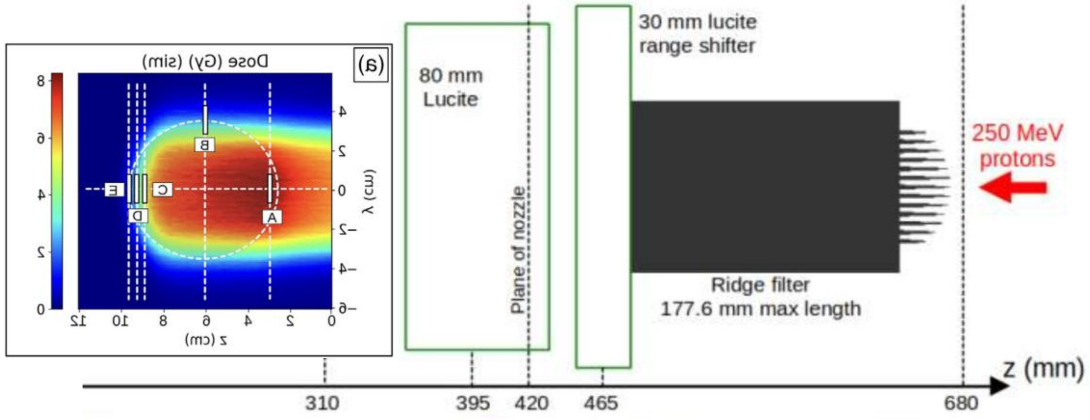
$$\dot{D}_i^{IDR} = \frac{D_i}{t_{sampling}}$$

Proton FLASH Approaches

First-in-human use of proton FLASH



Mascia, Anthony E., et al. "Proton FLASH radiotherapy for the treatment of symptomatic bone metastases: the FAST-01 nonrandomized trial." *JAMA oncology* 9.1 (2023): 62-69.



Harrison, Nathan, et al. "Characterizing devices for validation of dose, dose rate, and LET in ultra high dose rate proton irradiations." *Medical Physics* 51.11 (2024): 8411-8422.

Transmission Proton FLASH

- Single Energy Layer
- Simple hardware workflow
- Reduced distal OAR sparing

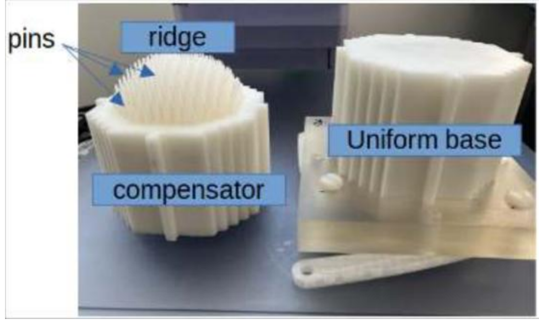
Conformal Bragg Peak FLASH

- Single Energy Layer
- Better distal OAR sparing
- Patient specific hedgehog/ridge filter
- Complicate hardware workflow

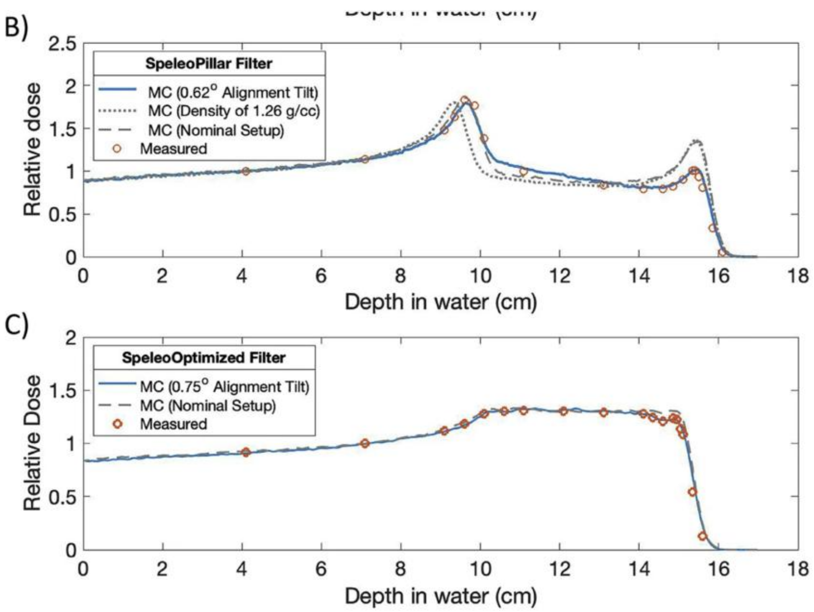
FLASH-RT QA: Clinical Need.

1. Determine if the treatment field can truly FLASH dose rate in the treatment volume.
2. Quality assurance measurement.

- 3D Printing error:
    - Resin WET consistency
    - SLA post-process shrinkage and warping
    - Missing/Broken Pins
- Filter alignment error:
    - Mounting Error: translation, rotation
    - Axis mismatch: beam not align with pillar axis



Harrison, Nathan, et al. *Medical Physics* 51.11 (2024): 8411-8422.



"manual alignment errors a 0.75° alignment offset resulted in a 2% dose deviation towards the distal portion of the measured PDD" Smith, Blake R., et al. *Communications engineering* 4.1 (2025): 139.

Our solution:

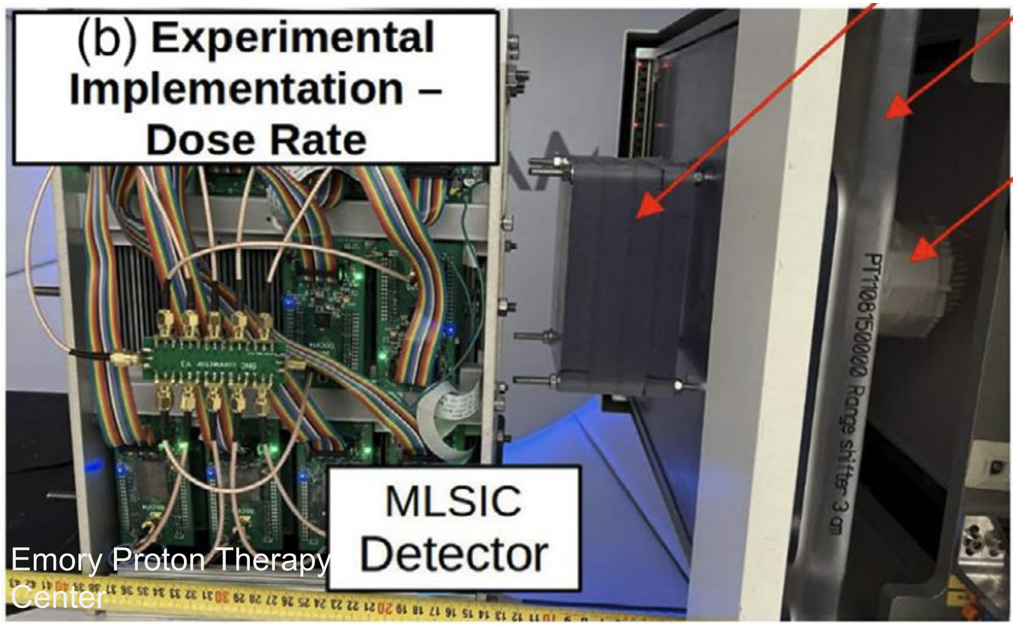
Current method:

- Log file method: No actual deposited proton distribution
- Ultra fast sensor: Can not measure 3D dose

Transmission Proton FLASH

Zhou, Shuang, et al. "Three-dimensional proton FLASH dose rate measurement at high spatiotemporal resolution using a novel multi-layer strip ionization chamber (MLSIC) device." *Medical physics* 52.10 (2025): e70033.

Conformal Bragg Peak FLASH



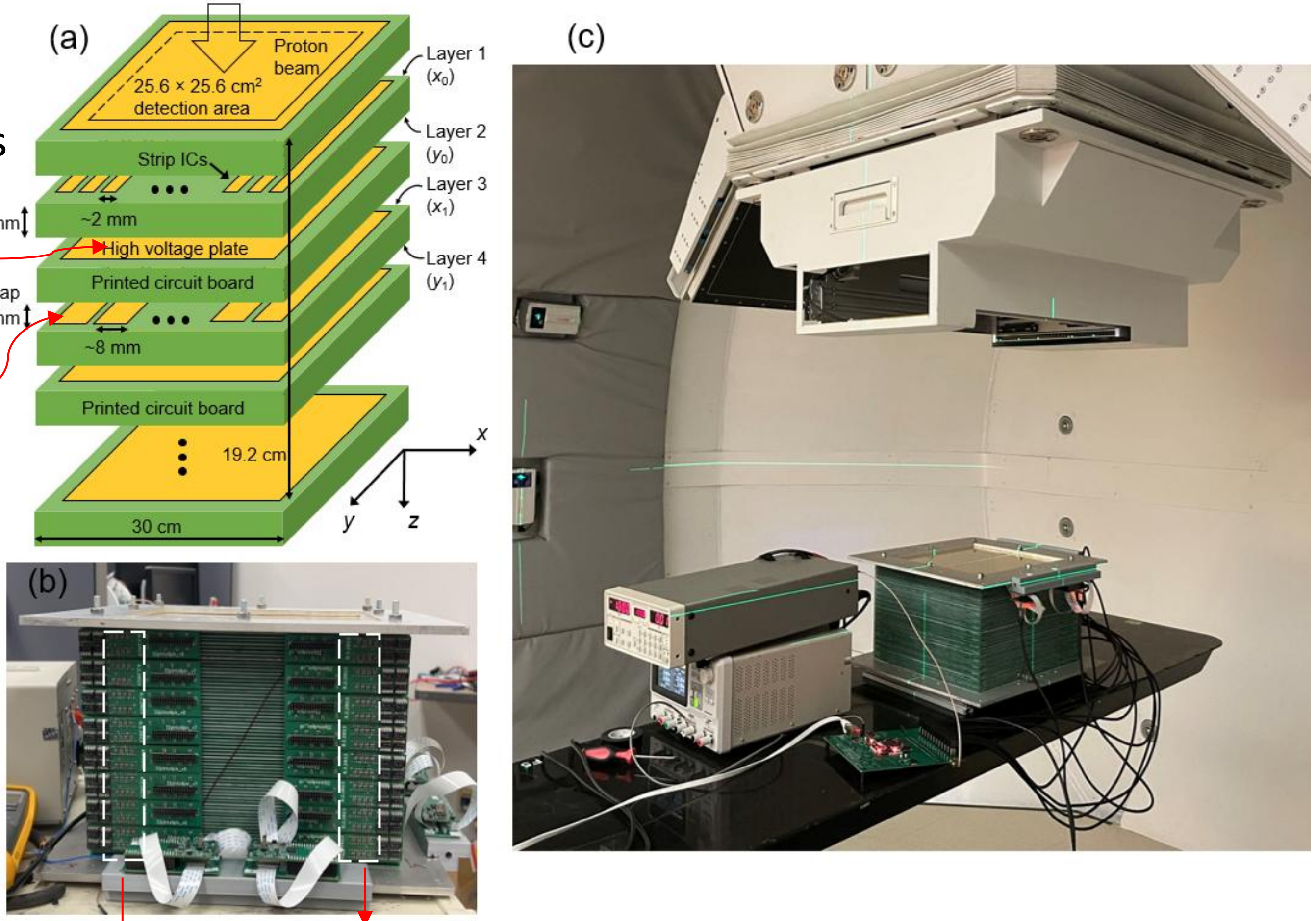
Harrison, Nathan, et al. "Characterizing devices for validation of dose, dose rate, and LET in ultra high dose rate proton irradiations." *Medical Physics* 51.11 (2024): 8411-8422.

3D dosimeter with high frame rate

MLSIC Architecture(1/2)

128 channels
2mm strip
High Voltage

8 channels
8mm strip

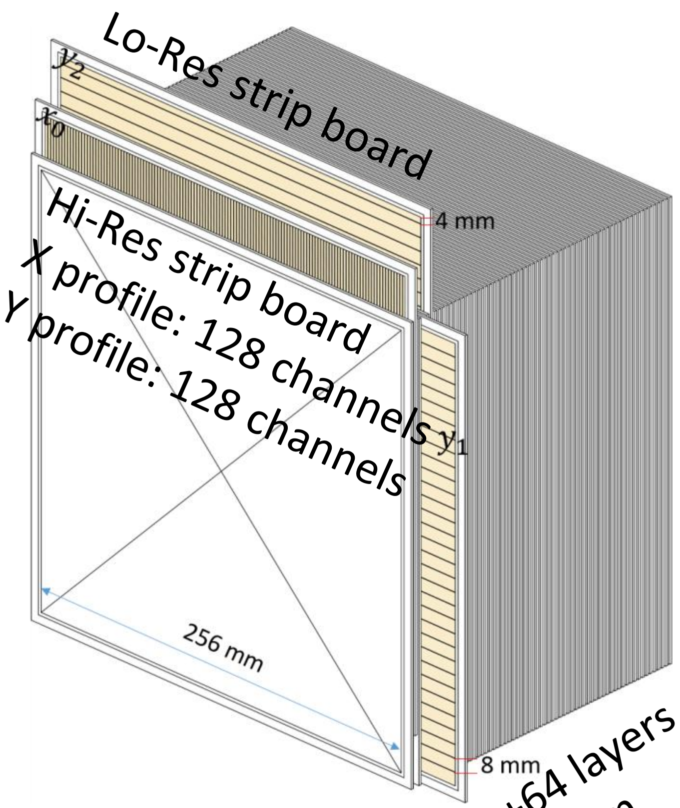


Attenuator for FLASH

Lo-Res X profile: 8×32 channels, 32 layers
Lo-Res Y profile: 8×32 channels, 32 layers

Lo-Res strip board

Hi-Res strip board
X profile: 128 channels
Y profile: 128 channels



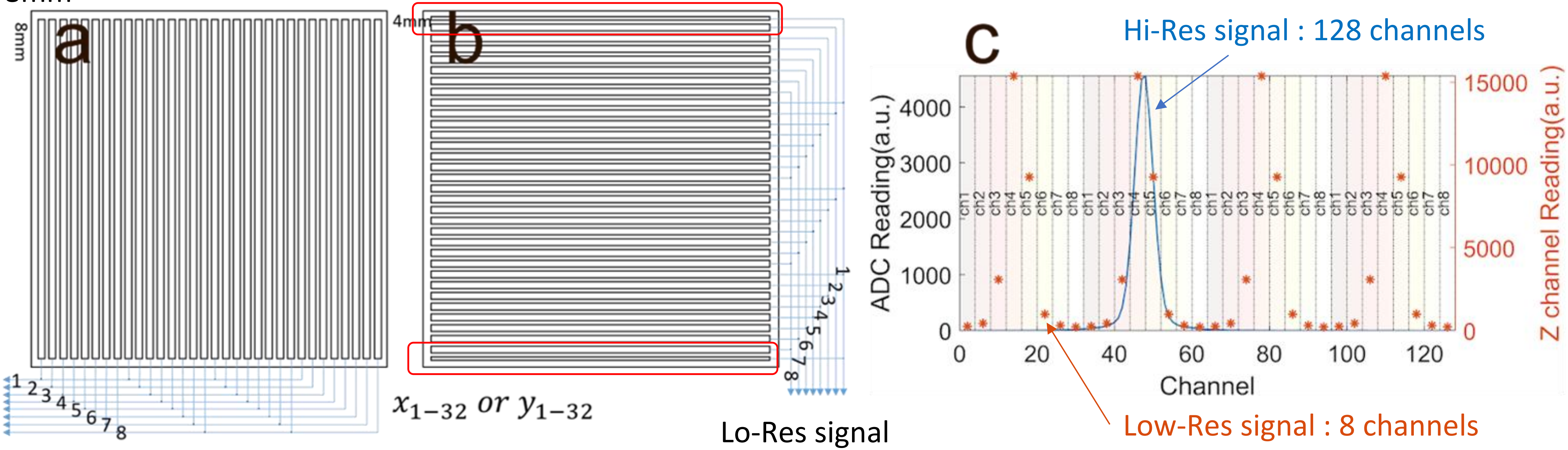
2+64 layers
19.2cm
Water equivalent

768 ADCs@16bit
160us ~ 6.25kHz

MLSIC Architecture(2/2)

8mm

Half strip offset



Lo-Res signal

32 strips to 8 ADC channels

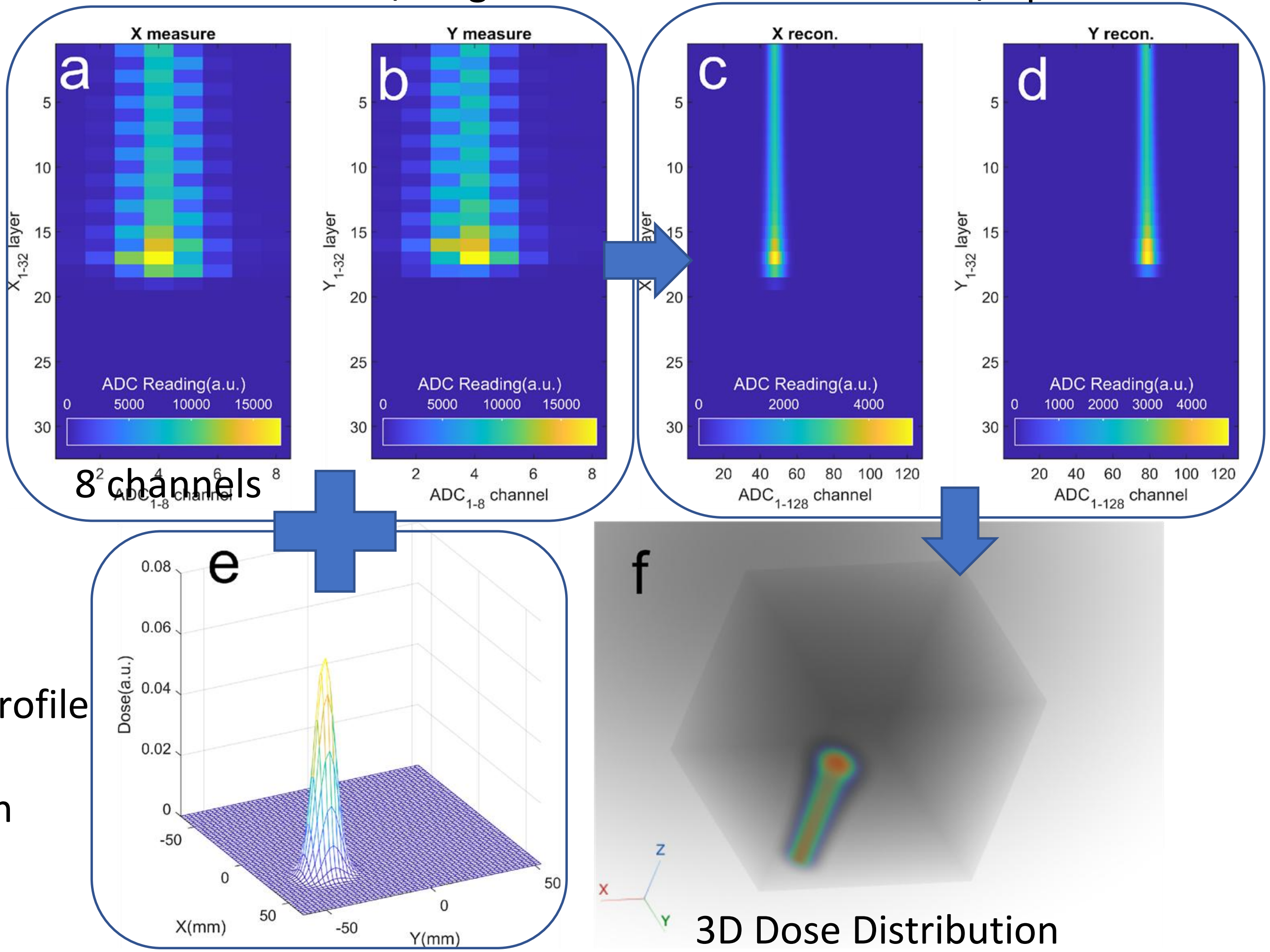
33 strips to 8 ADC channels

Dose reconstruction(1/2)

Measured Lo-Res X/Y signal

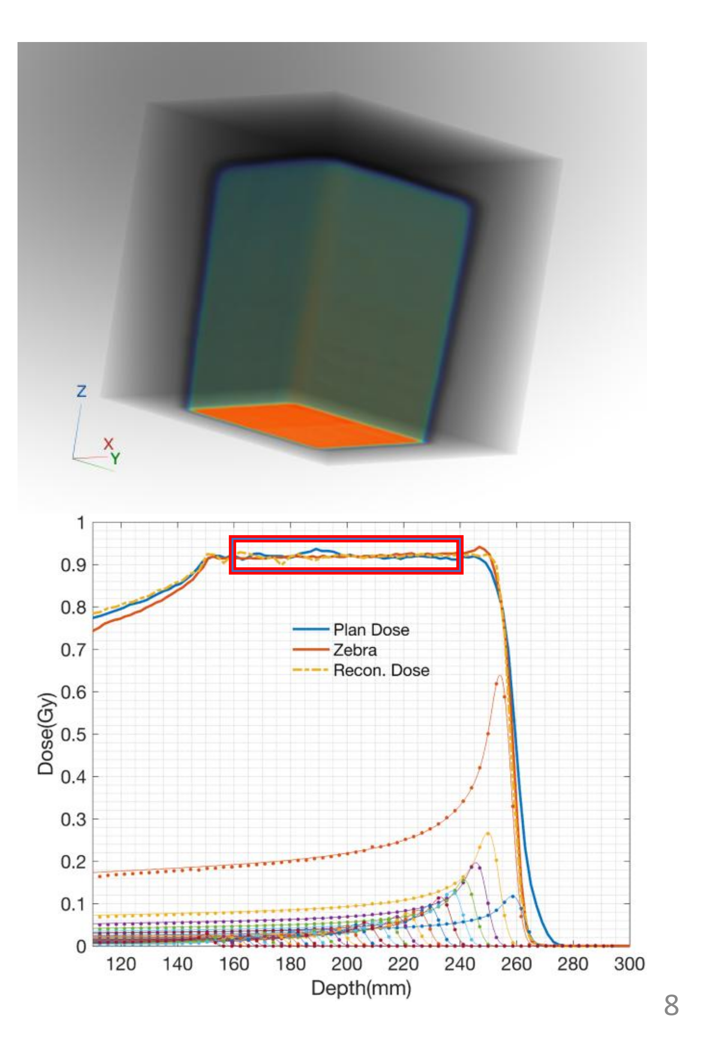
Reconstructed X/Y profile

32
Layers



Hi-Res X/Y profile
Beam sigma
Spot location

Dose Calibration with QA field



Dose Reconstruction(2/2)

Fit Hi-Res signal

$$f_{lpf}(x;\theta_x) = \frac{w_1}{\pi}\frac{\sigma_1}{(x-\mu)^2+\sigma_1^2} + \frac{w_2}{\sqrt{2\pi\sigma_2}}e^{-\frac{(x-\mu)^2}{2\sigma_2^2}} + \frac{w_3}{\sqrt{2\pi\sigma_3}}e^{-\frac{(x-\mu)^2}{2\sigma_3^2}}$$

Cauchy distribution Gaussian distribution

Total Variation
Smooth parameters between layers

$$\underset{\theta_{x,y}}{\arg\min}\left\|D_s\left(f_{x,y}\left(x,y;\theta_{x,y}(z)\right)\right)-m(z)\right\|^2+\mu_1\left\|\sum_{x,y}f_{x,y}\left(x,y;\theta_{x,y}(z)\right)-C(z)\right\|^2+\mu_2\left\|\theta_{x,y}(z)\right\|_{TV}$$

D_s : Down-sample operator, Hi-Res to Lo-Res conversion

$m(z)$: Measured Lo-Res X/Y profile

$C(z)$: Integrated Depth Charge (Bragg Peak Curve)

Constraints:

Beam alignment : $\frac{d\mu_x}{dz} = c_1, \frac{d\mu_y}{dz} = c_2$

$$\sigma(z) = c_3 * \left(0.18\frac{z}{R_{80}} + 0.82\left(\frac{z}{R_{80}}\right)^2\right) + c_4$$

The primary beam's σ should increase monotonically concerning depth (valid for pristine proton beams)
(Pedroni, Scheib et al. 2005, Hirayama, Takayanagi et al. 2016)

c_{1-4} are fitting parameters

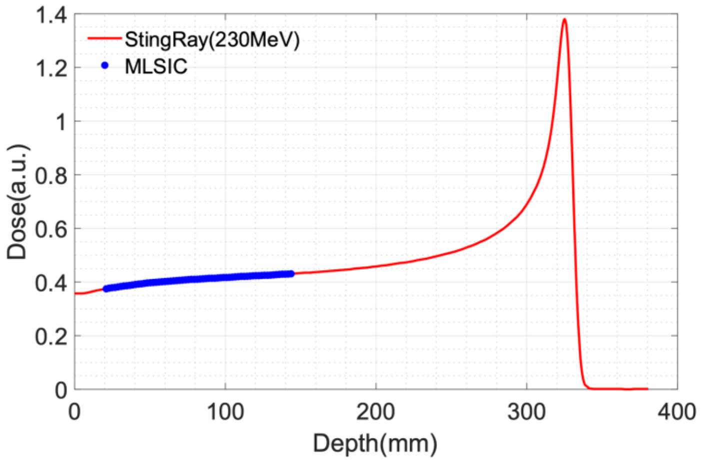
Recover 3D dose:

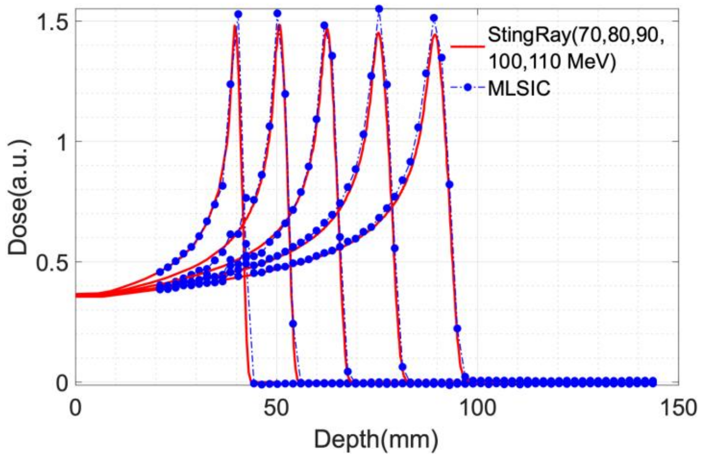
$$f_{3D}(x,y,z;\theta_x,\theta_y) = A(z)f_x(x;\theta_x(z))f_y(y;\theta_y(z))$$

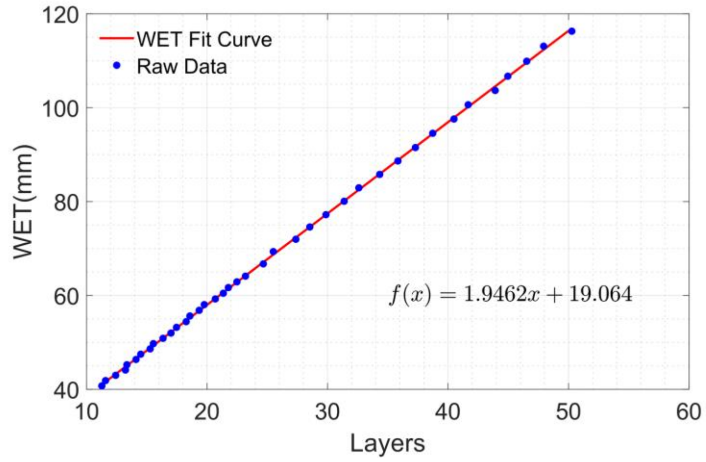
Zhou, Shuang, et al. "Proton 3D dose measurement with a multi-layer strip ionization chamber (MLSIC) device." *Physics in Medicine & Biology* 69.13 (2024): 135010.

Calibration

1 mm thick PCB : WET1.95 mm
1.6mm thick PCB: WET 2.91mm



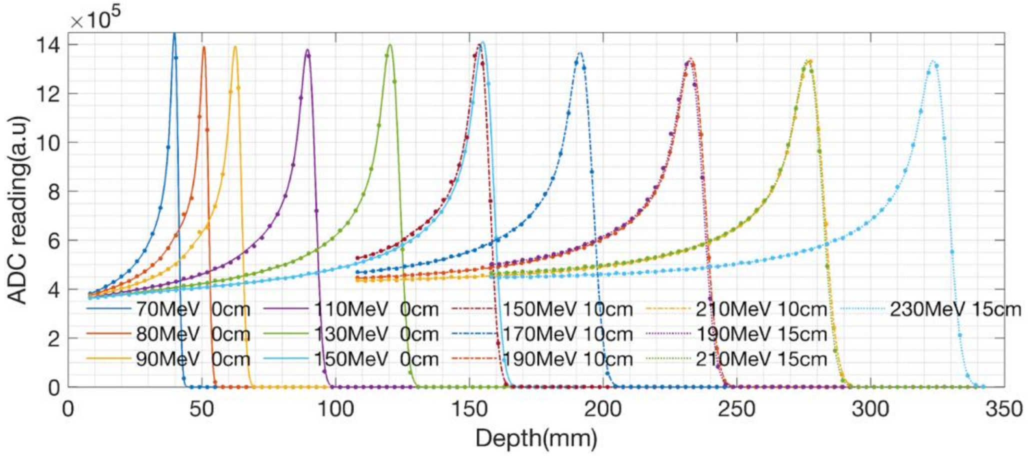


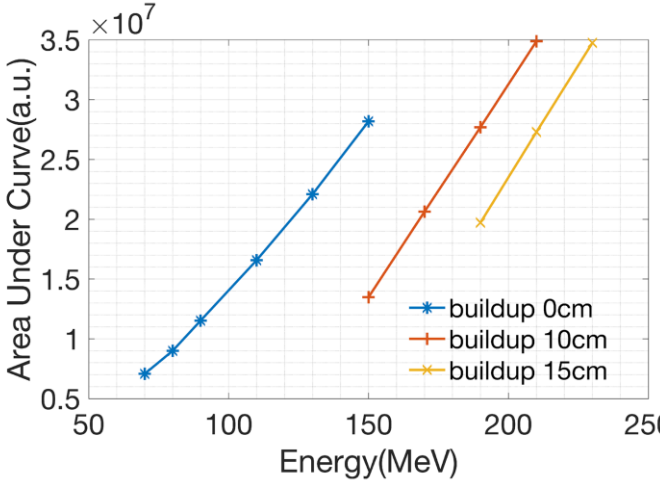


Depth sensitivity calibration

Range calibration

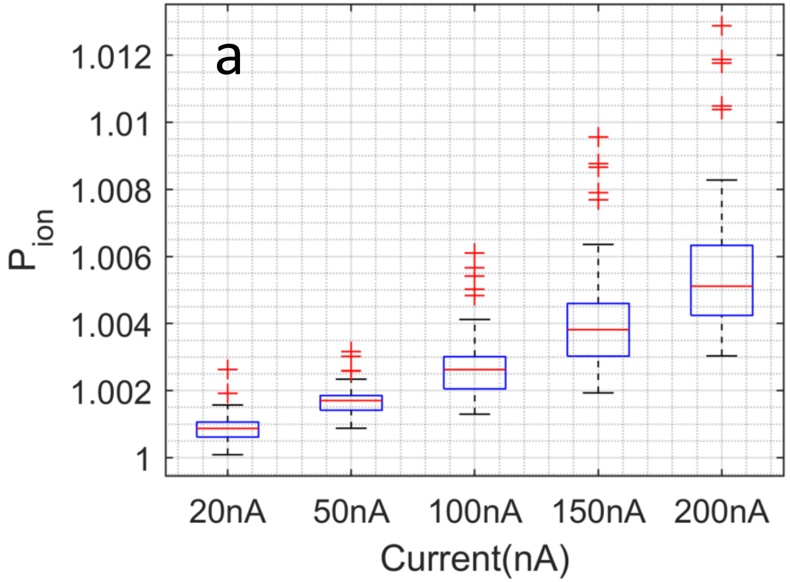
WET Fit





MU calibration

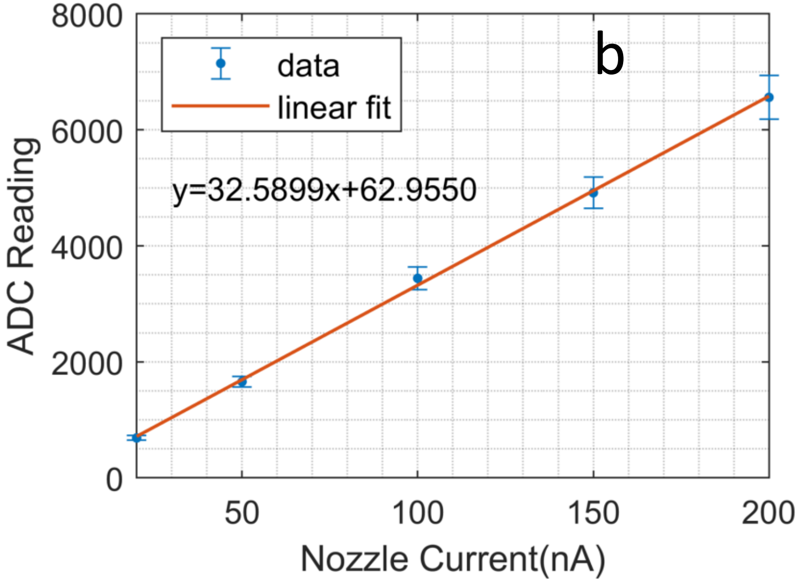
Recombination



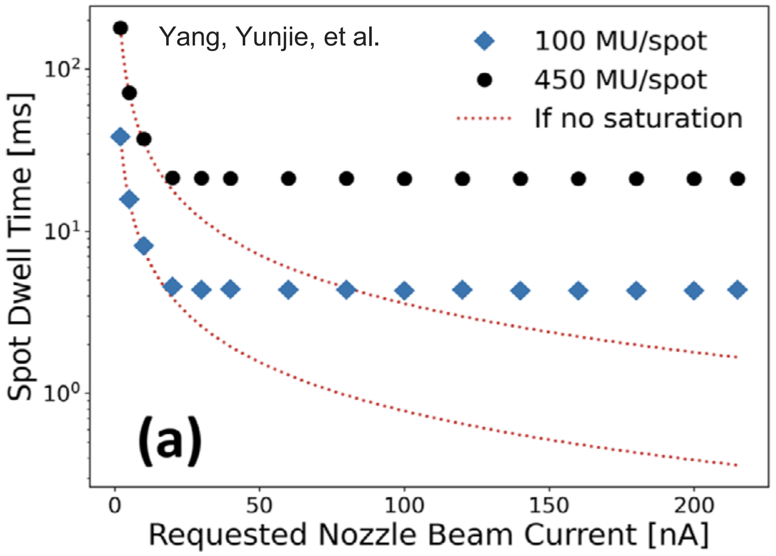
Recombination factor < 1%
Measured at 300V/600V, air gap 1.3mm.
E=4.62kV/cm

$$P_{ion} = a_0 + a_1 \frac{q_1}{q_2} + a_2 \left(\frac{q_1}{q_2}\right)^2$$

Weinhous, Martin S., and Jerome A. Meli. "Determining Pion, the correction factor for recombination losses in an ionization chamber." *Medical physics* 11.6 (1984): 846-849.



Data Linearity

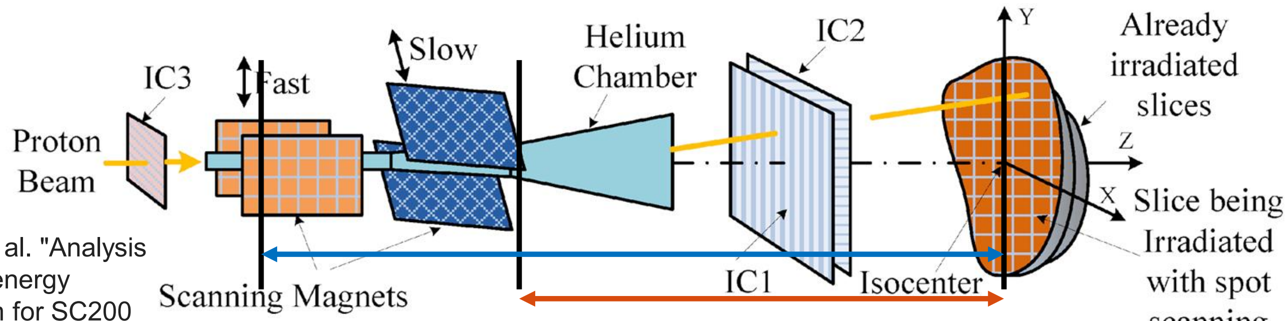


Spot Duration Time vs Nozzle Current with fixed MU per spot

Inverse-proportional relationship

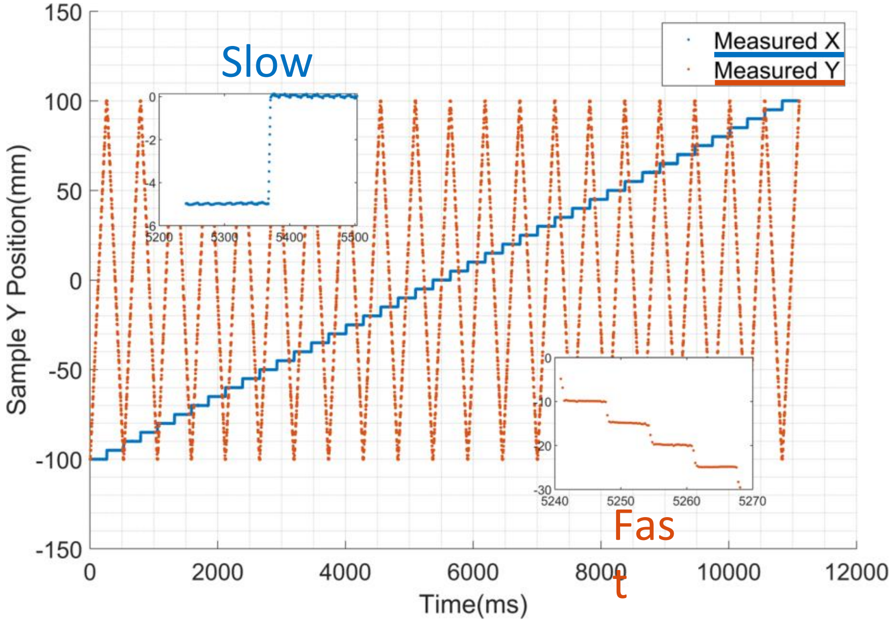
Yang, Yunjie, et al. "Commissioning a 250 MeV research beamline for proton FLASH radiotherapy preclinical experiments." *Medical Physics* 50.7 (2023): 4623-4636.

Physical Beam Trajectory(1/2)

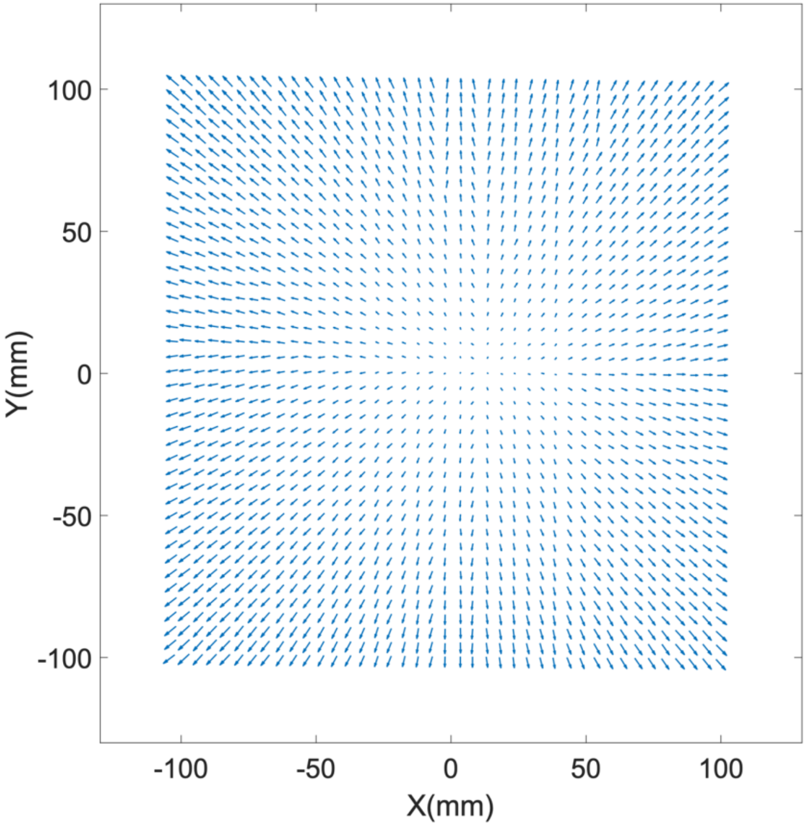


Virtual source-axis distance difference

Wang, Pengyu, et al. "Analysis and design of an energy verification system for SC200 proton therapy facility." *Electronics* 8.5 (2019): 541.



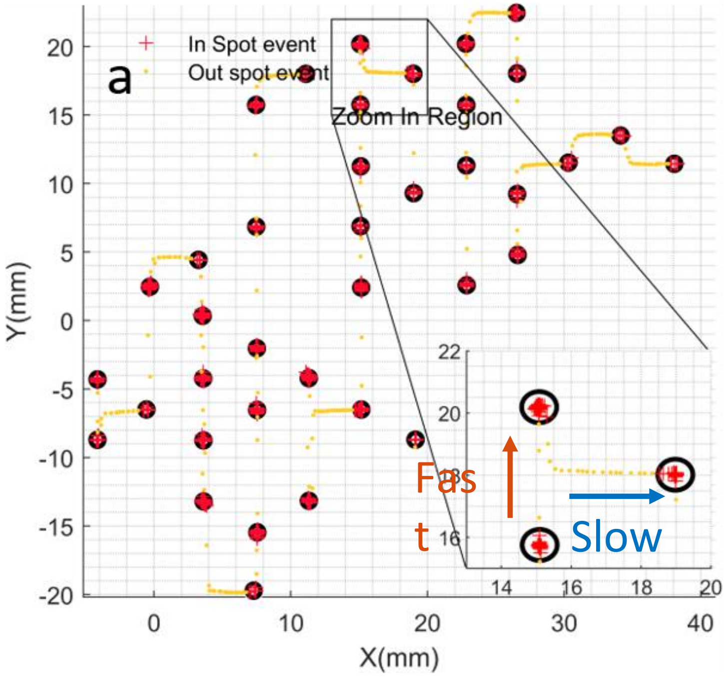
Continuous proton beam trajectory

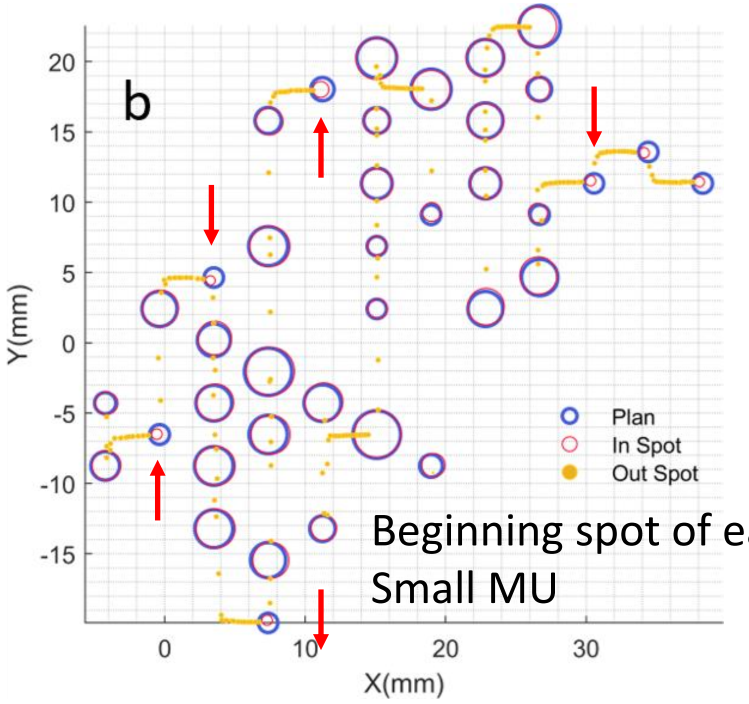


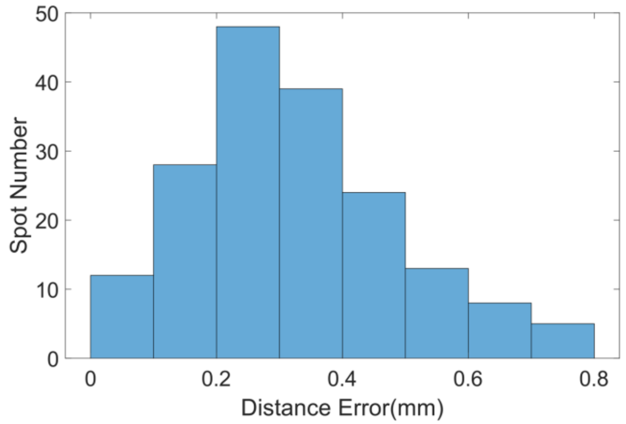
Proton beam cone angle/ divergence

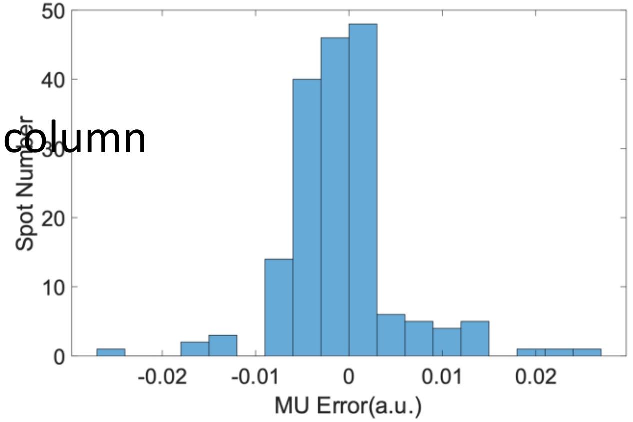
Physical Beam Trajectory(2/2)

Software defined spot location vs Actual proton trajectory









Beginning spot of each column

Small MU

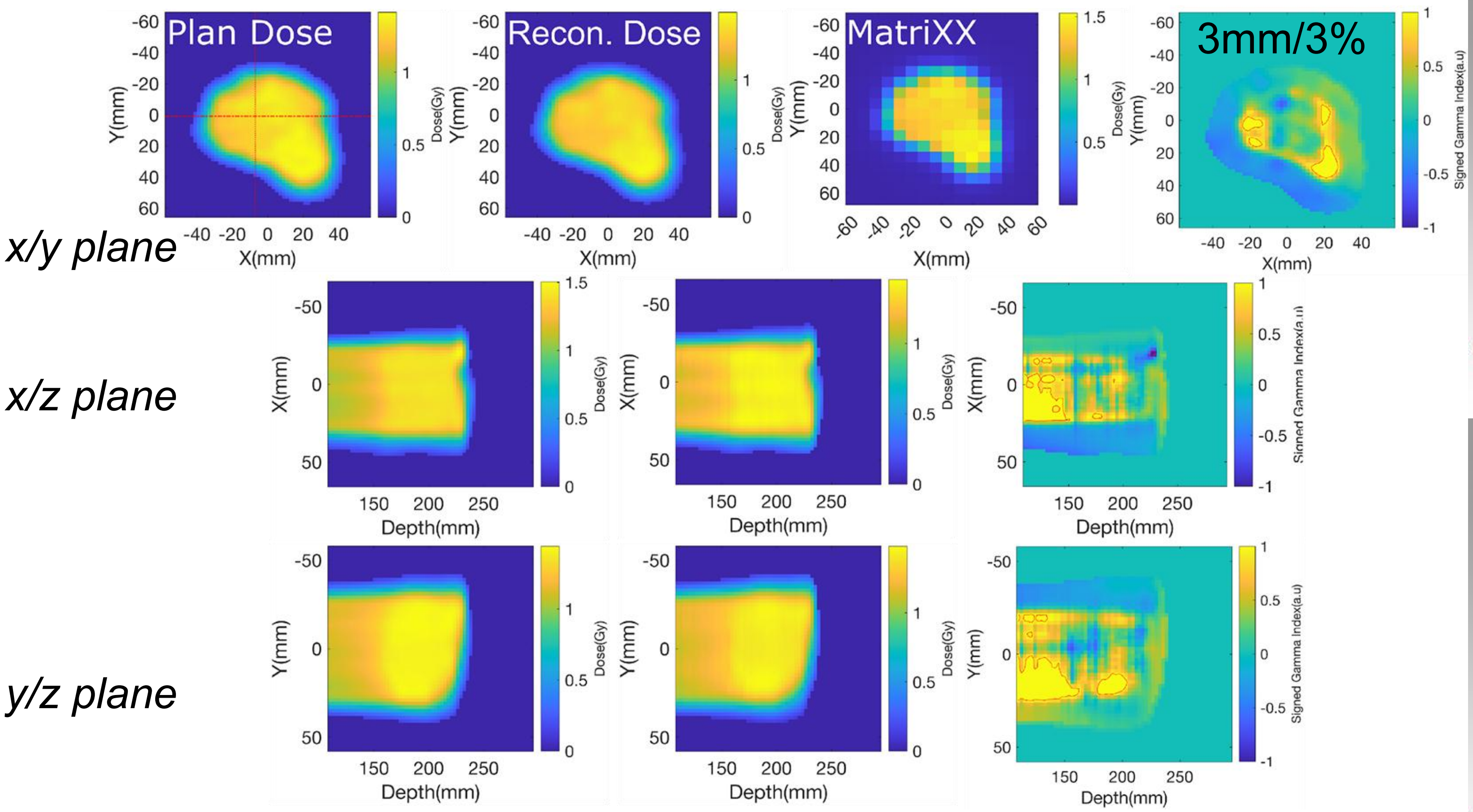
Circle size denotes MU

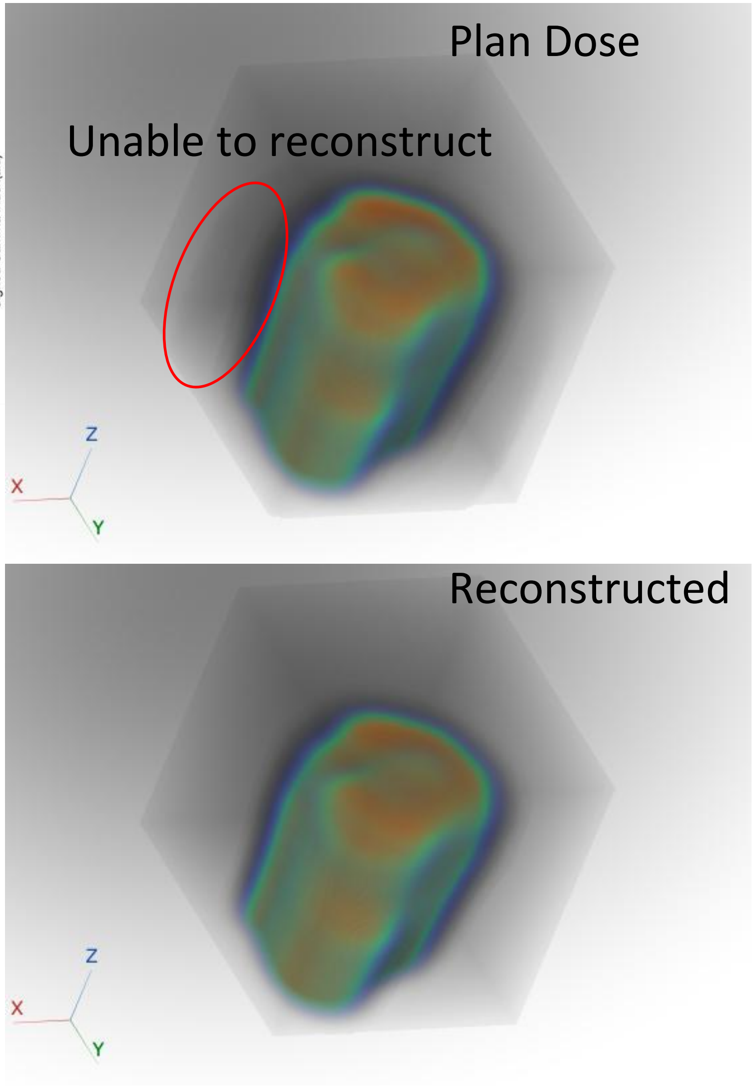
Assign dose to nearest spot

MU discrepancy <2.5%

IMPT Plan

Prostate treatment field with ProBeam



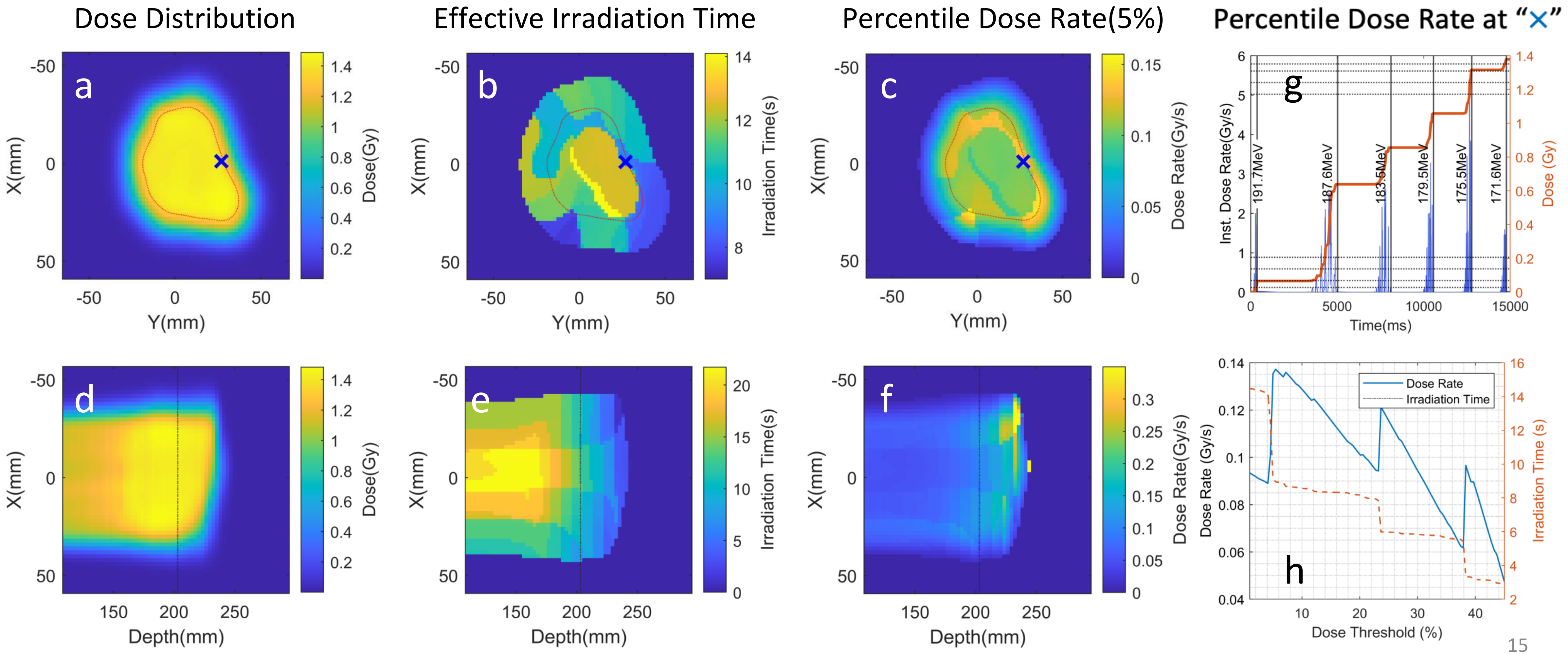


3D Gamma Index: 88.9%, 3mm/3%, 10% threshold
96.2%, based on a 5mm/5% criteria, 10% threshold

Conventional Dose Rate

1309 spots across 12 distinct energy layers. A total of 9832.3 MUs was delivered in 24.7 seconds

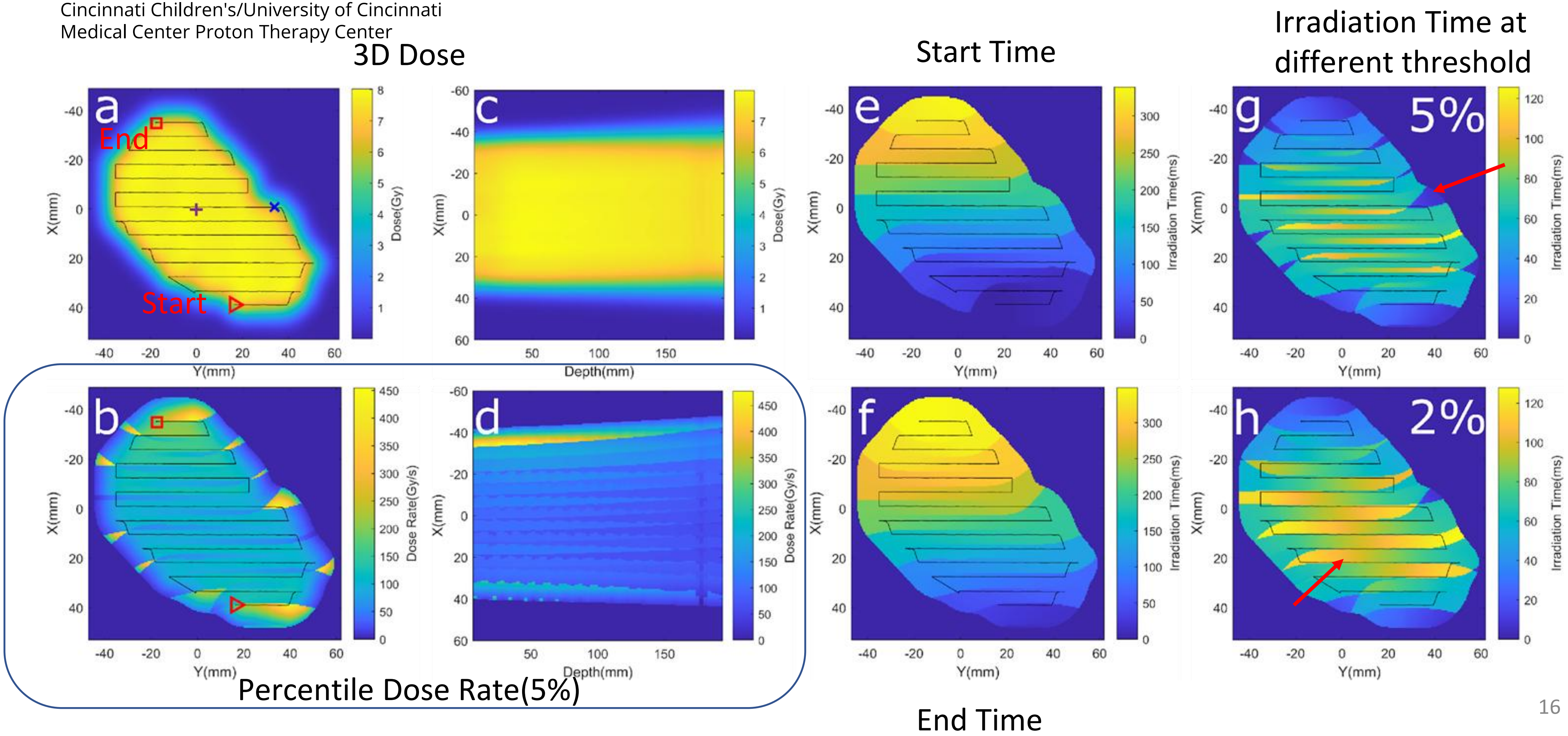
0.3566 s with 38 spots, 3.2909 s with 169 spots, 1.7997 s with 217 spots, 1.1605 s with 182 spots, 0.8851 s with 154 spots and 0.7077 s with 125 spots
Energy switching time: 1.3493 s, 1.2747 s, 1.2554 s, 1.2296 s and 1.1968 s



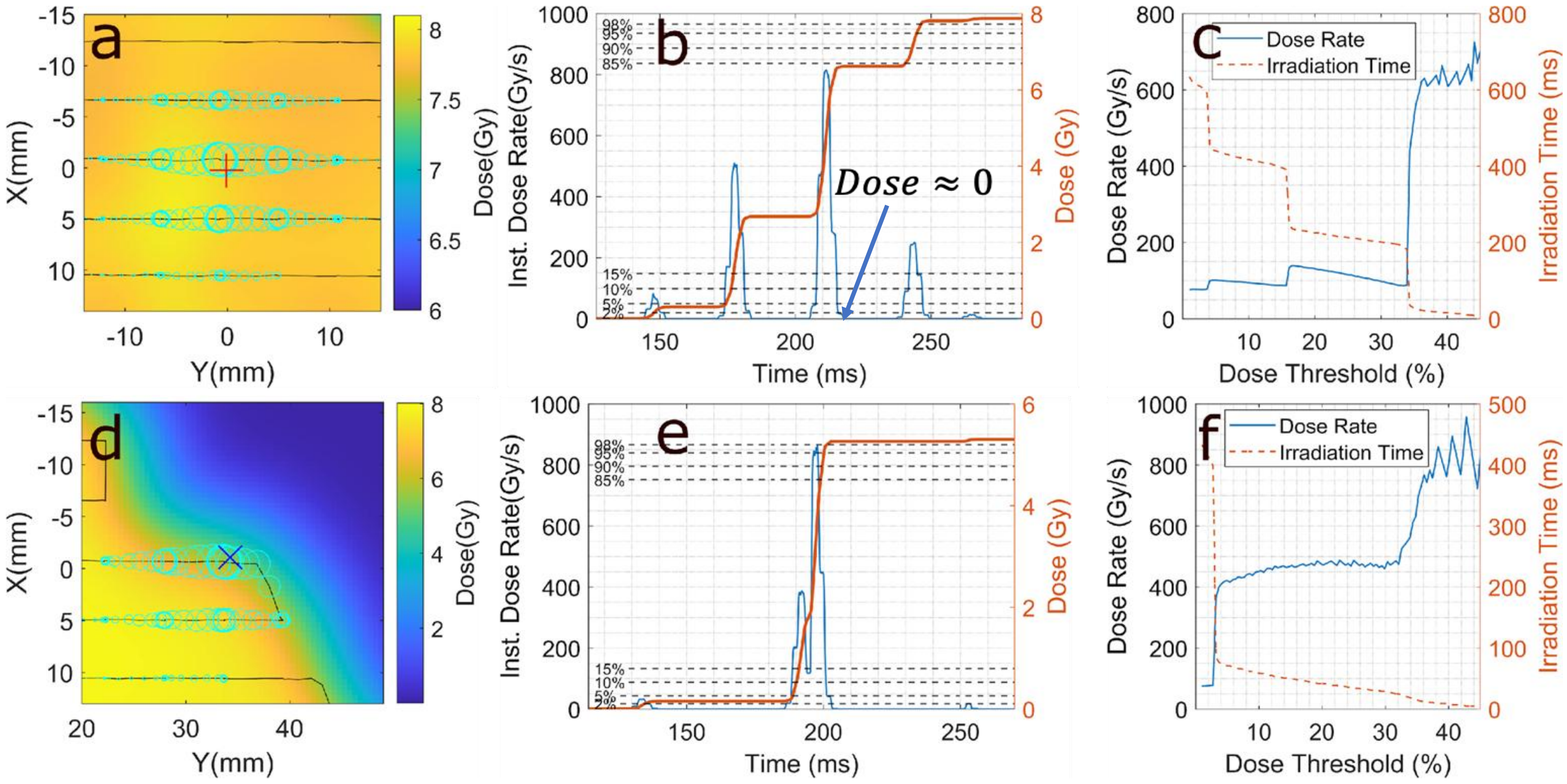
Transmission Proton FLASH Dose Rate(1/3)

141 spots; 111,672 MU in 0.34 seconds

FAST-02 (NCT05524064) clinical trial beam at the Cincinnati Children's/University of Cincinnati Medical Center Proton Therapy Center

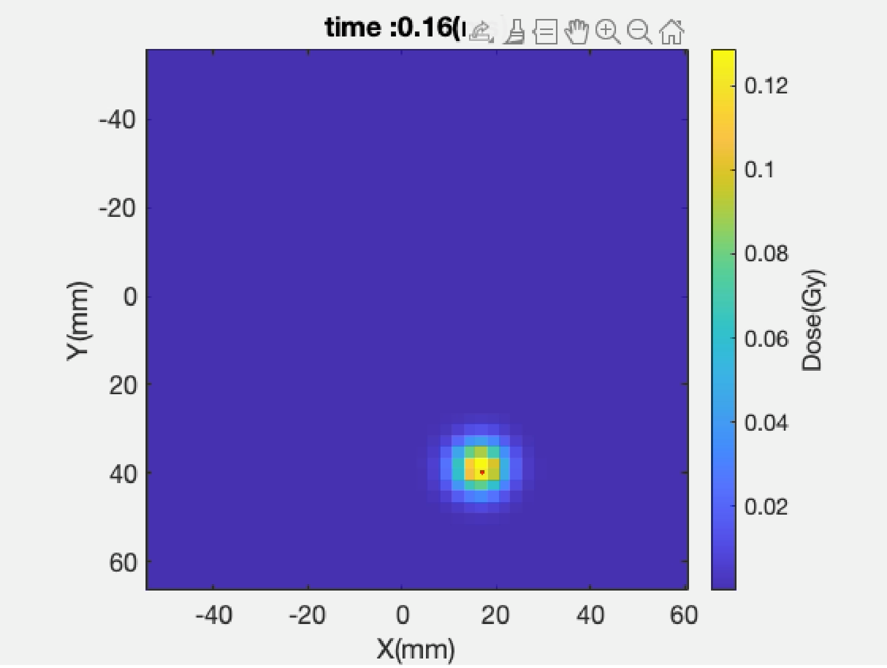


Transmission Proton FLASH Dose Rate(2/3)



Circle size ∝ Dose

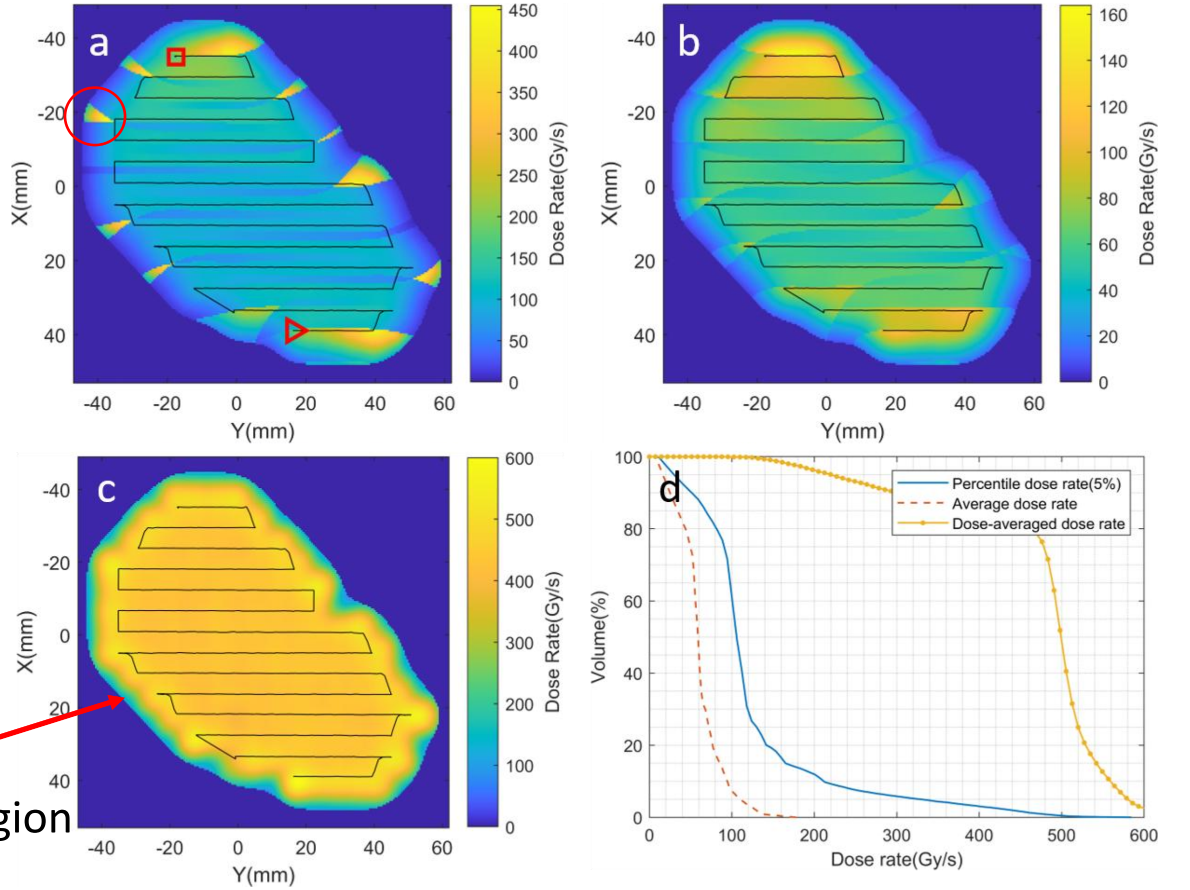
Transmission Proton FLASH Dose Rate(3/3)



High dose rate at turning point

Percentile dose rate(5%)

ADR



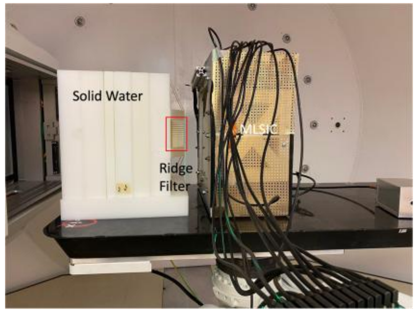
Low dose rate on boundary

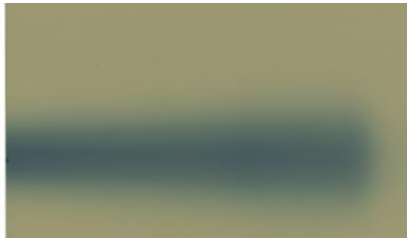
Uniform dose rate in center region

DADR

Dose rate volume histogram

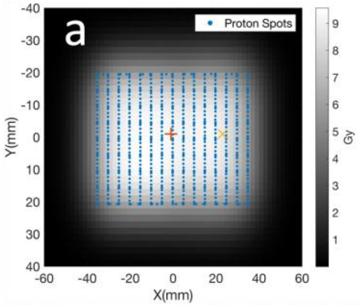
FLASH Dose Rate Measurement of Ridge Filter

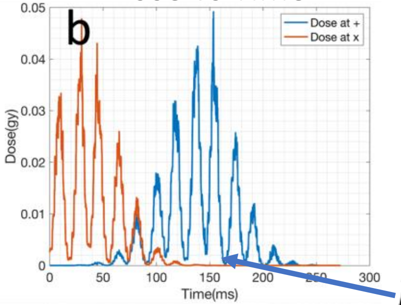




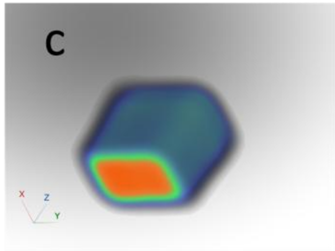
Single spot measured by EBT4 Film

Dose vs Time

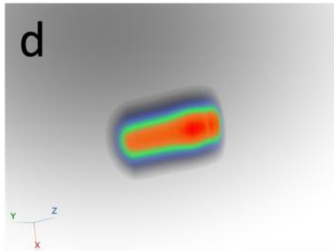




$Dose > 0$



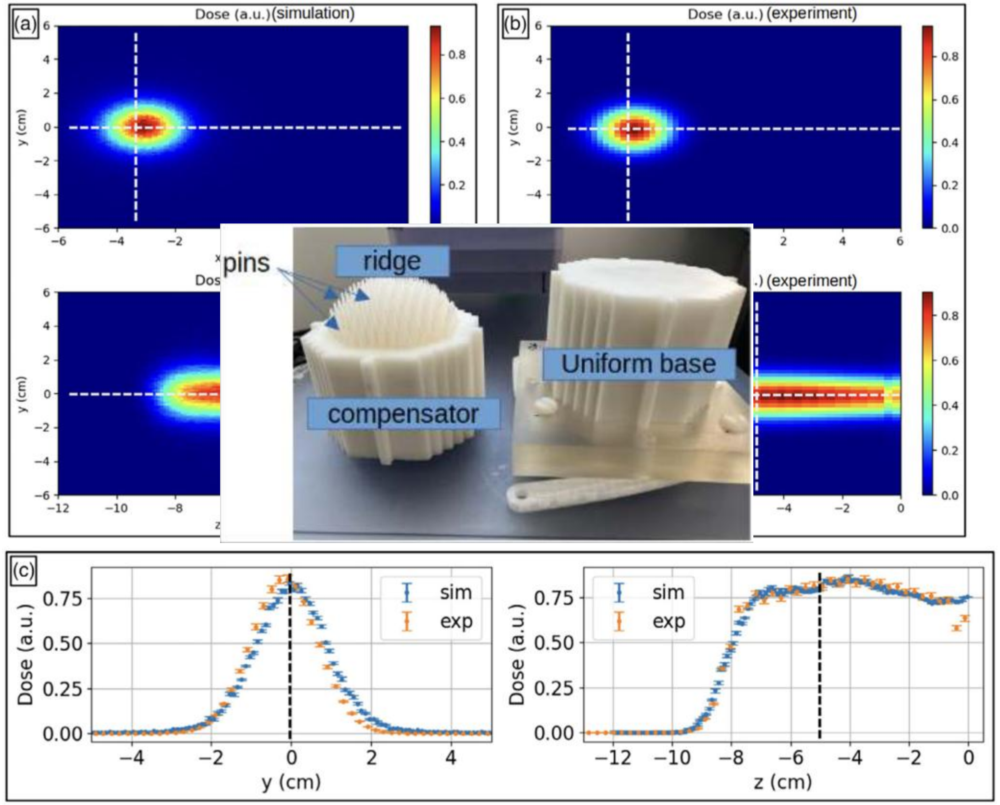
Field 3D dose



Single spot 3D dose

Simulation

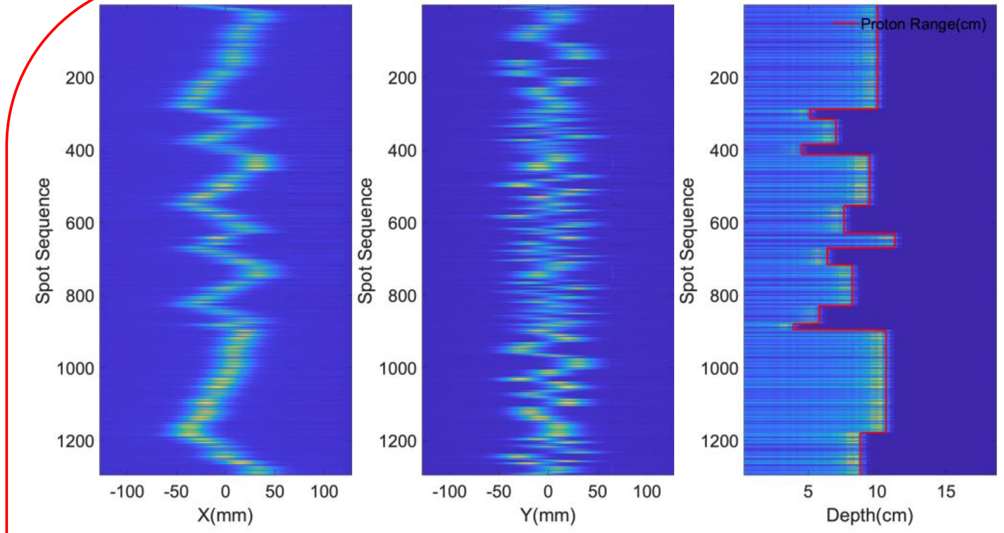
MLSIC

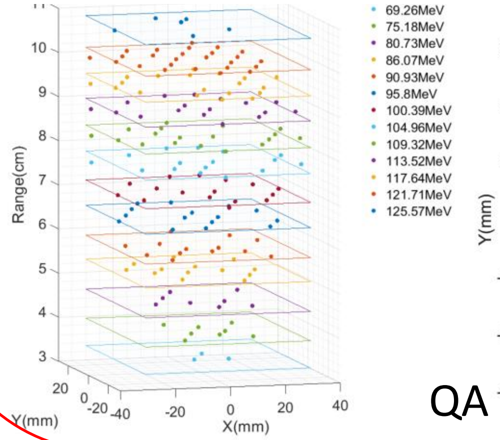


Harrison, Nathan, et al. *Medical Physics* 51.11 (2024): 8411-8422.

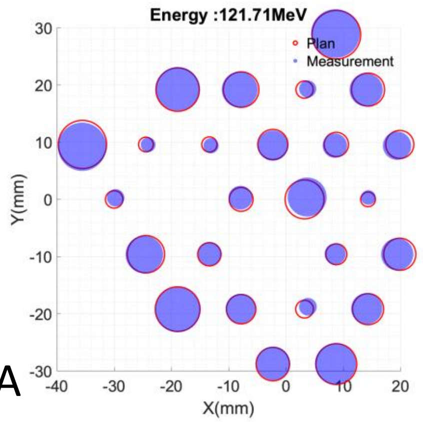
Other Clinical Uses of MLSIC

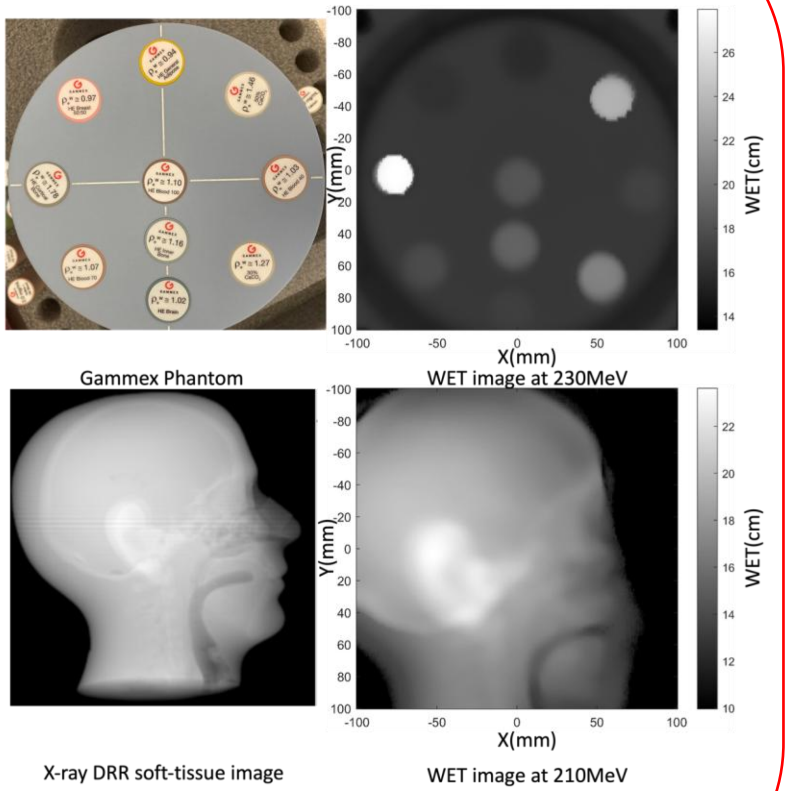
Efficient IMPT patient specific QA   Proton radiography for stopping power measurement





QA

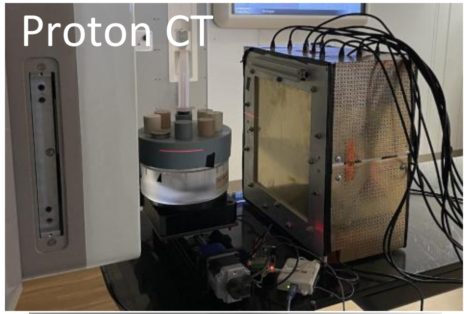




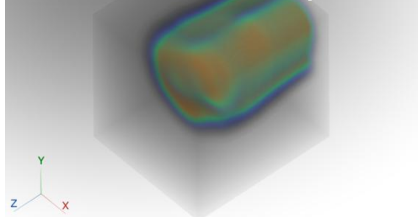
Proton Radiography
WET measurement

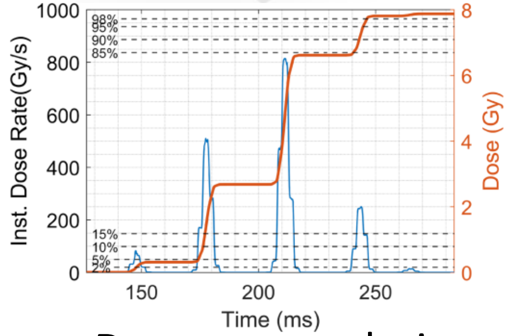
Real-Time Outputs

Proton CT



3D Dose analysis





Dose rate analysis

Offline Outputs

Conclusion

- High speed 3D dose and dose rate measurement device
- Depth dose curve, Lateral dose Profile, 3D dose and dose rate in one system

- Offline Reconstruction required
- Pre-treatment verification only

Acknowledgement

- NIH SBIR Contract #75N91024C00084
- NIH SBIR Contract # 75N91022C00055
- NIH/National Center for Advancing Translational Sciences (NCATS), CTSA grant UL1 TR002345.

- Foundation for Barnes-Jewish Hospital and their generous donors
- Washington University Institute of Clinical and Translational Sciences
- University of Cincinnati College of Medicine, Cincinnati Children's Hospital Medical Center
- Emory University, Emory Proton Therapy Center

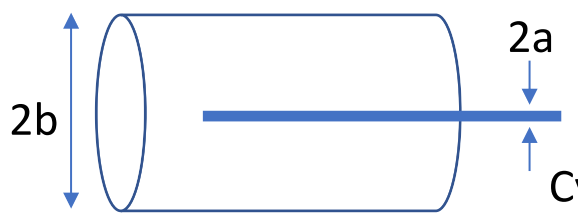
Questions

Review of dose measure tools

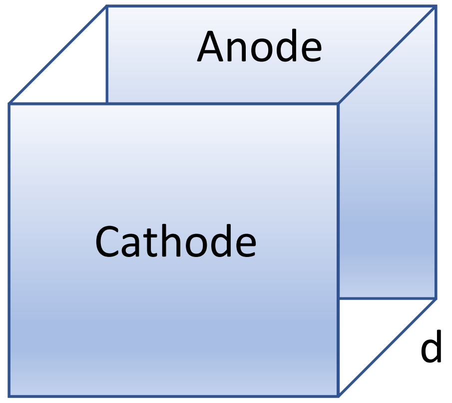
Method	Dimensionality	Sampling Rate	Observable	Representative systems
Water Tank	3D	<1Hz	Gas Ionization Charge	DigiPhant PT
1D Ion Chamber	Depth	~ 100Hz	Gas Ionization Charge	Giraffe, Zebra(100Hz)
Ion Chamber Planar arrays	Surface	10–100Hz	Gas Ionization Charge	MatrixxPT/One(50Hz), Octavius 1600XDR(10Hz) etc
Diode Planar arrays	Surface	20Hz	Semiconductor Charge	MapCHECK3
2D Strip Ion Chamber	Surface	20kHz	Gas Ionization Charge	Yang Y, Shi C, Chen C-C, et al.
Scintillator imaging	Surface	1kHz	Optical Photon	Vasyltsiv R, Harms J, Clark M, et al.
Radiation acoustic imaging	3D (Reconstructed)	Pulse-based	Acoustic Pressure	Zhang, W., Oraiqat, I., Litzenberg, D. et al.
MLSIC	3D (Reconstructed)	6.125kHz	Gas Ionization Charge	Our system

Cylinder ion chamber

Inner electrode radius: a
Outer electrode radius: b
Distance between parallel plates: d



Cylinder ion chamber



Parallel plate ion chamber

$$E(r) = \frac{V}{rln(b/a)}$$

$$t_{cyl} = \int_a^b \frac{rln(b/a)}{\mu V} dr = \frac{\ln(b/a)}{\mu V}(b^2 - a\hat{}2)$$

$$t_{para} = \frac{d^2}{\mu V}$$

Assume b = 3mm, a = 1.7mm, d = 1.3mm

$$t_{cyl} = \frac{0.57}{\mu V} * 6.11 = \frac{3.47}{\mu V}$$

$$t_{para} = \frac{1.3^2}{\mu V} = \frac{2.6}{\mu V}$$