KONWERSATORIUM

im.J.Pniewskiego i L.Infelda

Faculty of Physics, University of Warsaw

Warszawa, 5 Pasteura St., room **0.06**

Monday 10/**06**/2024

at **11.00** (coffee will be served at **10.30**)

prof. Karol Lang

University of Texas at Austin (USA)

Image-guided **FLASH** Proton **Therapy**

Image-guided FLASH Proton Therapy

Konwersatorium

Wydział Fizyki, Uniwersytet Warszawski

Karol Lang

University of Texas at Austin

June 10, 2024

Outline:

- The Big Picture
- Our background
- Proton Therapy
- Our PETs
- Recent FLASH experiments
- Plans

The Big Picture

Facts:

- 18 mln new cancer cases per year worldwide.
- 50% of patients receive radiation treatment.

A question:

- Can we apply radiation treatment better?

"Better"

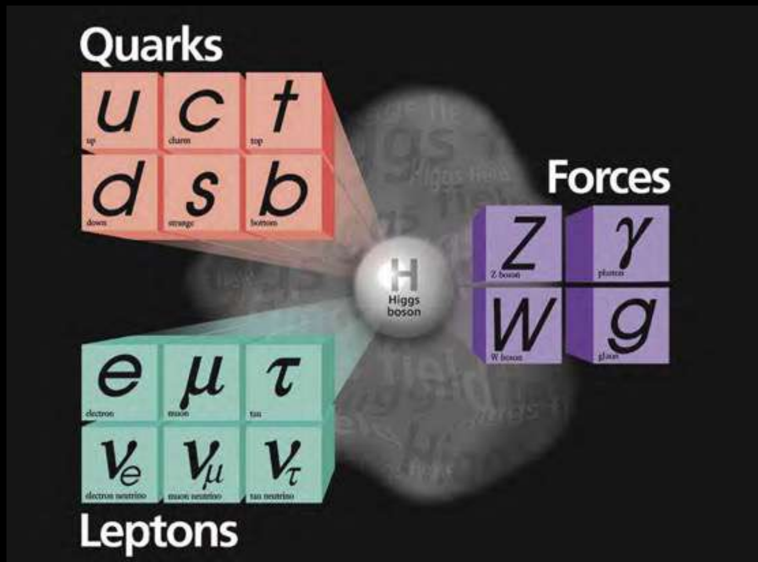
"Better" means

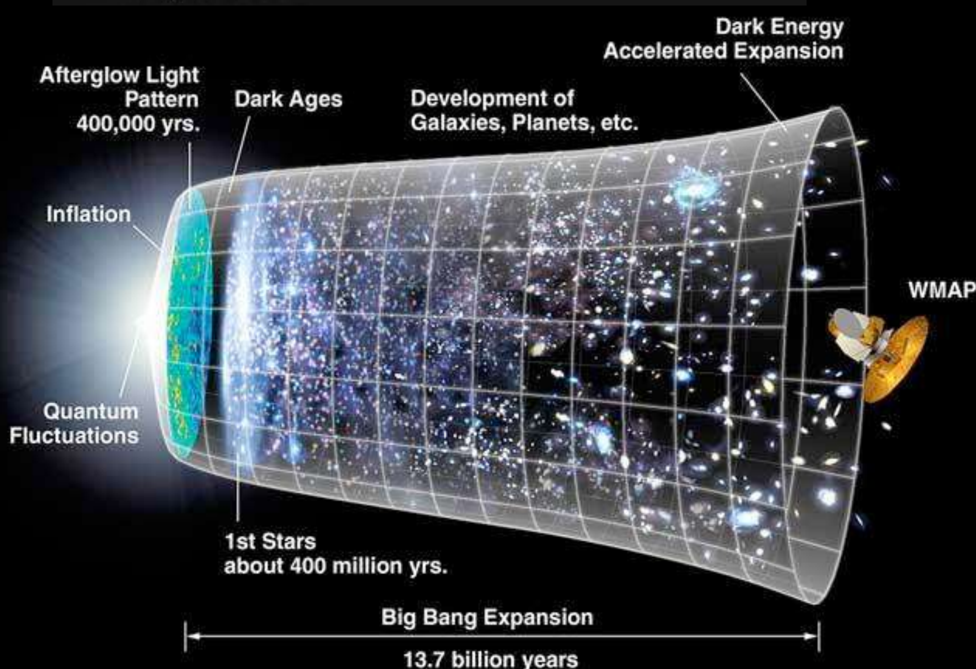
- Minimize or avoid post-radiation complications (toxicity)?
- Treat more patients with protons.
- Lower the cost of therapy.
- …(and more)

Our background

The standard view of the Universe:

("inner space and outer space")





Open questions

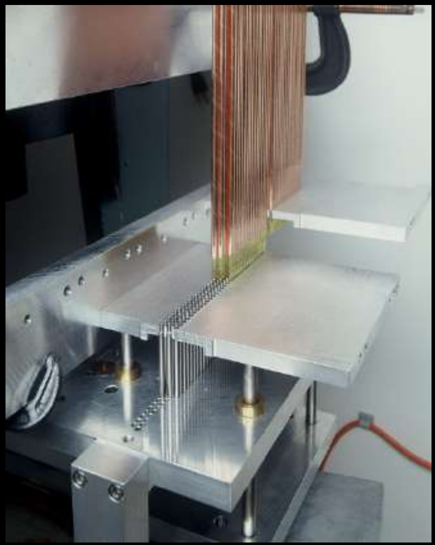
(i.e., mysteries that the SM can't explain) :

- ✓ 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!

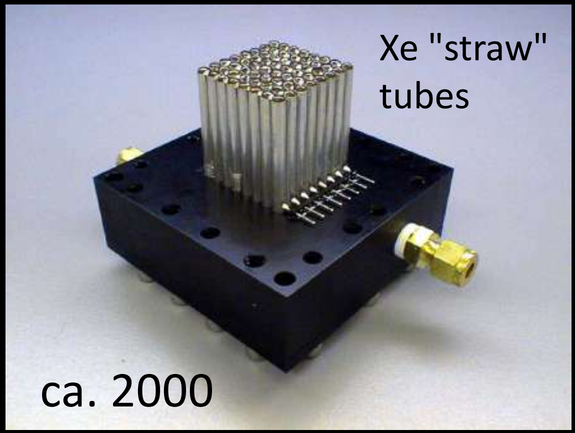
Better understand neutrinos

Experimental Particle Physics is our (main) business (so far)...



BNL 871

MINOS



"On the shoulder of giants …"

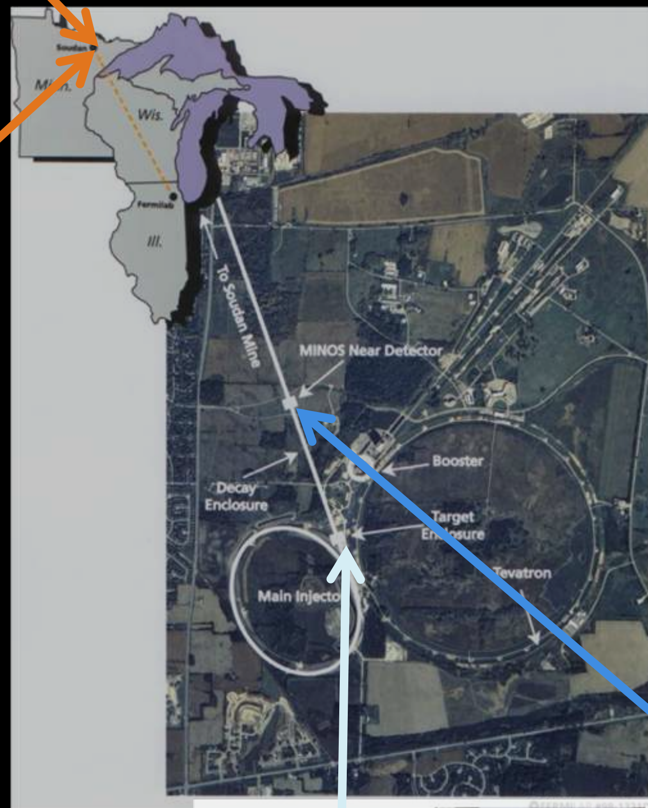
"When I saw groups with more than 1,000 physicists, I became scared. So I decided to switch to the application of my detectors to medicine and biology."

Nobel Prize in Physics 1992:
"for his invention and development of particle detectors, in particular the multiwire proportional chamber"

A typical banquet at Georges's laboratory with many colleagues around a table with wine, sausages and cheese he used to bring back from Corsica. From left to right some of his close collaborators: Leszek Ropelewski, D Anderson, Stan Majewski, Anna Peisert, Amos Breskin, Roger Bouclier, Martin Suffert and Vladimir Peskov.

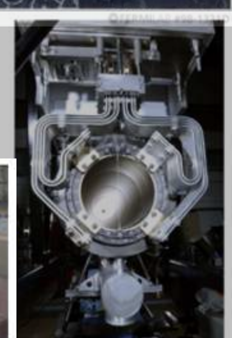
MINOS and NuMI @ FNAL (Fermilab)

- MINOS Experiment
- The Far Detector



- MINOS Experiment
- The Near Detector

- Neutrino Beam
- NuMI



Fermi National Accelerator Laboratory (Fermilab)

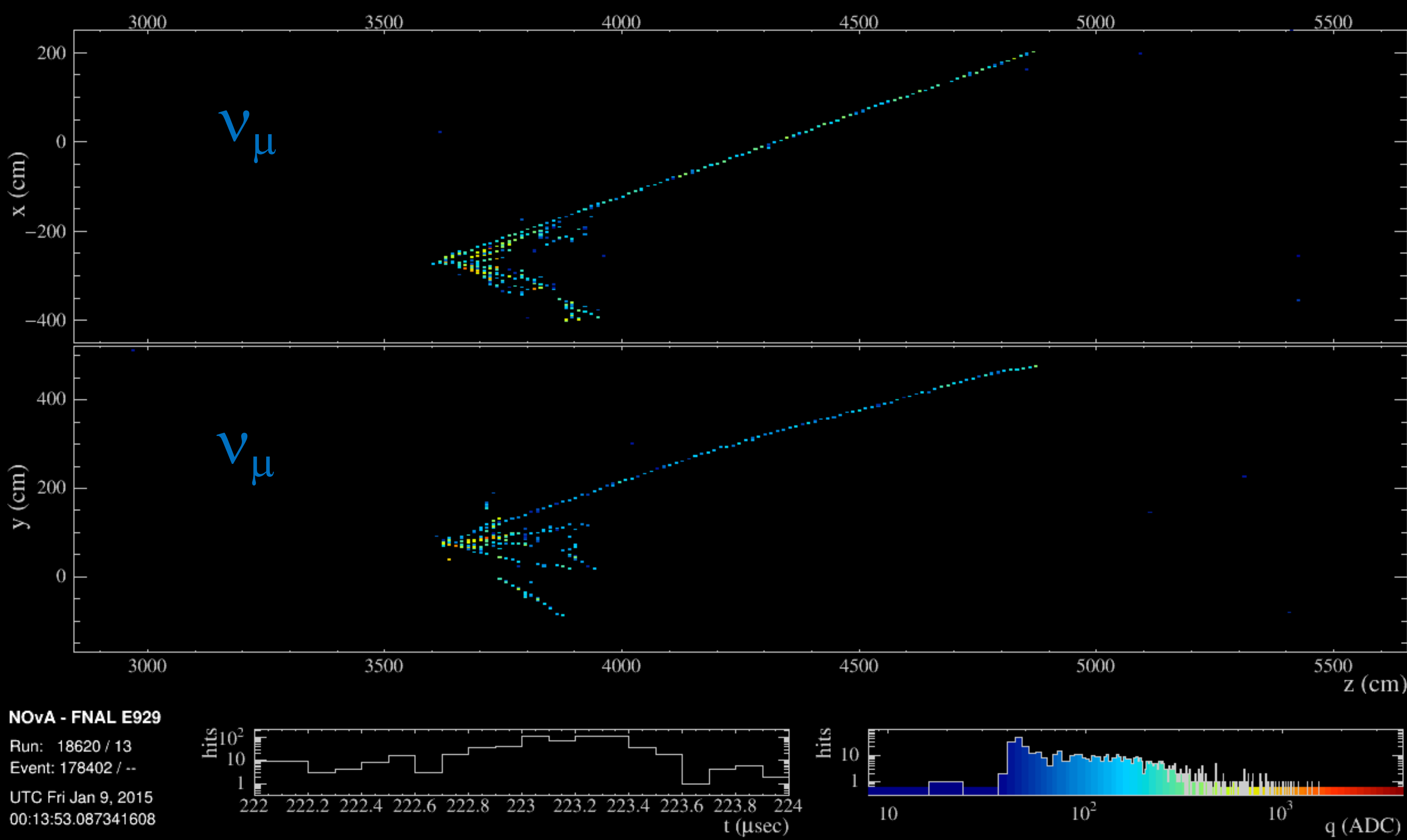
Robert Rathbun Wilson (1914 - 2000)

Wilson Hall
Fermilab

Fermilab's builder
and 1st director
1967-1978

Finding neutrino candidates in NOvA

Imaging neutrino interactions



1925-2015

"You can **observe** a lot by **watching**."

- Yogi Berra

PT

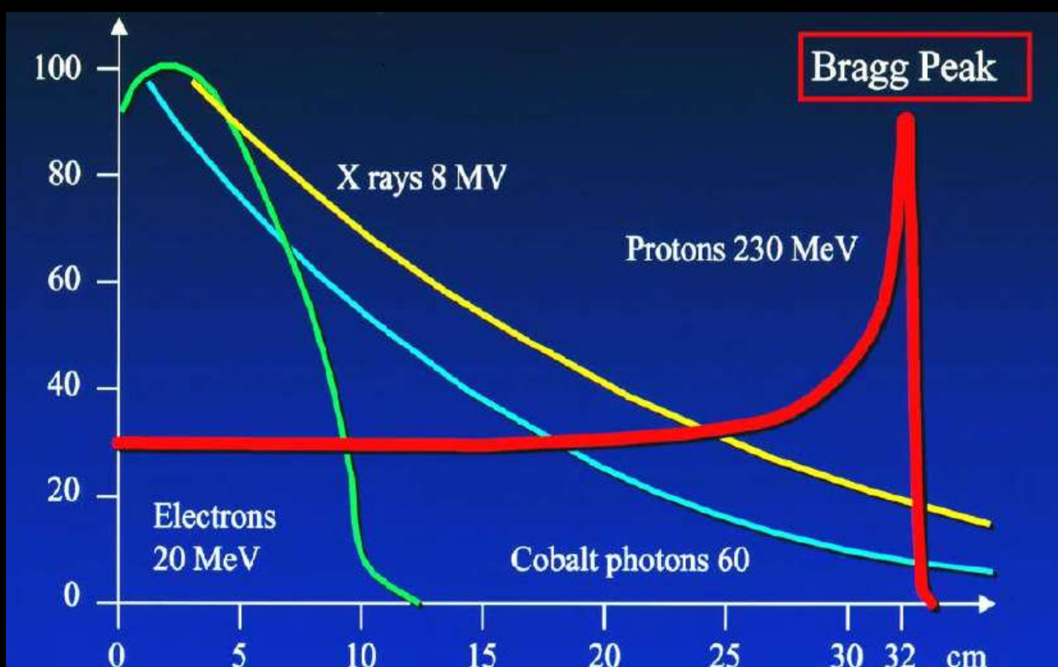
(**P**roton **T**herapy)

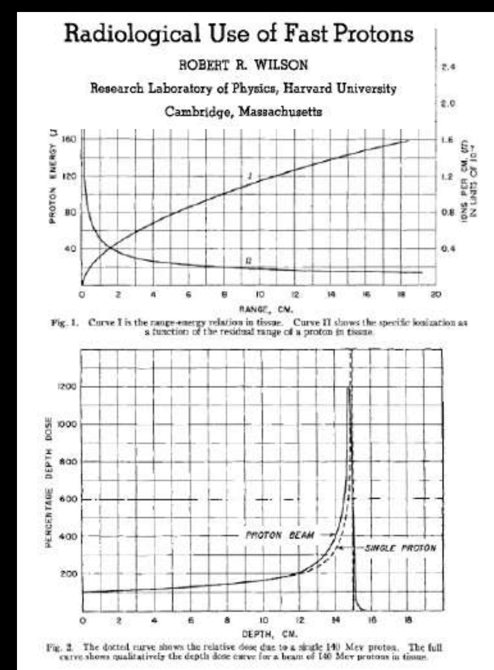
77+ years ago....

Robert Rathbun 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. .... [the] 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. [...][in a] **strictly 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**.''





Radiological Use of Fast Protons

ROBERT R. WILSON

Research Laboratory of Physics, Harvard University

Cambridge, Massachusetts

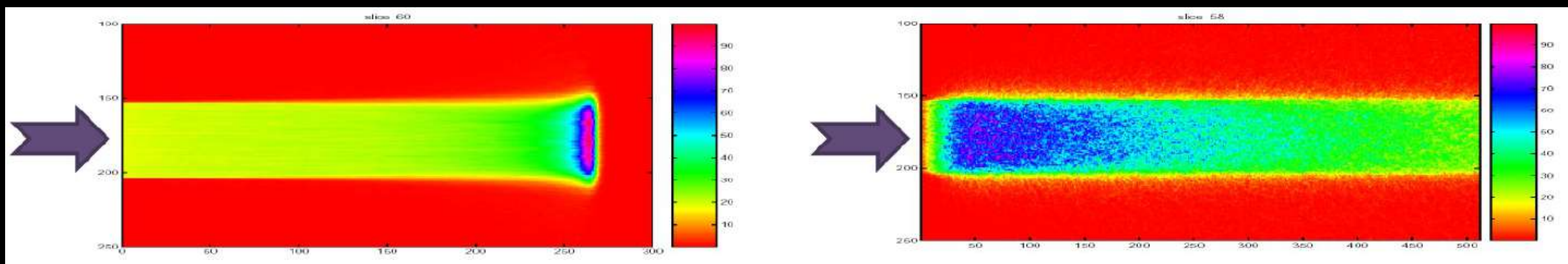
Fig. 1. Curve I is the range-energy relation in tissue. Curve II shows the specific ionization as a function of the residual range of a proton in tissue.

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.

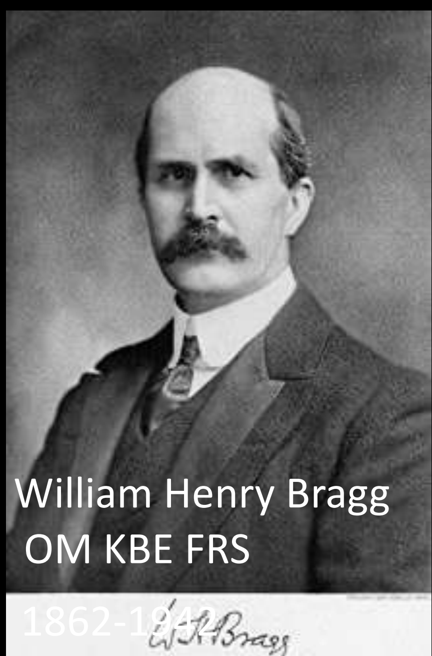
Less collateral damage (i.e., less toxicity)

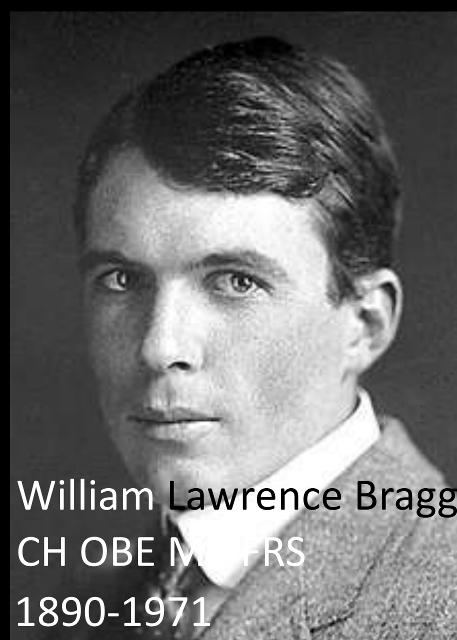
Protons stop and activate

Photons (X-rays) don't

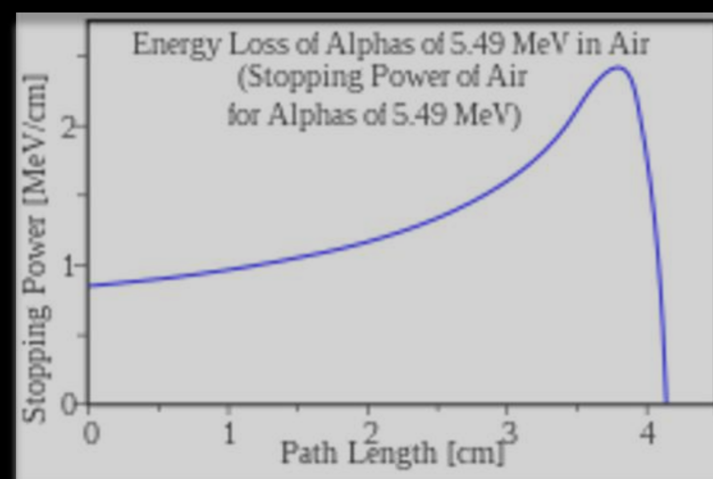


1915  "for their services in the analysis of crystal structure by means of X-rays"



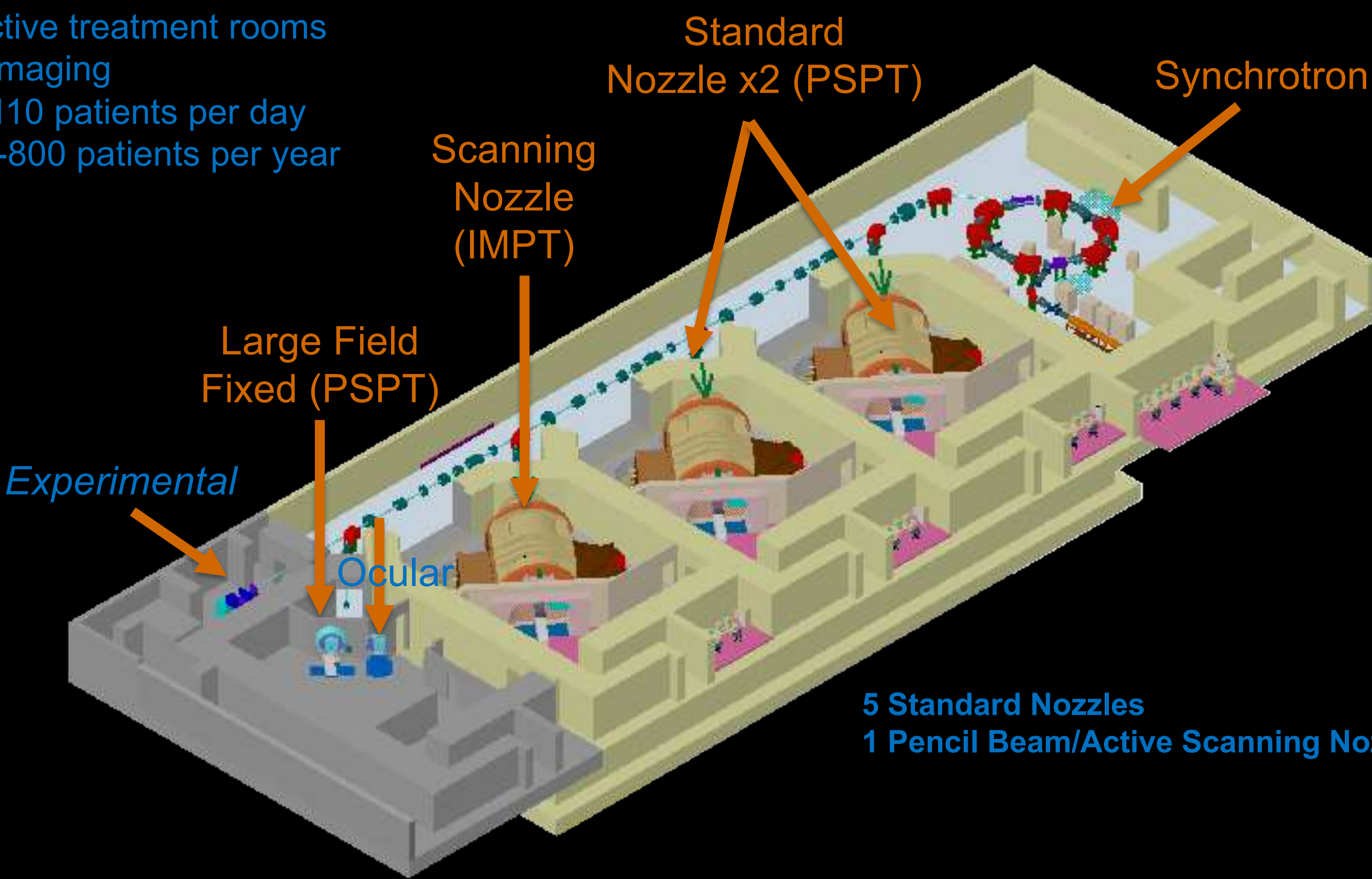


W. H. Bragg peak, 1903



MDACC Proton Therapy Center

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



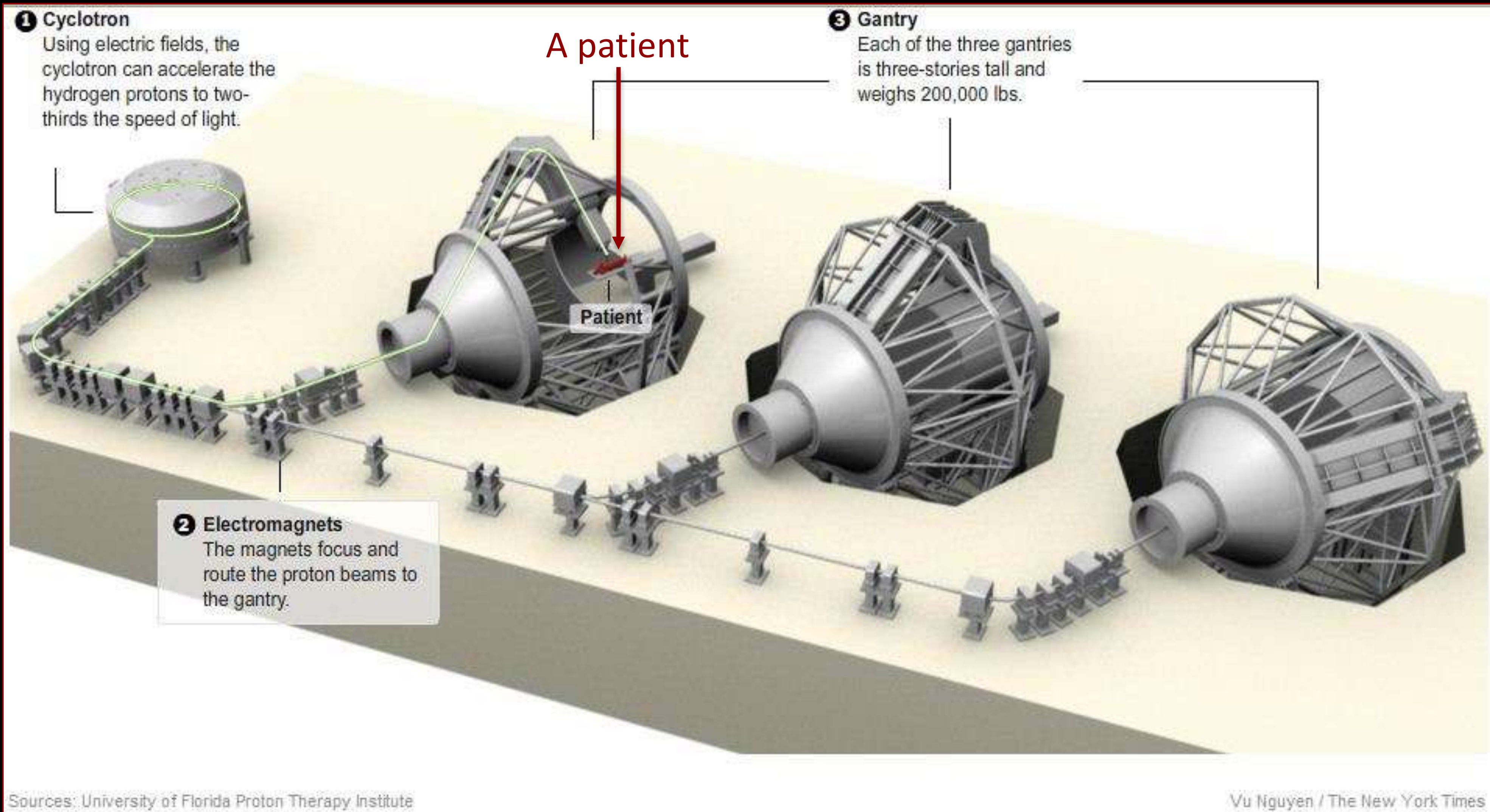
5 Standard Nozzles
1 Pencil Beam/Active Scanning Nozzle

passively-scattered proton therapy (PSPT)

Intensity modulated proton beam therapy (IMPT)

borrowed from Dr. Brandon Gunn

The scale ...



Florida Proton Therapy

IMRT vs IMPT

Intensity Modulated Radiation Therapy

(using X-rays)

Intensity Modulated Proton Therapy

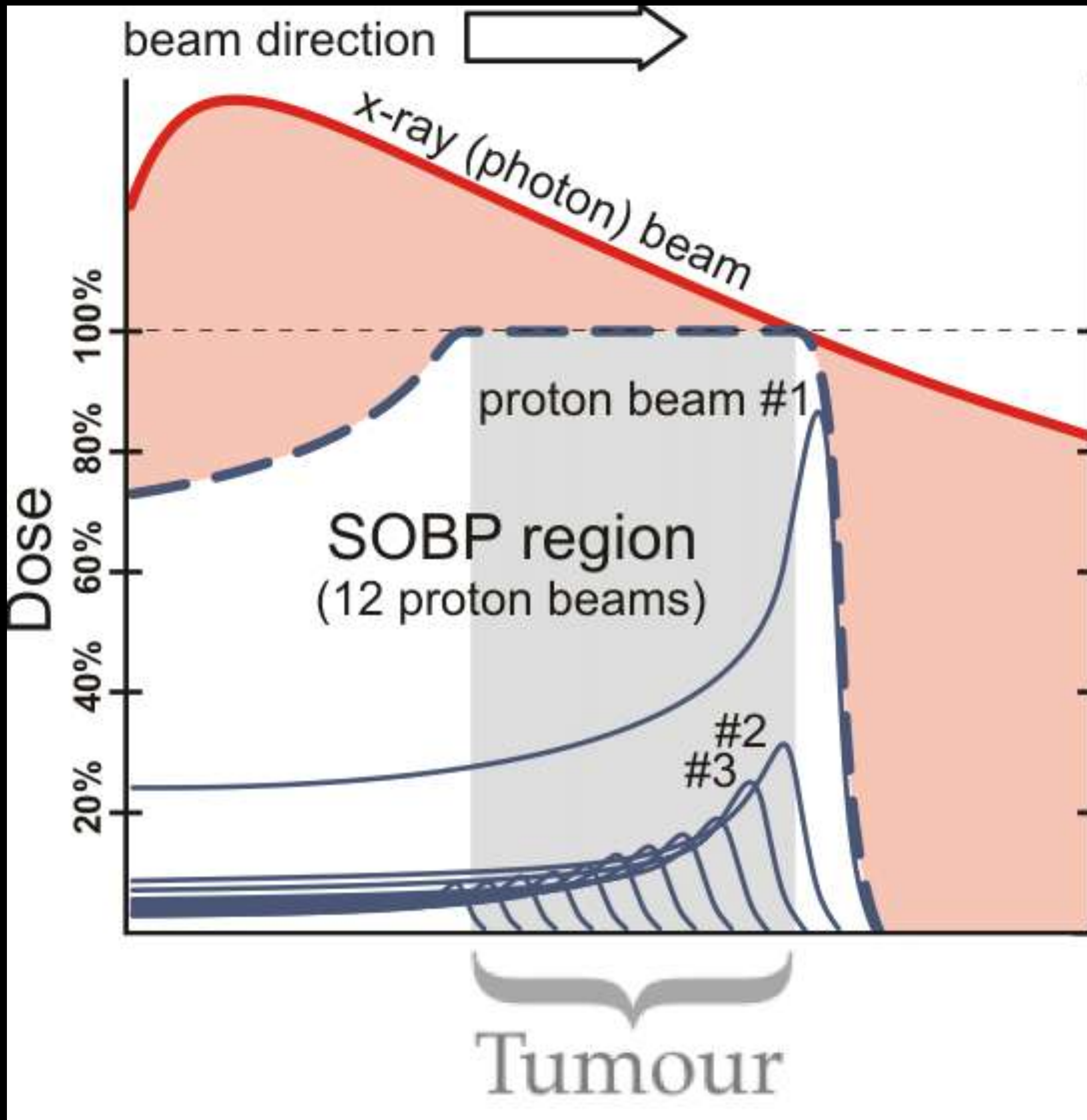
(using protons, ions, pions …)

Traditional X-ray (produces exit dose)

Proton Therapy (produces no exit dose)

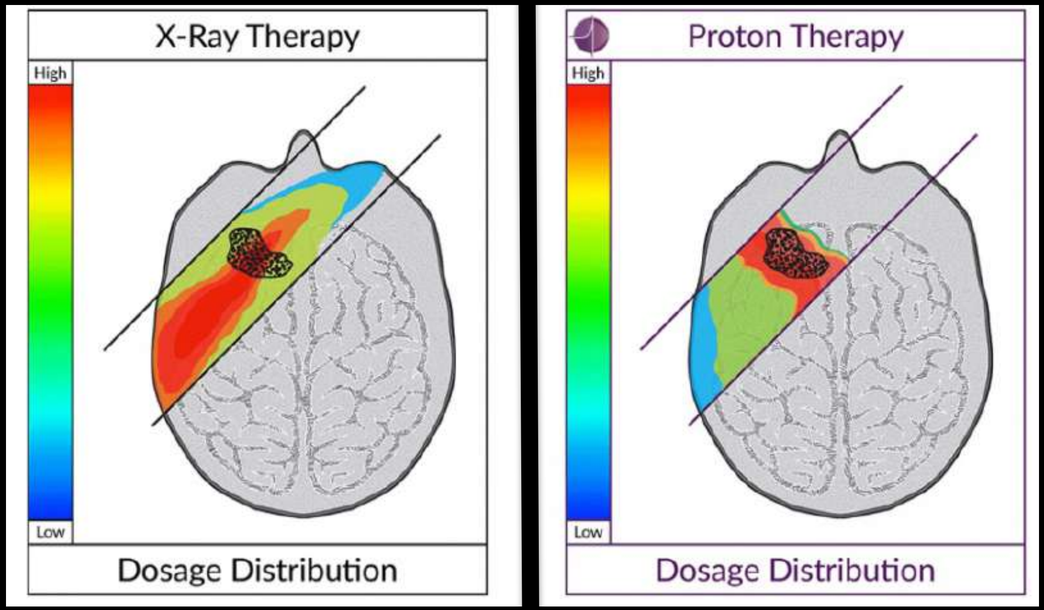
The above images illustrate the radiation benefits of proton therapy (right) in sparing healthy tissues compared to traditional x-ray (photon) therapy (left). Proton therapy deposits a high dose of radiation at the tumor and stops; this eliminates any "exit dose" of radiation, therefore reducing the risk of side effects in patients.

Spread-out Bragg Peak (SOBP)

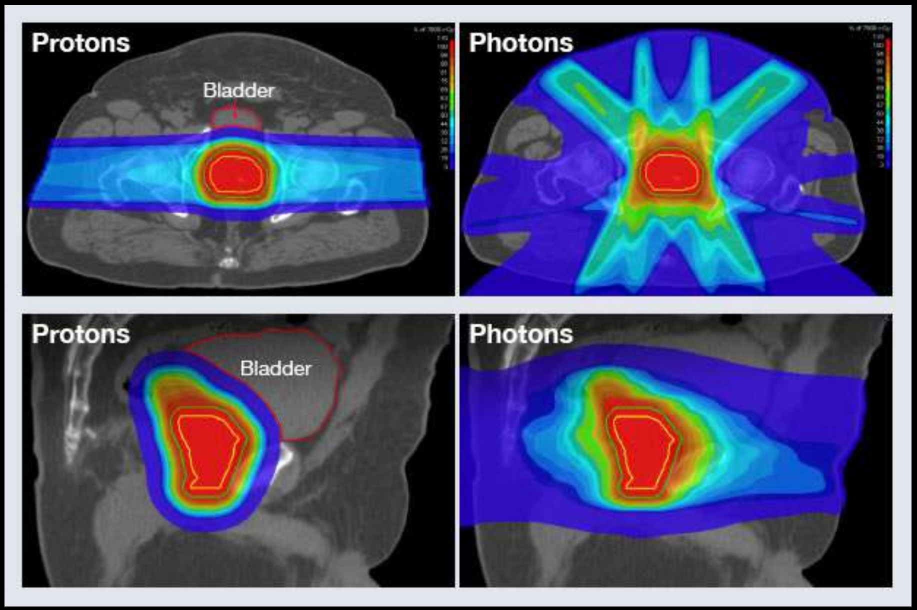


IMRT vs IMPT

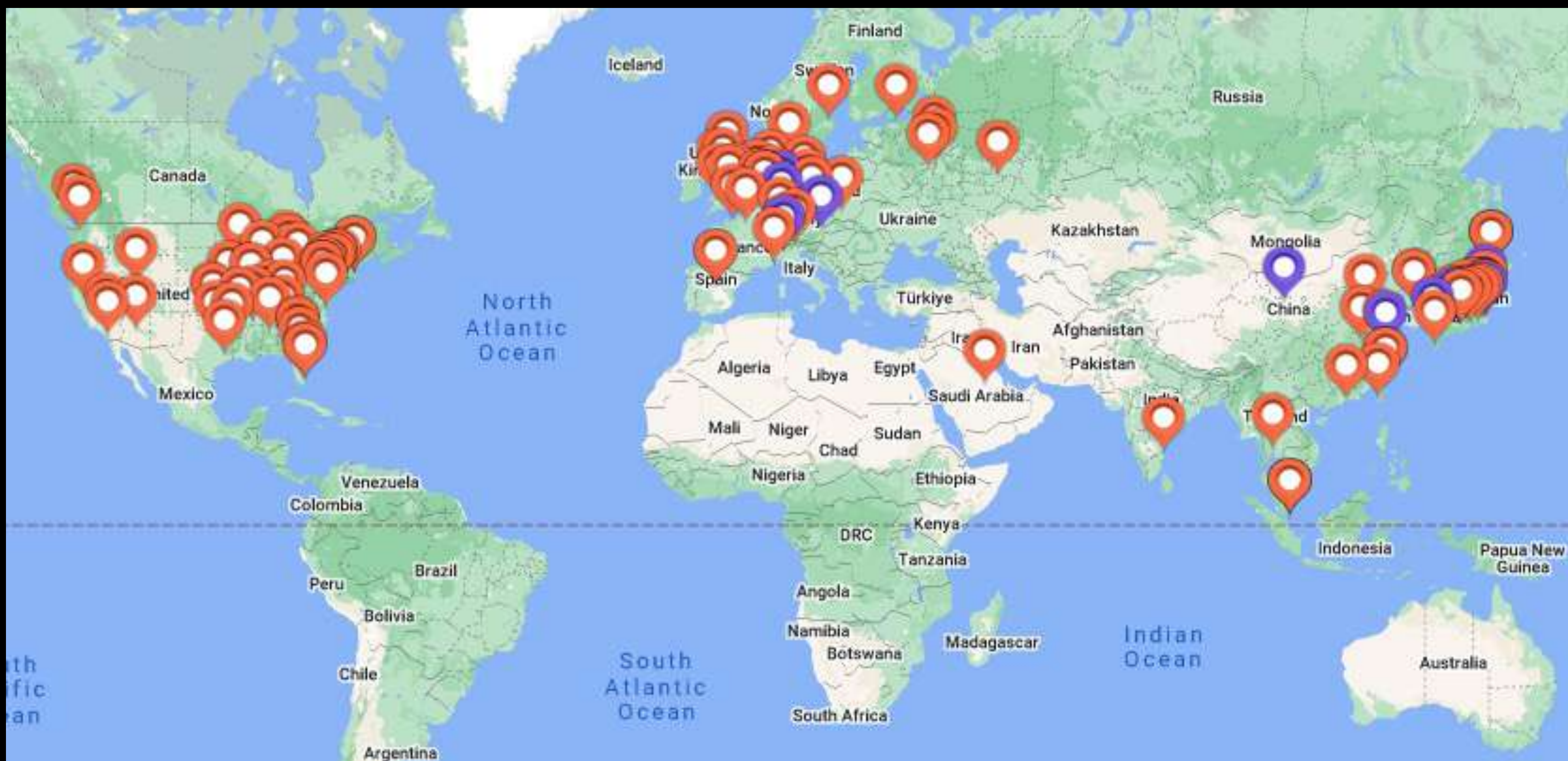
Photons Protons



Protons Photons



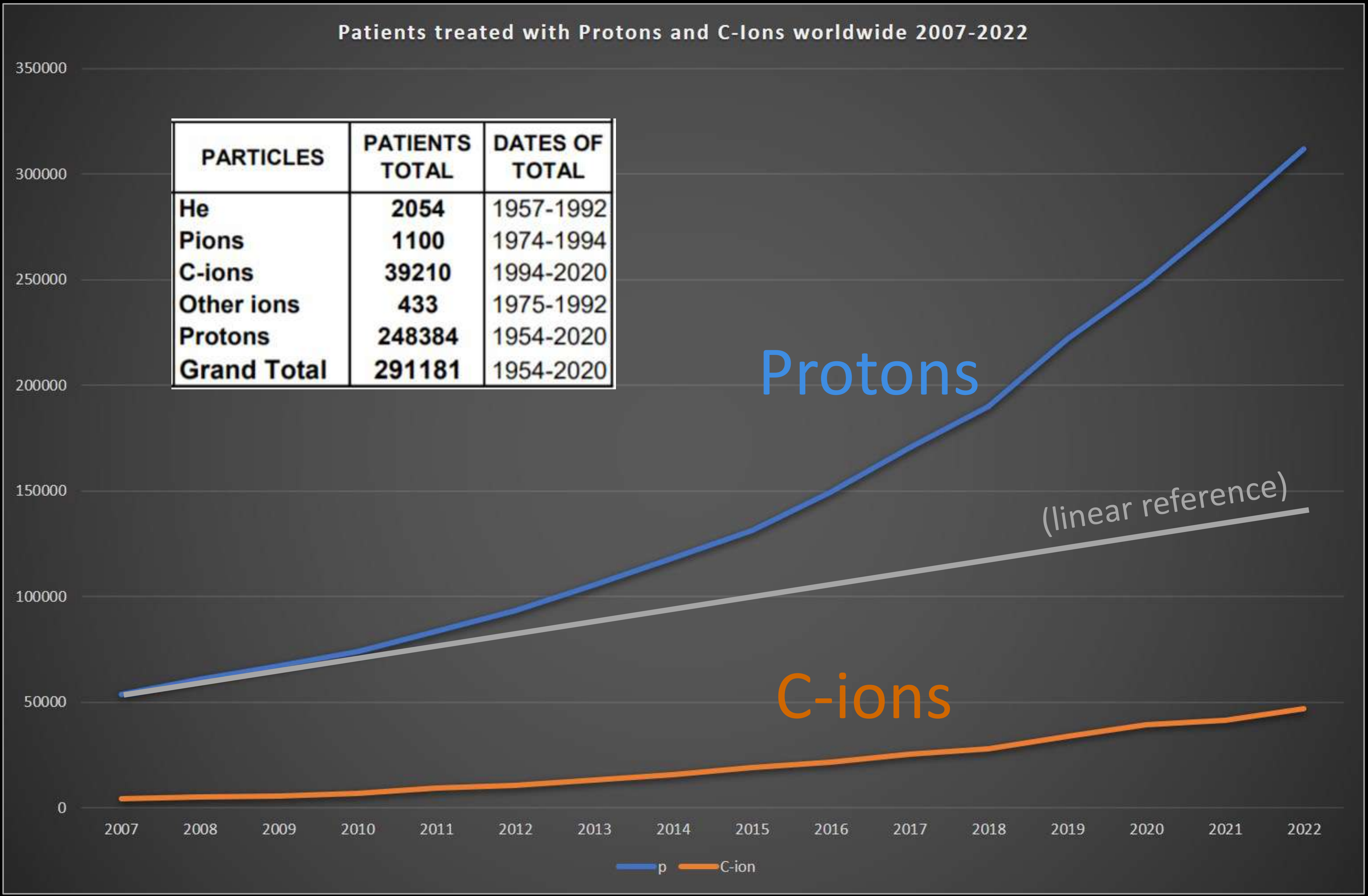
122 facilities worldwide, another >100 in various planning/construction stages



- 46 facilities in the USA .... 26 in Japan ... 7 in Germany ... 8 in China ... 3 UK, 3 Netherlands
  1 in Poland (CCB IFJ, Kraków)
- 3 in Texas: 2 at MD Anderson CC and at 1 @UT Southwestern Medical Center
- And 1 more to open in a new MD Anderson CC in Austin within 3-4 years…

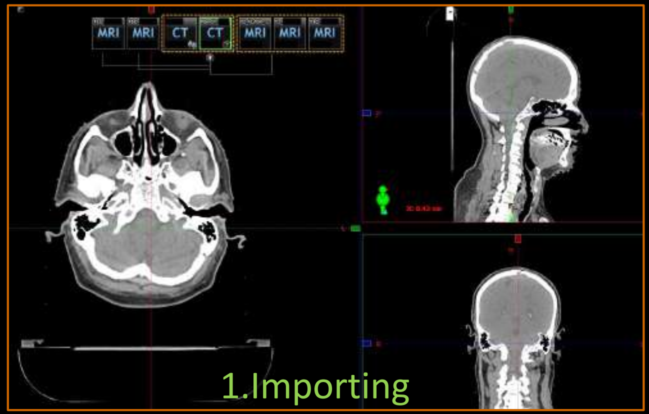
The future of radiation therapy... (PTCOG)

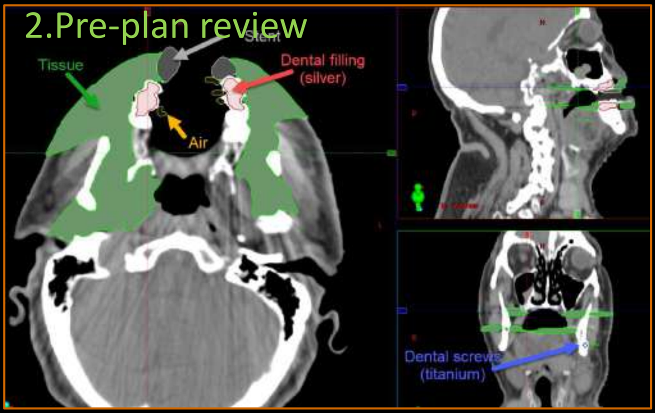
PARTICLES	PATIENTS TOTAL	DATES OF TOTAL
He	2054	1957-1992
Pions	1100	1974-1994
C-ions	39210	1994-2020
Other ions	433	1975-1992
Protons	248384	1954-2020
Grand Total	291181	1954-2020

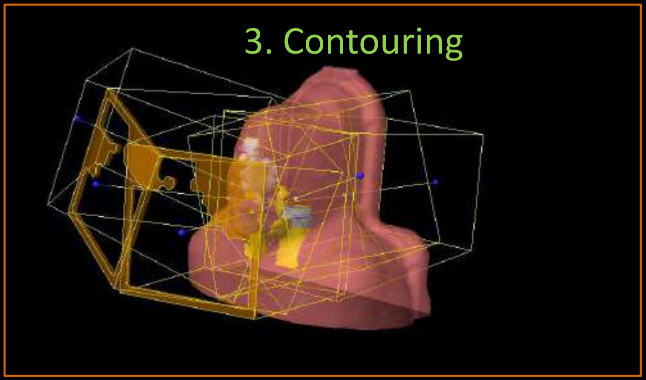


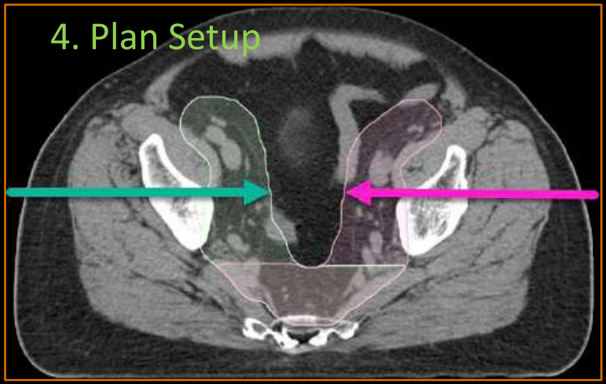
Treatment Planning

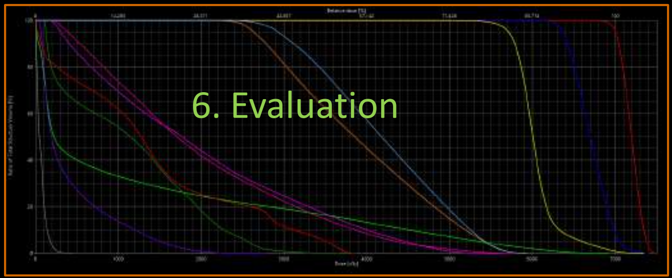
- Meticulous and sophisticated treatment planning ("well-oiled machine") – 5 days of intense preparations
  - 1. Importing
  - 2.Pre-plan Review
  - 3.Contouring
  - 4.Plan Setup
  - 5.Optimization
  - 6.Evaluation
  - 7.Summary











That's the end of good news ...

Impediments limiting the effectiveness of proton therapy

- Anatomy changes may perturb dose distributions to a significantly greater extent for protons than for photons
- High gradients in proton dose distributions are very sensitive to anatomy motion and changes, and to set up variations
- Gaps in the knowledge of relative biological effectiveness (RBE) of protons
  - Proton RBE is assumed to be a constant of 1.1
- Heterogeneity in patient population, tumor characteristics and treatment techniques may be obscuring the potential advantages of protons for subpopulations of patients
- Evolving treatment delivery and planning systems and techniques
- Limits to the applicability of knowledge and models based on photon therapy experience to protons
- High cost of proton therapy

A successful plan requires good communication and **m**ultitude of factors that need input from:
– Physician
– Dosimetry team
– Physics team
– Therapy team

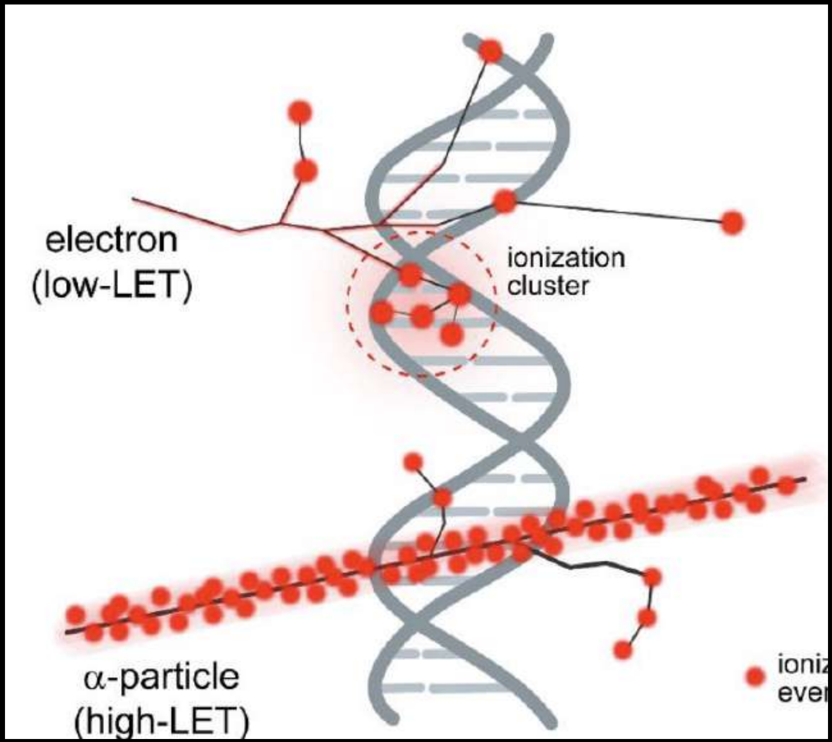
→

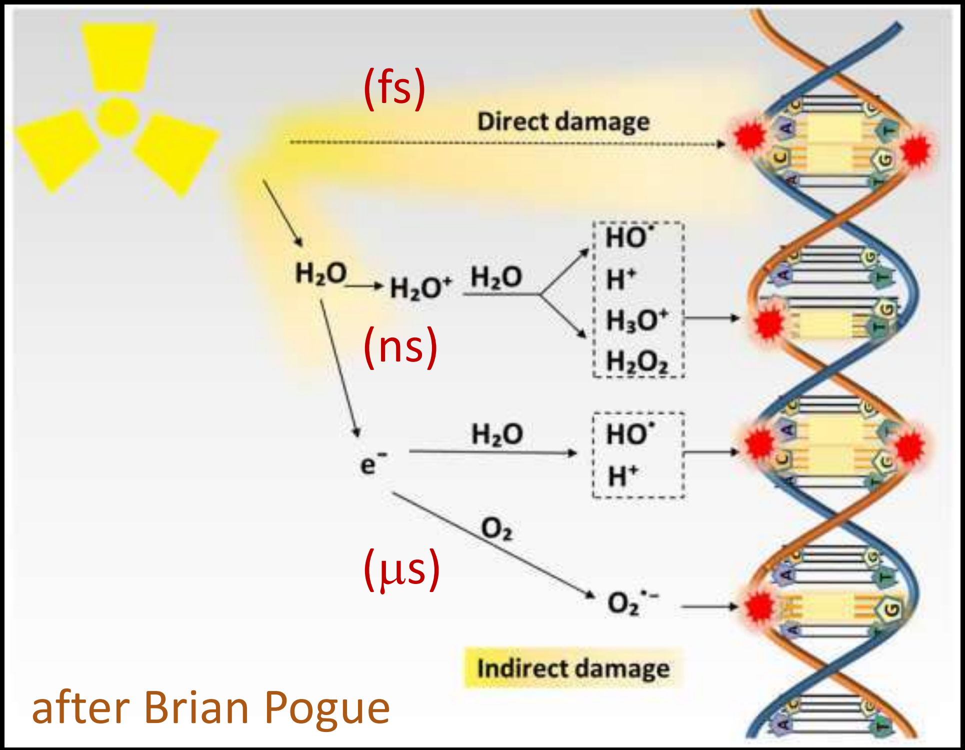
Much room for improved feedback of ongoing therapy
(a.k.a. proton range verification)

After Radhe Mohan, PhD

Destroying cancer or impeding its growth

oxygen radicals ...



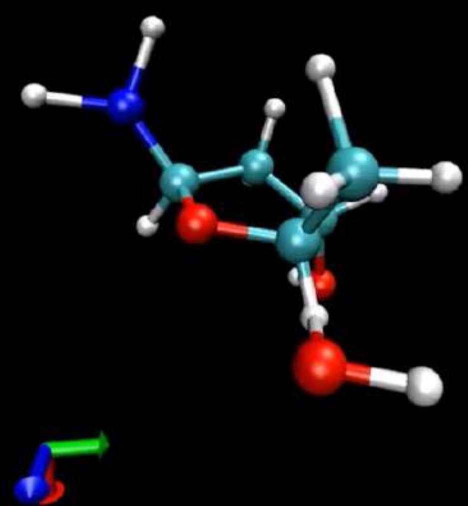


Do we understand the time and concentration dependence of effects of ionizing radiation on living cells/tissues?

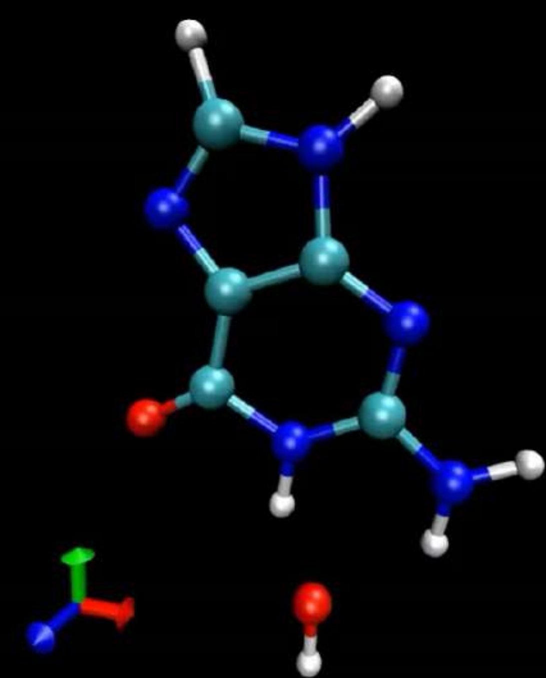
Reactive Oxygen Species (ROS)...

Atoms color code: C, O, N, H, P

DNA (outer)



DNA (inner)



$$OH^{-} + OH^{\cdot} \rightarrow {}^{\cdot}O^{-} + H_2O$$

R. Abolfath et al., JPC. 2009 / 2010

Our PETs

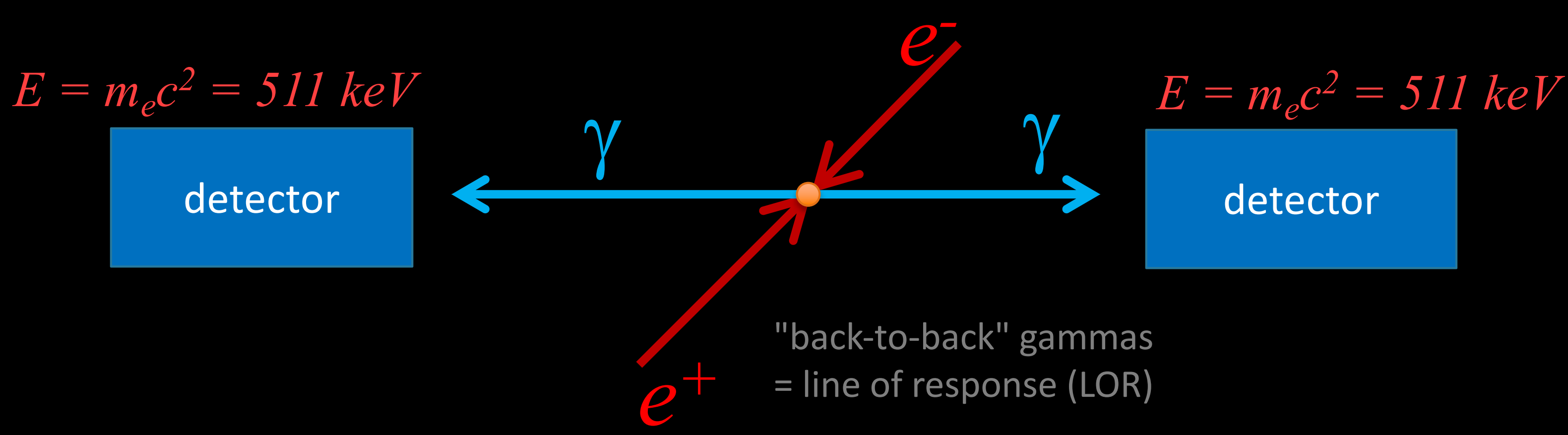
TPPT

(Time-of-Flight PET for Proton Therapy)

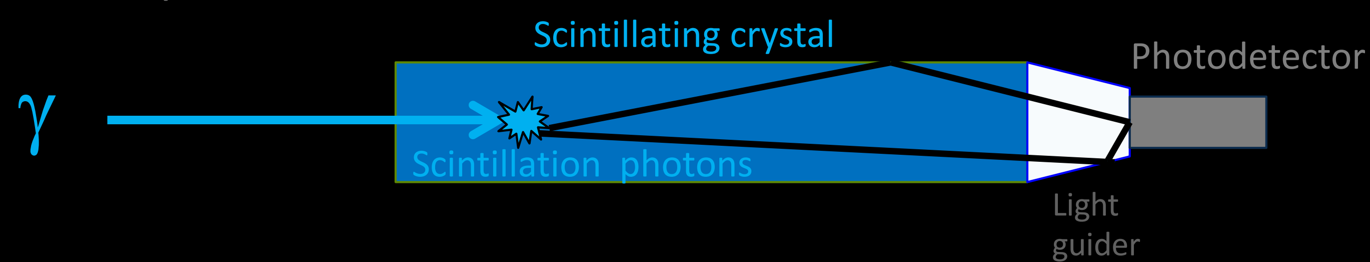
Positron Emission Tomography

Injection of ^{18}F-fluoro-deoxy-glucose (^{18}FDG)
or other suitable radio-pharmaceuticals

$$^{18}F \rightarrow {}^{18}O + e^{+} + \nu_e$$



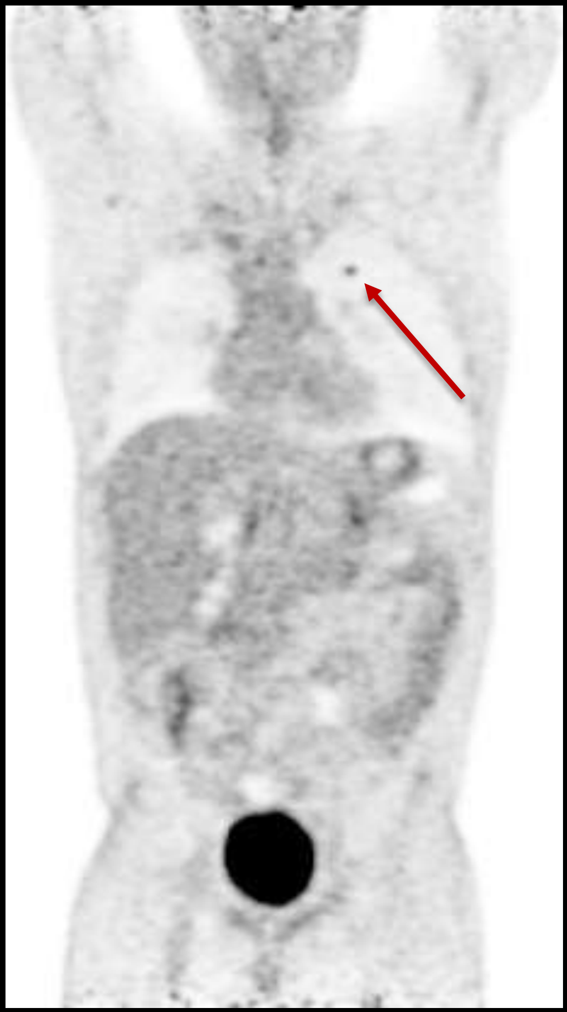
A conceptual detector



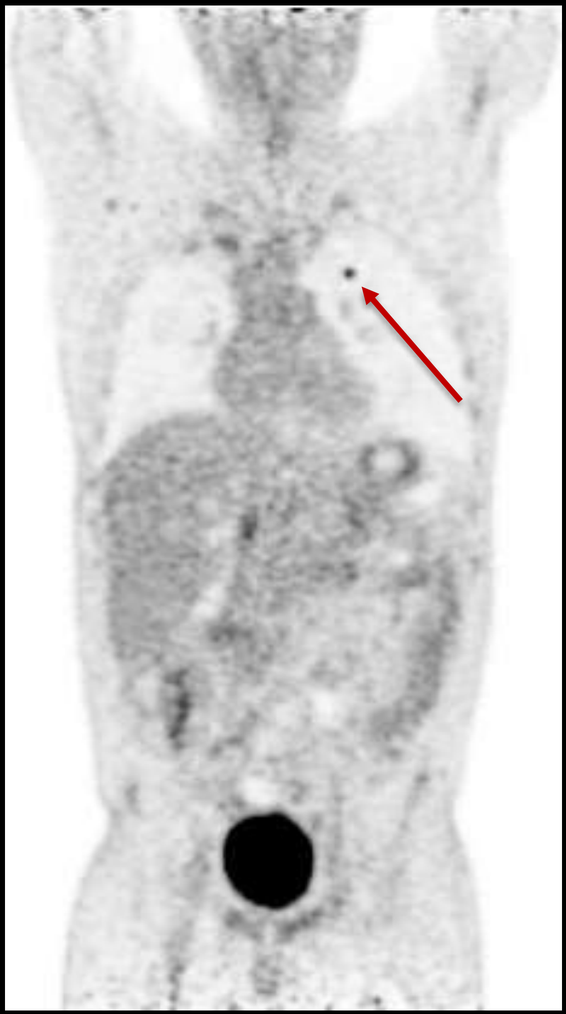
Time of Flight PET advantages: noise reduction and improved contrast recovery

3 minute/bed injection of ^{18}F-fluoro-deoxy-glucose (^{18}FDG)

Non-TOF



TOF (550 ps)



Borrowed from Dr. Maurizio Conti
Director, PET Physics and Reconstruction
Siemens Medical Solution USA, Inc, Knoxville, TN, USA

ToF PET for Proton Therapy (TPPT) concept

The concept:
proton range verification using activated positron emission tomography

C-11 ($T_{1/2}$=20min)
N-13 ($T_{1/2}$=10min)
O-15 ($T_{1/2}$=123sec)

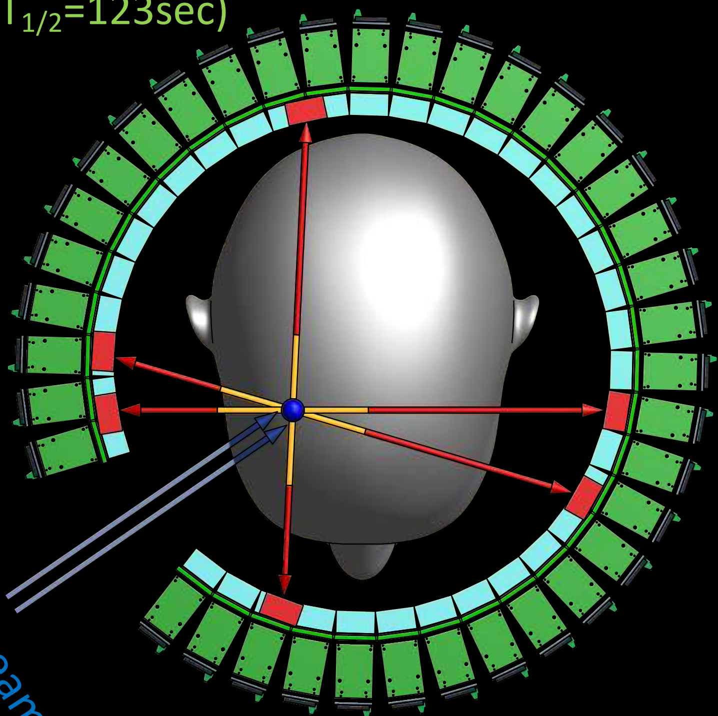
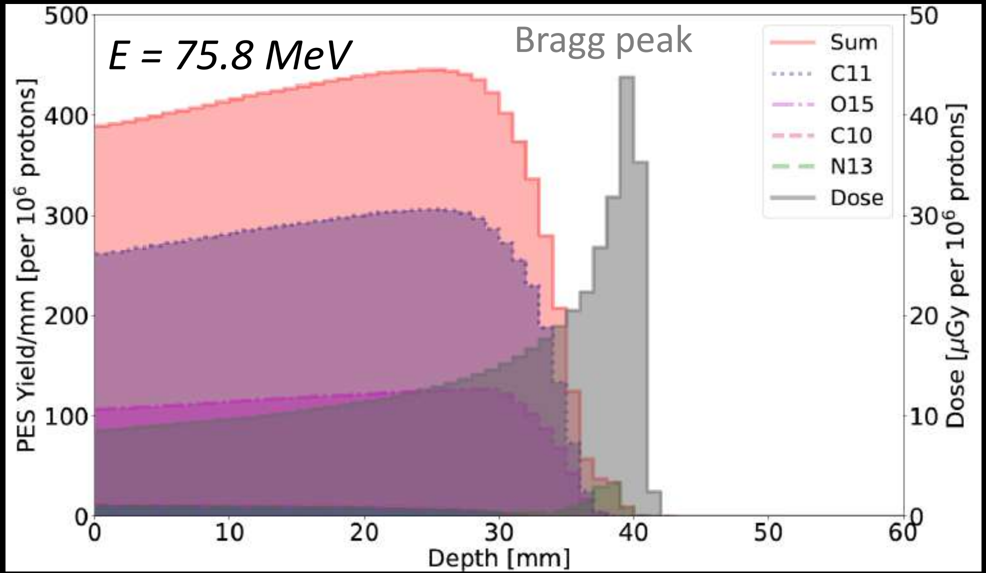


Image-guided proton therapy and theranostics

Production (proton activation), e.g.,

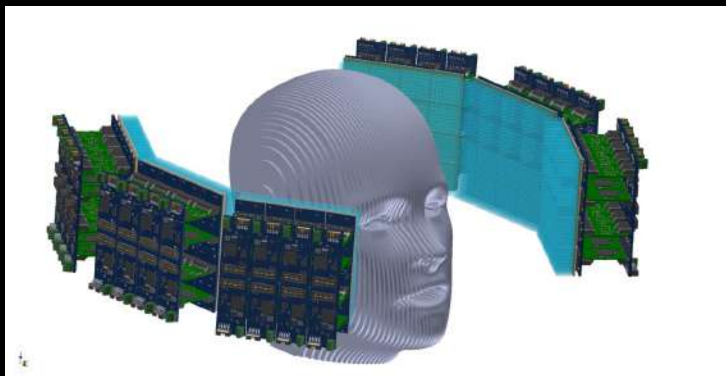
$$^{16}O(p,pn)^{15}O$$



β+ isotopes activated

Concept → engineering

Proposal



concept

U. of Texas at Austin, USA
PETsys Electronics, Lisbon, Portugal
LIP, Coimbra, Portugal
C^{2}TN, Instituto Superior Técnico, Lisbon, Portugal
ICNAS, U. de Coimbra, Portugal
U. of Texas MD Anderson Proton Therapy Center, USA

Available online at www.sciencedirect.com
SCIENCE DIRECT
ELSEVIER Nuclear Instruments and Methods in Physics Research A 525 (2004) 284–288
NUCLEAR INSTRUMENTS & METHODS IN PHYSICS RESEARCH Section A
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Charged hadron tumour therapy monitoring by means of PET

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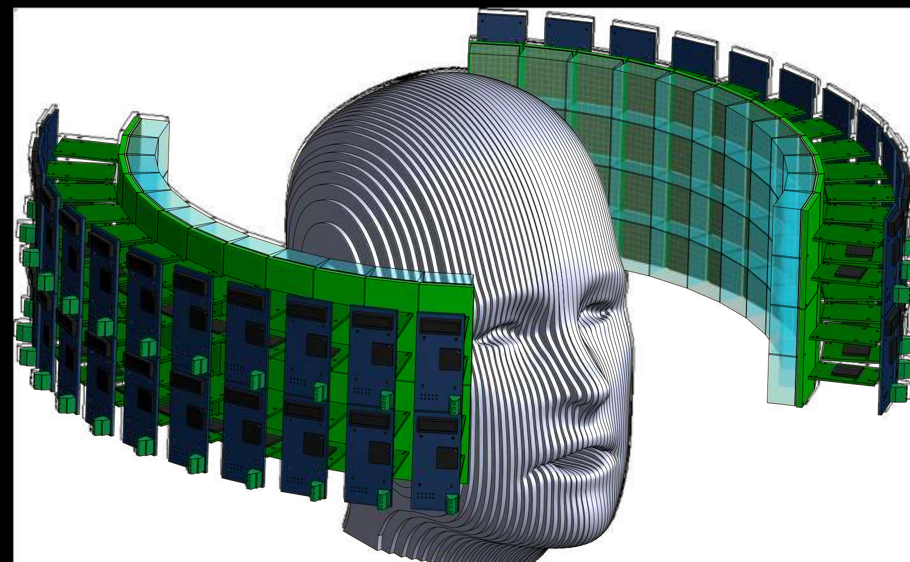
[a] Forschungszentrum Rossendorf e.V., Institute of Nuclear and Hadron Physics, Postfach 510119, D-01314 Dresden, Germany
[b] Hammersmith Imanet Ltd., Hammersmith Hospital, London, W12 0NN, UK

Design

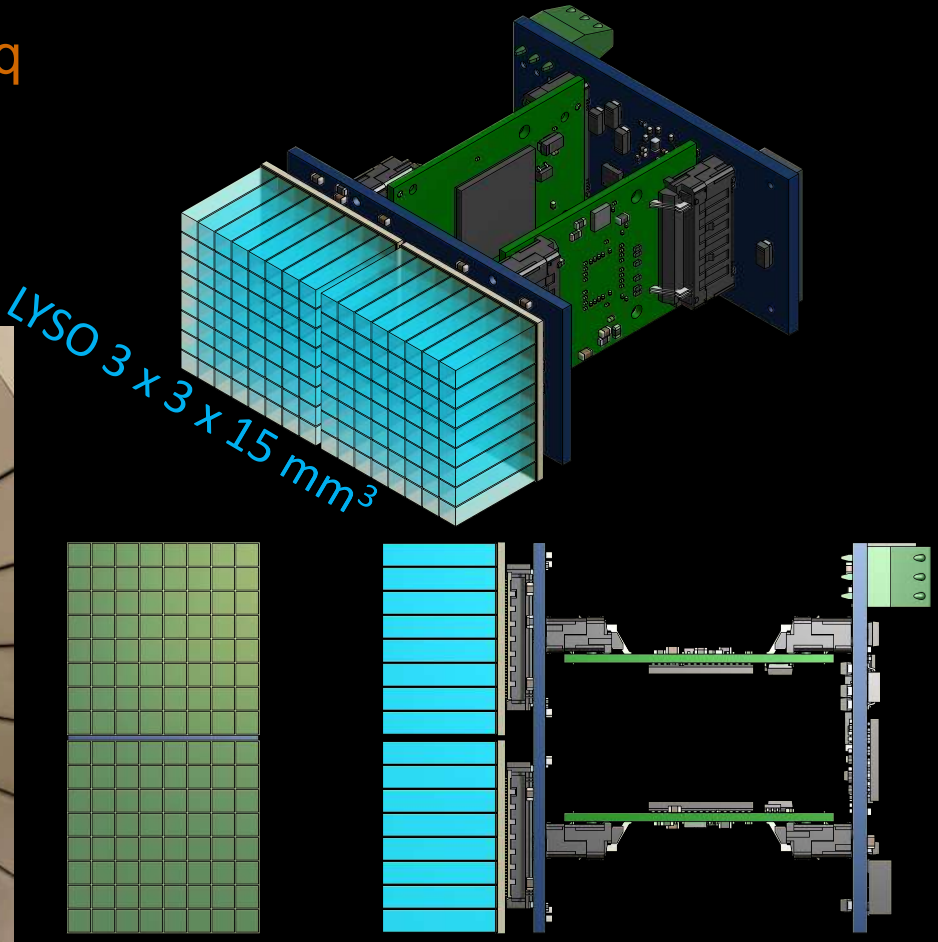


Consider: Symmetry
Cooling
Mechanics

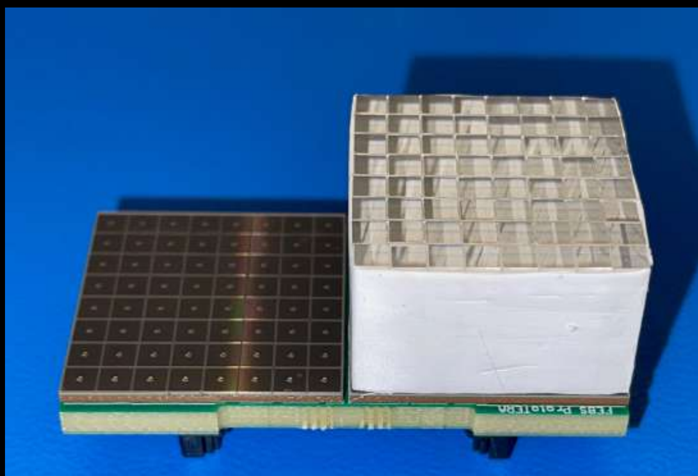
UTAustin Portugal

Design ingredients

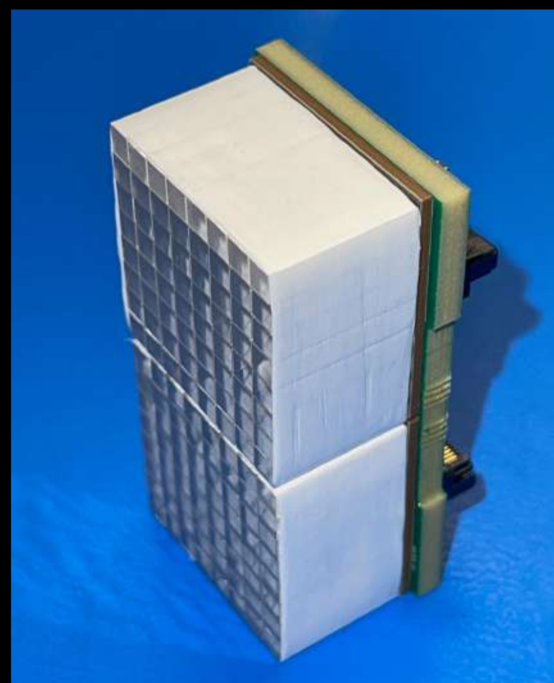
- Proton beam constraints
- PETsys front-end electronics + daq
- Commercial SiPM and LYSO
- constraints in $/€



Our “Lego” blocks



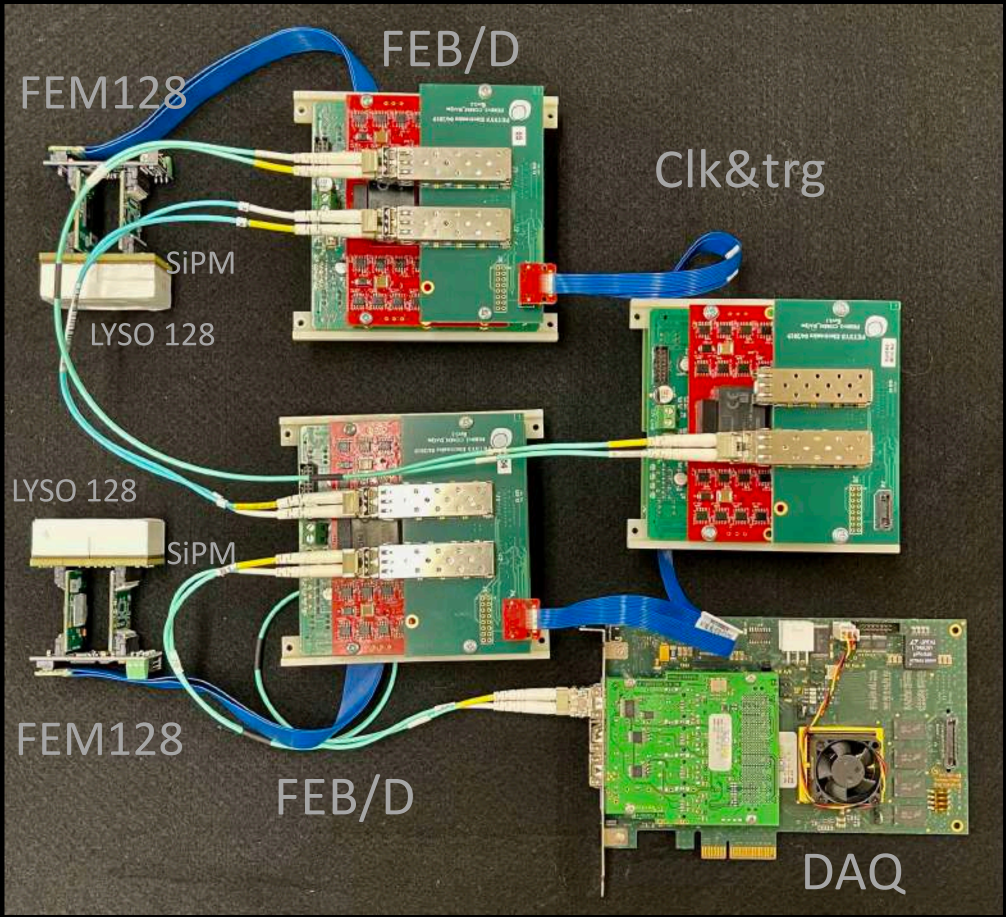
3 x 3 x 15 mm^3



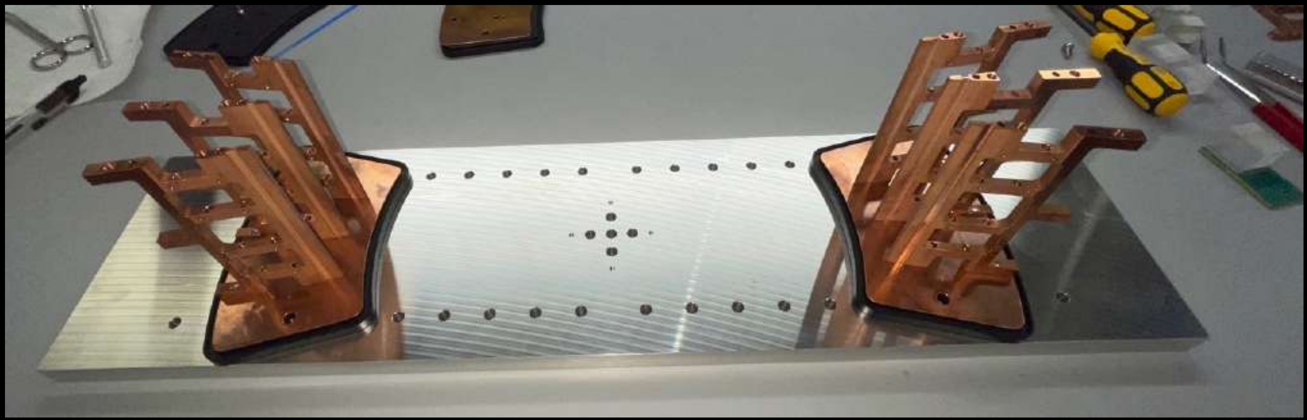
Hamamatsu

LYSO ($Lu^{1.8}Y.^{2}SiO^{5}:Ce$) is a Cerium-doped Lutetium-based scintillation crystal

PETsys front-end and daq



Need to check performance → mini-PET

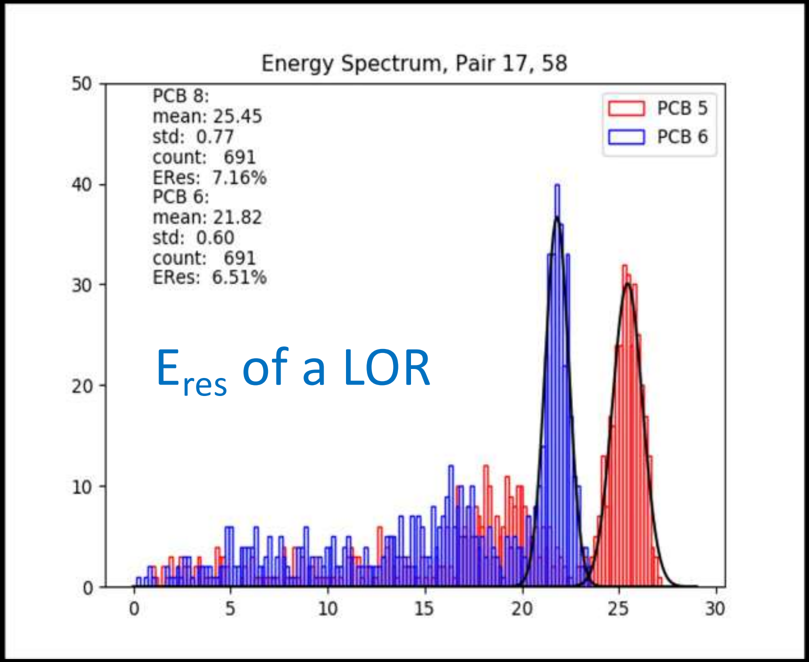


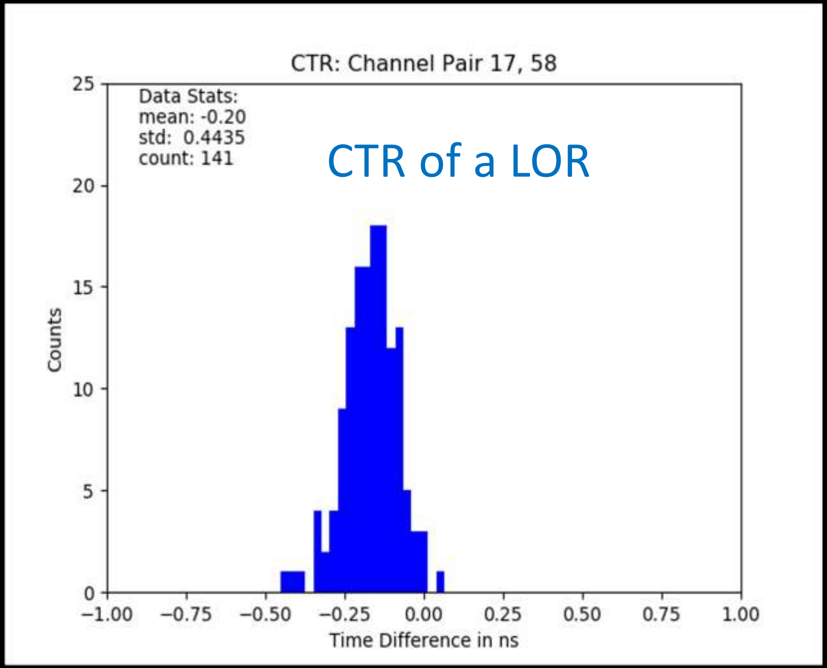
mini-PET data

Coincidence data:

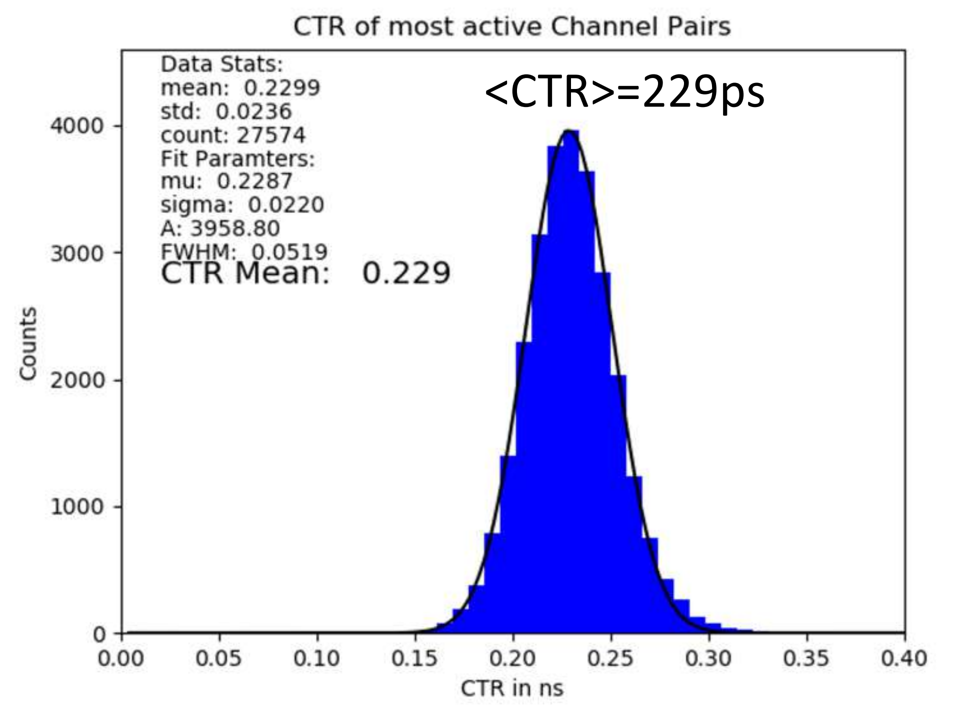
list mode from PETsys daq
pairs of channels on either side
lines of response

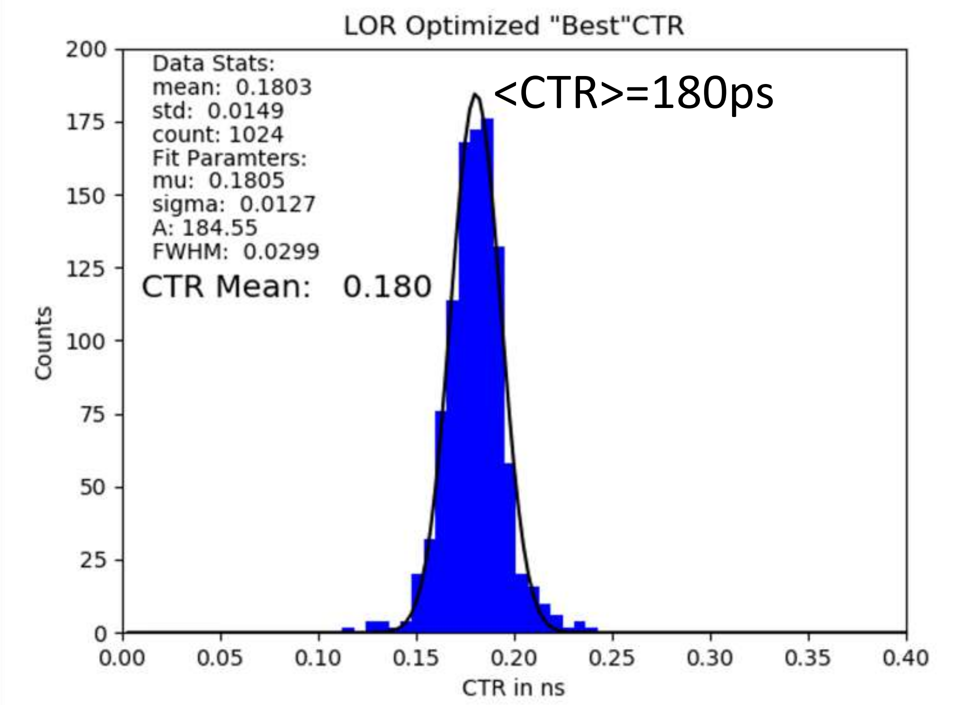
→ energy resolution
→ coincidence time resolution (CTR)



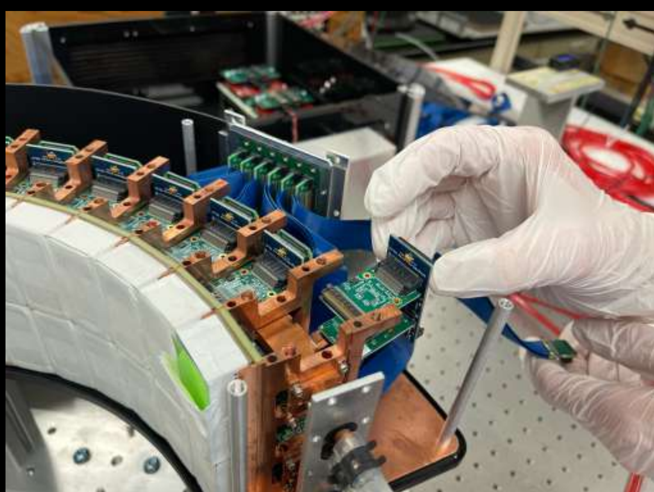


mini-PET Results

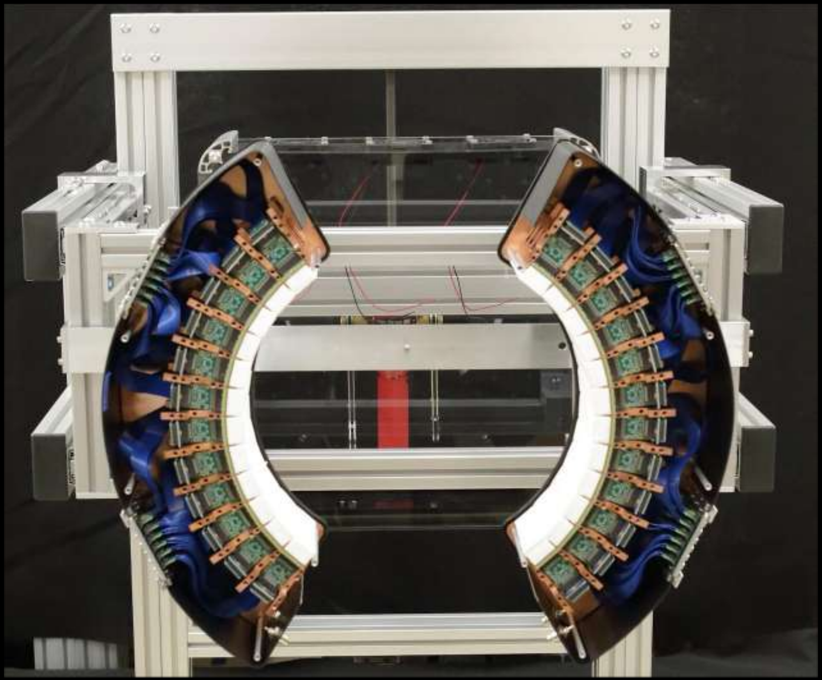


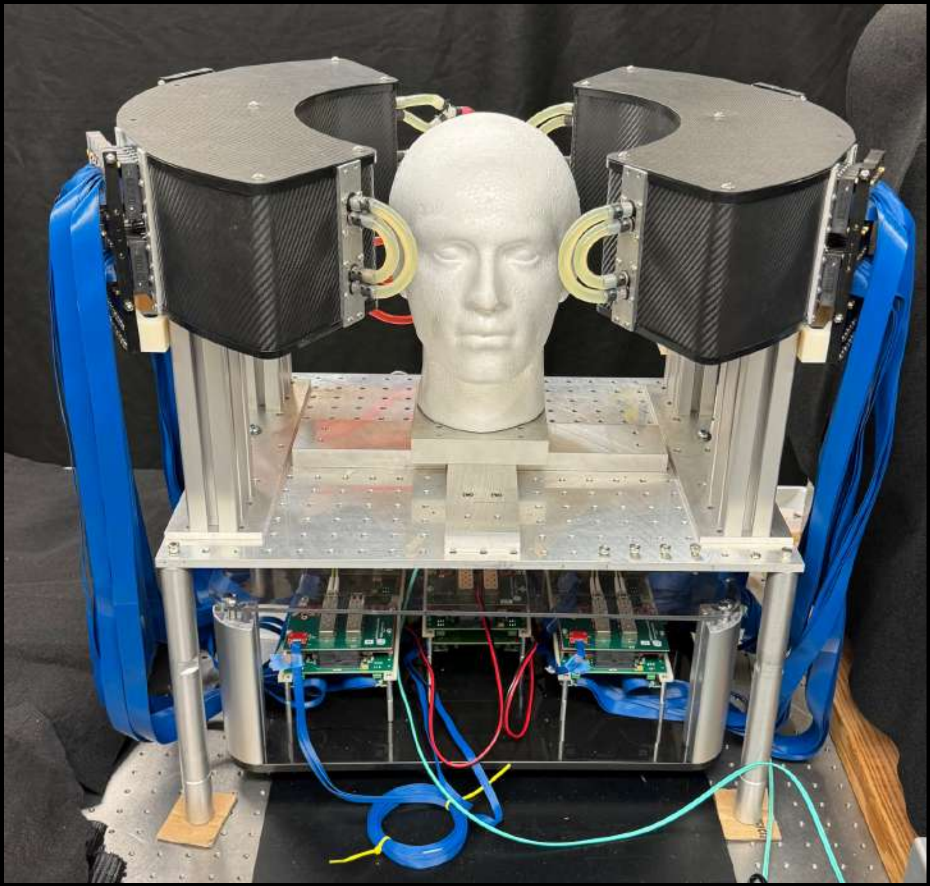


Full TPT scanner assembly



Dress rehearsal for MDACC





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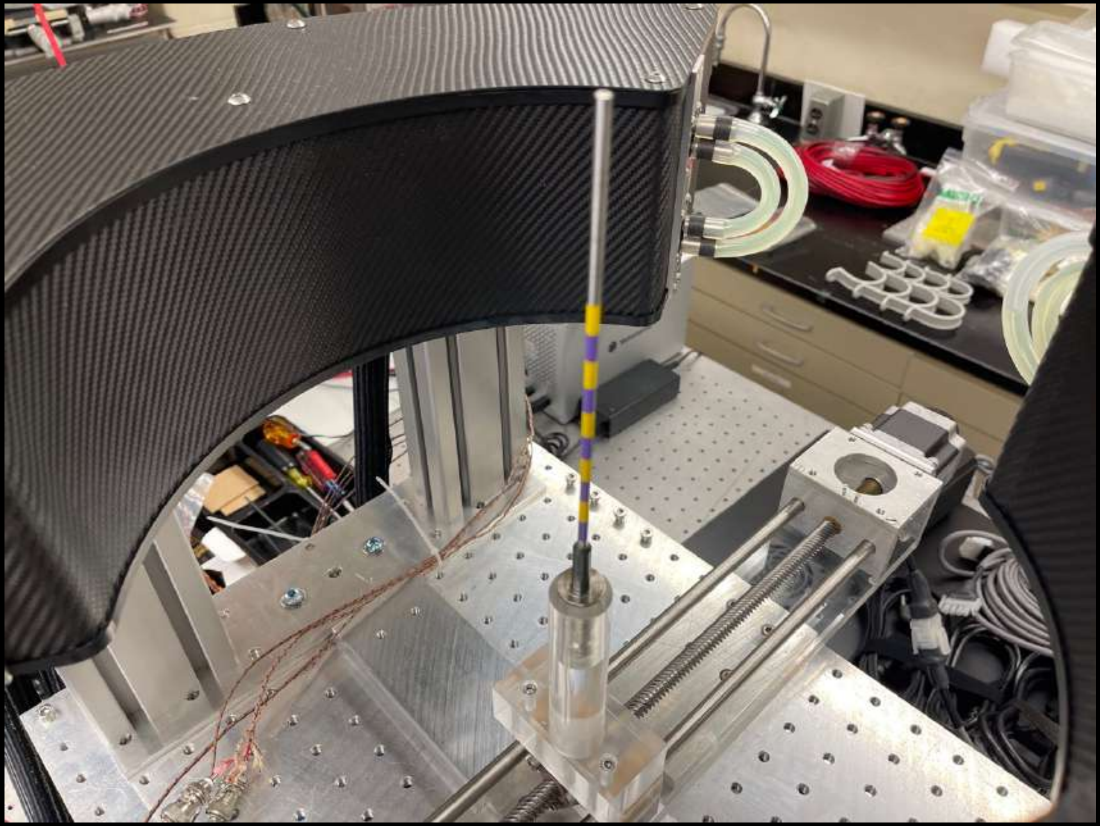
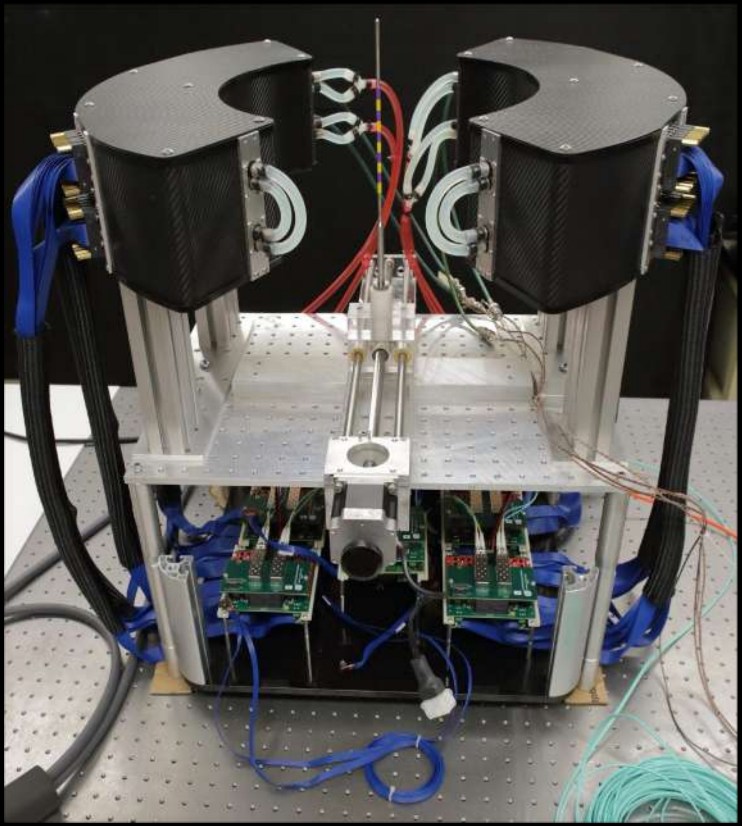
Current test bench setup

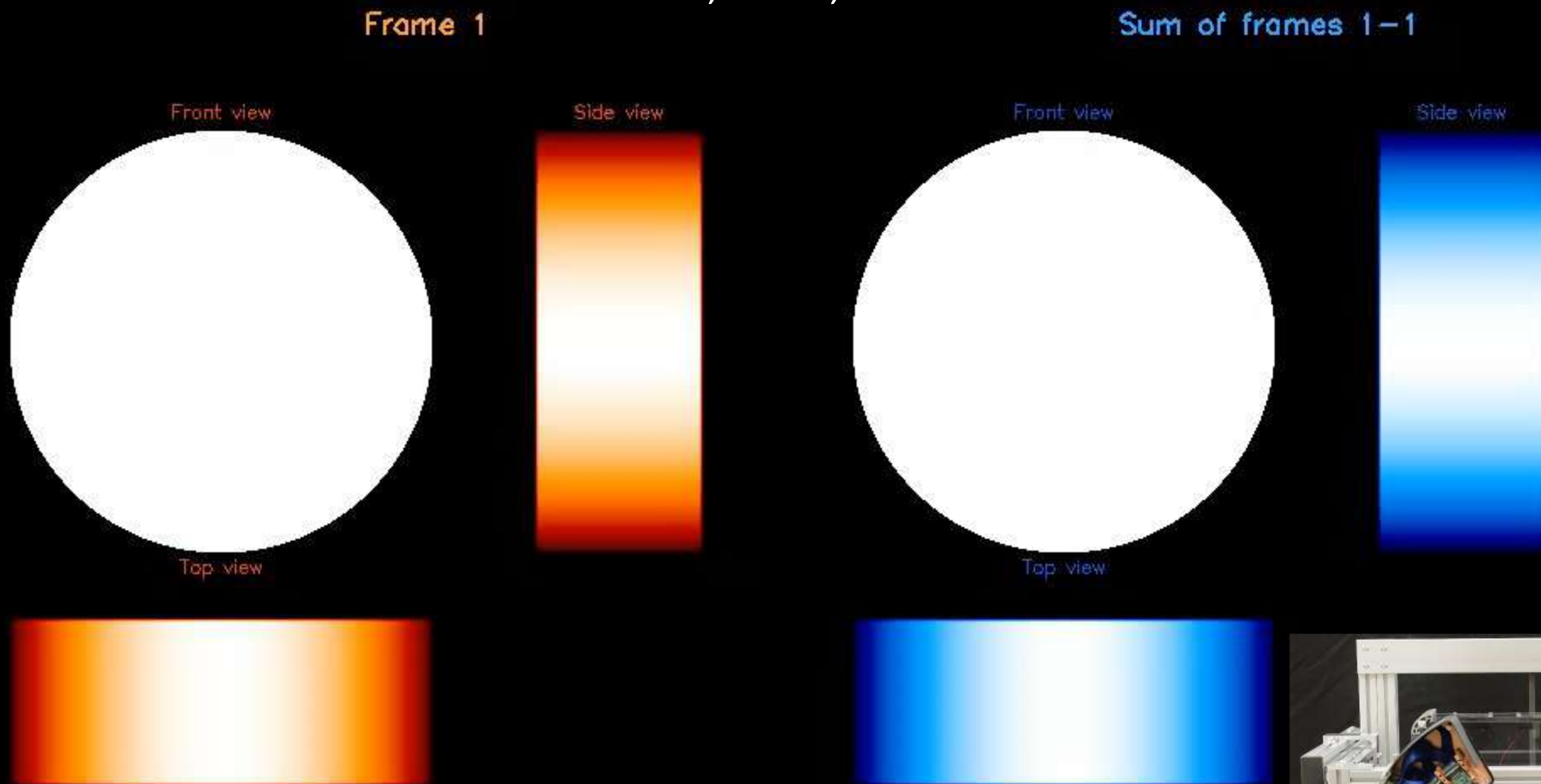


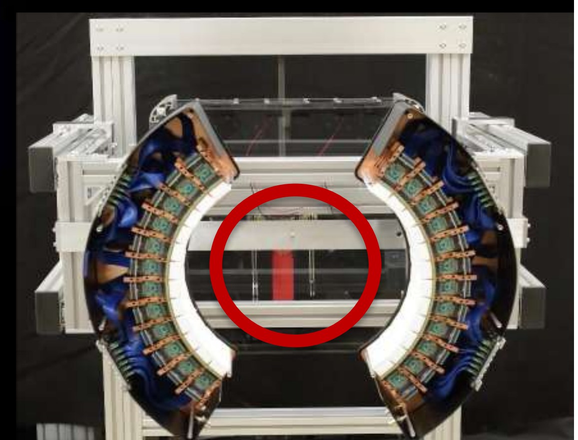


55

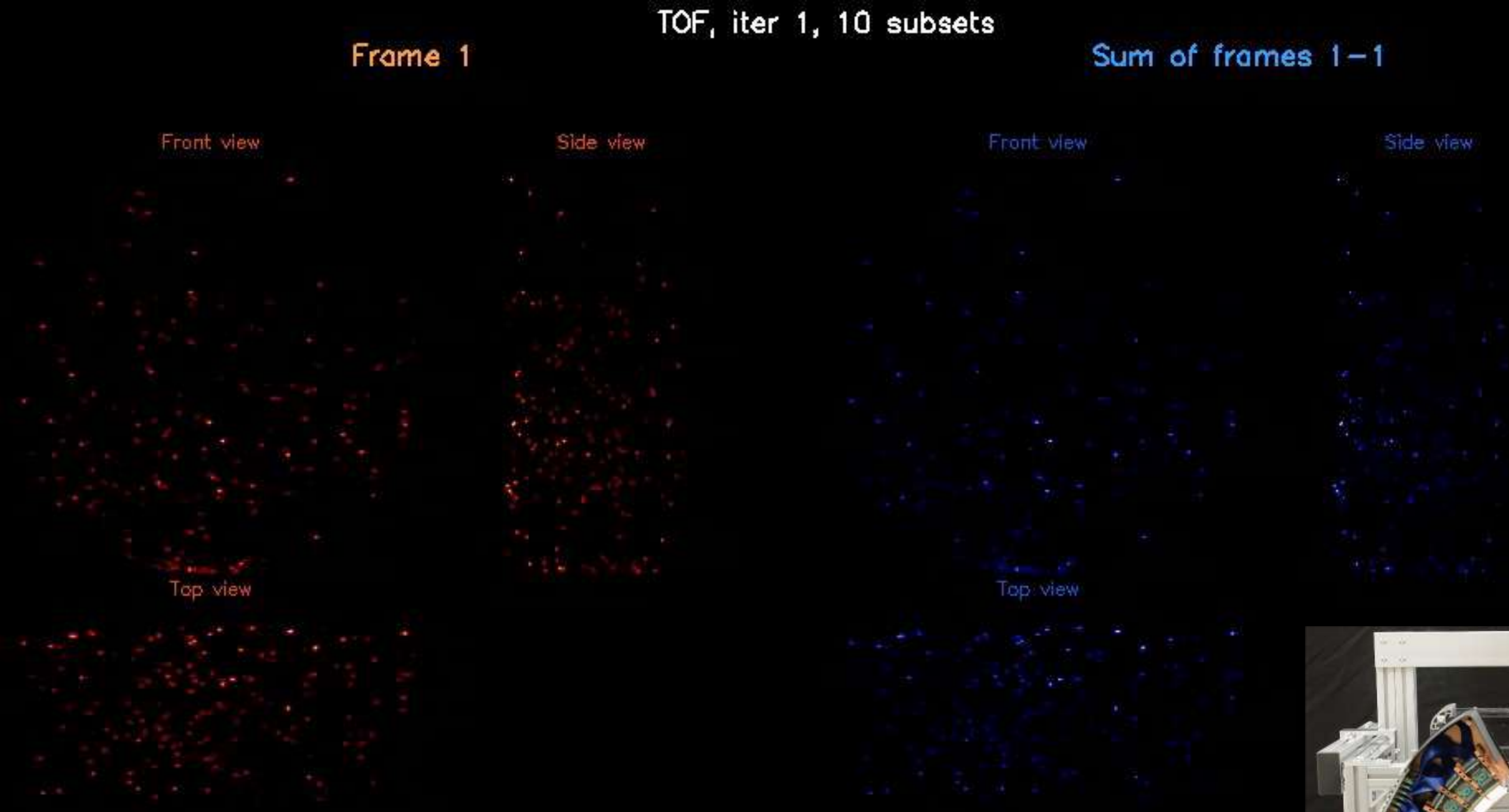
Calibration with ^{68}Ge line source (circular sweep)

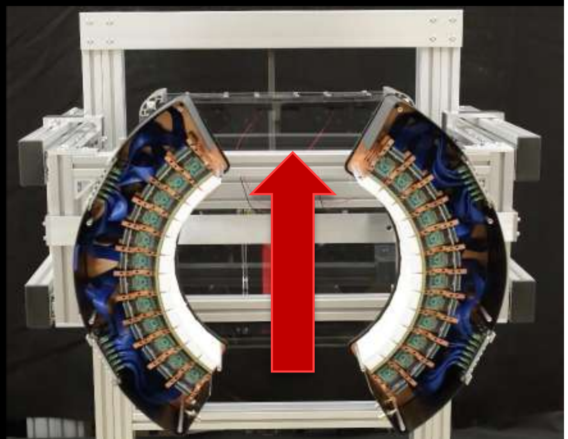
TOF, iter 6, 10 subsets



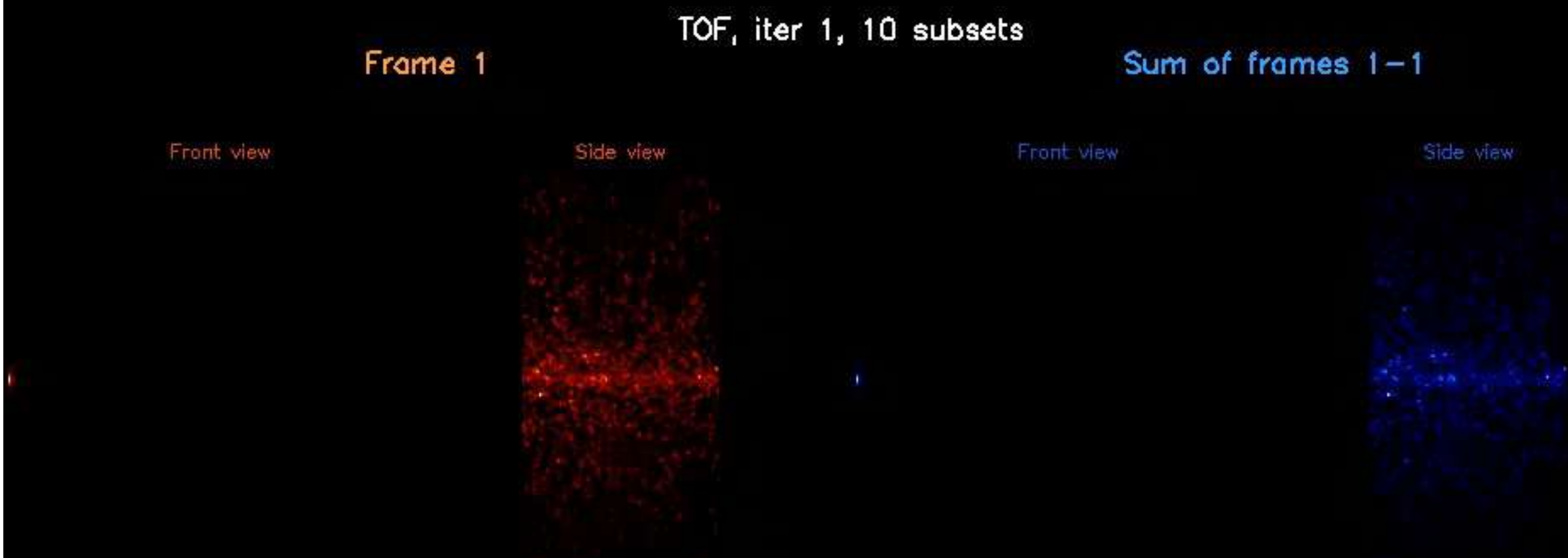


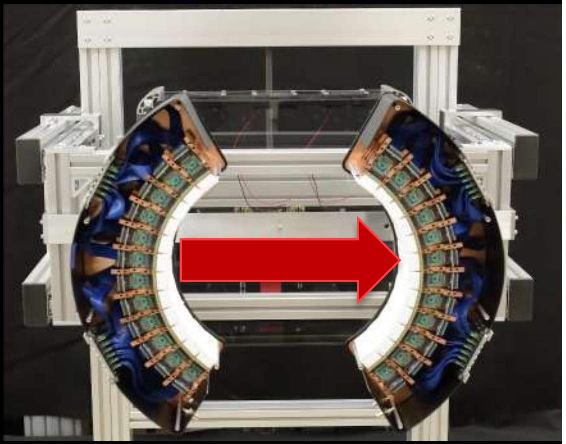
Calibration with ^{68}Ge line source (v sweep)





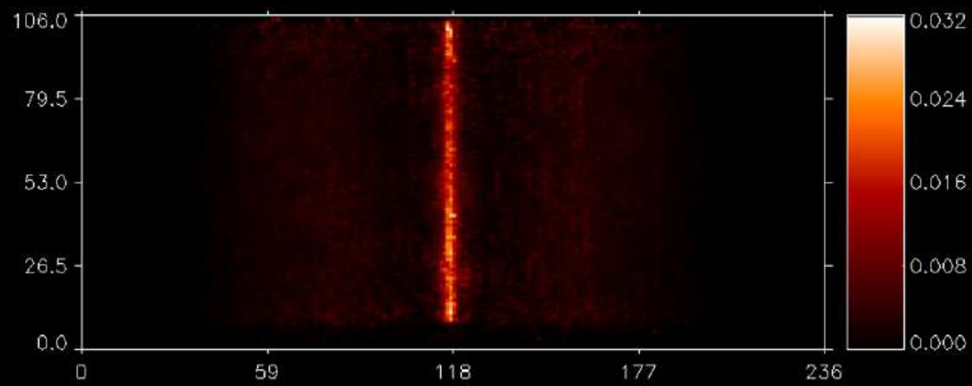
Calibration with ^{68}Ge line source (h sweep)



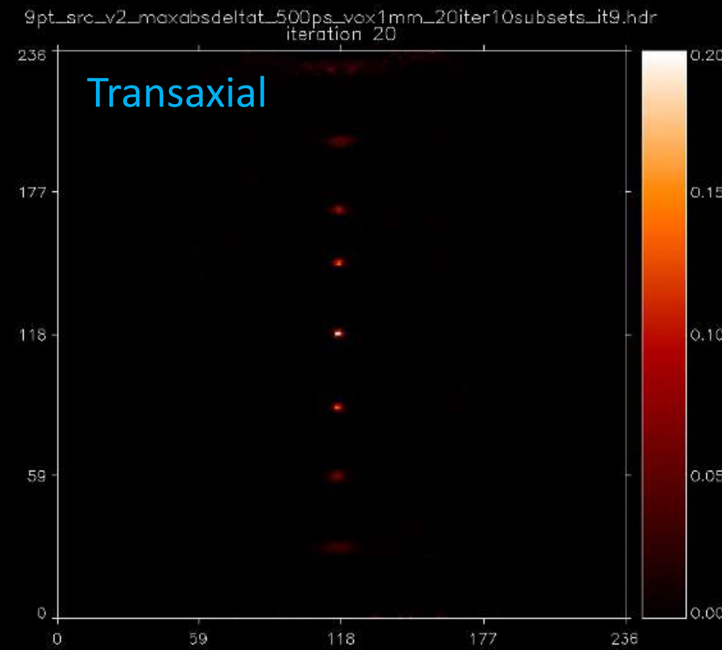


calibrations with linear ^{68}Ge source

Coronal

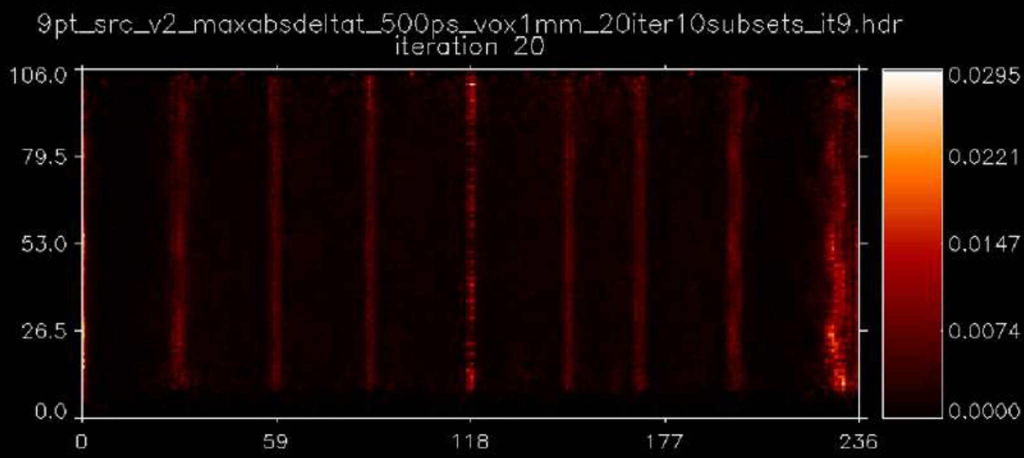


^{68}Ge line source moving across detector FOV



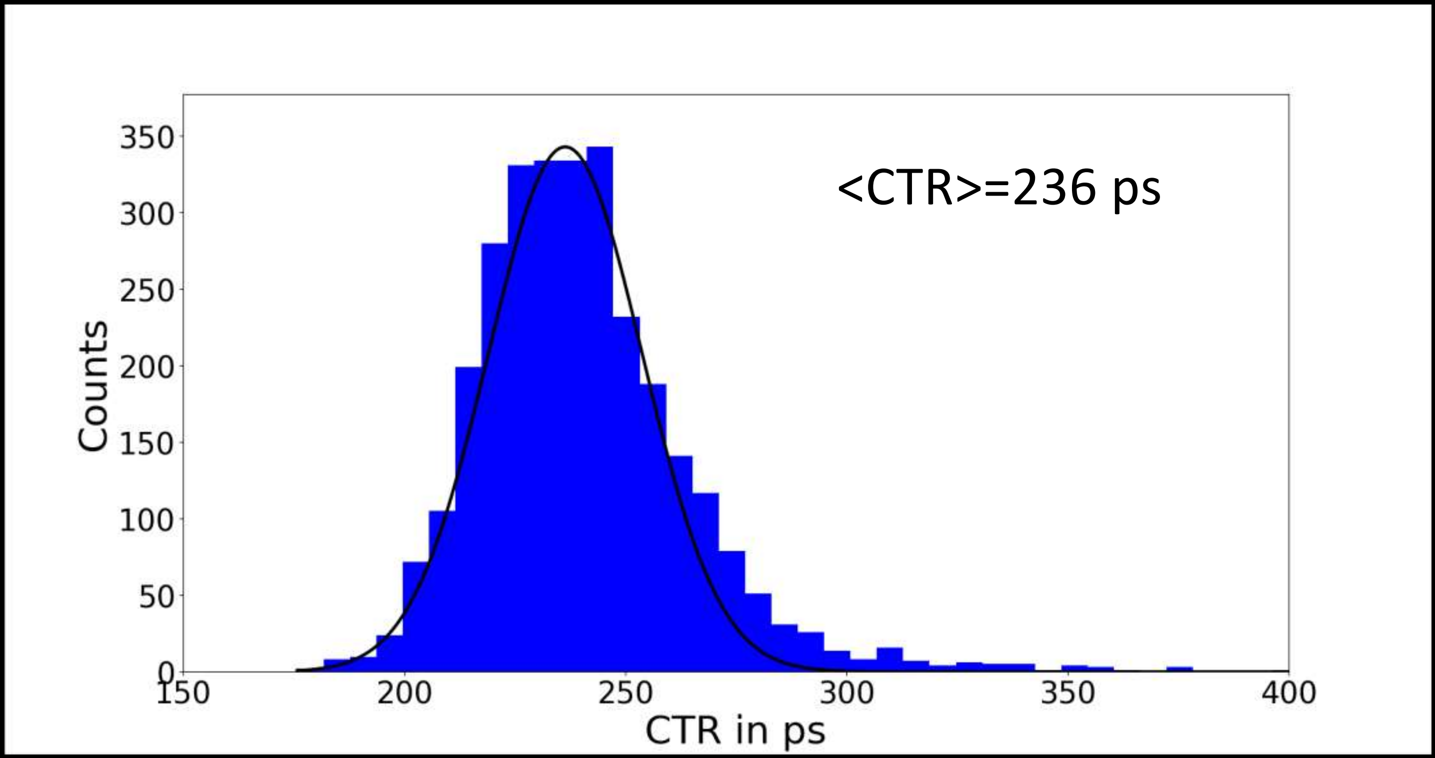
PRELIMINARY! Pre-calibrated scanner data…

Sagittal



60

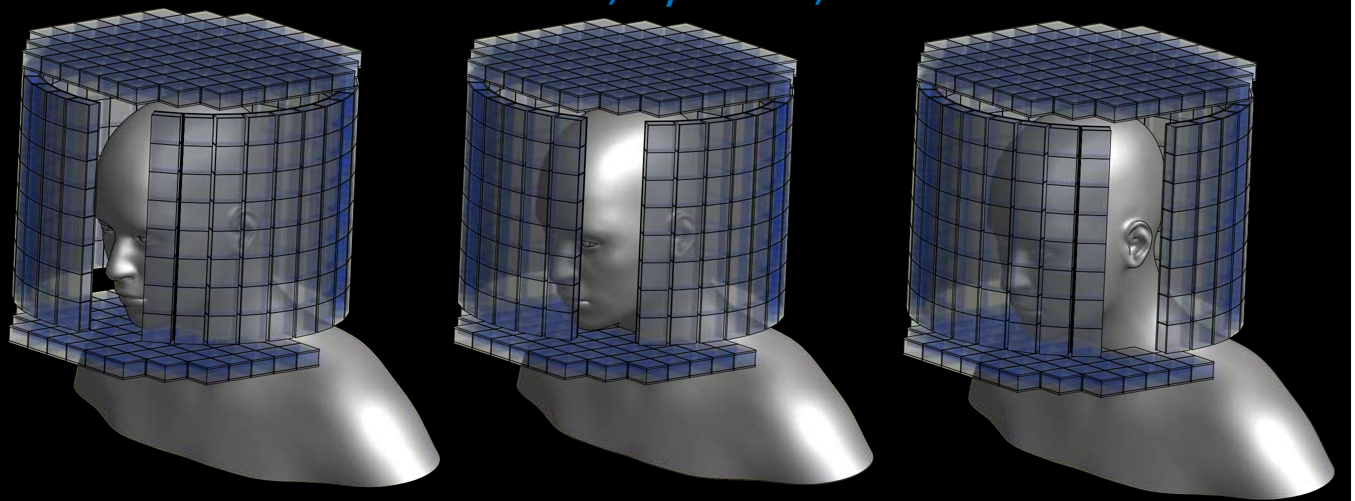
Current tests: full scanner CTR (Part of ongoing Threshold Optimization)

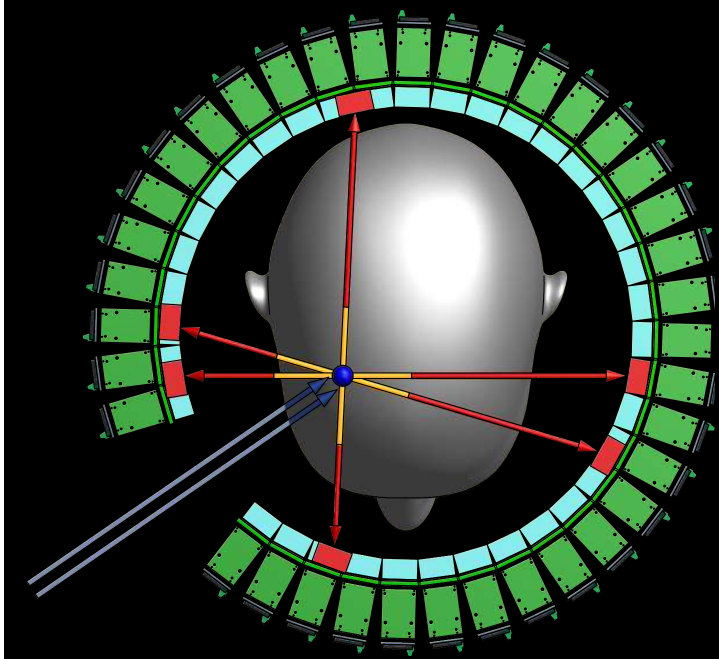


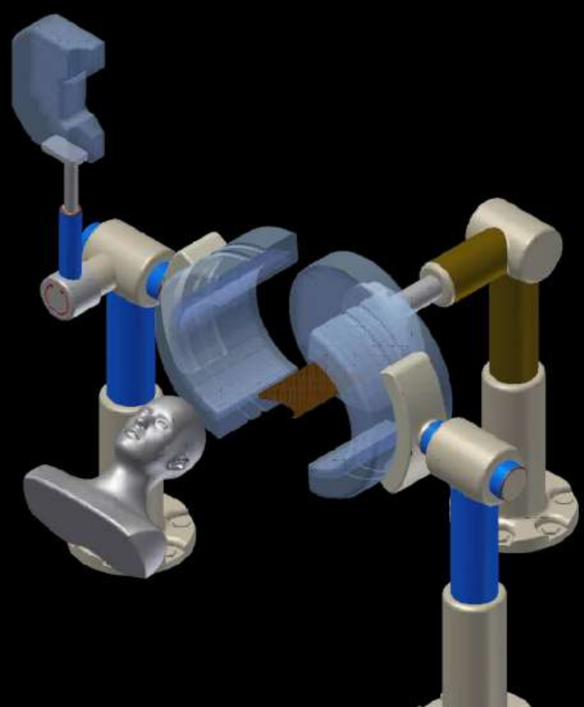
In-beam PET for Proton Therapy

C^3 = crown, cylinder, chin

PET-Image-driven therapy?
PT and radiopharmaceuticals?







FLASH effect
and our recent FLASH experiments

The FLASH effect

❑ Conventional treatment

(fractions) day 1 day 2 day 3 .... day 29 day 30

- each day: a dose of 2 Grays delivered over a few minutes (1 Gy = 1 J/1 kg)
- total of 60 Gy / treatment
- (mostly) no checks while the treatment is ongoing

❑ Recent (re?)discovery (pre-clinical, w/ animals)

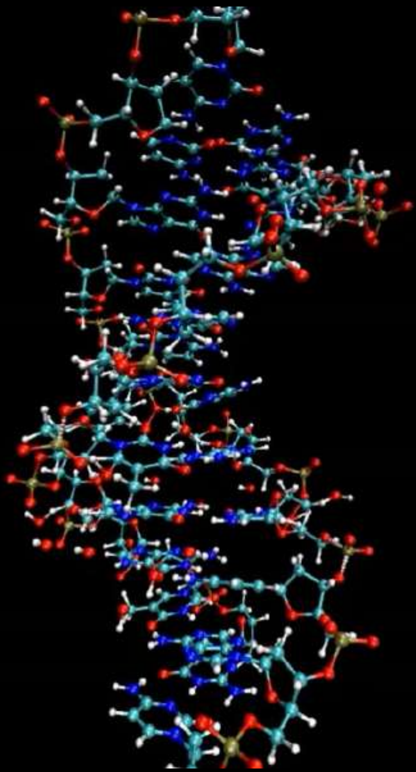
- compress the entire treatment to 1 fraction delivered in less than a second (FLASH)
- instantaneous dose 100-1000 larger
- appears as effective in eradicating cancer as conventional irradiation
- spares healthy tissue much better
- expect much less post-radiation toxicity (post-radiation "side effects")
- the effect is not understood

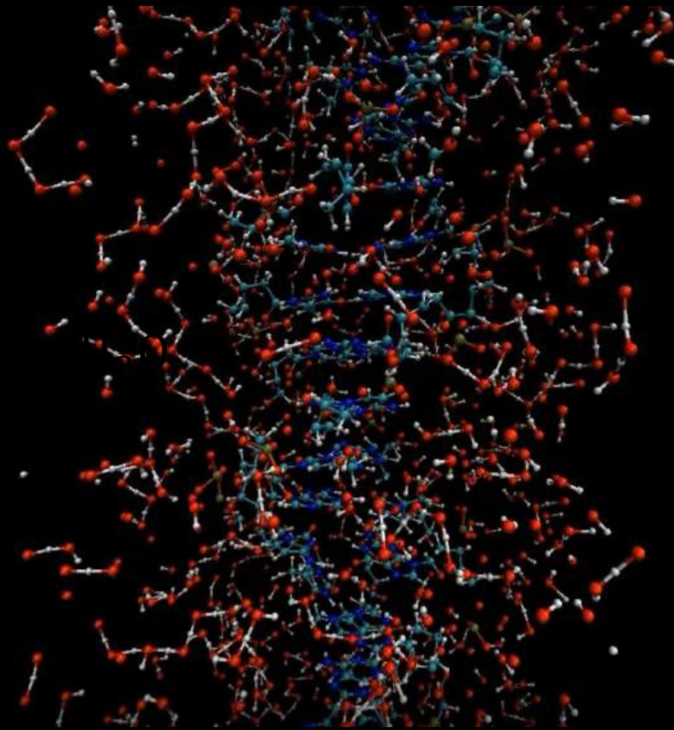
❑ Un-escapable conclusion

- we are missing some fundamentals !!!
- perhaps a large fraction of radiation patients can receive a better treatment

Theoretical approach...

Atoms color code: C, O, N, H, P





$$OH^- + OH^\cdot \rightarrow {}^\cdot O^- + H_2O$$

R. Abolfath et al., Frontiers in Phys. 2023

FLASH effect is a mystery

→ We *conducted* two FLASH experiments on January 9 and March 5, 2023
(for an NIH proposal)

→ Our goal is to provide an instrument that could elucidate the FLASH effect

Proton Therapy Center at MD Anderson Cancer Center

ocular beam (can be FLASH)

Physics in Medicine & Biology

PAPER • OPEN ACCESS

The first PET glimpse of a proton FLASH beam

F Abouzahr[1], J P Cesar[1], P Crespo[2,3], M Gajda[1], Z Hu[4], W Kaye[5], K Klein[1], A S Kuo[1], S Majewski[1,6], O Mawlawi[7], A Morozov[2], A Ojha[1], F Poenisch[8], J C Polf[5], M Proga[1], N Sahoo[8], J Seco[9,10], T Takaoka[11], S Tavernier[12], U Titt[4], X Wang[8], X R Zhu[8] and K Lang[1] − Hide full author list

Published 7 June 2023 • © 2023 The Author(s). Published on behalf of Institute of Physics and Engineering in Medicine by IOP Publishing Ltd

Physics in Medicine & Biology, Volume 68, Number 12

Citation F Abouzahr *et al* 2023 *Phys. Med. Biol.* **68** 125001

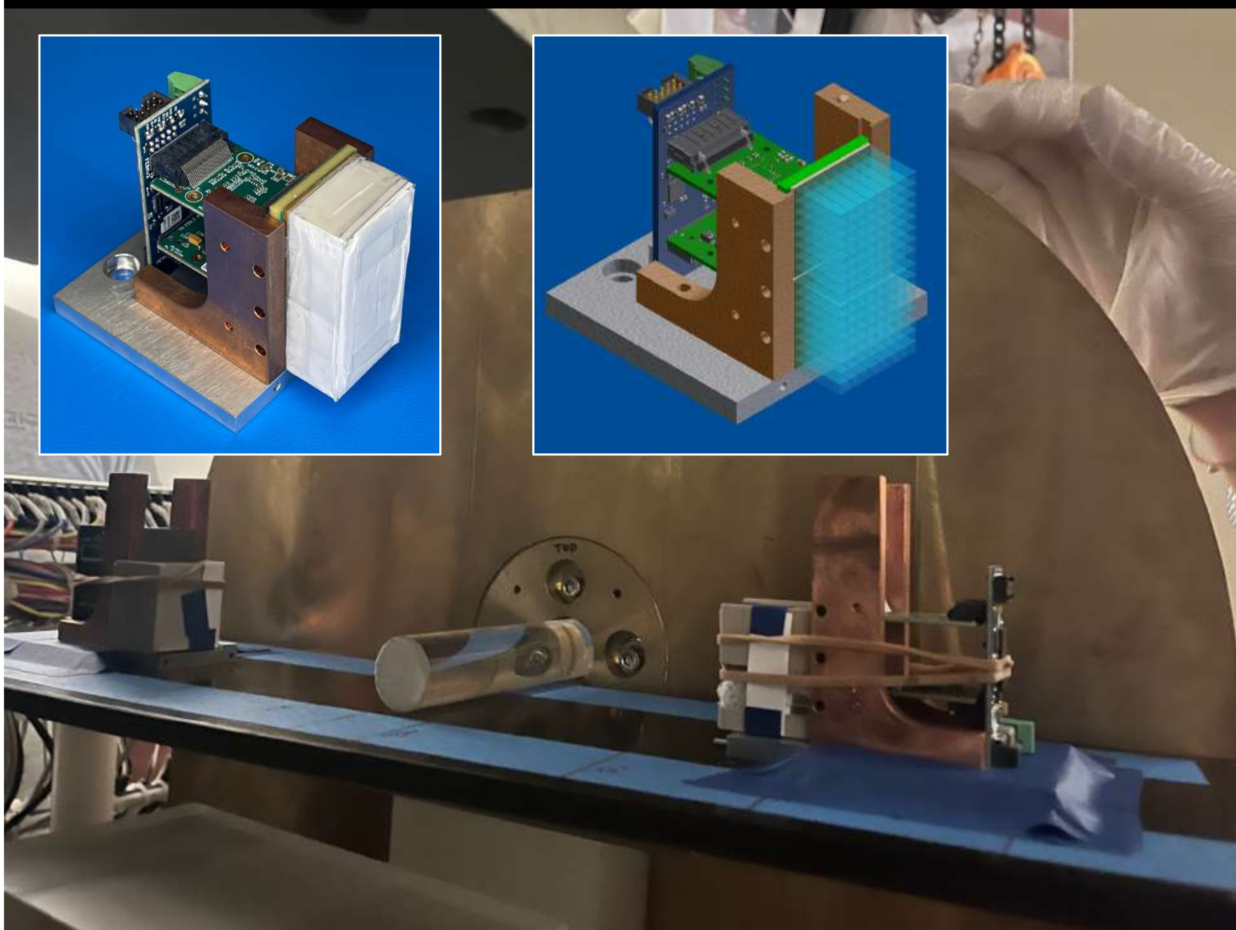
DOI 10.1088/1361-6560/acd29e

> 2500 downloads

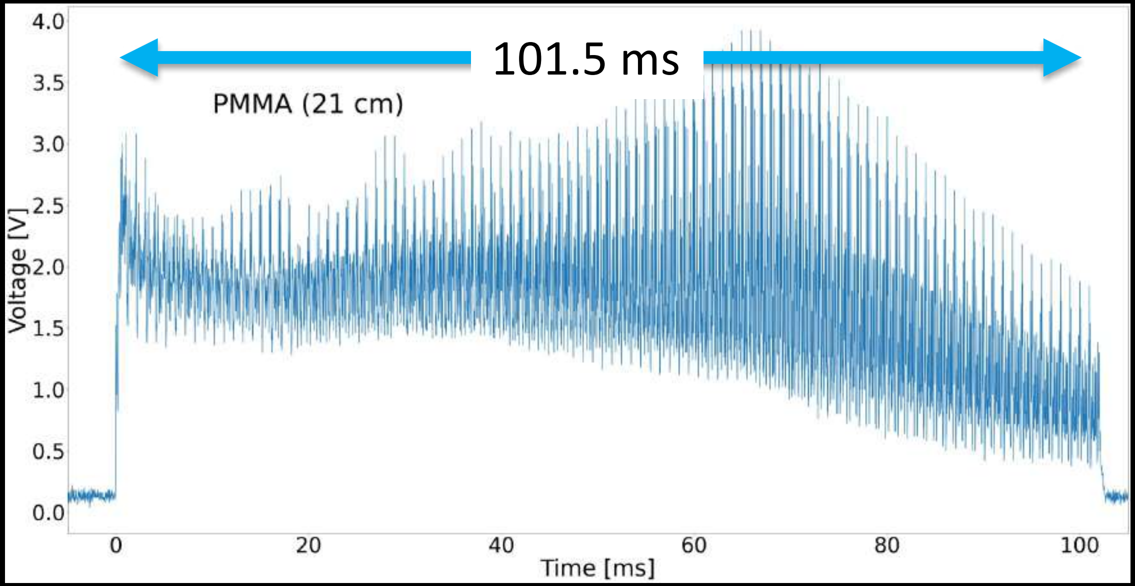
FLASH 1 (JAN 9, 2023)

FLASH 1 (January 9, 2023)

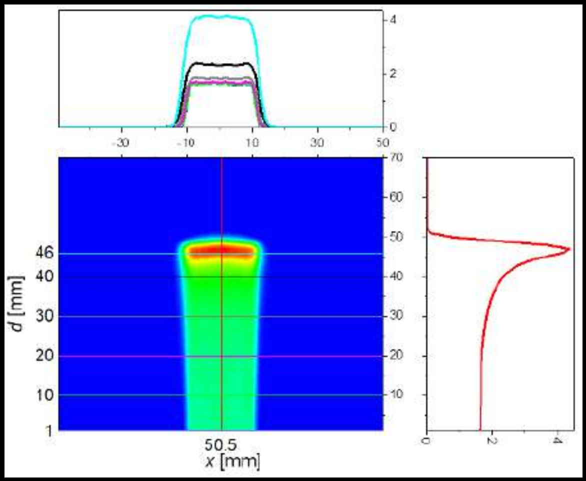
FLASH 1 (January 9, 2023)

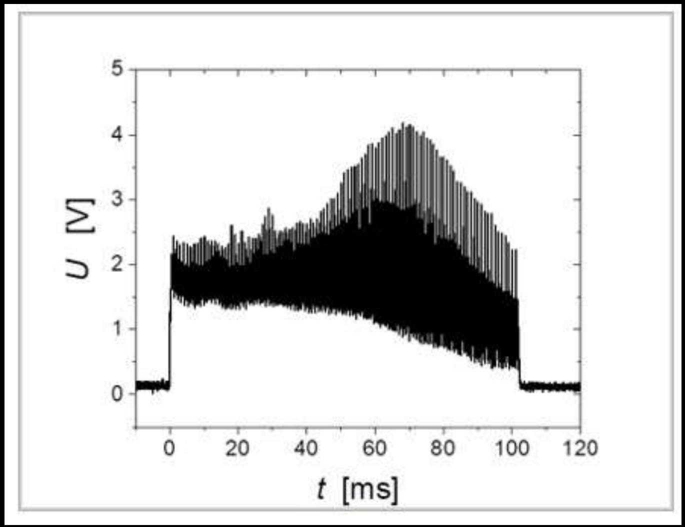


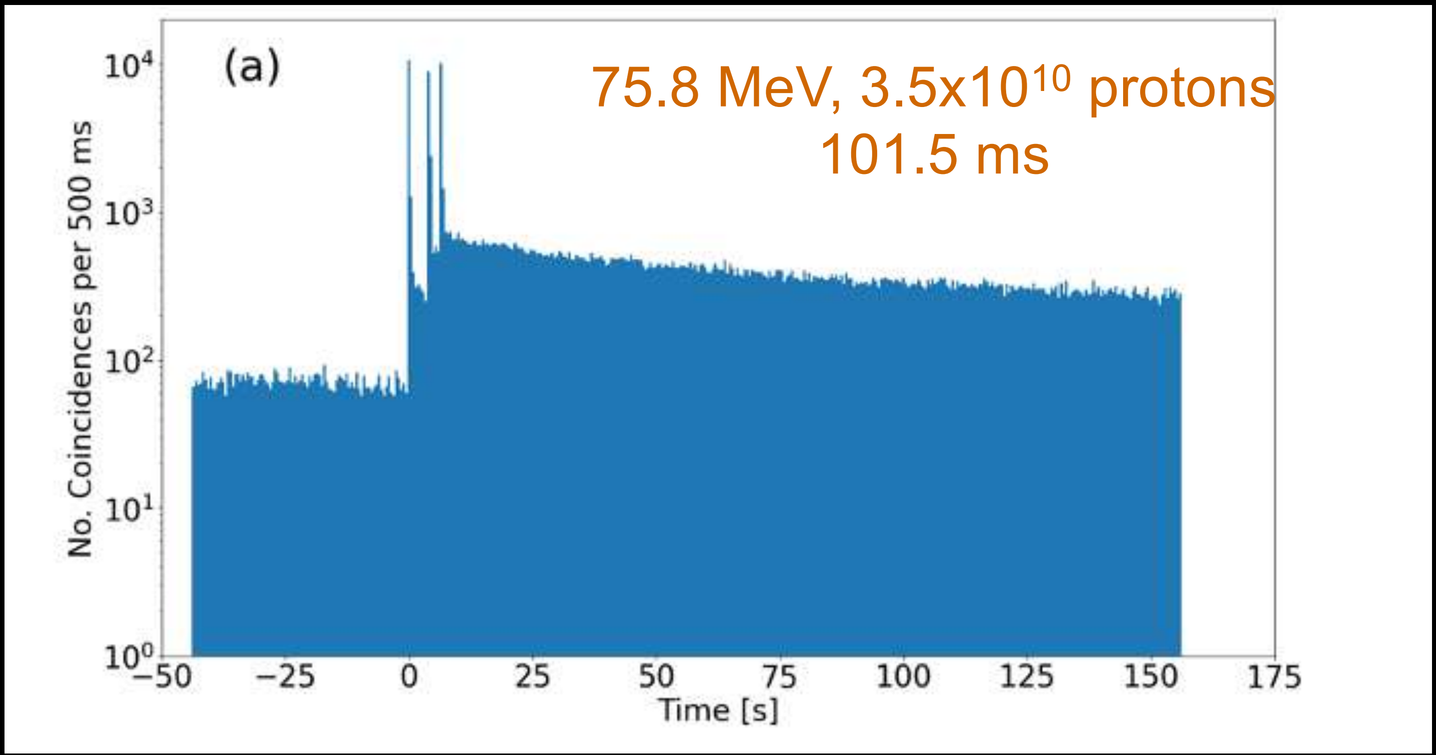
A Hitachi spill (101.5 ms)



FLASH 1 (January 9, 2023)





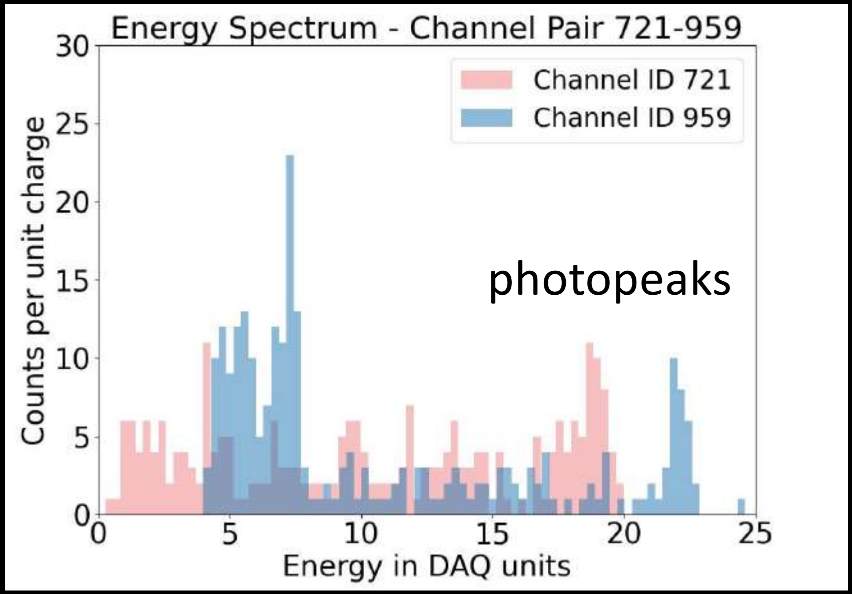


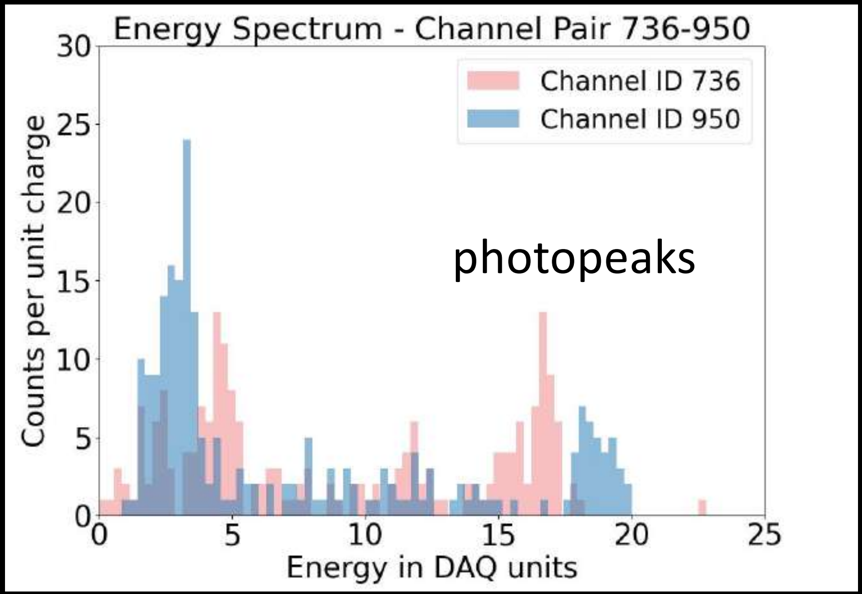
FLASH 1 (January 9, 2023)

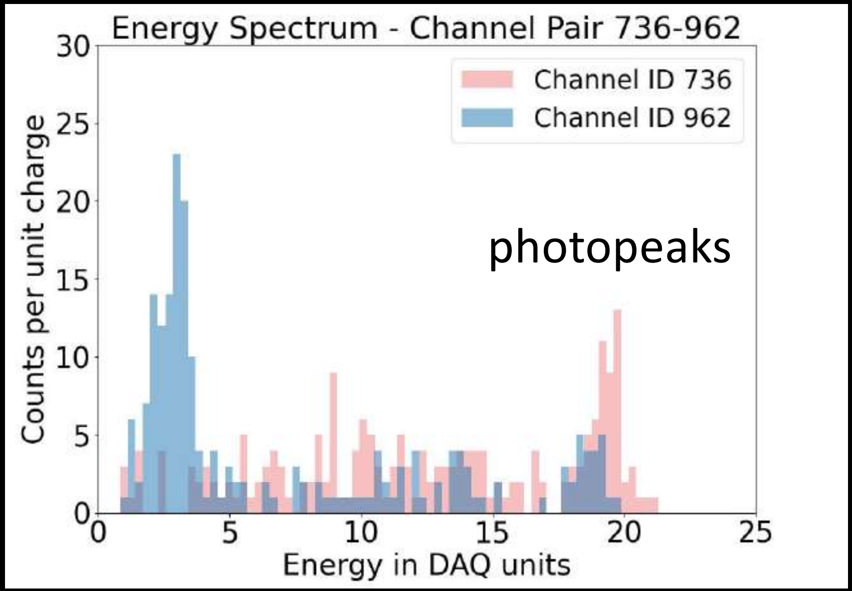
Energy response (post-spill)

3 LOR examples

(LOR = line of response)

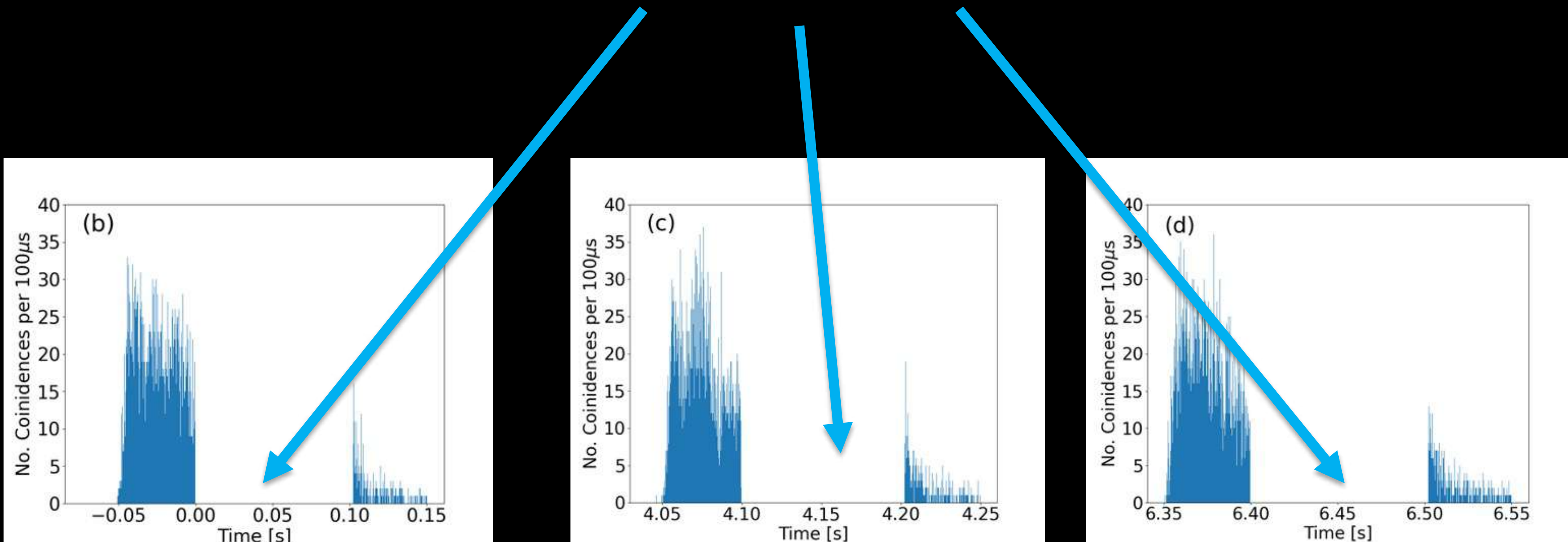






FLASH 1 (January 9, 2023)

in-spill deadtime



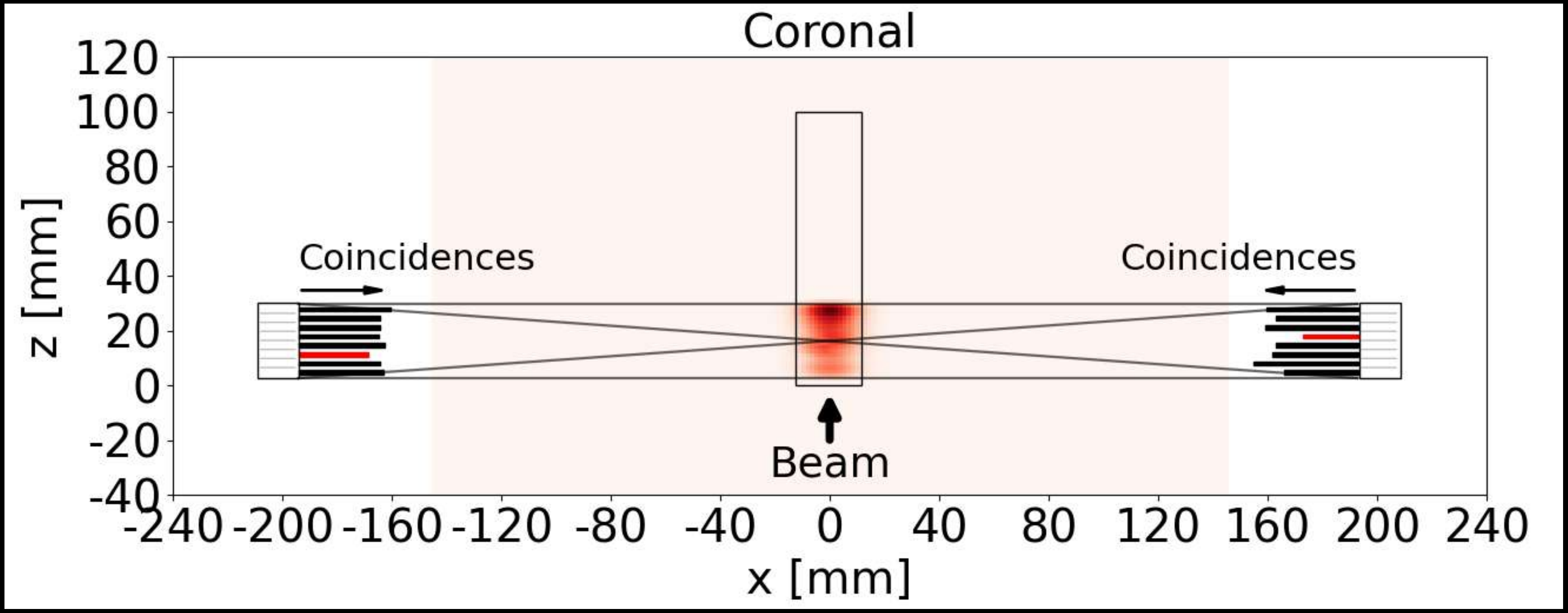
FLASH spill 1

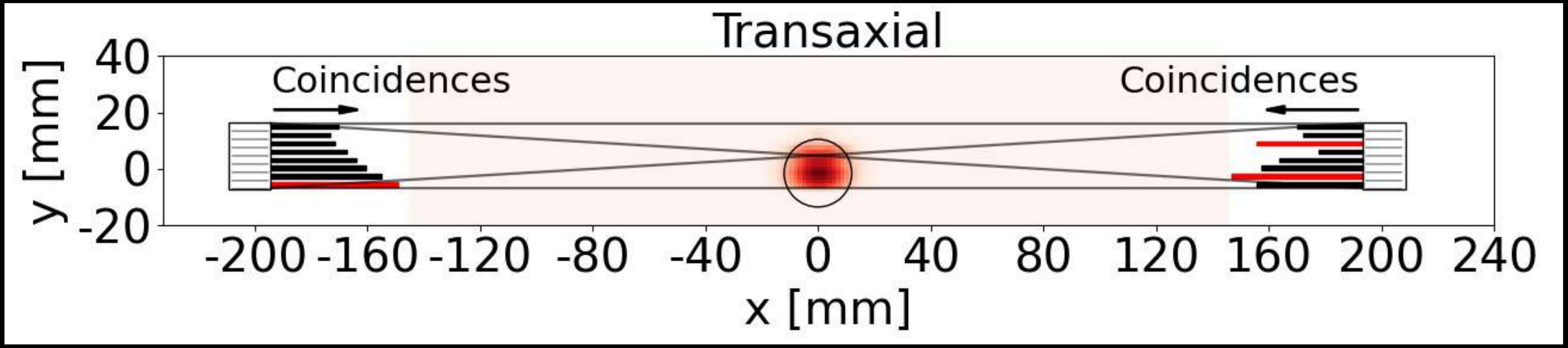
FLASH spill 2

FLASH spill 3

CASToR Imaging and our "dosimetry"

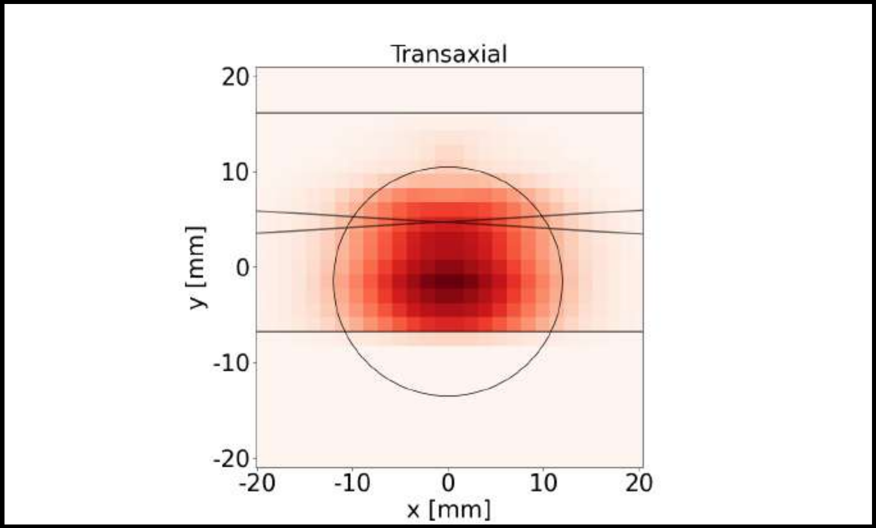
FLASH 1 (January 9, 2023)

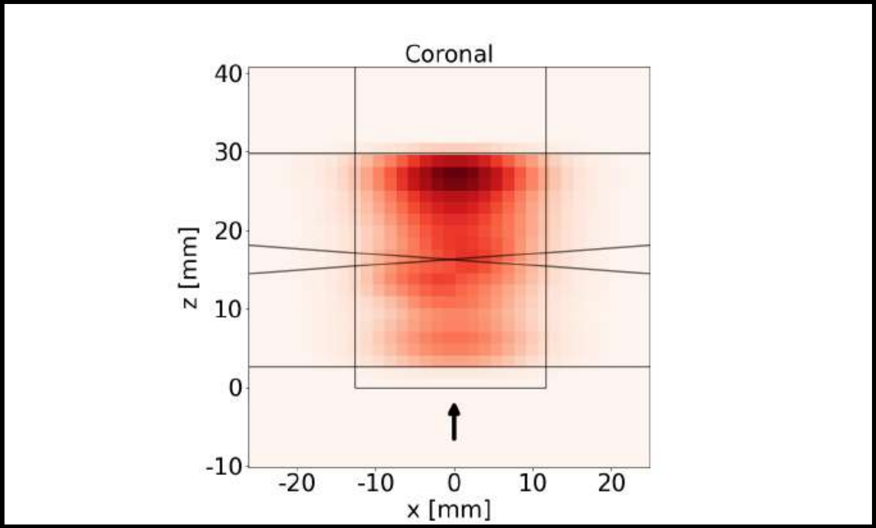


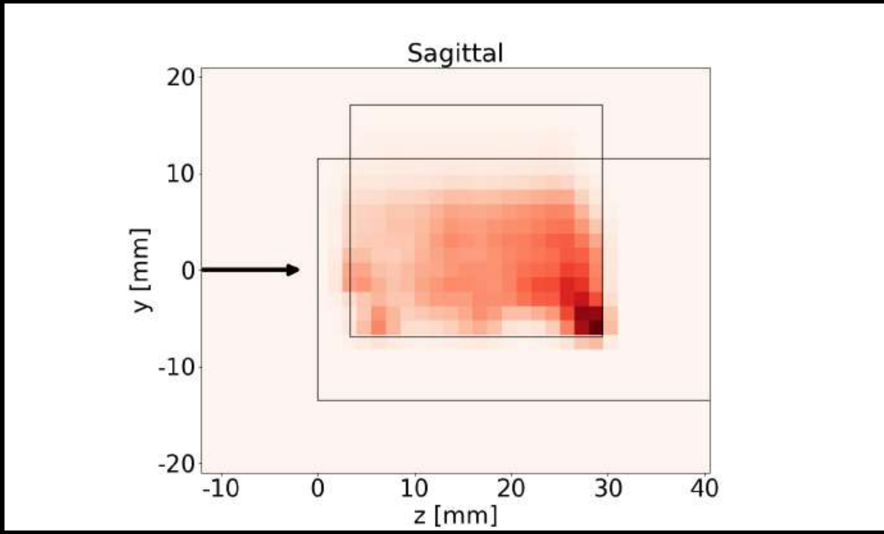


CASToR Imaging (magnified)

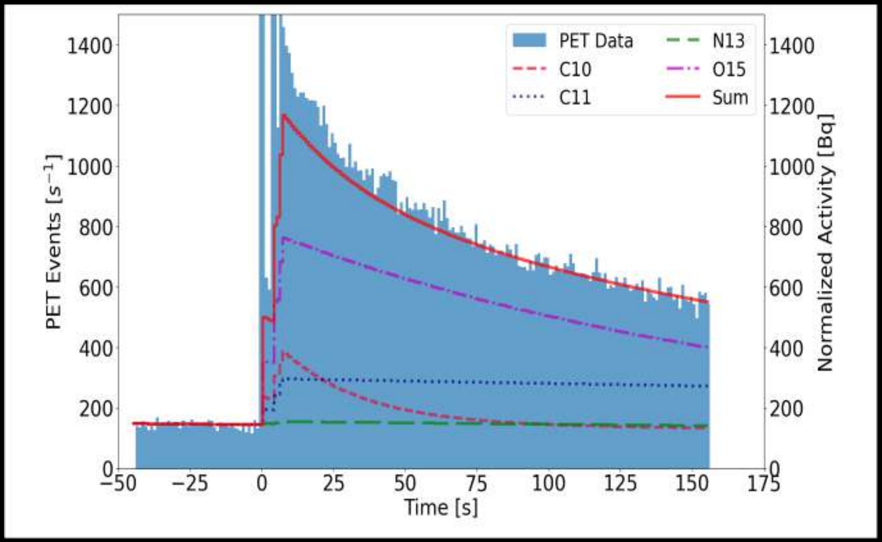
FLASH 1 (January 9, 2023)

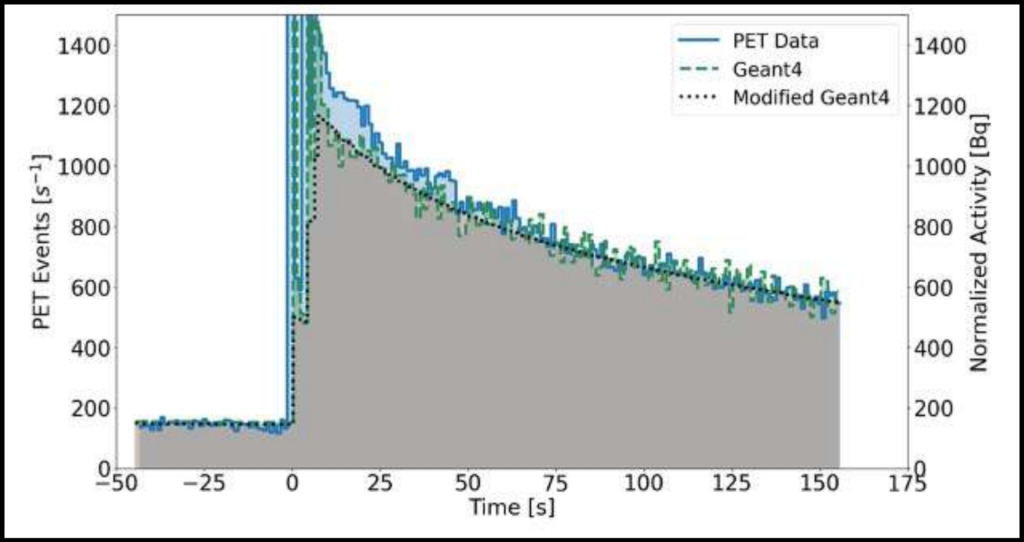


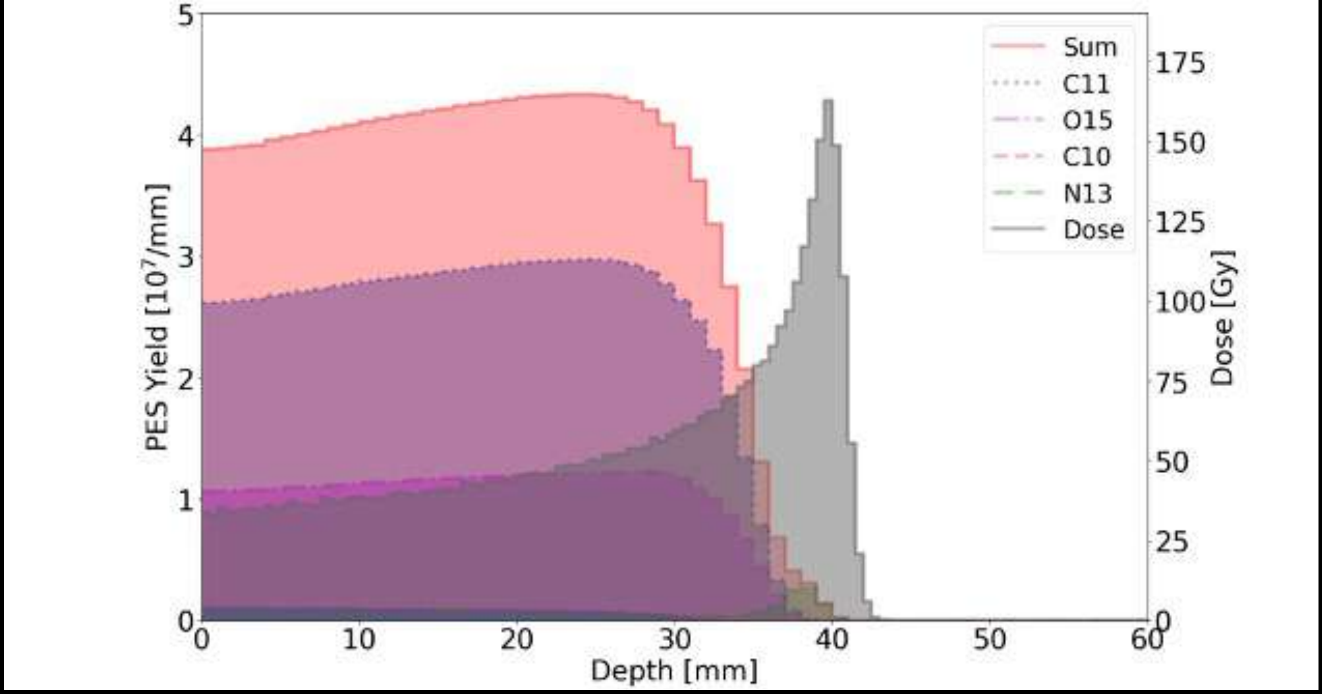




FLASH simulations and fits







Physics in Medicine & Biology

PAPER • OPEN ACCESS

The first probe of a FLASH proton beam by PET

F Abouzahr[1], J P Cesar[1], P Crespo[2,3], M Gajda[1], Z Hu[4], K Klein[1], A S Kuo[1], S Majewski[1,5], O Mawlawi[6], A Morozov[2], A Ojha[1], F Poenisch[7], M Proga[1], N Sahoo[7], J Seco[8,9], T Takaoka[10], S Tavernier[11], U Titt[4], X Wang[7], X R Zhu[7] and K Lang[1]

− Hide full author list

Published 23 November 2023 •

Physics in Medicine & Biology, Volume 68, Number 23

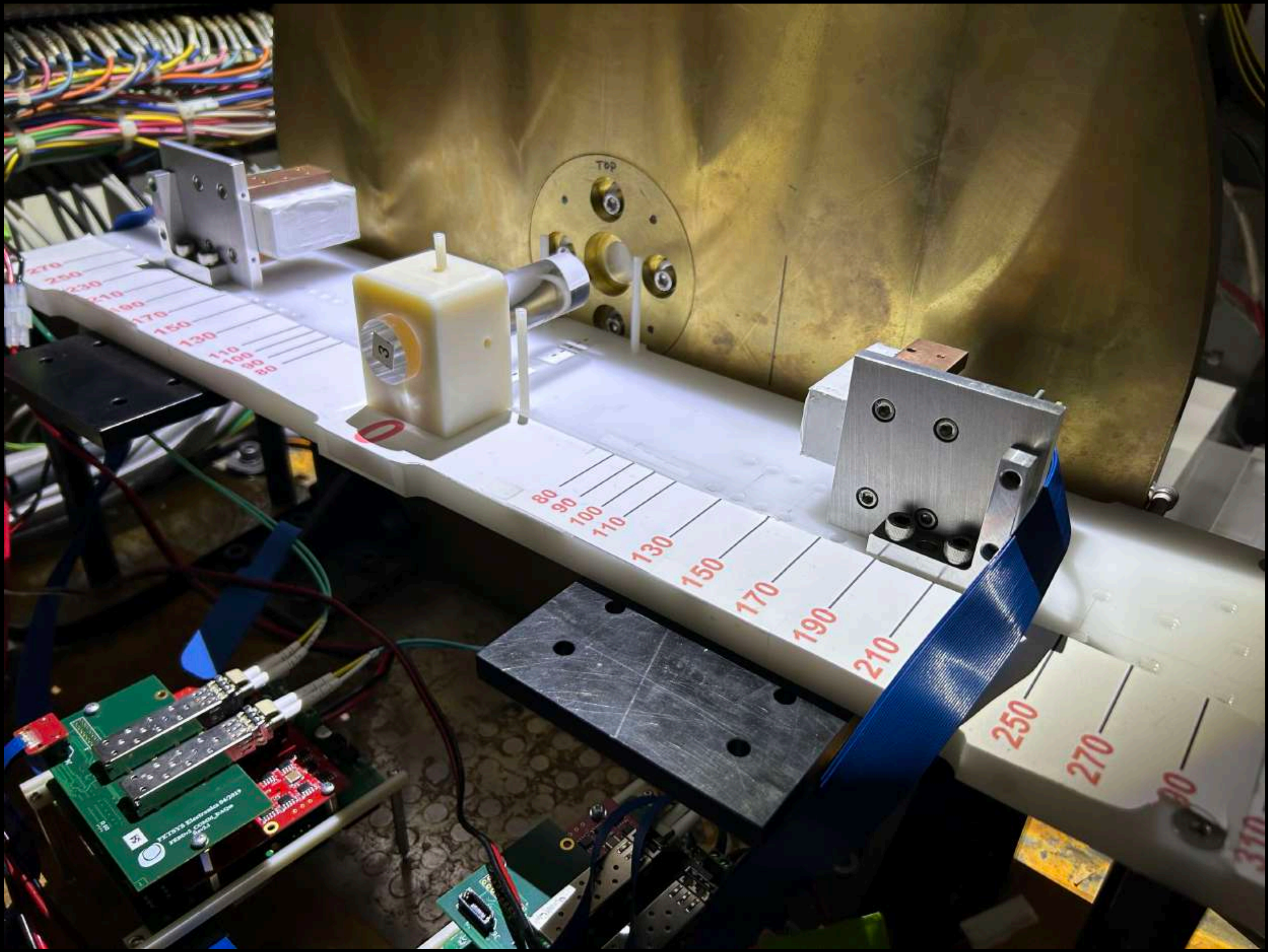
Citation F Abouzahr *et al* 2023 *Phys. Med. Biol.* **68** 235004

DOI 10.1088/1361-6560/ad0901

> 1,100 downloads

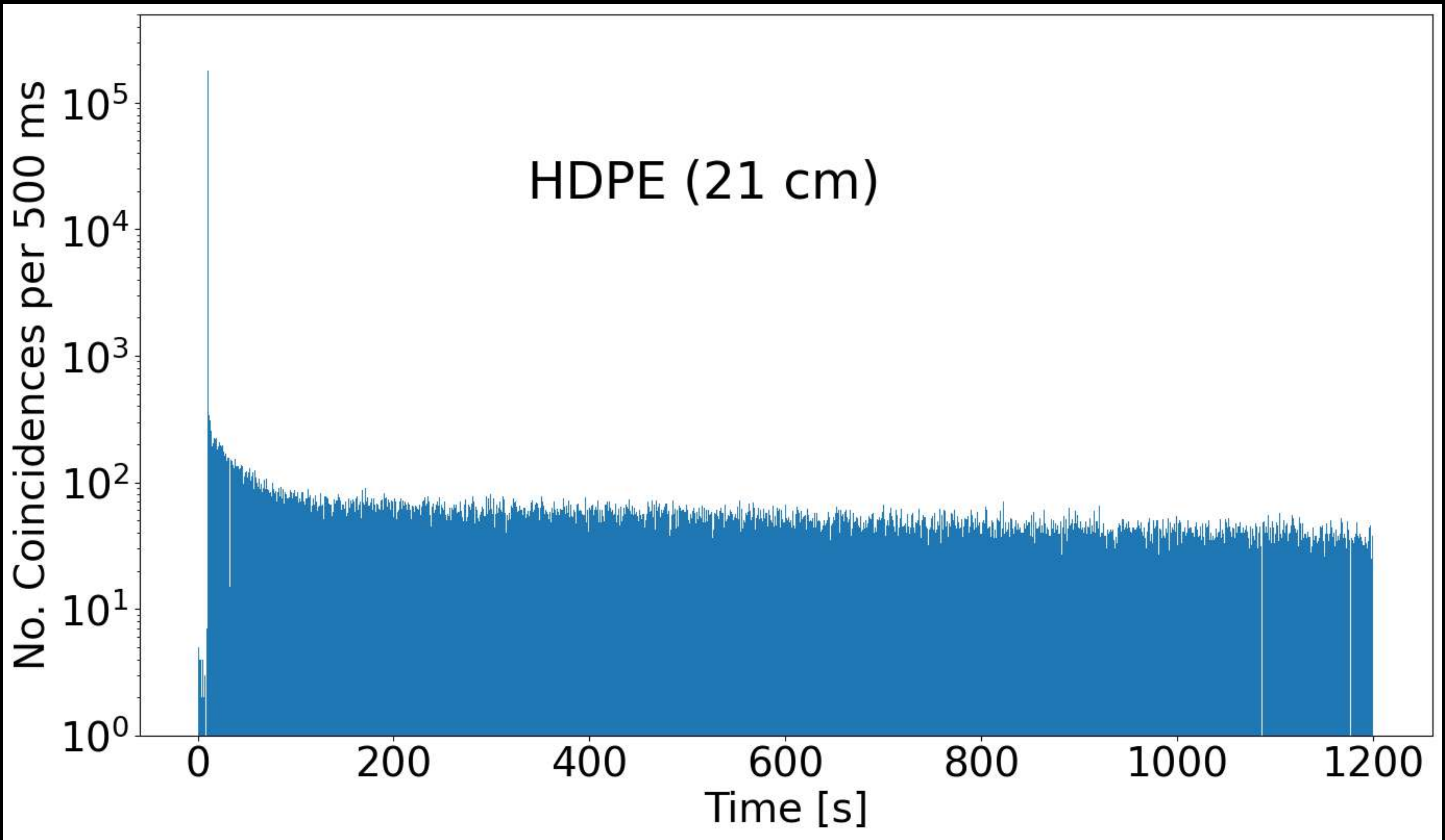
FLASH 2 (MAR 5, 2023)

75.8 MeV, 3.5x10^{10} protons, 101.5 ms



Run 5 – HDPE (21 cm)

A typical time spectrum

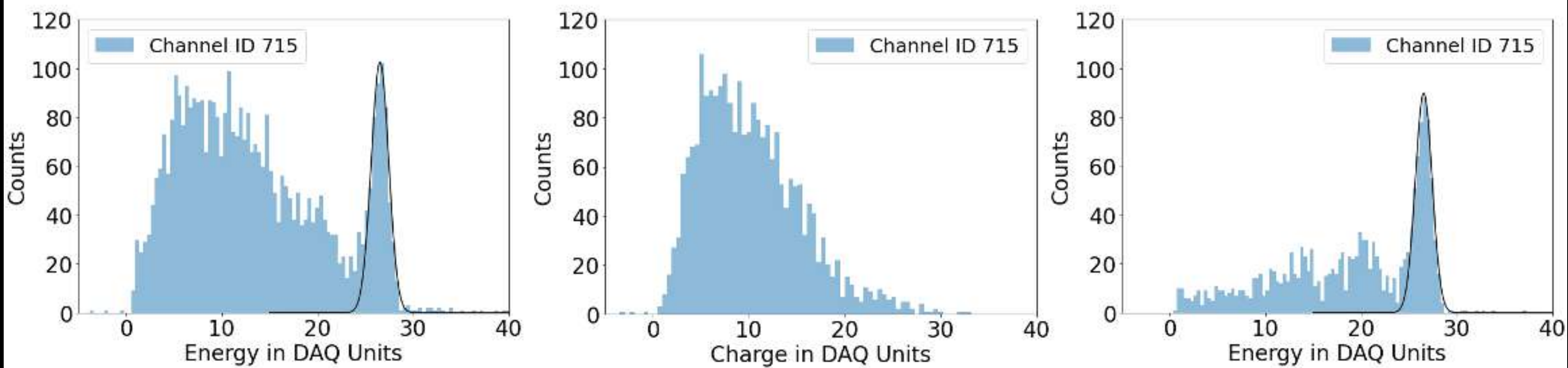


PMMA (21 cm)

Energy spectra

Below we plot the aggregate coincidence energy spectrum for one channel (715) from the PMMA 21 cm run for the entire run, in-spill data only, and post-spill data only.

Entire Run | In-Spill | Post-Spill

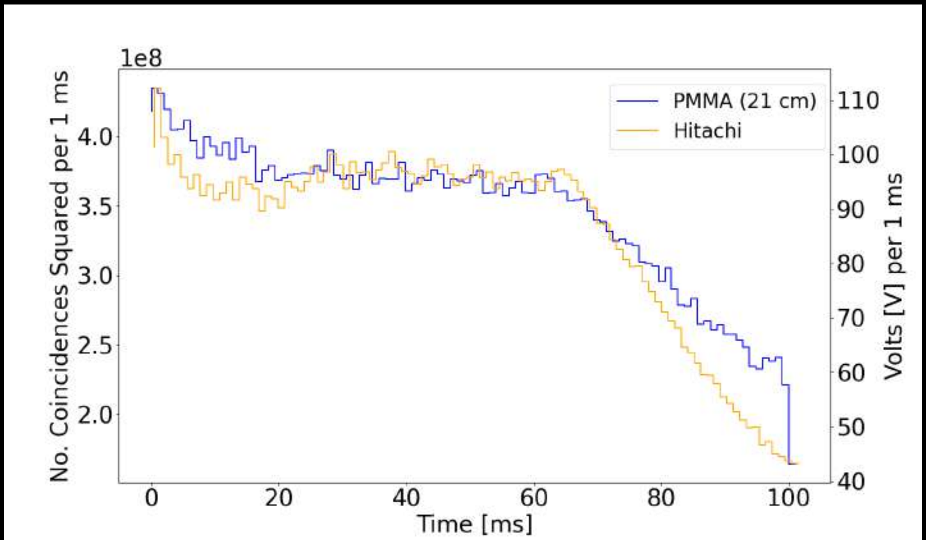


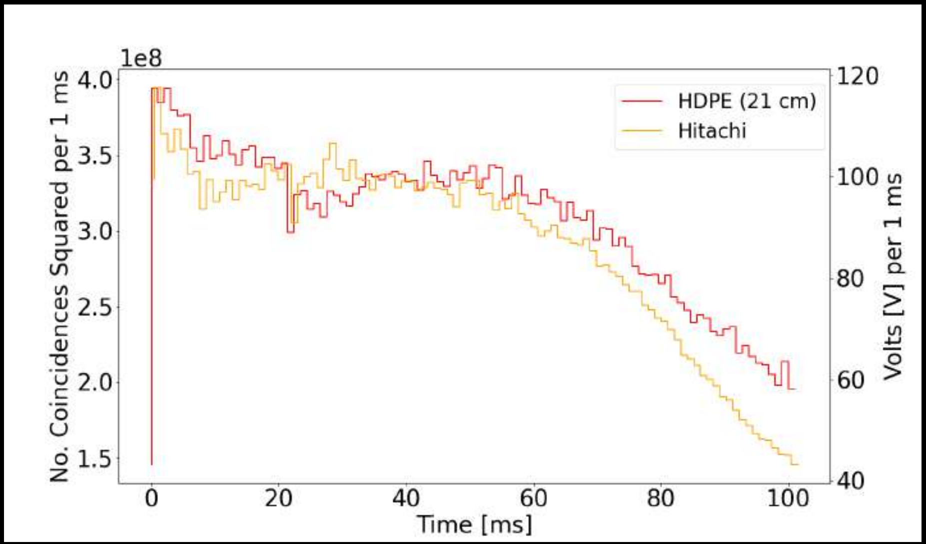
Entire Run: Total Counts: 3985, Photopeak Counts: 649

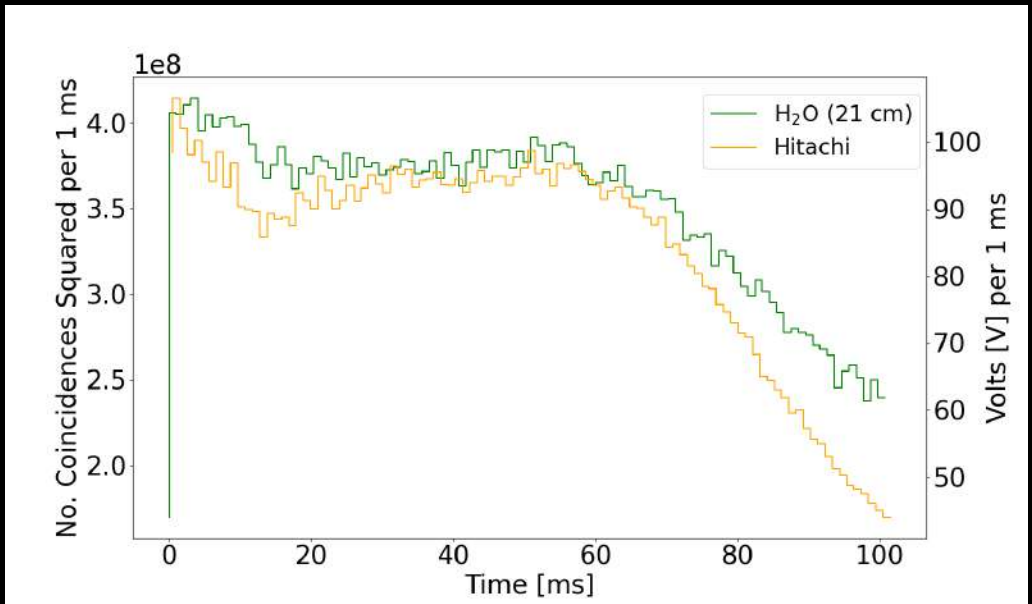
In-Spill: Total Counts: 2377, Photopeak Counts: n/a

Post-Spill: Total Counts: 1491, Photopeak Counts: 572

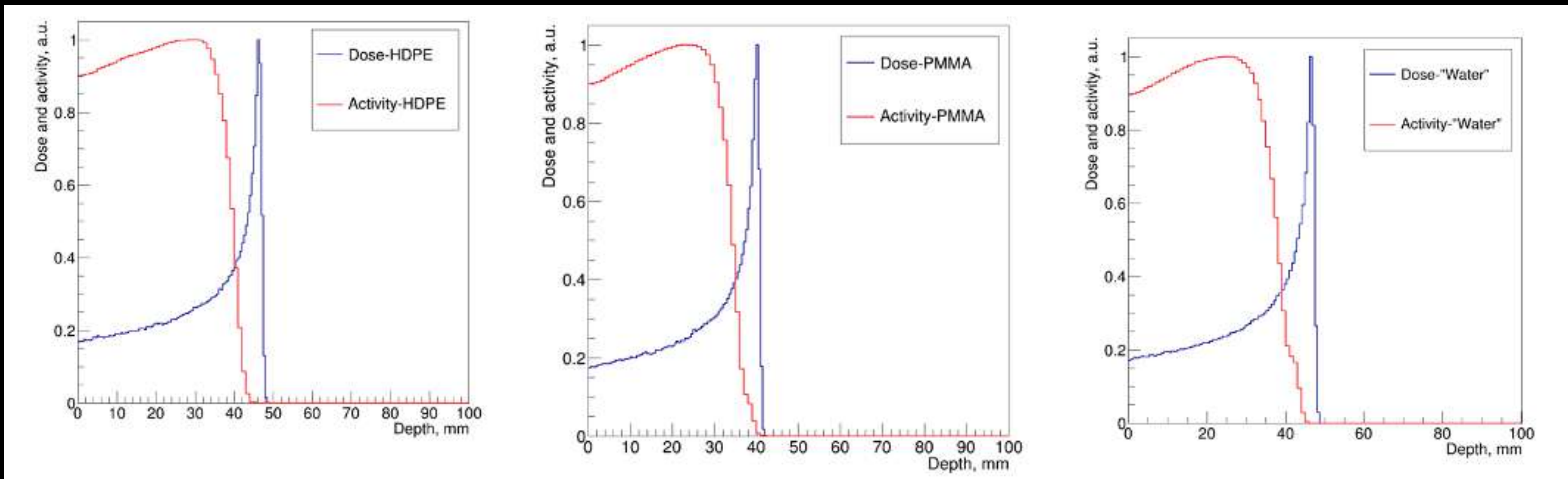
In-spill random coincidences



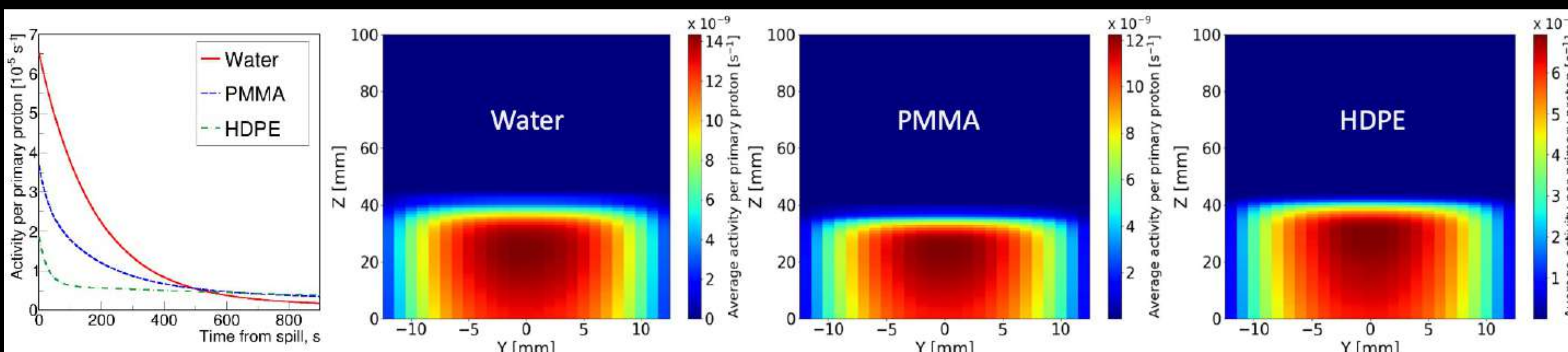




Ranges

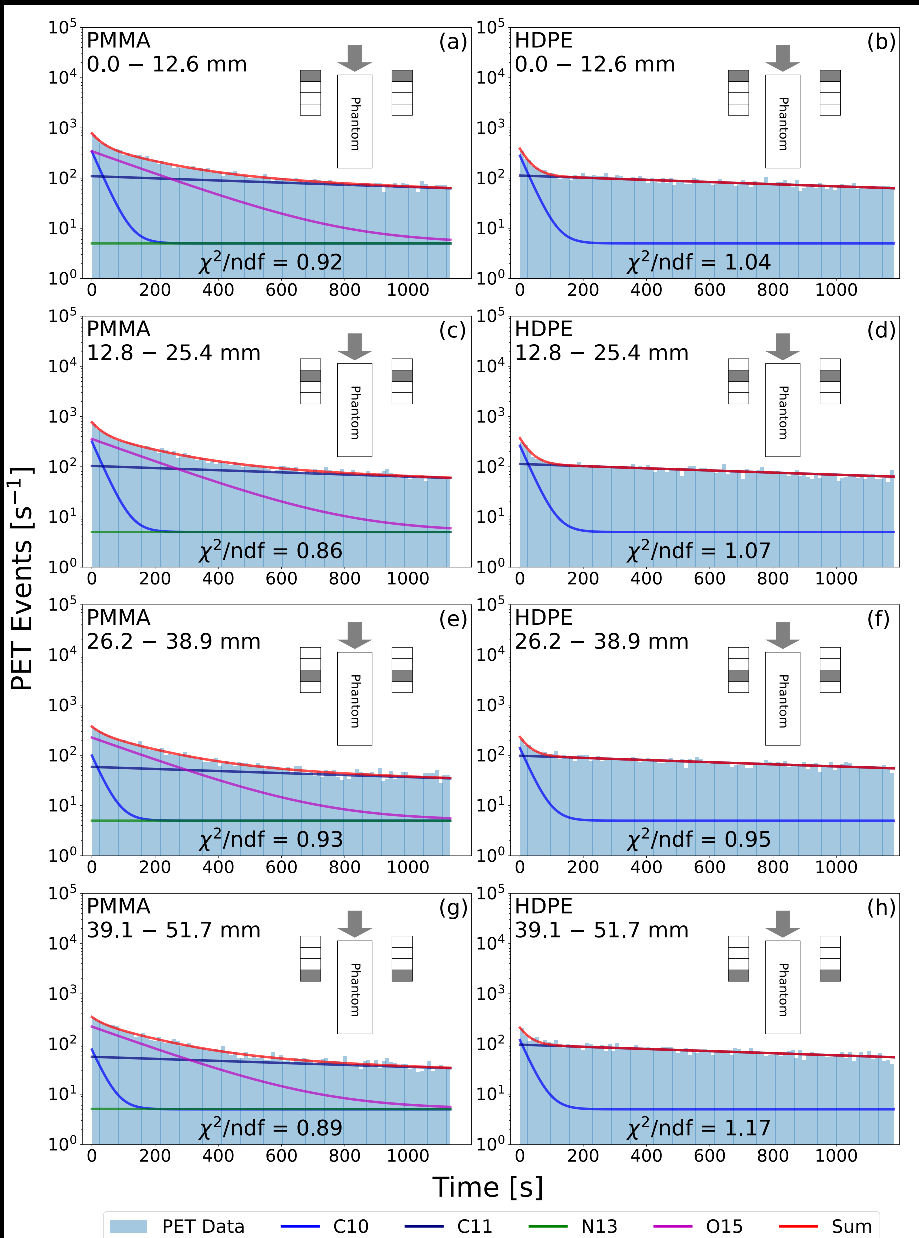


Dose-HDPE
Activity-HDPE
Dose and activity, a.u.
Depth, mm
Dose-PMMA
Activity-PMMA
Dose and activity, a.u.
Depth, mm
Dose-"Water"
Activity-"Water"
Dose and activity, a.u.
Depth, mm

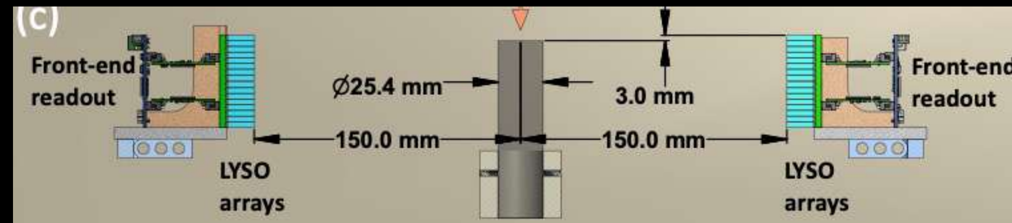


Water
PMMA
HDPE
Activity per primary proton [10⁻⁵ s⁻¹]
Time from spill, s
Water
PMMA
HDPE
Z [mm]
Y [mm]
Average activity per primary proton [s⁻¹]
x 10⁻⁹

Abundance as a function of depth

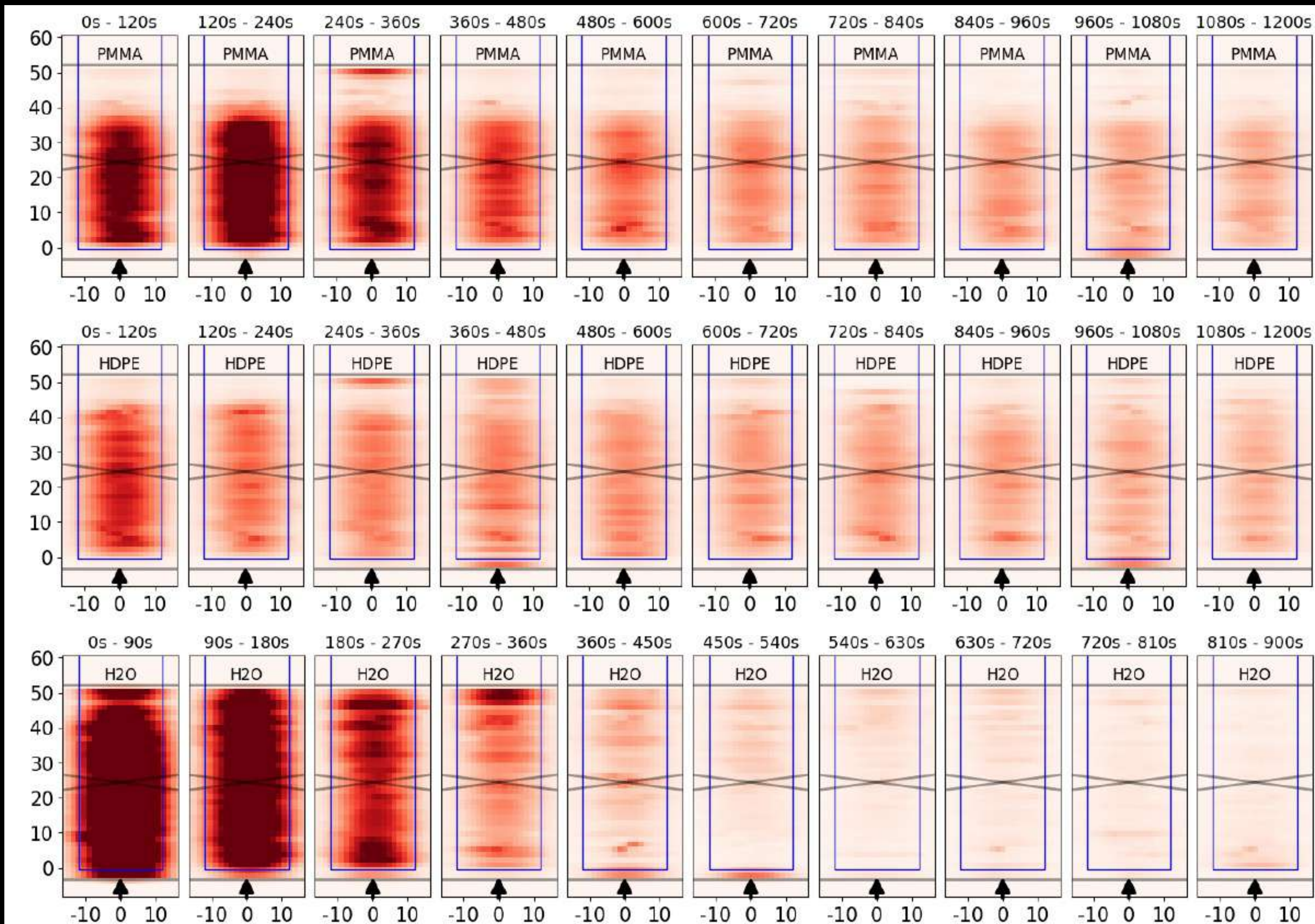


Beam

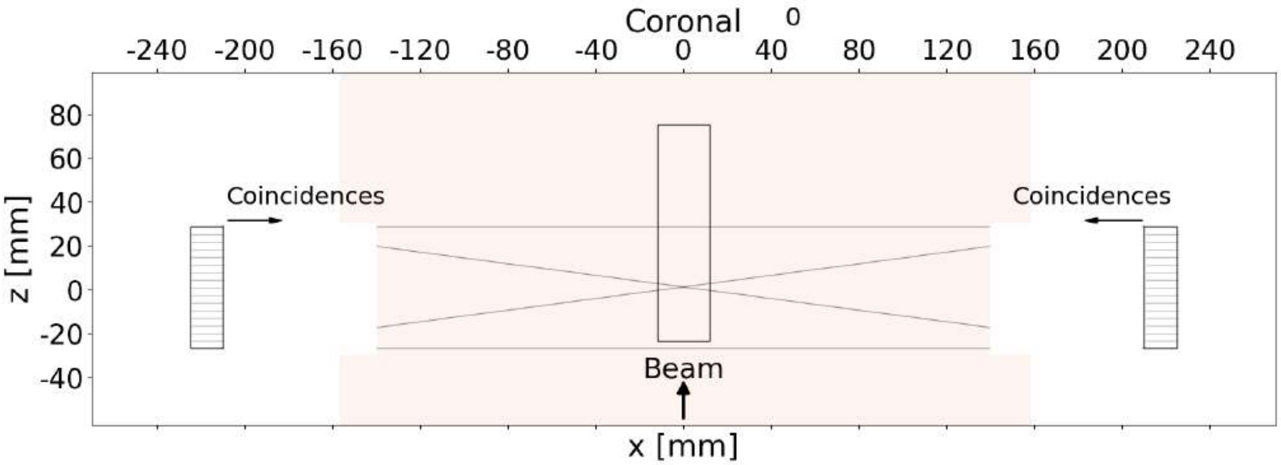


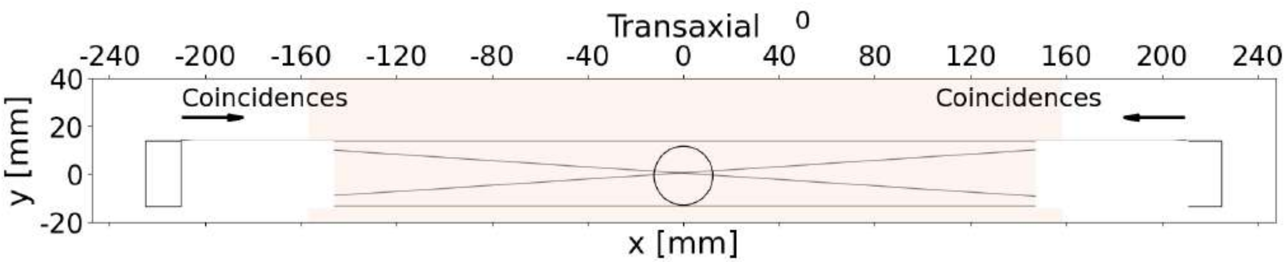
Phantom $T_{1/2}$[s] →	^{10}C 19.3	^{11}C 1220.4	^{15}O 122.4	^{13}N 597.9	χ^2/ndf
PMMA Depth					
0.0 - 12.6 mm	0.43	0.13	0.43	< 0.01	0.92
12.8 - 25.4 mm	0.41	0.13	0.46	< 0.01	0.86
26.2 - 38.9 mm	0.25	0.15	0.60	< 0.01	0.93
38.1 - 51.7 mm	0.21	0.15	0.64	< 0.01	0.89
HDPE Depth					
0.0 - 12.6 mm	0.72	0.28	–	–	1.04
12.8 - 25.4 mm	0.70	0.30	–	–	1.07
26.2 - 38.9 mm	0.59	0.41	–	–	0.95
38.1 - 51.7 mm	0.55	0.45	–	–	1.17

Time evolution of activations – PET imaging

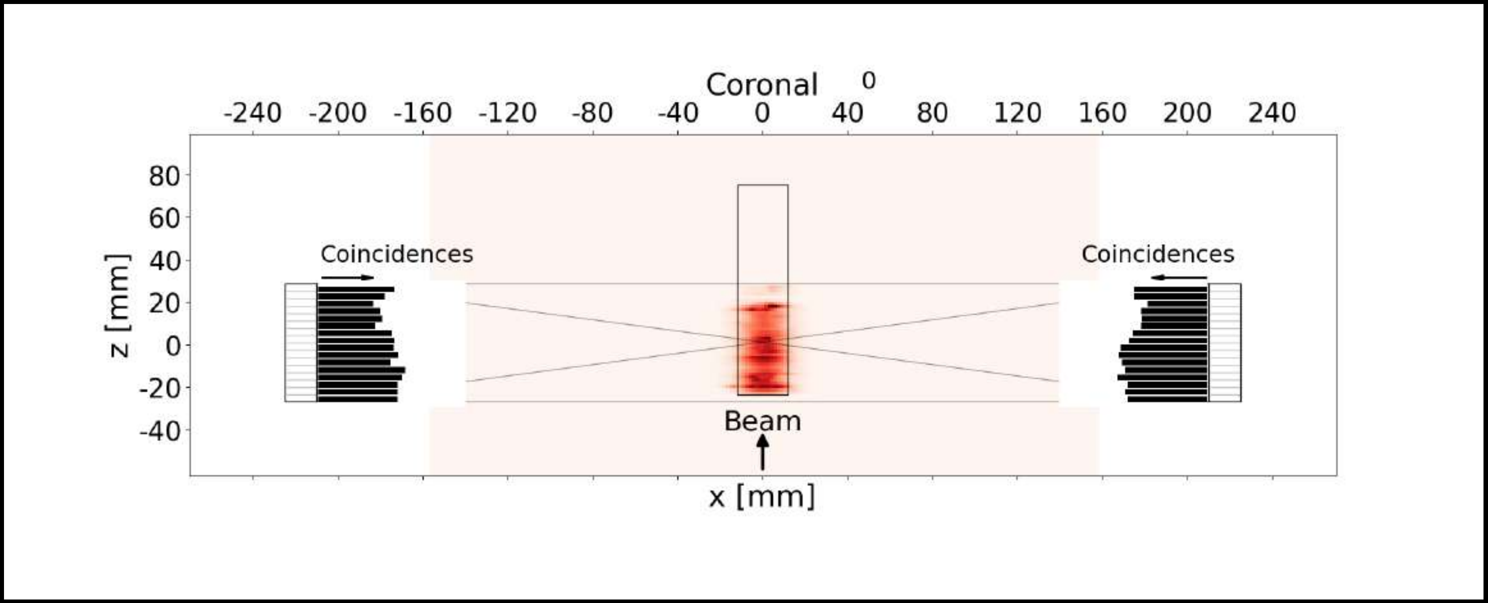


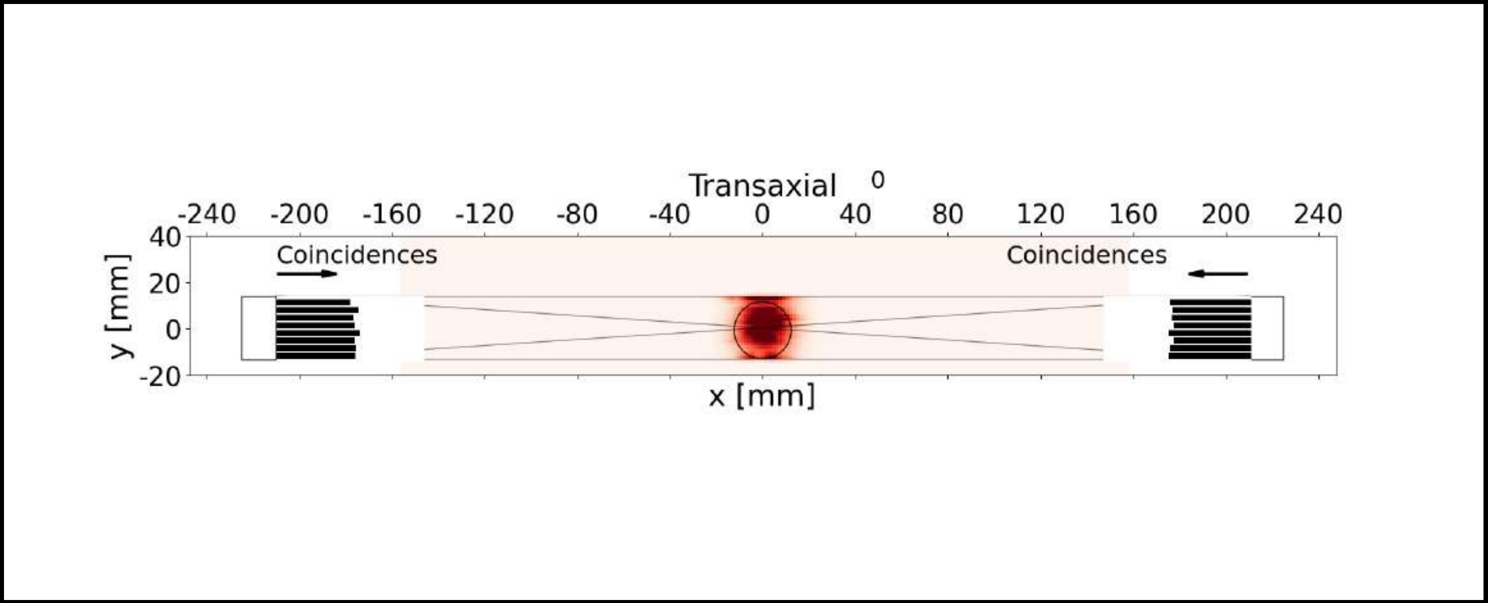
PMMA – PET flow



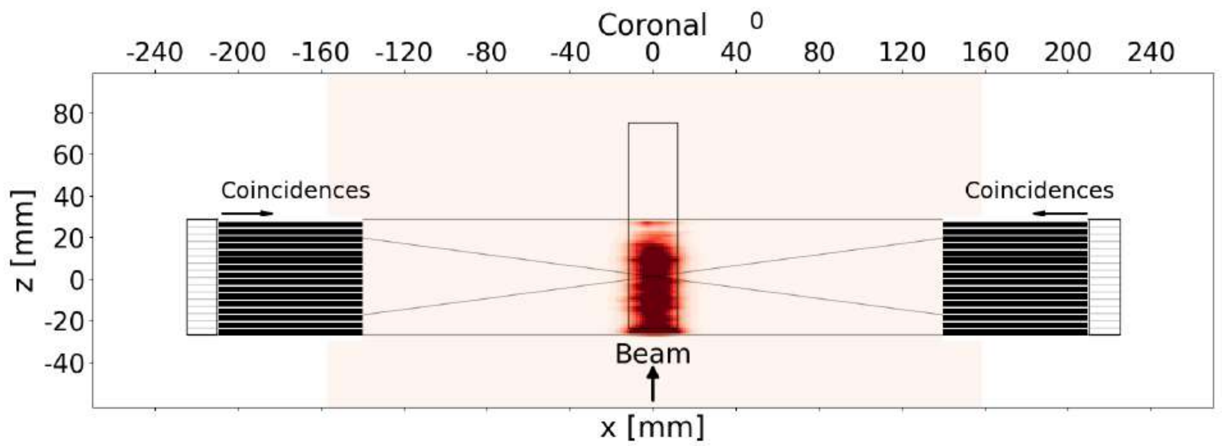


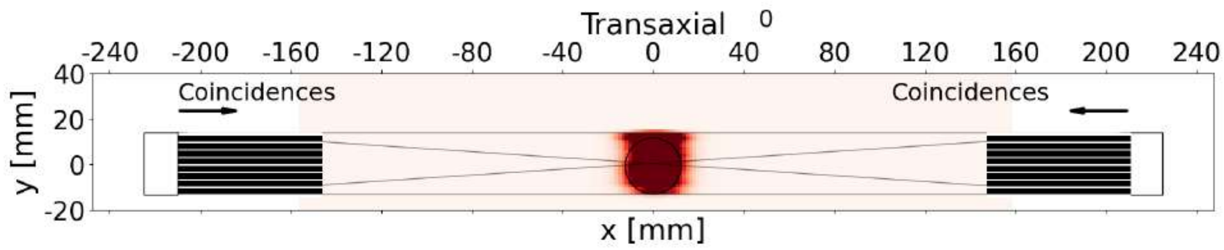
HDPE – PET flow



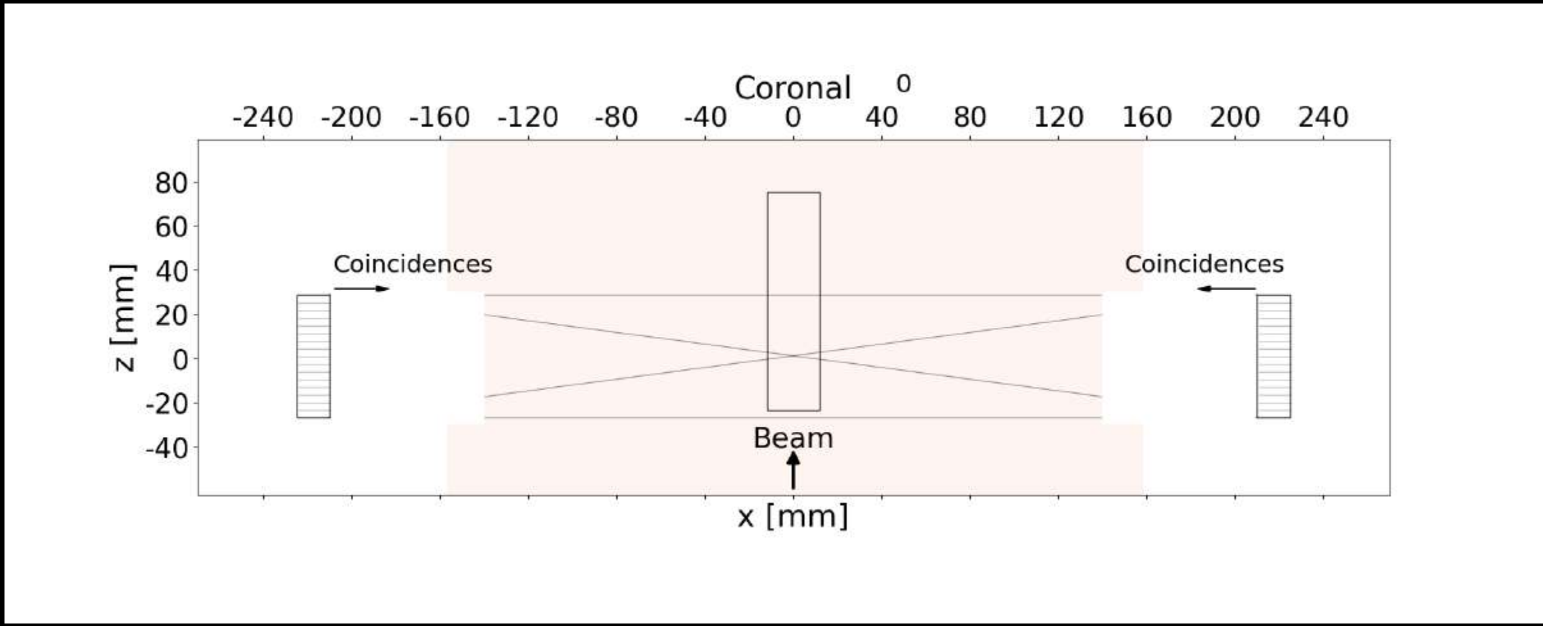


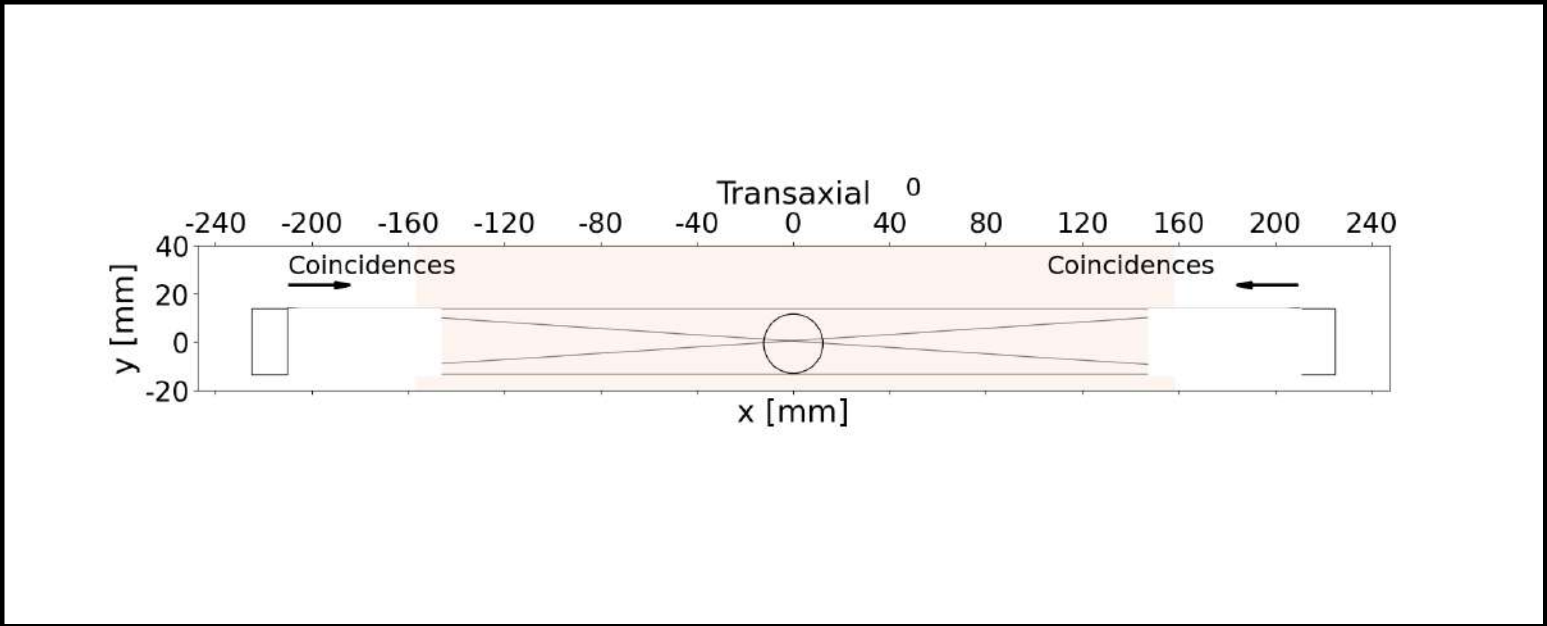
Water – PET flow





Air – PET flow


Coronal 0
-240 -200 -160 -120 -80 -40 0 40 80 120 160 200 240
80
60
40
20
0
-20
-40
z [mm]
Coincidences
Coincidences
Beam
x [mm]


Transaxial 0
-240 -200 -160 -120 -80 -40 0 40 80 120 160 200 240
40
20
0
-20
y [mm]
Coincidences
Coincidences
x [mm]

A wish list…

- New detector
  - Capable to provide dosimetry and functional imaging of FLASH
  - PGI – SPECT – PET

- New pharmaceuticals
  - Image-enhancing and therapeutic (radio-sensitized, e.g., AuNP)

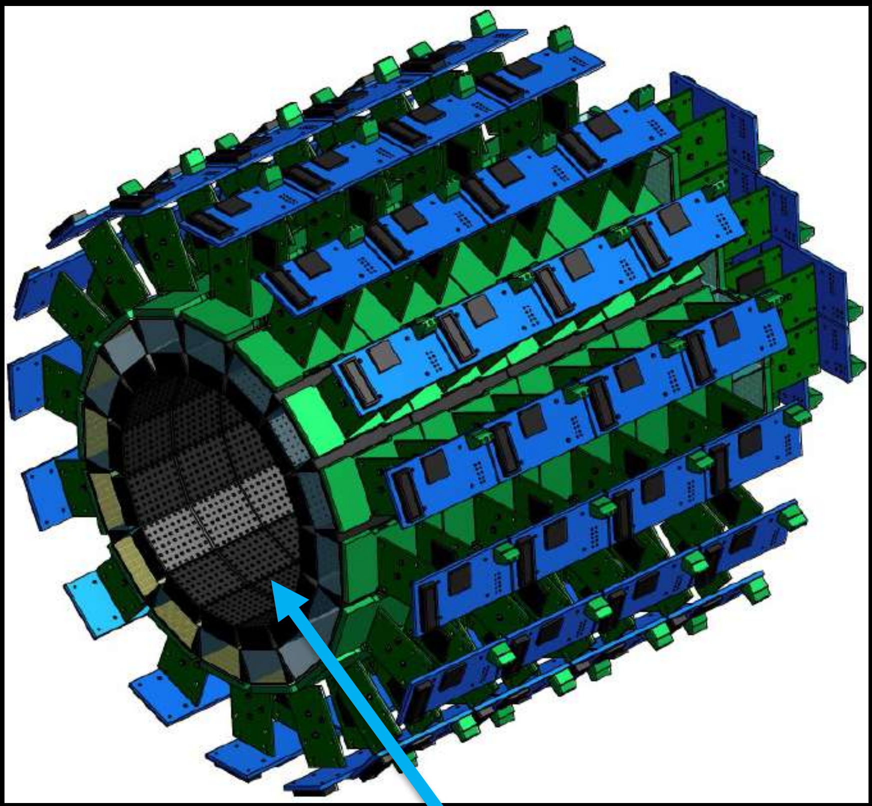
- New software (ML, AI ...)
  - enable fast assessment of each radiation
  - adjust proton treatment plan

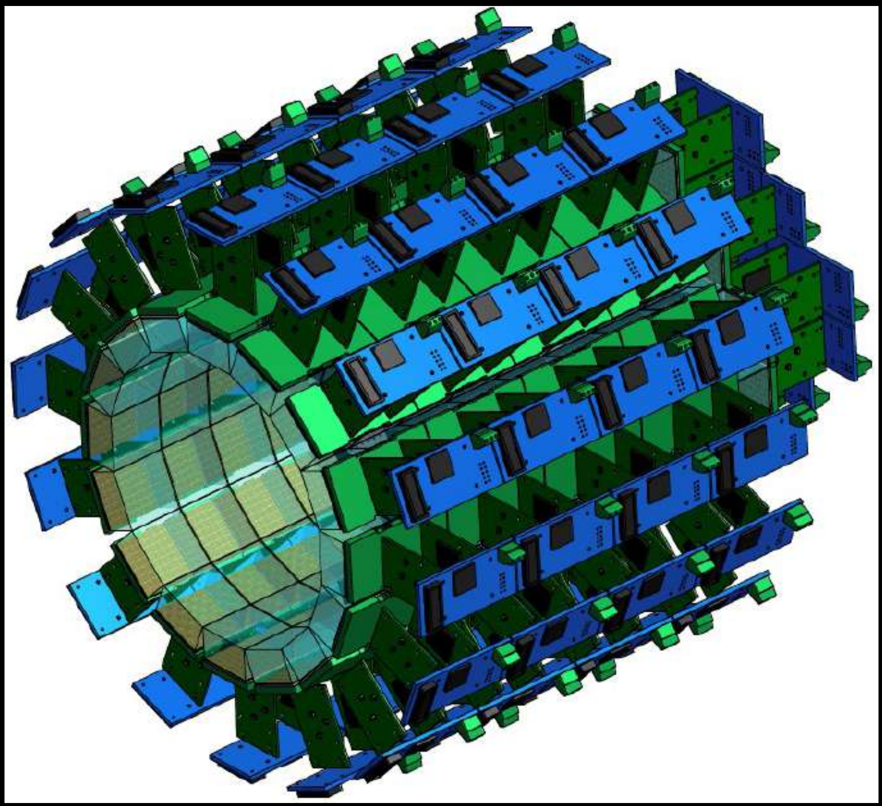
- New protocols
  - Image-guiding (i^3): irradiate-image-improve-irradiate-….
  - FLASH therapy can be fast(er)

- Cheaper and better beams (mini-spots conformity)

PET PGI SPECT

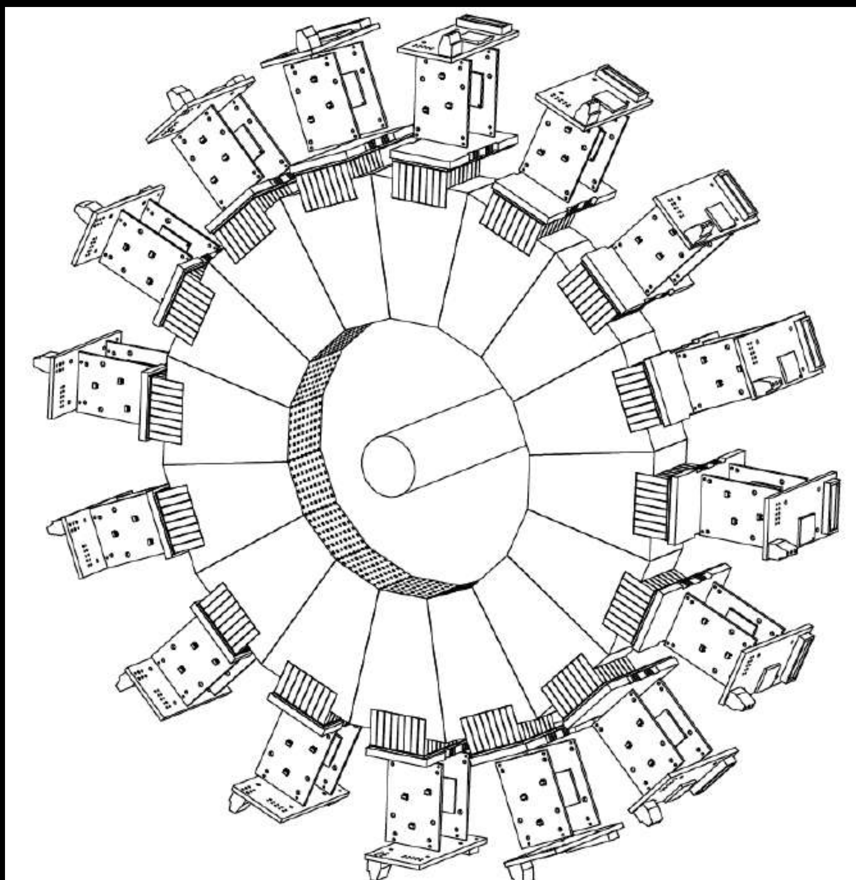
mini replica of a C^3 PET with PGI / SPECT

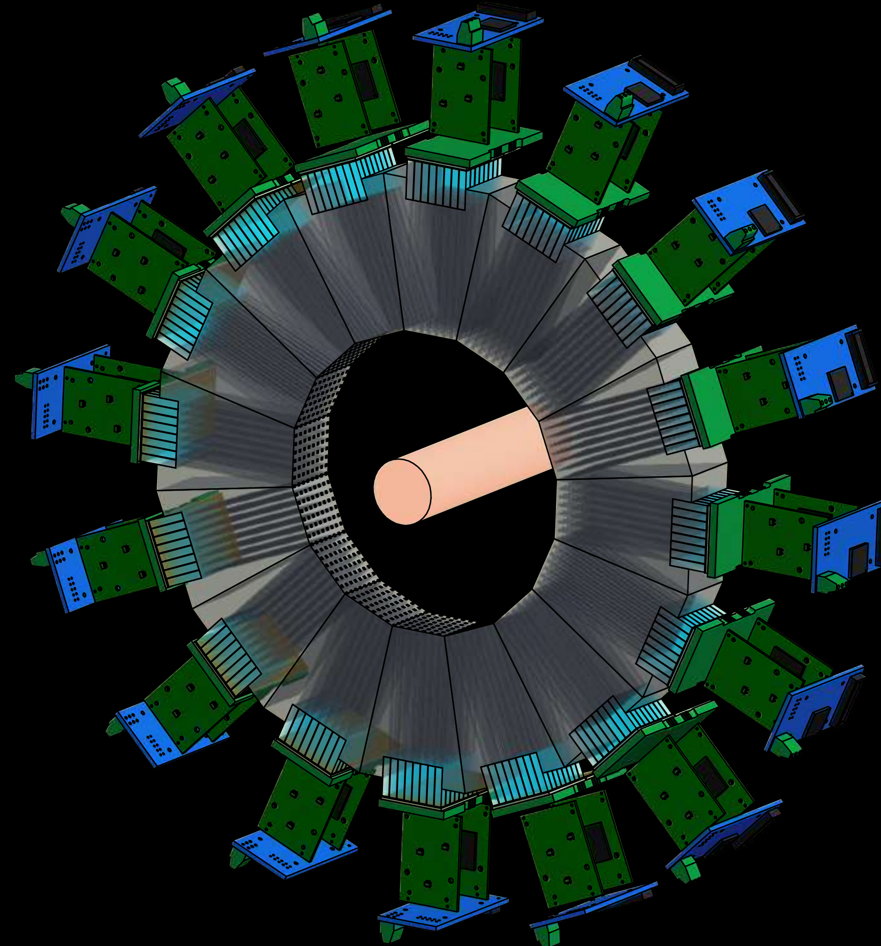




tungsten collimator

PET PGI SPECT option





~~Final~~ Initial thoughts

We are "watching" together with our few closest friends ...

“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.

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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.

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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

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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.

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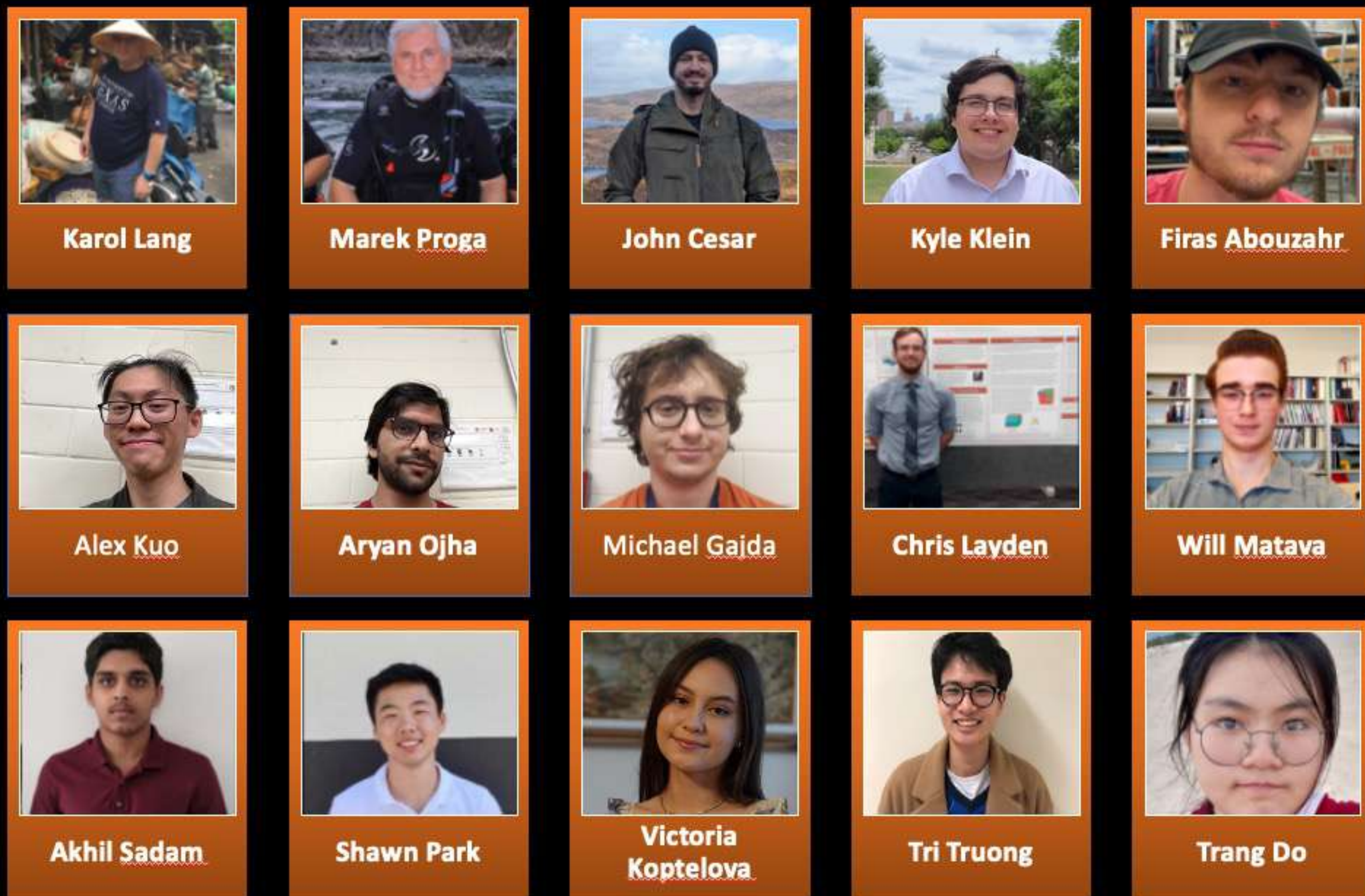
Can an effective collaboration be formed, modeled on research projects in experimental particle physics, that would accomplish in nuclear medical imaging what has not been accomplished over the last few decades by a number of small and isolated groups world-wide?

- We have been working on it ...



TPPT @ Tagus Park (June 16, 2023)