Meeting the Detector Challenges for Pre-Clinical Proton and Ion Computed Tomography

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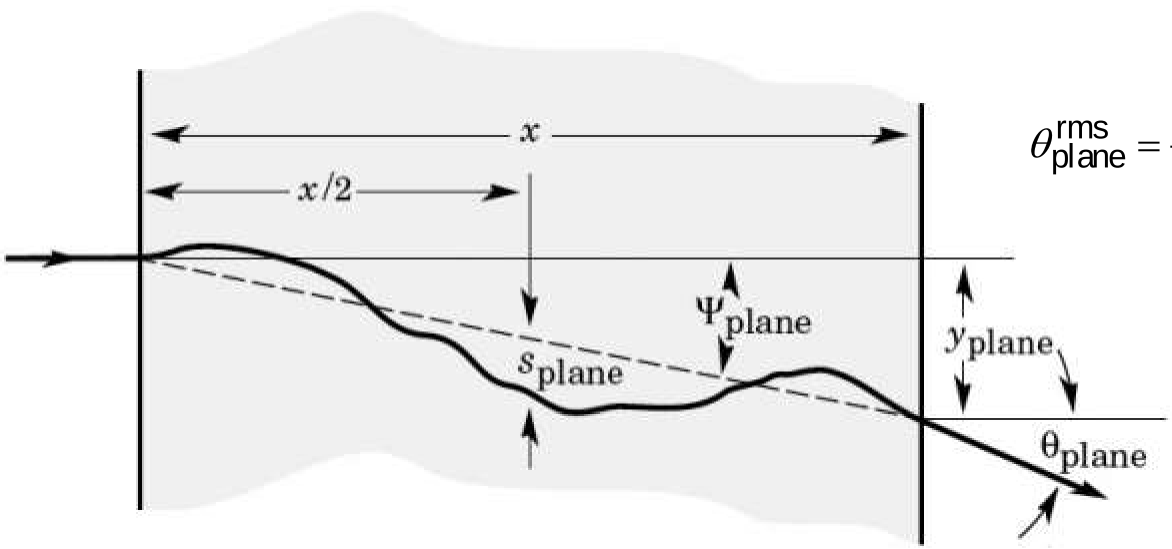
Abstract

Ion computed tomography and radiography have the potential to improve treatment planning for hadron therapy. However, more than 40 years following initial efforts, no ion-imaging scanner has been introduced into clinical use. Numerous research prototypes have been built and tested, and a few existing devices routinely achieve promising results. Technological advances in particle detection, data acquisition, and data processing certainly indicate that by now it should be possible to build a clinically relevant instrument, and some ambitious new projects are in development. This presentation will review some of the technical requirements and the technologies being utilized to meet them. Then it will review a few of the existing systems, and discuss what improvements in design and engineering are needed in order to have a practical device suitable for pre-clinical testing.

Why Ion Computed Tomography?

- Treatment planning—solve the range problem posed by ambiguities in conversion of x-ray Hounsfield units to ion WEPL.
  - A lot of contemporary work has been going into solving this problem by use of dual or multi-energy x-ray CT.
  - Using an ion beam pre-treatment as well as for treatment is expensive – the improvement in treatment planning had better be significant.
  - Also emphasize other advantages of ion CT: freedom from beam-hardening; no artifacts created by metal; very low dose.
  - Ion radiography: the ion CT scanner might get employed more often to make radiographs for last-minute verification of the treatment plan and/or patient positioning. Or CT calibration (Mara Bruzzi's talk yesterday).
- Tests using an existing ion-CT system showed that pCT, He-CT and DECT are competitive in treatment-planning quality
  - L Volz et al, 2021, PMB **66** 235010; G. Dedes et al, PMB 64 (2019) 165002.
  - It is clear that to generate interest in a clinical ion-CT scanner, we have to make substantial improvements relative to existing work!

Multiple Coulomb Scattering

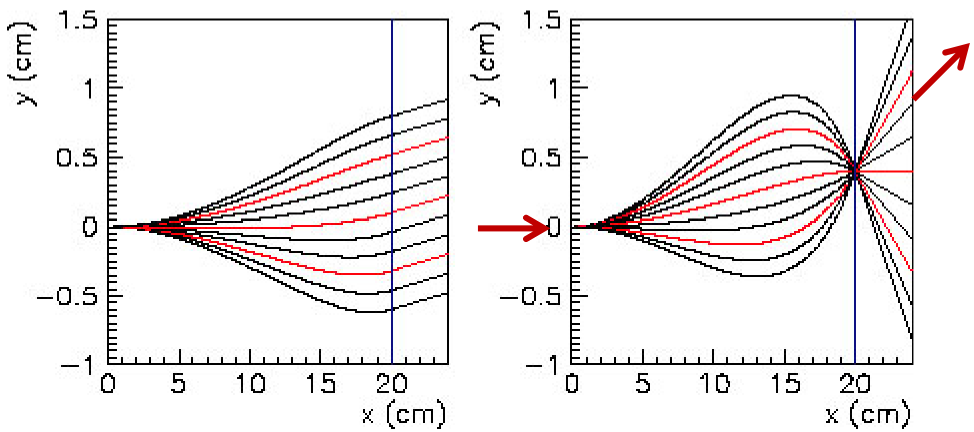


$$\theta_{\text{plane}}^{\text{rms}} = \frac{13.6\,\text{MeV}}{\beta cp}\sqrt{\frac{x}{X_0}}\cdot\left[1+0.038\ln(x/X_0)\right]$$

Charged particles do not travel in straight lines through material!

The amount of scattering scales as the inverse of the particle kinetic energy.

D.C. Williams, Phys. Med. Biol. vol. 49, #13, p. 2899 (2004).



Most Likely Path (MLP)

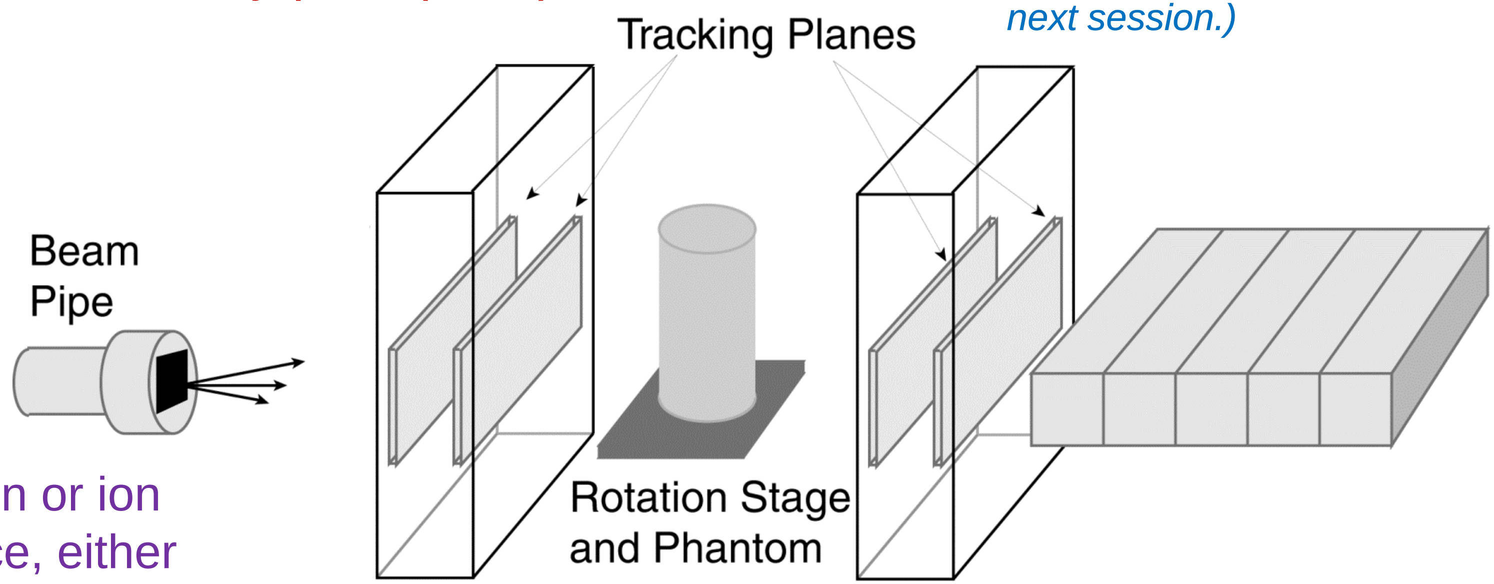
This helps significantly (factors of 2 or more) in CT *and* radiography but requires measuring the particles <u>one at a time</u> ("list mode").

C.A. Collins-Fekete et al, PMB 61, 2016, 8232

Basic Instrument Concept

Measure each particle trajectory ***individually***, so that we can calculate the most likely path (MLP) for each one.

(But see Ryan Fullarton's talk in the next session.)



Proton or ion source, either cone-beam or scanned pencil beam.

Tracking detectors measure the entry and exit vectors of each and every proton, used to predict the *MLP* through the phantom.

The energy detector stops the proton and measures its residual energy or range, used to infer its "water equivalent path length" (*WEPL*) through the phantom.

V.A. Bashkirov, et al, NIM Advances in Detectors and Applications for Medicine 809, 2016, 120.

Instrumental Requirements: Energy

- Measure at least 5 million ions per second, in order to acquire a CT image data in less than one minute.
  - For radiographs, ≈1 MHz is more than adequate (and already achieved).
- Pileup must be managed by fast measurements and/or spatial segmentation.
  - Event overlaps generally destroy the necessary good energy resolution.
  - But moderate spatial segmentation is helpful only if pencil beams are not used.
  - Small pixels can do the job in fine pencil beams.
- Range-straggling fluctuations will be 3 to 4 mm WET (at 200 MeV kinetic energy), so the instrumental resolution on the residual range should be no worse.

Instrumental Requirements: Tracking

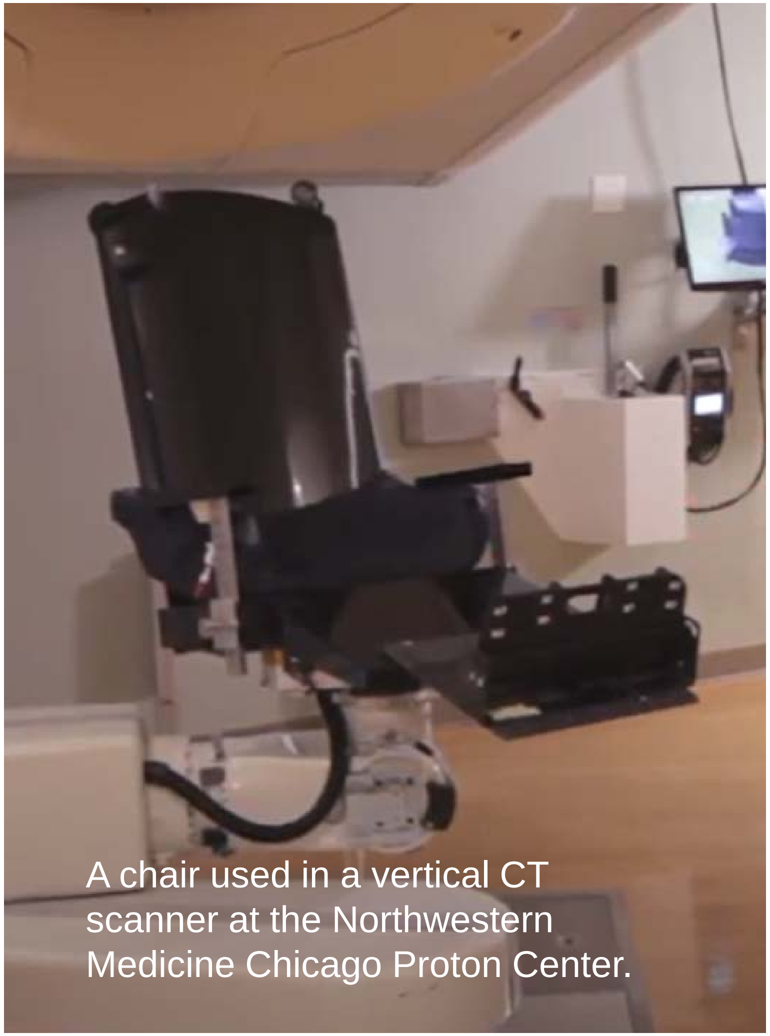
- The same rate requirement as for the energy measurements.
  - *Must manage pileup, especially for pencil beams.*
- High hit efficiency (i.e. ≥98%), to do the tracking with zero or minimal redundant layers.
  - This requires detectors with high signal/noise!
- Cracks and overlaps should be avoided, because they may produce artifacts in the image.
- Hit spatial resolution is not critical, because of large scattering in the phantom.
  - The range 0.1 mm to 1 mm is probably adequate in all cases.
- Detector thickness is not critical, again because most of the scattering material will generally be in the phantom.
  - e.g. no real advantage in choosing more complex double-sided silicon-strip detectors over single-sided.
- Radiation hardness:
  - Not difficult if only the low-intensity imaging is seen by the detector.

Variations on the Theme

- ***Is a front tracking detector necessary?*** Eliminating it would greatly simplify a clinical setup.
  - Only *one* highly-efficiency layer is needed in the typical case that the proton direction is well known.
  - *Or none at all if a scanning beam is employed and its instantaneous position is known.*
    - J.R. Solie et al, *Image quality of list-mode proton imaging without front trackers,* PMB **65** (2020) 135012.
- Not having the front tracker does reduce spatial resolution and increase image noise to some extent.
- Good results require extending the MLP formalism to account for particular geometric parameters and measurement uncertainties.
  - N. Krah et al, PMB **63** (2018) 135013.
- The beam spot size relative to its spacing has to be carefully considered to avoid image artifacts.

Rotations

- A rotating stage works well for CT development work using phantoms.
- Ion CT in a clinic might use a gantry to illuminate the patient from all directions, *but such a complex interface seems highly unlikely in the beginning*.
- A rotating chair is a simpler proposition.
  - This idea goes back at least 40 years.
  - It has already been employed in x-ray CT.



A chair used in a vertical CT scanner at the Northwestern Medicine Chicago Proton Center.

Other Types of Energy Detectors

The energy detector does not necessarily have to stop the particles and suffer from range straggling and N interactions.

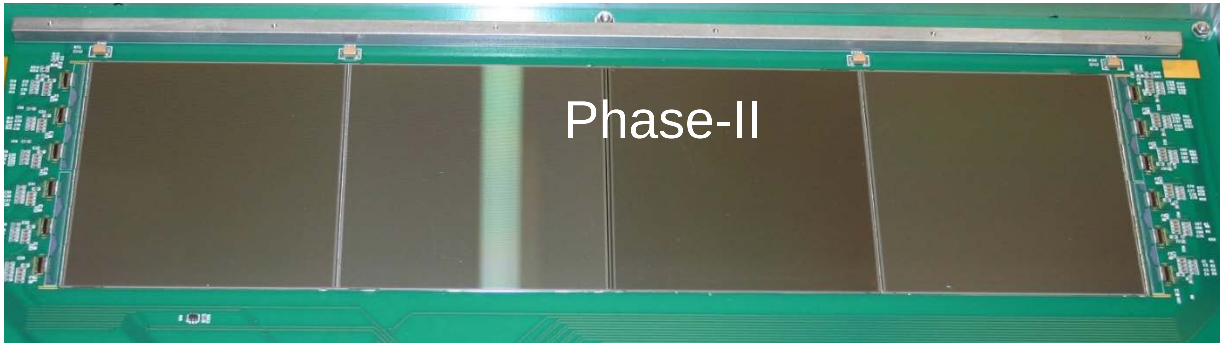
- Magnetic spectrometer: can have exquisite resolution, but generally too massive and expensive to accommodate the large bore needed for ion CT.
  - Example: Y. Takada et al, NIM-A **410** (1988) 410.
- Time-of-Flight: for readily achievable time resolution, the necessary distance may be too long.
  - At 100 MeV residual kinetic proton energy, a ±3% uncertainty corresponds to ±30 ps for a 50 cm path length.
  - LGAD silicon pixel detectors have observed ≈30 ps resolution over small areas, but uniform instrumentation of a large area that achieves that resolution has not yet been achieved
    - N. Cartiglia et al, NIM-A **850** (2017) 83.
    - *See the talk today by Felix Ulrich-Pur.*

Tracking Technologies

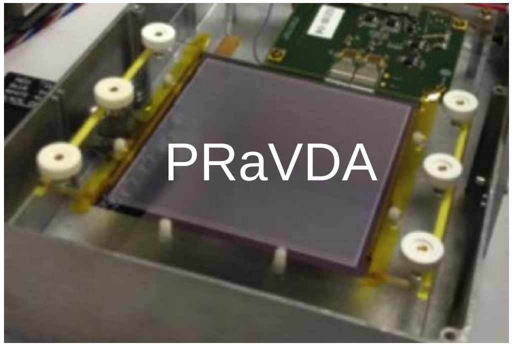
Silicon Strips (e.g. PRaVDA, LLU/UCSC/Baylor Phase-II, PRIMA/RDH, etc.)

- Very high S/N (near 100% efficiency with near zero noise).
- Easy to integrate into detector assemblies using automated manufacturing processes.
- Solid-state, with very stable operation and calibration.

- *But,* impossible to integrate into large planes without cracks and/or overlaps.
  - Keep the gaps as small as possible to avoid potential artifacts.
- Relatively slow, except in small sizes with high power (e.g. LHC).
  - Pulse shaping makes pileup a potential issue in pencil beams.
- Strips measure only one coordinate (ambiguities in multi-track events, unless extra U/V layers are added, a la PRaVDA, *and* tracks are widely separated).



R.P Johnson et al, IEEE Trans Nucl Sci **63** (2016) 52

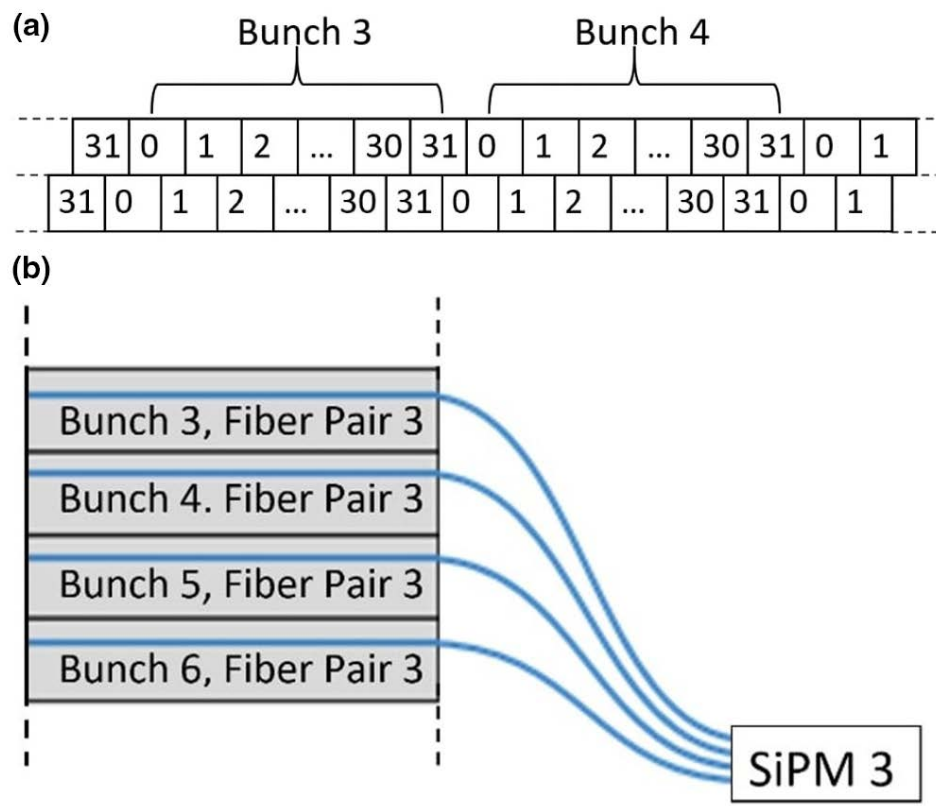


J.T. Taylor et al, JINST **10** (2015) C02015

Tracking Technologies

Scintillating fibers (e.g. Proton VDA)

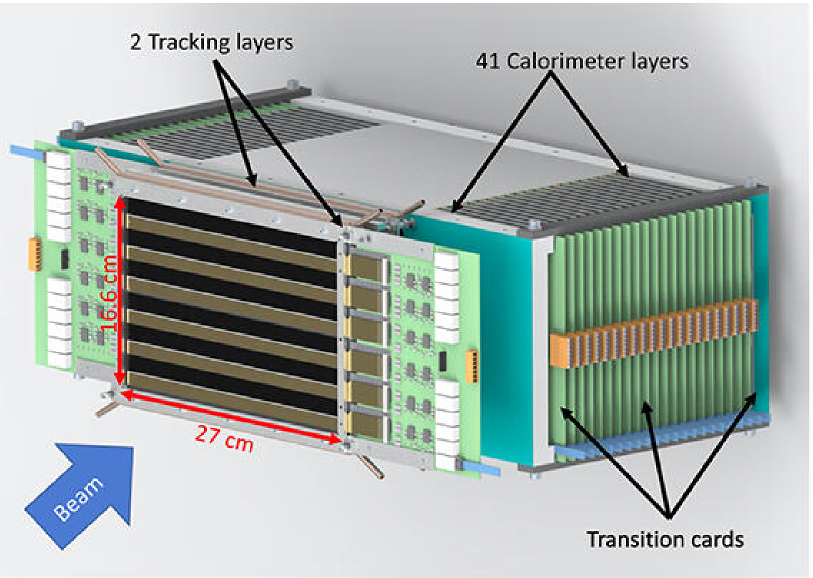
- Can instrument a large detector plane without cracks (using double layers).
- Can be significantly faster than large-format silicon-strip detectors.
  - Proton-VDA:10 MHz design (but appears to be used thus far at rates $\leq$ 2 MHz).
- Signal/noise is poor compared with Si strips, but acceptable if relatively large (e.g. 1 mm) fibers are used.
- Like SSDs, measures only a single coordinate.
- Proton VDA connects 12 fiber pairs to each SiPM, relying on knowledge of the pencil-beam location to resolve ambiguities.
  - Avoids the use of VLSI ASICs to instrument a large number of channels.



Tracking Technologies

Monolithic Active Pixel Sensors (MAPS, e.g. Bergen)

- Very fine segmentation (and resolution): $30 \times 27\ \mu m^2$ pixels.
  - Avoids pile-up problems with 2 μs peaking-time signals.
- Each pixel has its own integrated amplifier/discriminator.
- Tracking extends all the way through a range counter.
- Prototype measured 10^6 protons per second at 2 kHz readout rate, i.e. 500 tracks per frame. Maximum layer occupancy of 0.42%.
- Current design assumes 10μs frames and 10^7 protons/s, i.e. 100 tracks per frame. *No trigger.*
- *Rear detector only.*
  - Cannot match tracks between front and rear detectors.
- About 10 GB/s of data.
- Full CT scan in 30s.



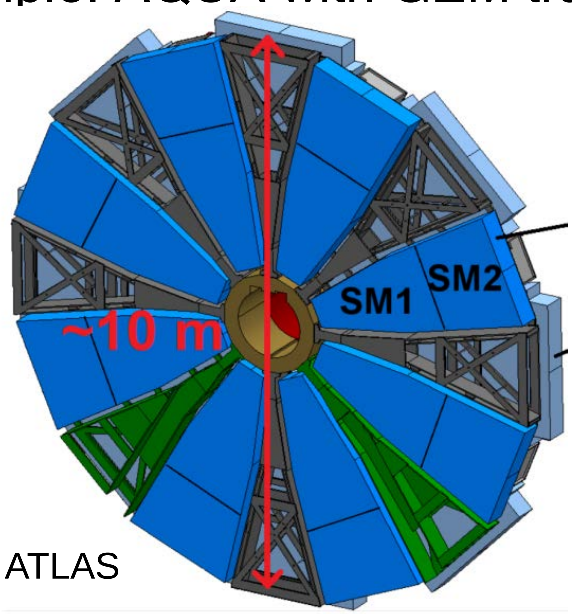
J. Alme et al, Front. Phys. 8 (2020) 568243.

See Dieter Röhrich's talk from yesterday.

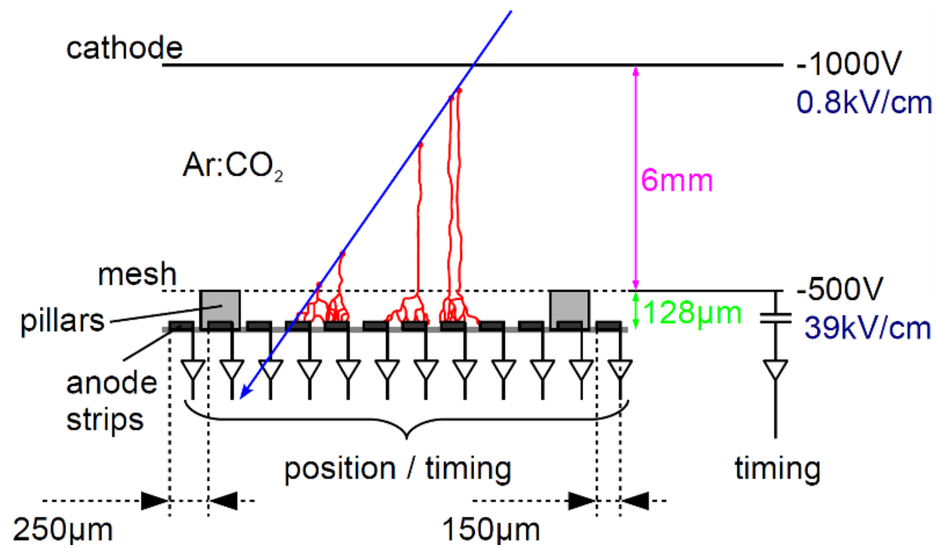
Tracking Technologies

Micro pattern gas detectors, *GEM* and *MicroMegas*

- Fast signals (<100 ns) with high gas amplification (>10^4).
  - No need for long integration to keep noise down, as in Si strip detectors.
- Large area coverage without gaps (LHC ATLAS muon detectors!).
- Strip readout with pitch appropriate to ion-CT (0.25 to 0.5 mm).
- Technologies advanced by the CERN RD51 collaboration.
- Example: AQUA with GEM tracking (U. Amaldi et al, NIM-A **732** (2013) 564)



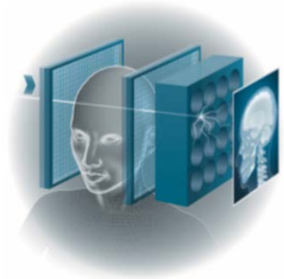
LHC ATLAS



Energy or Range Detector Technologies

Calorimeter (measure directly the residual energy)

- Very high energy resolution is needed for small-WEPL (1 to 2%)
  - *A large residual energy is subtracted from the beam energy to give the WEPL.*
- Segmented doped-CsI crystals tended to produce artifacts due to cracks and non-uniform coverage, *and were much too slow.*
  - LLU/NIU/UCSC Phase-1 scanner, R.F. Hurley et al., Med Phys **39** (2012) 2438.
  - See Carlo Civinini's talk yesterday for discussion of corrections for proton sharing.
- YAG:Ce crystals are much faster: V. Sipala et al., JINST **10** (2015) C03014
- Plastic scintillators are fast but relatively low resolution. Two solutions have been employed to always measure a small residual energy:
  1. Multi-stage calorimeter (V. Bashkirov et al, Med Phys **43** (2016) 664)
     - LLU/UCSC/Baylor Phase-II scanner (5 identical stages)
     - Calibration of protons stopping near the interfaces is difficult, giving ring artifacts.
  2. Modulate the beam energy, to be low in low-WEPL regions, etc.
     - Proton-VDA: 16 PMTs read a single scintillator block.
     - Program a-priori knowledge into beam delivery, or scan the entire phantom multiple times.
     - Potentially complicates the interface with beam delivery.



Energy or Range Detector Technologies

Range Detector

- Make the detector spacing commensurate with range straggling
  - 3 to 4 mm, or 64 to 100 stages, for a 200 MeV beam
- The WEPL resolution will not be good enough (i.e. below 1%) if a simple threshold is used
  - Nuclear interactions in the detector have too much negative impact
- Digitize every pulse height from scintillators with WLS fibers
  - PSI FROG: 64 stages; PMT with *discriminators only* (radiography)
    - *P. Pemler et al, NIM-A **432** (1999) 483*
  - AQUA: 48 stages; SiPM with 12-bit pipelined ADCs
    - *M. Bucciantonio et al, NIM-A **732** (2013) 564*
  - NIU/FNAL: 96 stages; SiPM with 12-bit pipelined ADCs
    - *S.A. Uzunyan et al, arXiv:1409.0049*

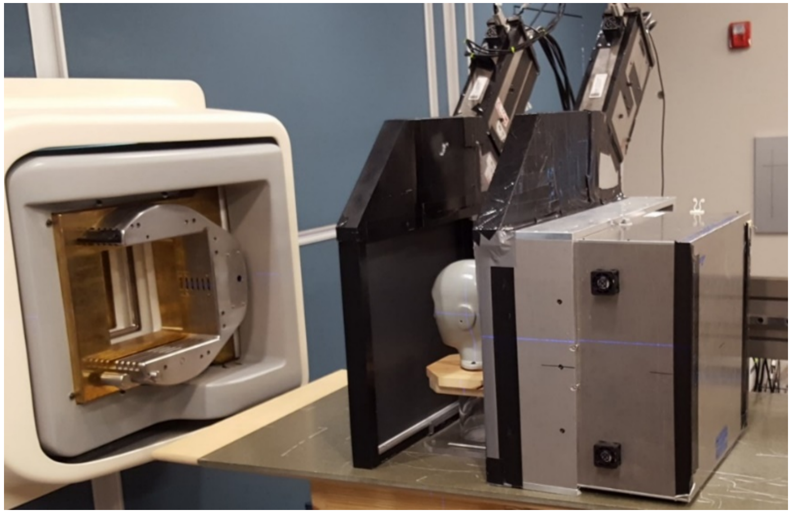
AQUA PRR30

- Or track the particles throughout the detector
  - Bergen: MAPS
    - *J. Alme et al, Front. Phys. **8** (2020) 568243*
  - PRaVDA: Si strips, 21 stages of Si and 2 mm PMMA (up to 80 MeV)
    - *M. Esposito et al, Phys Med **55** (2018) 149*

Operational Prototype Systems

Proton-VDA

- Our only commercial venture
  - (PROTOM claims to be working on pCT also, but I've never found any technical information or results)
- Emphasizes low cost
  - Relatively few electronics channels
  - Tracking layers do not measure direction
  - Emphasis on radiography as well as CT
- Specifically designed for scanning pencil beams
  - Uses knowledge of the beam position for data analysis
  - Requires modulation of beam energy to cover full WEPL range
- 10 MHz design goal
  - A "few" MHz demonstrated.



- *A Comparison of Proton Stopping Power Measured with Proton CT and X-Ray CT in Fresh Post-Mortem Porcine Structures,* Med Phys **48** (2021) 7998.
- *Technical Note: A fast and monolithic prototype clinical proton radiography system optimized for pencil beam scanning,* Med Phys **48** (2021) 1356.
- *Analysis of characteristics of images acquired with a prototype clinical proton radiography system,* Med Phys **48** (2021) 2271.
- Reconstructed and real proton radiographs for image-guidance in proton beam therapy, J. Radiat Oncol 8 (2019) 97.

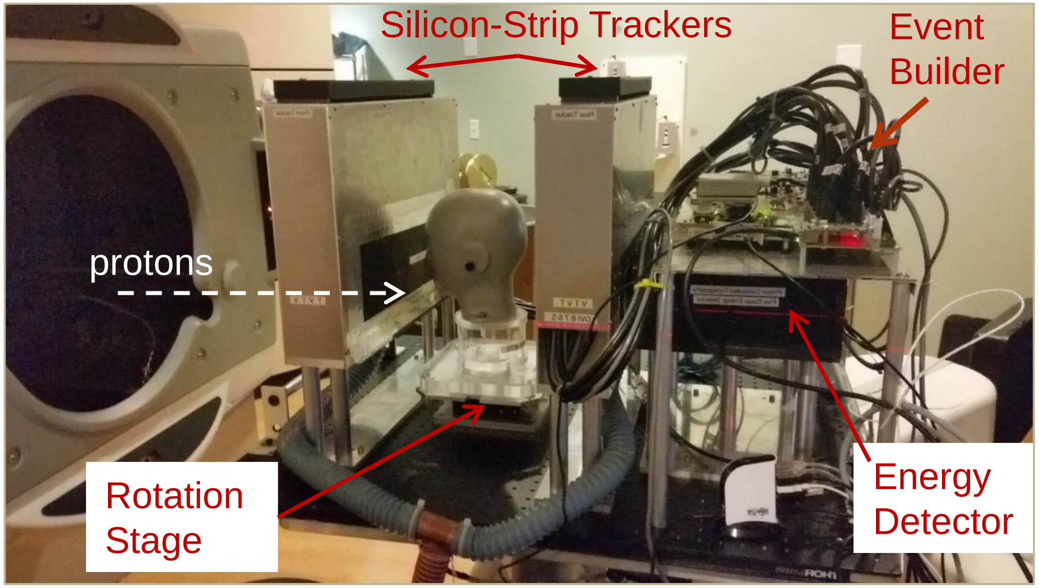
Large aperture can view the entire head at once.

See talk today by Ethan DeJongh

Operational Prototype Systems

Phase-II pCT Scanner

- 9×36 cm^2 aperture
- > 1 MHz rate
- Good quality CT scans in 6 minutes with continuous rotation.
- Used by multiple groups since 2014 to produce a large body of work. A few examples:



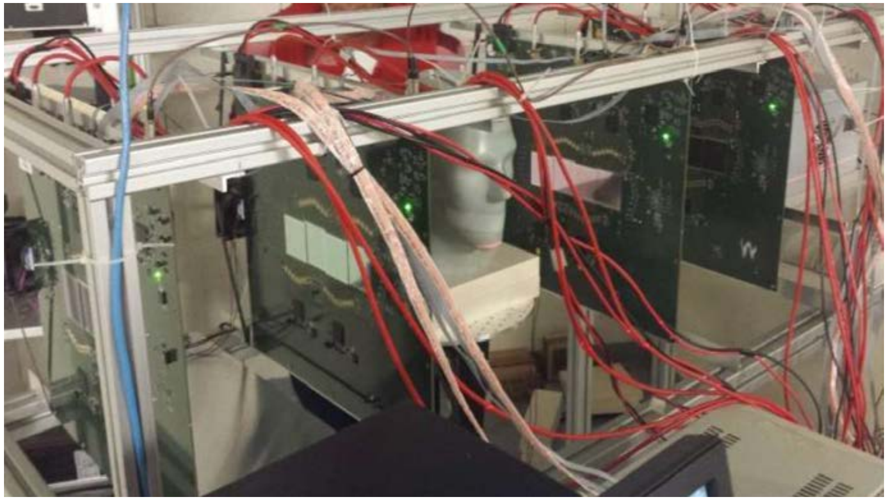
R.P. Johnson, et al., IEEE Trans Nucl Sci ***63*** *(2015) 52.*

- G. Dedes et al., *Comparative accuracy and resolution assessment of two prototype proton computed tomography scanners*, Med. Phys. **49** (2022) 4671. (Phase-II versus Proton-VDA)
- L. Volz, et al., *The accuracy of helium ion CT base particle therapy range prediction: an experimental study comparing different particle and x-ray CT modalities,* Phys. Med. Bio. **66** (2021) 235010.
- G. Dedes et al., *Experimental comparison of proton CT and dual energy X-ray CT for relative stopping power estimation in proton therapy*, Phys. Med. Bio. **64** (2019) 165002.
- G. Dedes et al., *Experimental fluence-modulated proton computed tomography by pencil beam scanning.* Med. Phys., **45** (2017) 3287.
- T. Plautz et al., *An Evaluation of Spatial Resolution of a Prototype Proton CT Scanner,* Med. Phys. **43** (2016) 6291.

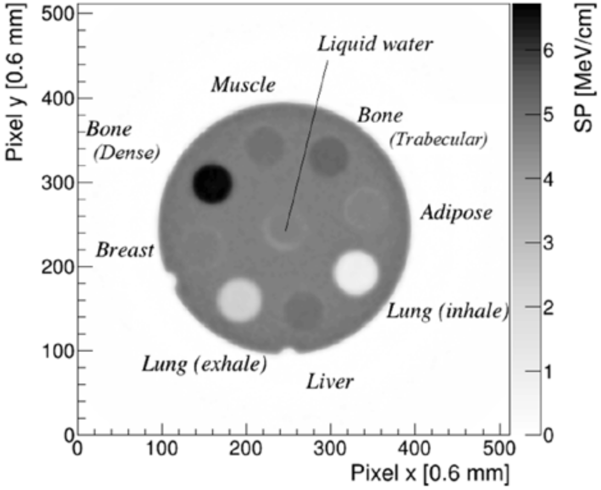
Operational Prototype Systems

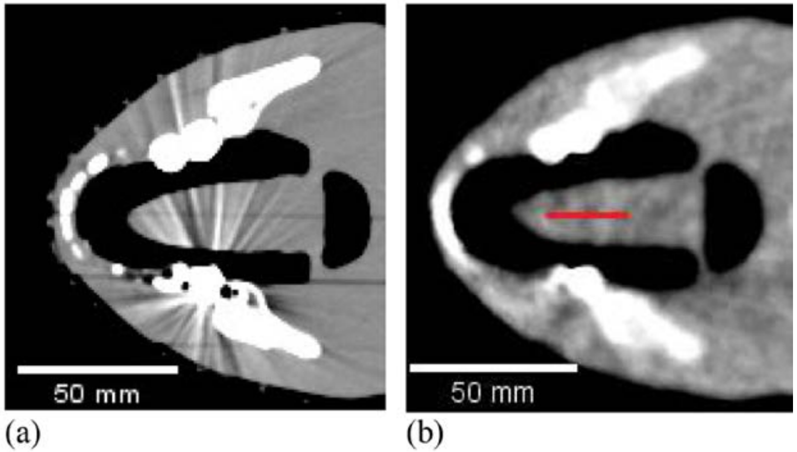
INFN Prima-RDH system

- 5×20 cm^2 aperture
- 80 kHz rate
- YAG:Ce calorimeter



- C. Civinini et al., *Relative stopping power measurements and prosthesis artifacts reduction in proton CT*, Phys Med Biol **65** (2020) 225012.





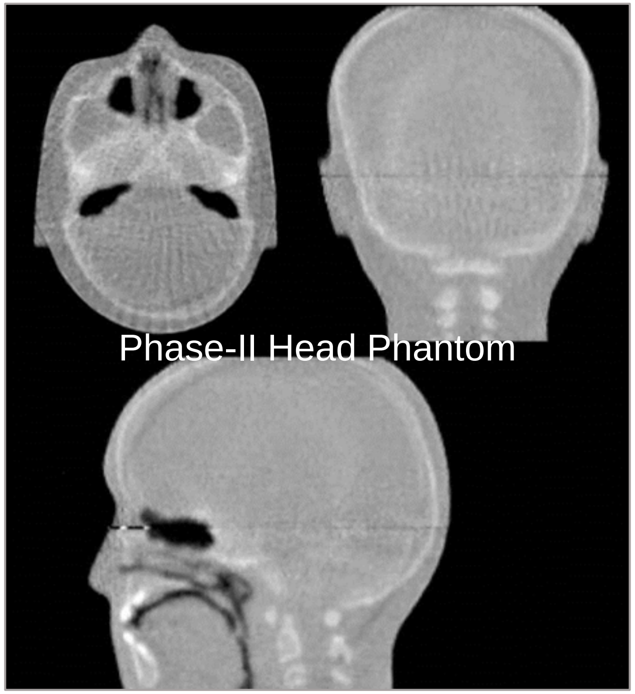
X-ray CT proton CT

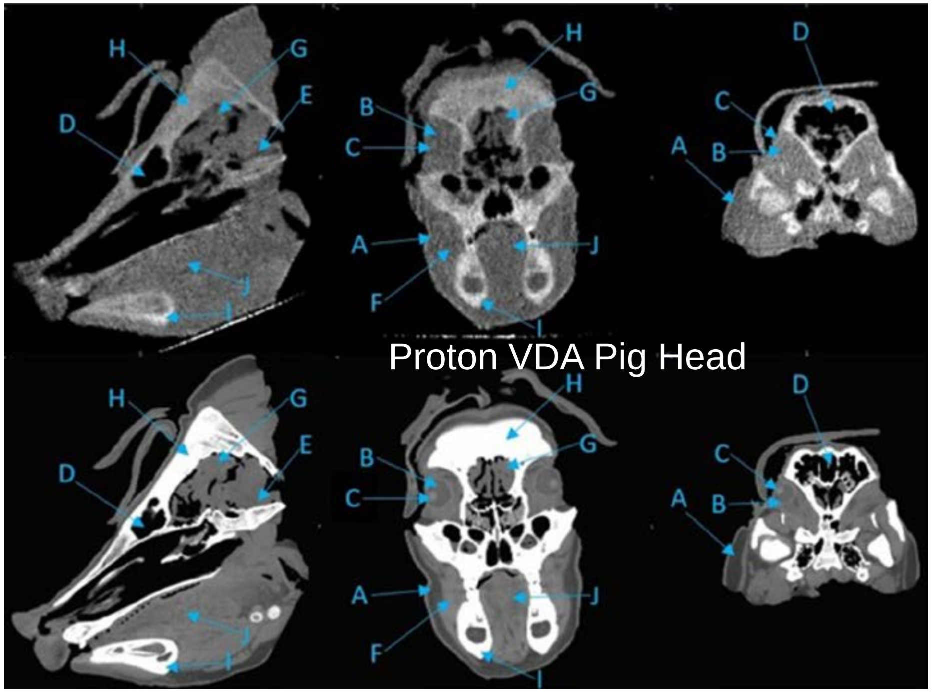
See talks yesterday by Carlo Civinini and Mara Bruzzi.

Operational Prototype Systems

From G. Dedes et al., Med. Phys. **49** (2022) 4671: *(See George's talk today)*

In terms of RSP accuracy, both scanners achieved the same MAPE of 0.72% when excluding the porous sinus insert from the evaluation. The ProtonVDA scanner reached a better overall MAPE when all inserts and the body of the phantom were accounted for (0.81%), compared to the Phase-II scanner (1.14%). The spatial resolution with the phase-II scanner was found to be 0.61 lp/mm, while for the ProtonVDA scanner somewhat lower at 0.46 lp/mm.





Med Phys **48** (2021) 7998

Engineering a True Pre-Clinical System

- Turnkey: one power plug, one switch, integrated DC and HV supplies, integrated DAQ, simple GUI control, clean & fast data transmission to analysis computers.
  - *Should not look like a particle physics experiment!*
  - *Cost is a real-world issue that cannot be ignored!*
- Quick, painless calibration, done once per day at most.
- Integration with the beam-control and safety systems.
  - I think this may be the hardest part: how do we get the ion-therapy system vendors interested in working on this?
  - Positioning the patient and scanner, plus rotation control.
    - Modern pencil-beam scans can avoid the need to have beam at all angles in therapy, but CT requires it. *(Simple radiography would be much easier.)*
  - Feedback to the accelerator operators, and safety interlocks.
    - Typically their instruments cannot monitor the low-intensity beam.
  - Acquiring data on angle, beam energy, and beam position during a scan.
- Hardware data-acquisition speed.
- Data reduction and image feedback after only a few minutes.

Outlook

- After more than 40 years of on/off development, proton radiography and CT still have not made it into any clinic.
  - But technology not available in 1980 suggests better prospects now.
- Several promising efforts with small-scale prototypes have promised a next generation large enough (≈40 cm) and fast enough (>1 MHz) to make realistic CT images, but then seem to have faded away.
- Radiography is easier, but even there some promising starts have faded or were dormant for several years.
  - PSI proton radiograph of a live dog:
    - U. Schneider et al, Med Phys 31 (2004) 1046.
  - TERA AQUA PPR-30 (now used for pCT tests at MedAustron).
    - F. Ulrich-Pur et al., NIM-A 978 (2020) 164407. (Tracking by Belle-II DSSDs)
- The Proton-VDA scanner is probably the best realization so far of a practical pre-clinical device.
  - See Ethan DeJongh's talk later in this session.

Outlook

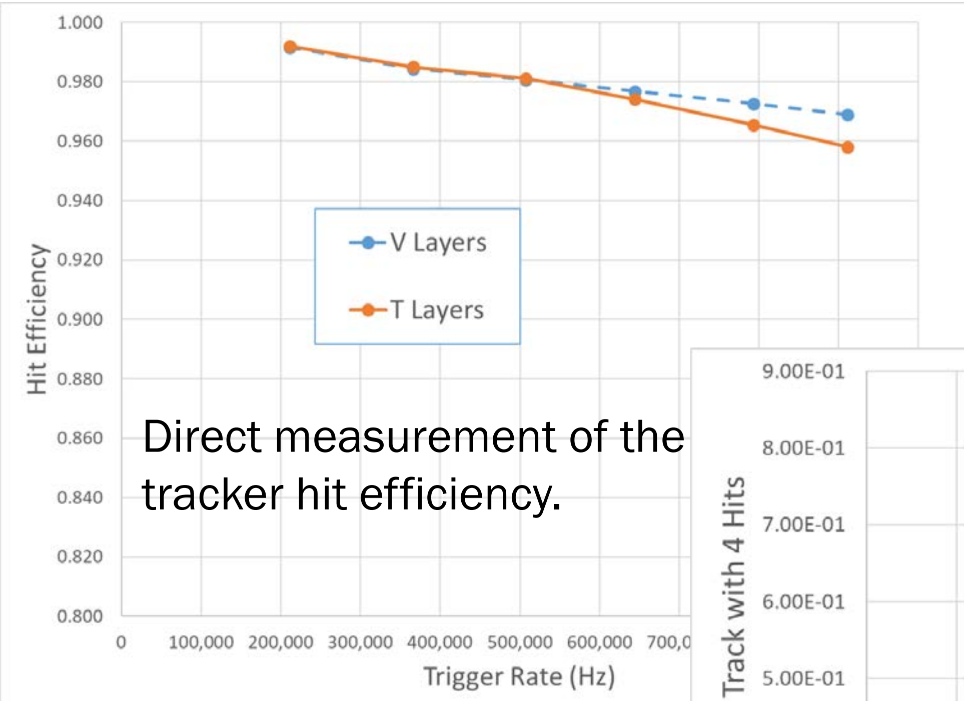
- The Bergen pCT project is working toward an ion-CT scanner with perhaps the ultimate capability:
  - Dieter Röhrich's talk yesterday.
- The Phase-II collaboration is actively working on a new proposal.
  - Up to factor of 5 increase in ion rate.
  - Larger aperture.
  - More turnkey, for ease of use.
- MedAustron plans: Albert Hirtl's talk yesterday.
- PRaVDA/OPTima pCT: Michela Esposito's talk yesterday.
- TOF ion-CT: Felix Ulrich-Pur's talk later in this session.
- Integrated-mode system: Ryan Fullarton's talk in next session.

It is exciting to see the continuing interest exhibited in this workshop.

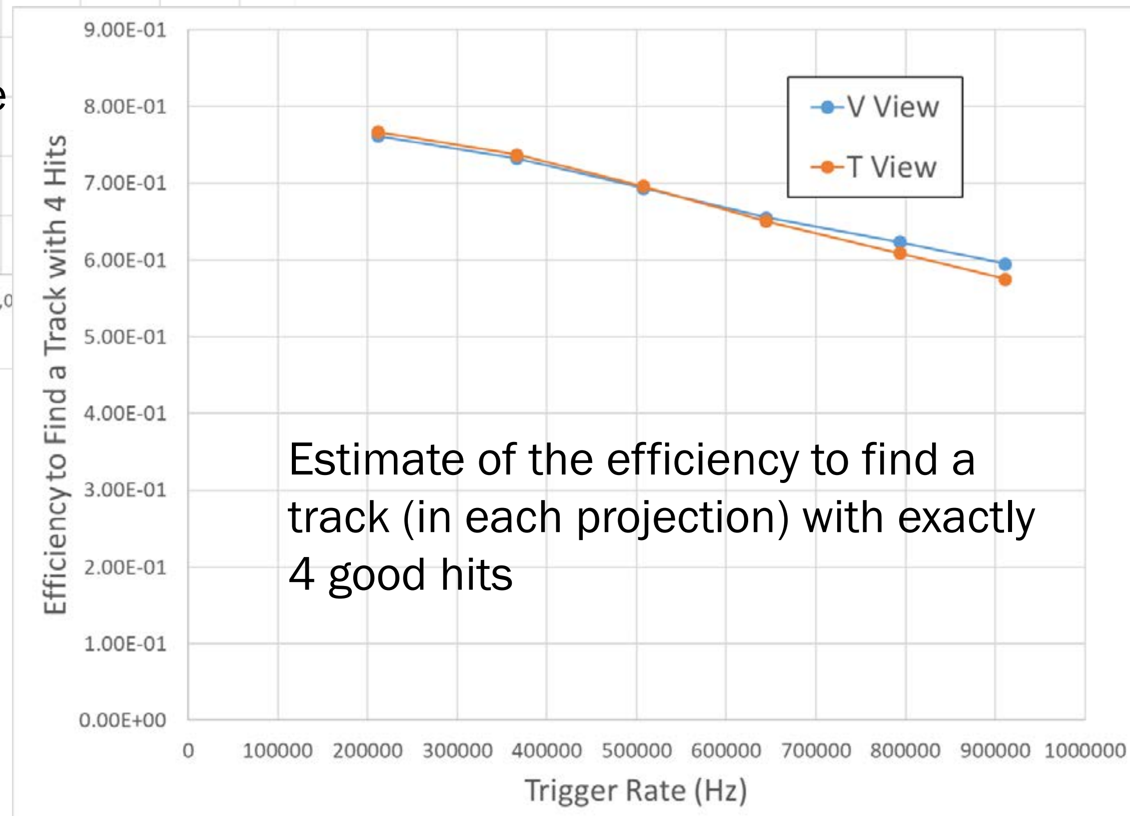
I would like to see an increasing emphasis on engineering a pre-clinical device (i.e. one that could conceivably used in a clinic, even if not yet achieving approval for use with humans) that will excite interest from the ion therapy industrial providers.

Backup Slide: pileup in the Phase-II

Data from a November 2017 run at the Chicago Proton Center, using scanned pencil beams with no phantom (with a phantom the pileup in the rear tracker will be substantially reduced).



Direct measurement of the tracker hit efficiency.



Estimate of the efficiency to find a track (in each projection) with exactly 4 good hits