Towards High Sensitivity and High-Resolution PET Scanners

Image-guided Proton Therapy and Total Body imaging

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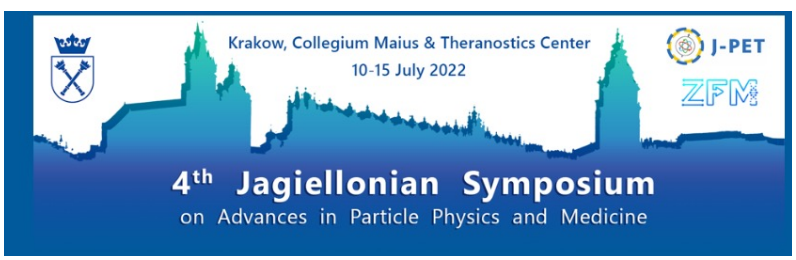
University of Texas at Austin

On behalf of the TPPT Consortium
July 13, 2022

Outline:

- Proton Therapy
- Our PETs
  - brain scanner
  - total body
- (In lieu of) Conclusions

UTAustin Portugal



The University of Texas at Austin
Department of Physics
College of Natural Sciences

This is the time of genocidal war going on just next door...

We, the civilized world, must not condone it!

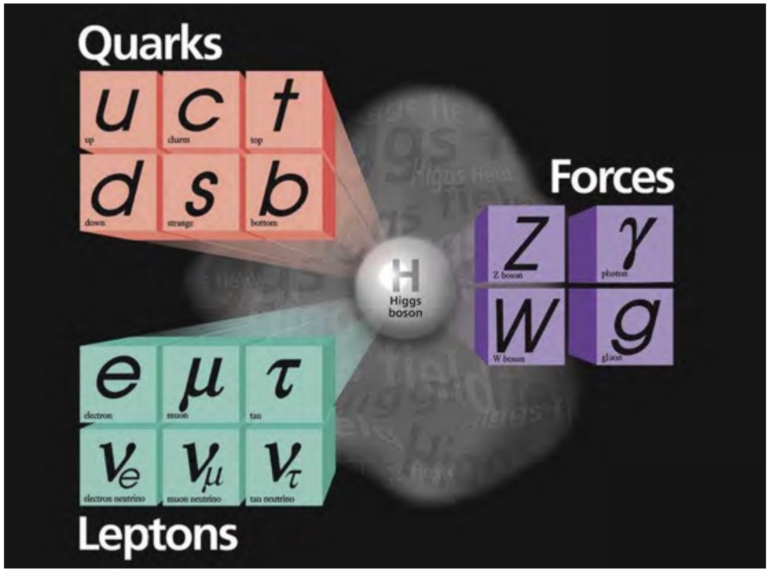
I would like to dedicate this talk, just as I have done with all talks since the war broke out,
to future peace and prosperity of Ukraine...

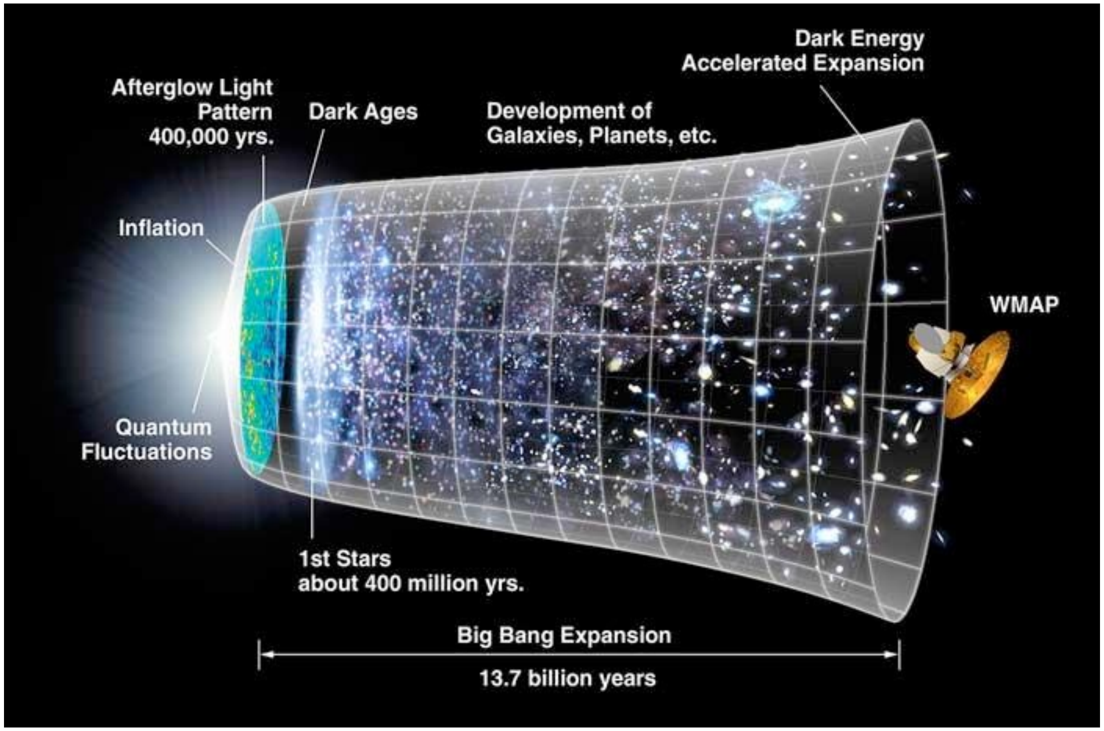
Good will prevail!

“You can **observe** a lot by **watching**.”

- Yogi Berra

Our origins:
The standard view of the Universe:
("inner space and outer space")





Open questions

(i.e., mysteries that the SM can't explain) :

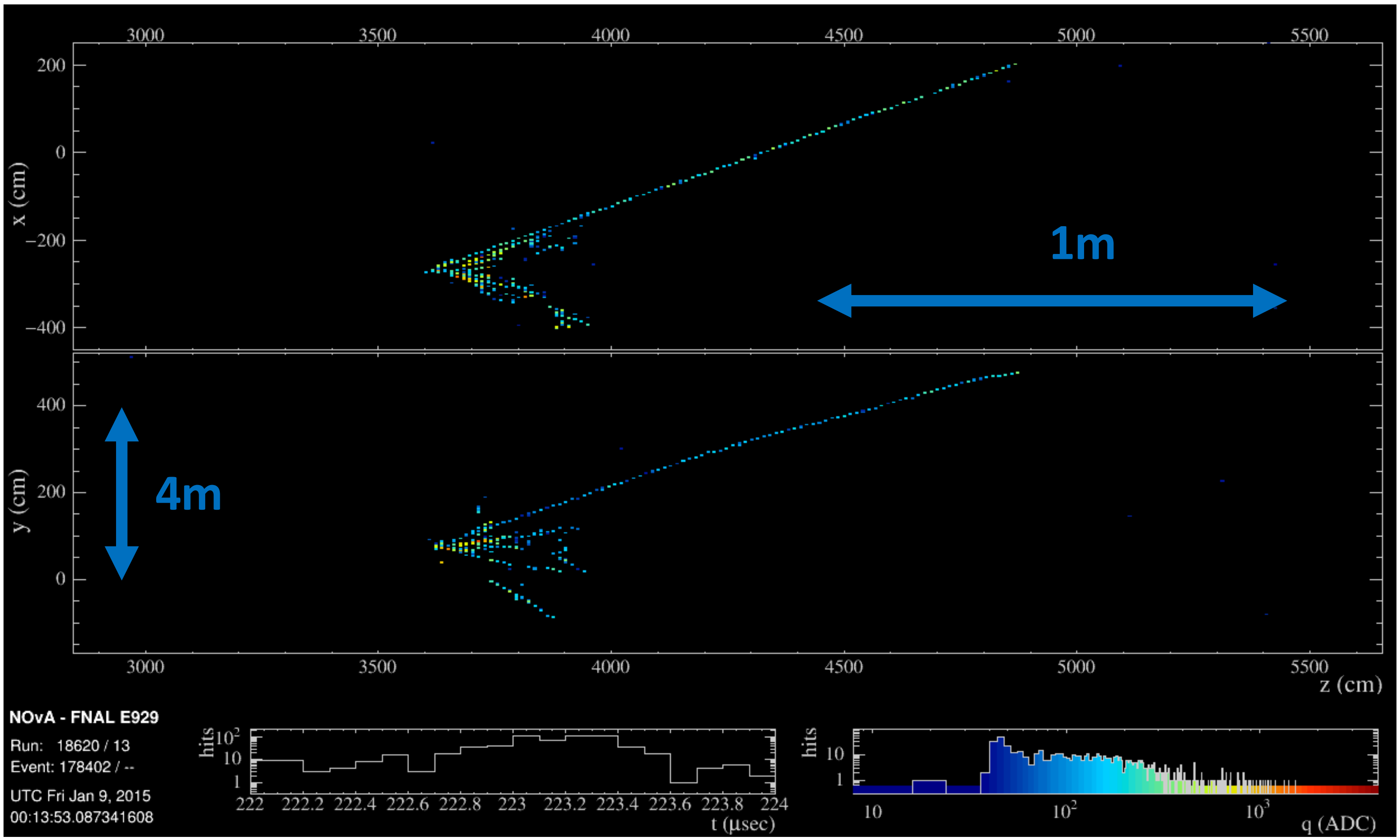
- ✓ Why this structure?
- ✓ What is dark energy ?
- ✓ What is dark matter ?
- ✓ Why matter-antimatter asymmetry?
- ✓ Why / are L, B numbers conserved?
- ✓ Are neutrinos Majorana type: $\nu \equiv \bar{\nu}$
- ✓ How do neutrinos get their mass?
- ✓ What about gravity?
- ✓ …

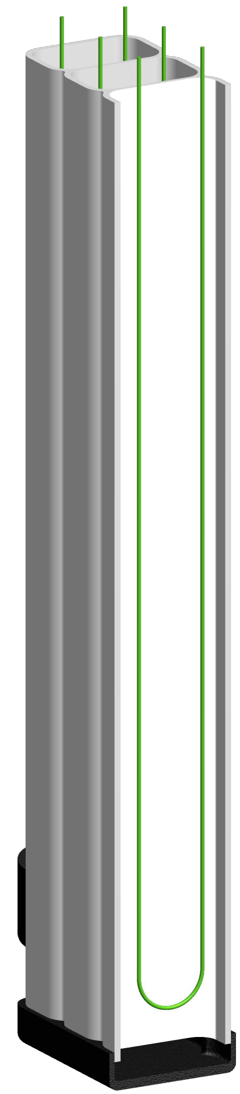
Neutrinos are implicated in all these questions!

Better understand neutrinos

Finding neutrino candidates in NOvA

Zooming in spatially can see a candidate neutrino interaction.



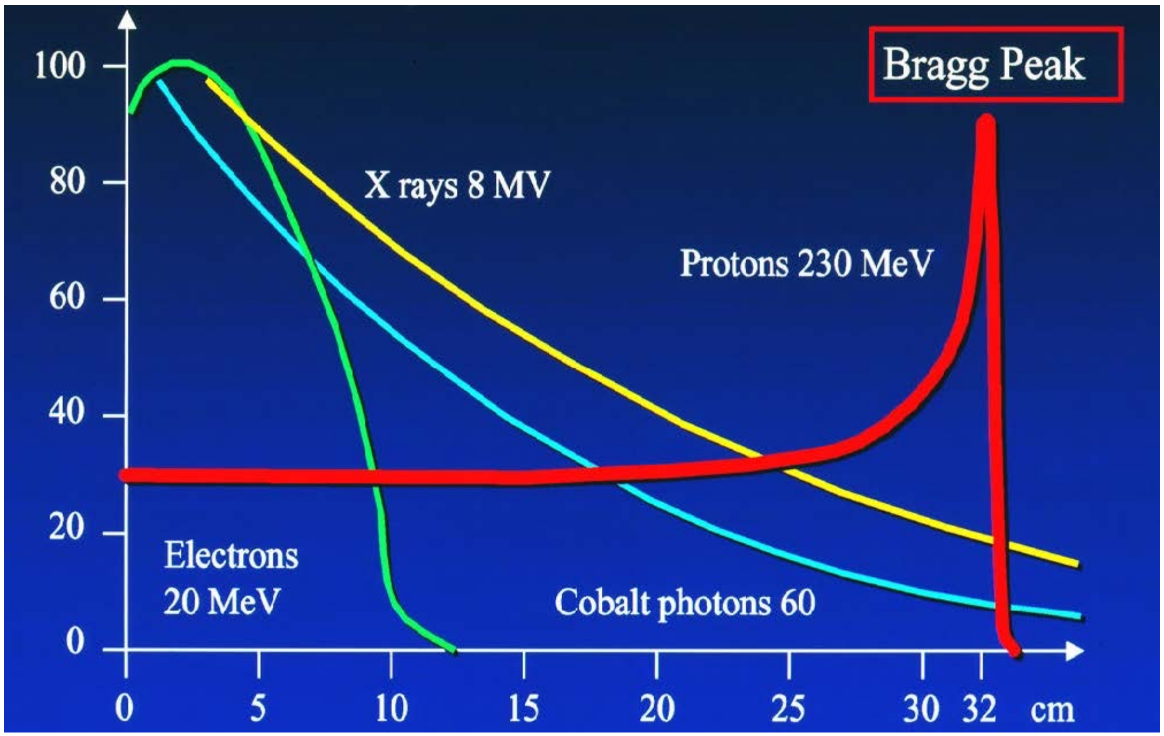


76 years ago....

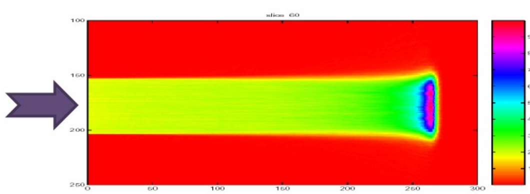
R. R. Wilson, Harvard University

Radiological use of fast protons, Radiology **47**, 487-491 (1946) doi:10.1148/47.5.487.

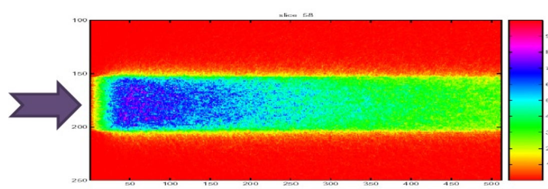
``The proton proceeds through the tissue in very nearly a straight line, and the tissue is ionized at the expense of the energy of the proton until the proton is stopped. [...] Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest. These properties make it possible to irradiate intensely a localized region within the body, with but little skin dose. It will be easy to produce well collimated narrow beams of fast protons, and since the range of the beam is easily controllable, precision exposure of well defined small volumes within the body will soon be feasible.''



Protons stop



Photons (X-rays) don't



Radiological Use of Fast Protons

ROBERT R. WILSON
Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

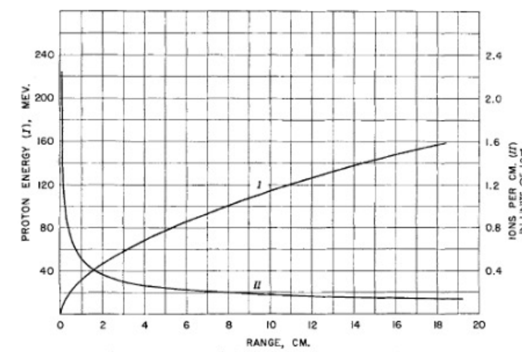


Fig. 1. Curve I is the range-energy relation in tissue. Curve II shows the specific ionization as a function of the residual range of a proton in tissue.

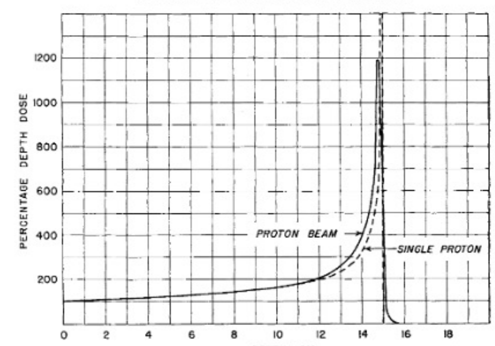
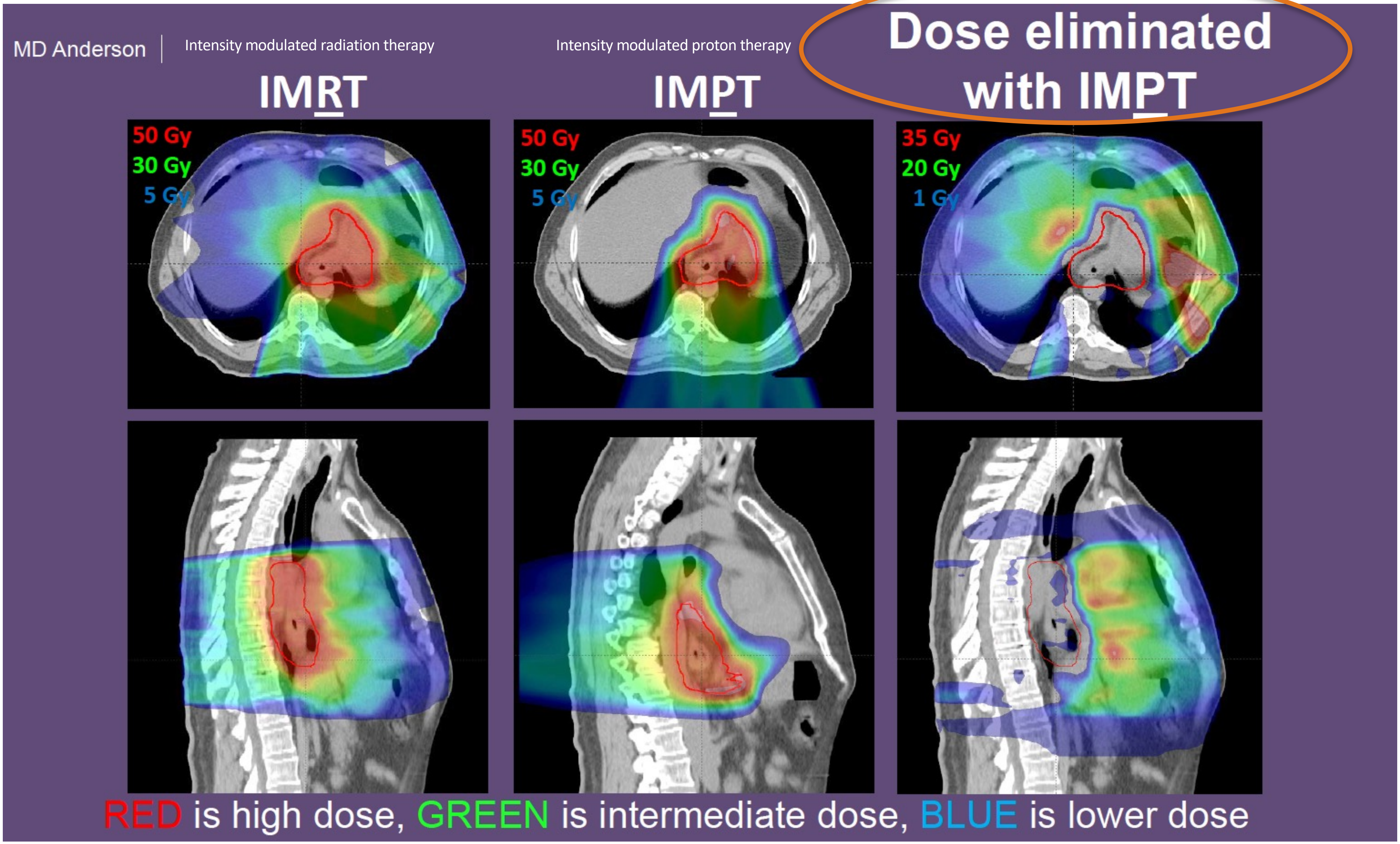


Fig. 2. The dotted curve shows the relative dose due to a single 140 Mev proton. The full curve shows qualitatively the depth dose curve for a beam of 140 Mev protons in tissue.

Life-saving improvements ...

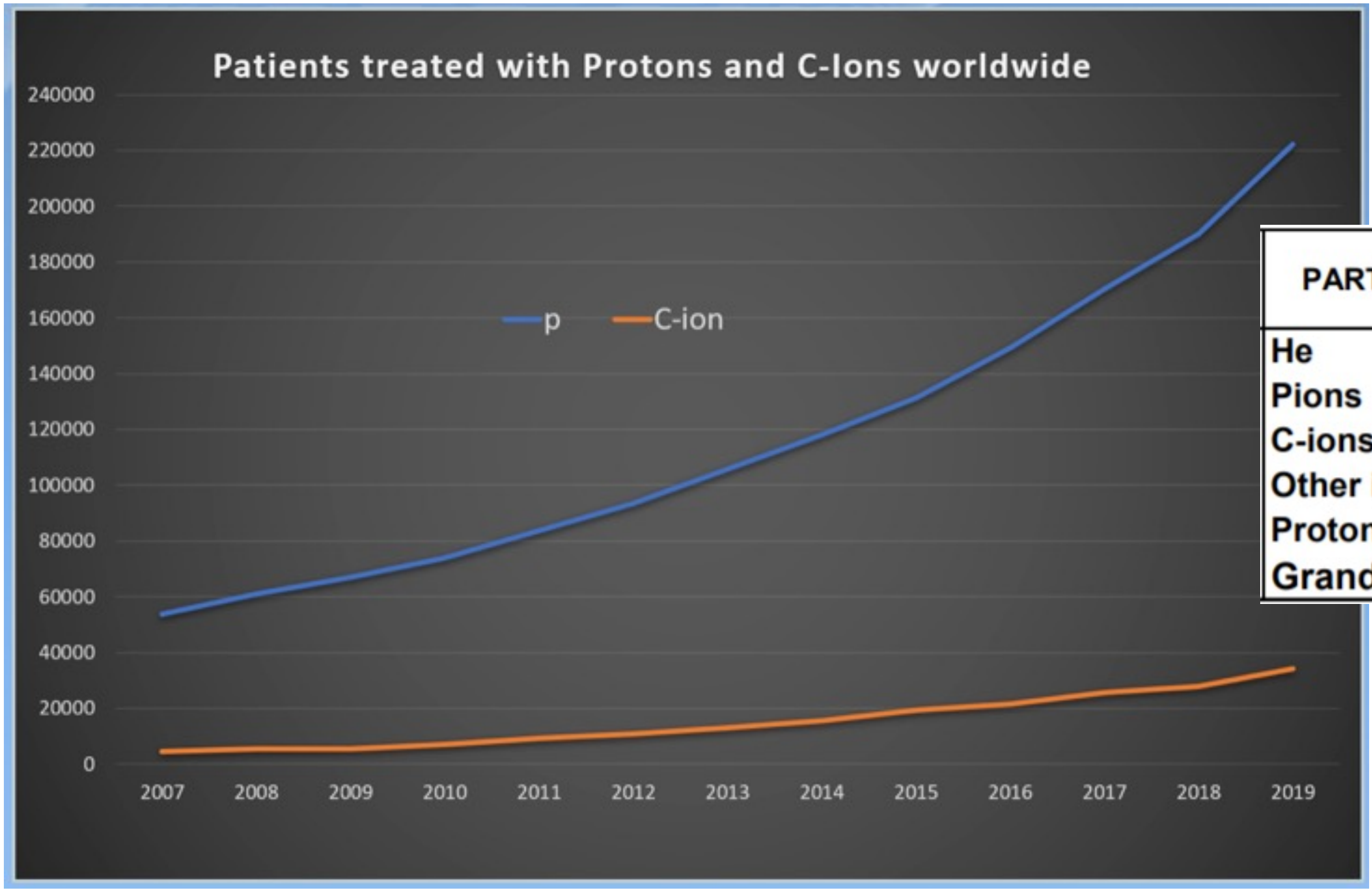


borrowed from Dr. Brandon Gunn

- Arguably, the (main) method of choice of future radiation therapy.
- About 100 particle facilities worldwide now.
- About 150 in various stages of planning and/or realization.

Poland	**IFJ PAN, Krakow**	p	C 230	1 horiz. fixed beam, 2 gantries	2011, 2016	687	Dec-20

The future of radiation therapy... (PTCOG)



PARTICLES	PATIENTS TOTAL	DATES OF TOTAL
He	2054	1957-1992
Pions	1100	1974-1994
C-ions	39210	1994-2020
Other ions	433	1975-1992
Protons	248384	1954-2020
Grand Total	291181	1954-2020

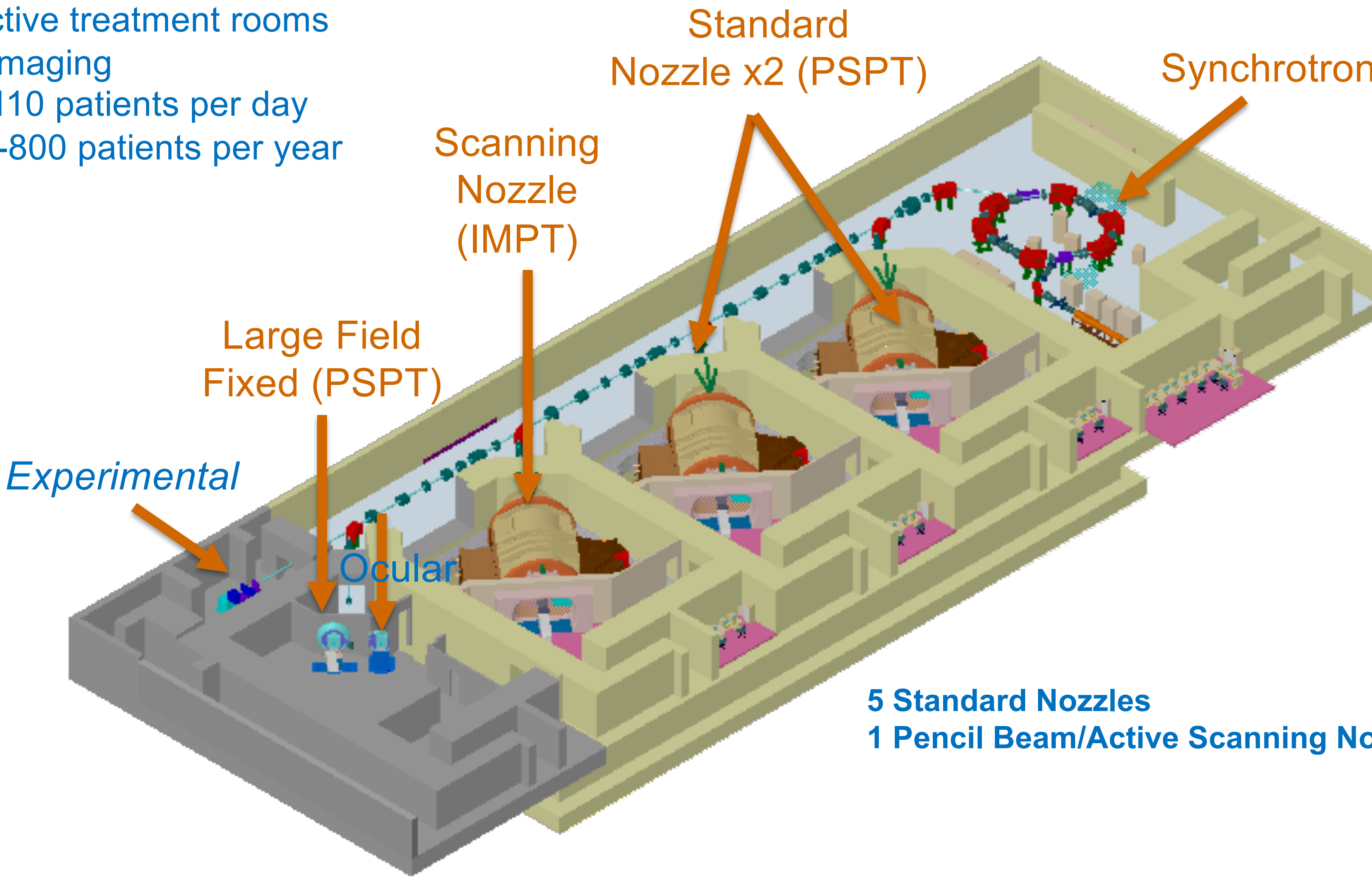
There is much clinical evidence that PT

- leads to lower toxicity and complications
- requires fewer long-term interventions
- better overall outcomes
- requires more initial resources ($$)

The Pentagon's budget request in the 2022 fiscal year for hypersonic research was $3.8 billion which was up from $3.2 billion they year before.

MDACC Proton Therapy Center

- 4 active treatment rooms
- kV imaging
- 90-110 patients per day
- 700-800 patients per year



5 Standard Nozzles
1 Pencil Beam/Active Scanning Nozzle

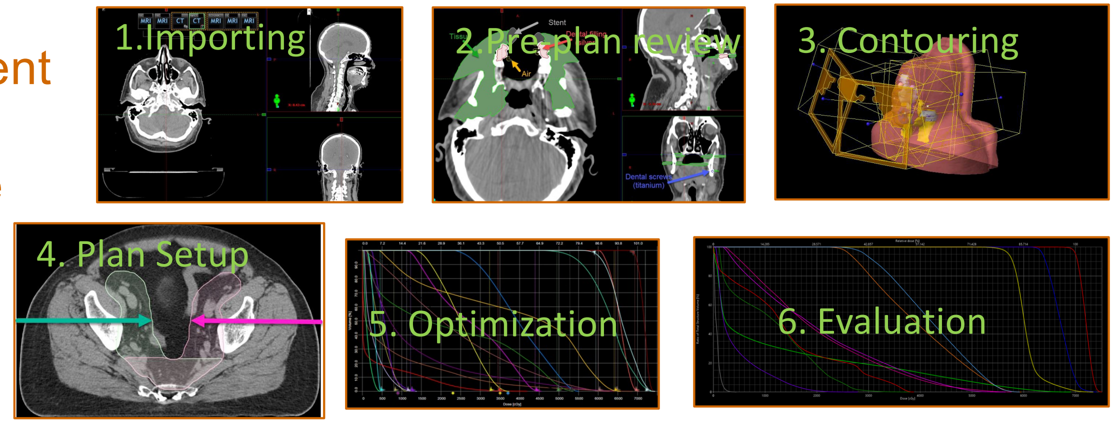
passively-scattered proton therapy (PSPT)

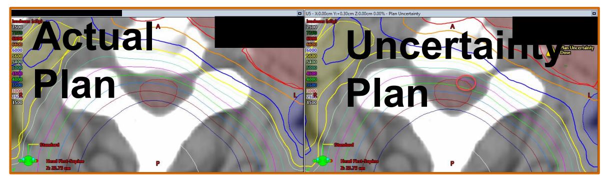
Intensity modulated proton beam therapy (IMPT)

borrowed from Dr. Brandon Gunn

After Christine Chung
Research Dosimetrist
and Radhe Mohan

Treatment Planning: good news and bad news





- Meticulous and sophisticated treatment planning ("well-oiled machine") – 5 days (Monday → Friday) of intense preparations

- Impediments limiting the effectiveness of proton therapy
  - Anatomy changes
  - High gradients in proton dose distributions
  - Evolving treatment delivery
  - Gaps in the knowledge
  - Heterogeneity in patient population
  - Limits to the applicability of knowledge and models based on photon therapy experience to protons

A plan requires good communication and multitude of factors that need input from:
–Physician
–Dosimetry team
–Physics team
–Therapy team
→
Much room for improved feedback of ongoing therapy
(a.k.a. proton range verification)

Employ a PET scanner ("holy grail")…

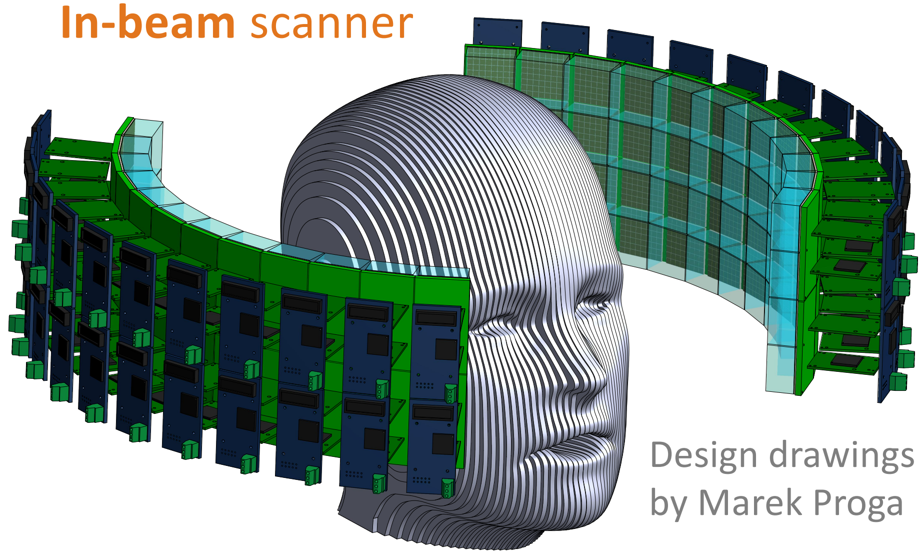
- Not a new idea
  - not practiced
  - new technologies

- Three years ago we formed a consortium to compete in the U. Texas - Portugal funding competition and were lucky to be selected:
  1. **U. of Texas MD Anderson Proton Therapy Center**
  2. **U. of Texas at Austin**
  3. **PETsys Electronics**
  4. **LIP, Laboratorio de Instrumentação e Fisica Experimental de Particulas (Coimbra)**
  5. **Centro de Ciências e Tecnologias Nucleares (C^2TN), Instituto Superior Técnico (Lisbon)**
  6. **Instituto de Ciências Nucleares Aplicadas à Saúde (ICNAS), Universidade de Coimbra**

- We proposed a "feedback" PET scanner to register nuclides activated in proton irradiations:
  - C-11 ($T_{1/2}$=20min)
  - N-13 ($T_{1/2}$=10min)
  - O-15 ($T_{1/2}$=123sec)

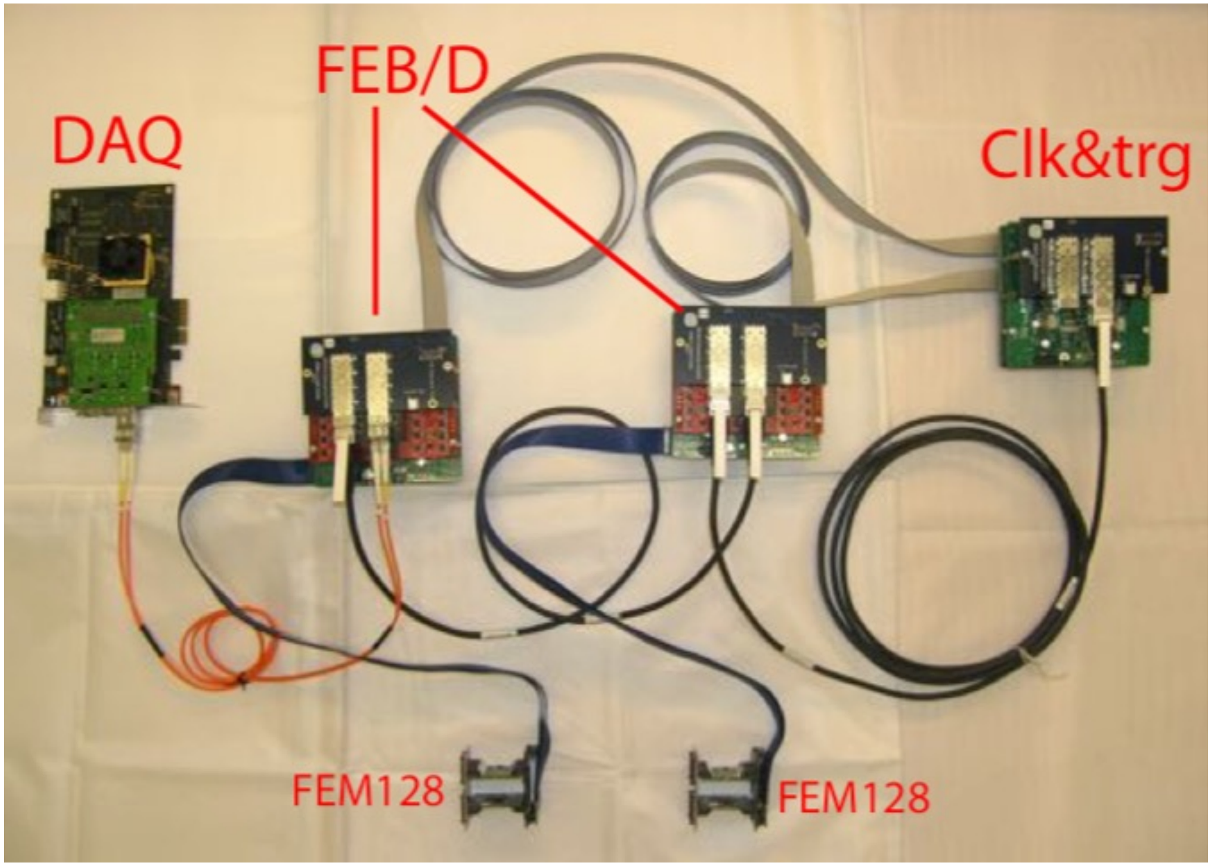
ToF PET for PT = TPPT

In-beam scanner



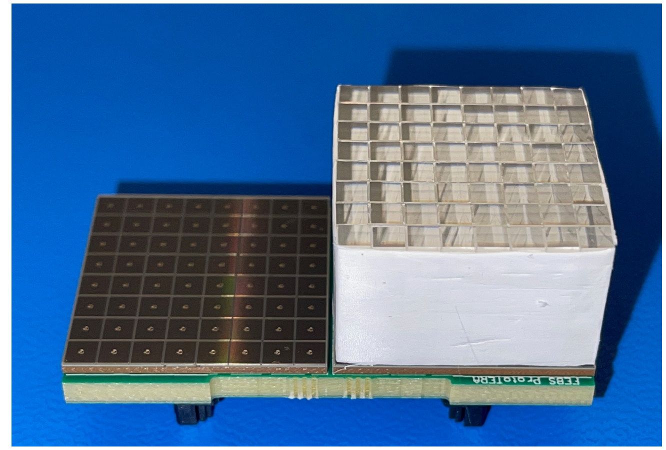
Design drawings by Marek Proga

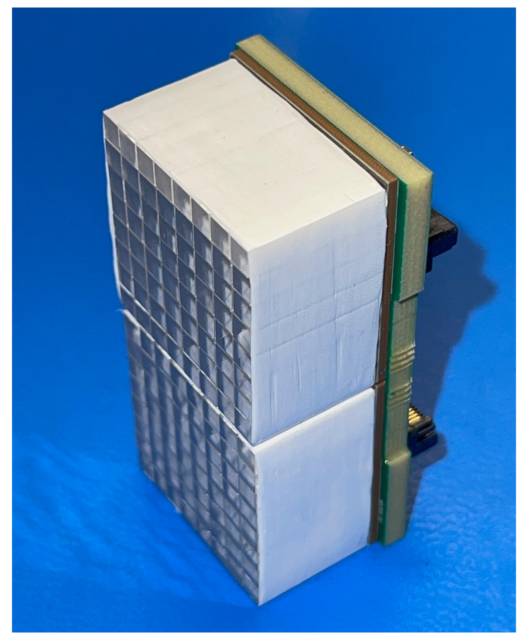
Building blocks



PETsys FE electronics

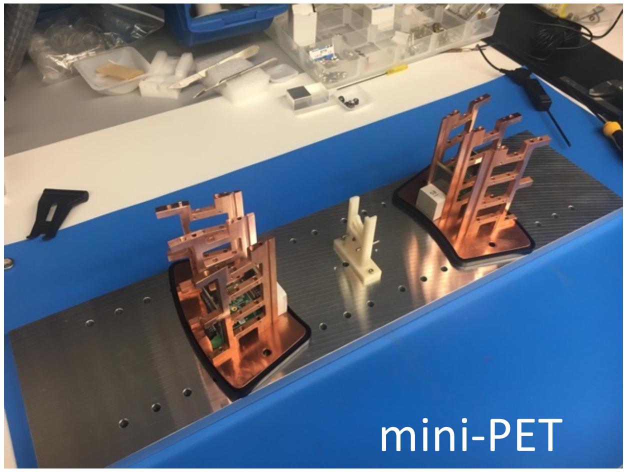
LYSO/SiPM

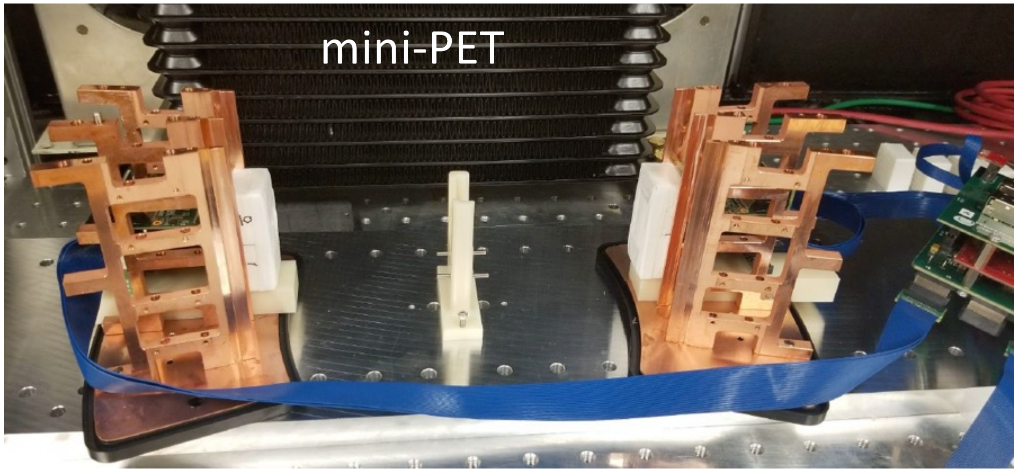


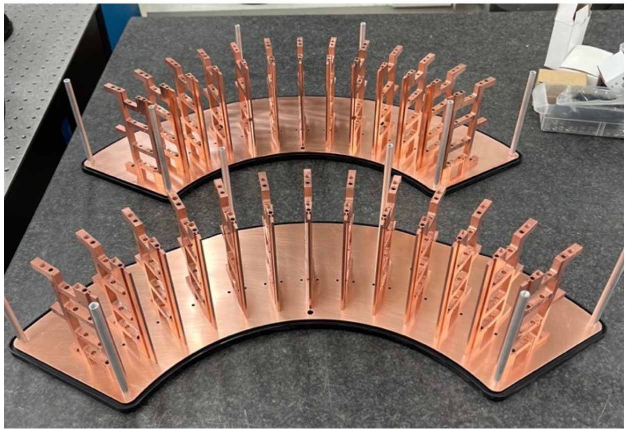


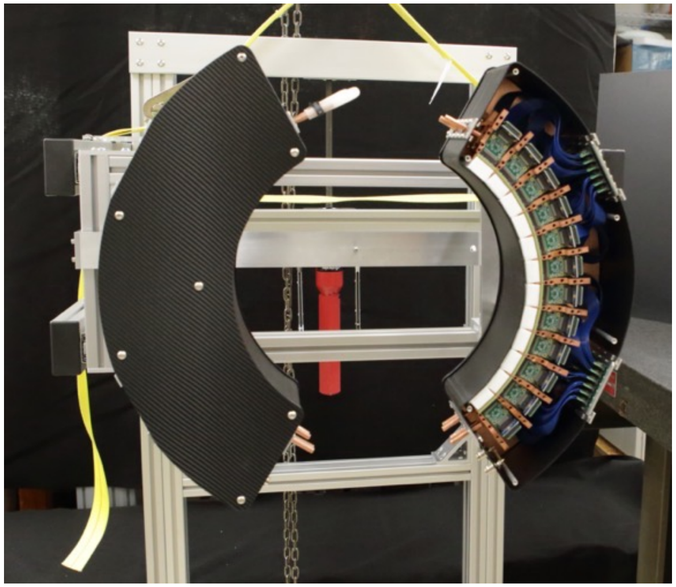
A picture is worth 1000 words

"Rome wasn't built in a day"

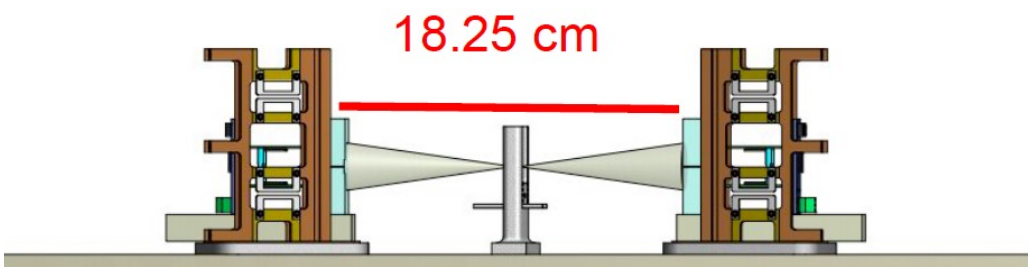


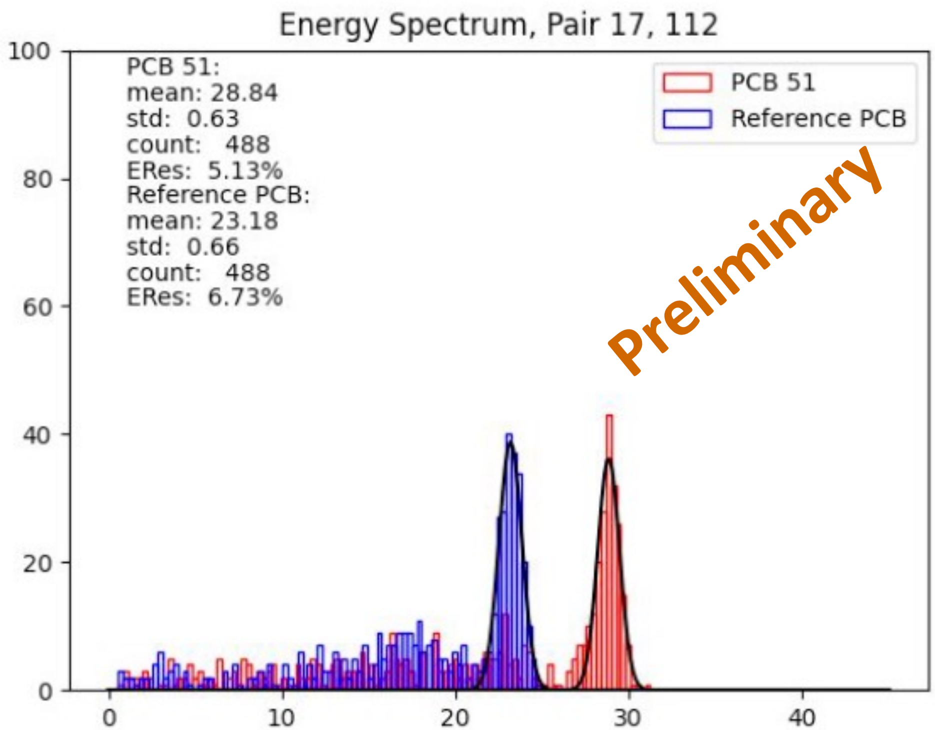




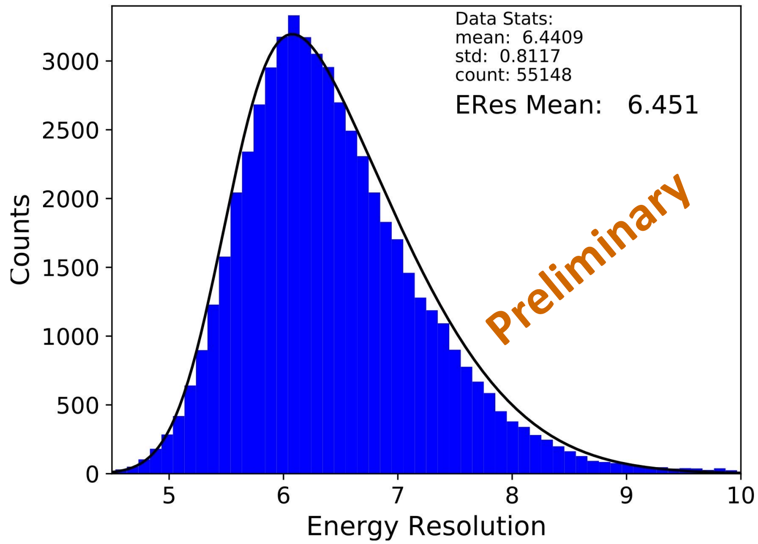


Mini-PET results

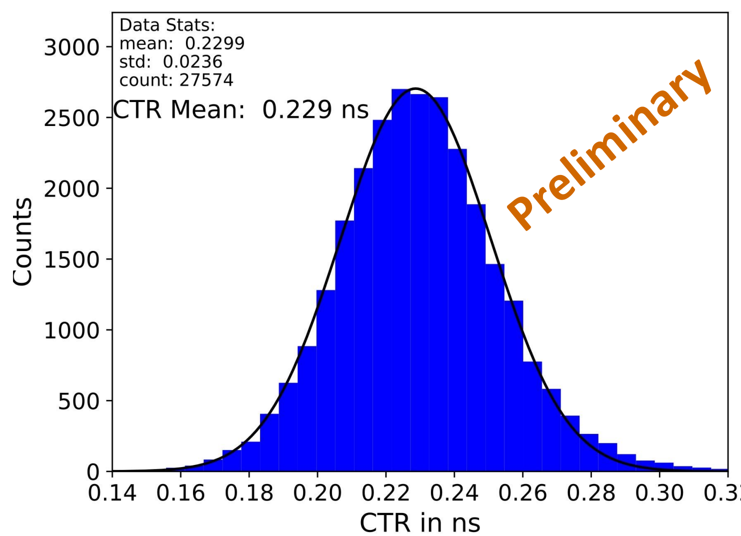




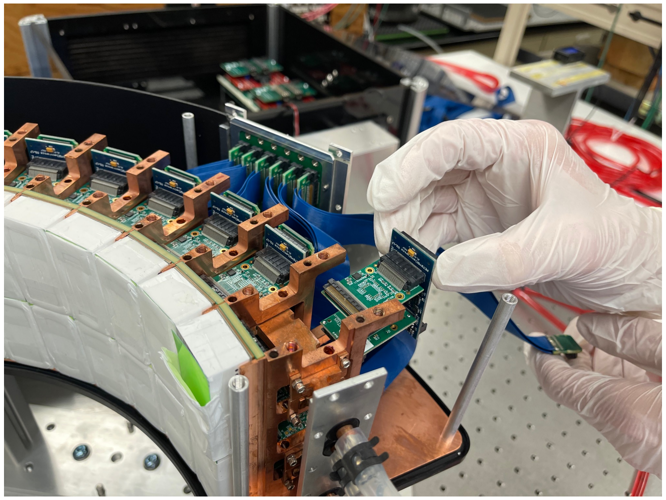
Energy resolution (FWHM) 6.5%

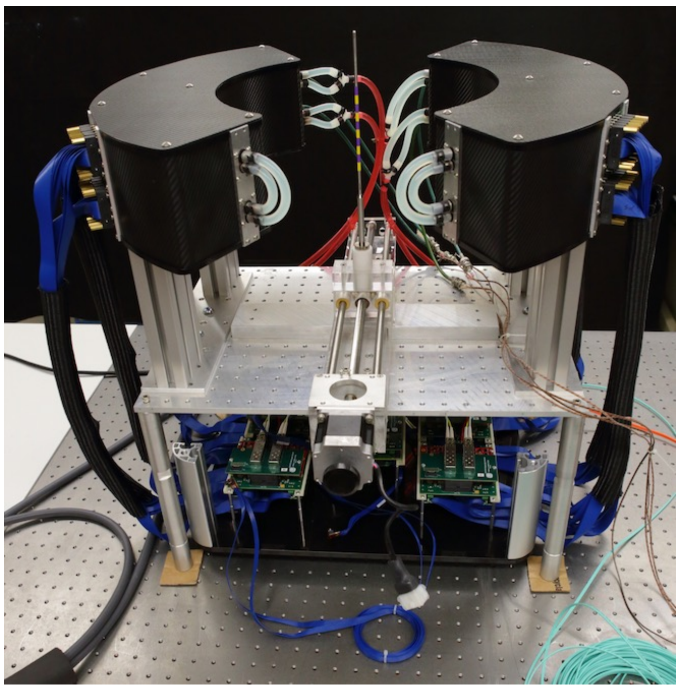


Coincidence Time Resolution (FWHM) 230ps

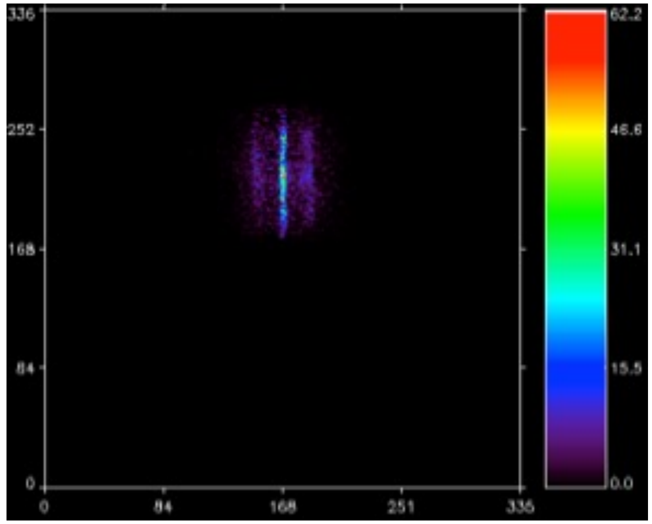


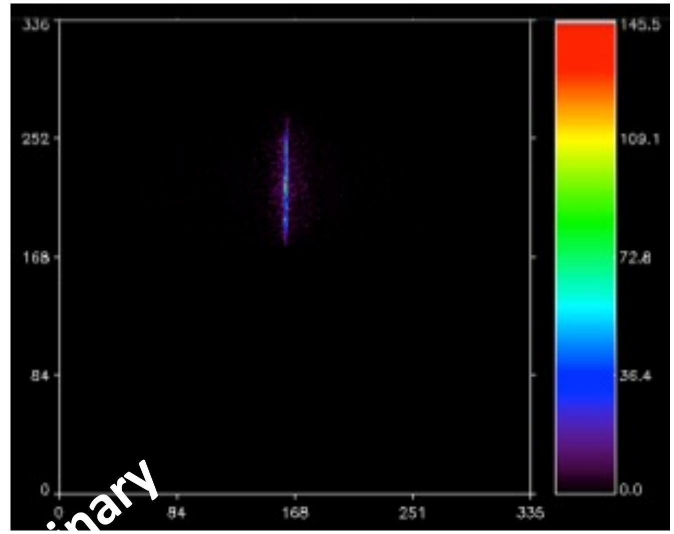
Full scanner (being commissioned)

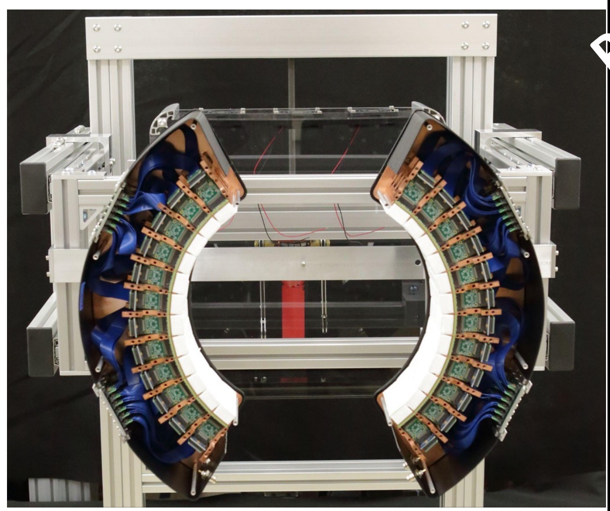


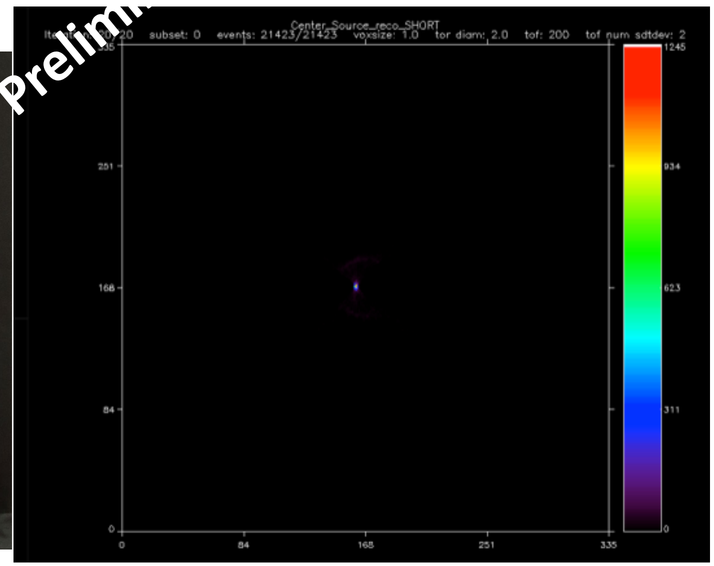


Ge-68 Line source





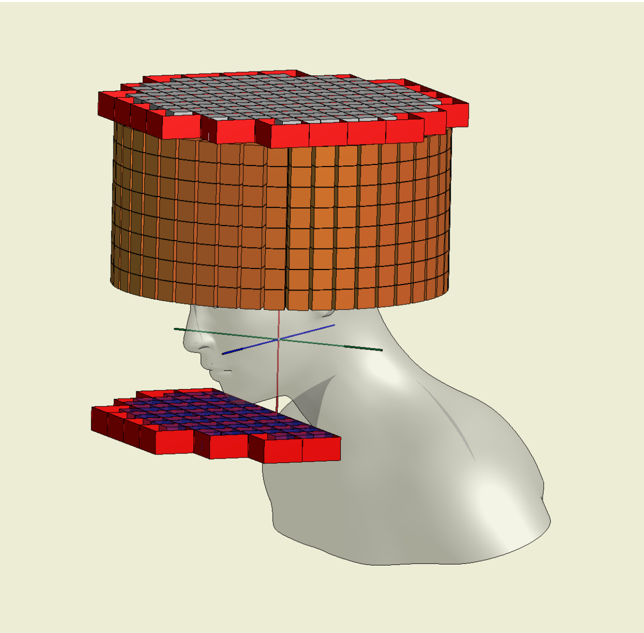


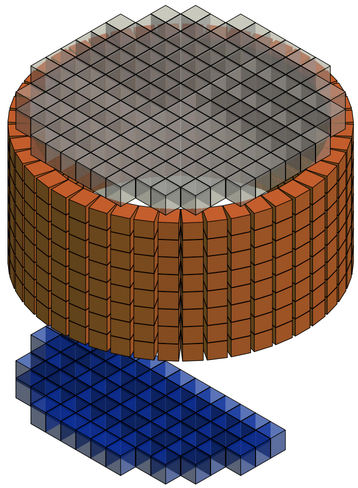


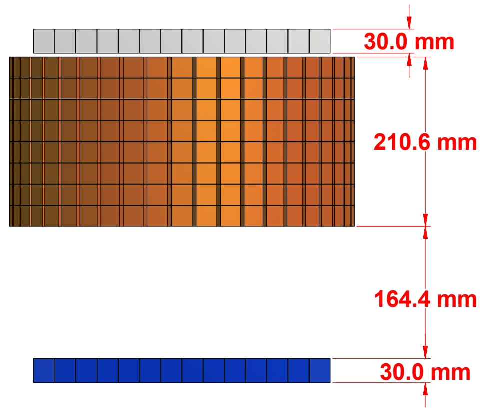
Design and modeling of a high resolution and high sensitivity PET brain scanner with double-ended readout

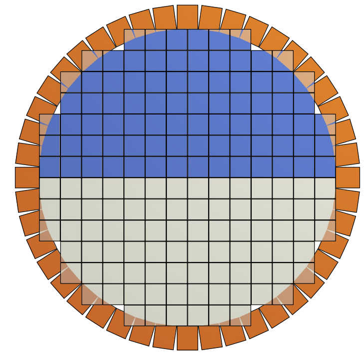
Christopher Layden[1,*], Kyle Klein[1], William Matava[1], Akhil Sadam[1], Firas Abouzahr[1], Marek Proga[1], Stanislaw Majewski[2], Johan Nuyts[3] and Karol Lang[1]

C³-PET
(Chin-Crown-Cylinder PET)

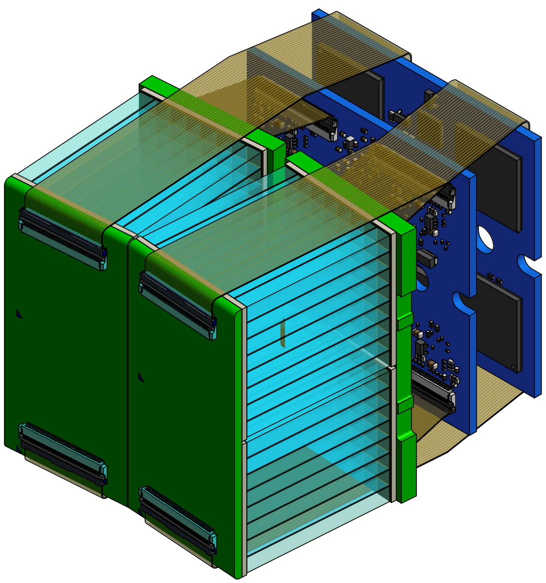








Double-ended readout for DOI



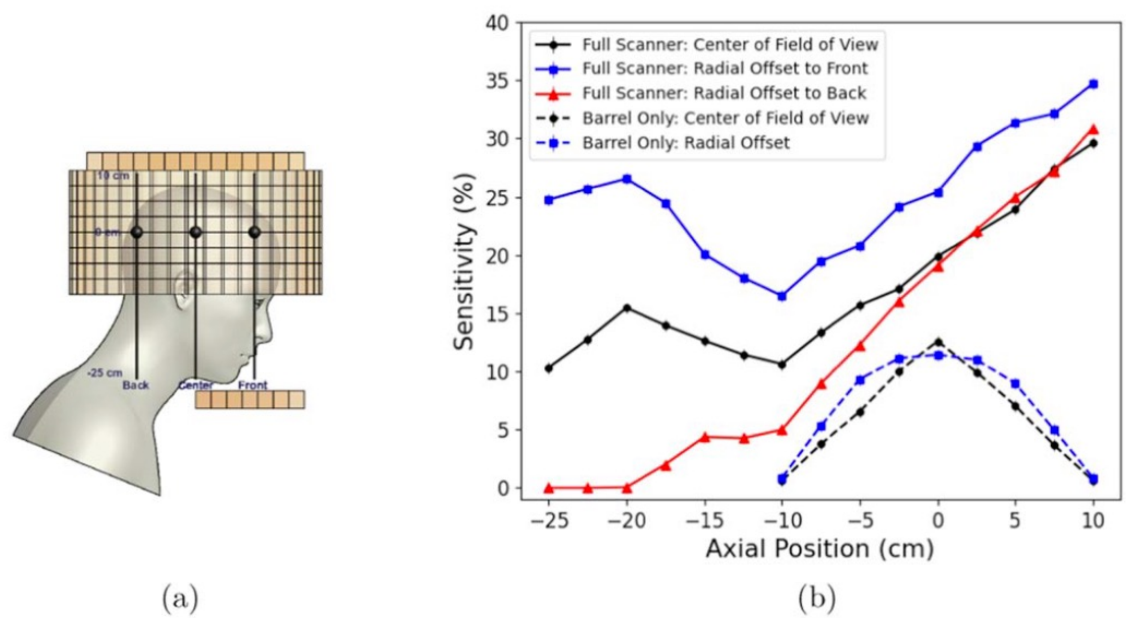
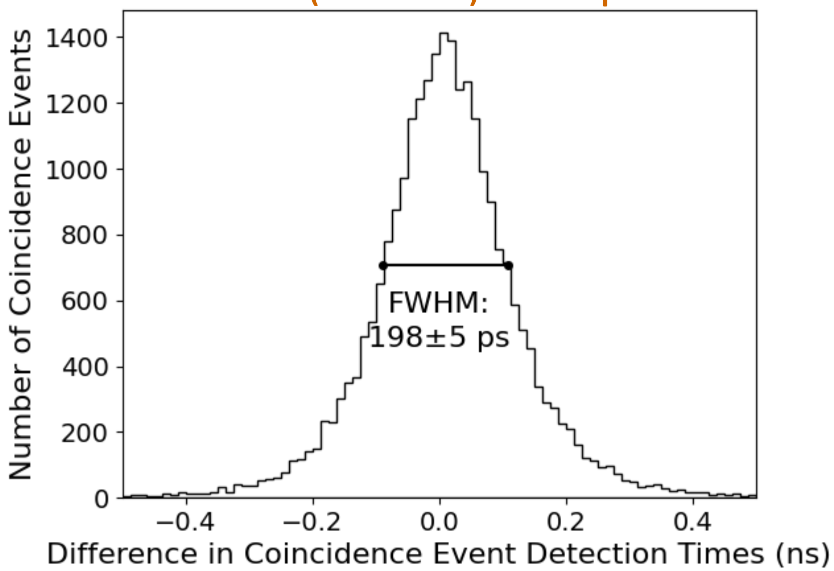


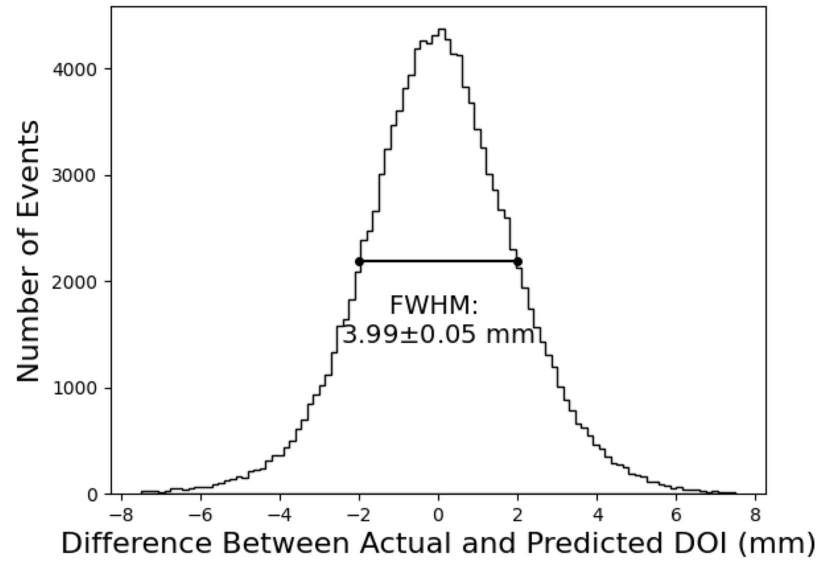
Figure 3. (a) Positions of line sources used for sensitivity predictions. (b) Absolute sensitivities for point sources placed along the line sources, for both the full scanner and barrel module alone, at the center of the radial field of view and at 10 cm radial offsets.

Double-ended readout → DOI

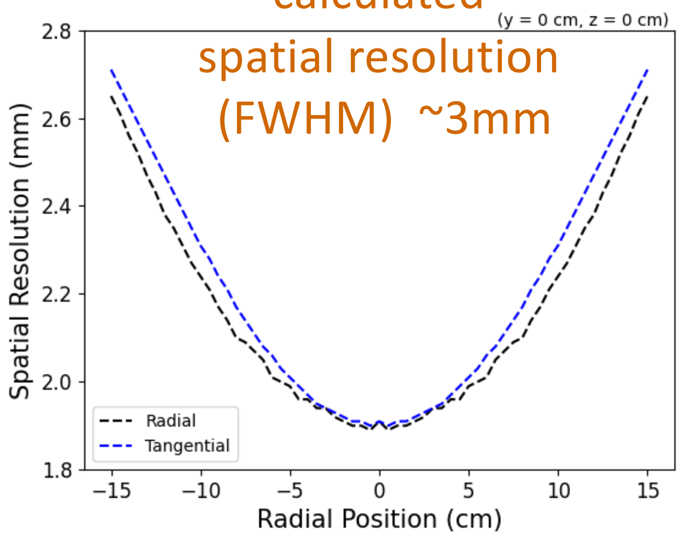
CTR (FWHM) ~200ps



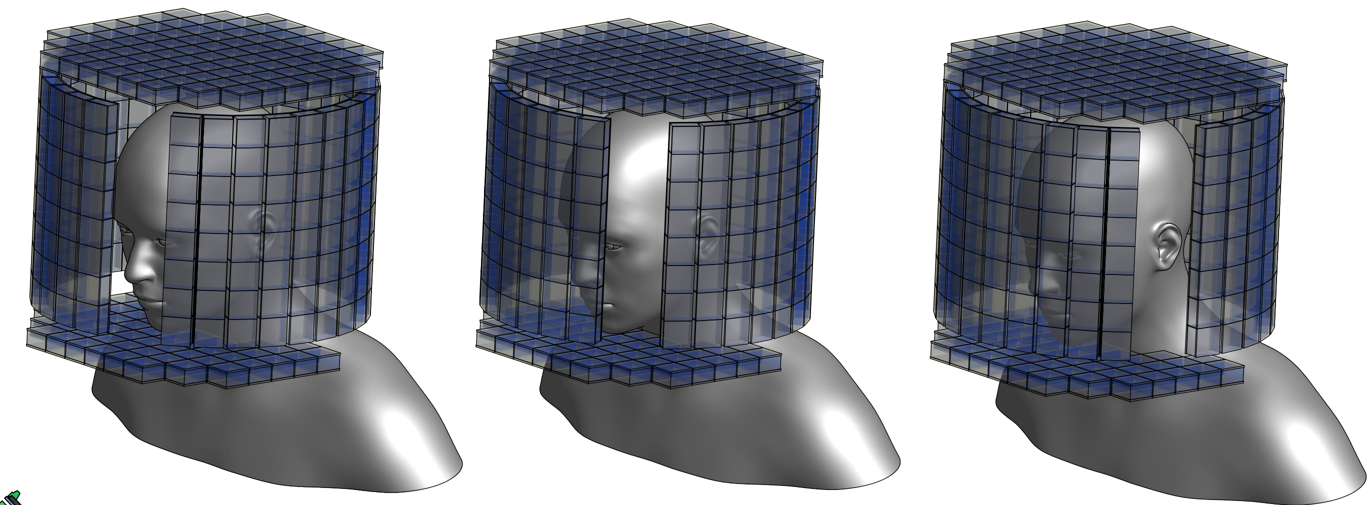
DOI (FWHM) ~4mm

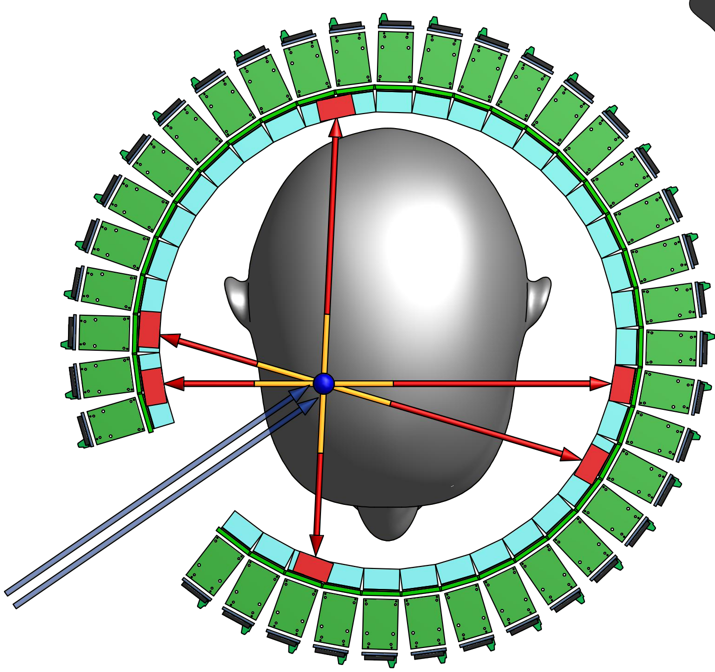


calculated spatial resolution (FWHM) ~3mm



Improved C^3-PET for Proton Therapy

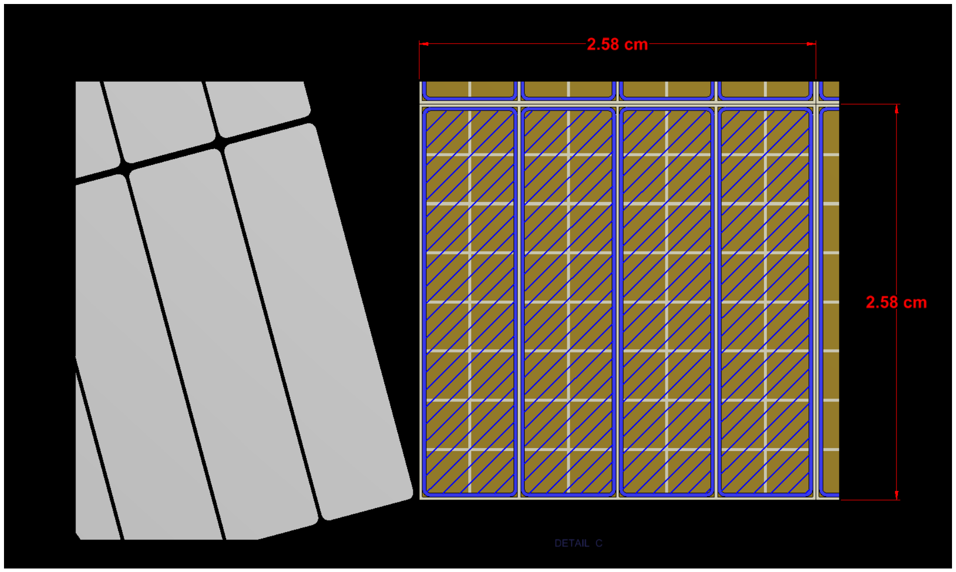


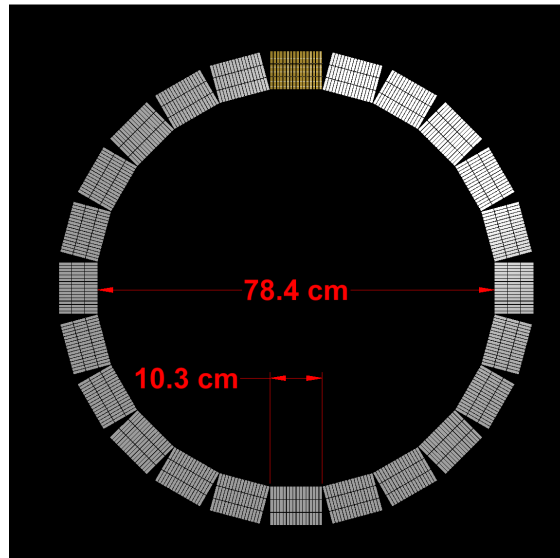


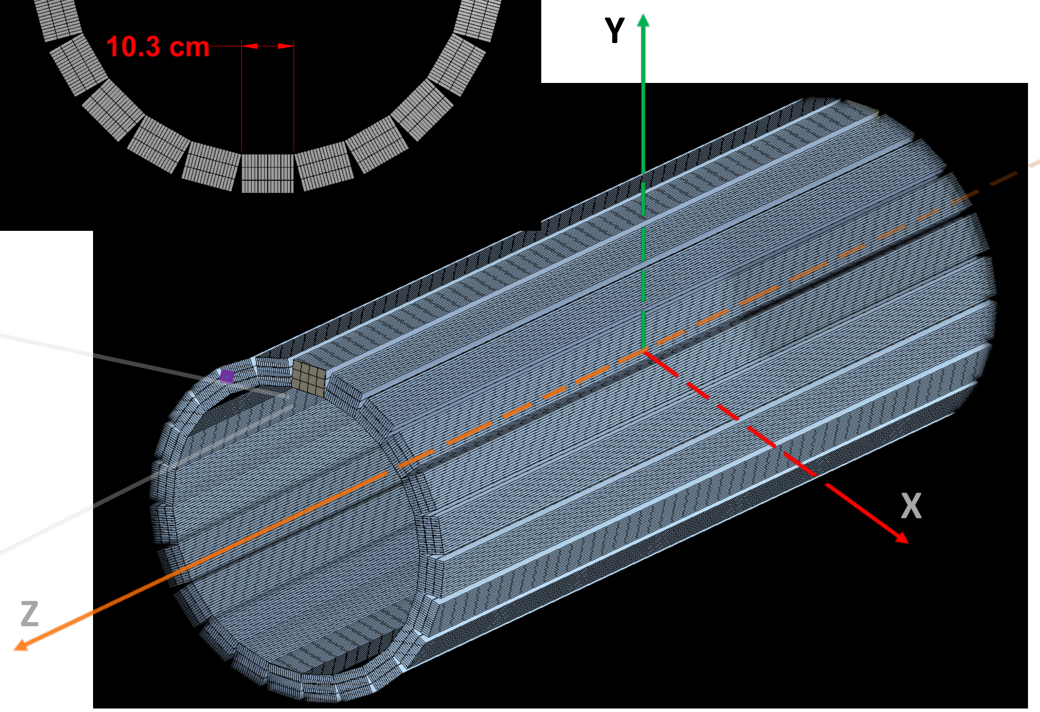
- PET-Image-driven therapy?
- PT and radiopharmaceuticals?
- PT and "SPECT" pharmaceuticals
- FLASH?

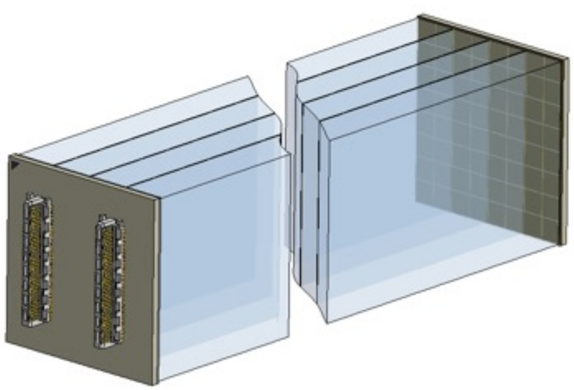
Total Body - Detector geometry

- 1m long barrel PET (2.54 x 0.62 x 100cm scintillator)
- 1152 plastic scintillator strips and 576 SiPMs.









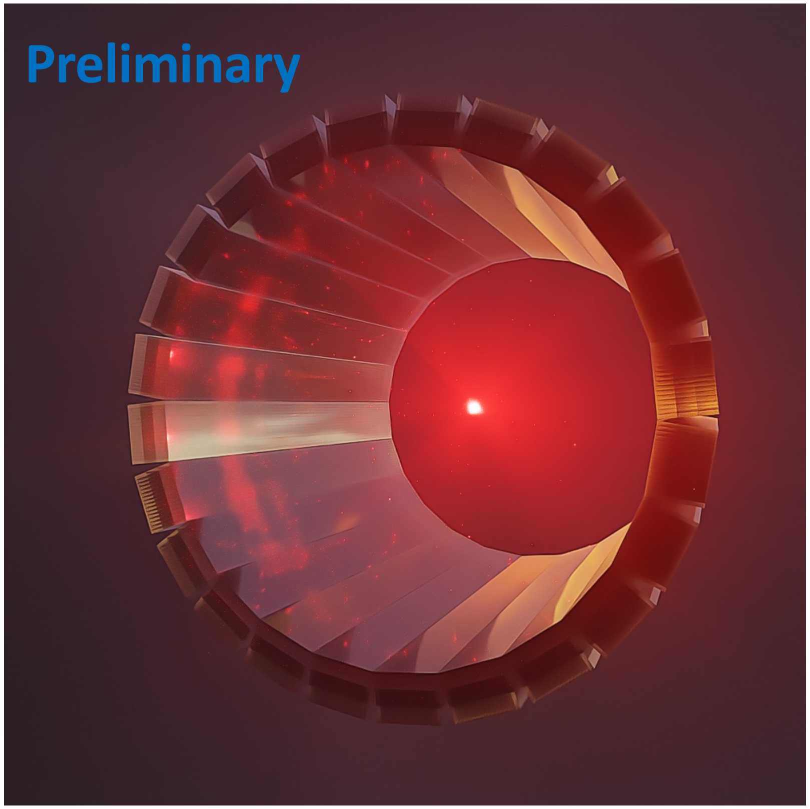
Total body: Plastic or crystals?

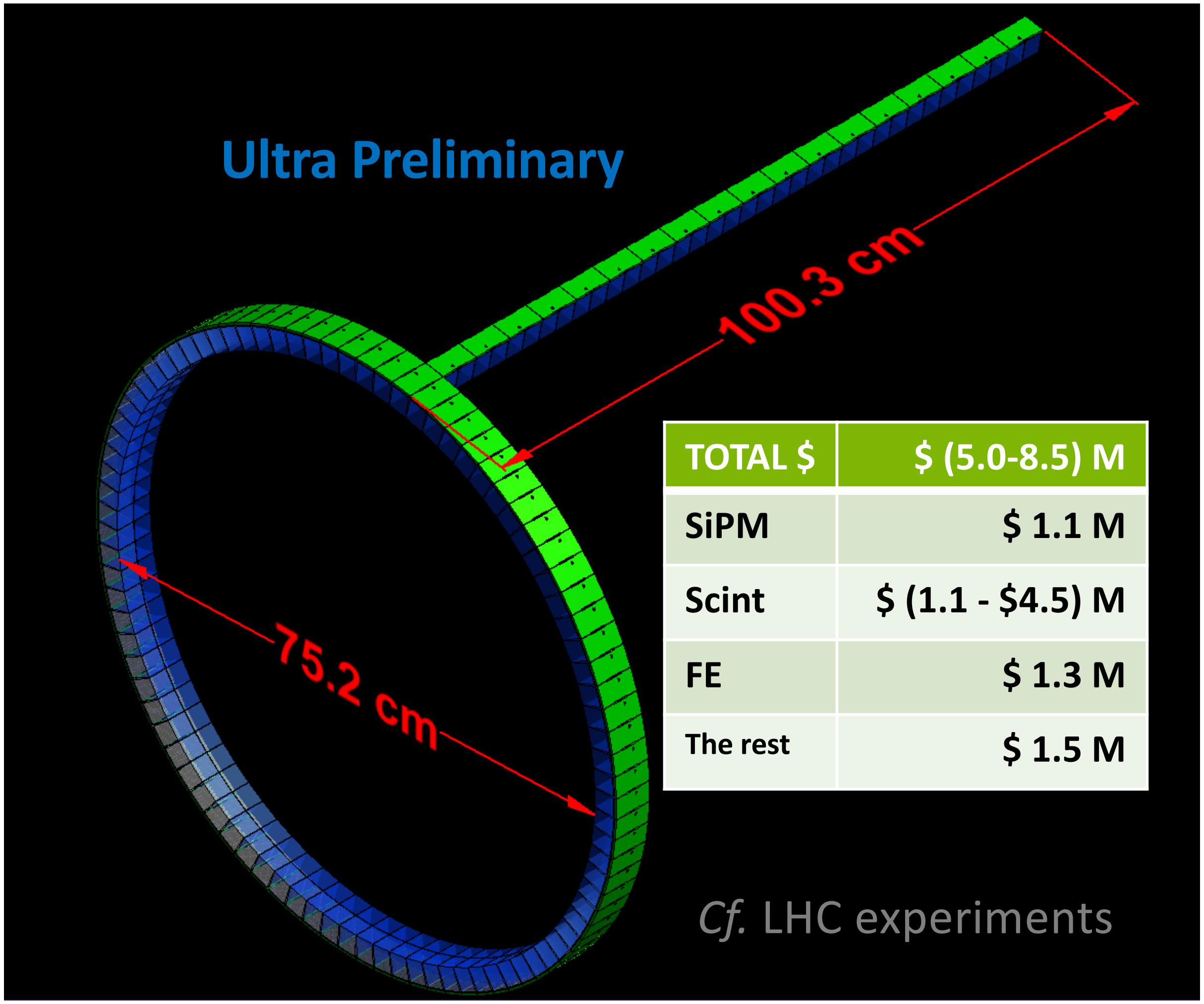
kNN-based resolutions, imaging,...

TOTAL $	$ 2.1 M
SiPM	$ 0.2 M
Scint	$ 0.4 M
FE	$ 0.5 M
The rest	$ 1.0 M

Informed gue$$timates
(1m long, 75 cm dia)

Sparsy-fied?
BGO-fied?
Insert-fied?



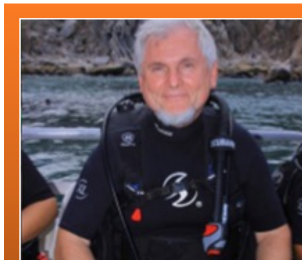


TOTAL $	$ (5.0-8.5) M
SiPM	$ 1.1 M
Scint	$ (1.1 - $4.5) M
FE	$ 1.3 M
The rest	$ 1.5 M

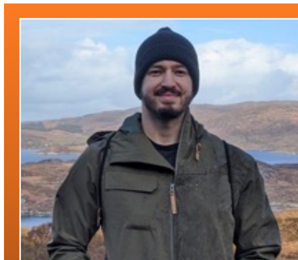
Cf. LHC experiments

(In lieu of) Conclusions: We are working on it …

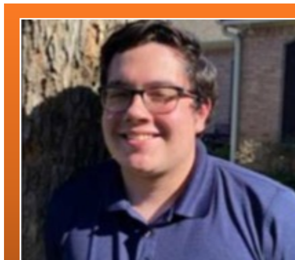
Karol Lang



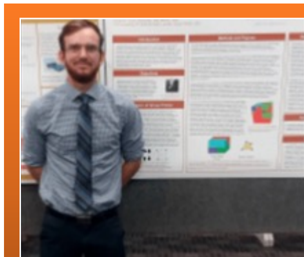
Marek Proga



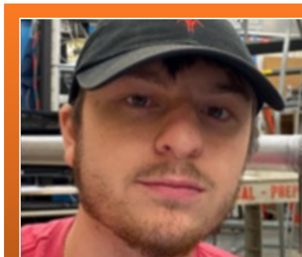
John Cesar



Kyle Klein

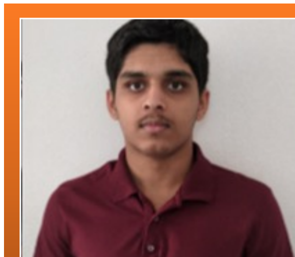


Chris Layden

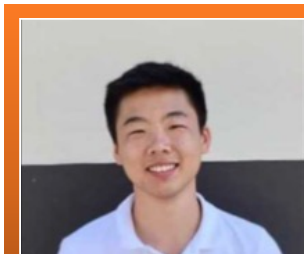


Firas Abouzahr

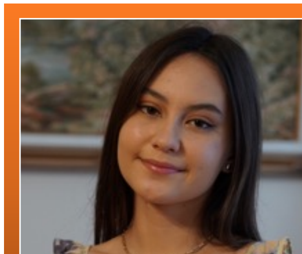
Will Matava



Akhil Sadam



Shawn Park



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~~Final~~ Initial thoughts

"Bridging Barriers"

Development and Demonstration of 5D Positron-Emission Tomography

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"Bridging Barriers"
Development and Demonstration of 5D Positron-Emission Tomography

1. The Question: Full-body, high-resolution and low-cost medical diagnostic imaging may arguably be one of the most significant obstacles in efficiency of practicing future medicine. Nuclear medical imaging offers a huge potential for internal medicine yet, despite appearances, has almost stagnated in technology while escalating in cost. While a number of new MRI, SPECT, and PET scanners enter the market every year, they adopt and/or adapt only limited scope of progress made in particle and nuclear physics instrumentation which is the essential core of this technology. In other words, new imaging devices evolve relatively slowly and only incrementally improve their technical capabilities. The field suffers from fierce competition and proprietary vendor protocols that induce lack of openness or sharing of information, despite specialized conferences and publications. It is quite clear that a breakthrough is needed in most, if not all, aspects of the field. New concepts and comprehensive collaborative approach in modeling, development, prototyping, and demonstration as well as properly-structured funding are needed. Thus, the question is this:

> Can an effective collaboration be formed, modeled on research projects in experimental particle physics, that would accomplish in nuclear medical imaging what has not been accomplished over the last few decades by a number of small and isolated groups world-wide?

We assert that this may have never been tried before on a scale that we envision and thus propose to explore possible collaborative options leveraging our extensive experience and knowledge of necessary methodology.

[...]

rather than, as currently, only by large hospitals.

The University of Texas would play the key role in coordinating activities and leading the technical progress, prototyping and demonstration of working devices. It could result in propelling the State of Texas into fostering a 21st century technology that would go far beyond the current state-of-the-art diagnostic PET. This could be just a start of an open-ended endeavor for improved technology of future medicine.

2

2. The Approach: One of the main reasons for the current technology stagnation is that collaborative teams are small and have limited expertise. We propose to model our approach on organizations of particle physics experiments practicing "the big science". Essentially all modern particle physics experiments involve groups of experts bringing together a broad range of expertise and technical capabilities. In most cases, they successfully engage industrial partners in reaching their objectives. There is a large number of examples of experiments at Fermi National Accelerator Laboratory near Chicago, CERN near Geneva, Brookhaven National Laboratory in New York, SLAC at Stanford, KEK lab in Japan, SNOlab in Canada, and many more smaller labs around the world.

The expertise portfolio needed and practiced by all particle physics experiments can be grouped into five areas: (`i`) high-fidelity modeling of physics processes and detectors, (`ii`) development of new detector technology (e.g, crystals, cryogenic noble gases, photodetectors), (`iii`) development of largely integrated (e.g., ASIC) front-end electronics and data acquisition systems, (`iv`) detector prototyping and large system integration, and (`v`) data mining, analysis, imaging and interpretation. Obviously, development of a medical instrument would not only benefit technically from the involvement of radiologists and radio-pharmacists but we would need their knowledge and understanding of socio-economic aspects of the field.

3. The Interdisciplinary Team: Development and demonstration (i.e., prototyping) of 5DPET requires expertise that only minimally extends beyond what is required now in large particle physics experiments. We have been involved in several such endeavors and our acquired knowledge, experience, and developed laboratory infrastructure are directly applicable towards forming a collaboration that we envision as necessary for PET. Assuming that we would mostly operate on campus, we (at the Department of Physics) would solicit

[...]

and imaging software. Some or most of these activities would employ high-power computing (e.g., TACC).

We would also argue, based on our experience, that necessary ingredients of this team work will be industrial partners, national laboratories, and various research groups worldwide that could be enticed in joining in. Again, the openness and large collaboration will be the key to success.

3

Can an effective collaboration be formed, modeled on research projects in experimental particle physics, that would accomplish in nuclear medical imaging what has not been accomplished over the last few decades by a number of small and isolated groups world-wide?

Our few closest friends

Some ponderings by *Yogi*

- Easy things are done → *The future ain't what it used to be.*
- Choose wisely → *No one goes there nowadays, it's too crowded.*
- Be persistent → *It ain't over till it's over.*
- Be decisive →When you come to a fork in the road, take it.