Demonstration of LGADs and Cherenkov detectors for prompt gamma timing range verification of proton therapy

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Proton therapy range verification

- Protons potentially offer better targeting of tumor than x-ray therapy, thanks to Bragg peak.
- But, requires aim in 3D, not just 2D
- In practice, treatment planned with very conservative margins, negating a lot of the potential benefit.

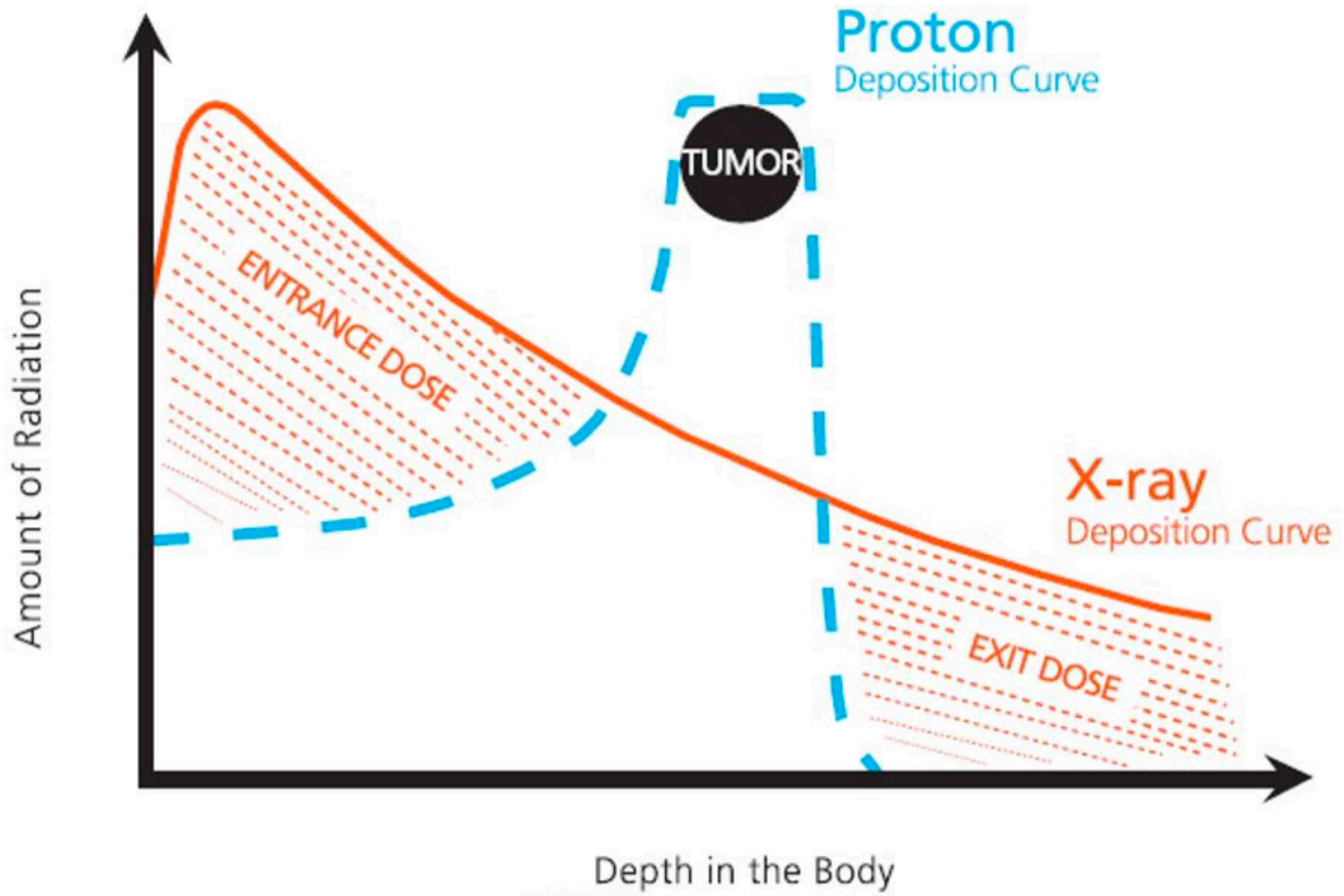

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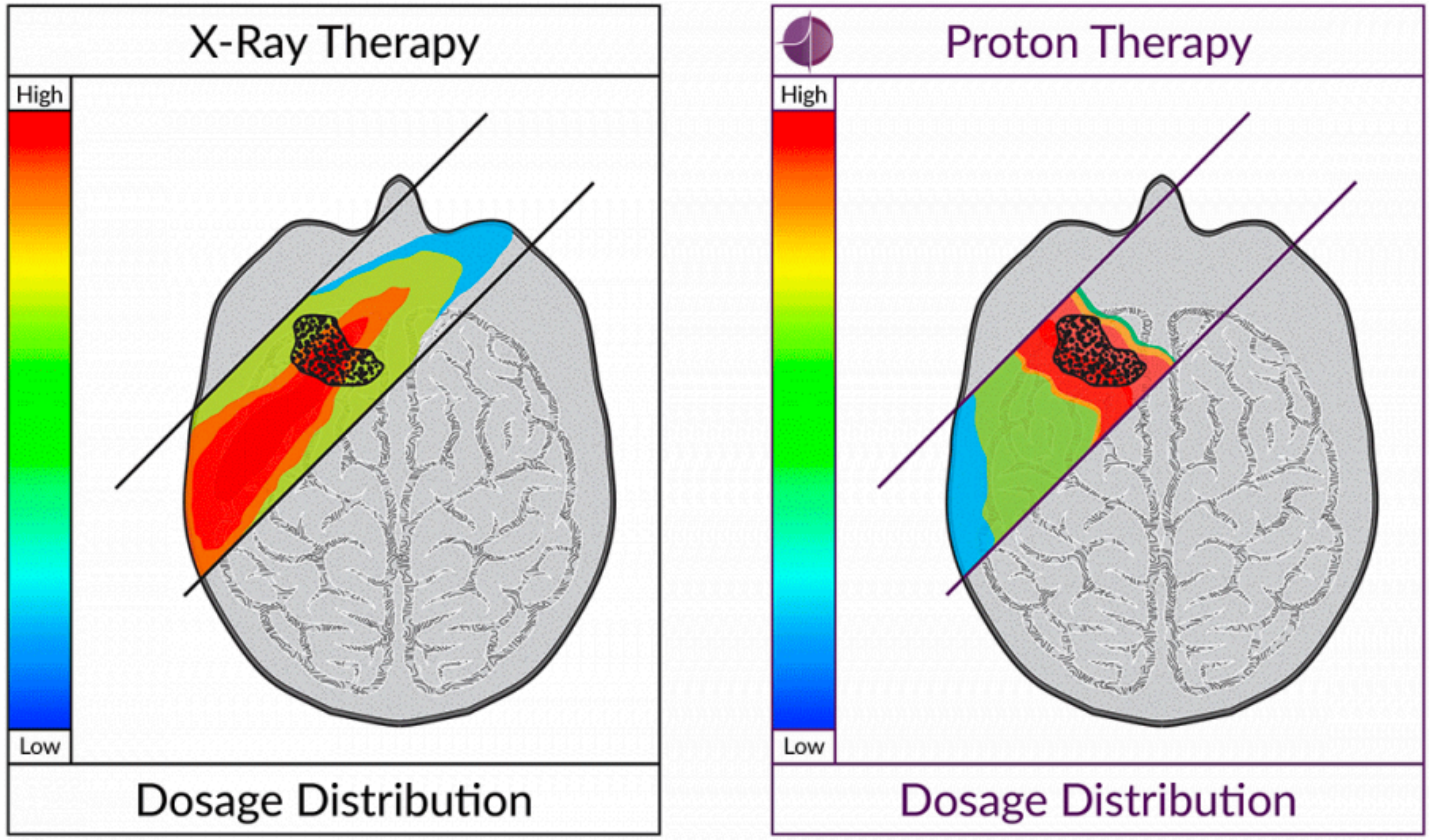
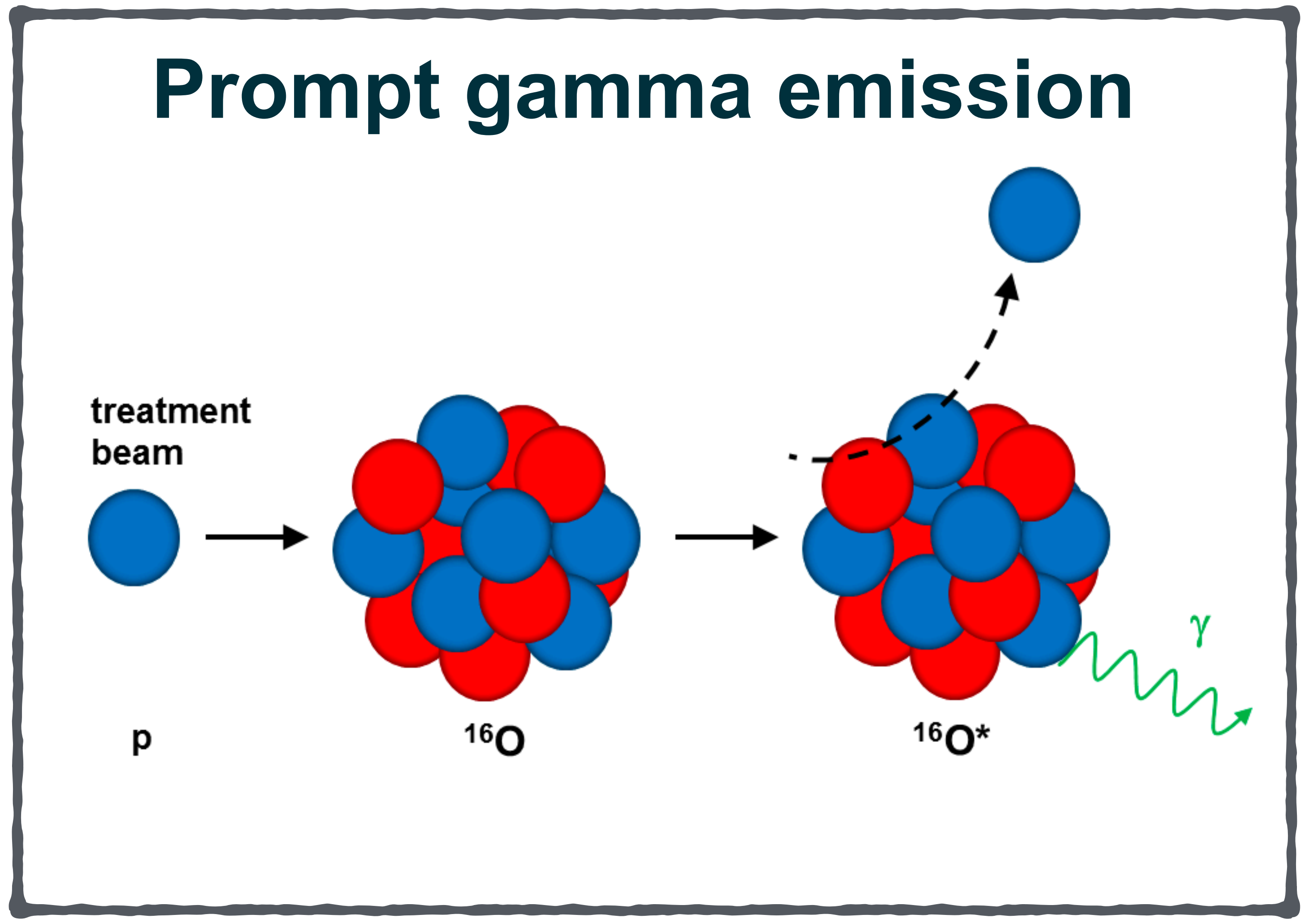
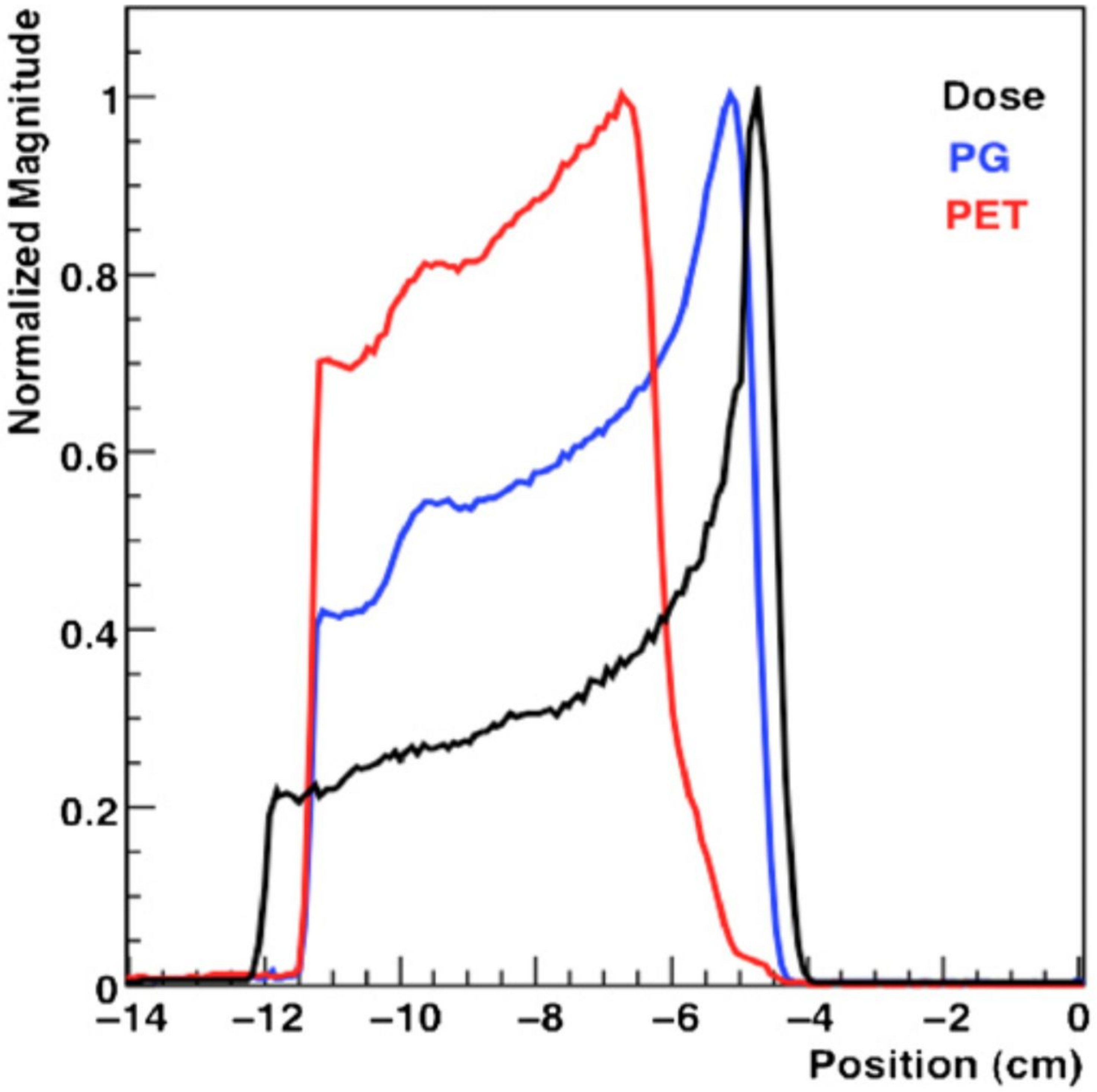
Figure 2. Comparing the relative percent depth dose of x-rays and protons.



Range verification techniques

- Many viable approaches using secondary particle emission
- PET, in-beam / post-beam
  - Mature systems, but require extra acquisition time & susceptible to biological washout.
- Prompt gamma rays—immediate emission and closer correspondence to dose.
  - Direct imaging (PGI):
    - Compton camera: susceptible to combinatorics at high rate & BG
    - Collimation: sacrifice sensitivity
  - Prompt gamma timing (PGT)
    - Time of flight proportional to depth
    - No collimator, and only single detection per PG


Prompt gamma emission



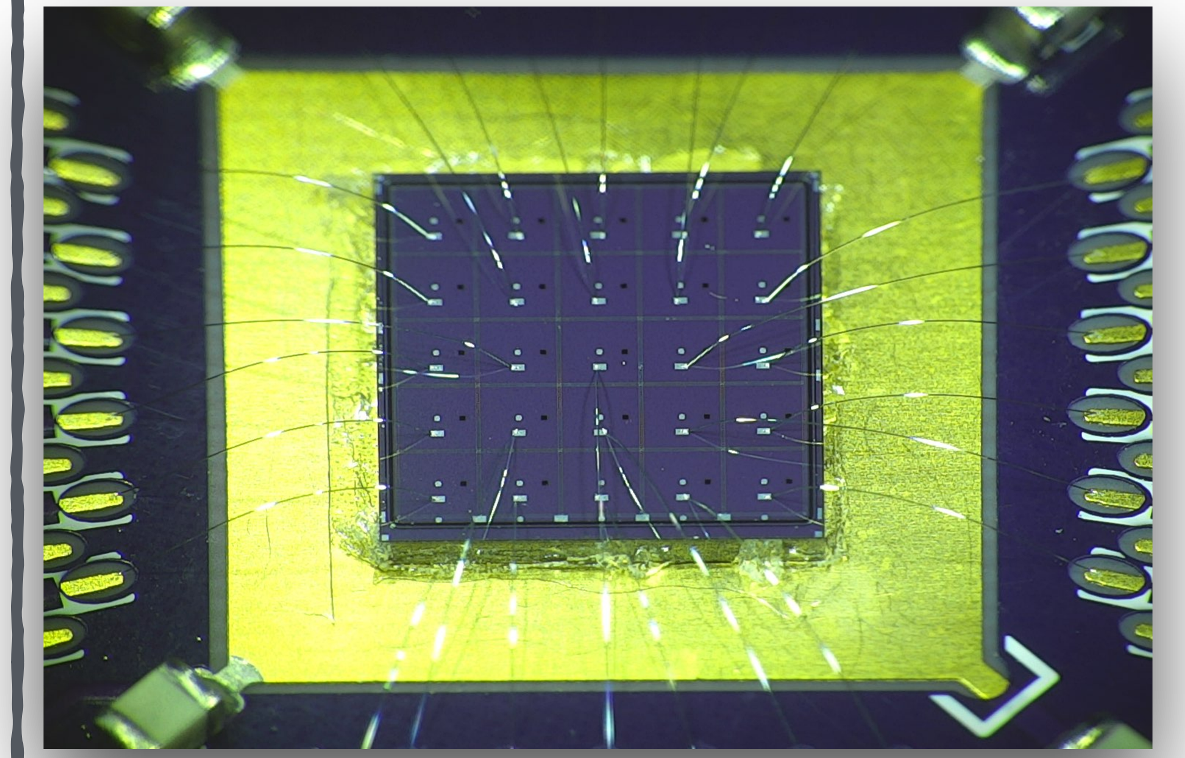
Moteabbed, España, Paganetti, Phys. Med. Biol. 2011

Prompt gamma timing

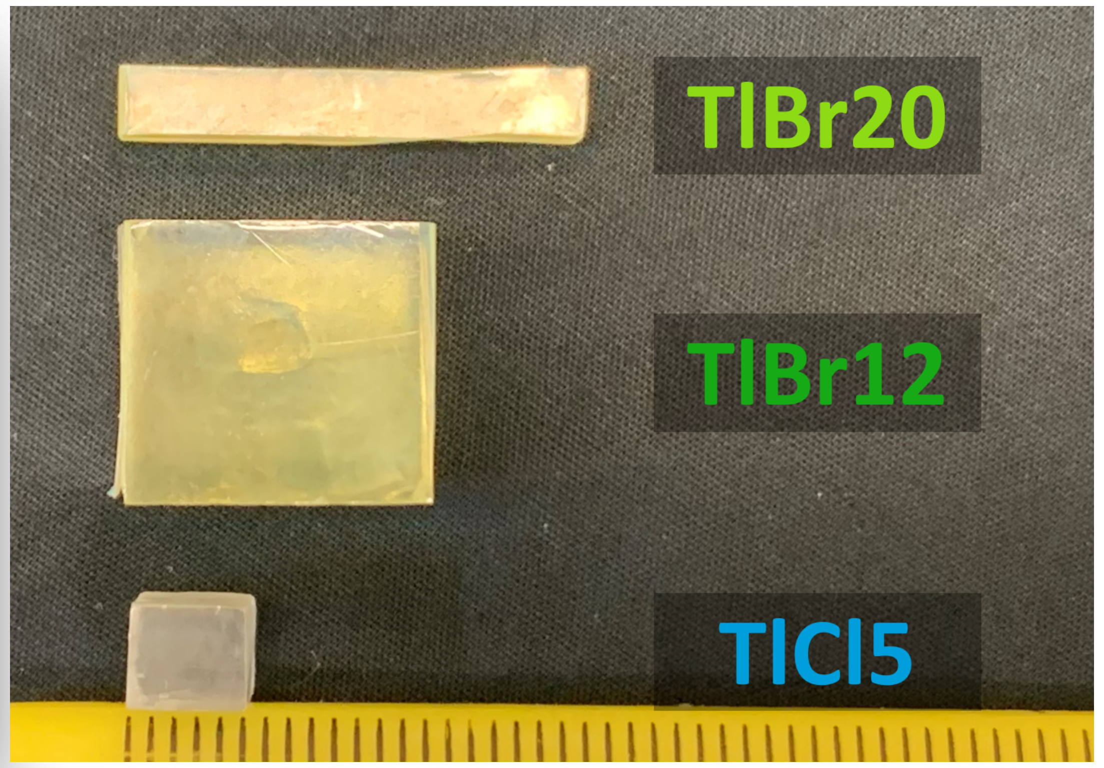
- Key challenges
  - Pushing limits of time resolution
  - High signal intensity / pileup / repetition rate
  - Backgrounds (neutrons, gammas)
  - Radiation damage to start detector

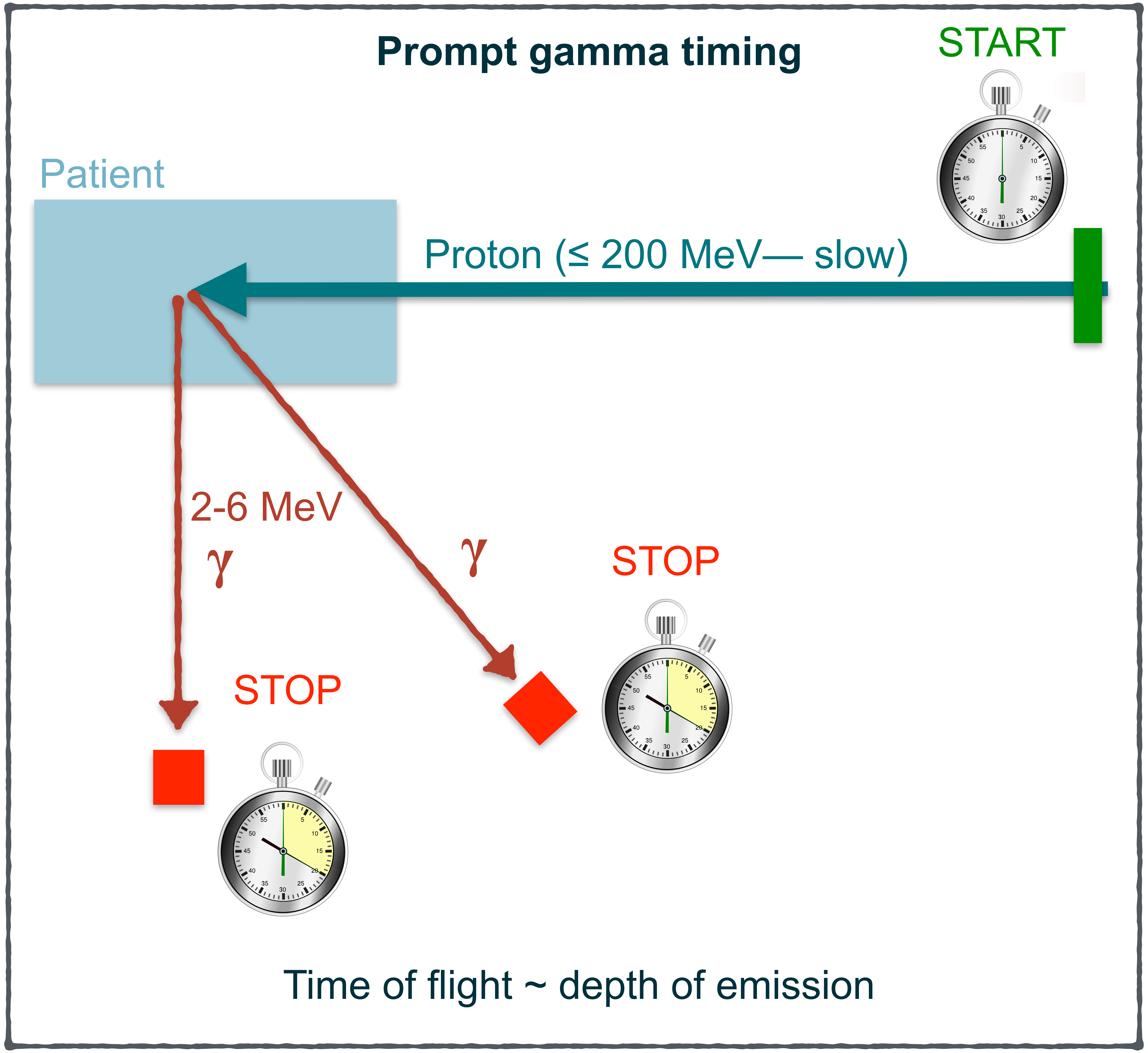
Our approach:

Start
Low Gain Avalanche Detector (LGAD)



Stop
Pure Cherenkov emitters

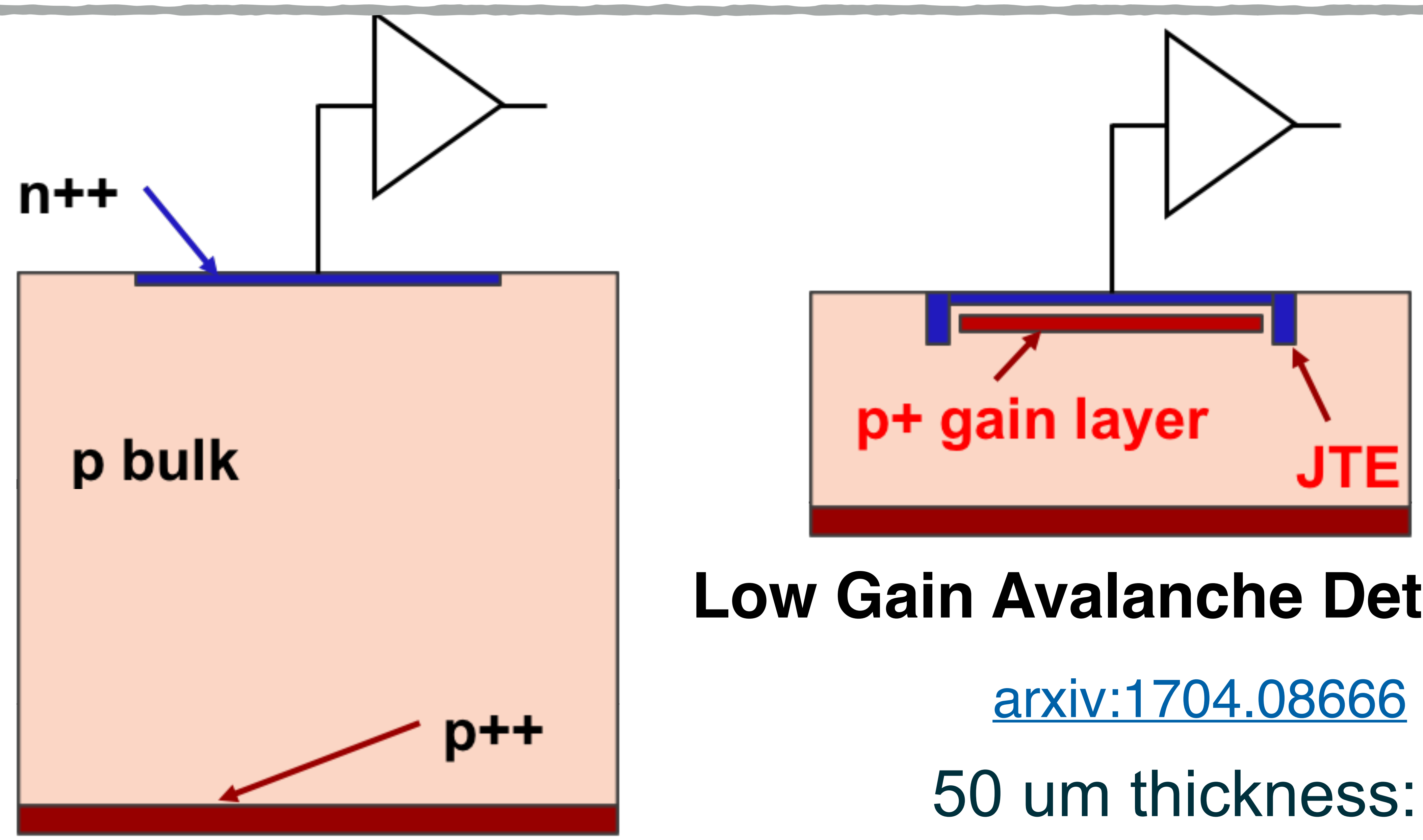




Time of flight ~ depth of emission

Low Gain Avalanche Diodes (LGAD)

- Silicon ionization sensors optimized for timing: Low Gain Avalanche Detectors (LGADs)
  - Thin depletion region (50 micron): fast & uniform signals
  - Modest internal gain (x10-40): boost signal-to-noise. Analogous to APD, not SiPM
- Note for charged particles, thinness does not harm sensitivity
- Time resolution σ = 30 ps for MIPs, likely 20-25 ps for 50-200 MeV protons



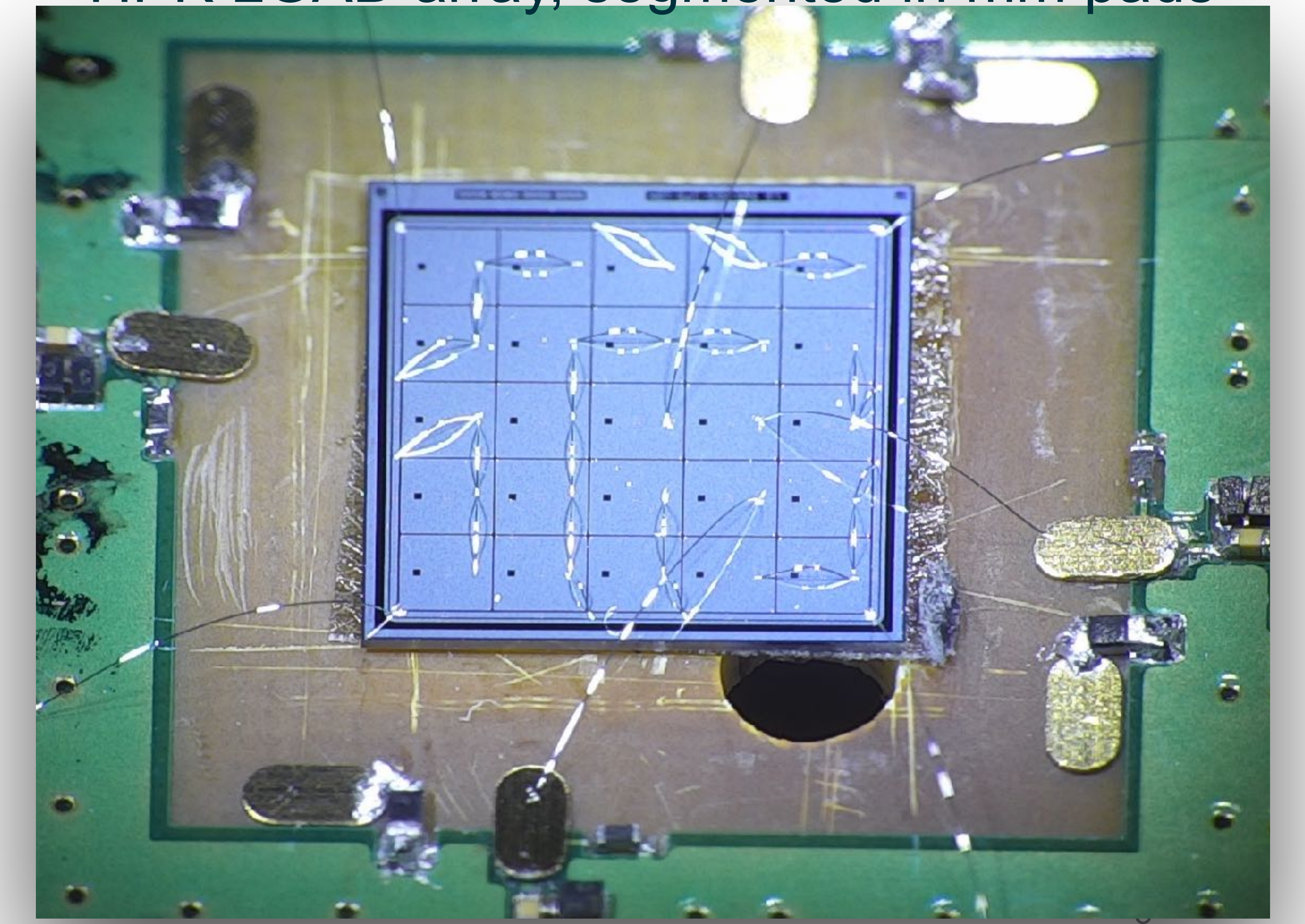
Traditional Si diode detector

Low Gain Avalanche Detector

[arxiv:1704.08666](https://arxiv.org/abs/1704.08666)

50 um thickness:
σ = 30 ps

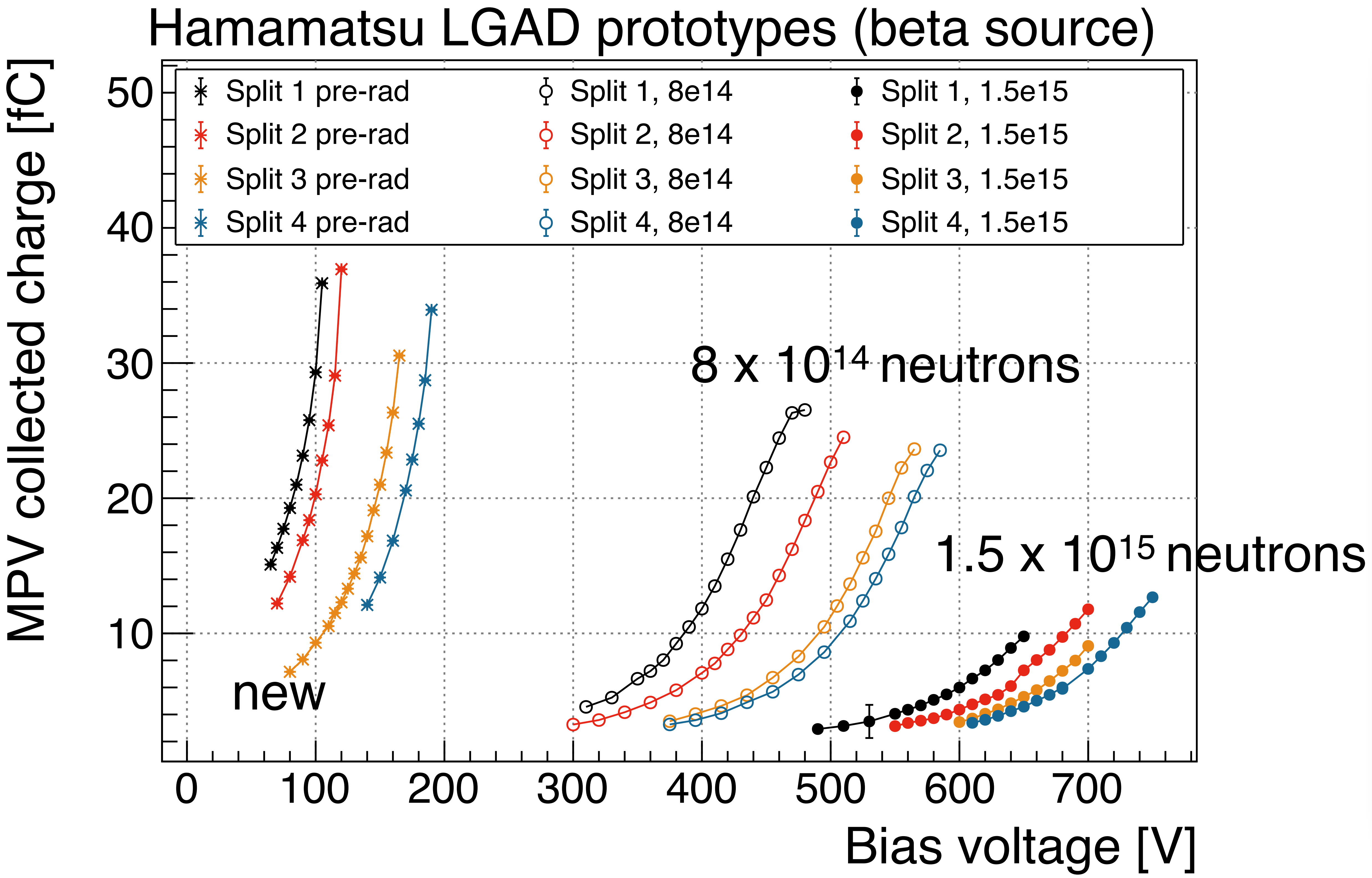
HPK LGAD array, segmented in mm pads

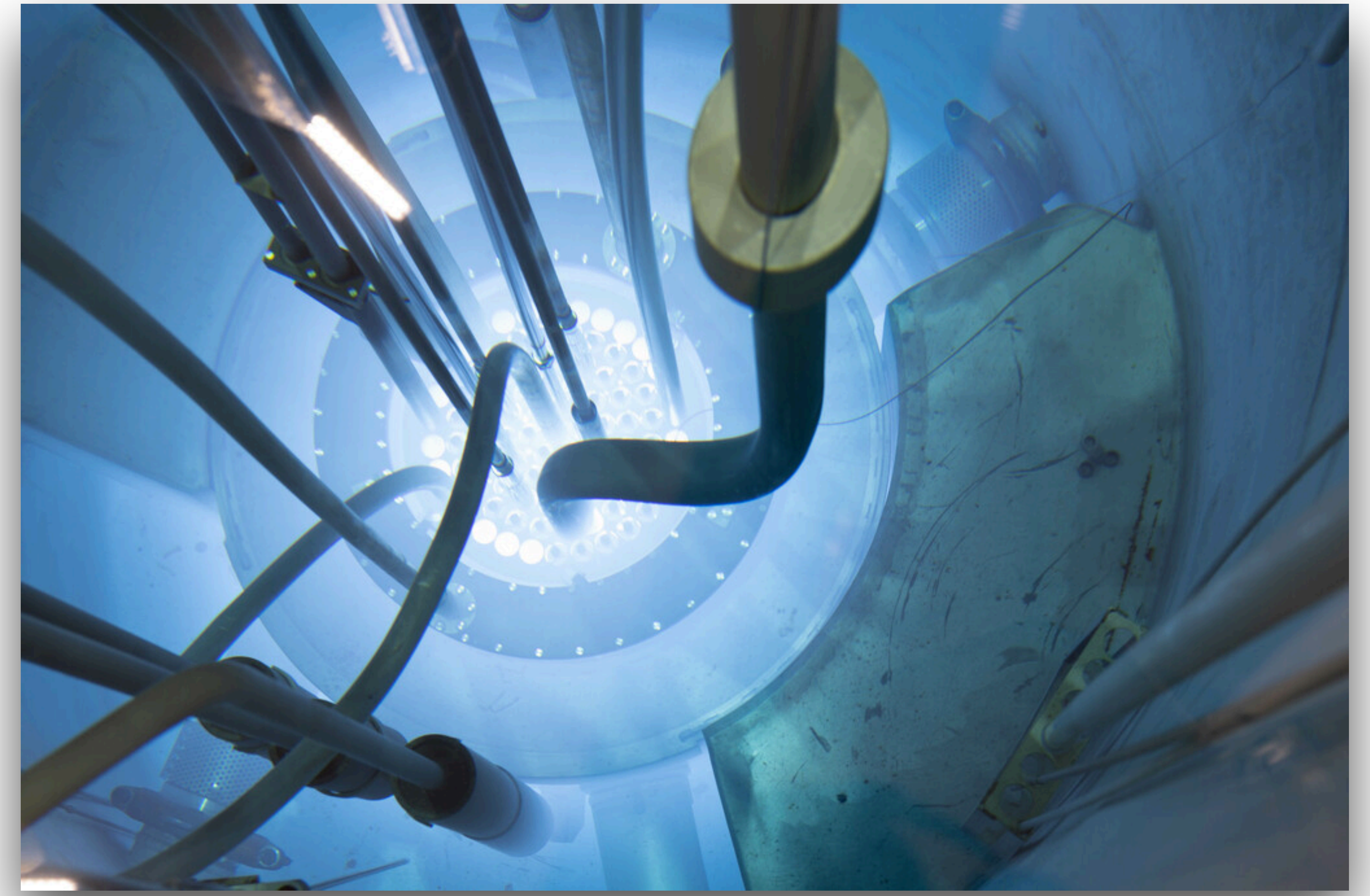


LGAD (UFSD) also proposed for PGT by [Pennazio, Ferrero et al]()

LGAD radiation hardness

- Originally developed for hadron colliders — radiation and hit rate tolerance are critical.
- Study radiation hardness w/ nuclear reactor (up to 1.5 x 10^{15} neutrons / cm^2)





TRIGA reactor at JSI, Ljubljana, Slovenia

- Gain layer de-activates at very large fluence, but compensate by increasing bias voltage

LGAD radiation hardness

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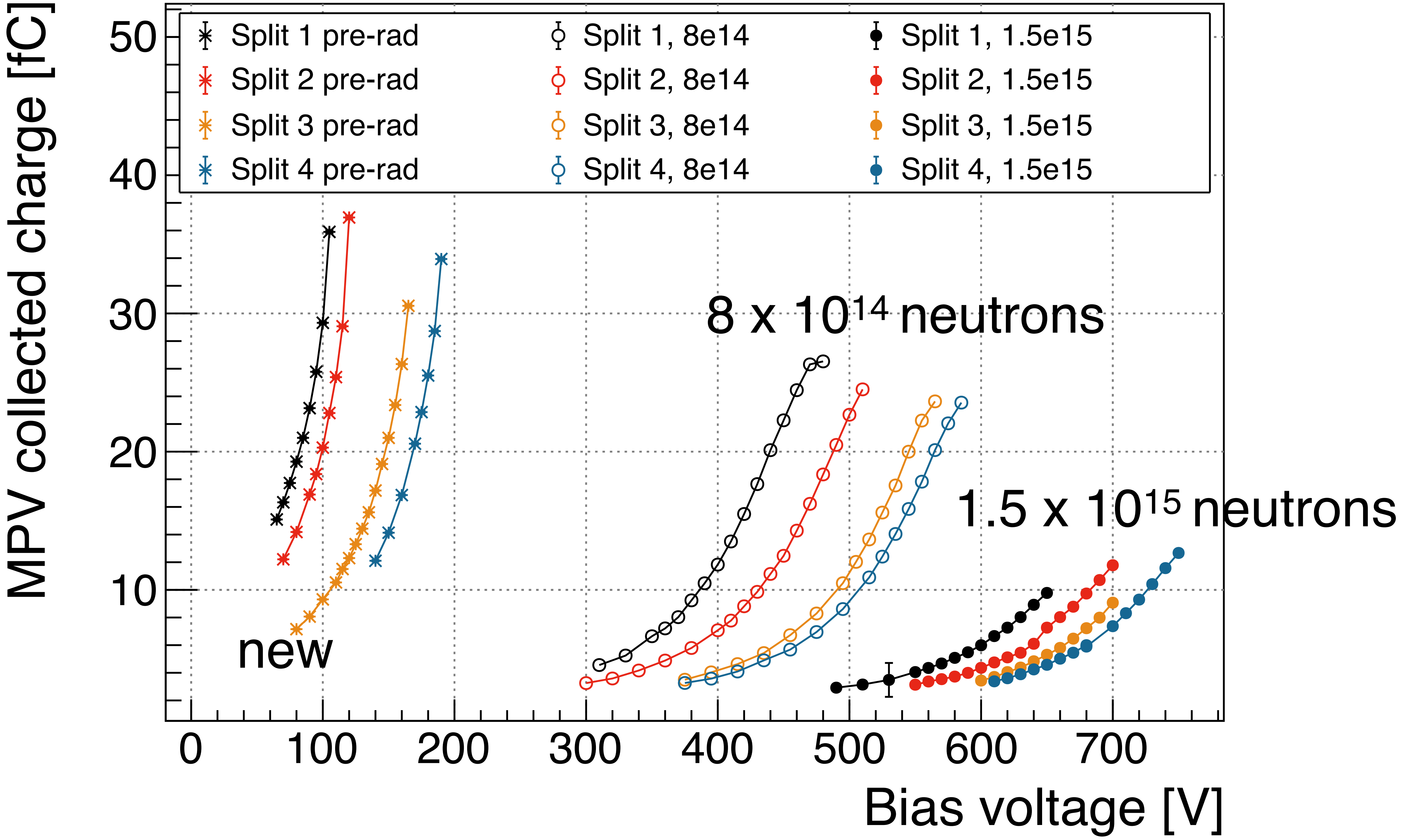
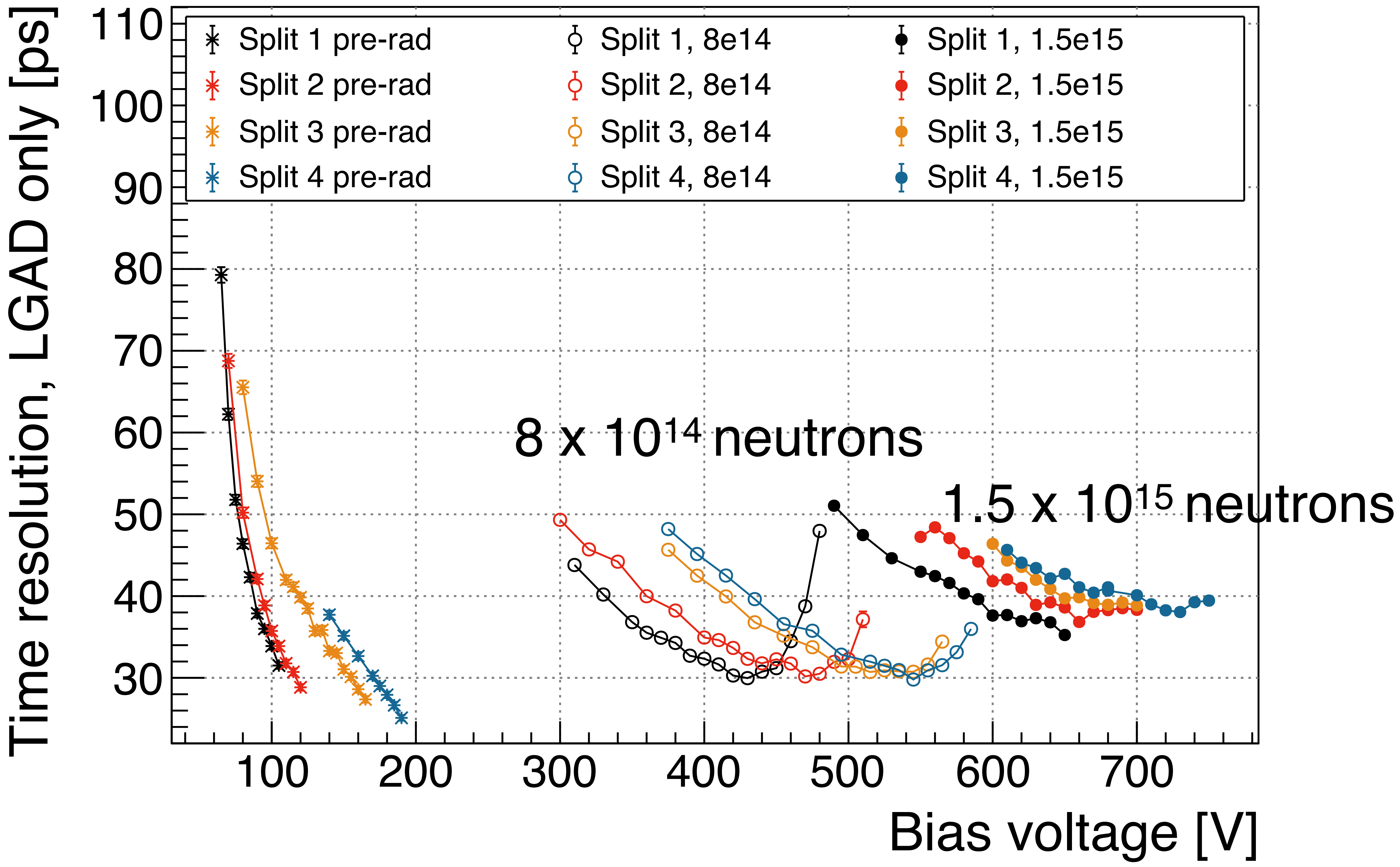
Hamamatsu LGAD prototypes (beta source)



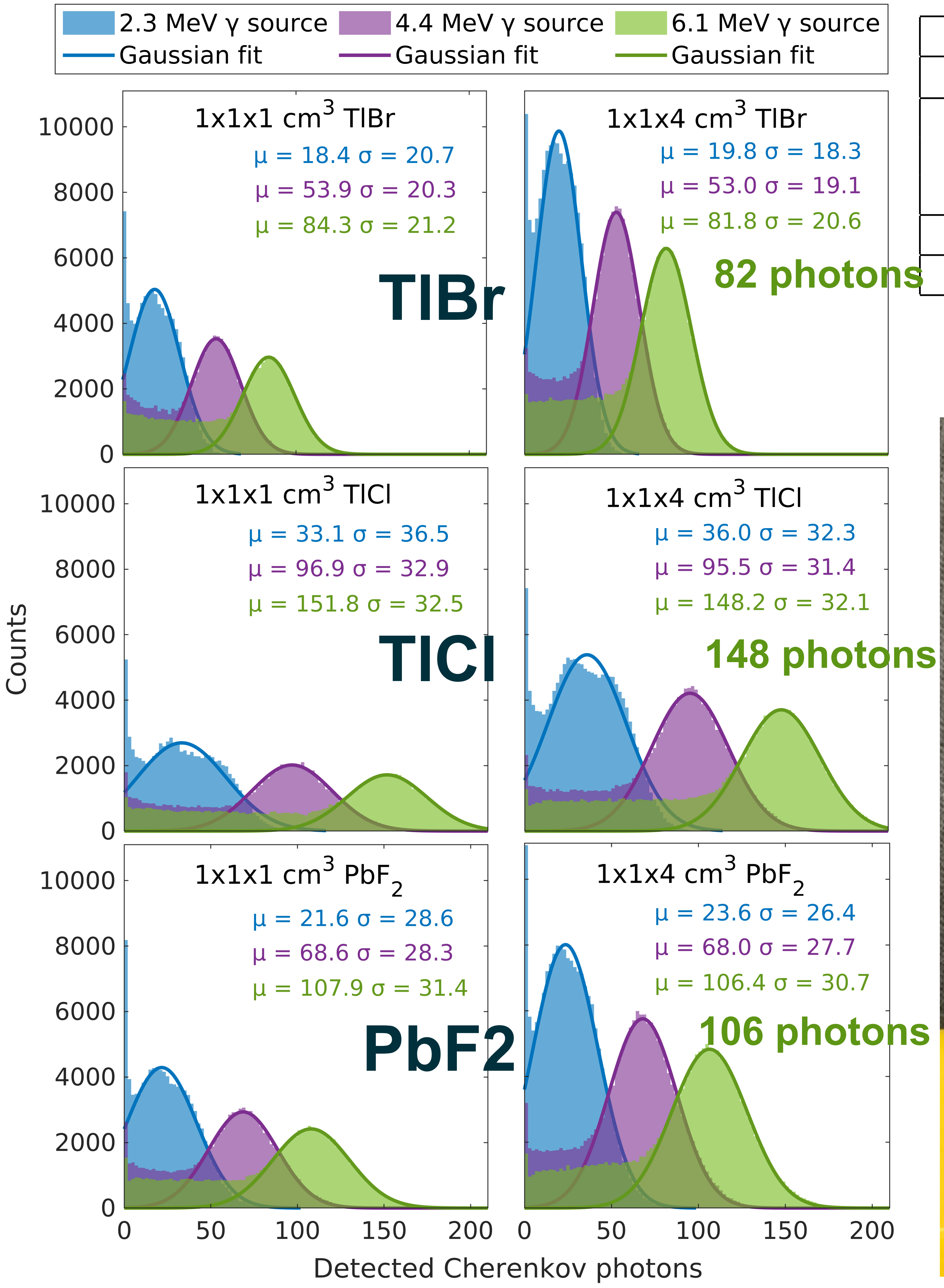


- Maintain timing performance up to 10^{15} protons/cm^2, or roughly 10^5 treatment fractions
- Replace LGAD every 1-2 years in clinical system.

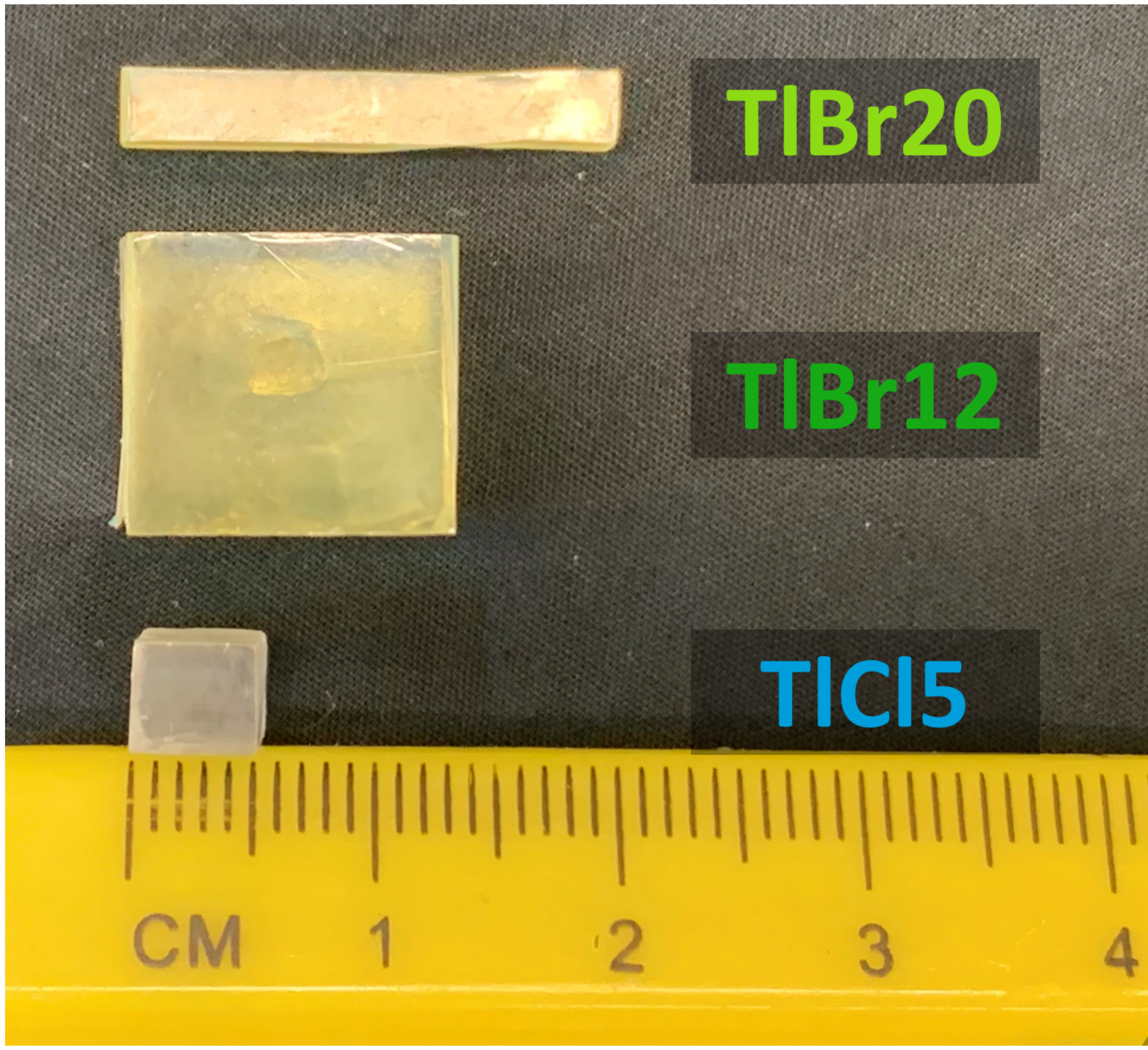
Cherenkov detectors

- Pure Cherenkov emission: instantaneous light. Ideal for timing and pileup tolerance
- Several good options: PbF_2, TlBr, TlCl
  - TlBr: can operate as semiconductor detector
  - TlCl: higher Cherenkov yield. Can be doped for scintillation
  - PbF_2: slightly higher stopping power
- Light yield heavily dependent on energy
  - 511 keV → detect few photons
  - 2-6 MeV → detect tens or hundreds
  - Set threshold to reject BG
- 3 prototypes studied: TlBr $(12\ mm)^3$, TlBr $3x3x20\ mm^3$, TlCl $(5\ mm)^3$

2.3 MeV **4.4 MeV** **6.1 MeV**

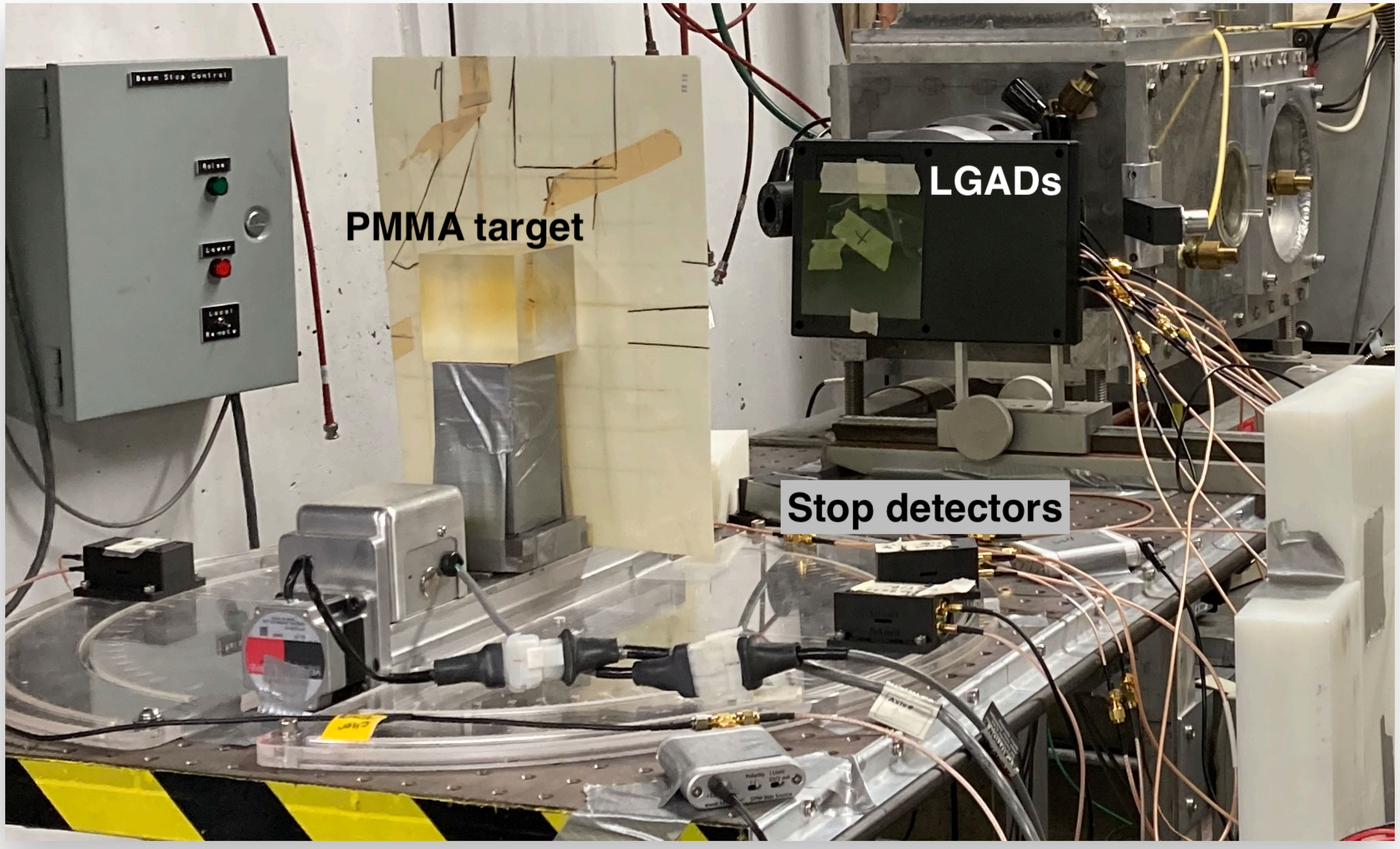


Properties		TlBr	TlCl	PbF_2
Density [g/cm^3]		7.5	7.0	7.8
Attenuation length [cm]	2.3 MeV	3.1	3.3	3.0
	4.4 MeV	3.4	3.5	3.2
	6.1 MeV	3.3	3.4	3.1
Refractive index at 550 nm		2.48	2.32	1.78
Cutoff wavelength [nm]		440	380	250



Ellin et al 2024 Phys. Med. Biol. 69 115002
Rebolo et al, 2023 IEEE TRPMS
Ariño-Estrada et al 2019 Phys. Med. Biol. 64 175001

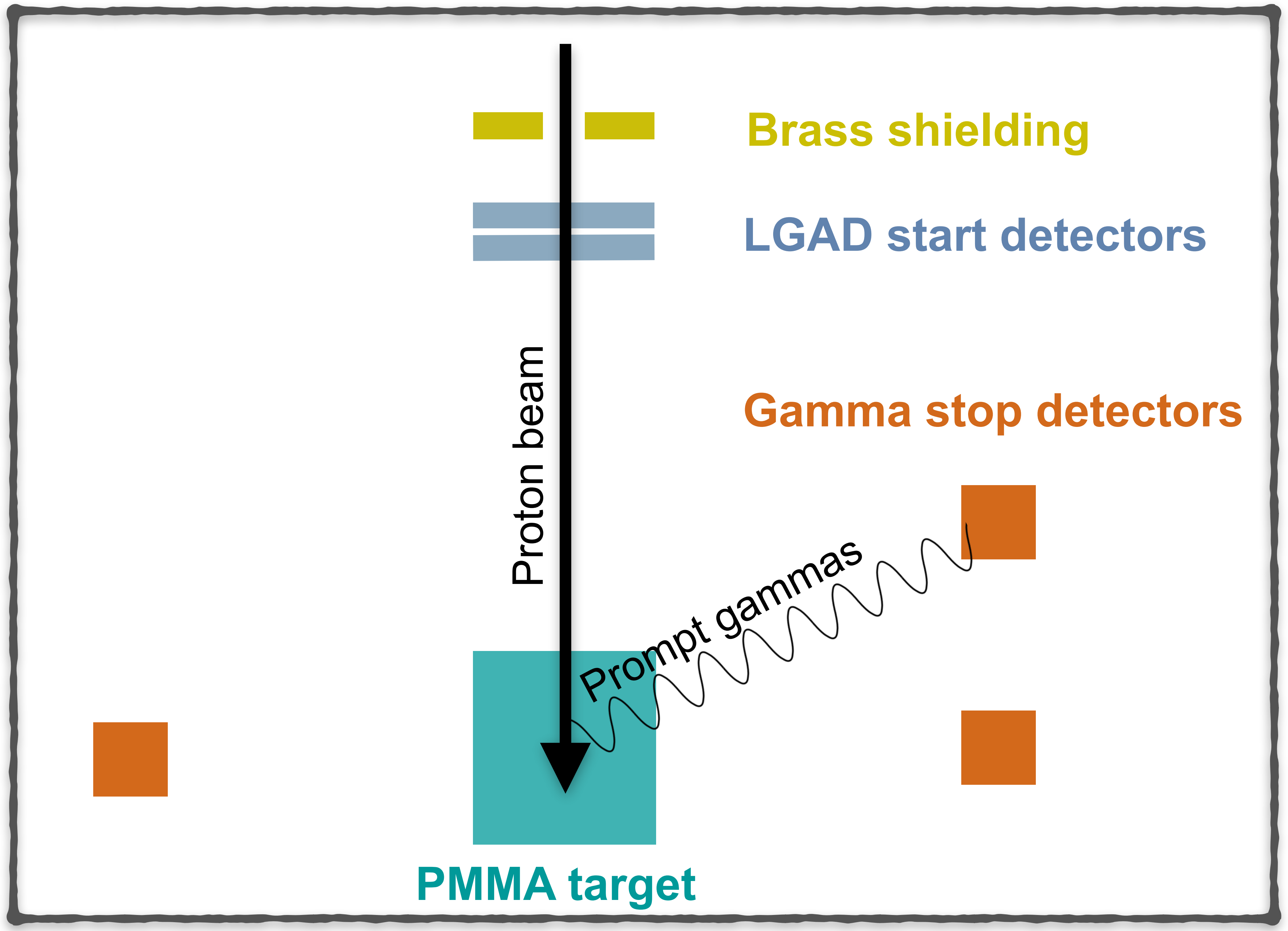
Beam demonstration at UC Davis Crocker Cyclotron



Capture waveforms with CAEN DT5742 (DRS4)

Trigger on stop detectors with DRS4 USB module

- 67.5 MeV proton beamline used to treat ocular cancers. Operate at 225 pA
- Beam impinges on PMMA target on motion stage
- Scan target position over 12 mm range—aim to detect range shift based on ToF.



Time of flight analysis

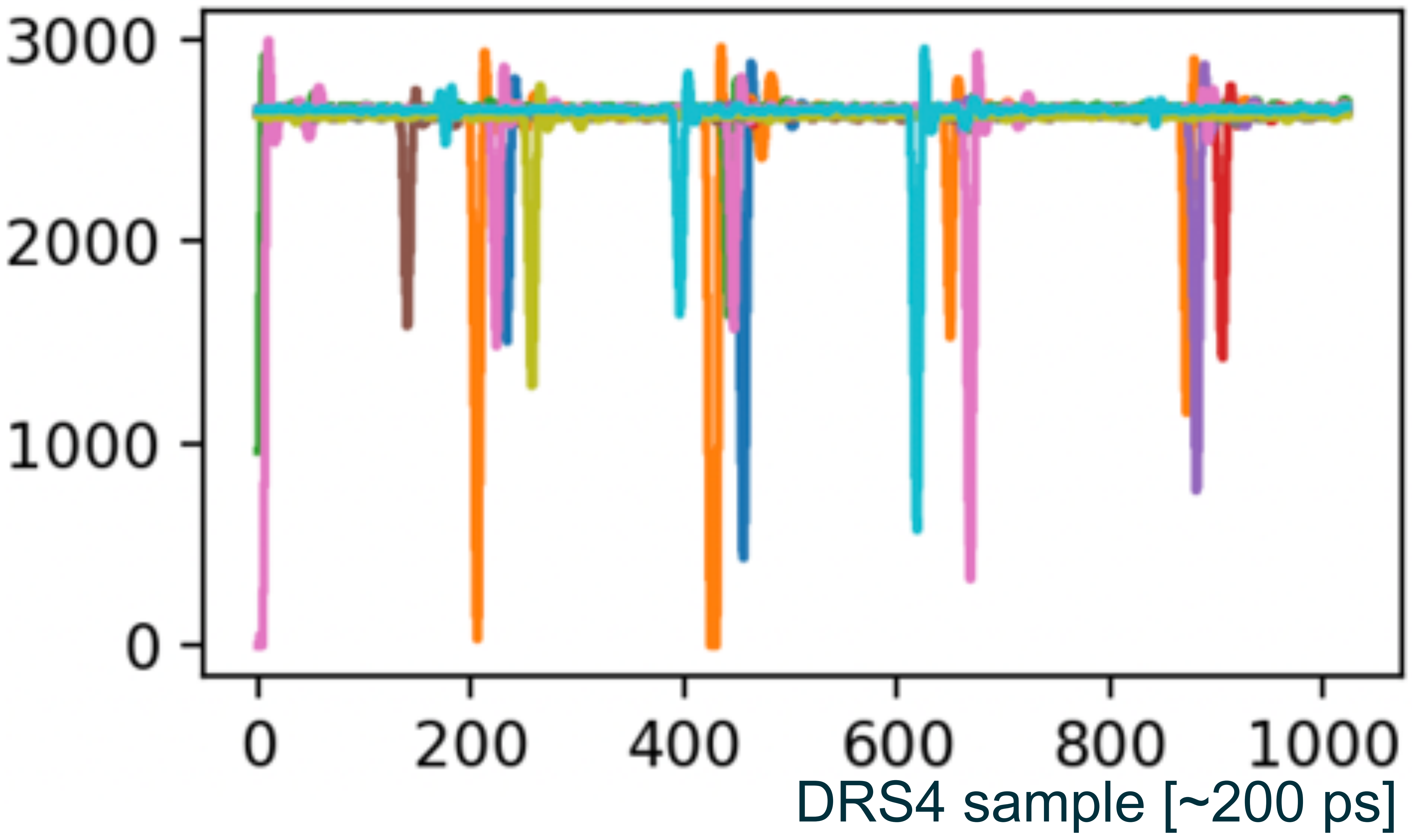
- Approach for time of flight depends on beam structure:

Each bunch: O(50) protons
O(500 ps) width

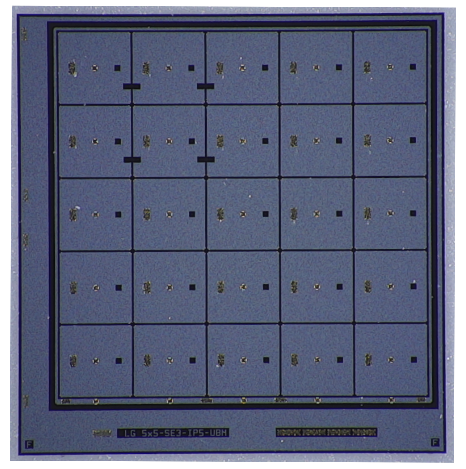
Time-averaged current: 225 pA

44.4 ns spacing

1 LGAD pixel, 10 events in different colors

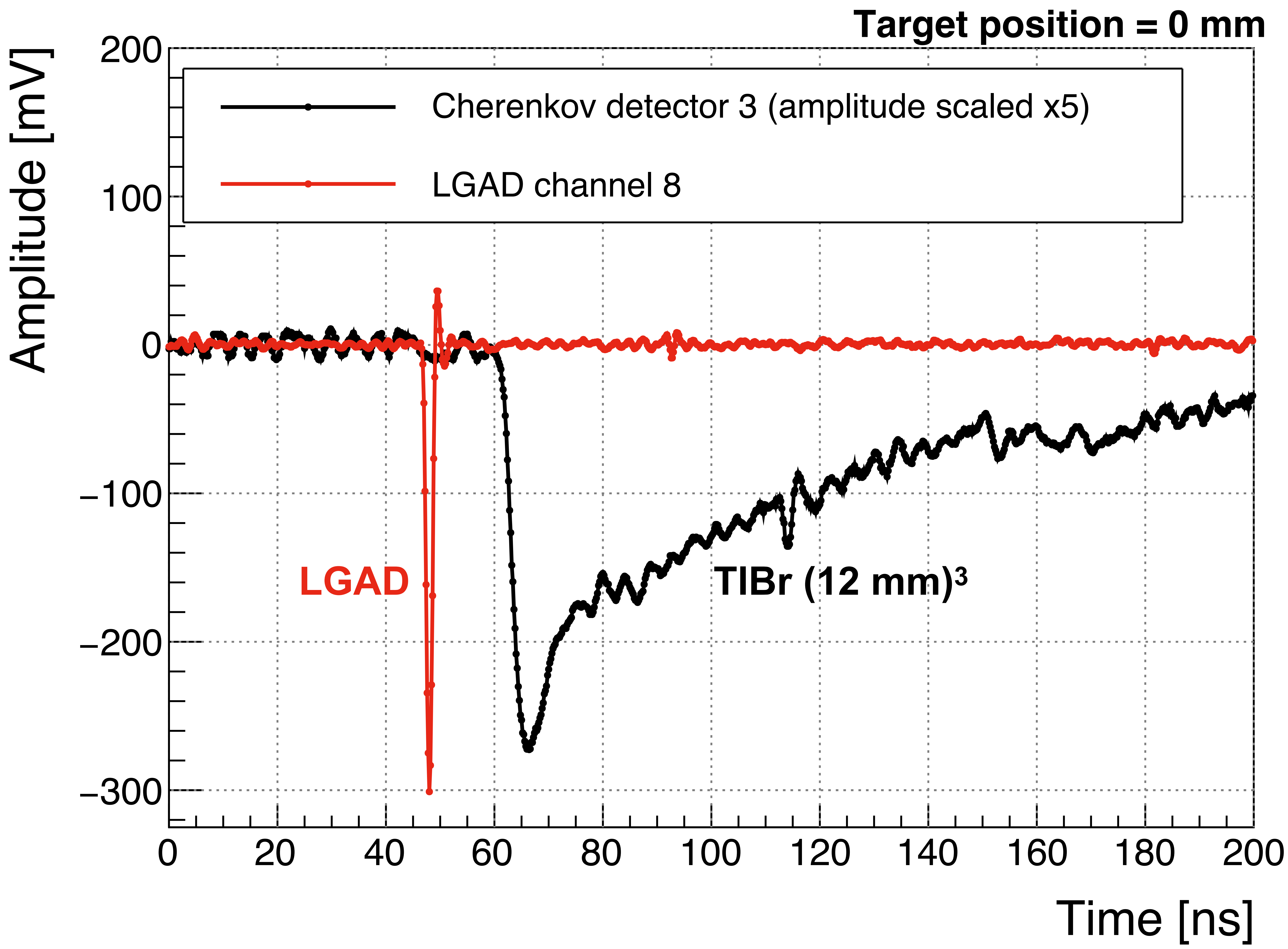


- LGAD could time single protons with σ ~ 30 ps
- This case—can’t associate gamma with parent
- Instead, trigger on gamma, search for bunch timestamp. Multiple chances per event:
  - 4x bunches per window (modulo 44.4 ns)
  - 5x LGAD pixels



- ToF resolution dominated by bunch width.

Example event

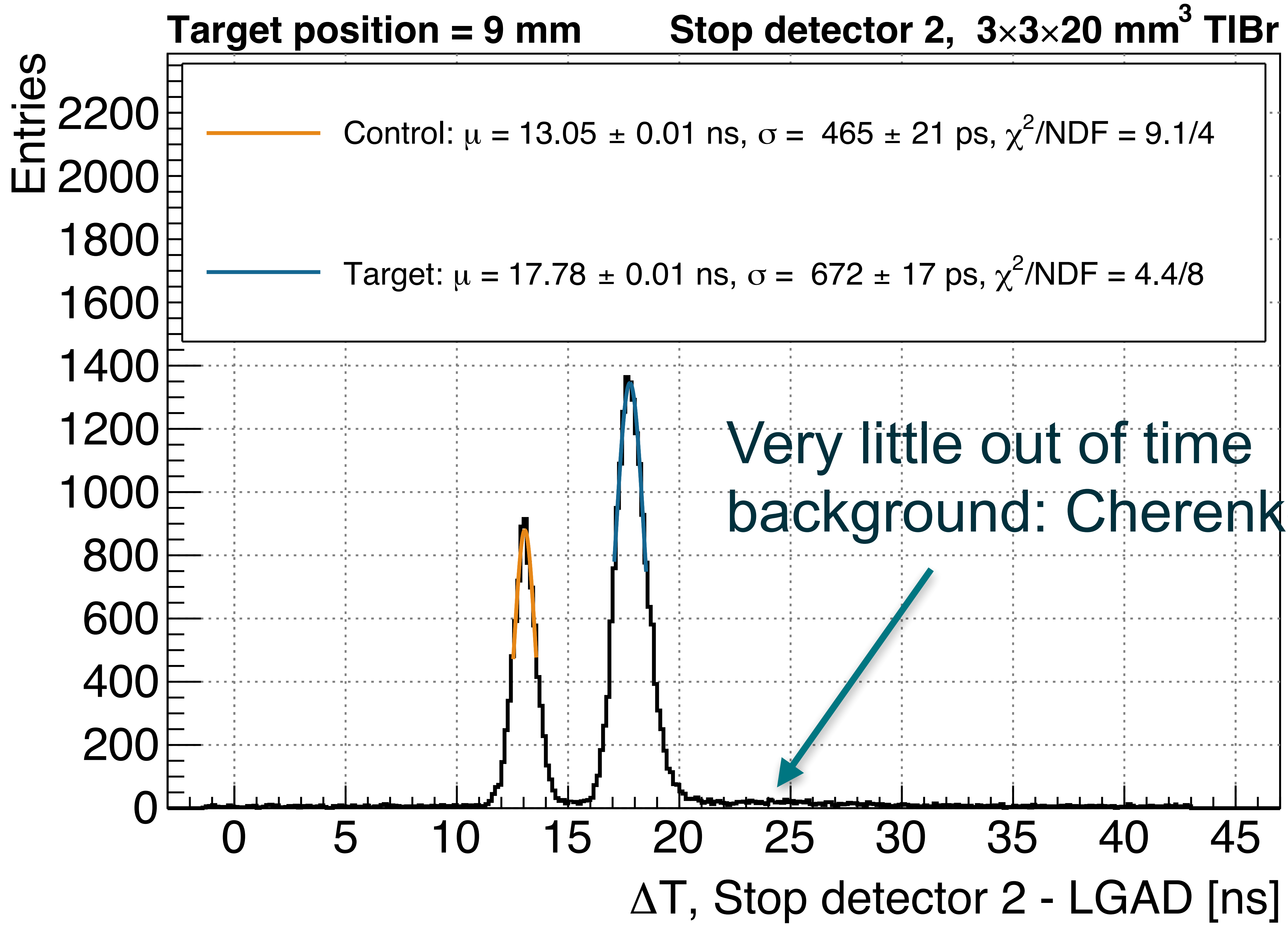


- LGAD signal resolves in 2 ns: ideal for high rate timing
- Cherenkov light production instantaneous, in this case long tail due to electronics—can also resolve much faster.
- Timestamp both LGAD and Cherenkov detectors at 20% CFD

Time of flight distributions

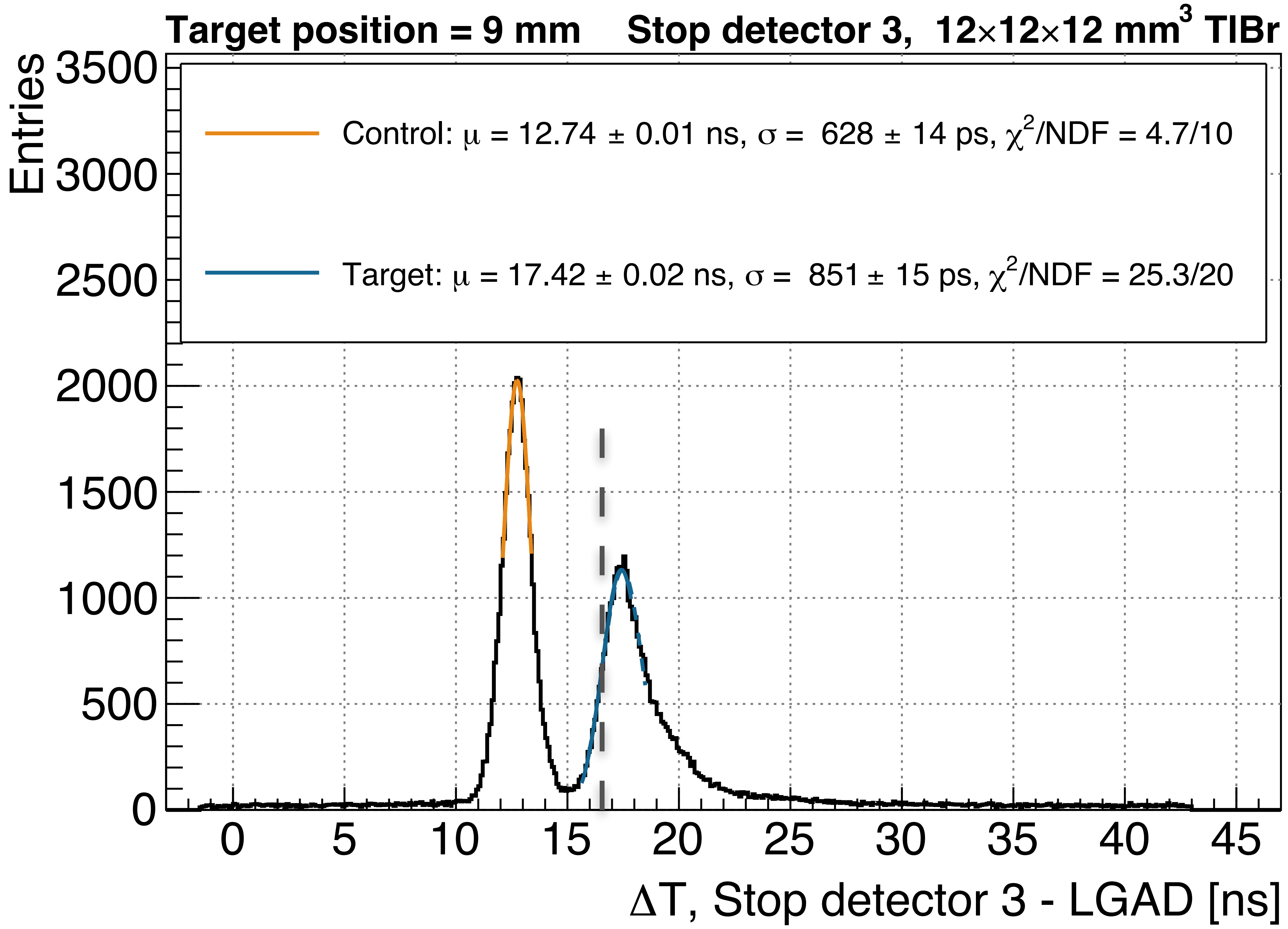
- Two populations in time of flight:
  - “Control”: prompt gammas from upstream collimator
  - “Target”: from PMMA phantom
- For range shift analysis, want robust marker for typical time. Fit each population with Gaussian, track position of mean - sigma

3x3x20 mm^3 TlBr



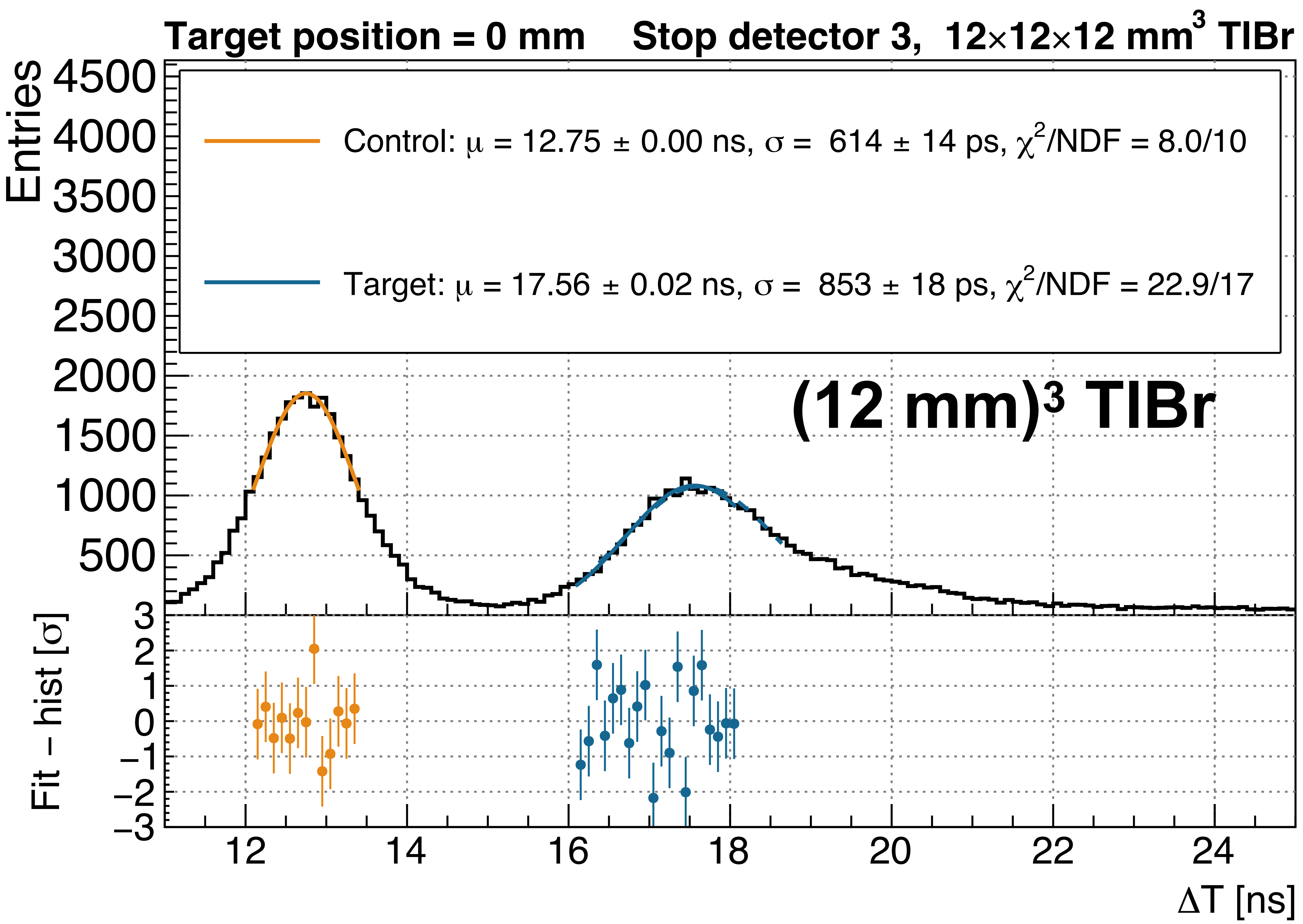
Very little out of time background: Cherenkov.

(12 mm)^3 TlBr

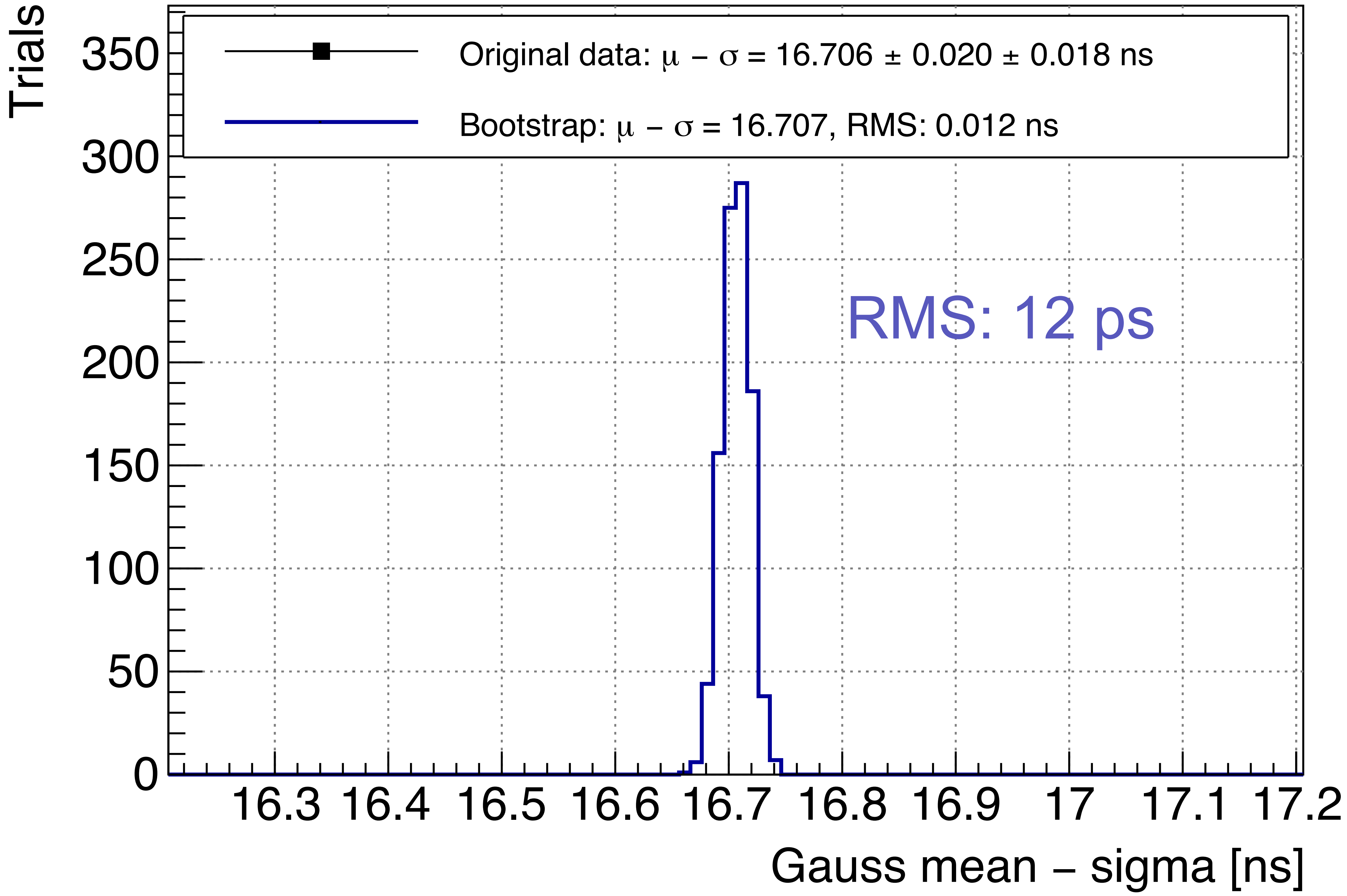


Statistical uncertainty, from bootstrap

- Generate random histograms using poisson fluctuations around fit, re-perform fit to extract time
- Take RMS of extracted times as statistical uncertainty



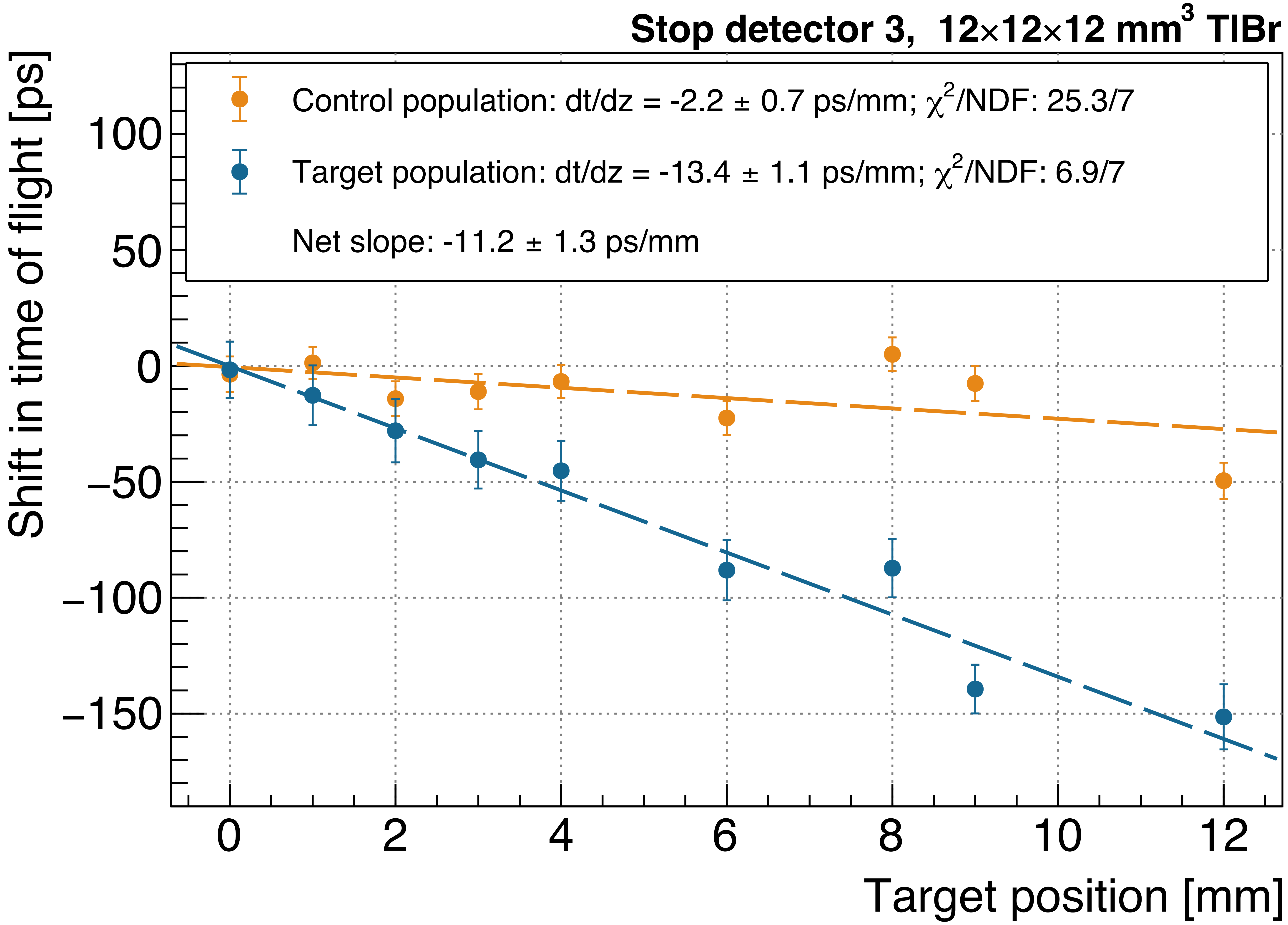
Histogram of mean - sigma variations



- Statistical uncertainty 10-12 ps for best performing detector (12 mm)^3 TlBr, 25 ps for others.
- For 67 MeV protons, 1 mm ~ 9.3 ps. Roughly σ = 1.3 mm statistical uncertainty on range shift.

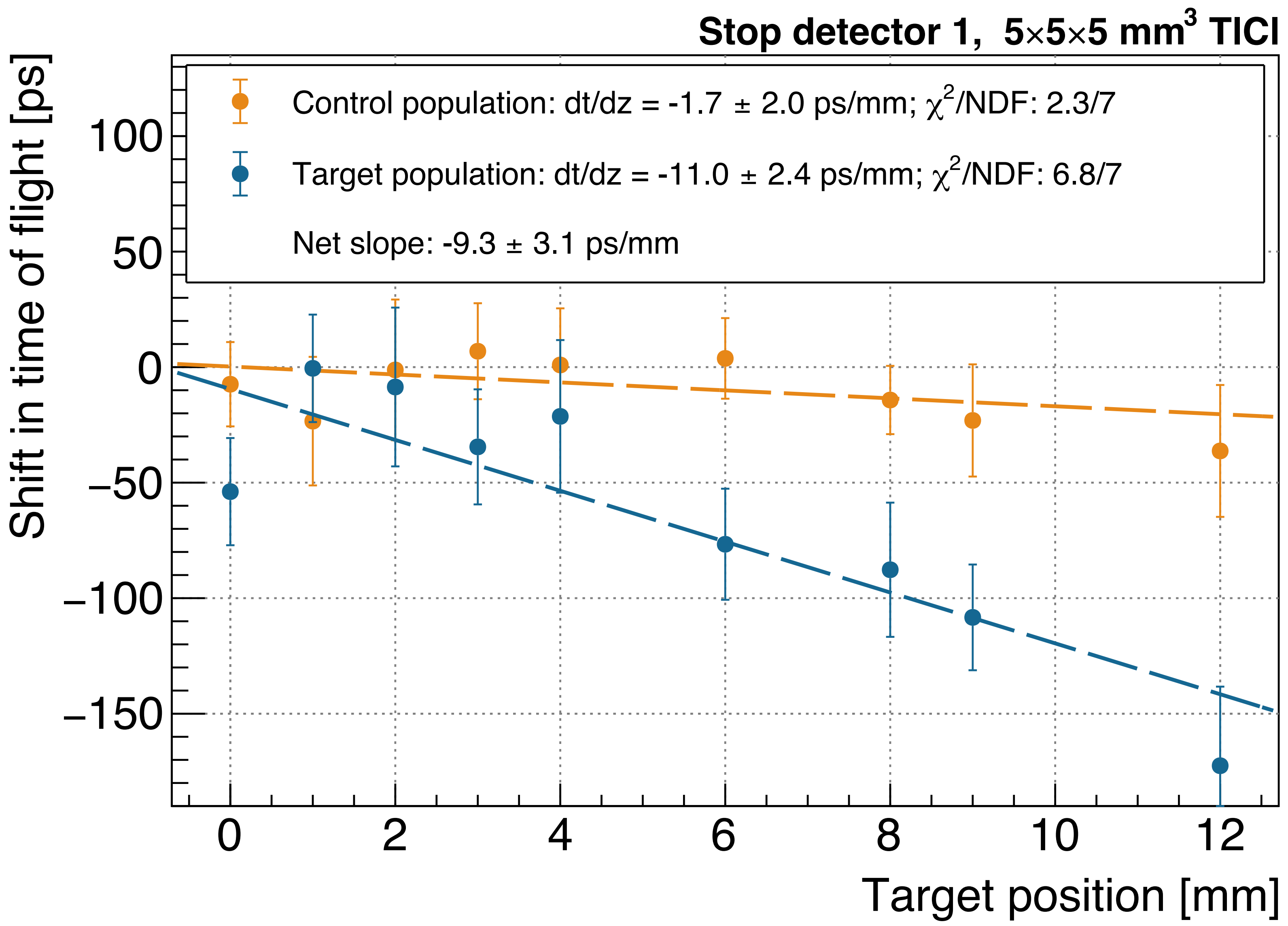
Range shift analysis

- Took data at 9 different target positions spanning 12 mm total
- Plot time shift vs position for both populations
- Accuracy check: slope should correspond to proton velocity at 67.5 MeV— **9.3 ps/mm**
- Control population: useful check for timing drifts & systematic effects!

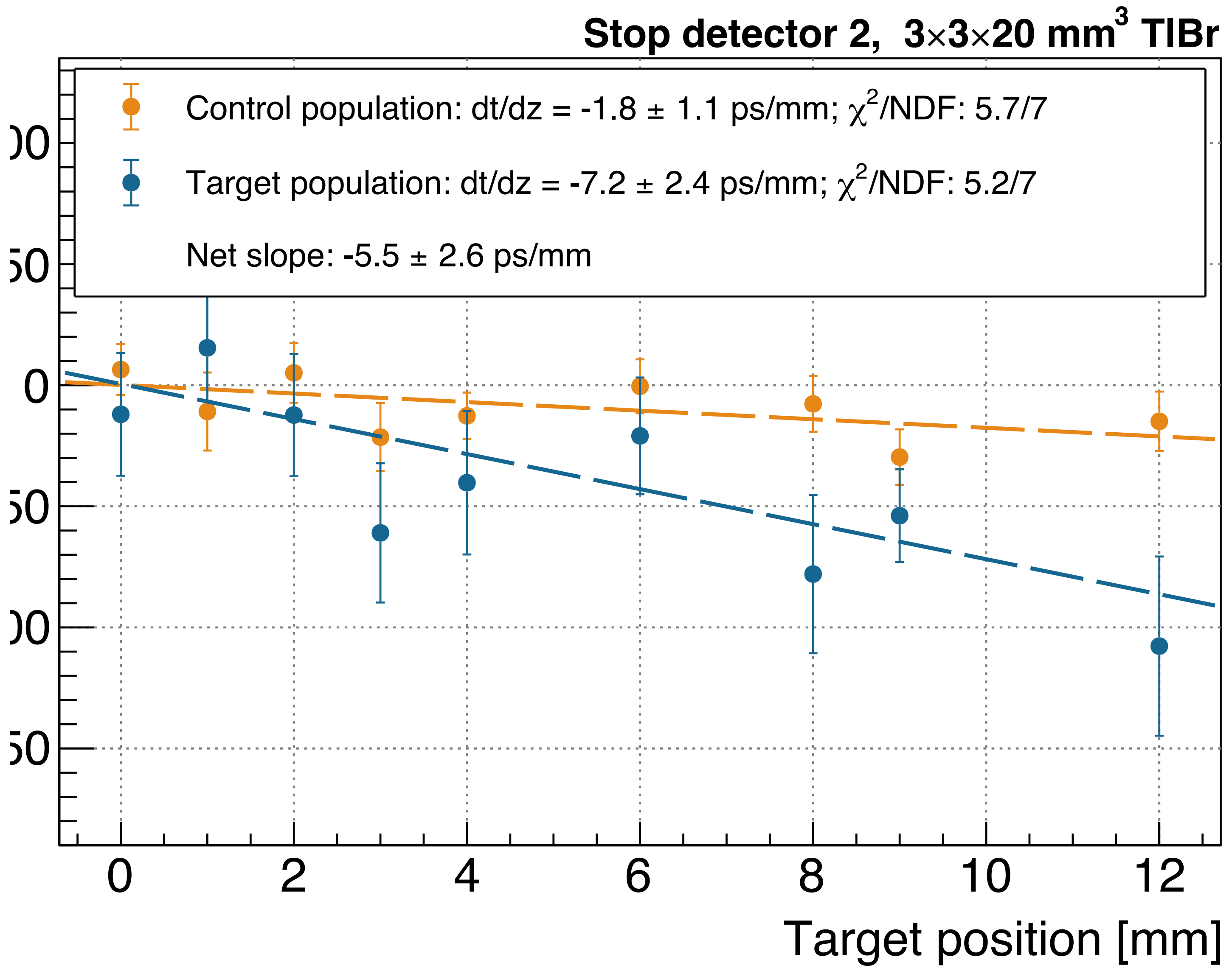


Range shift analysis

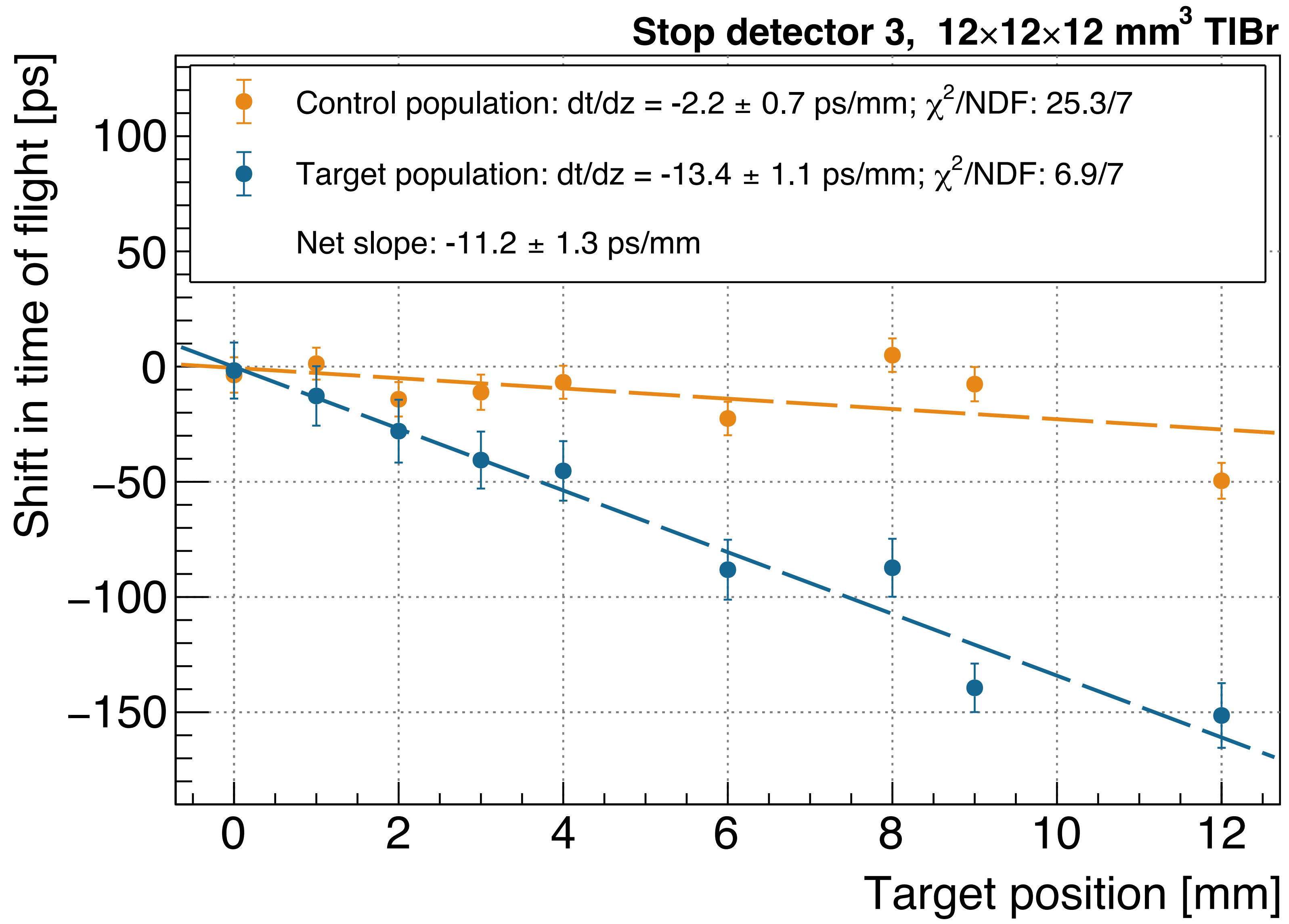
(5 mm)^3 TlCl



3x3x20 mm^3 TlBr



(12 mm)^3 TlBr

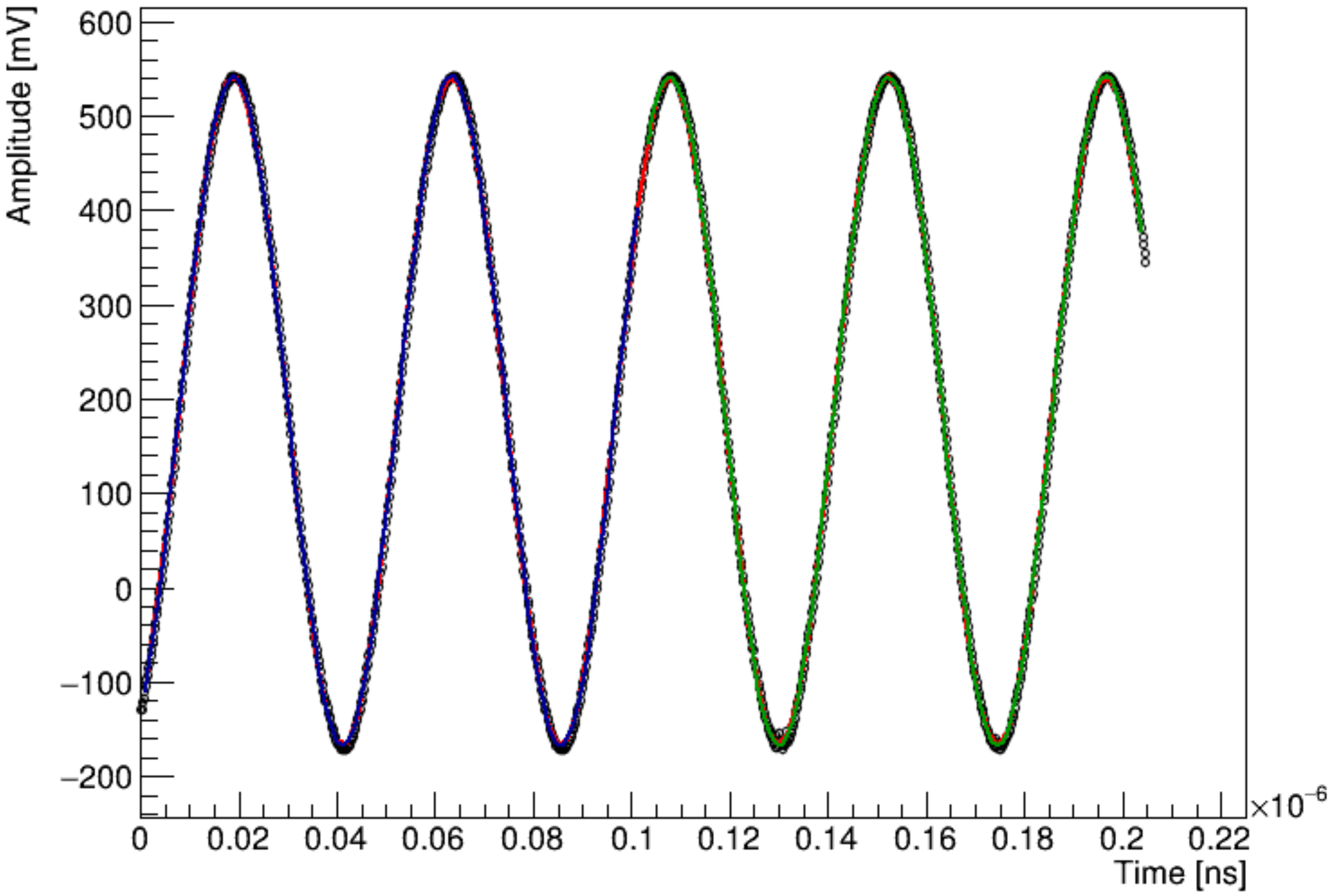


- Observe systematic drift in Control population with all detectors, at roughly 2 ps / mm
- Eventually understood as LGAD-related drift. Correct Target population based on Control slope
- Ultimately all velocities consistent with 9.3 ps/ms expectation—
  - (12 mm)^3 TlBr: 11.2 ± 1.1 ps/mm, (5 mm)^3 TlCl: 9.3 ± 3.1 ps/mm, 3x3x20 mm^3 TlBr: 5.5 ± 2.6

Accelerator RF phase as start indicator?

- Typically, RF signal from accelerator is readily accessible. Can we use it to time the bunch, rather than a dedicated start detector?

22.5 MHz sine wave digitized every event.
Fit phase with 10 ps precision



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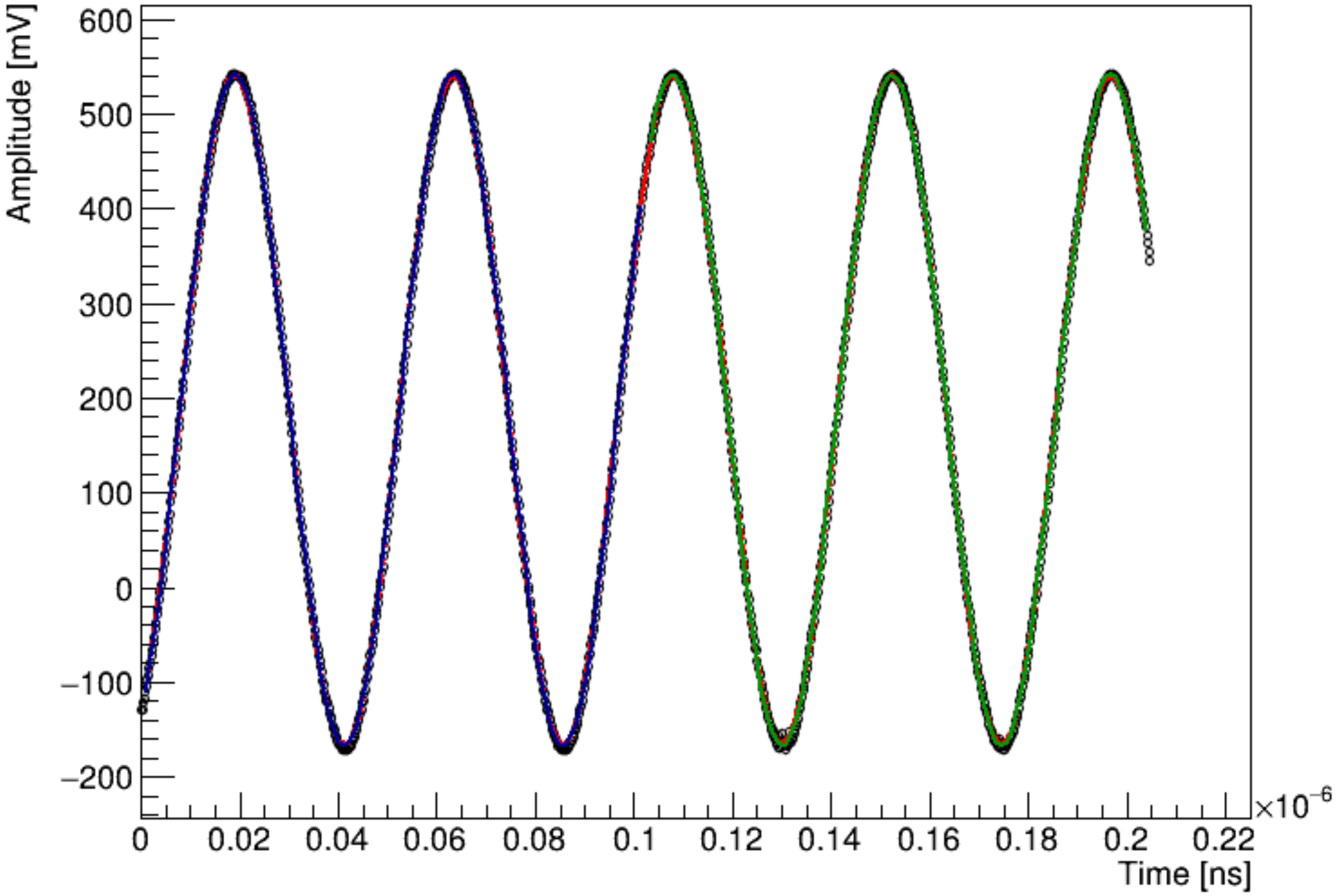
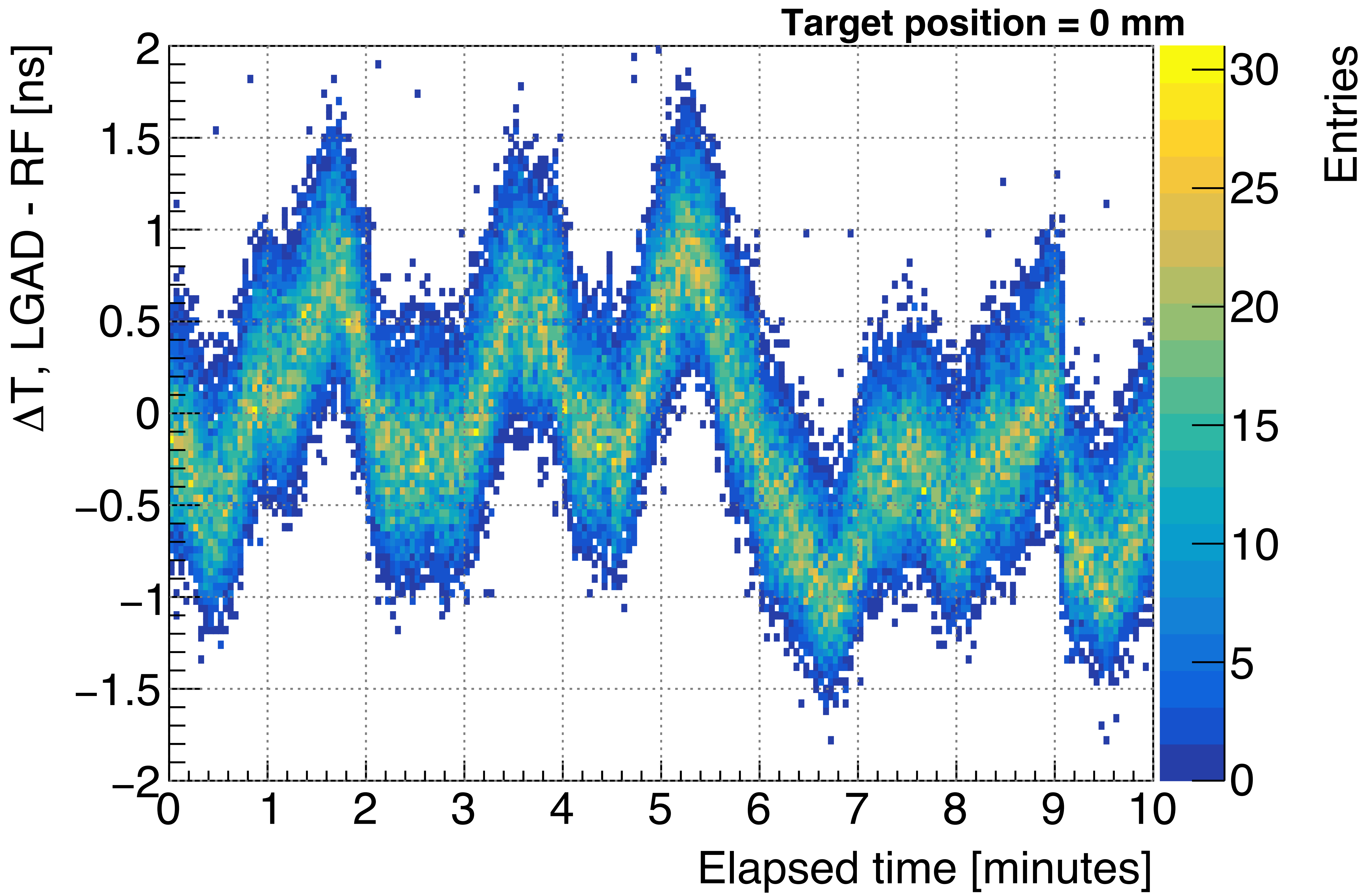
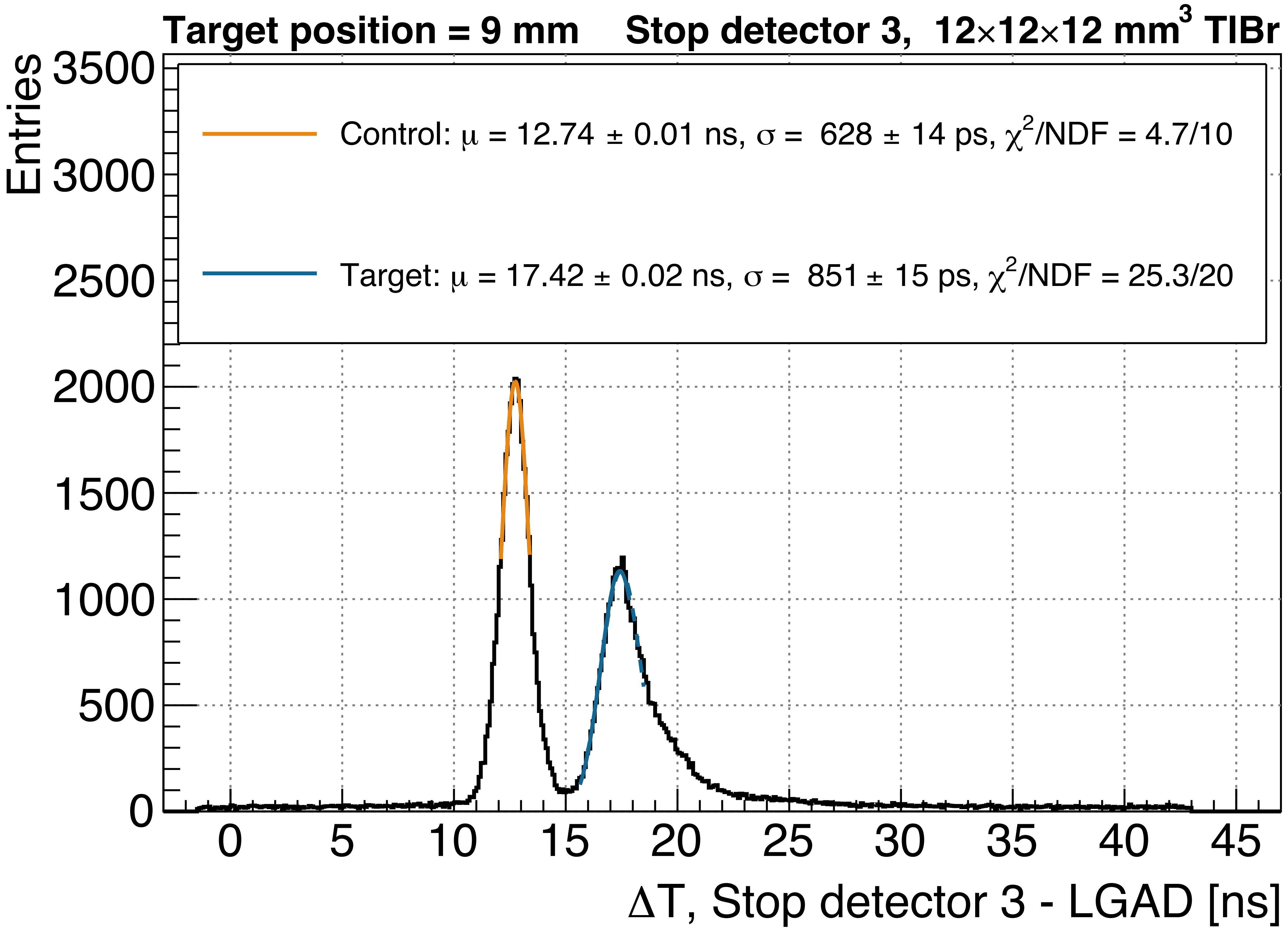


RF phase - LGAD time over ten minutes:



- No! RF phase drifts by O(ns) on timescale of minutes. Start detector is needed! (At least, at this beamline.)

Concluding remarks



- Achieve 1.3 mm precision with sample size of 20-30k prompt gammas
  - Typical pencil beam spot: 10^8 protons, 10^7 PG *
  - Implies clinical system needs efficiency only 0.2-0.3% — very reasonable.

- Background is barely visible: SNR ~ 40
  - Thanks to Pure Cherenkov emission
  - Thanks to narrow time window
  - Both factors could benefit PGI system w/ modest timing information, too.

*Pausch et al, NIM A, 2020

Summary

- Successful demonstration of prompt gamma timing system with LGADs and Cherenkov detectors
- Detectors tolerate high rate and are relatively insensitive to background
- Achieve 12 ps / 1.3 mm uncertainty (RMS) on range shift & accurately reconstruct proton velocity
- Control population at constant time extremely useful experimental tool
- Detector concepts promising for scaling towards full clinical system.

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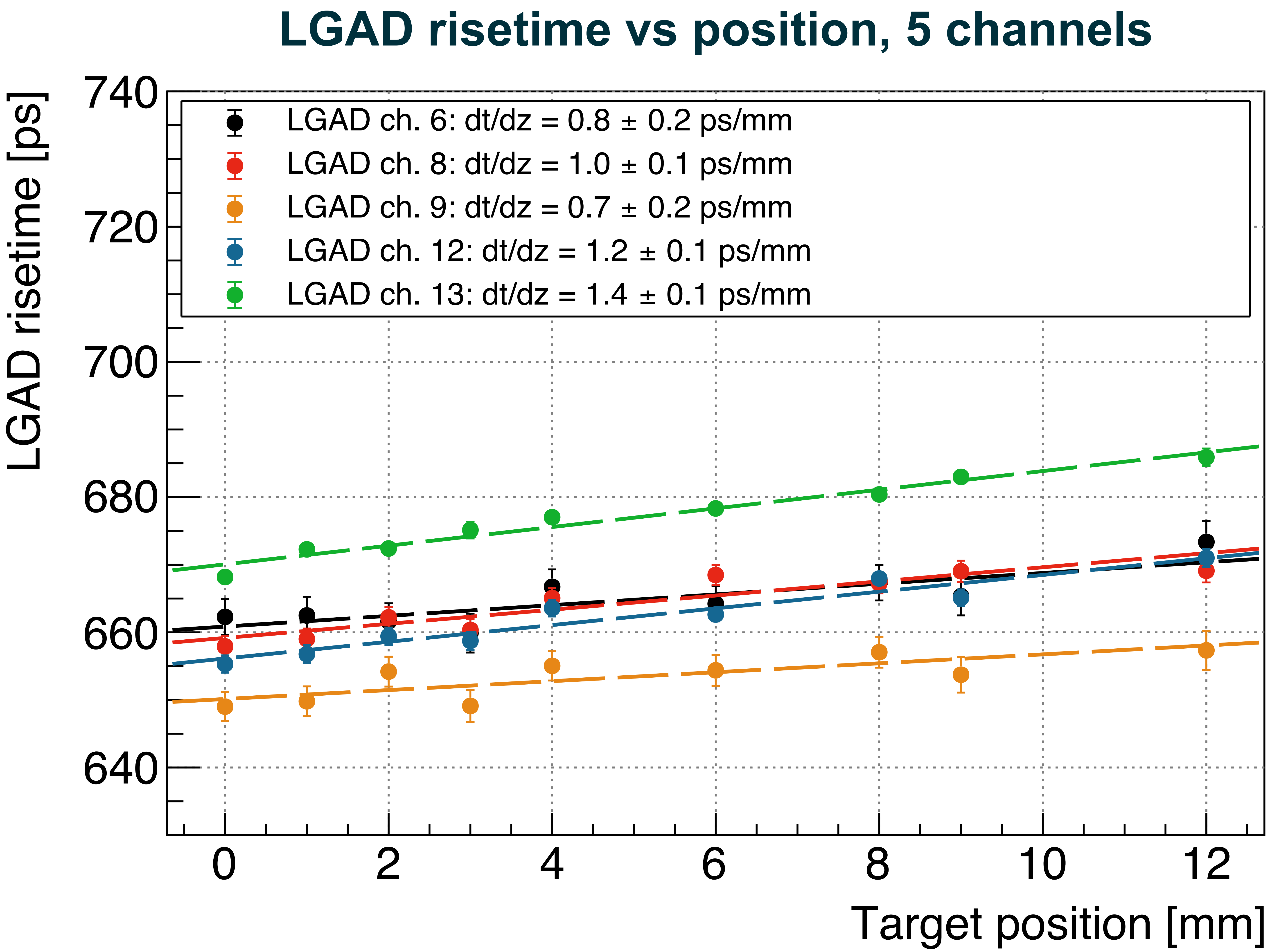
LGAD risetime drift



- LGAD risetime (10-90%) steadily increasing: 660 ps to 670 ps
- What is happening? Exaggerated radiation damage
  - Total flux: 10^{13} protons (~1000 treatment fractions)
  - Setup not optimized for radiation tolerance
    - Max bias voltage: 210 V
    - Uncontrolled temperature (≥ 30 C)
  - Result: defects from rad damage increase leakage current, cause few volt droop in bias, reducing E-field and drift velocity in LGAD.
- This effect not relevant in clinical operation. Would operate at -20 C & scale voltage with damage.
- LGAD will perform for ~ 10^5 fractions, > 1 year.