Scintillator Based Real-Time Particle FLASH Therapy Monitoring

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Collaborators

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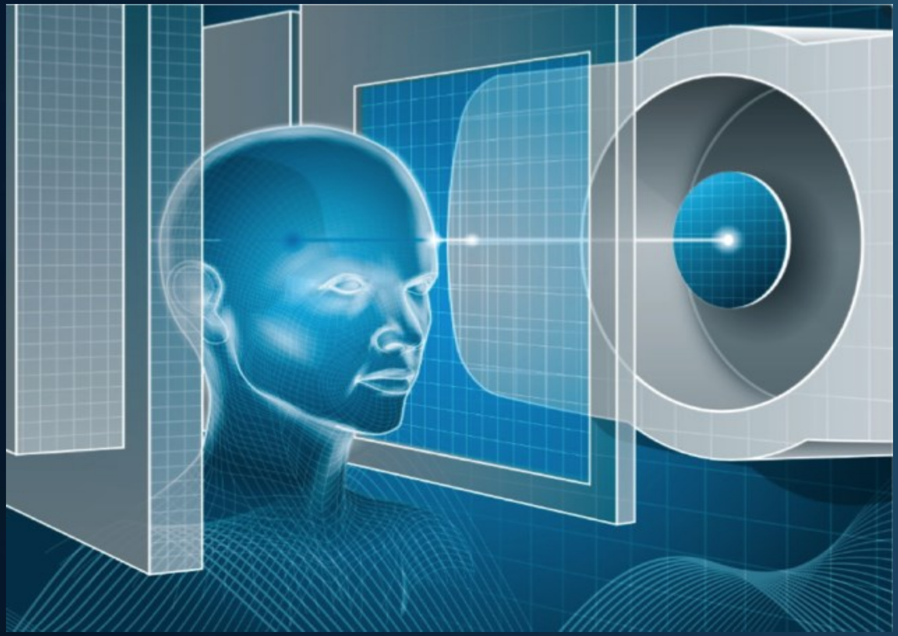
Safety Problem: Monitoring FLASH Delivery

- Challenge: To be clinically approved (FDA/NIH/IRB) FLASH-RT must be monitored in real-time so the beam can be ***immediately*** terminated if a problem develops given the **100-1000X higher dose rates** and **~ 0.1 to 0.5 sec** total delivery time.

- Conventional beam monitors are not capable of large-area 2D imaging with full analysis in real-time at FLASH rates.

- Our Solution: **F**LASH **B**eam **S**cintillator **M**onitor (FBSM) that continuously images & analyzes beam every **50 μs** as the patient is irradiated.

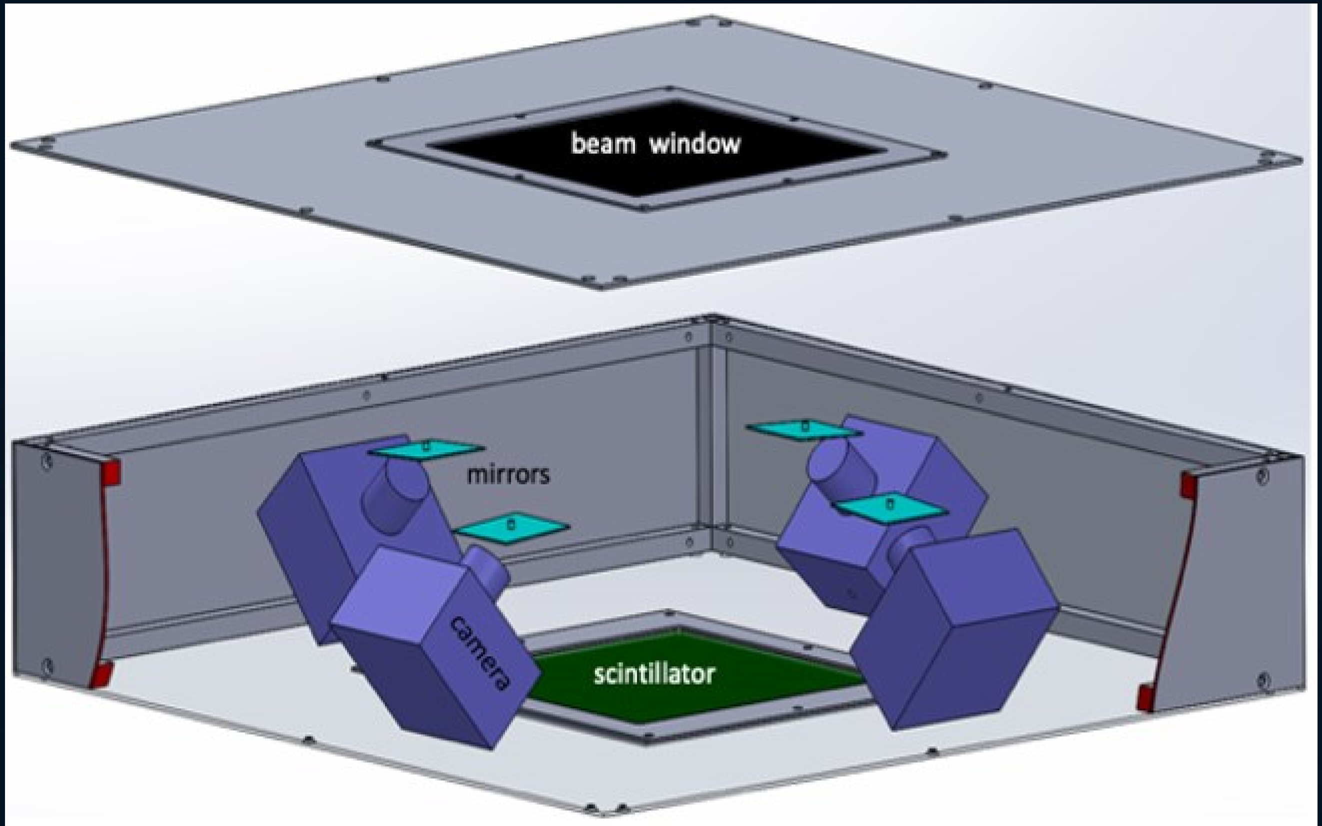


Performance Objectives

✓= achieved

- Fast, real-time response to produce beam interlock, IEC compliant (in progress)
  - **Deliver < 10% of total dose** (or < 10% deviation from treatment plan) **in case of fault**
  - Scanning ***proton*** beams: process at **50 μs** → 20,000 fps, analysis in **~ 1 μs** ✓
  - Pulsed ***electron*** beams: data acquisition/process rate 100-1000 Hz → **1 ms** (in progress)
- Spatial resolution: **<** 100 μm on centroids ✓
- Dynamic range: beam center to tails span 2 orders-of-magnitude ✓
- Low mass & thin profile: < 0.8 mm WE and profile/depth of ~ 10-11 cm ✓
- Large area: 15 cm x 15 cm ✓ to 30 cm x 30 cm (in progress)
- Real-Time Dosimetry (within ~ 50 μs for protons): < 4% ✓
- Radiation resistance: > 1 year of clinical usage (5 d/wk; 50 wk/yr) < 1% signal loss/yr ✓

Large-Area FLASH Beam Scintillator Monitor*



** 1st Generation **FBSM** Conceptual Design*

- Large 30 cm x 30 cm sensitive area
- Quadrant system with 4 cameras
- Thin 11 cm profile with folded optics
- Ultrafast machine-vision cameras
- Triggered or quasi-free-running modes
- FPGA data processing & analysis
- Low mass profile < 800 µm WE

**NIH-NCI $1.9M "Direct-to-Phase-II" SBIR Award 2021-2024*

Large-Area Proprietary Scintillators

Type 1: **Hybrid Material (HM)** – Inorganic polycrystalline ceramic hybrid

- Thin < 800 µm WE

Type 2: **Polymer Material (PM)** – Semicrystalline

- Ultrathin to Thin: tested 2 µm to < 300 µm WE

Both Types 1 & 2 have favorable properties:

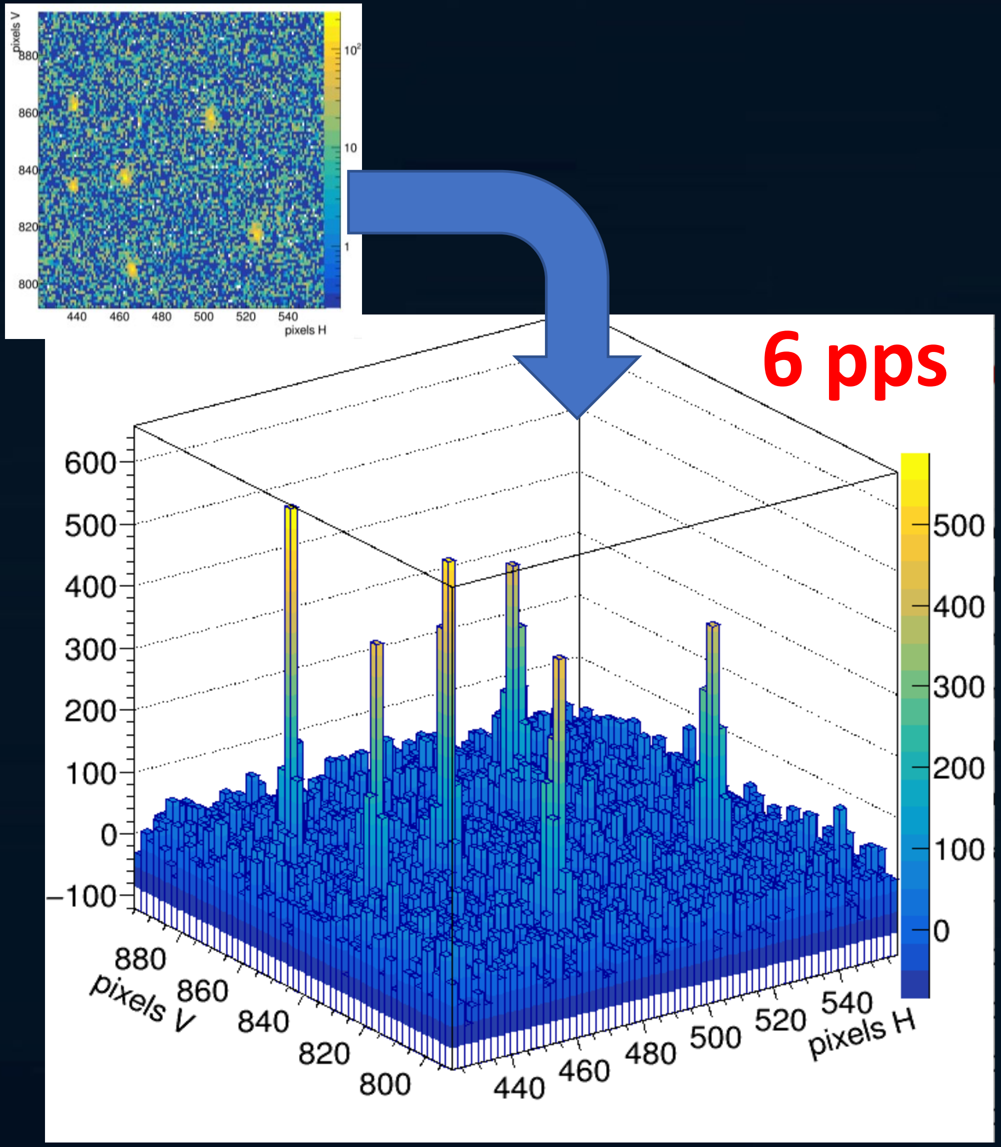
- Radiation hard
- Sharp images – no internal reflections
- Non-hygroscopic
- Highly transmissive
- Extremely high light emittance for their respective type

Test Beam Results for Prototypes

*at **FLASH Dose Rates***

Notre Dame Radiation Laboratory…….	e^-	8 MeV,	0.2-200 Gy/s
U. Michigan Ion Beam Laboratory ……	p+	5 MeV,	> 300 Gy/s
Facility for Rare Isotope Beams …….	$^{86}Kr^{+26}$	2.75 MeV/u,	~0-50 Gy/s*

Single - Particle to FLASH Dose* with $^{86}Kr^{+26}$



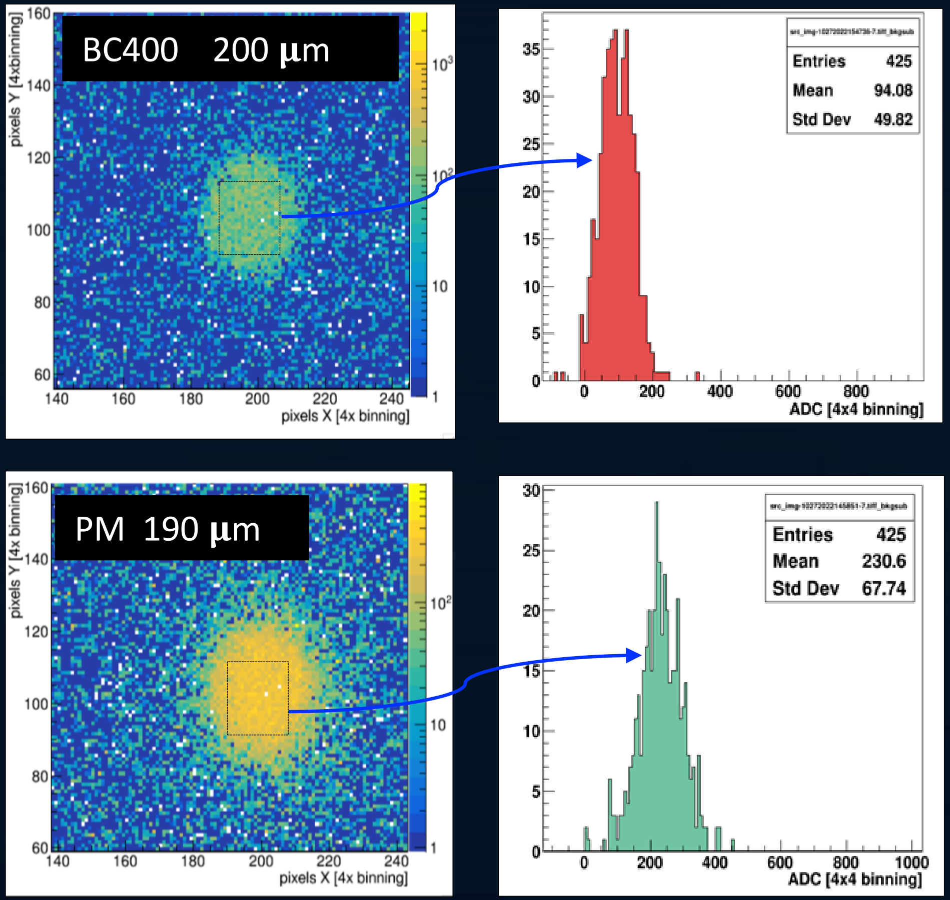
36
Kr
Krypton
83.80

*Krypton is a mixture of six stable isotopes with ^{86}Kr being the heaviest of its natural isotopes.

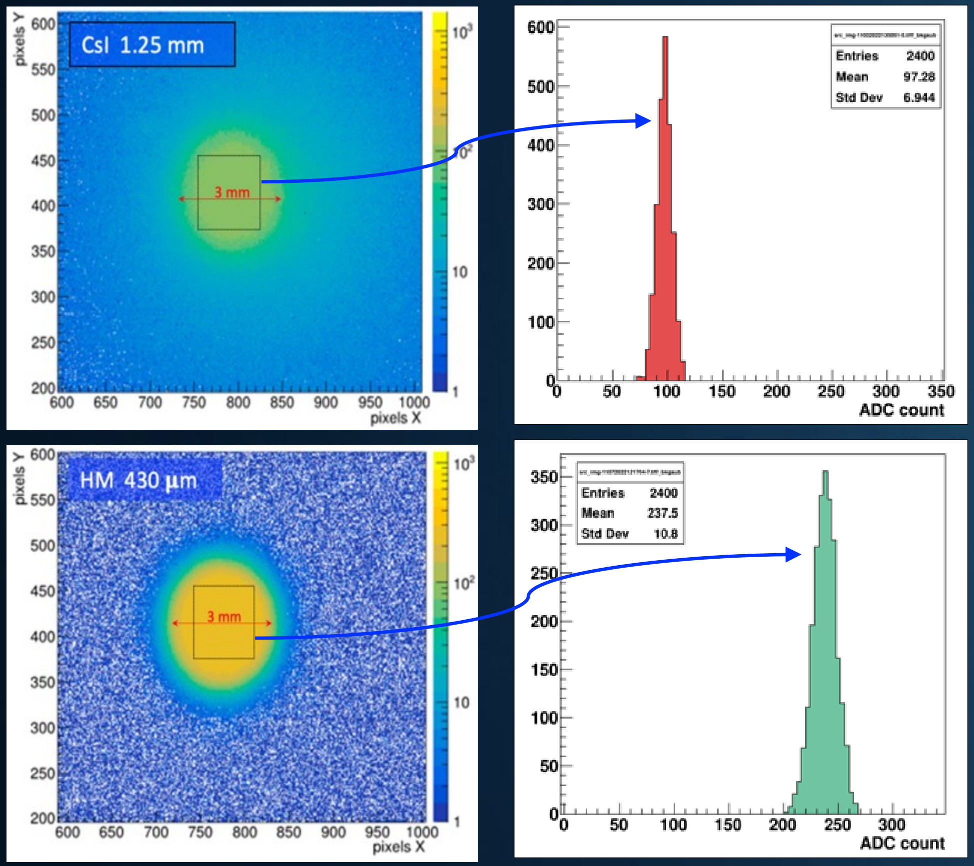
Scintillator Efficiency Comparisons to Benchmarks

3 mm collimated electron beam (β^- source ^{90}Sr)

PM type

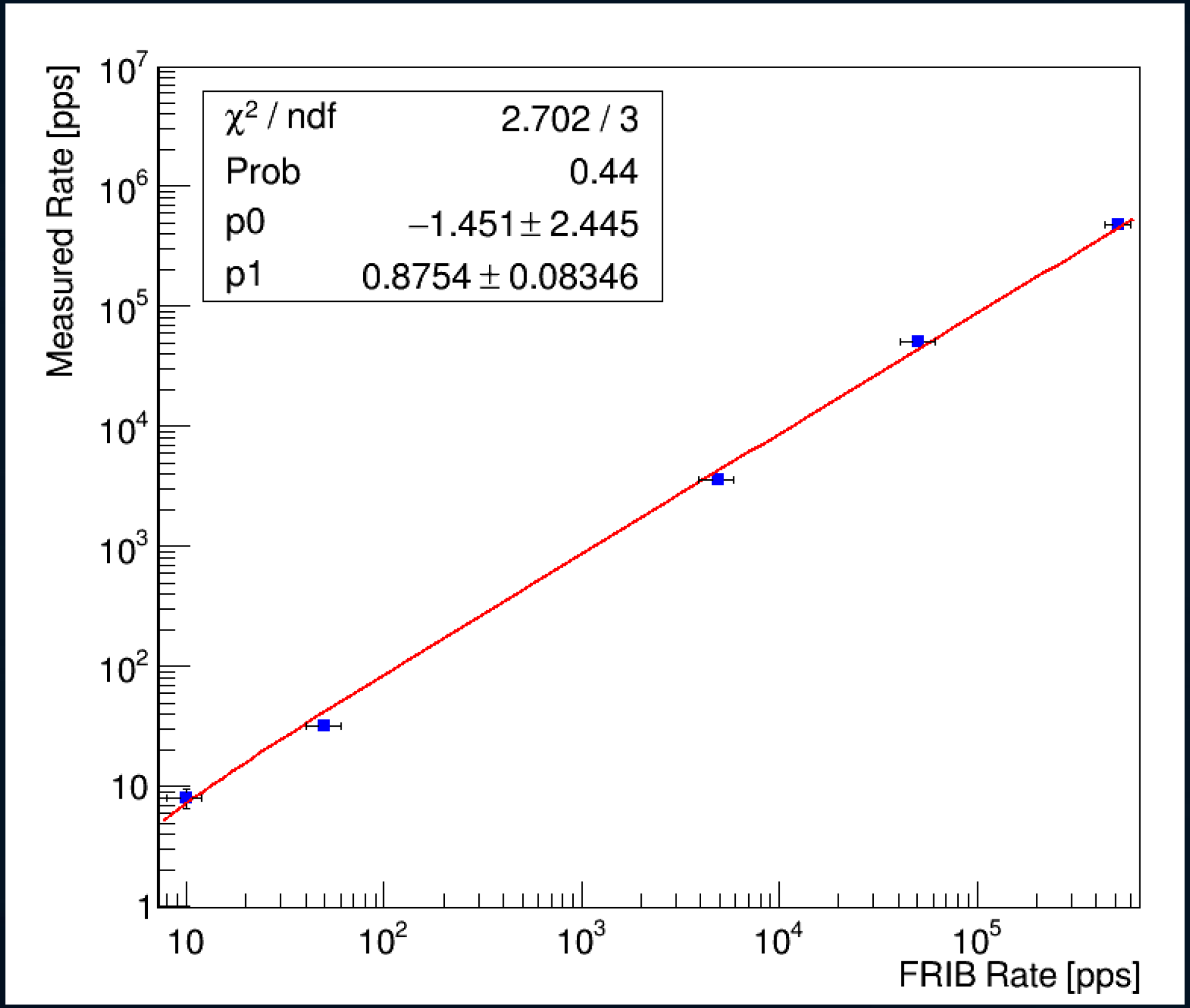


HM type



Beam Current in HM Scintillator

Kr^{+26} Beam Monitor Rate vs FRIB Instruments Rate



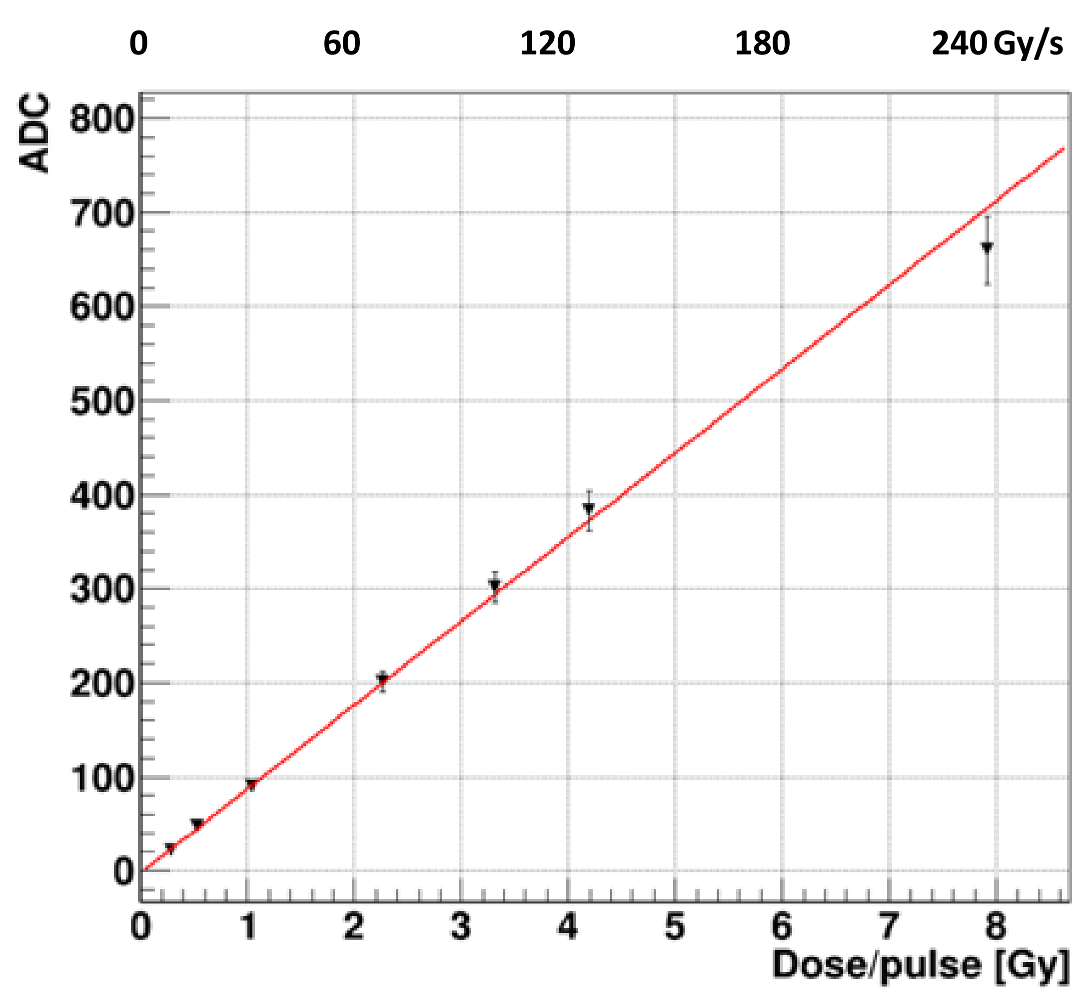
➔ Result 1: Beam monitor measures currents over range covered by *4 different FRIB devices*

- Faraday Cup
- Calibrated beam attenuator
- MCP detector
- Silicon detector

➔ Result 2: **Linear for 5 decades up to FLASH dose rates**

Dose Response in HM Scintillator

8 MeV Electron Beam at 30 Hz (Notre Dame Lab)



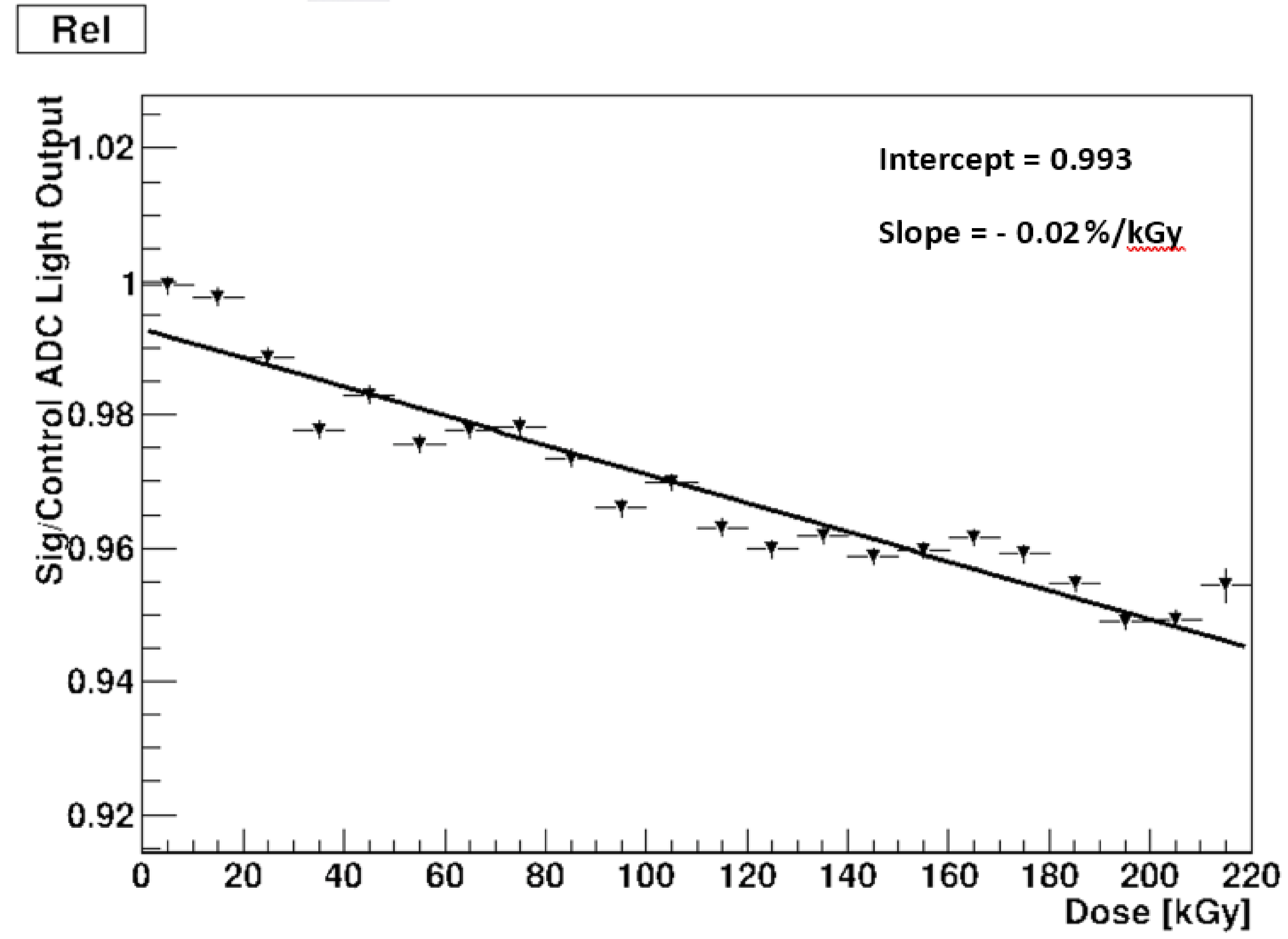
Each data point = average of 100 pulses.

Pulse width in all cases ~2 ns.

At 30 Hz, average dose rate ranges from **~6 to >200 Gy/s**, which is well beyond the required 40 Gy/s for FLASH.

Linear response to *high dose* FLASH rates.

Radiation Hardness of HM Scintillator

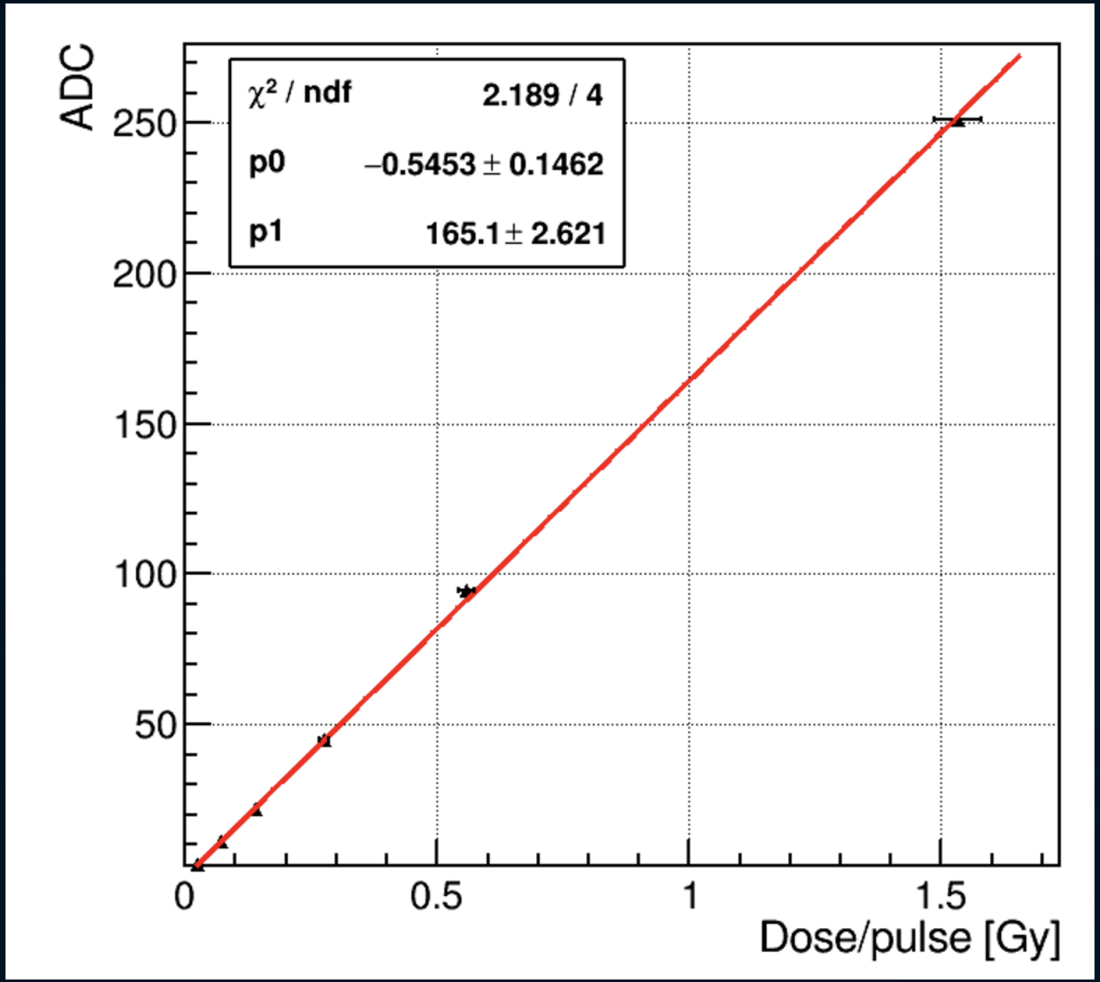


Low signal loss of 0.02%/kGy measured over 212 kGy in 15 minutes (acceleration factor of ~ 150,000x or five-OOM !).

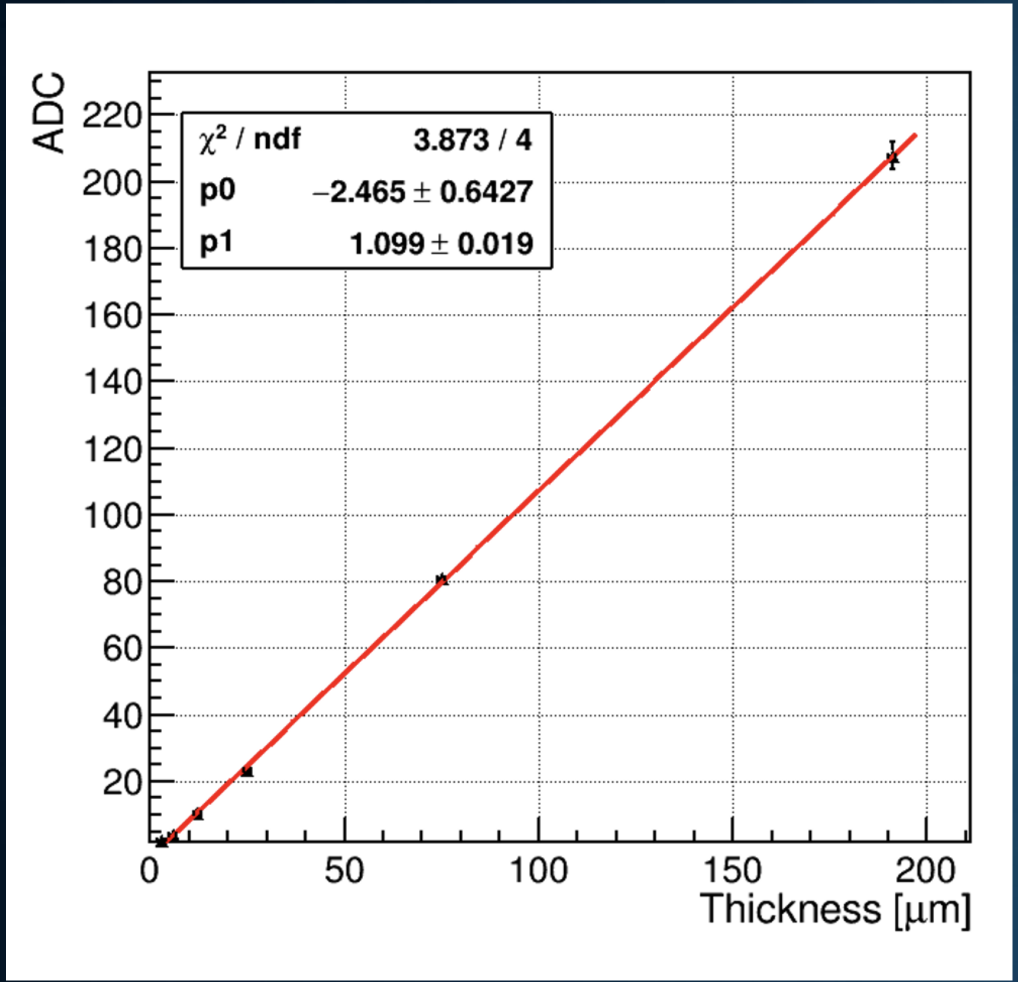
> 1 yr of continuous FLASH patient use (~ 50 kGy) yields < 1 % signal loss.

Signal loss is correctable with internal UV calibration system.

PM Scintillator Response to Dose & Thickness



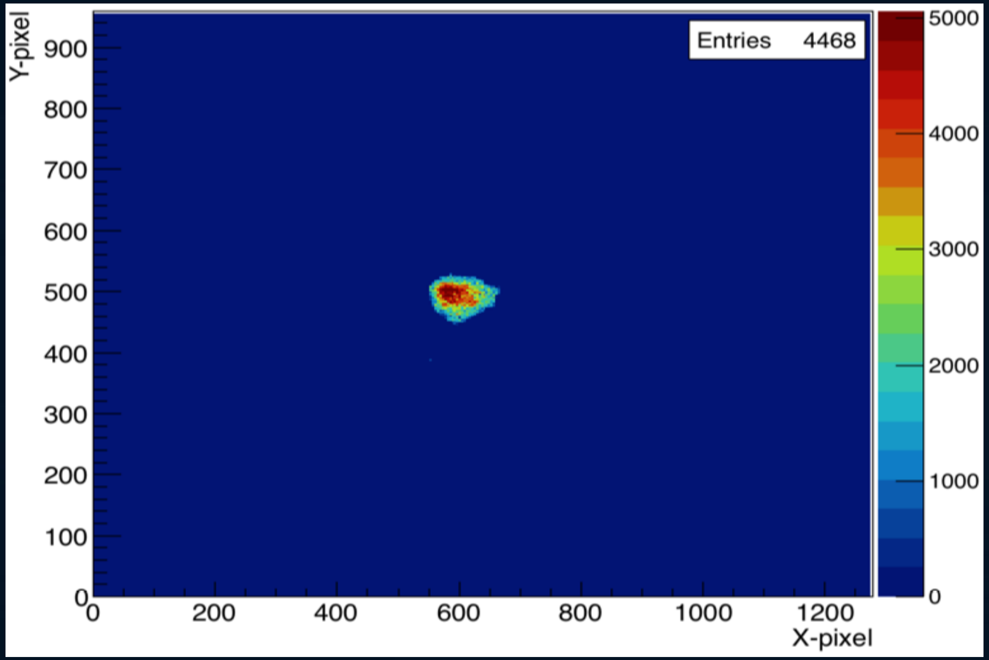
Result 1: Signal scales with dose

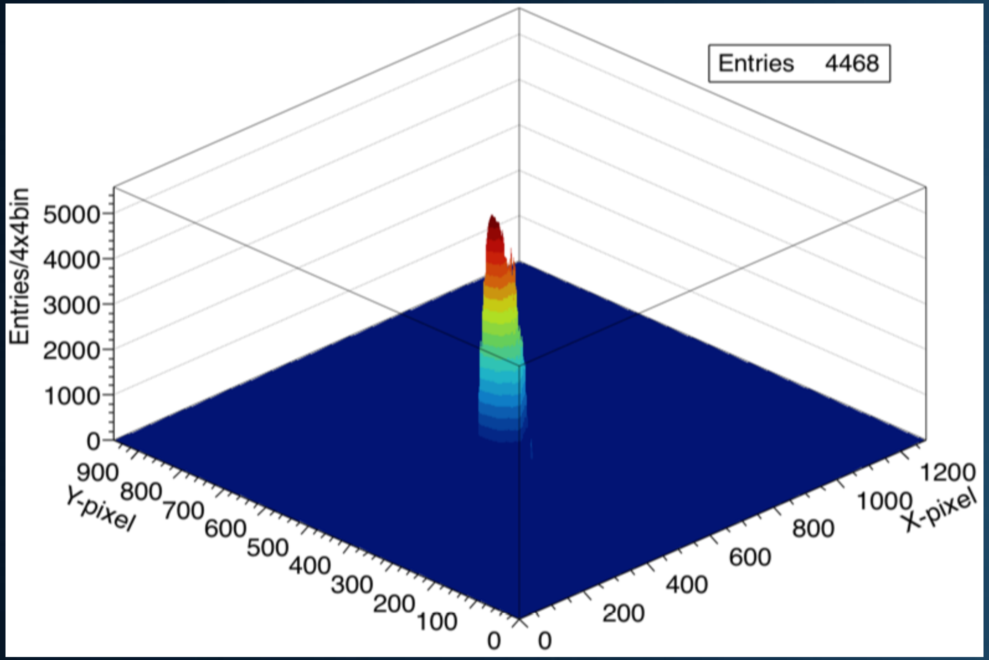


Result 2: Signal scales with thickness

PM-Scintillator Image at FLASH Dose Rate

Moving *proton beam image* (color coded) captured with *10 μs exposure**





*10 nA beam of 5.4 MeV protons **moving at 80 mm/ms**, through 190 μm thick PM-scintillator with diameter of ~2.5 mm. Particle flux corresponds to ***FLASH dose rate of ~200 Gy/s***.

Beam Energy Loss & Scattering

(in Beam Monitor with 190 μm thick PM)

*Proton Beam Energy Loss through Beam Monitor**

< 0.30 MeV at 70 MeV, **< 0.18 MeV** at 140 MeV, **< 0.14 MeV** at 210 MeV

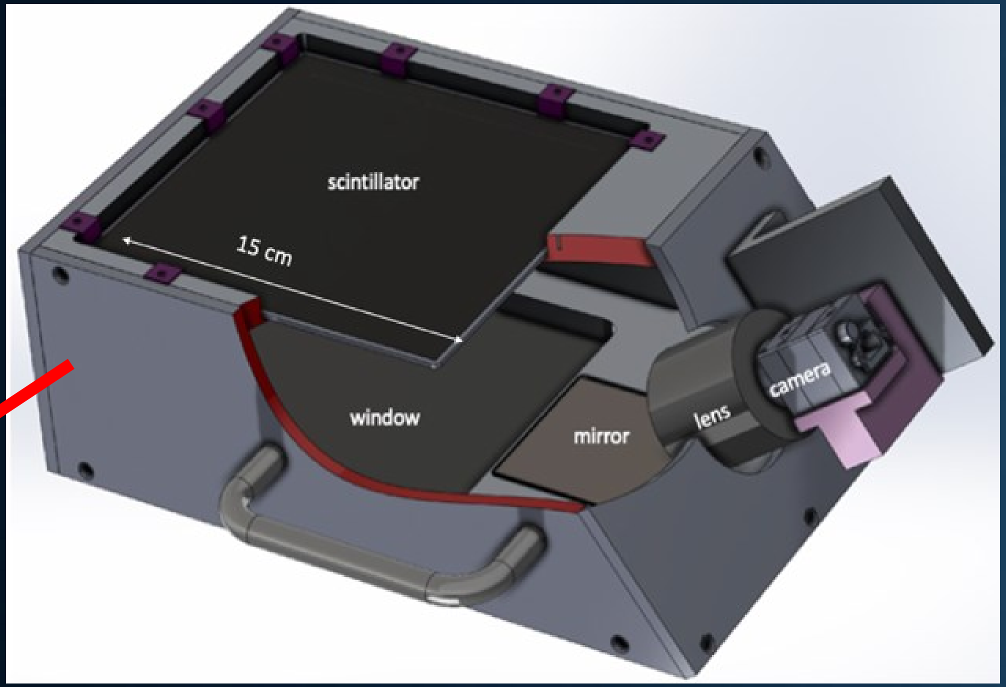
*Beam Spread 70 cm Downstream from Monitor Materials**

≤ 0.017 mm at 70 MeV, **≤ 0.006 mm** at 140 MeV, **≤ 0.003 mm** at 210 MeV

* *~90% of beam energy loss & beam spread due to air (calculations by Geant4 simulations)*

Beam Tests at U. Michigan Radiation Oncology

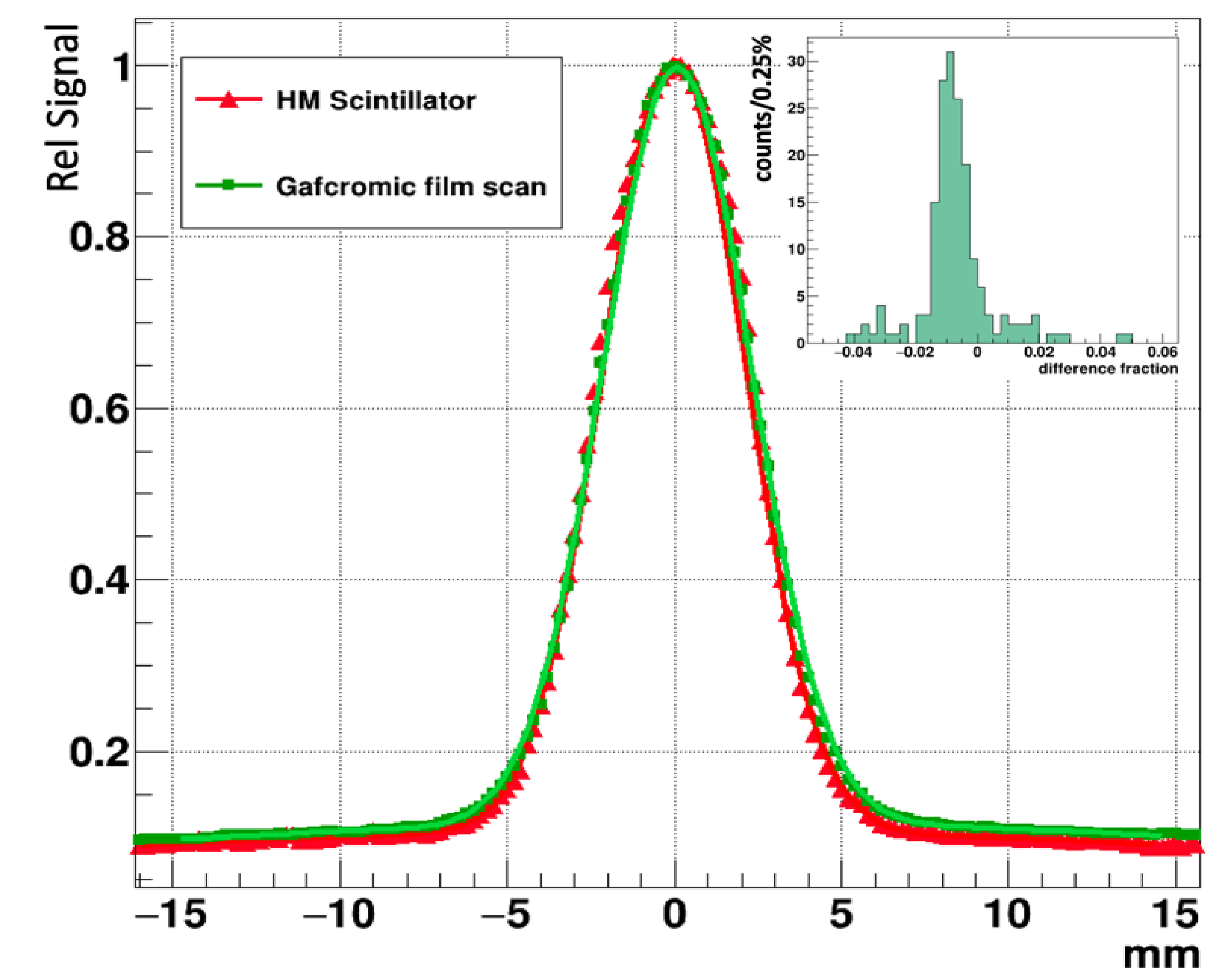
Varian linac: electron energy 6-16 MeV
Conventional dose rate = 1 – 10 Gy/min



Protoype FLASH Beam Scintillator Monitor (FBSM) single camera, 15 cm x 15 cm

Beam Shape & Spatial Resolution

HM Scintillator vs Gafchromic Film

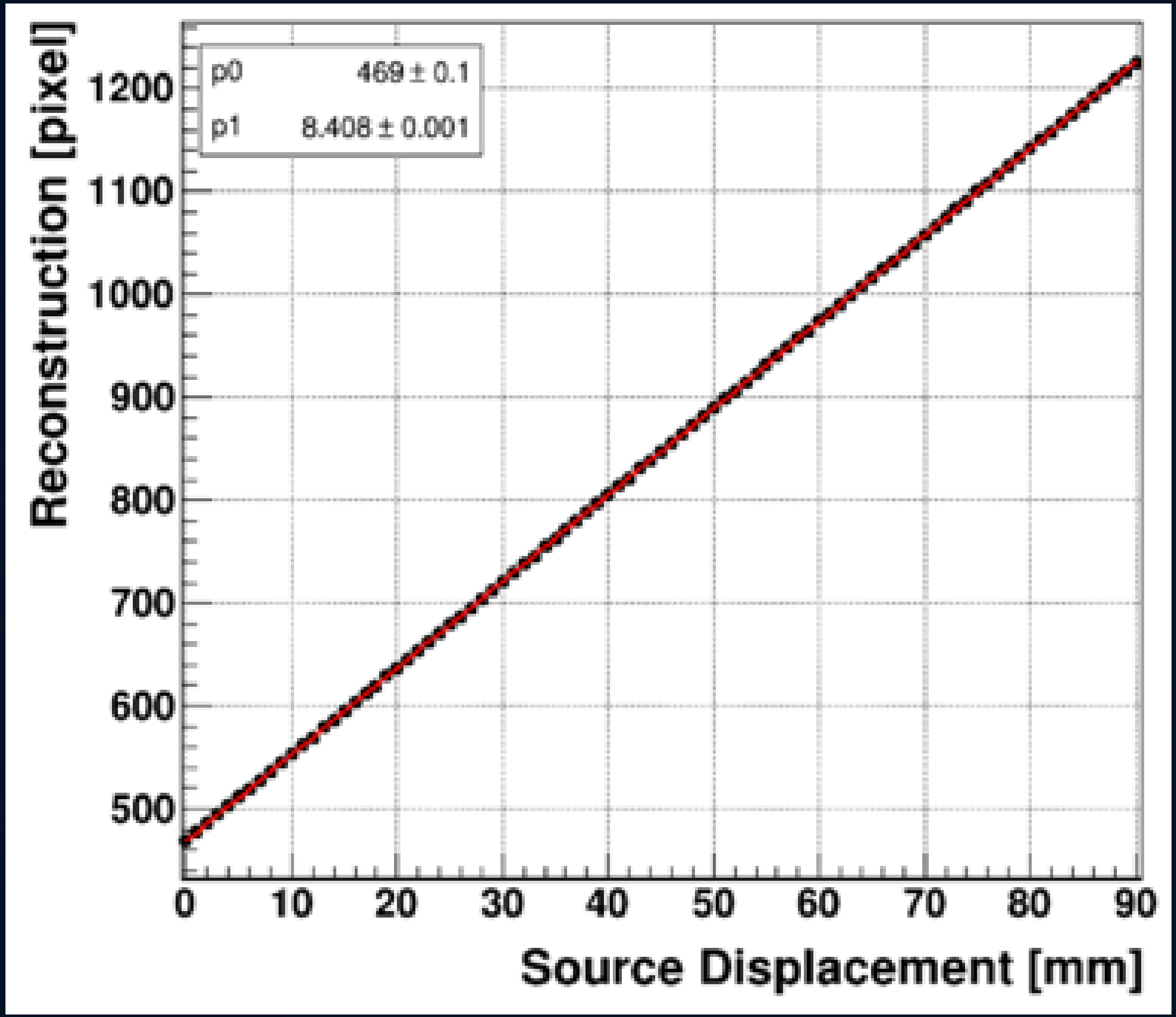


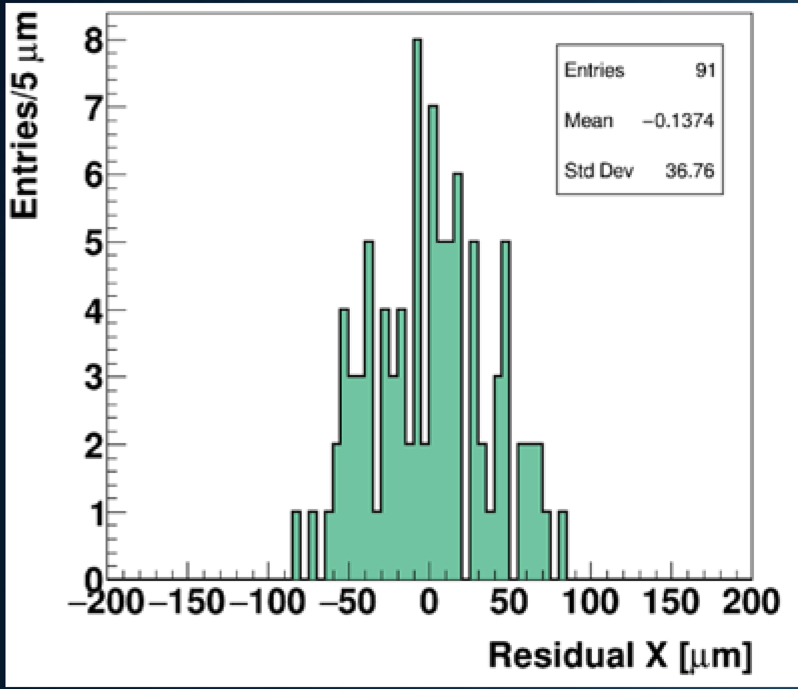
HM scintillator resolution is similar to Gafchromic film resolution (≲ 25 μm).

2D beam profiles are nearly identical.

Beam monitor primary advantage is real-time analysis

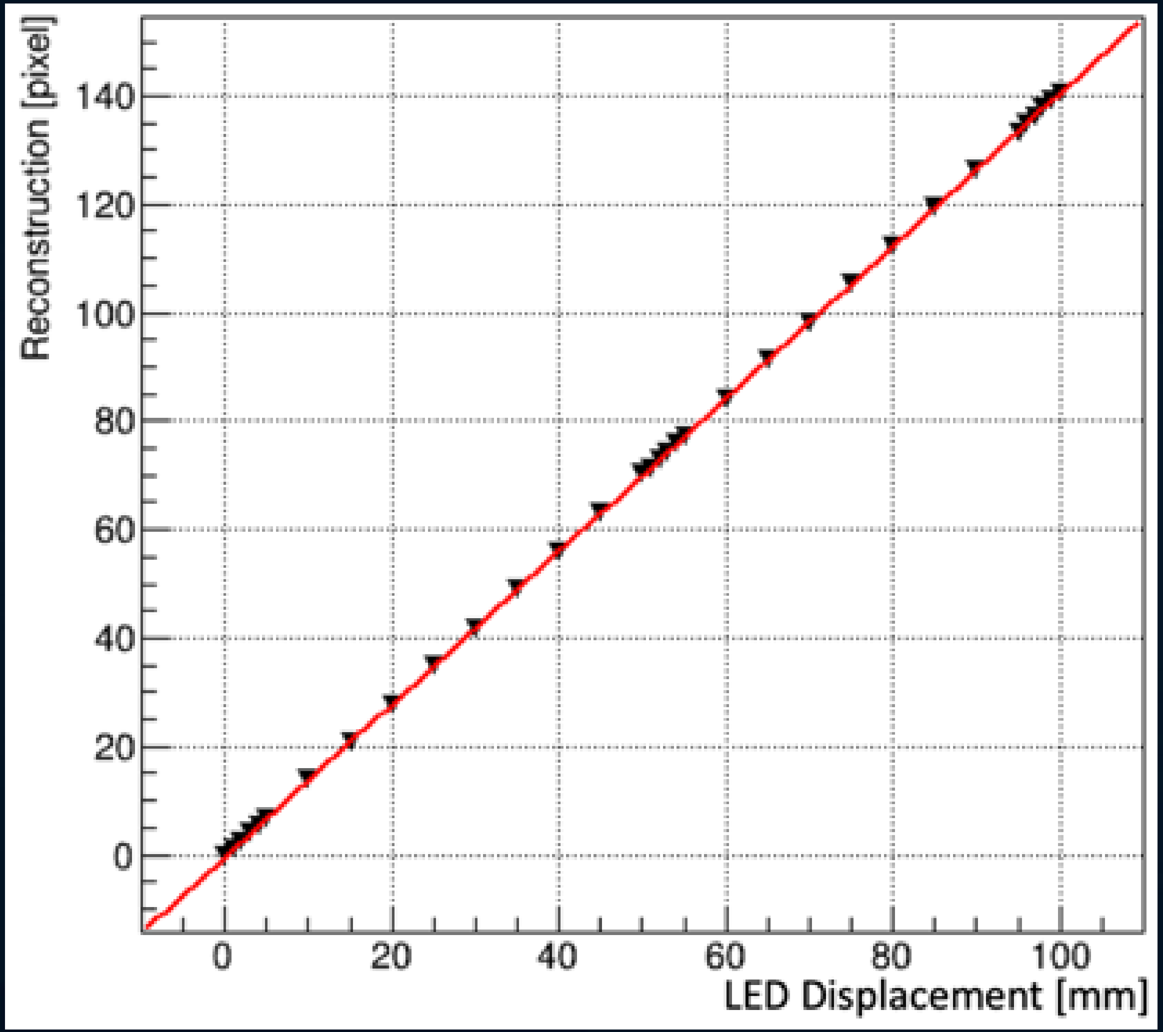
FBSM Spatial Resolution at 200 fps

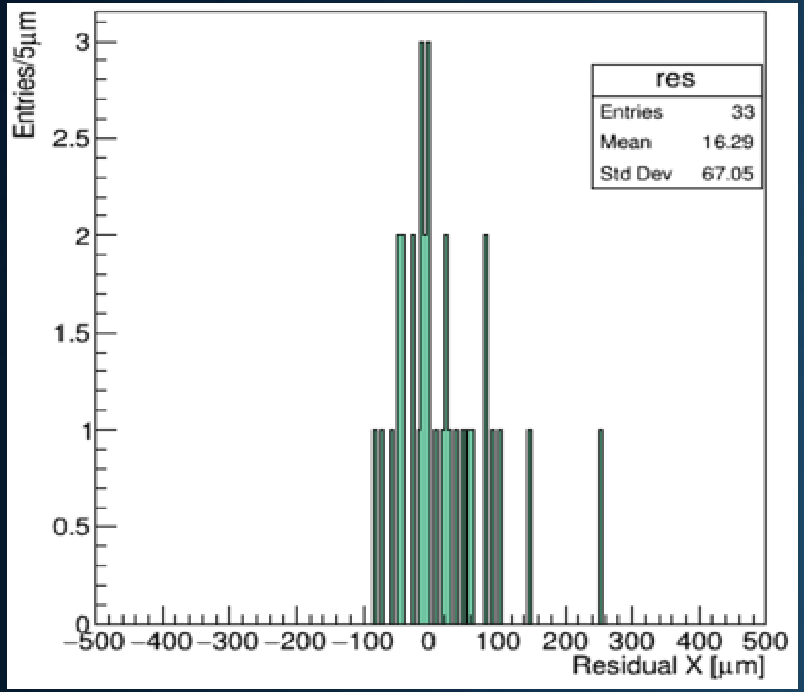




(Left) reconstructed beam centroids in pixel units plotted against precise location of a 3 mm beta source translated along the X coordinate of the FBSM. (Right) The residual distribution of the reconstructed positions yields spatial resolution of **37 µm** (RMS of fit residuals using Camera-E at **200 fps**).

FBSM Spatial Resolution at 20,000 fps



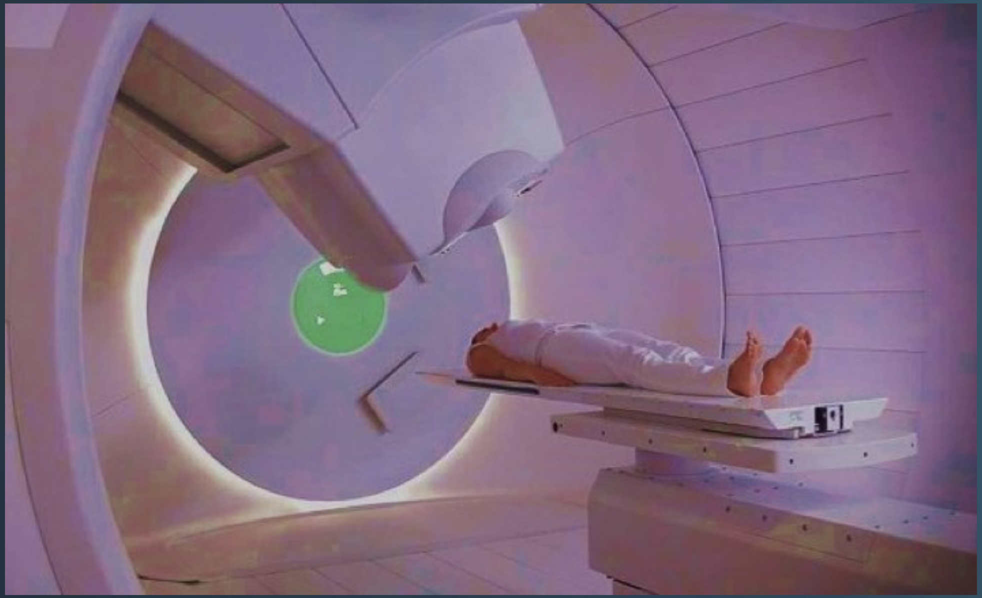


(Left) reconstructed beam centroids in pixel units plotted against precise location of a 10 mm LED source translated along the X coordinate of the FBSM. (Right) The residual distribution of the reconstructed positions yields spatial resolution of **67 μm** (RMS of fit residuals using Camera-P at **20,000 fps**).

FBSM Competitive Advantages

Our beam monitor is a patented, enabling technology for FLASH-RT

- Two New High Efficiency Scintillators
  - ➢ PM-scintillator (polymer) ultra-thin rolls
  - ➢ HM-scintillator (hybrid) highest efficiency
- Innovative / Patented Configurations
  - ➢ Ultra-fast beam analysis ~ **1 μs** *(continuous)*
  - ➢ Real-time dosimetry, beam position, 2D shape
  - ➢ High spatial resolution (≤ **70 μm**)
  - ➢ Water-equivalent thickness ~ 2 μm to < 800 μm
  - ➢ Internal calibration
  - ➢ Multiple cameras & folded optics
  - ➢ Detector area: up to ~ 30 cm x 30 cm



Applications

- **FLASH-RT** (electrons, protons, ions, photons / x-rays)
- Advanced EBRT including heavy-ions (helium, carbon ions, etc.)
- Electron – FLASH – IORT (intraoperative radiation therapy)
- Beamline Monitoring (medical EBRT & scientific apps. – e.g., DOE at FRIB, ANL)
- High-Resolution, Volumetric Patient Specific QA (FLASH & conventional EBRT)
- Boron Neutron Capture Therapy (BNCT beam monitoring)

Validation & Collaborations

Radiotherapy *(NIH-NCI) and* ***Nuclear Physics*** *(DOE-NP)*

- Leading Academic & Government Institutions
  - University of Michigan
  - Loma Linda University
  - Stanford Cancer Institute
  - University of Texas / MD Anderson
  - Texas A&M
  - Notre Dame University
  - Florida State University
  - DOE Argonne National Laboratory
  - DOE Facility for Rare Isotope Beam

Technical Summary

✓ = achieved

*We have **demonstrated** prototype monitors for FLASH-RT beams ✓*

- **2D Imaging** with large area 15 cm x 15 cm ✓ 30 x 30 cm in development
- **High sensitivity & dynamic range**: single-particles to FLASH-RT dose rates ✓
- **Linear response:** up to highest FLASH dose rates ✓
- **Spatial resolution** < 70 µm, comparable with Gafchromic film ✓
- **Excellent radiation hardness** ✓
  - PM scintillator radiation damage: none observed to 9 kGy ✓
  - HM scintillator radiation damage: overall -0.02 %/kGy, tested to 212 kGy ✓
- **Real-time FLASH data processing** ✓
  - 20 kHz for protons with < 1 µs required for data analysis ✓
  - 1 kHz electrons (in progress)

2024 Technology Plans

- ***Electron*** and ***Photon*** FLASH-RT collaborations being discussed with prototype FBSM demonstrations planned.

- ***Proton*** FLASH beam demonstration of our FBSM being discussed at one of several possible university-based facilities.

- **High Resolution, Volumetric PSQA** (Patient Specific Quality Assurance) to be pursued.

- **BNCT** real-time beam monitoring application being discussed with several interested parties.

Conclusions

- Enabling technology for faster, safer & lower cost radiotherapy
- Technology validated and protected
- Development partners in place for NIH-NCI and DOE-NP programs
- Non-dilutive financing leverage:
  - NIH-NCI **$3.9M** Phase-II Awards for real-time/FLASH beam monitoring
  - DOE-NP **$1.7M** Phase-II Awards for real-time particle beam monitors
- We are looking to collaborate with additional technology partners