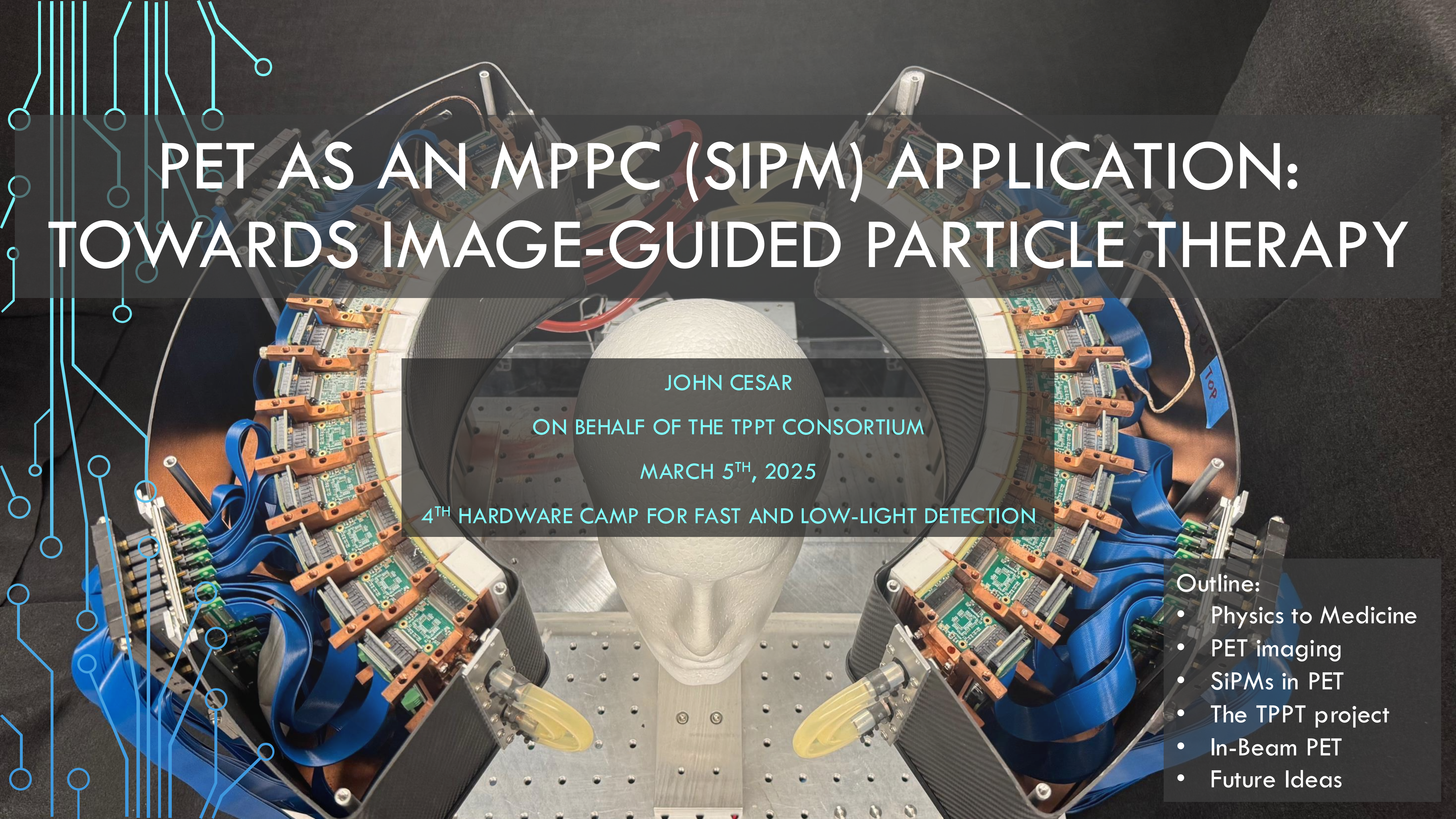
PET AS AN MPPC (SIPM) APPLICATION: TOWARDS IMAGE-GUIDED PARTICLE THERAPY

JOHN CESAR

ON BEHALF OF THE TPPT CONSORTIUM

MARCH 5TH, 2025

4TH HARDWARE CAMP FOR FAST AND LOW-LIGHT DETECTION



Outline:

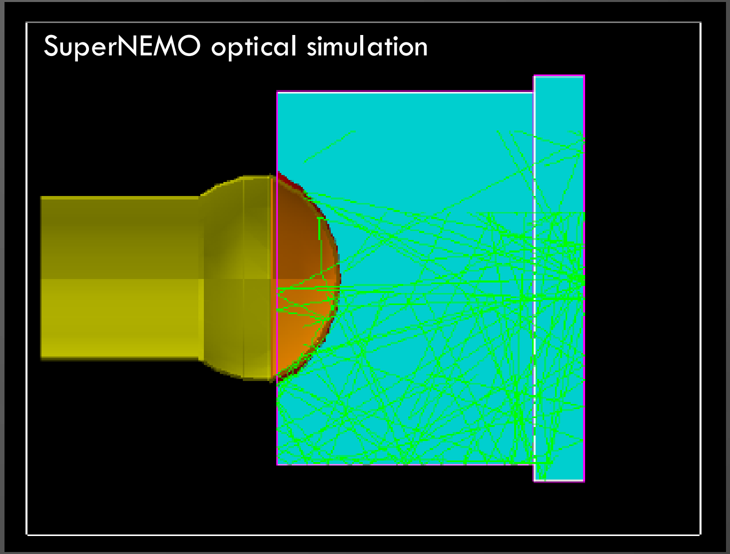
- Physics to Medicine
- PET imaging
- SiPMs in PET
- The TPPT project
- In-Beam PET
- Future Ideas

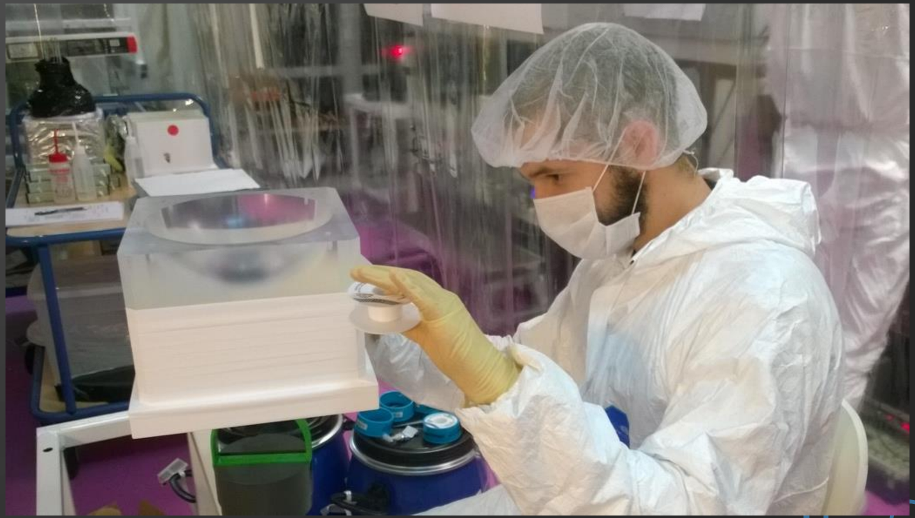
PHYSICS TO MEDICINE

From particle physics to medical physics…(but basically still doing particle physics!)

PHYSICS TO MEDICINE: BACKGROUND

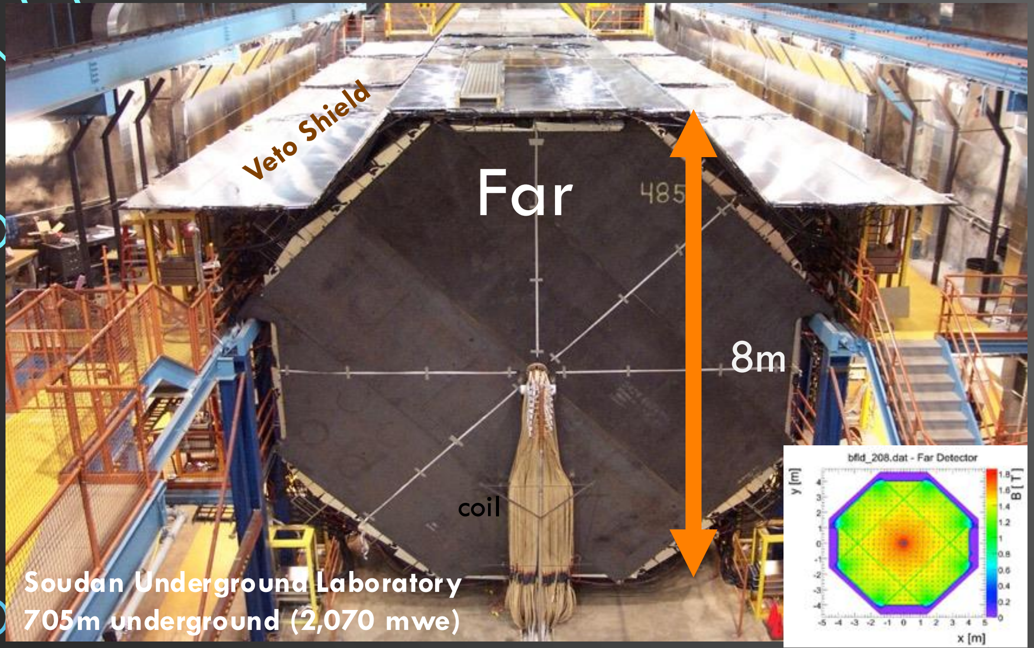
- Particle physics researchers at UT Austin
- Who want to help advance medicine
- The best way we know how: detector technology!
  - Many years working in radiation detection:
    - BNL 871, MINOS, NOvA, NEMO-3/SuperNEMO, LEGEND, DUNE, etc.
  - Hardware: experience in design, fabrication, calibration, commissioning of detector systems
  - Software: data analysis and simulations

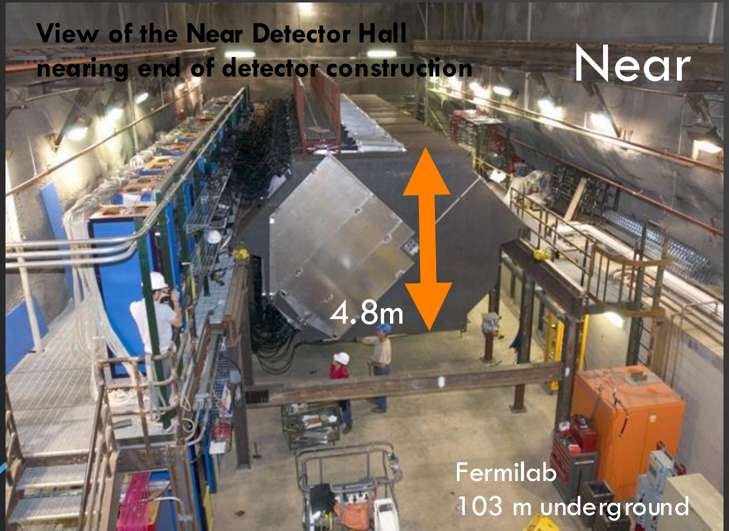




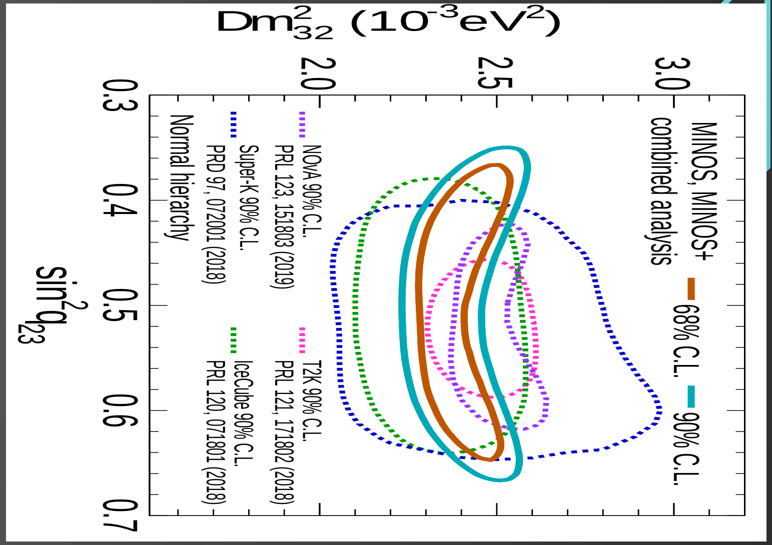
Preparation of a SuperNEMO calorimeter module

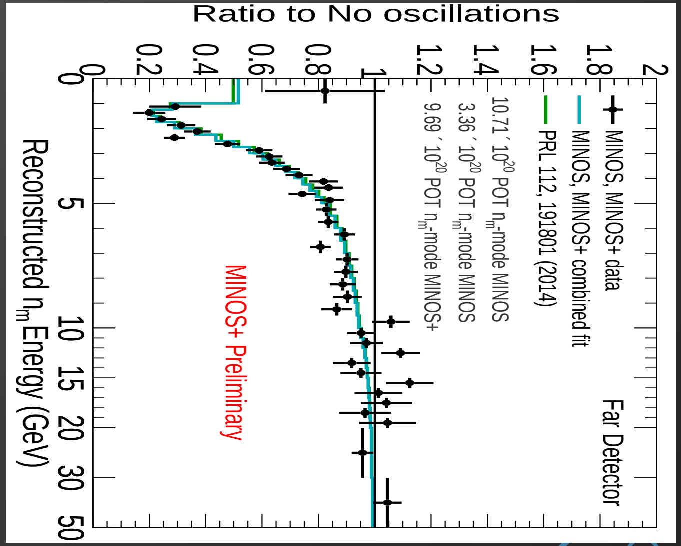
PHYSICS TO MEDICINE: MINOS/+





- Large-scale, long base-line neutrino oscillations experiment
- Detected neutrinos produced using the NuMI beamline at Fermilab
- Operated 2005 - 2016
- Precision measurements of mixing parameters
- Detector design:
  - Alternating planes of steel and plastic scintillator strips
  - Embedded fiber optics delivers scintillation light to PMTs

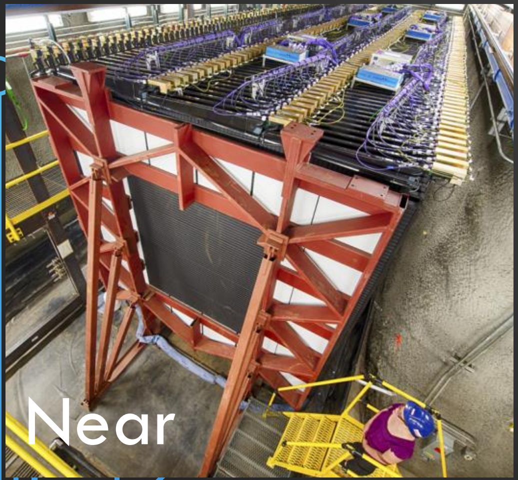




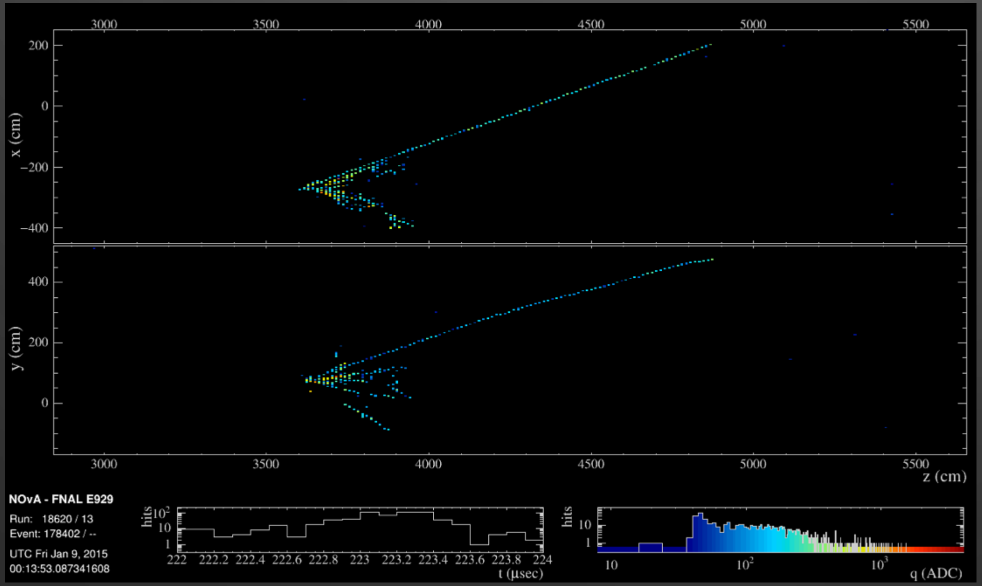
Normal $\Delta m^2_{32} = +2.41\,^{+0.08}_{-0.08}$ $(\times 10^{-3} eV^2)$ Inverted $\Delta m^2_{32} = -2.47\,^{+0.09}_{-0.07}$ $(\times 10^{-3} eV^2)$

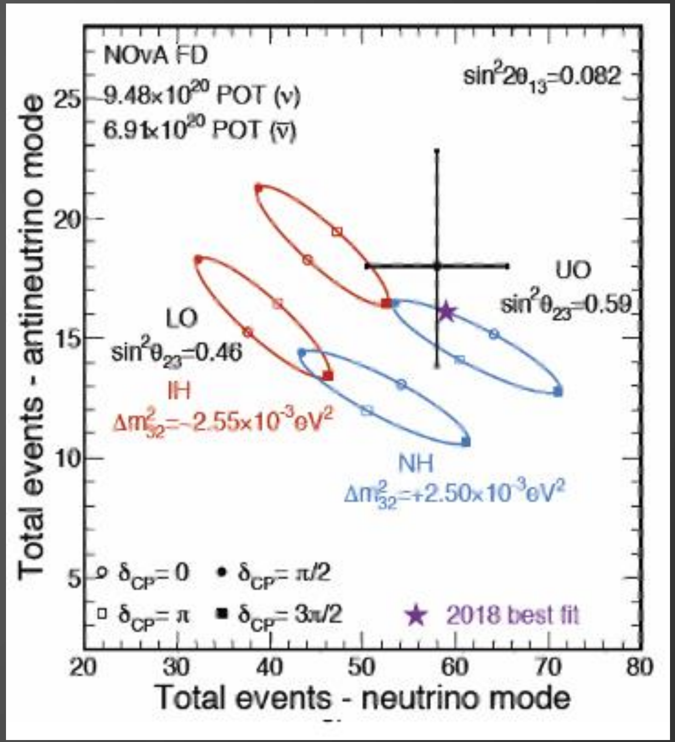
$sin^2\theta_{23} = 0.42\ (0.38 \leftrightarrow 0.48)$ $sin^2\theta_{23} = 0.42\ (0.38 \leftrightarrow 0.48)$

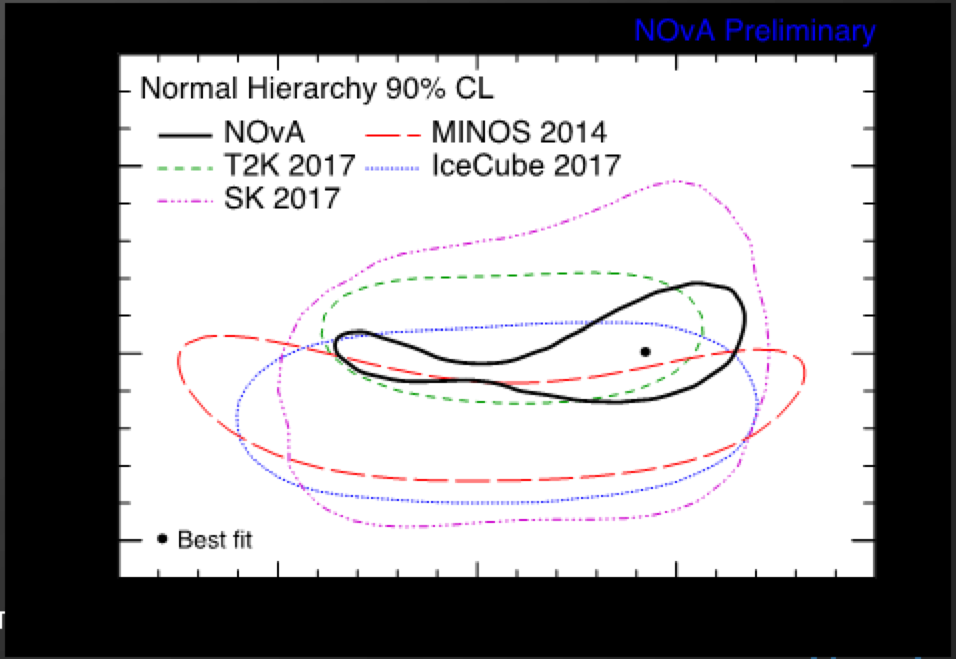
PHYSICS TO MEDICINE: NOVA



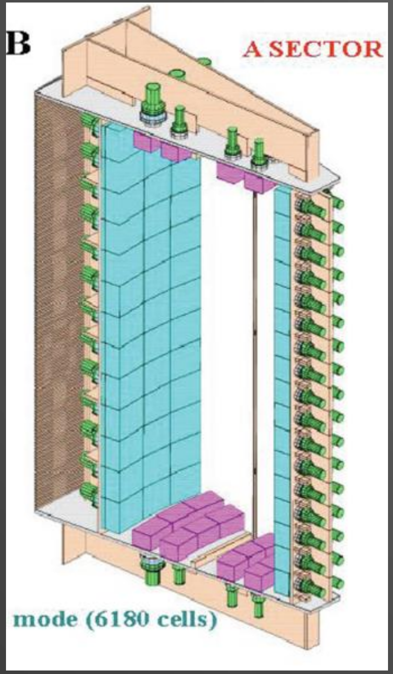
- Successor to MINOS, operating from 2014 - present
- Observes off-axis portion of NuMI beamline
- Precision measurements of mixing parameters
- Potential mass hierarchy resolution
- Detector design:
  - Plastic extrusions filled with liquid scintillator
  - Embedded fiber optic cable collects and delivers light to APDs



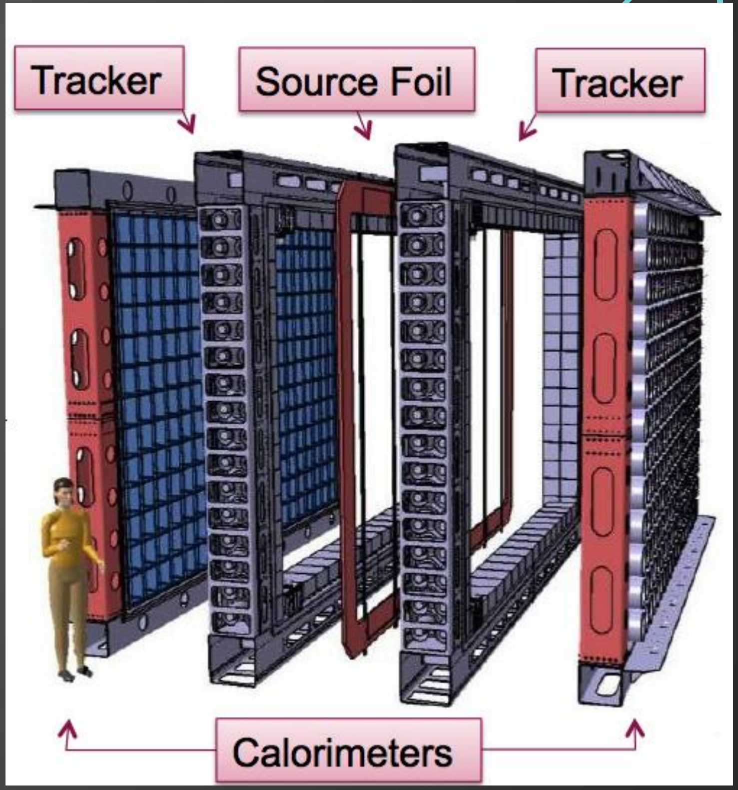


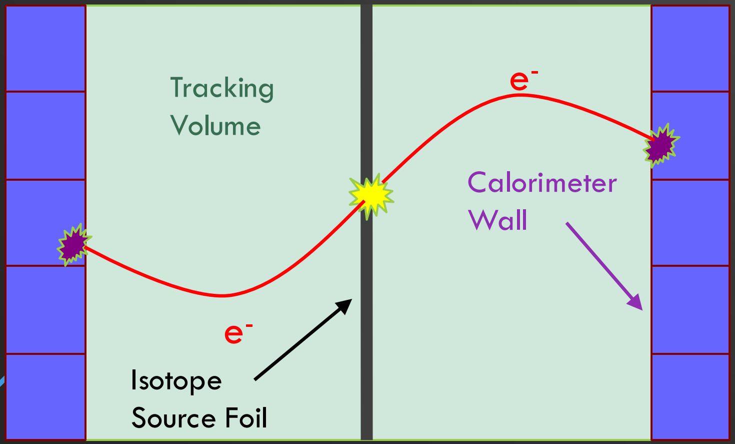


PHYSICS TO MEDICINE: NEMO

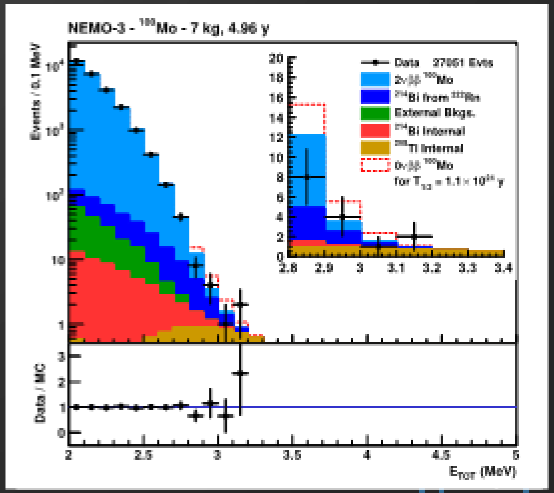


- Neutrinoless double-beta decay search experiment
- Multi-observable multi-isotope approach
- NEMO-3: 2003 -2011
- SuperNEMO demonstrator module currently being commissioned
- Detector design:
  - Isotopic source foils surrounded by tracking and calorimeters
  - Calorimeter = plastic scint. + PMTs





Isotope	$T^{0\nu}_{1/2}$ ($\times 10^{25}$ y)	$\langle m_{\beta\beta} \rangle$ (eV)	Experiment	Reference
^{48}Ca	$> 5.8 \times 10^{-3}$	$< 3.5 - 22$	ELEGANT-IV	(157)
^{76}Ge	> 8.0	$< 0.12 - 0.26$	GERDA	(158)
	> 1.9	$< 0.24 - 0.52$	MAJORANA DEMONSTRATOR	(159)
^{82}Se	$> 3.6 \times 10^{-2}$	$< 0.89 - 2.43$	NEMO-3	(160)
^{96}Zr	$> 9.2 \times 10^{-4}$	$< 7.2 - 19.5$	NEMO-3	(161)
^{100}Mo	$> 1.1 \times 10^{-1}$	$< 0.33 - 0.62$	NEMO-3	(162)
^{116}Cd	$> 1.0 \times 10^{-2}$	$< 1.4 - 2.5$	NEMO-3	(163)
^{128}Te	$> 1.1 \times 10^{-2}$	—	—	(164)
^{130}Te	> 1.5	$< 0.11 - 0.52$	CUORE	(124)
^{136}Xe	> 10.7	$< 0.061 - 0.165$	KamLAND-Zen	(165)
	> 1.8	$< 0.15 - 0.40$	EXO-200	(166)
^{150}Nd	$> 2.0 \times 10^{-3}$	$< 1.6 - 5.3$	NEMO-3	(167)



PET IMAGING

PET = **P**ositron **E**mission **T**omography
and a PET scanner is fundamentally just
a small particle detector (scintillator +
optical sensor)

PET IMAGING: A SUBSET OF MEDICAL IMAGING

CT (Computed Tomography)

MRI (Magnetic Resonance Imaging)

PET (Positron Emission Tomography)

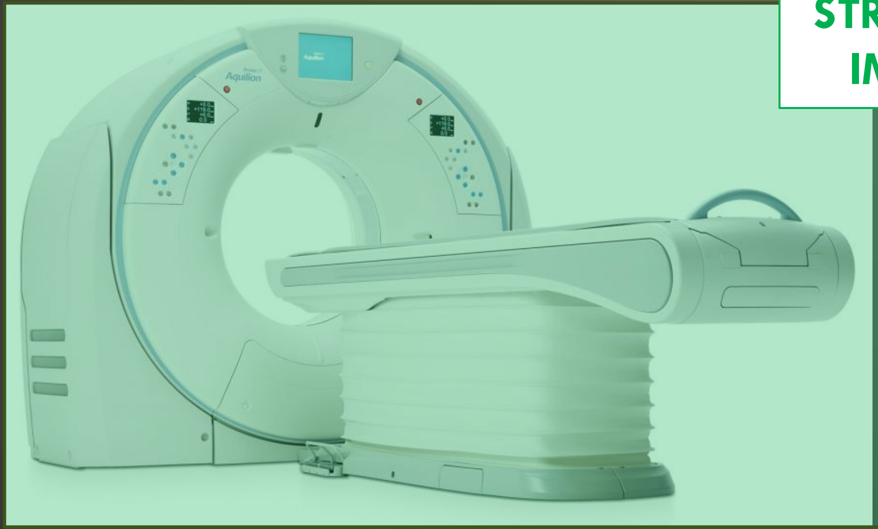
And there are others:

- **SPECT imaging**
- X-ray imaging
- Ultrasound imaging
- …

PET IMAGING: A SUBSET OF MEDICAL IMAGING

STRUCTURAL IMAGING

CT (Computed Tomography)



MRI (Magnetic Resonance Imaging)

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PET IMAGING: A SUBSET OF MEDICAL IMAGING

CT (Computed Tomography)

MRI (Magnetic Resonance Imaging)

PET (Positron Emission Tomography)

FUNCTIONAL IMAGING

PET and SPECT are <u>nuclear</u> medical imaging techniques

- Radiation being used/detected is **internal** rather than external
- Employ radiopharmaceuticals
- Emphasis on imaging **<u>function</u>** (metabolism, etc.) not **<u>structure</u>** (anatomy)

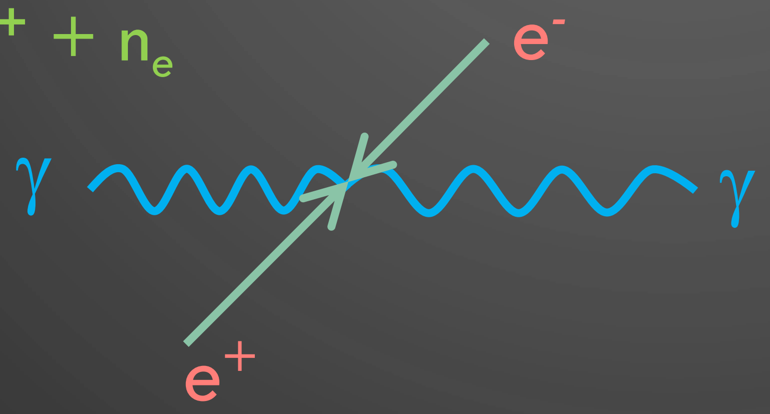
And there are others:

- **SPECT imaging**
- X-ray imaging
- Ultrasound imaging
- …

PET Imaging: Positron Emission

- Imaging biological → cellular metabolism
  - Cancer cells are highly metabolic!
- ^{18}F-fluorodeoxyglucose (^{18}FDG) is a radiopharmaceutical "tracer" for metabolic activity

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

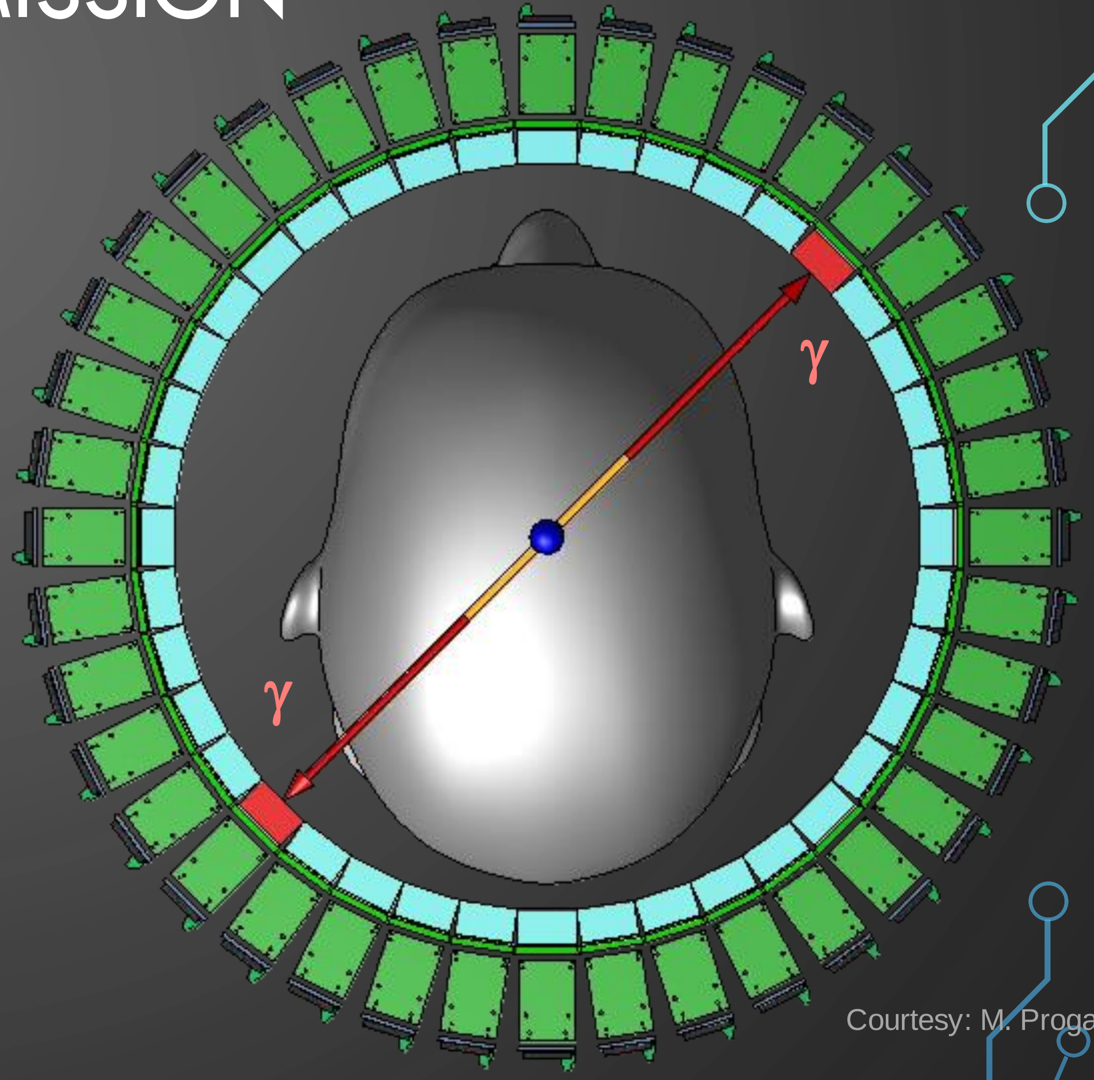


$e^{+} + e^{-} \rightarrow \gamma + \gamma$

$E = mc^2$

Mass of electron = mass of positron = 511 keV

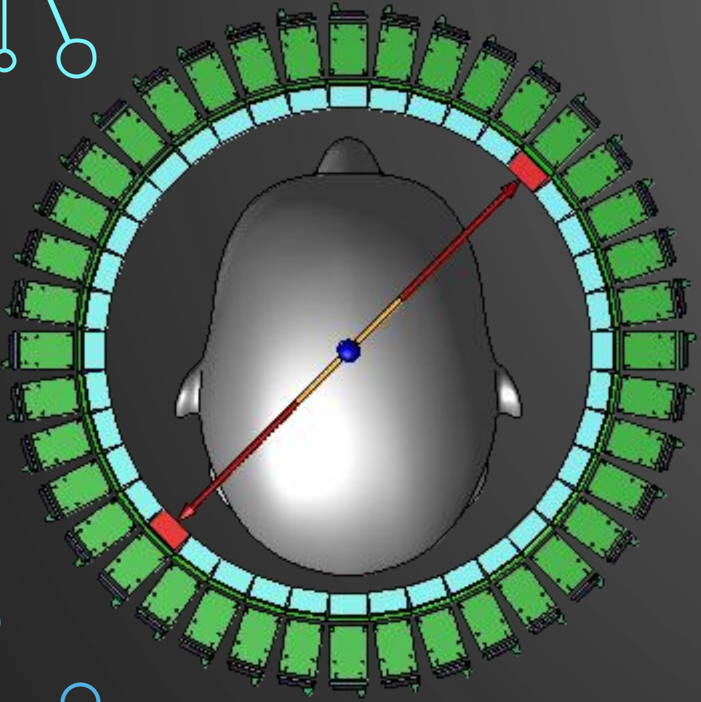
Therefore, E_{γ} = 511 keV



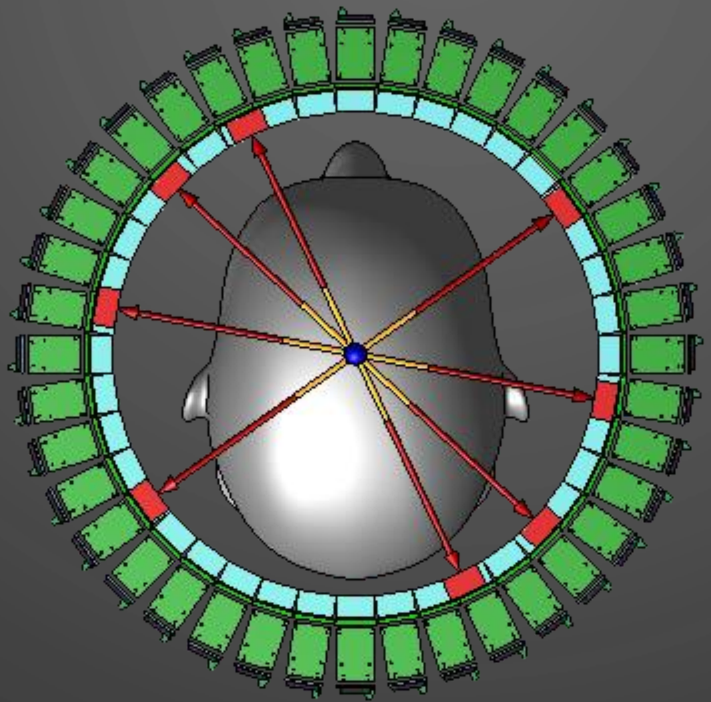
Courtesy: M. Proga

LOR = line of response = the line formed by the trajectories of the two back-to-back gammas

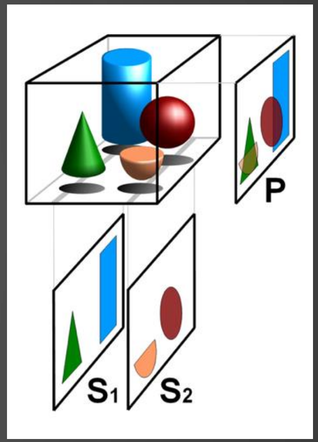
PET IMAGING: TOMOGRAPHY

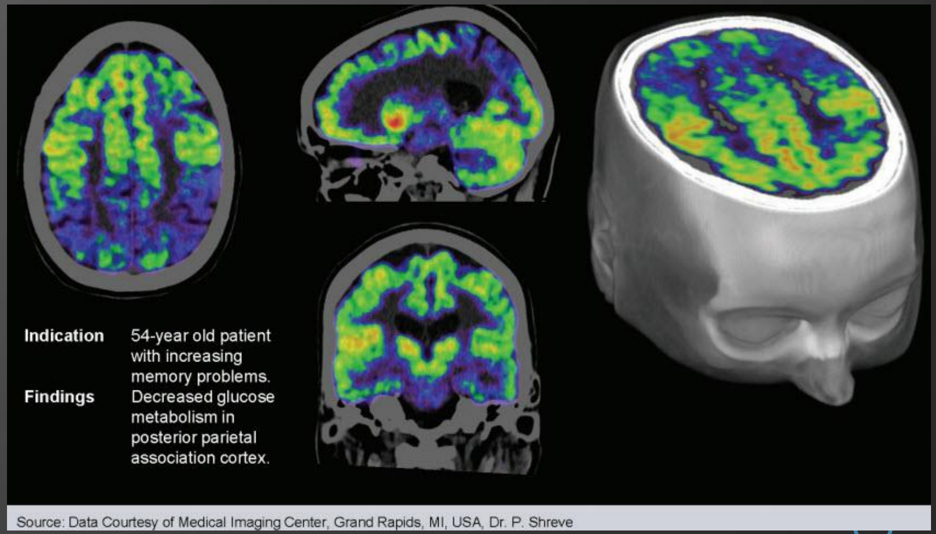


One LOR is not enough to pinpoint the emission site



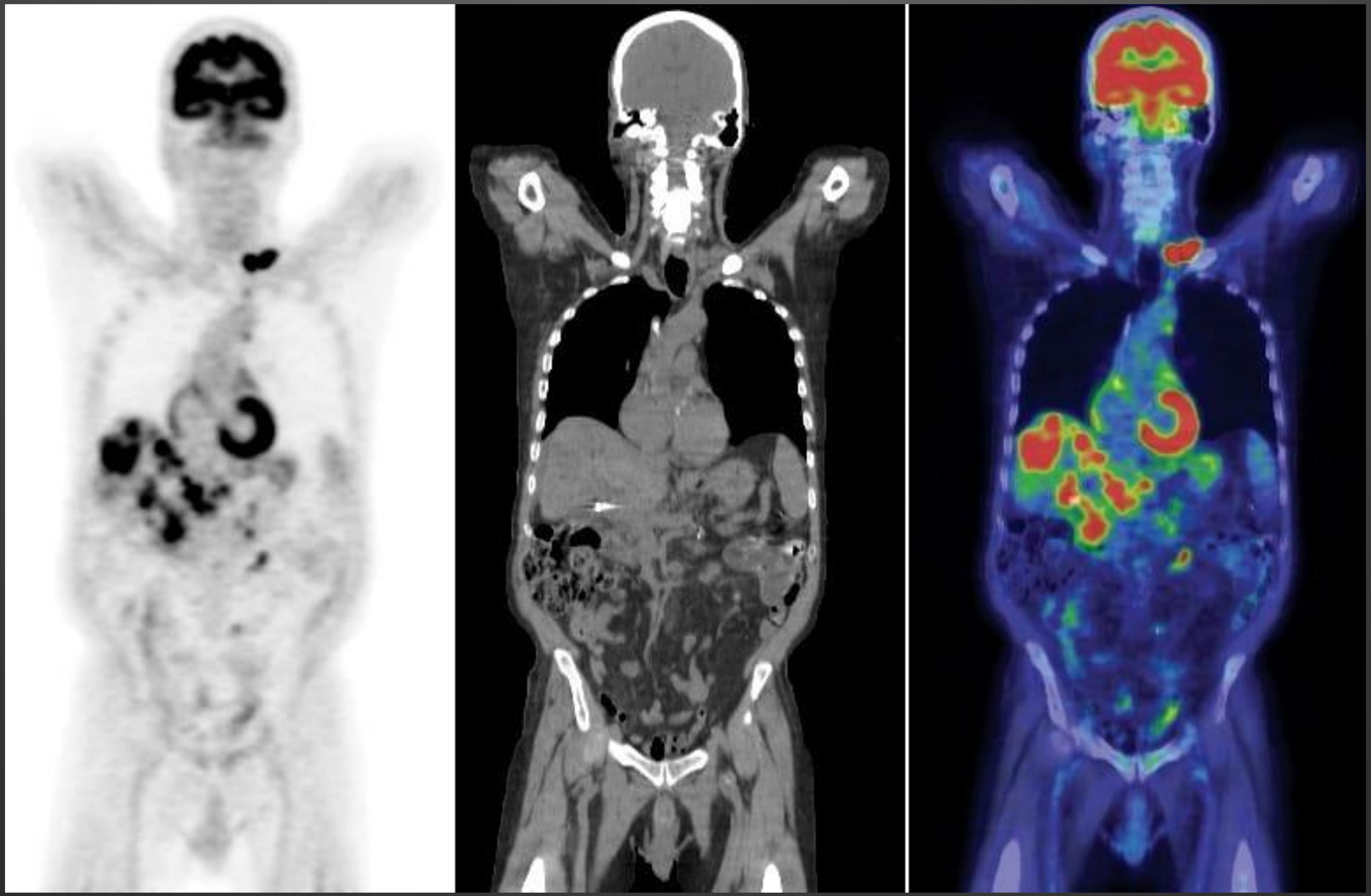
With many LORs from the same region, their intersections yields a source





Performing this along different planes then allows for full 3D image reconstruction of activity

PET IMAGING: CONVENTIONAL PET + CT



PET CT PET + CT

Recall:
CT = structural
PET = functional

SIPMS IN PET

Modern PET scanner technology: from PMTs to SiPMs

SIPMS IN PET: EARLY PMT-BASED SCANNERS

- Need to detect and localize emitted gammas
  - Space → gives us LORs
  - Time → Define coincidences
    - Minimizes randoms
- Early PET scanners used scintillators + PMTs
- But PMTs often have larger surface areas
  - Pixelization from scintillator geometry
  - Via clever light sharing mechanisms…

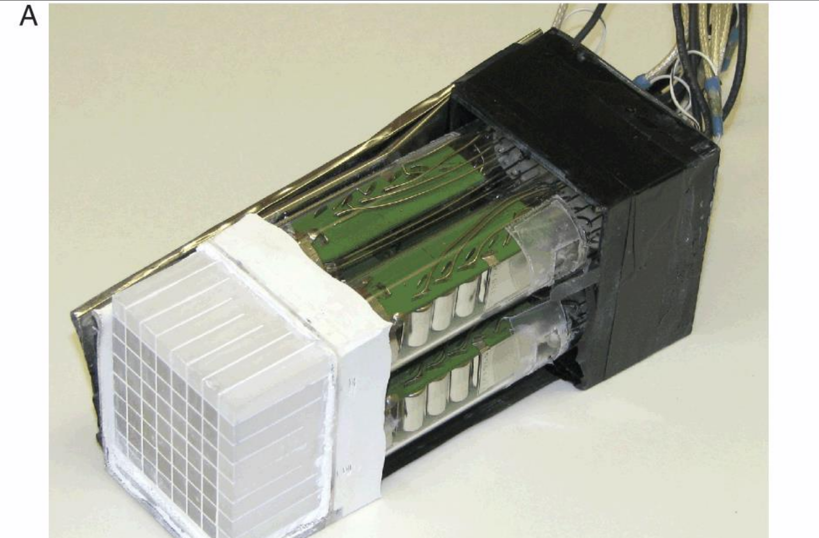
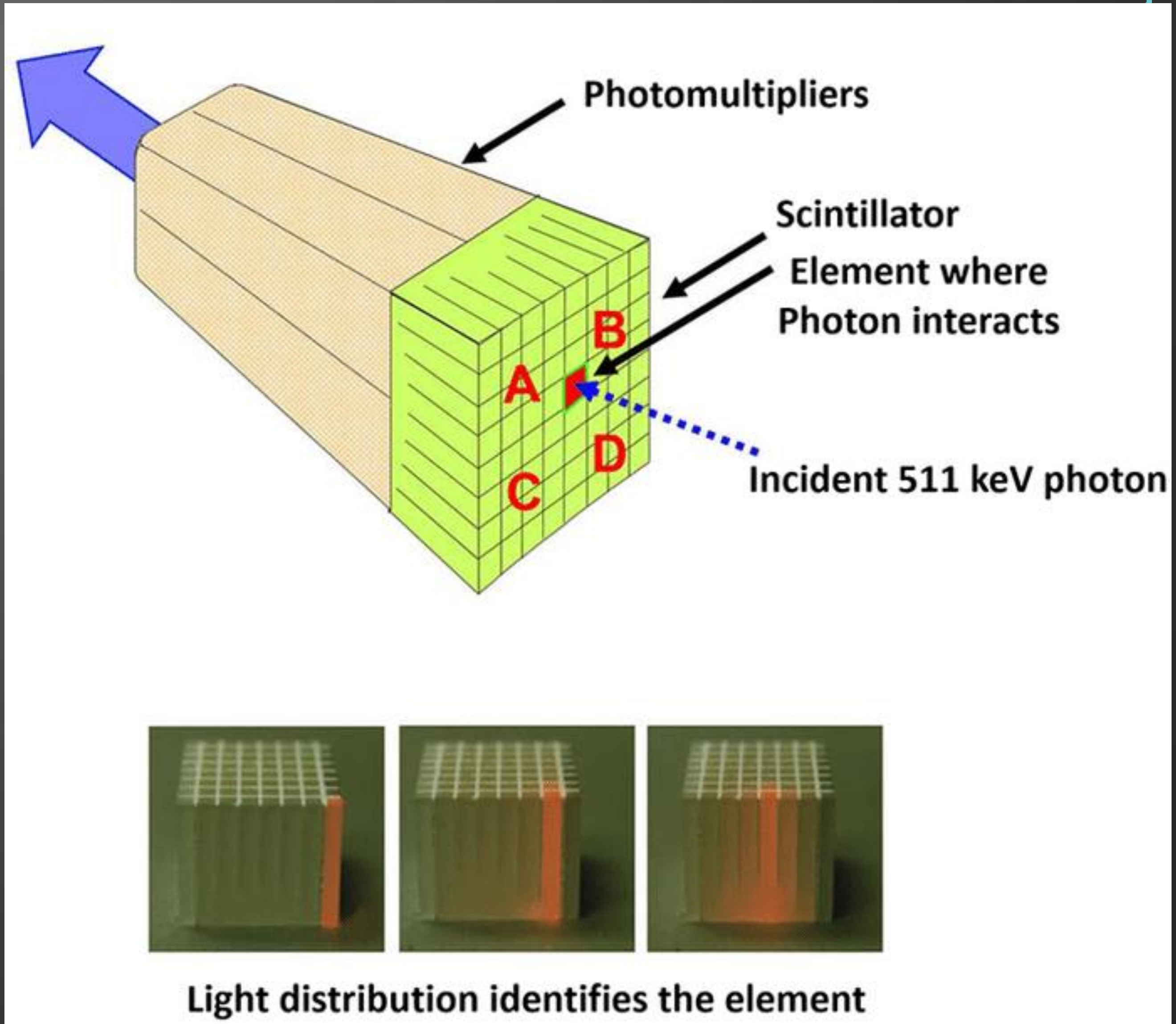


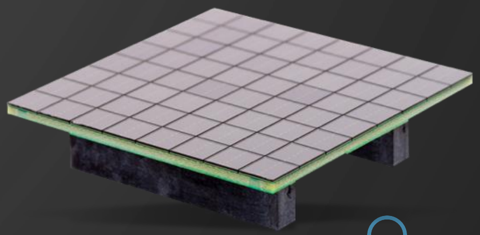
Image from: https://doi.org/10.1017/CBO9781139088268.007



SIPMS IN PET: OPTICAL SENSOR COMPARISON

	PD	APD	MPPC	PMT
Gain	1	10^2	to 10^6	to 10^7
Quantum efficiency	Highest	High	Medium	Low
Operation voltage	5 V	100 to 500 V	30 to 60 V	800 to 1000 V
Large area	No	No	Medium	yes
Multi channel with narrow gap	Yes	Yes	Yes	No
Readout circuit	Complex	Complex	Simple	Simple
Noise	Low	Middle	Middle	Low
Uniformity	Excellent	Good	Excellent	Good
Energy resolution	High	Medium	High	High
Temperature sensitivity	Low	High	Medium	Low
Ambient light immunity	Yes	Yes	Yes	No
Magnetic resist	Yes	Yes	Yes	No
Compact & Weight	Yes	Yes	Yes	No

PMT Examples



MPPC (SiPM) Example

Image courtesy of https://www.hamamatsu.com/eu/en/product/optical-sensors/mppc/what_is_mppc.html

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Noise	Low	Middle	Middle	Low
Uniformity	Excellent	Good	Excellent	Good
Energy resolution	High	Medium	High	High
Temperature sensitivity	Low	High	Medium	Low
Ambient light immunity	Yes	Yes	Yes	No
Magnetic resist	Yes	Yes	Yes	No
Compact & Weight	Yes	Yes	Yes	No

Comparable gain to PMTs and better QE

Better pixelization (spatial resolution) and less dead space

Allows combination of PET + MRI (function + structure imaging)

Compactness opens new opportunities for PET…

Image courtesy of https://www.hamamatsu.com/eu/en/product/optical-sensors/mppc/what_is_mppc.html

SIPMS IN PET: TIME-OF-FLIGHT

- Fast gamma detection opens new opportunities
  - Time-of-Flight (ToF) localization
- Three ingredients:
  - Fast **scintillators**
  - Fast **photodetector**
  - Fast **front-end electronics**
- Leads to improved image reconstruction
  - Less noise in final images

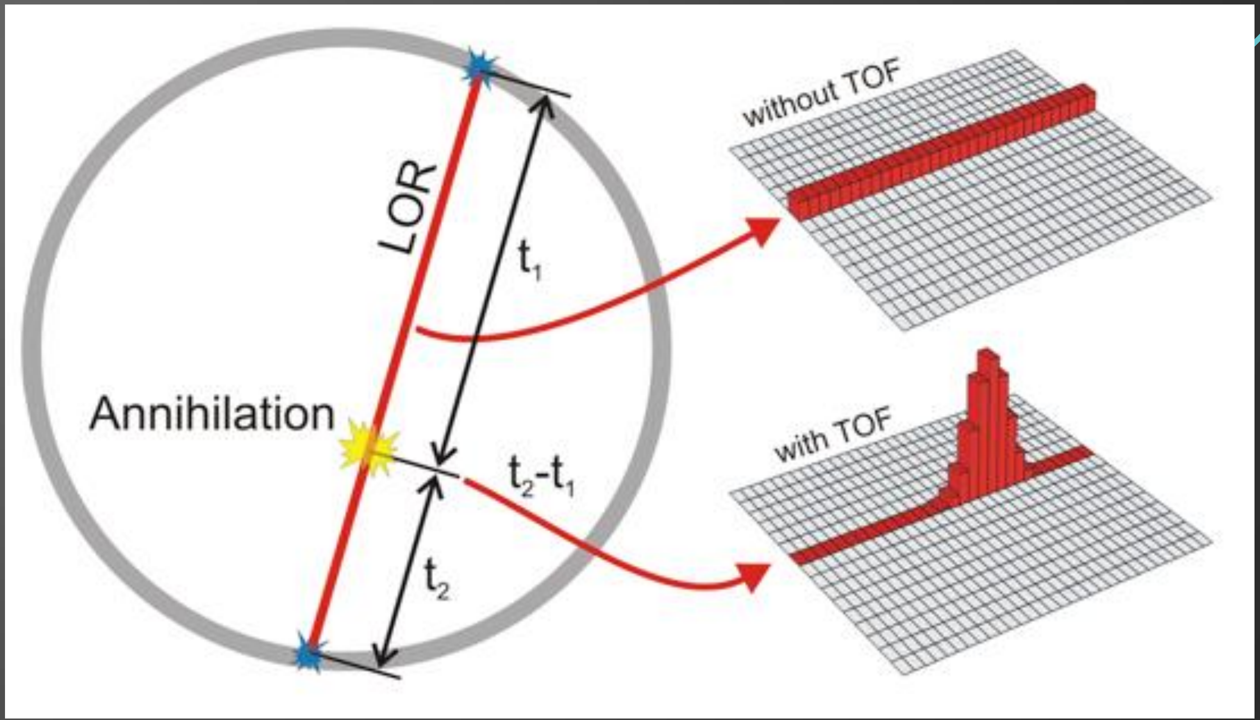
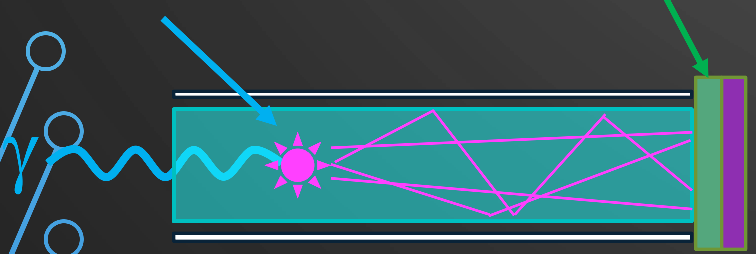
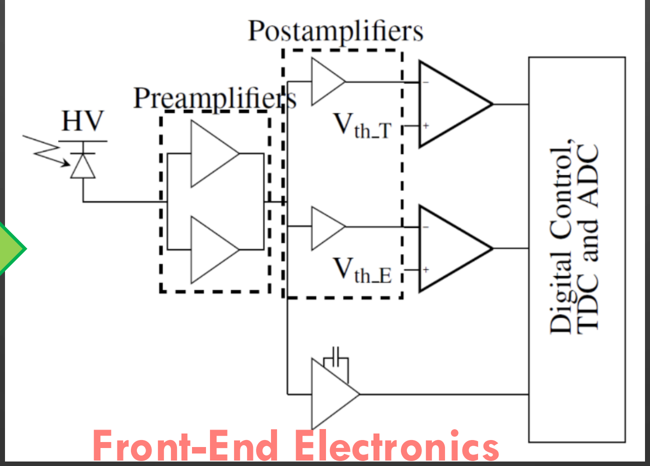


Image courtesy of https://the10ps-challenge.org/



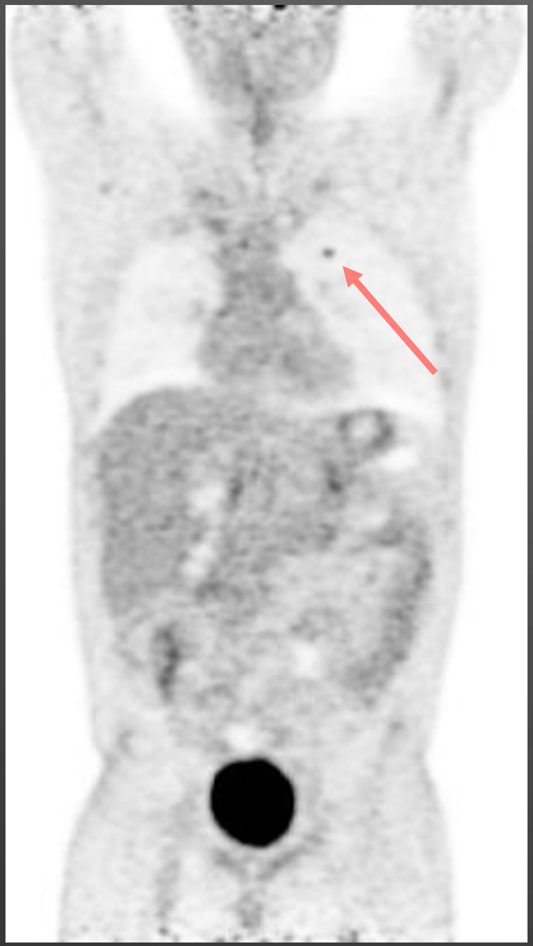


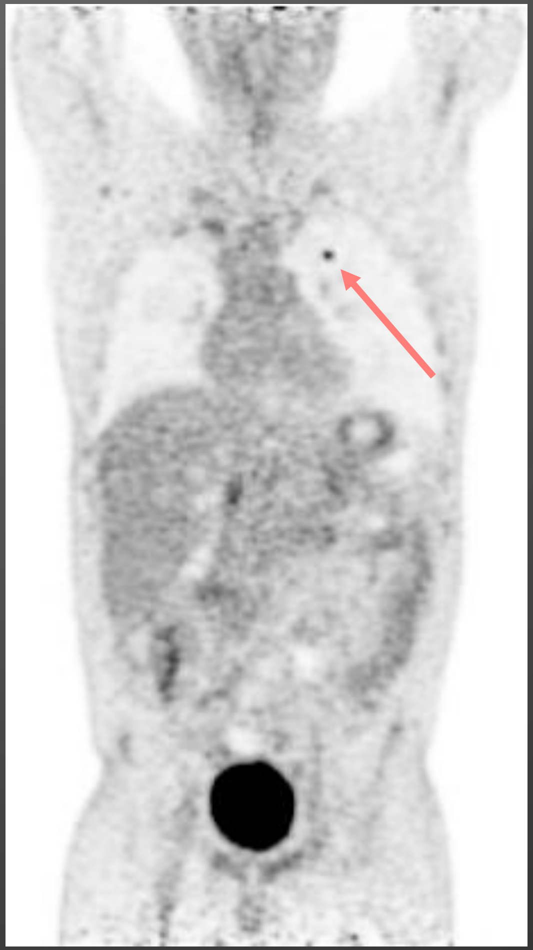
$\Delta X = c\,\Delta T/2$

$\Delta T = t_2 - t_1$

SIPMS IN PET: TIME-OF-FLIGHT PET

Non-TOF
Enabled
Reconstruction



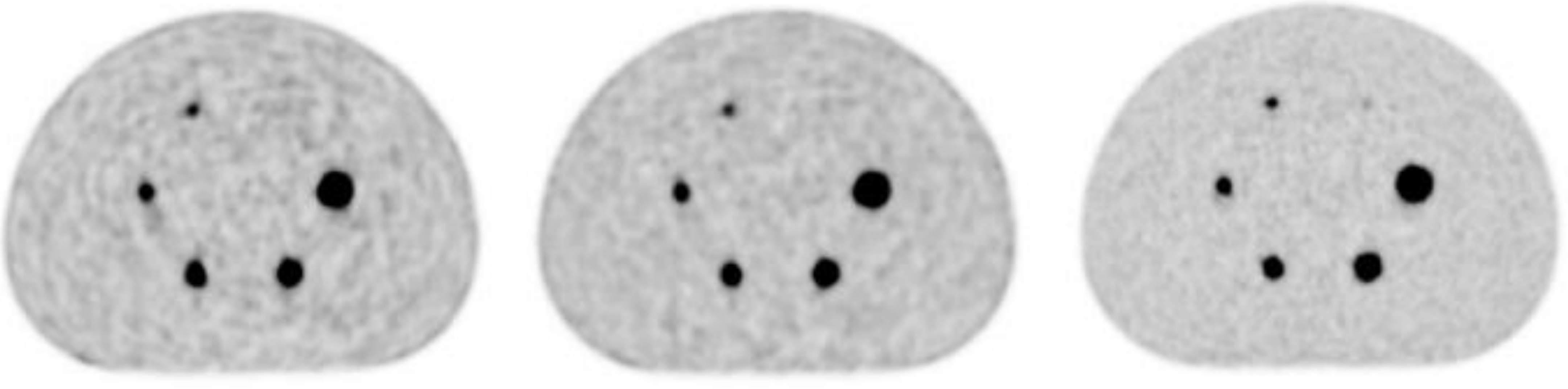


TOF (550 ps)
Enabled
Reconstruction

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

SIEMENS Healthineers

SIPMS IN PET: TIME-OF-FLIGHT PET



(a) nonTOF (b) TOF, 527ps (c) TOF, 210ps

SIPMS IN PET: COMPACT SIZE

- Compactness of SiPMs also present new opportunities
  - In-beam PET imaging
    - Reconstruct path of therapeutic beam
    - Monitor and verify delivered dose

Image courtesy of https://www.siemens-healthineers.com/en-us/molecular-imaging/pet-ct/biograph-vision

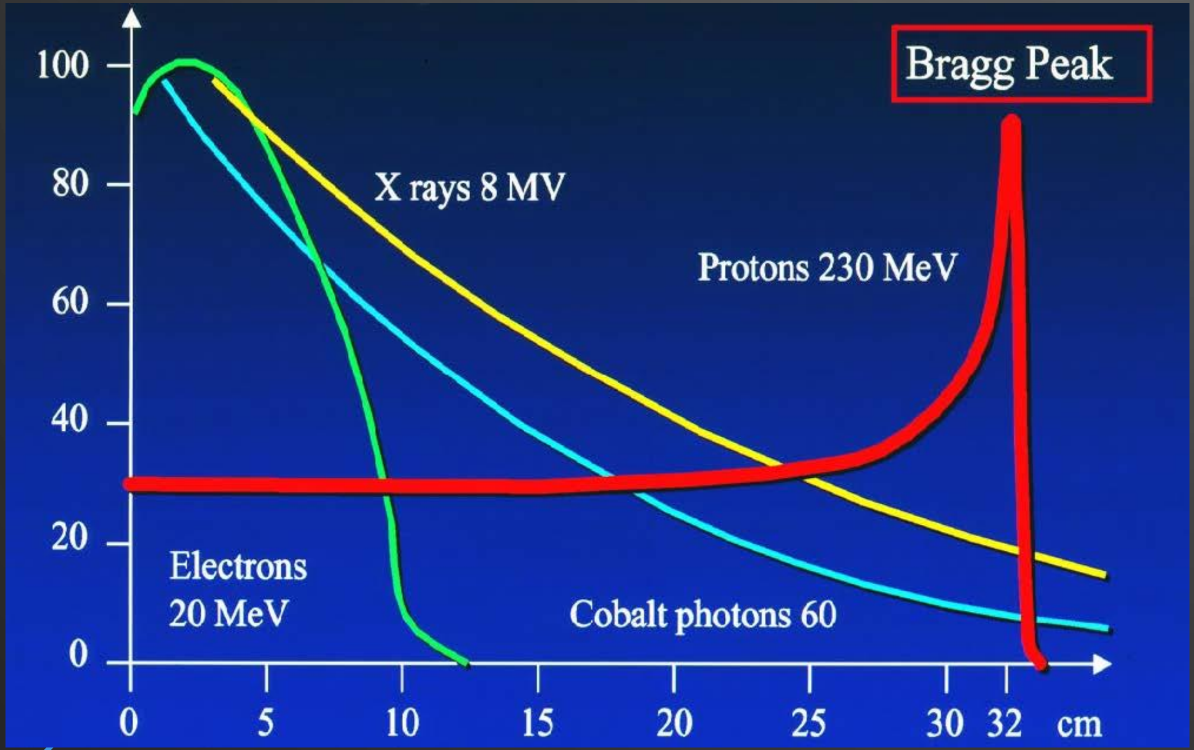
THE TPPT PROJECT

Time-of-Flight PET for Proton Therapy: Towards Image-Guided Particle Radiotherapy

THE TPPT PROJECT: PROTON THERAPY HISTORY

``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…**

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



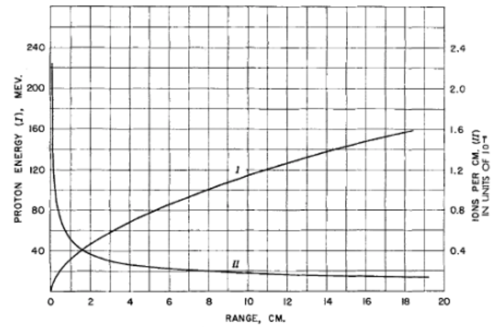


Fig. 1. Curve I is the range-energy relation in tissue. Curve II shows the specific ionization as a function of the residual range of a proton in tissue.

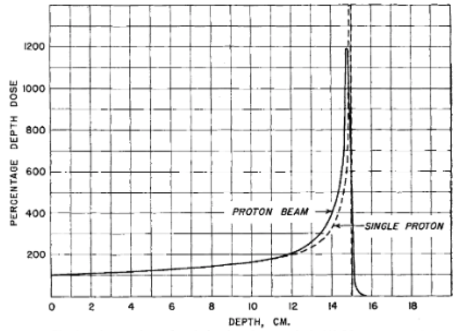
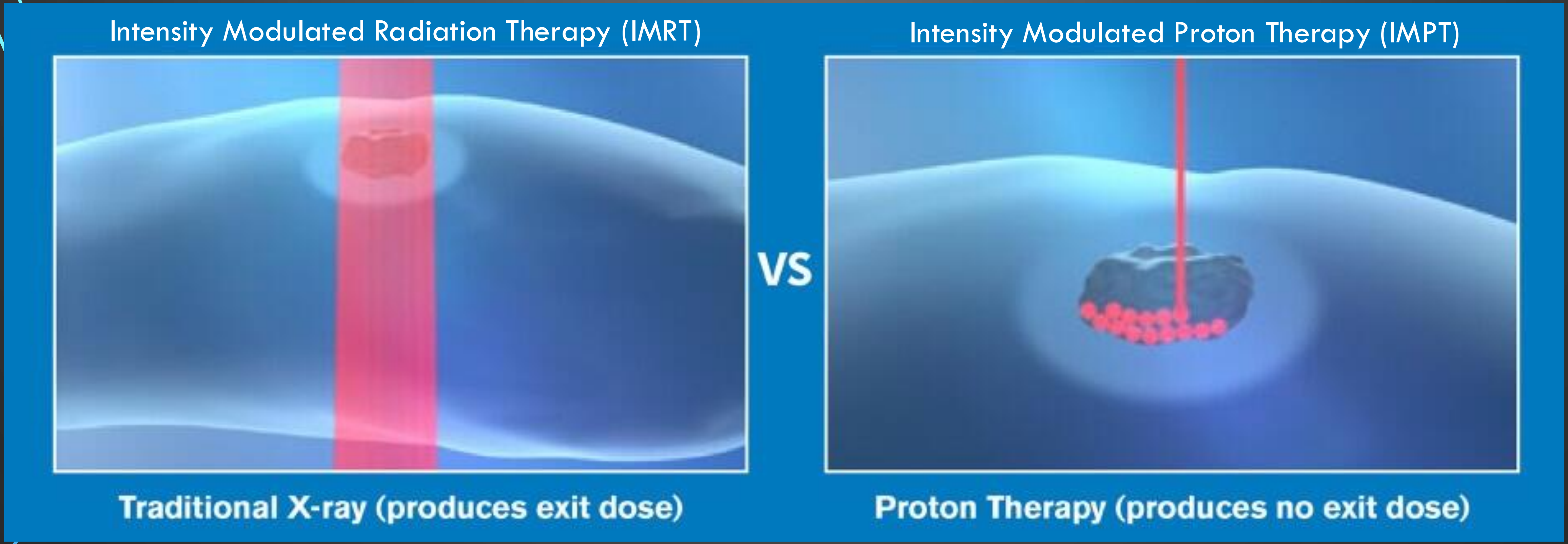
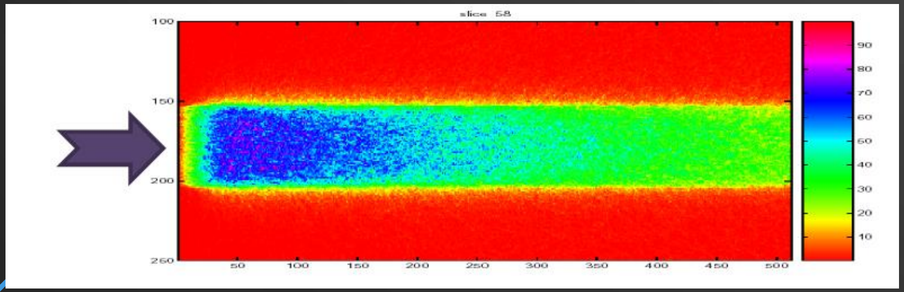


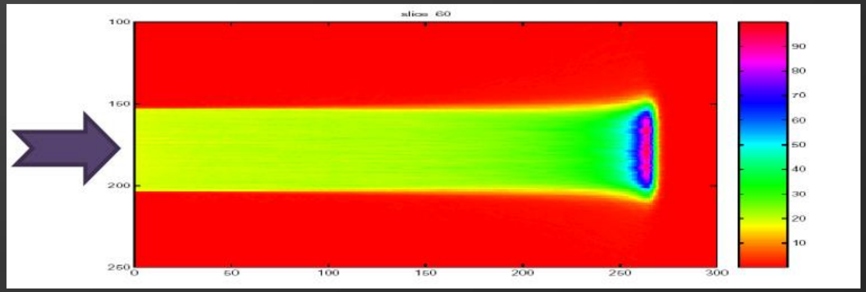
Fig. 2. The dotted curve shows the relative dose due to a single 140 Mev proton. The full curve shows qualitatively the depth dose curve for a beam of 140 Mev protons in tissue.

79 years ago!

THE TPPT PROJECT: PROTON THERAPY (PT)

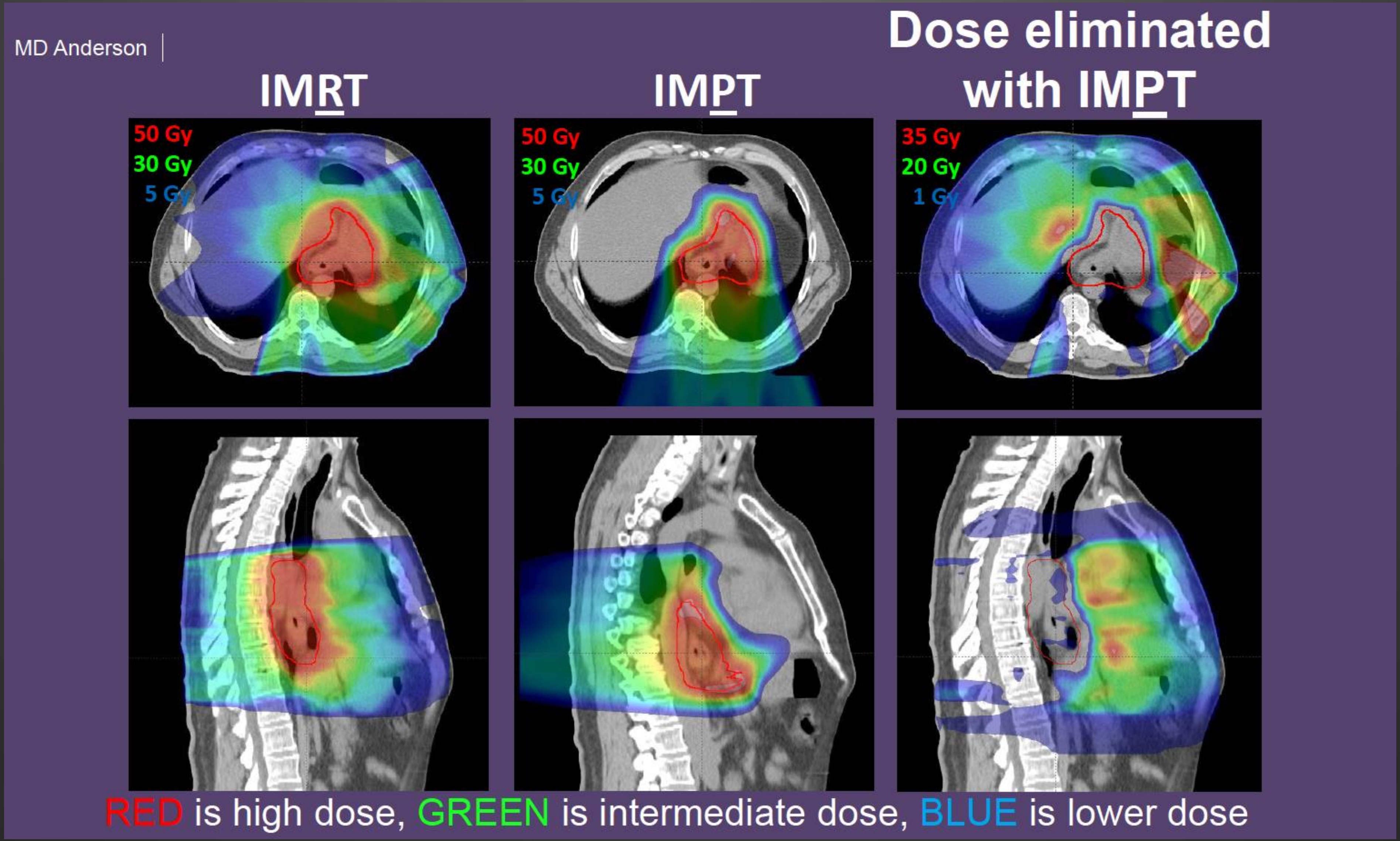






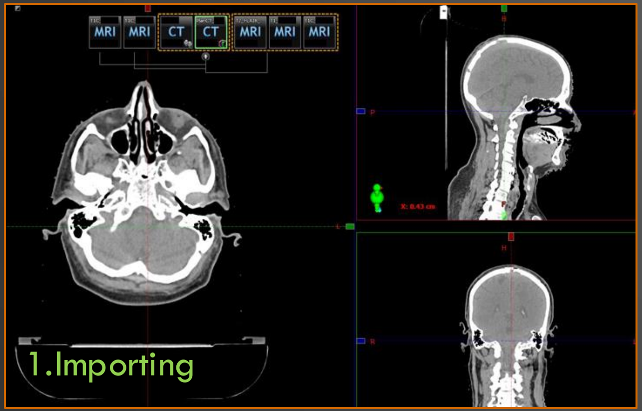
Uncertainty Plan

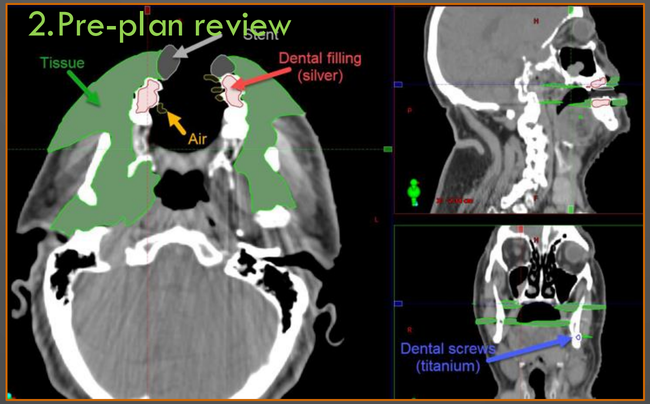
THE TPPT PROJECT: PROTONS VS. PHOTONS

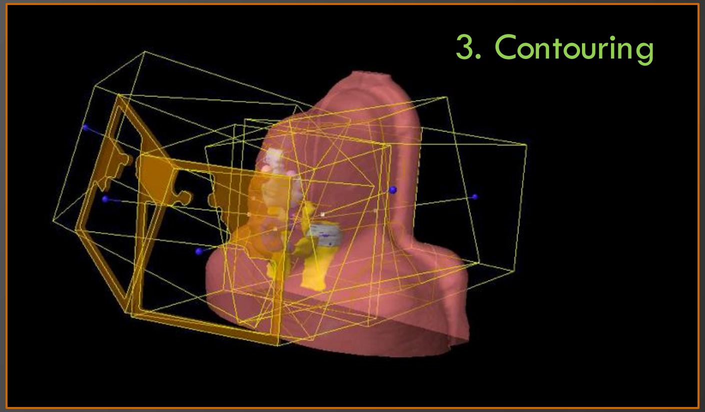


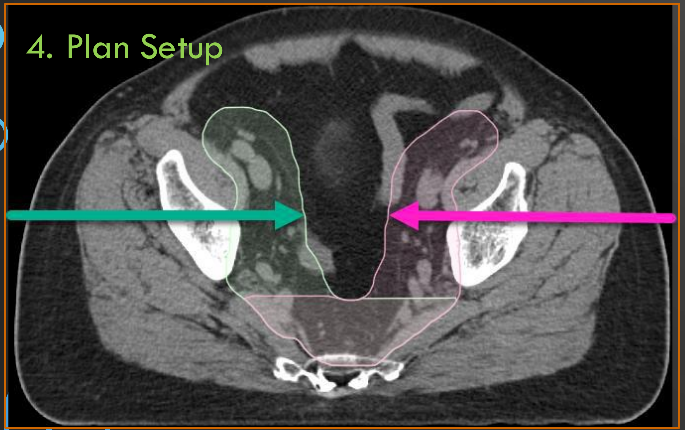
THE TPPT PROJECT: PT TREATMENT PLANNING

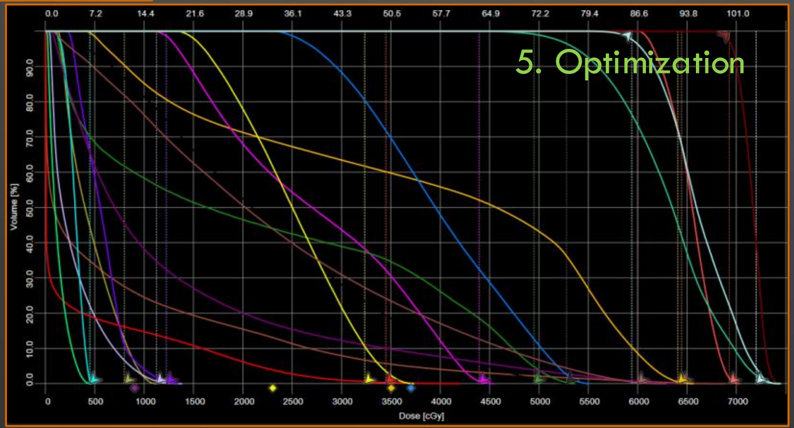
- High dose localization means that accuracy in PT is **paramount**
- Meticulous and sophisticated treatment planning – 5 days of intense preparations PER patient
- Imaging done before and after course of treatment (30 days of irradiation sessions) – NOT DURING!

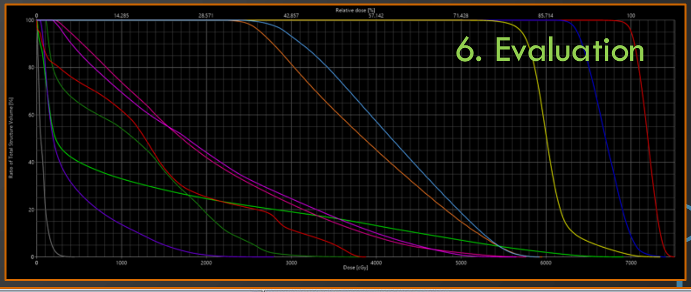


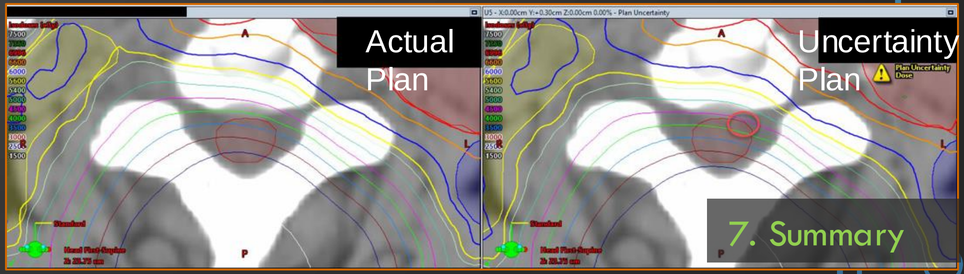










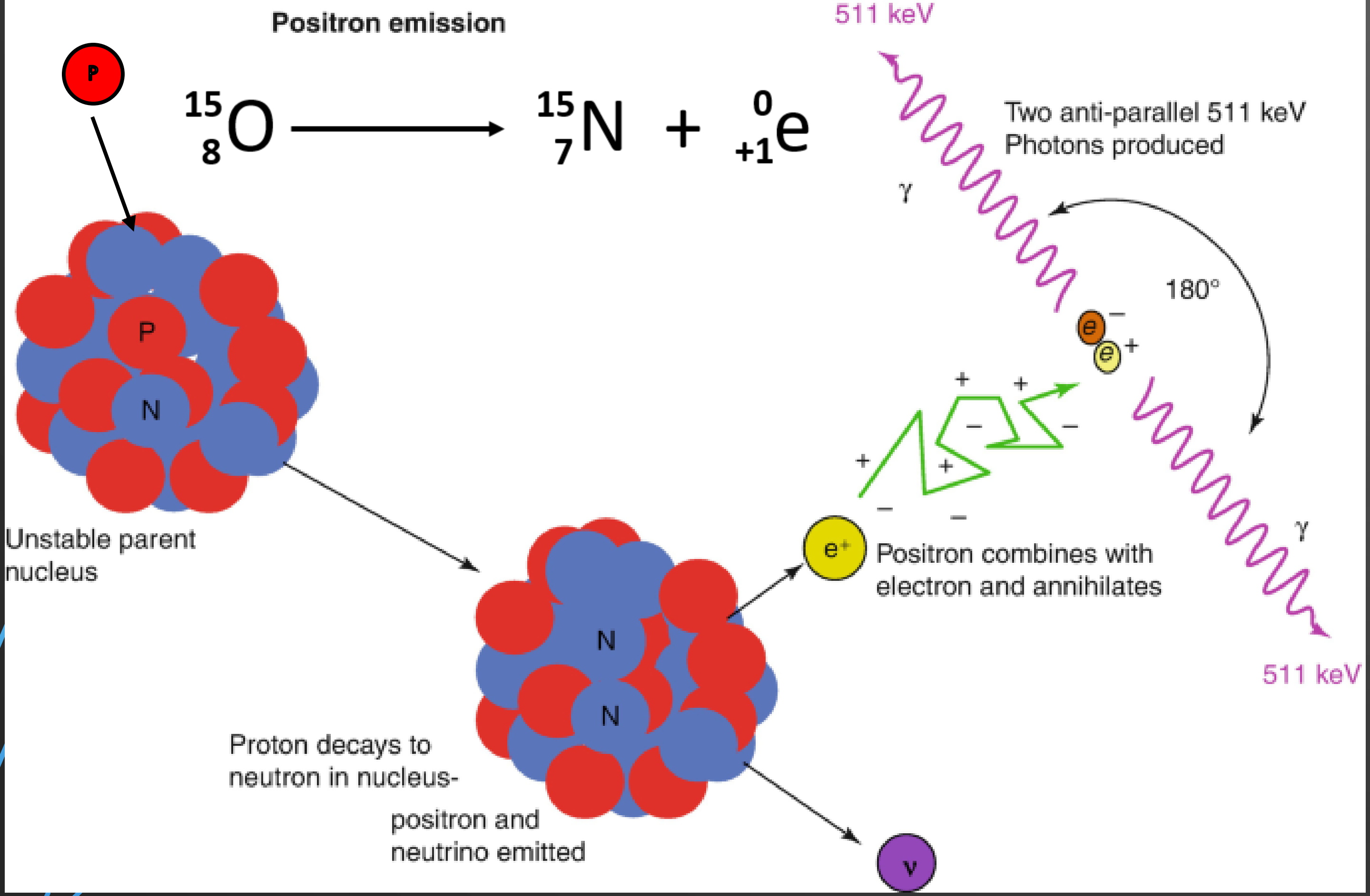


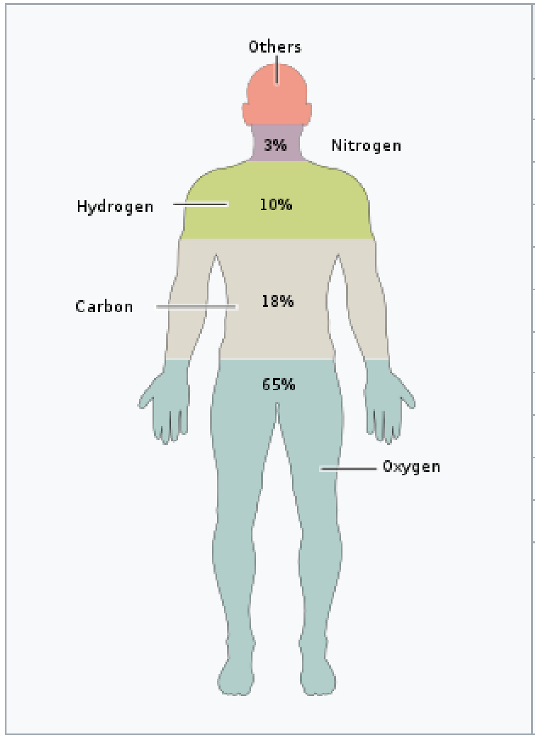
Can we "guide" PT treatments to make them safer, more effective, etc.? → Adaptive Treatment Protocols

From Christine Chung, MS, CMD, Research Dosimetrist

THE TPPT PROJECT: IN-BEAM PET

- Goal: asses, in-vivo, the range and dose of each proton beam irradiation, a.k.a. **Proton Range Verification**
- Approach: use activated positron emitters to monitor beam!





Element	Symbol	percent mass	percent atoms
Oxygen	O	65.0	24.0
Carbon	C	18.5	12.0
Hydrogen	H	10	62.0
Nitrogen	N	3.2	1.1
Calcium	Ca	1.5	0.22
Phosphorus	P	1.0	0.22
Potassium	K	0.4	0.03
Sulfur	S	0.3	0.038
Sodium	Na	0.2	0.037
Chlorine	Cl	0.2	0.024
Magnesium	Mg	0.1	0.015
All others		< 0.1	< 0.3

The main elements that compose the human body molecules (including water) can be summarized as CHNOPS.

Studenski MT *et al*. Proton therapy dosimetry

Table 1 Relevant positron emitter reactions in tissue from proton therapy

Reaction	Threshold energy (MeV)	Half life (min)	Positron energy (MeV)
$^{16}O(p, pn)^{15}O$	16.79	2.037	1.72
$^{16}O(p, \alpha)^{13}N$	5.66	9.965	1.19
$^{14}N(p, pn)^{13}N$	11.44	9.965	1.19
$^{12}C(p, pn)^{11}C$	20.61	20.390	0.96
$^{14}N(p, \alpha)^{11}C$	3.22	20.390	0.96
$^{16}O(p, \alpha pn)^{11}C$	59.64	20.390	0.96

THE TPPT PROJECT: IN-BEAM PET

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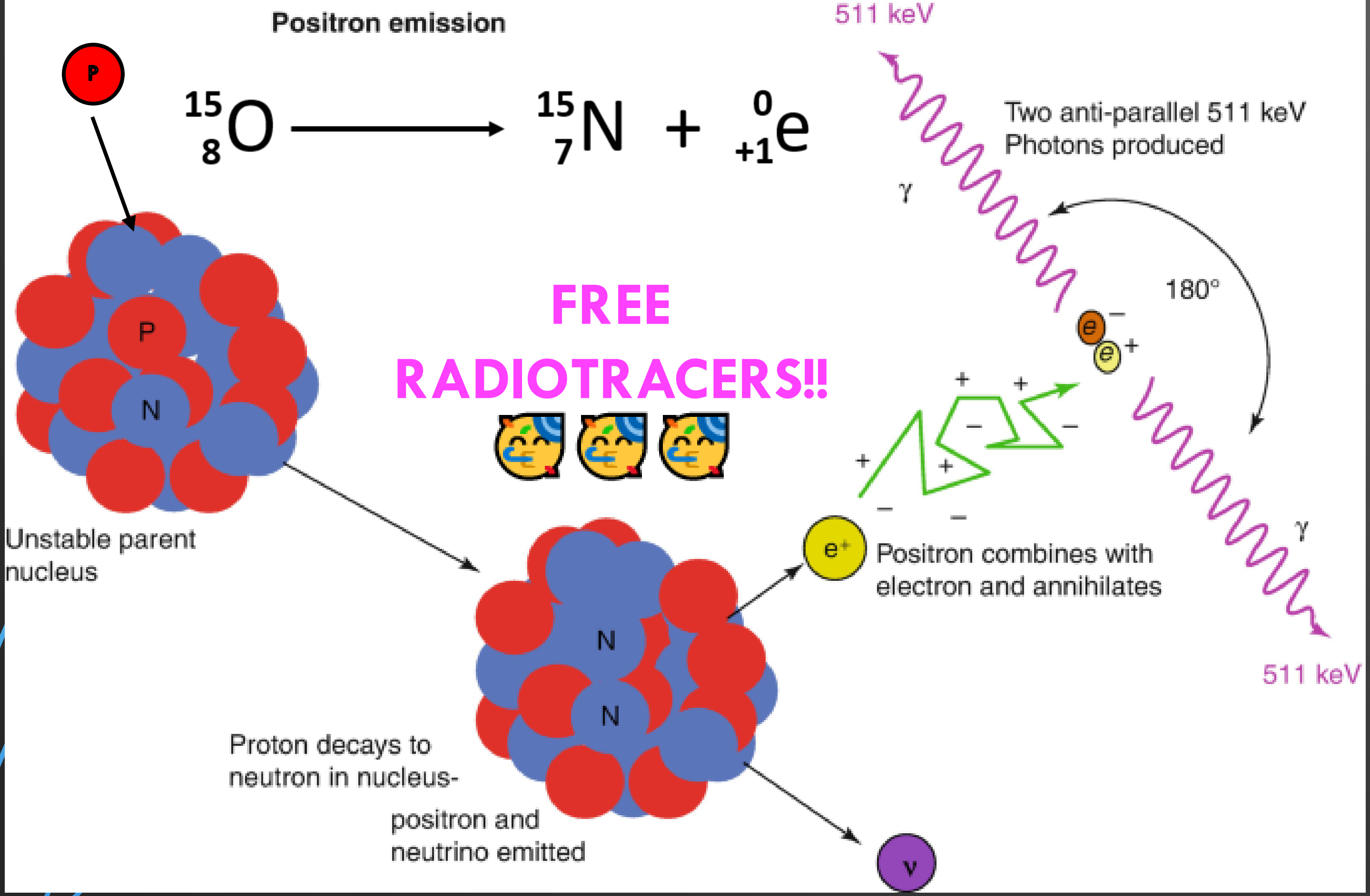

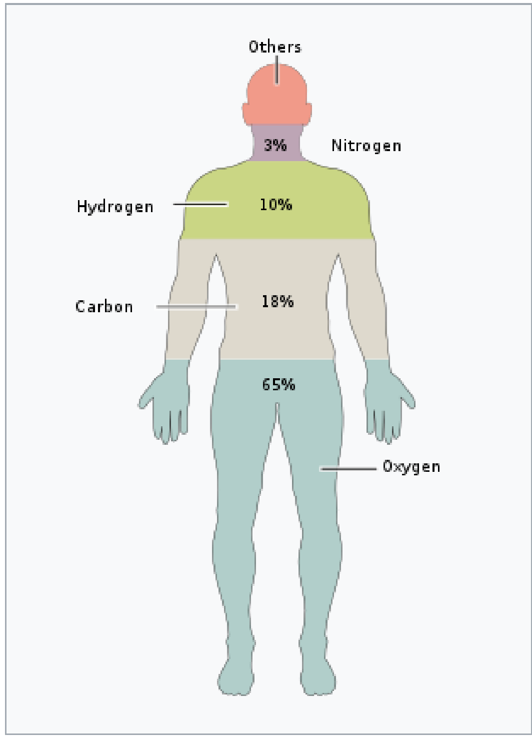

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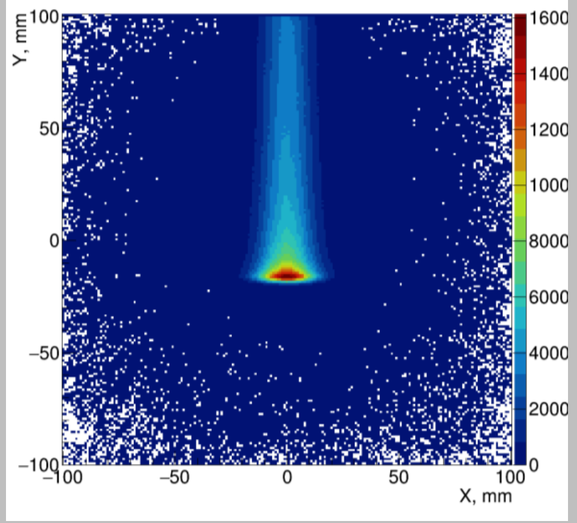
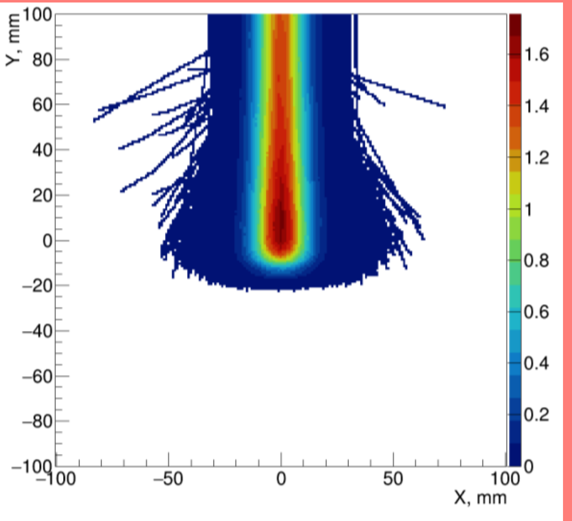
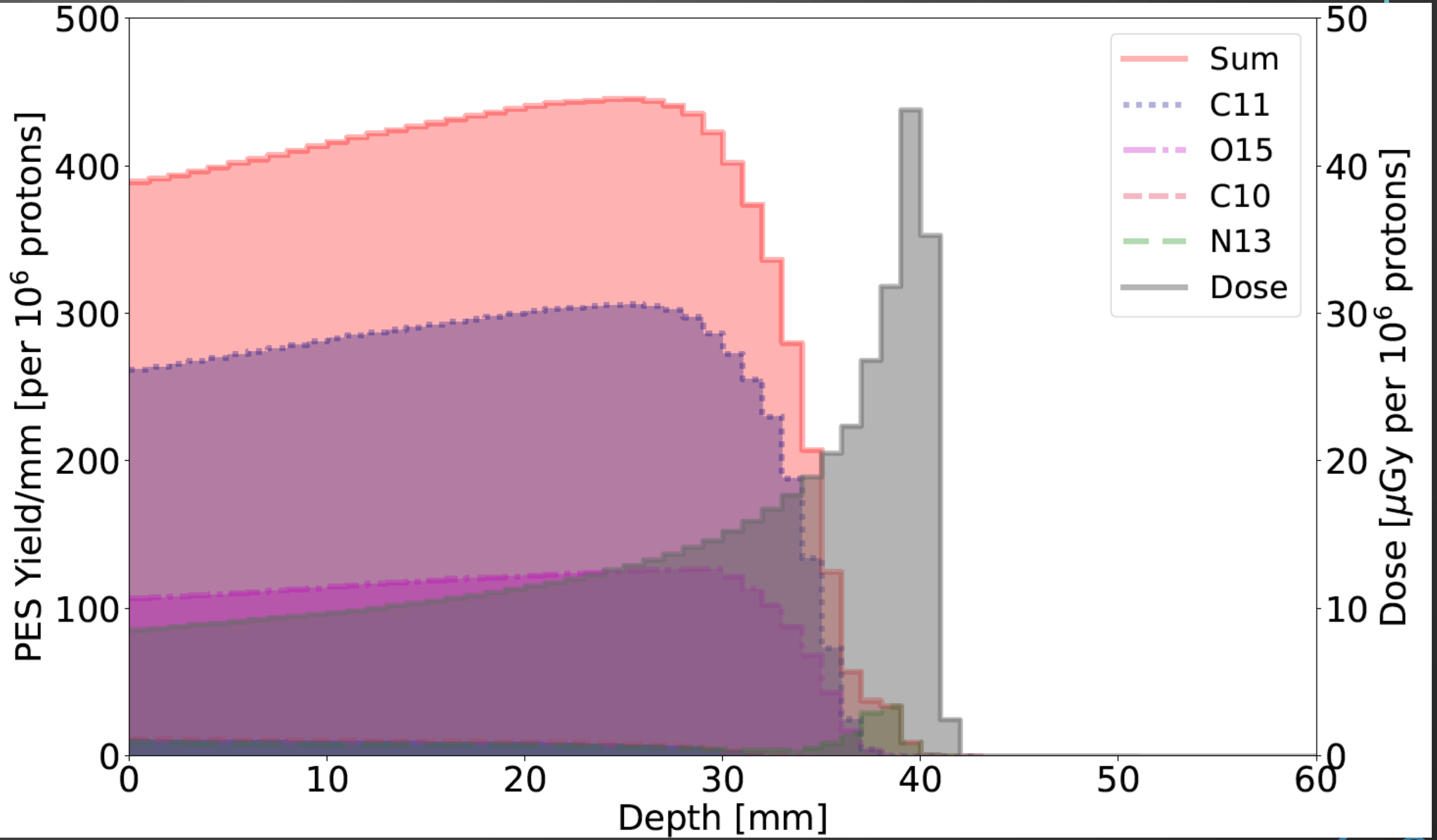
THE TPPT PROJECT: PROTON RANGE VERIFICATION

2D projection along beam of dose (Bragg Peak) due to **protons**



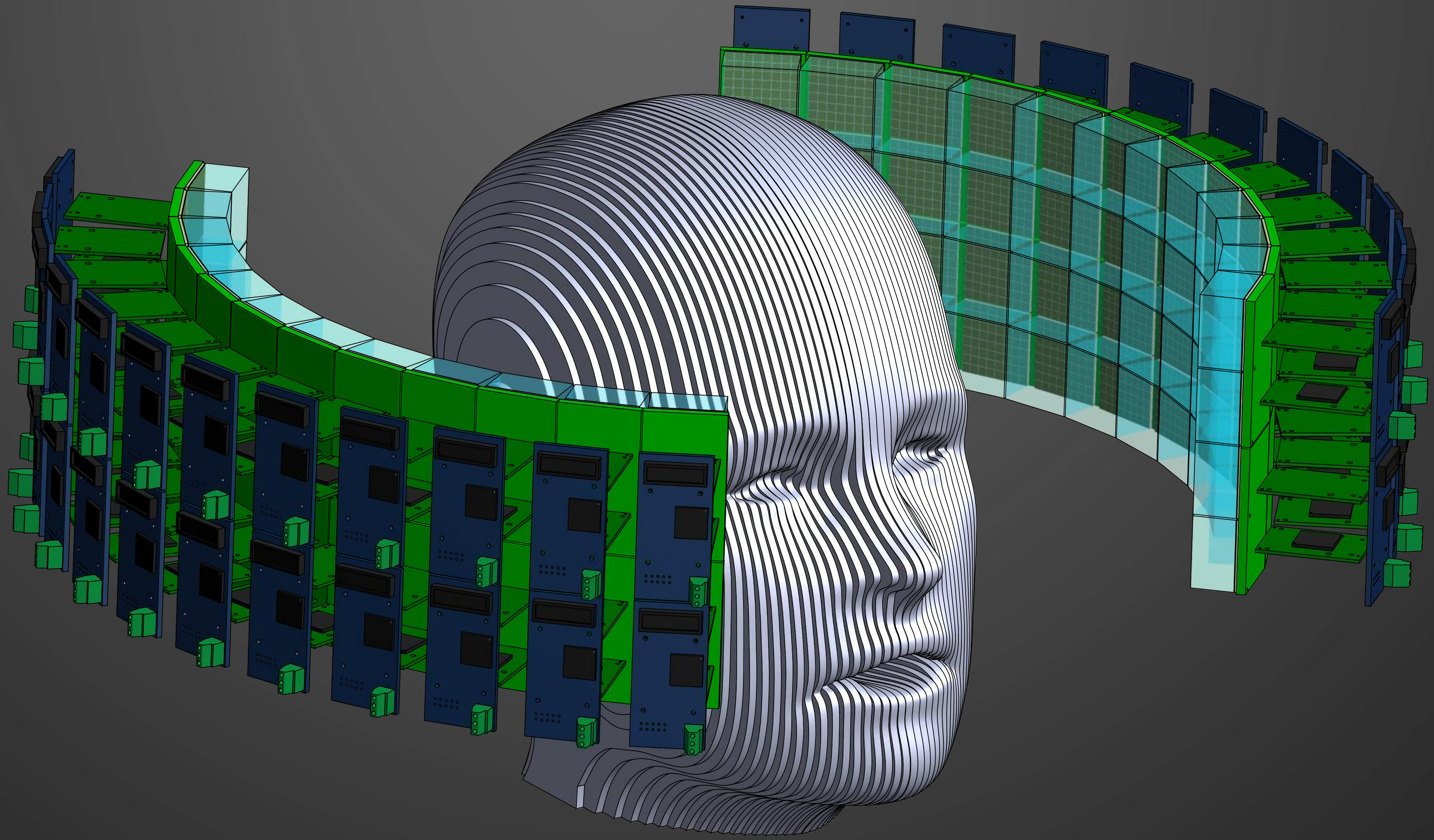
2D projection along beam of **PES** activity





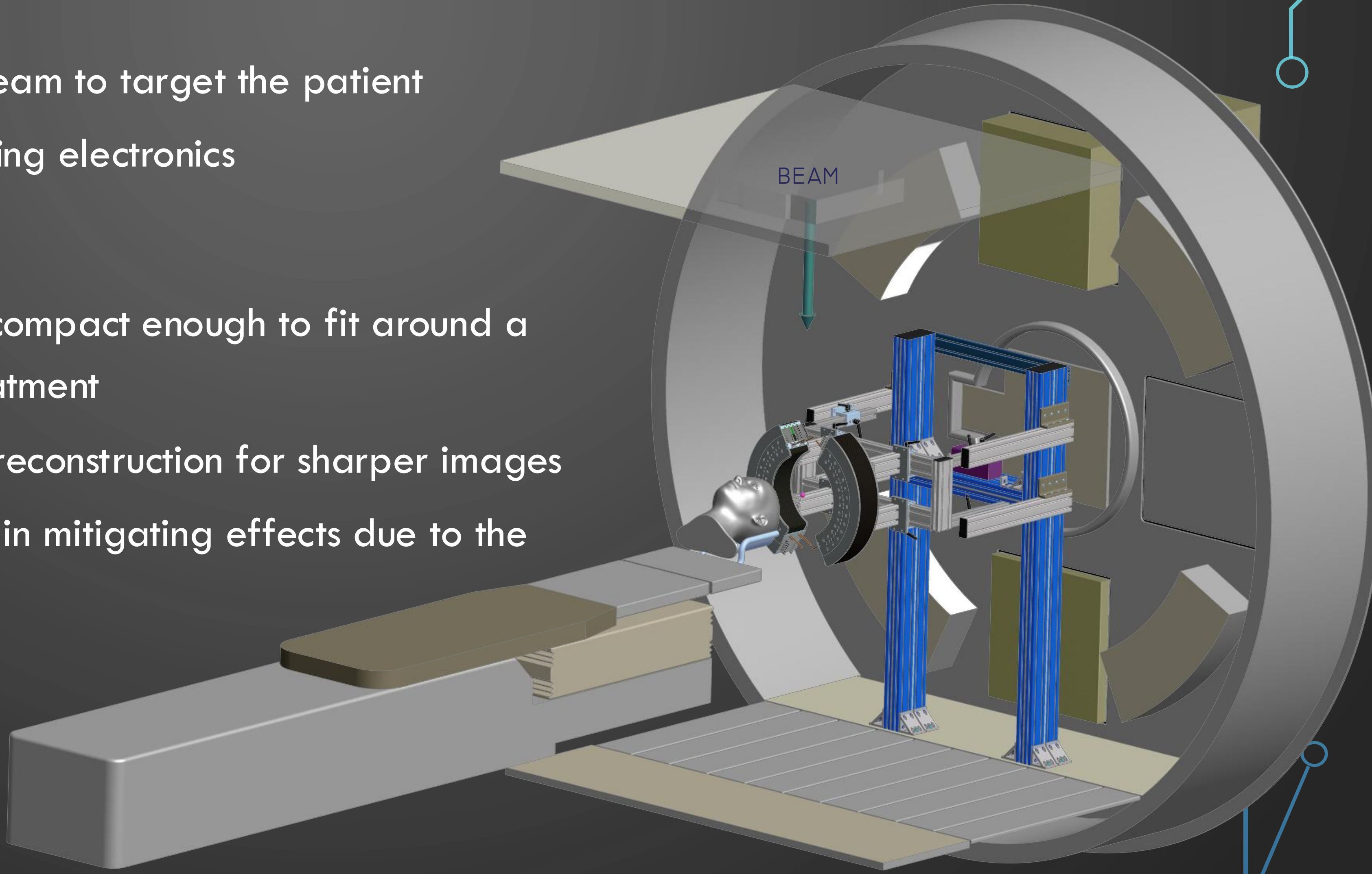
- PET imaging of PES can give feedback on proton beam dose and range
- Biological guidance? Tumor structure?

THE TPPT PROJECT: SCANNER DESIGN

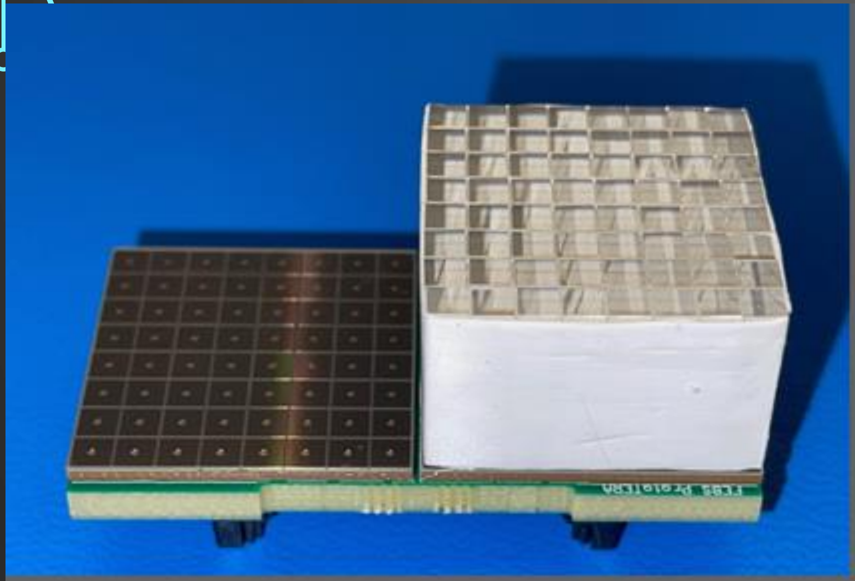


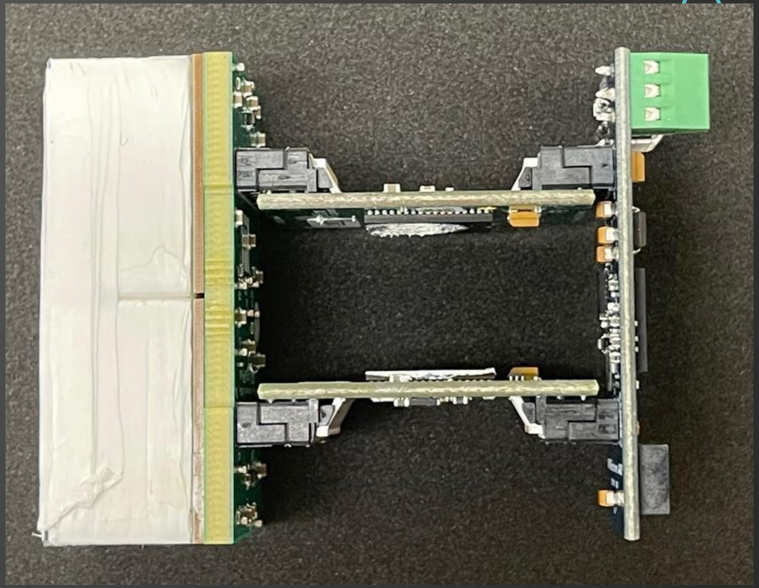
THE TPPT PROJECT: SCANNER DESIGN

- Partial ring design:
  - Openings allow for the beam to target the patient
  - Avoid irradiation/damaging electronics
- Use of SiPMs:
  - Allows the scanner to be compact enough to fit around a patient's head during treatment
  - Fast enough to allow ToF reconstruction for sharper images
  - ToF imaging is also useful in mitigating effects due to the partial ring design
- Needs high sensitivity
  - For short acquisitions
  - Due to short half lives



THE TPPT PROJECT: THE BASIC BUILDING BLOCKS





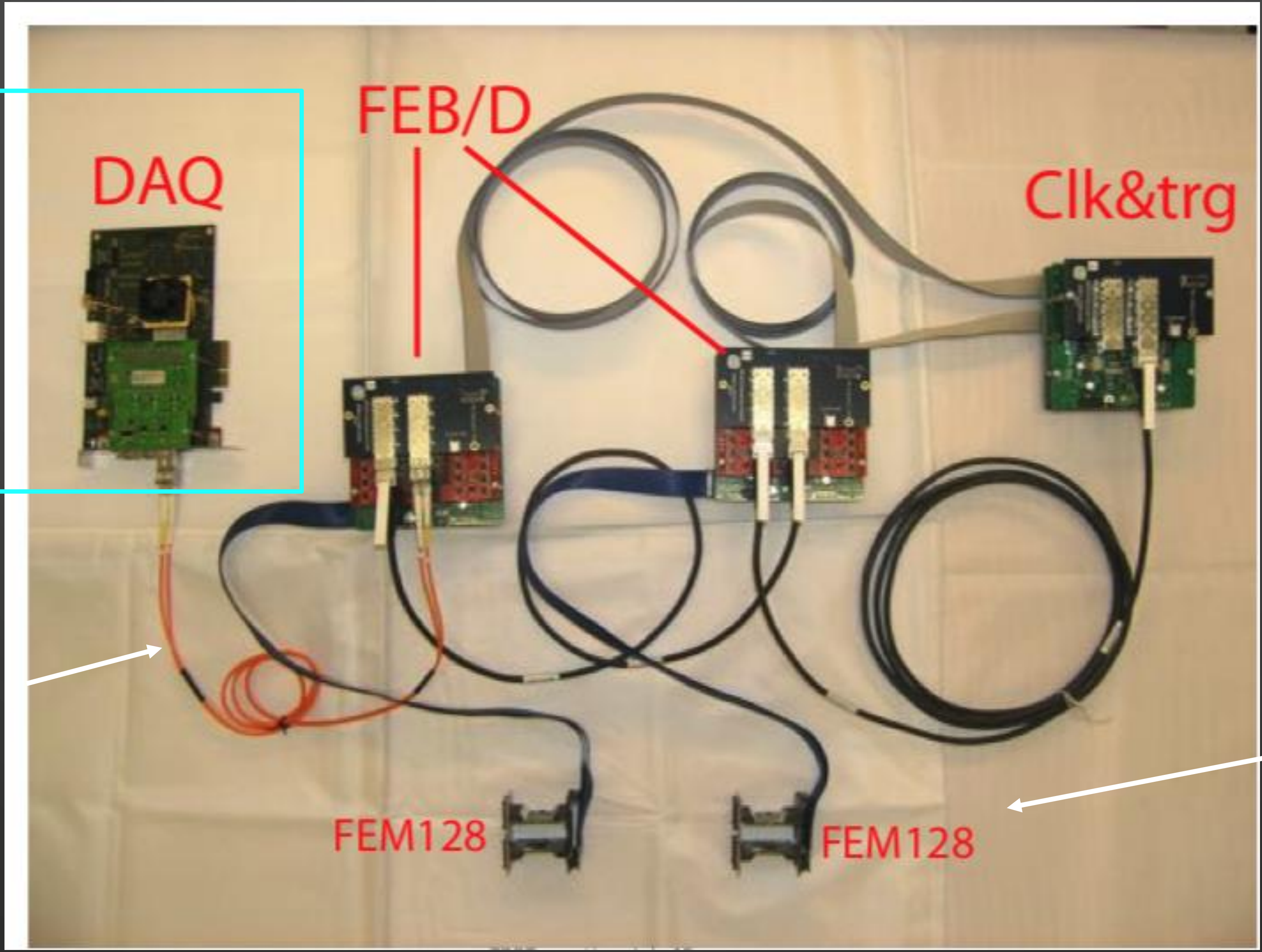
A Single TPPT "Module"

- Two 8x8 arrays of LYSO crystals coupled 1:1 to Hamamatsu SiPMs
  - This is a PET optimized MPPC!
- Crystals dimensions of 3mm x 3mm x 15mm
- ESR + Teflon between and around crystal surfaces
- Front-end electronics from collaborators at PETsys Electronics

THE TPPT PROJECT: PETSYS ELECTRONICS

Data Acquisition (DAQ) PC

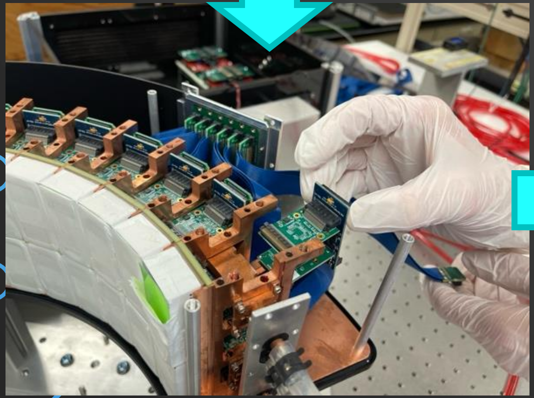
Fiber optic communication between system and DAQ PC

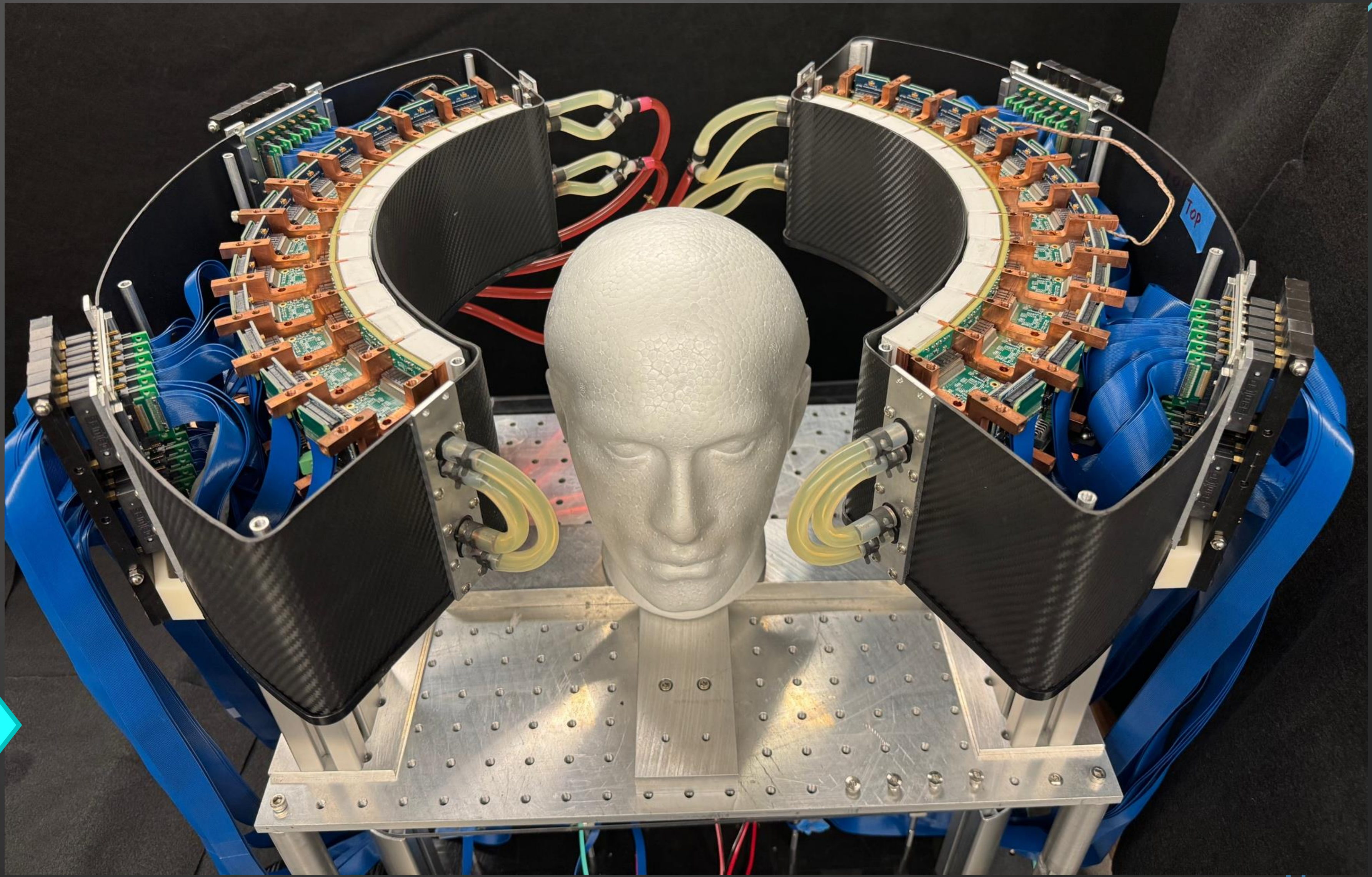


x 48 modules for full scanner

6144 total channels

THE TPPT PROJECT: THE COMPLETE SCANNER





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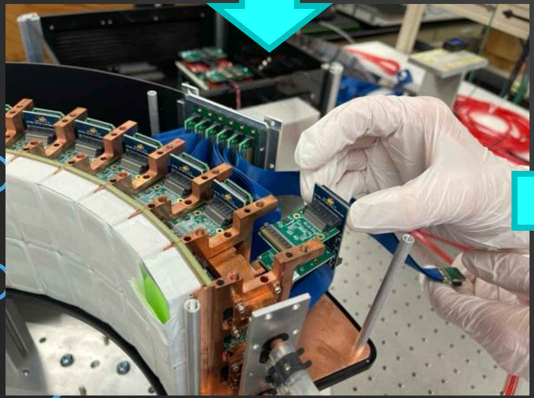
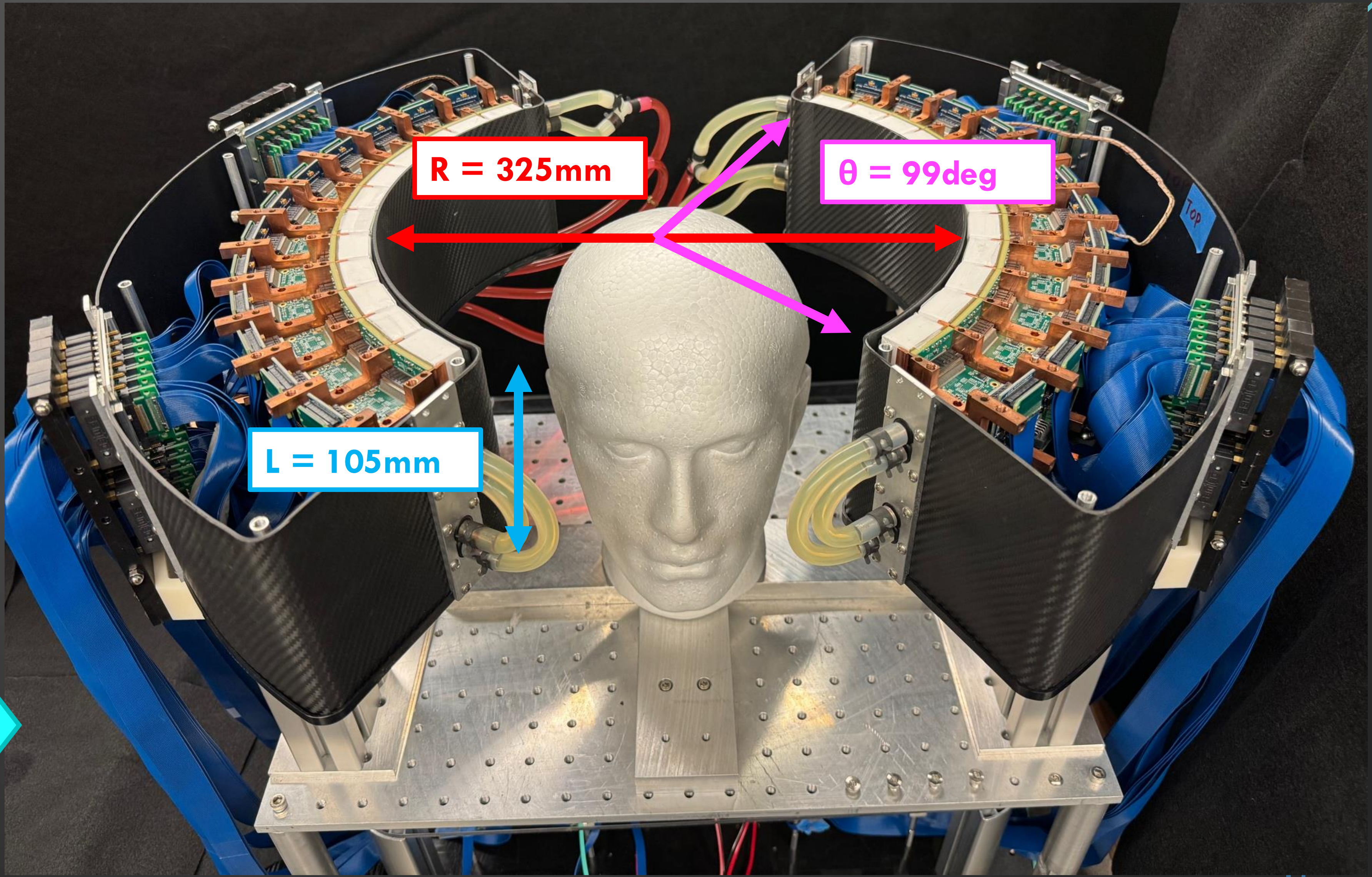
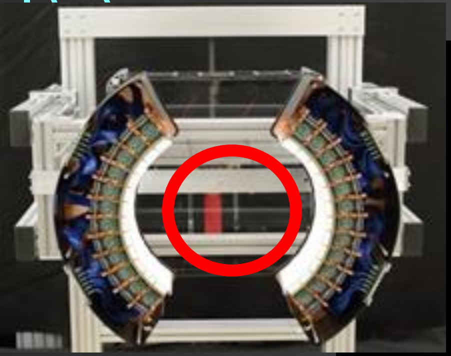
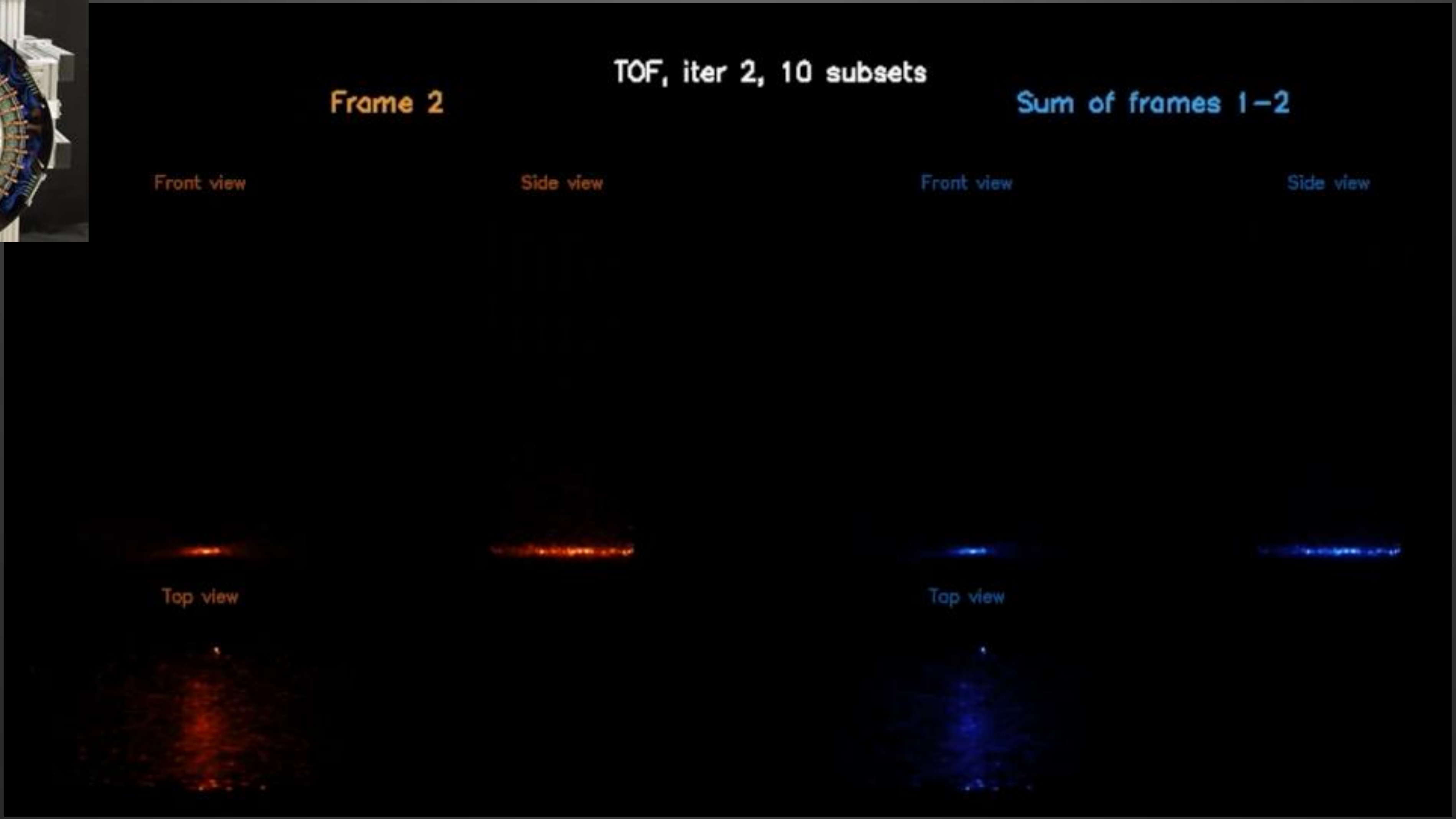




THE TPPT PROJECT: FIRST RECONSTRUCTED IMAGES!

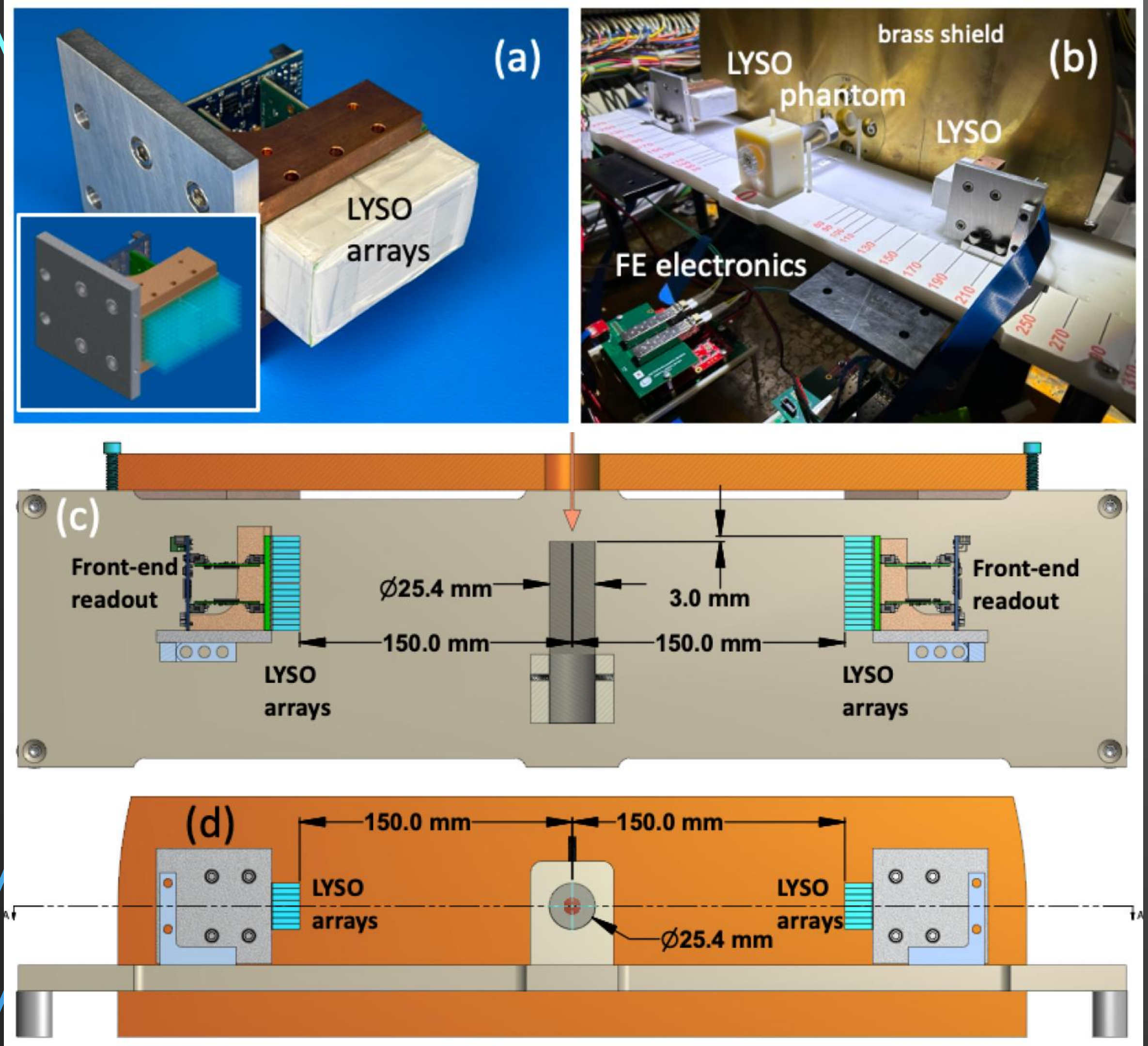




IN-BEAM PET

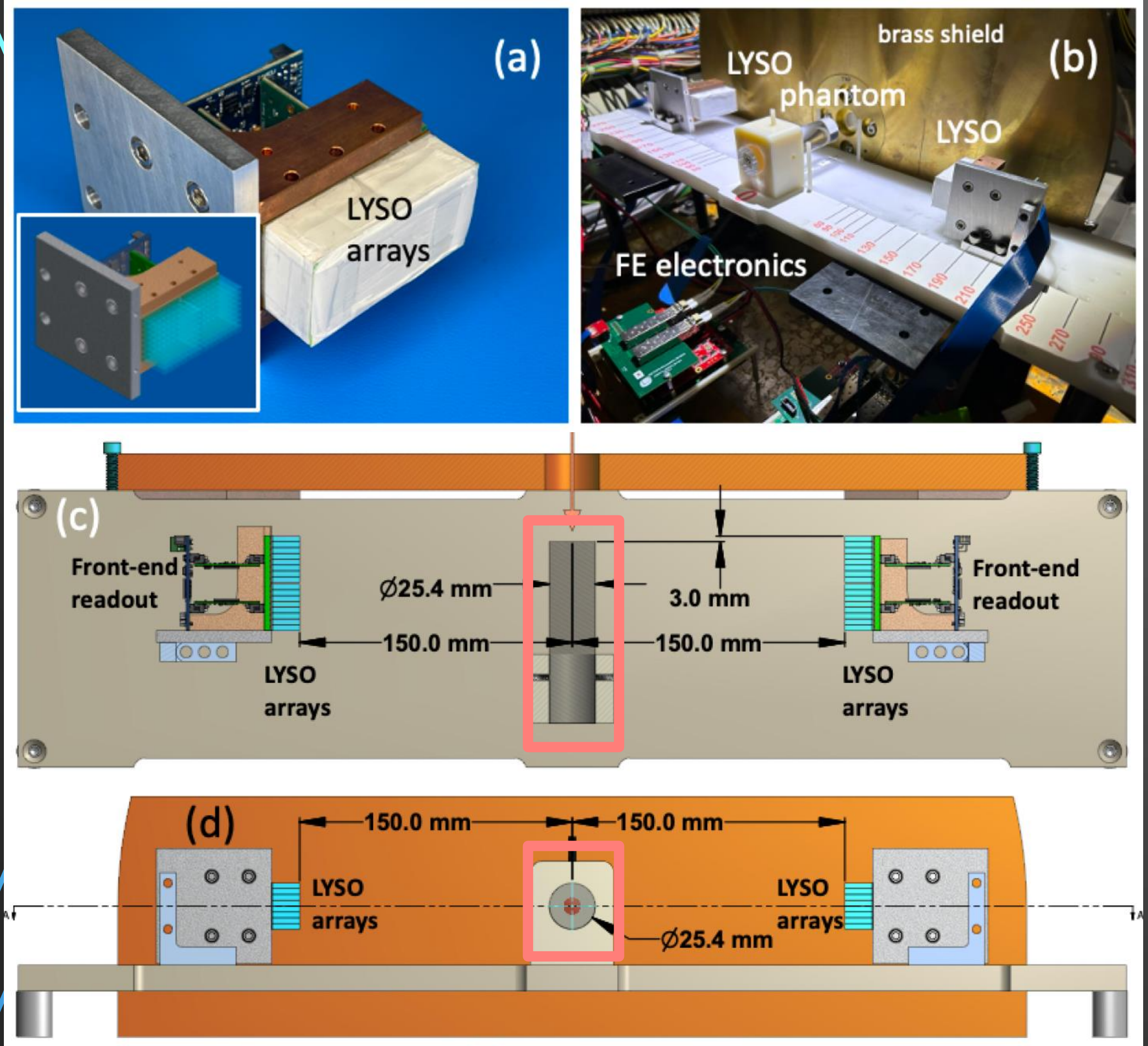
Can the TPPT scanner ”see” a proton beam?...

IN-BEAM PET: FIRST STUDIES



- Collaborated with MD Anderson Cancer Center in Houston, TX
- Granted access to a non-clinical ocular fixed beamline
- Novel beam was setup for **FLASH** delivery
  - 75.8 MeV protons
  - **164 Gy/s (Conventional = <1Gy/s)**
  - **101.5 ms beam spill (Conventional = O(sec))**
  - ~3.5×10^{10} protons/spill
- First visits were very exploratory
  - Used two TPPT modules to create a "MiniPET" scanner
- Target (phantom) = plastic cylinders
  - Plastics are mostly C, H, O just like humans!

IN-BEAM PET: FIRST STUDIES



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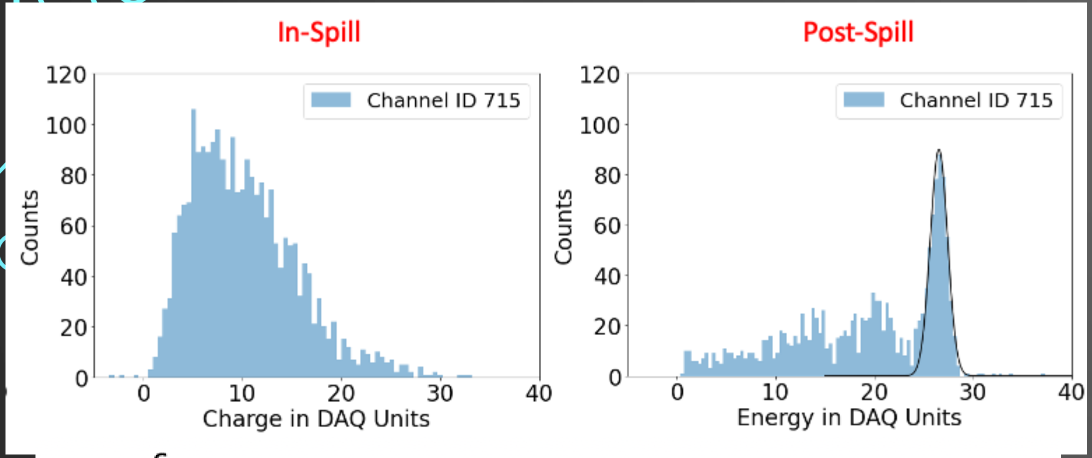
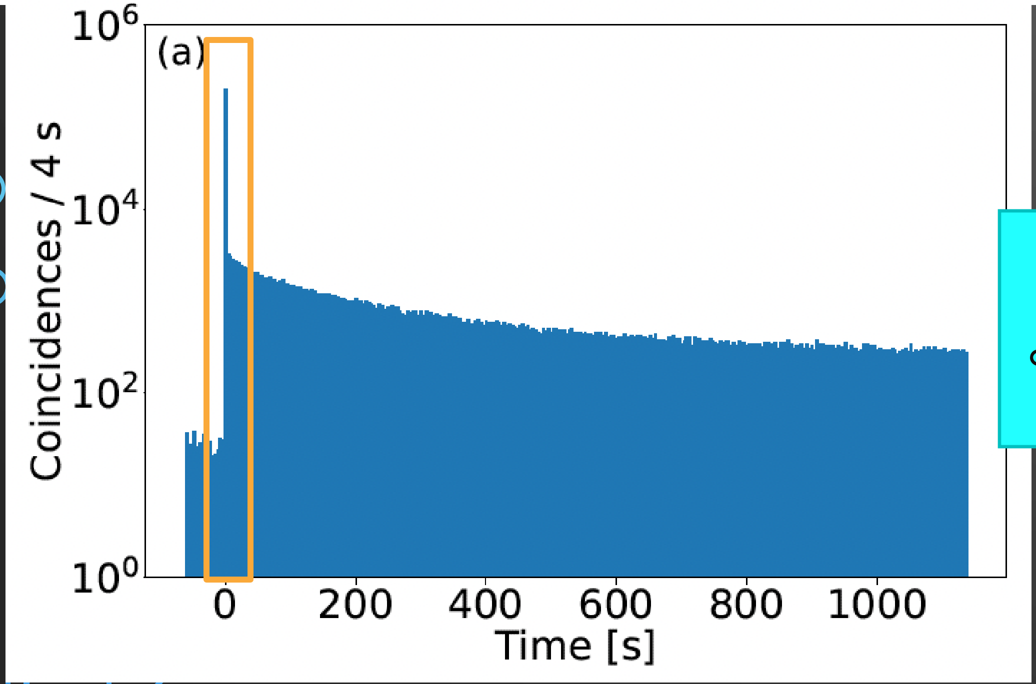
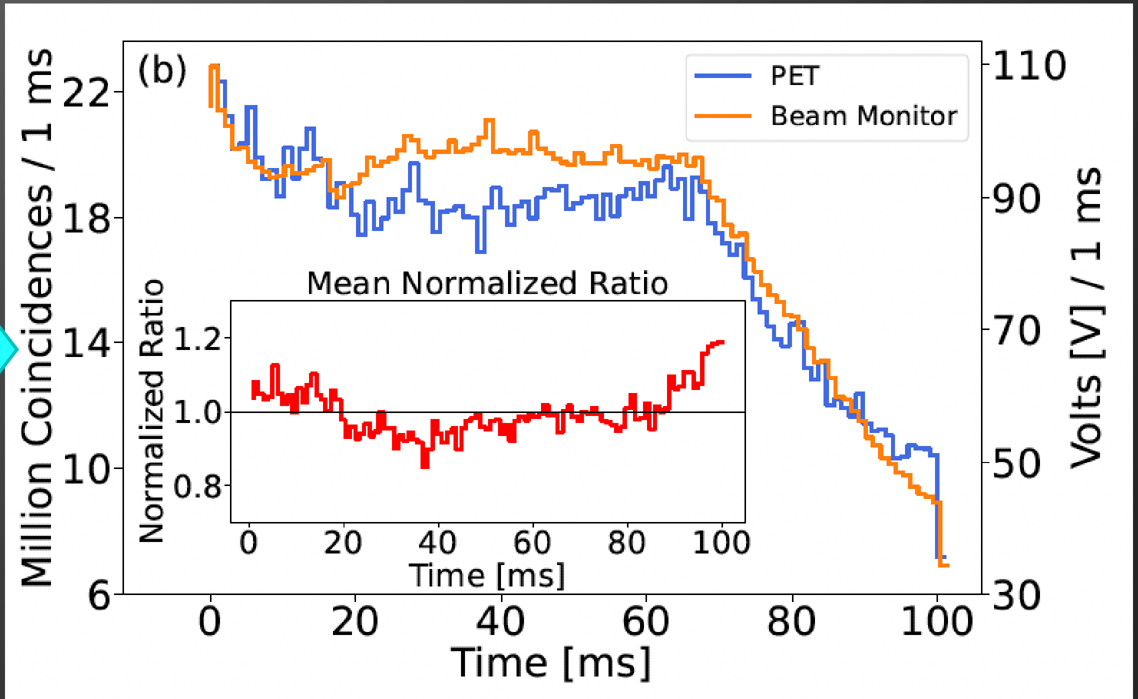
IN-BEAM PET: NOVEL USE OF PROMPT GAMMAS



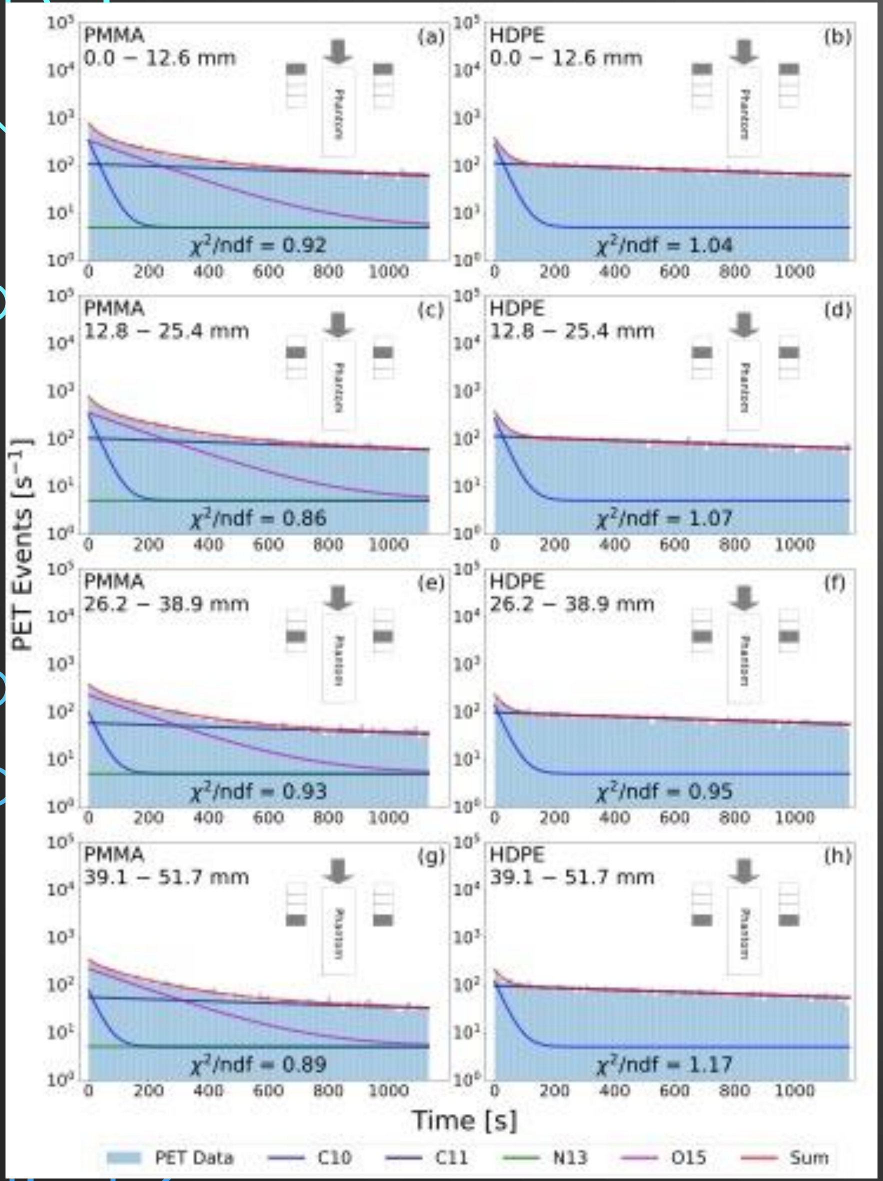
- Typically, only care about post-beam PES but…
- Prompt Gammas successfully used to reconstruct a proxy for the beam intensity during the 100ms spill
- Matched well with upstream beam monitor



Squared rate of random coincidences in 1ms window



IN-BEAM PET: PES ABUNDANCE MEASUREMENTS



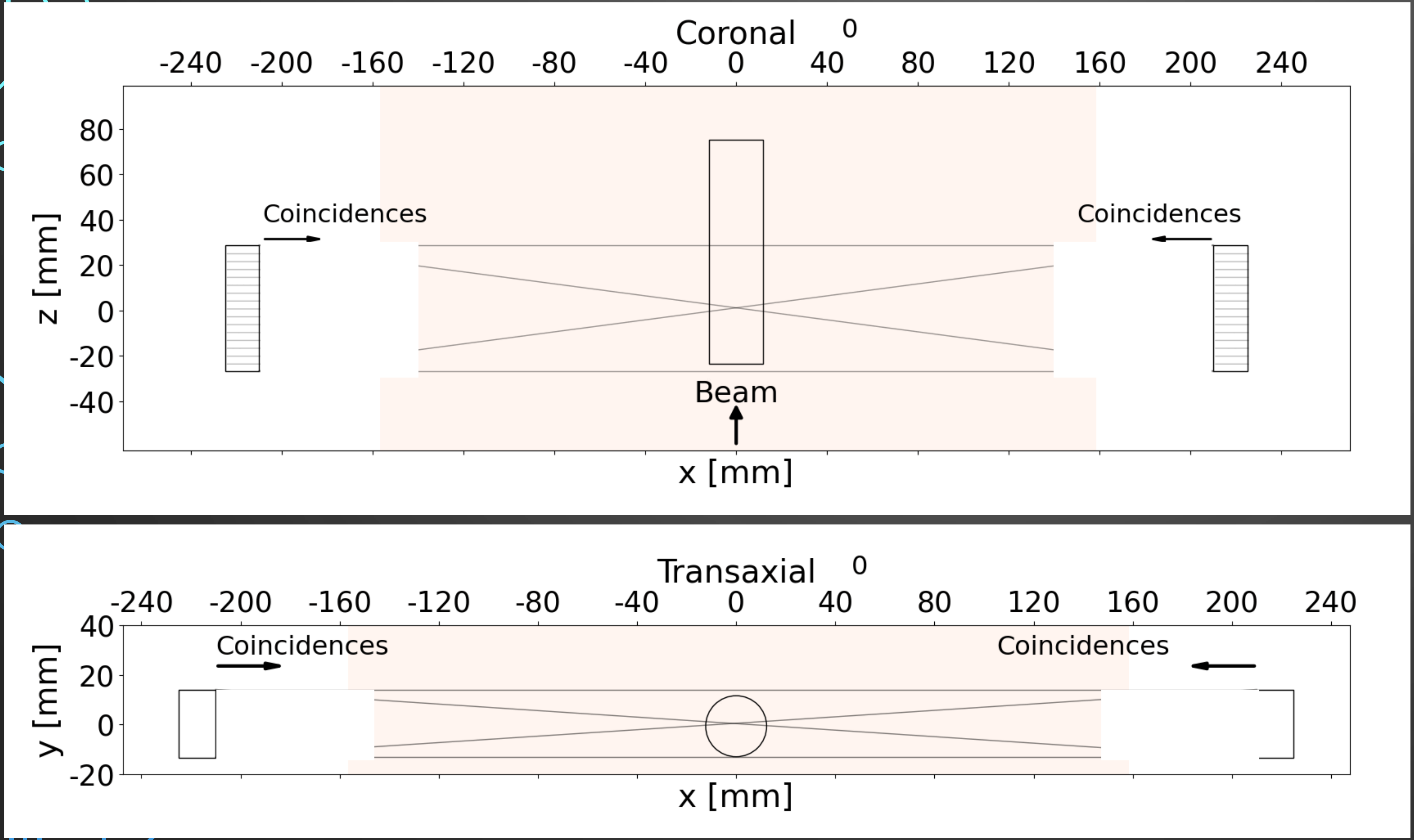
- Divided our modules into 4 sections (each consisting of 4 columns of crystals)
- Studied relative abundance of PES isotopes as a function of penetration depth into our target (phantom)

Phantom	^{10}C	^{11}C	^{15}O	^{13}N	χ^2/ndf
$T_{1/2}$[s] →	19.3	1220.4	122.4	597.9	
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
39.1–51.7 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
39.1–51.7 mm	0.55	0.45	—	—	1.17

PMMA = $(C_5H_8O_2)_n$

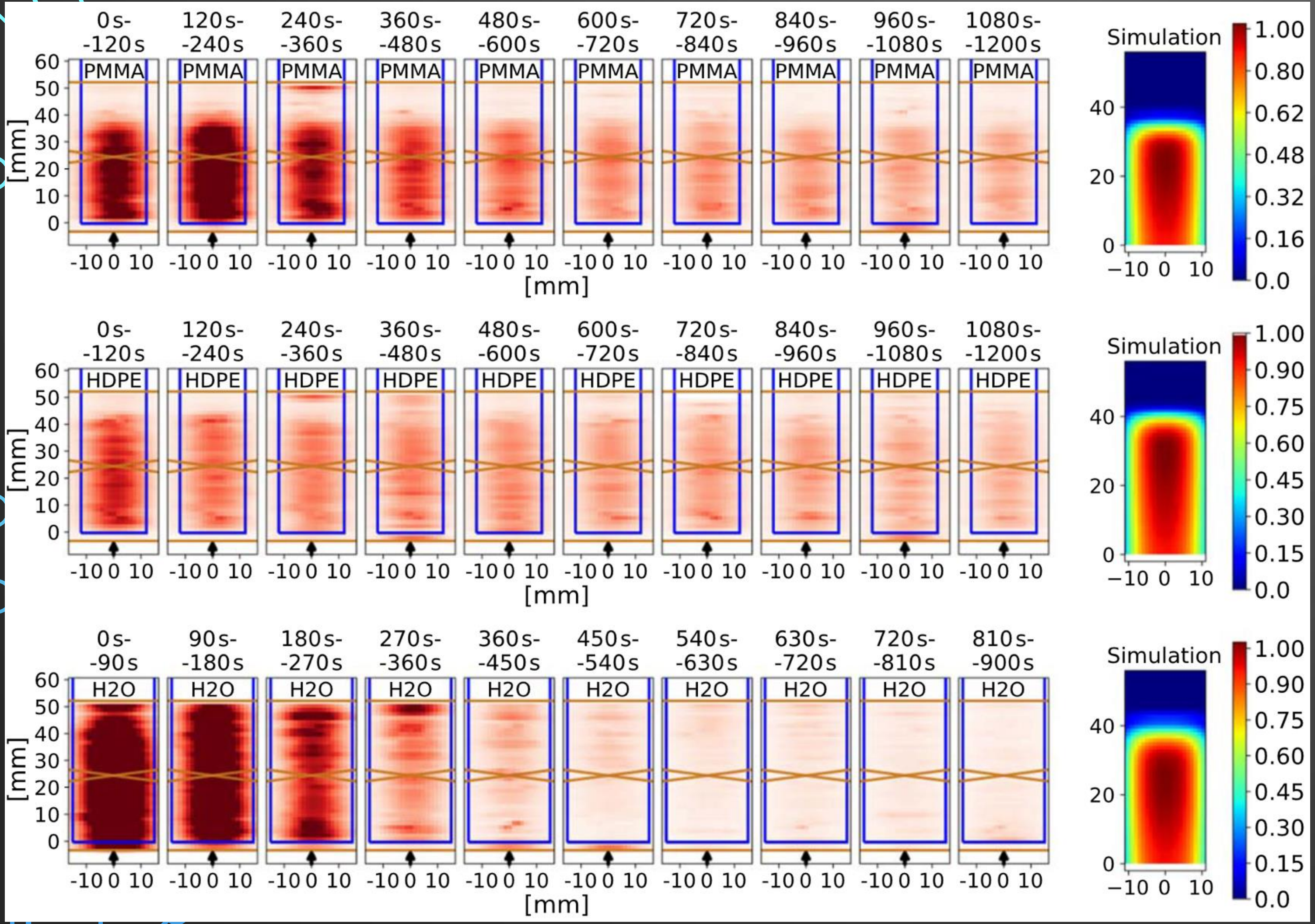
HDPE = $(C_2H_4)_n$

IN-BEAM PET: DYNAMIC IMAGING



- Dynamic reconstruction of PES activity
  - 30sec/frame
- Can see temporal and spatial distribution of PES activity
- Just two PET modules!
  - Localization along x-direction almost entirely due to ToF properties!

IN-BEAM PET: DATA AND SIMULATIONS



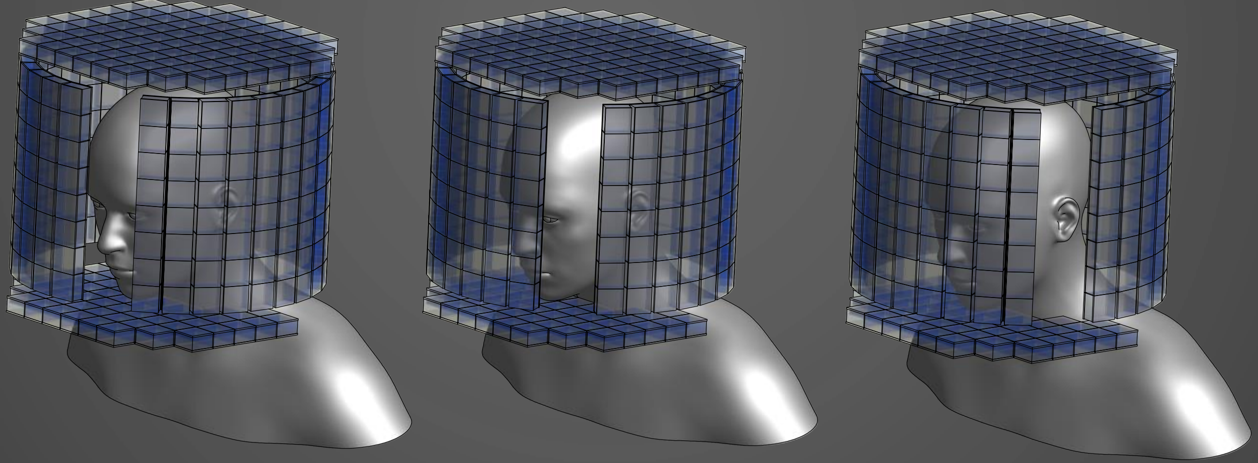
- GEANT-4 simulations agree well with ranges obtained in imaging
  - Even with Limited FOV
- Short acquisitions (3-5 minutes) can yield valuable range measurements!
- Temporal and spatial distributions of PES may yield new insights into response to treatment
  - Radio-sensitivity, tumor micro-environment, etc.
- Studies with water proved difficult due to diffusion effects
- In-Beam results with full scanner forthcoming soon!...

FUTURE IDEAS

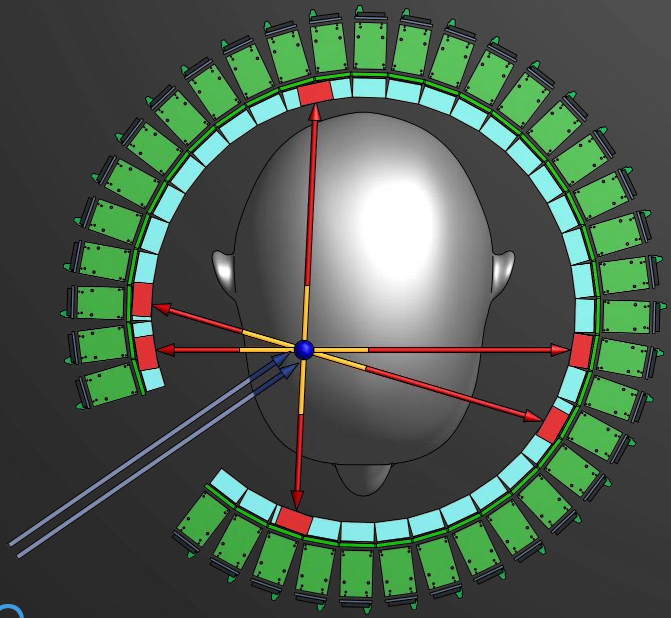
Novel PET designs that are only achievable with SiPMs

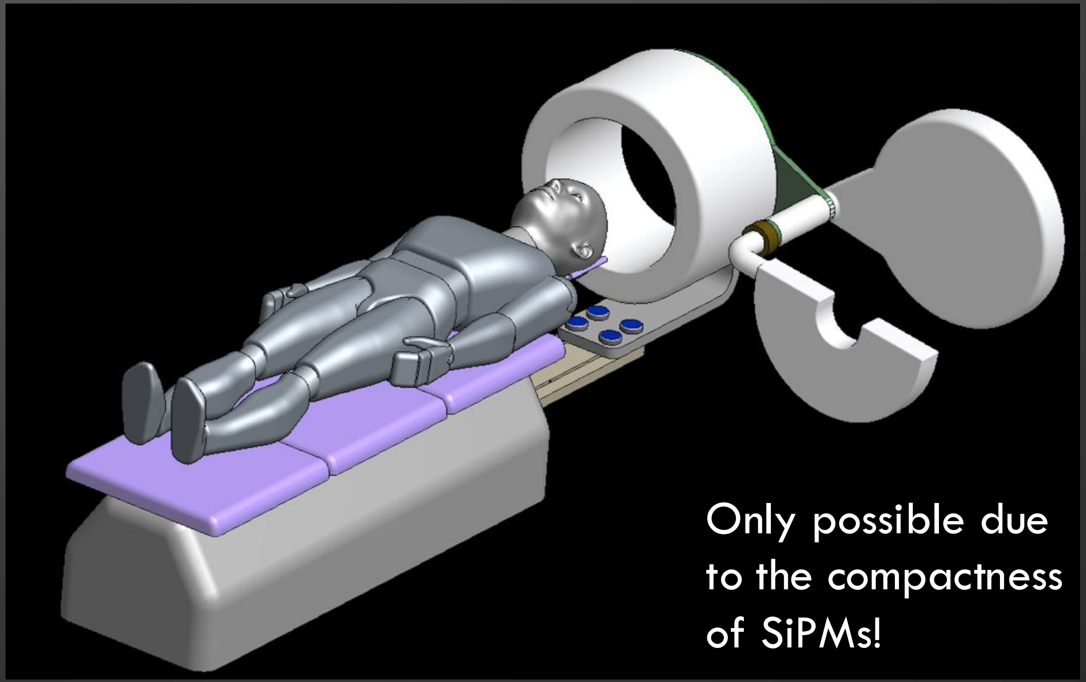
FUTURE IDEAS: C^3-PET + PROTON THERAPY

Chin -
Crown -
Cylinder - **PET**



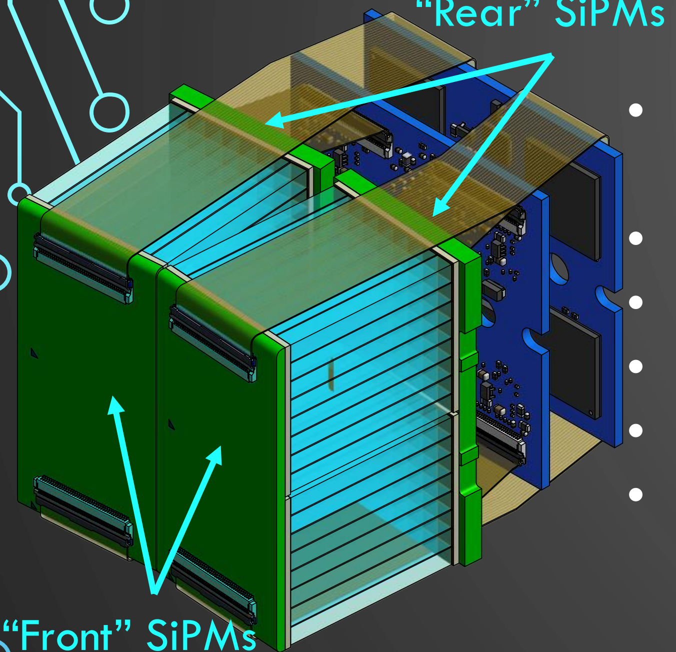
Rotating helmet-style design with gap allows for beam delivery at any angle



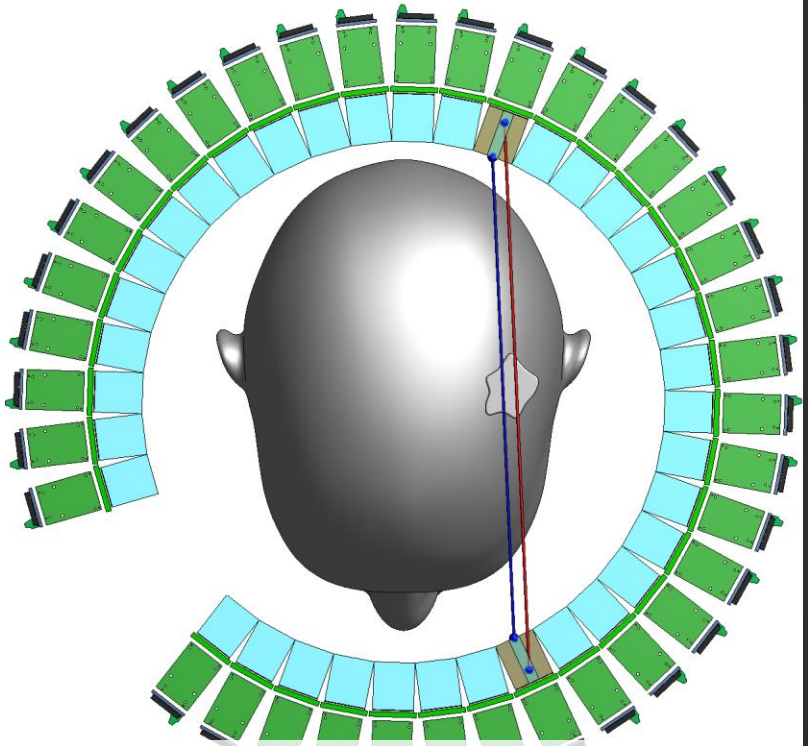


Only possible due to the compactness of SiPMs!

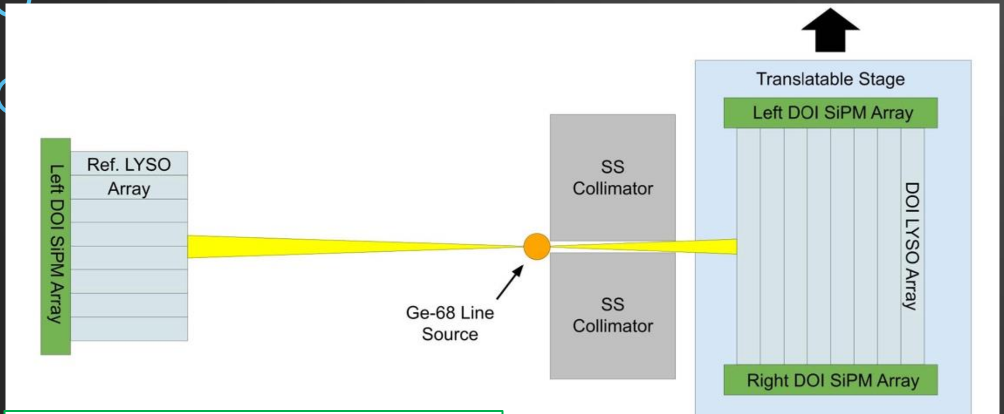
FUTURE IDEAS: PET + DOI



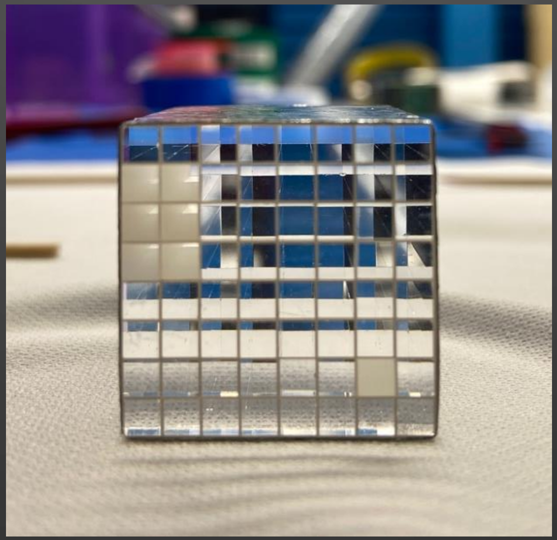
- Can we obtain depth-of-interaction (DOI) information from PET systems?
- Sandwich crystals between 2 SiPM arrays
- Use relative intensities to extract DOI
- Helps eliminate parallax error
- Potential to greatly improve image quality
- Studying effects of crystal properties on DOI resolution

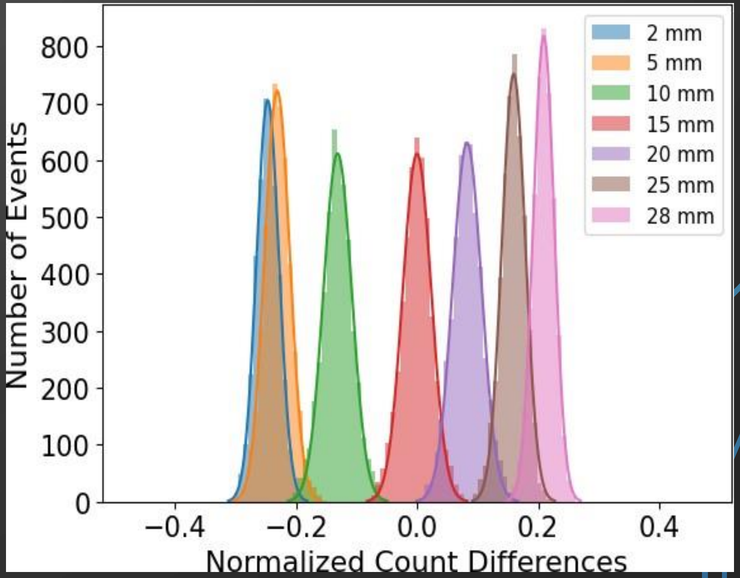


Ex: parallax error resulting in shifted LOR



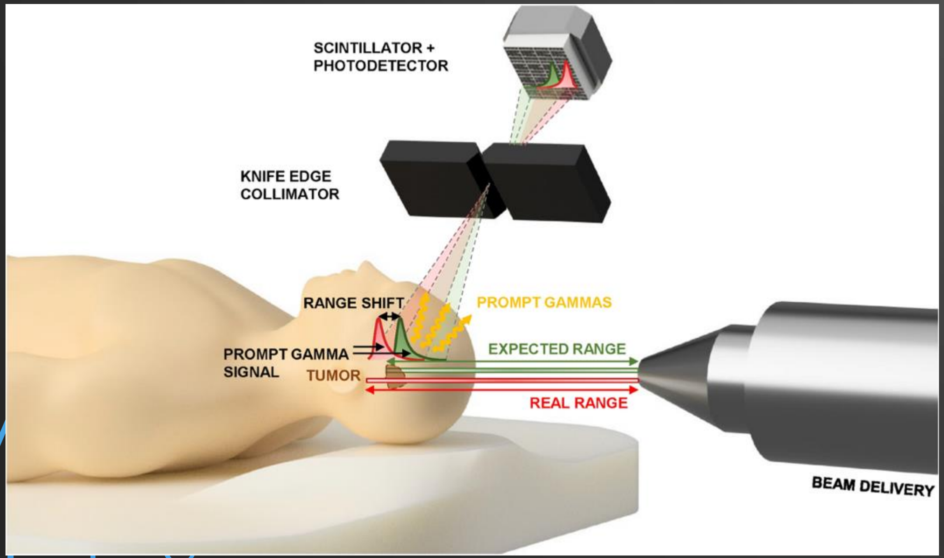
DOI Testing Setup at UT

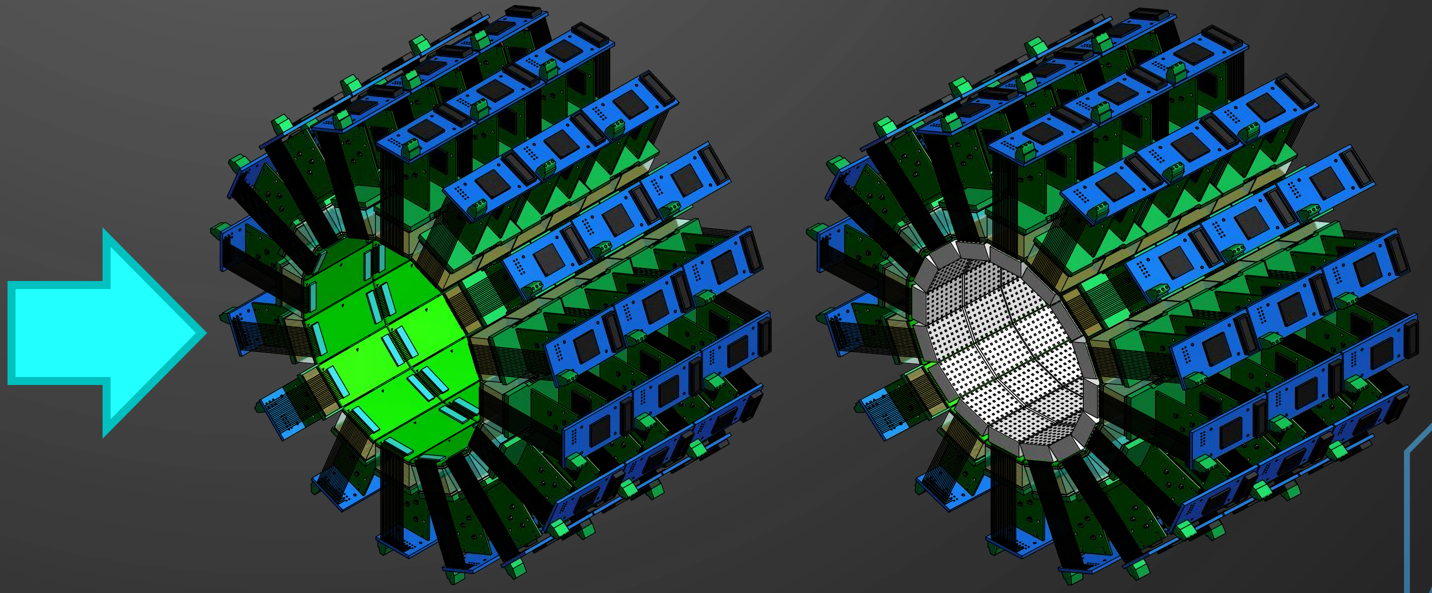




FUTURE IDEAS: PET + PGI/SPECT

- Another method of in-beam imaging is PGI (prompt gamma imaging)
- Uses the prompt gamma created by the beam (in nanoseconds)
  - No need to wait for PES to decay (in seconds or minutes)
- Quick "snapshot" of the beam → Reduces biological washout effect
- Can they be combined: PET + PGI/SPECT? Requires collimation…





DOI PET with removable collimator

SUMMARY AND CONCLUSIONS

- Physicists **CAN** help in the fight against cancer!
  - Medical professionals are incredibly valuable and talented but also very busy!
  - We can apply our long history and expertise in detector technology to advance the field
  - Help improve treatment outcomes for PT patients
- … And SiPMs have been crucial in this effort!
  - They offer numerous advantages over PMTs in PET imaging:
    - Fast timing, pixelization, compactness, functionality in magnetic fields fields (for integration with MRI)
  - Can be used to create novel scanner designs to push PET into new territory
- The TPPT Scanner is one such example of a next-gen SiPM-based PET system
- Have demonstrated the power of in-beam PET with early exploratory studies
  - **Rich data set from using just two PET modules!**
  - **And we were able to image a FLASH beam no less! It had never been done before!**
- Data taken in-beam with the full scanner forthcoming!

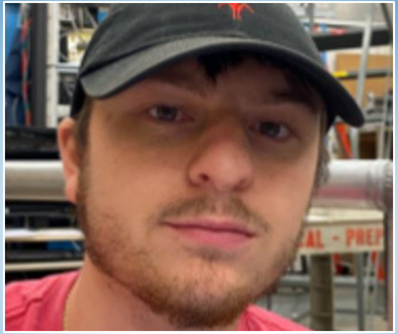
THANK YOU!

Karol Lang

Marek Proga

John Cesar

Kyle Klein



Firas Abouzahr

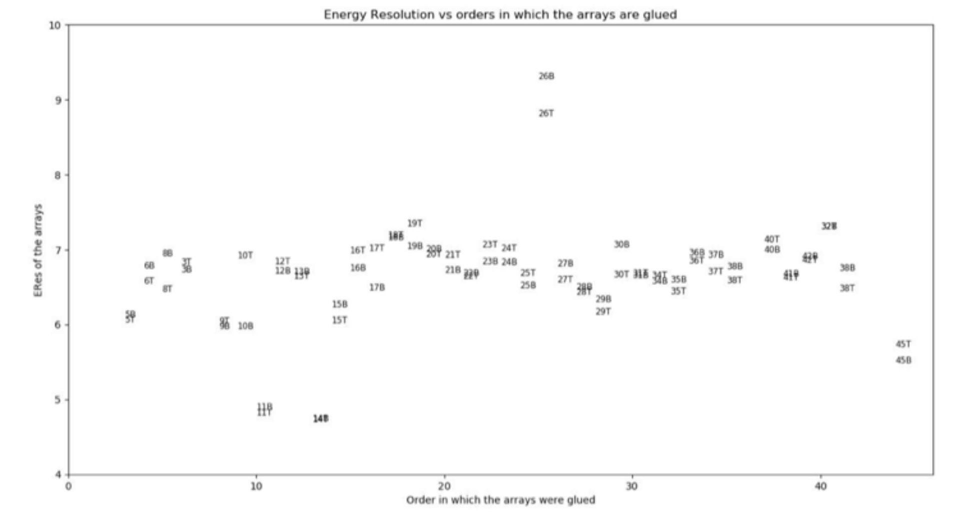
Alex Kuo

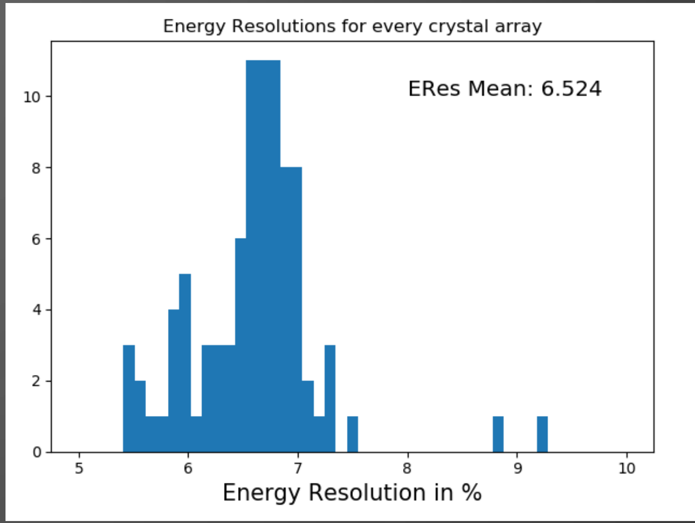
Aryan Ojha

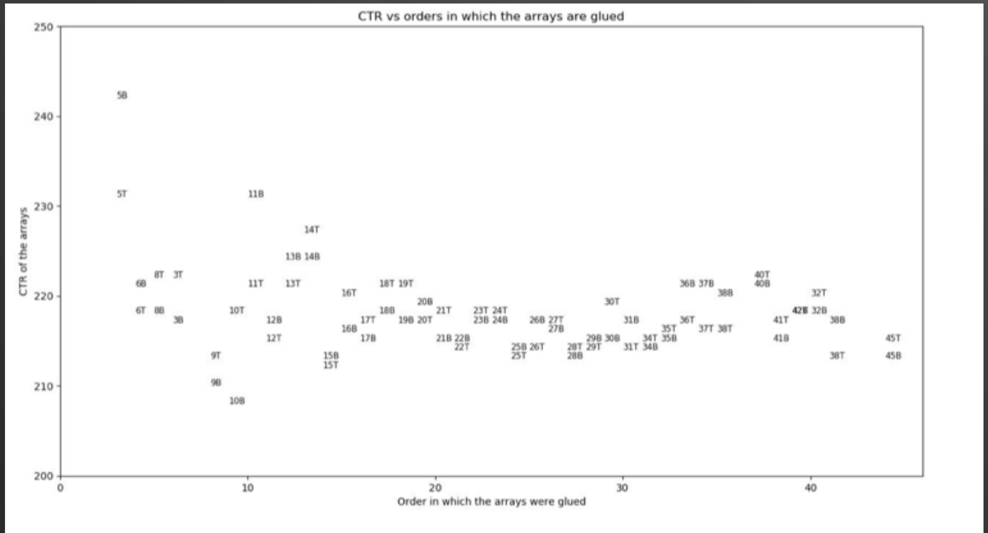
Michael Gajda

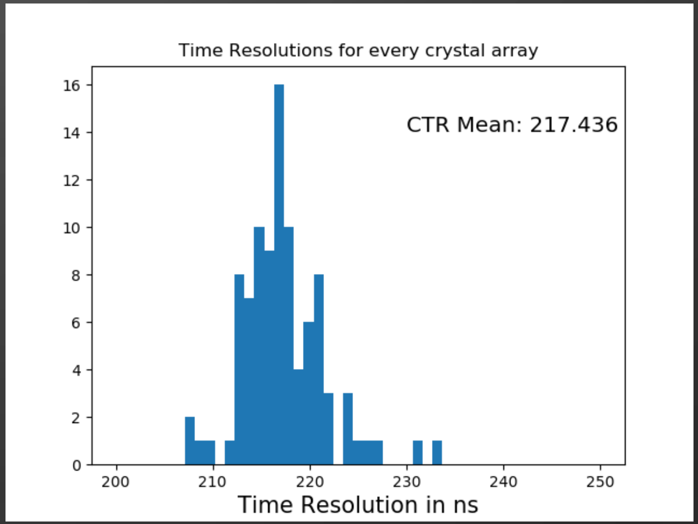
BACKUP SLIDES

THE TPPT PROJECT : MINI-PET RESULTS



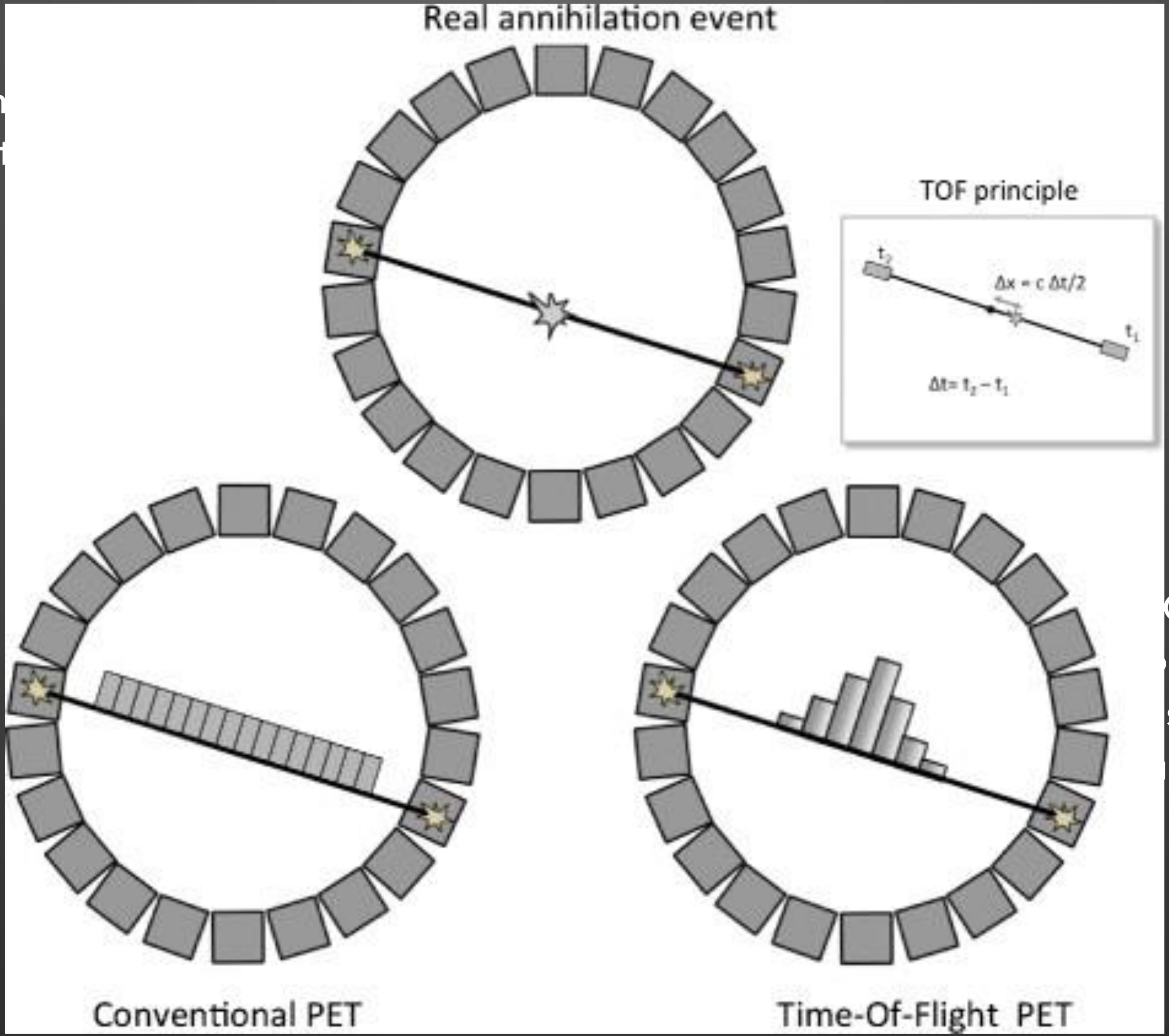






PET IMAGING: TIME-OF-FLIGHT PET

Real event: annihilation location
what's measured is just the posit
each hit in the detector

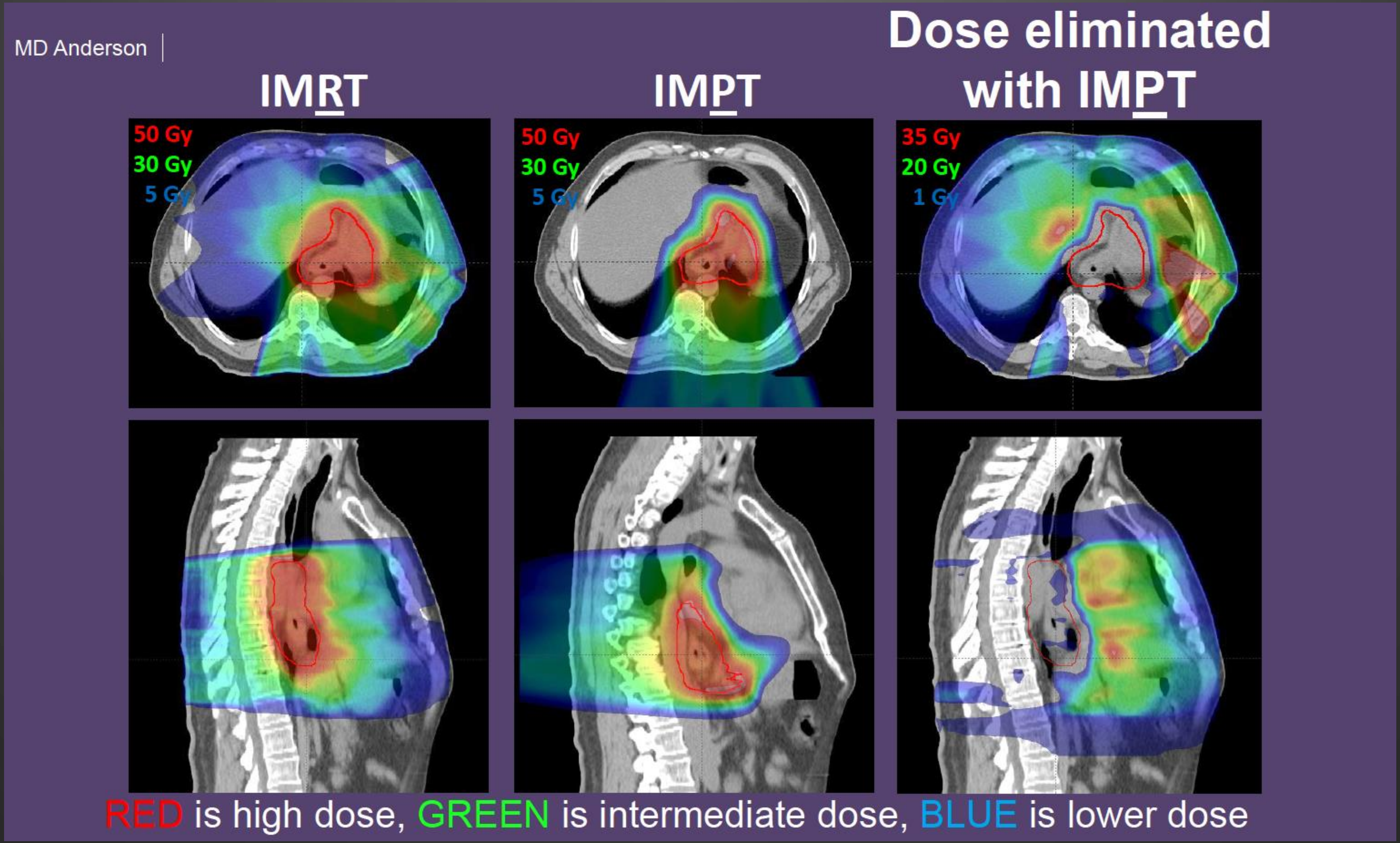


Traditional PET: Annihilation location probabilities uniformly distributed along LOR

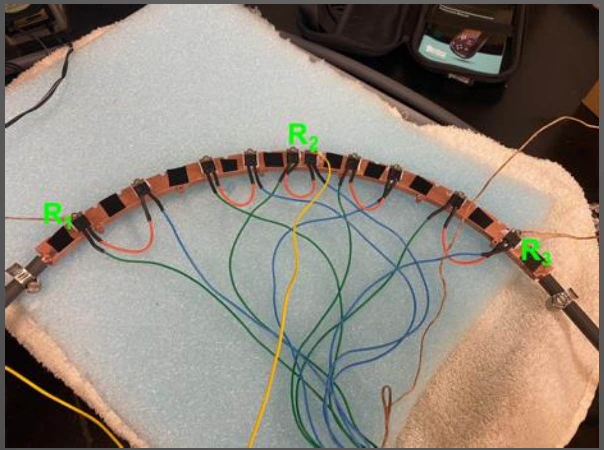
OF PET: Time difference
etween detections used to
stimate annihilation location
long LOR

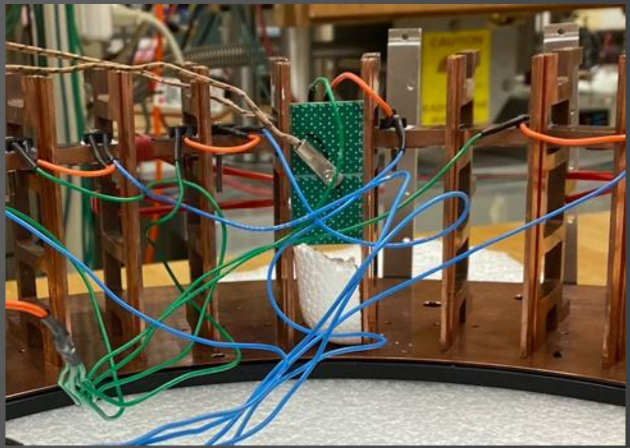
- Gaussian width determined by timing resolution

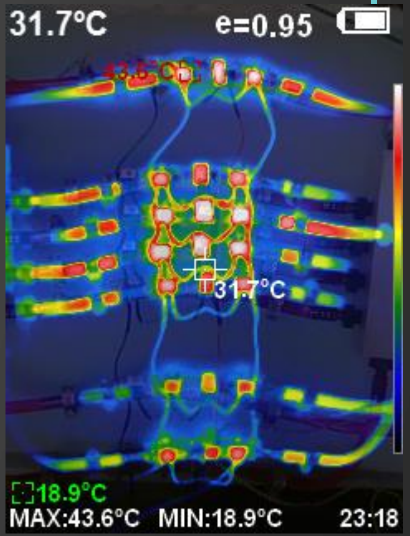
RADIATION THERAPY: PROTONS VS. PHOTONS



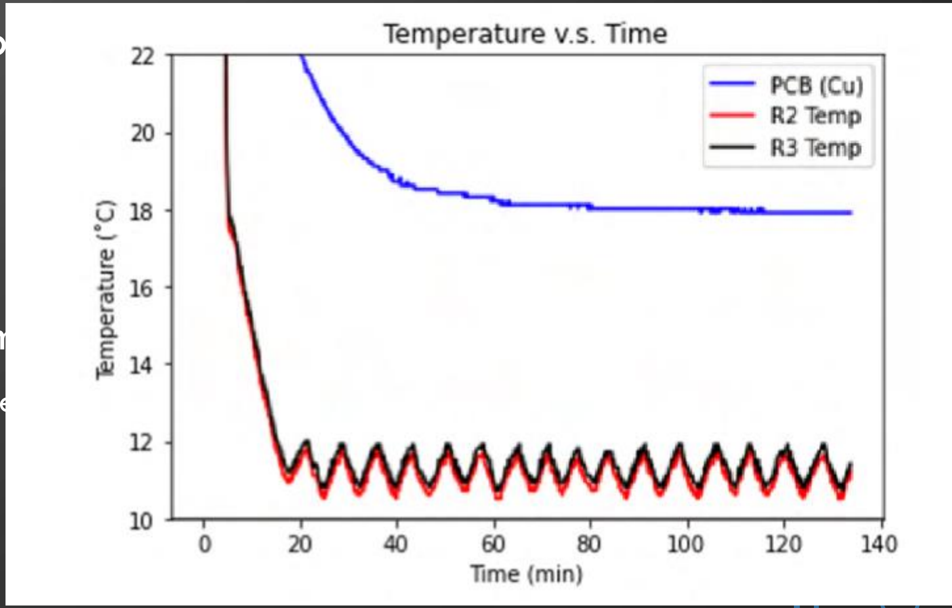
TPPT HARDWARE: COOLING SYSTEM



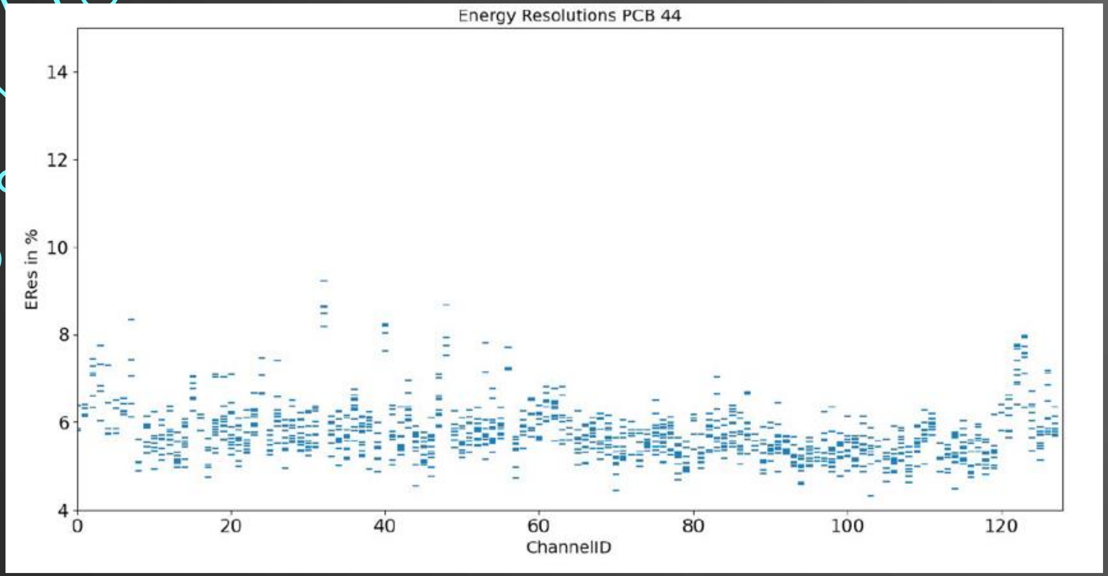


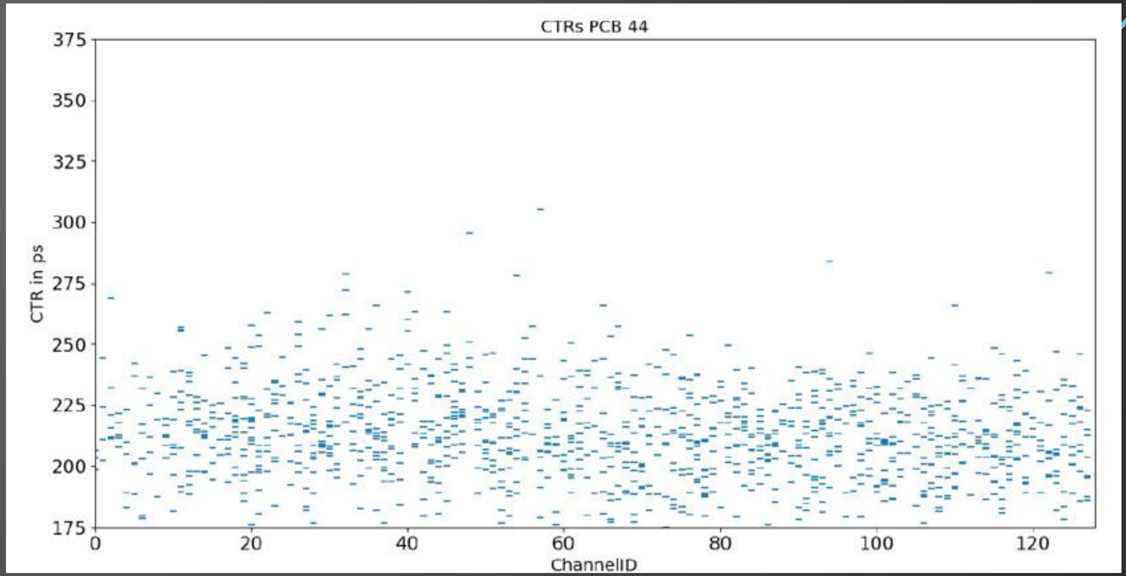


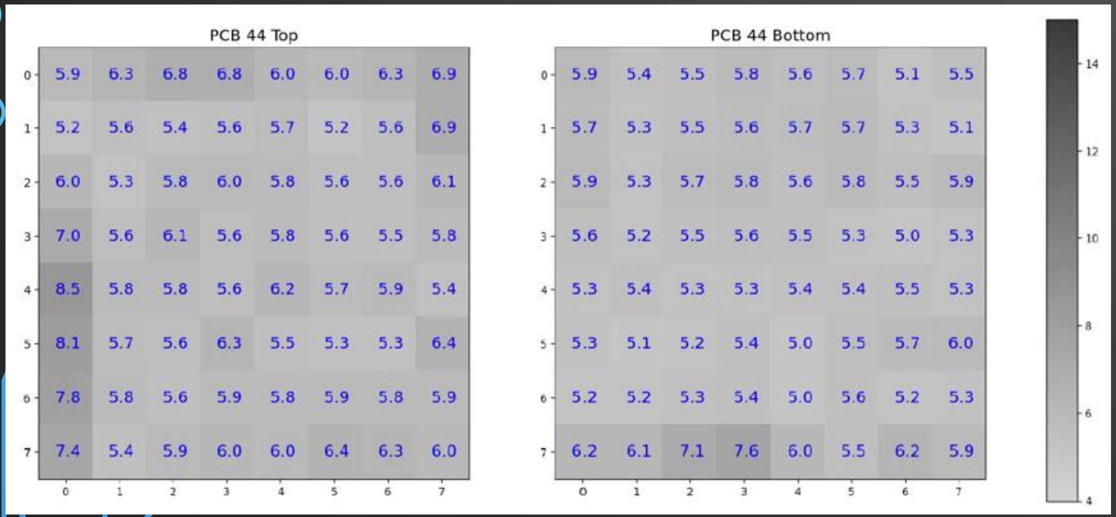
- ~1W dissipation per ASIC (2 x ASIC p module, 96 total)
- ASICs require stable temperature for calibration and operation
- Developed custom liquid cooling system
    - Copper elements circulate coolant and make thermal contact with ASICS and internal structure

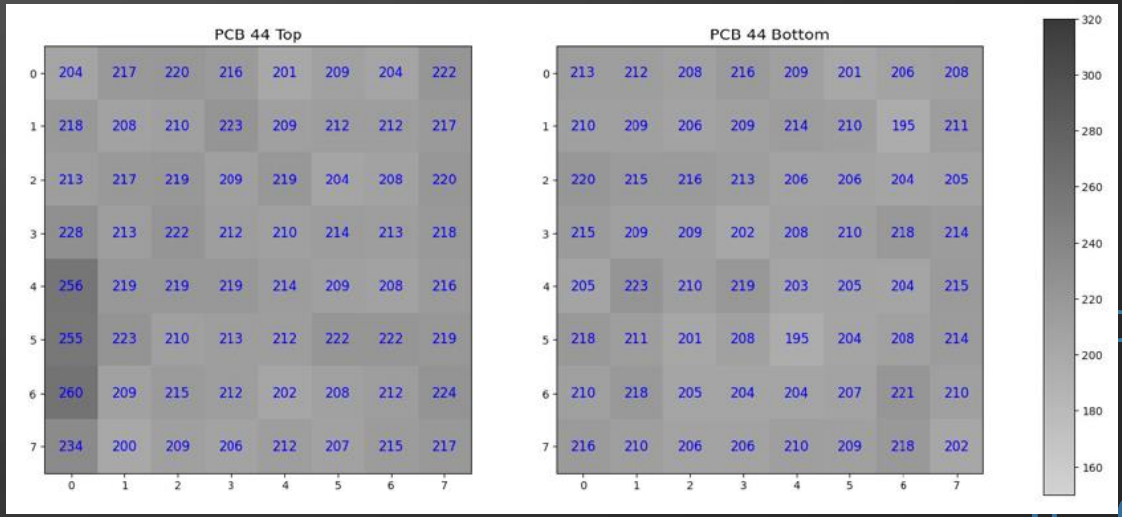


THE TPPT PROJECT : MINI-PET RESULTS



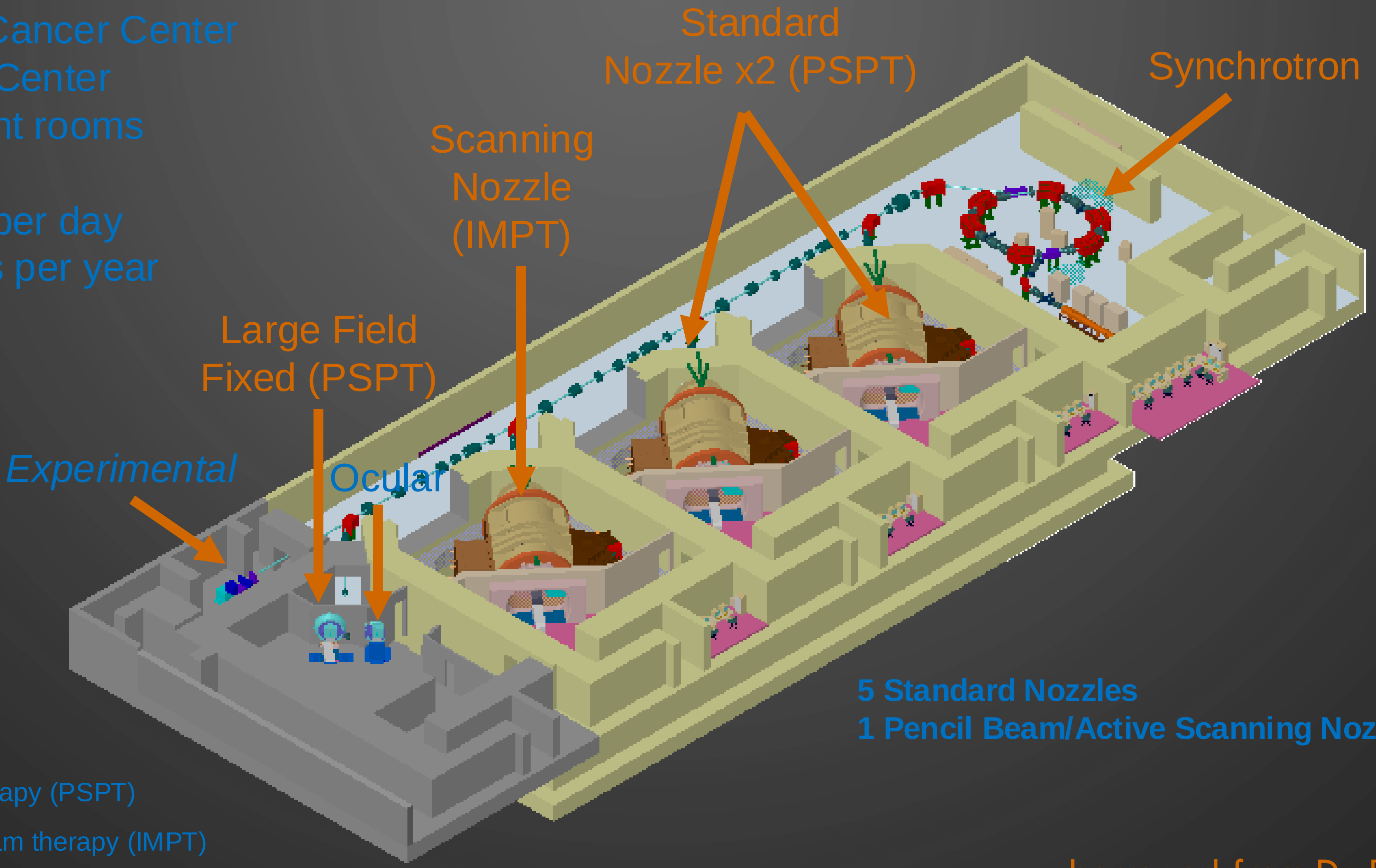






PROTON THERAPY: MDACC BEAMLINE

- M.D. Anderson Cancer Center Proton Therapy Center
- 4 active treatment rooms
- kV imaging
- 90-110 patients per day
- 700-800 patients per year



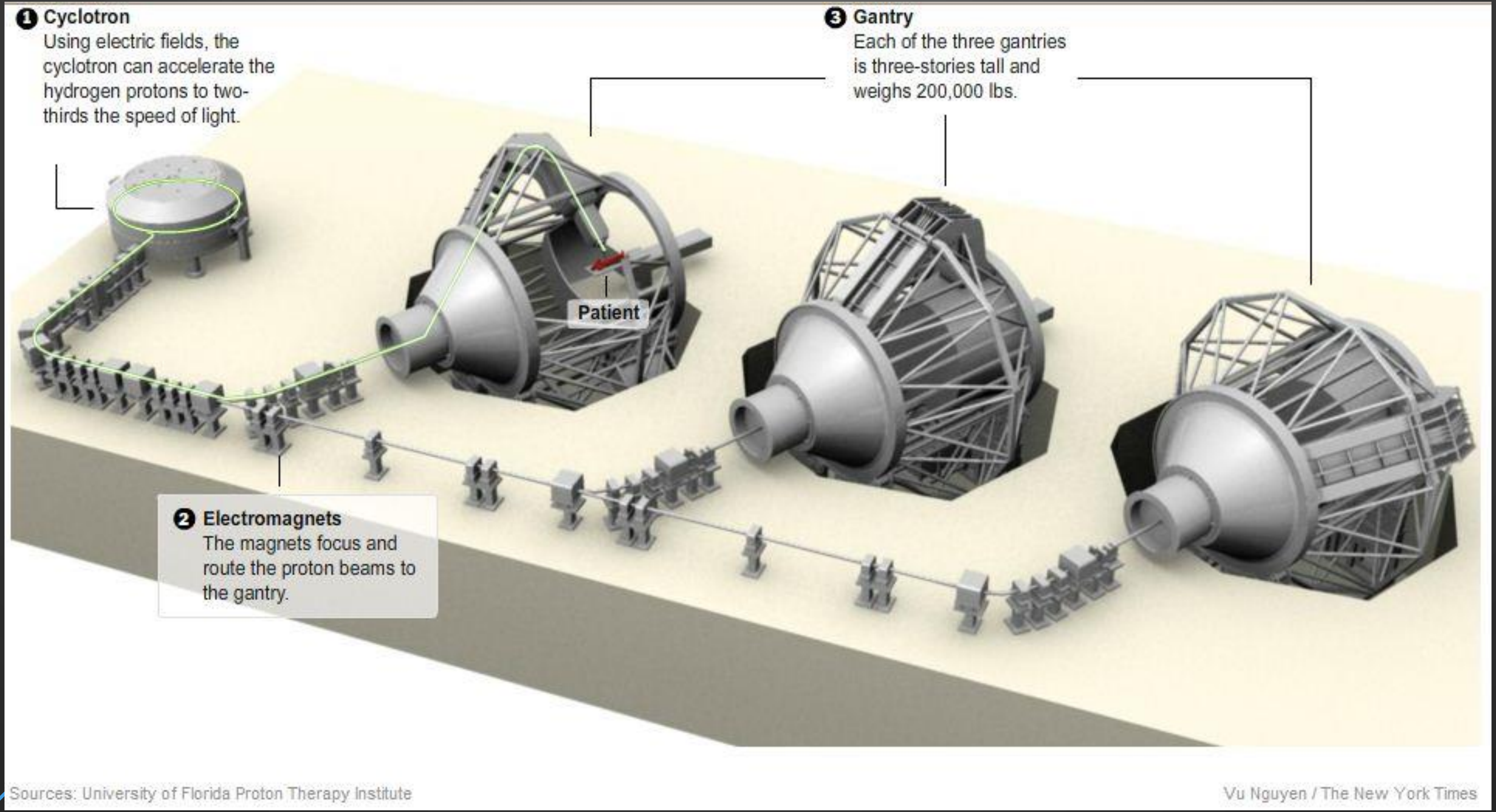
5 Standard Nozzles
1 Pencil Beam/Active Scanning Nozzle

passively-scattered proton therapy (PSPT)

Intensity modulated proton beam therapy (IMPT)

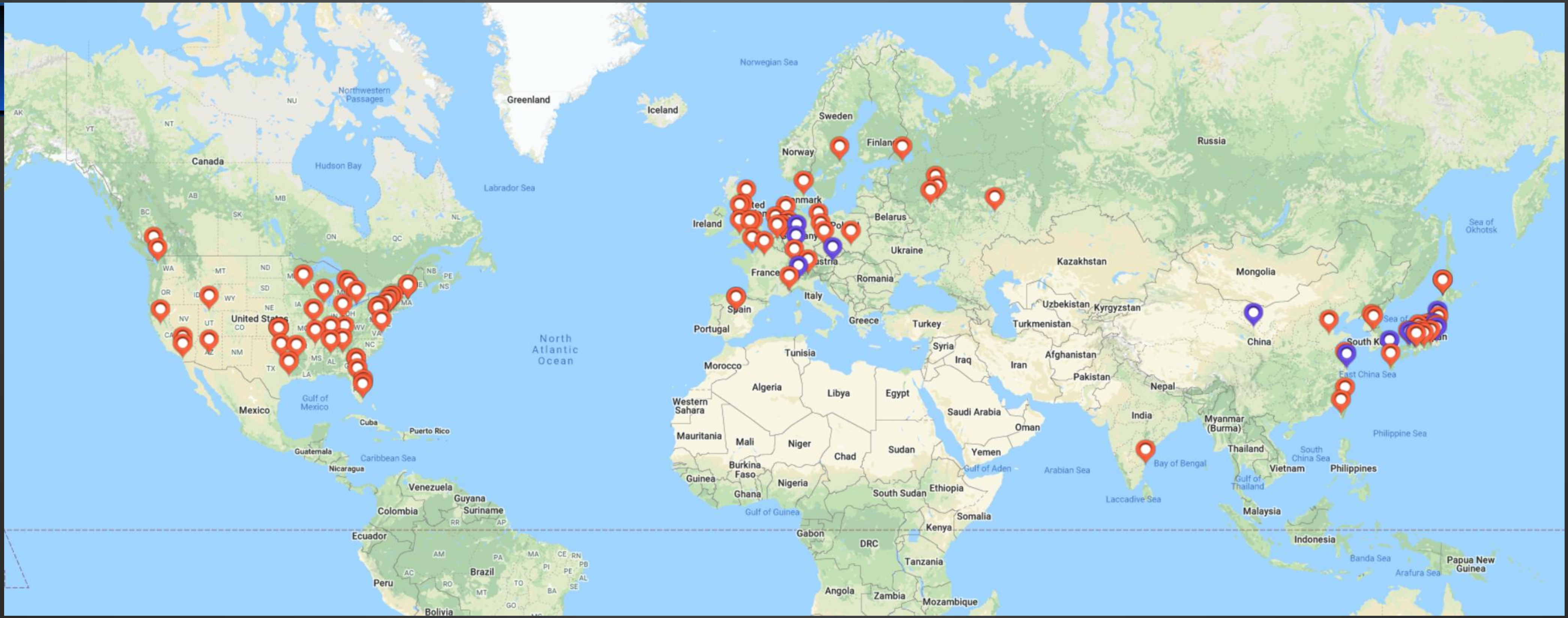
borrowed from Dr. Brandon Gunn

PROTON THERAPY: THE SCALE …



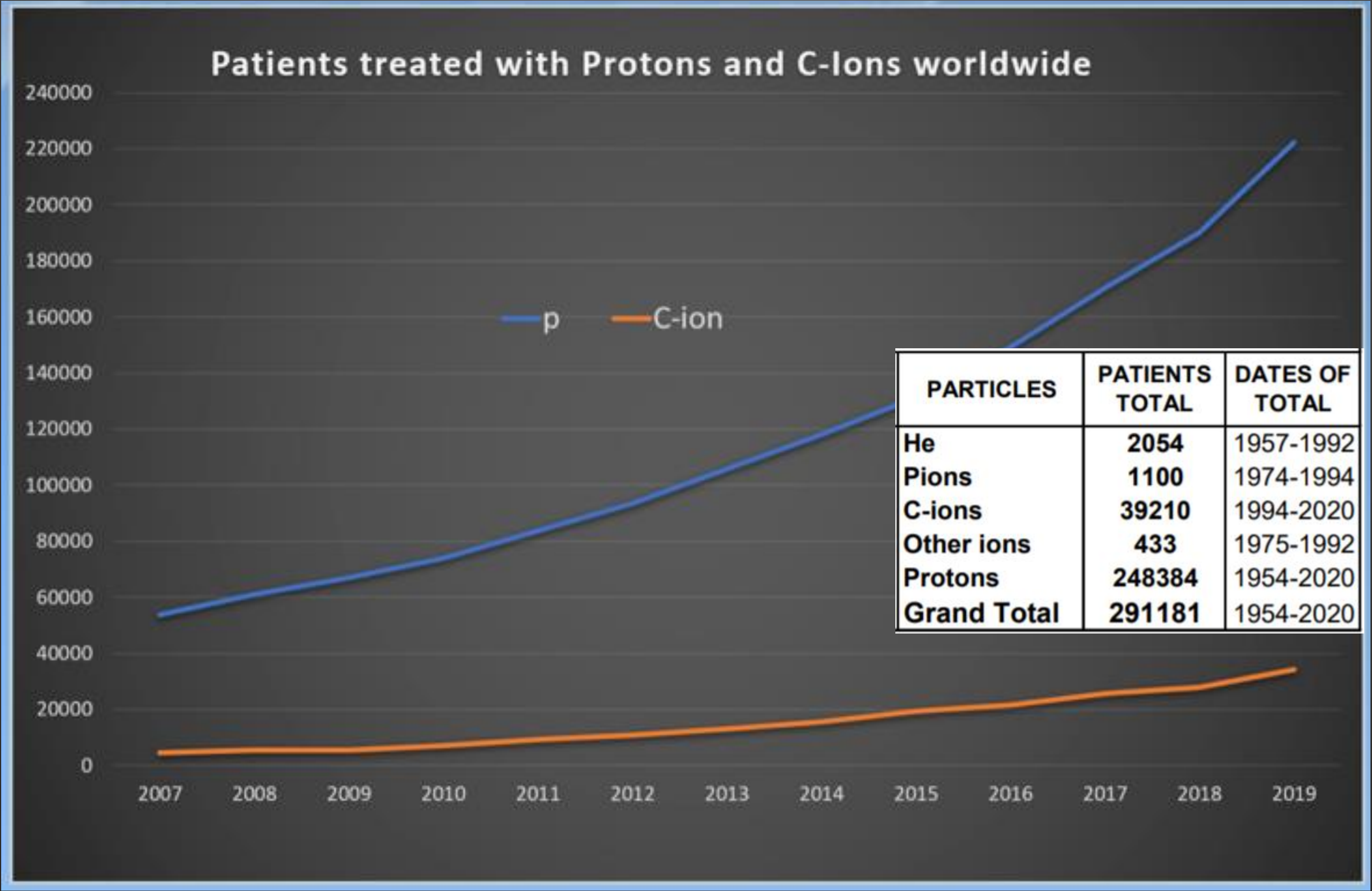
PROTON THERAPY: ON THE RISE….

112 facilities worldwide, another ~100 in various planning stages



- 42 facilities in the USA …. 26 in Japan … 7 in Germany … 7 in China … (3 Netherlands)
- 2 in Texas: MD Anderson CC and at UT Southwestern Medical Center
- 1 more to open soon at MD Anderson

PROTON THERAPY: ON THE RISE….



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

THE TPPT PROJECT: ISSUES FACING PT

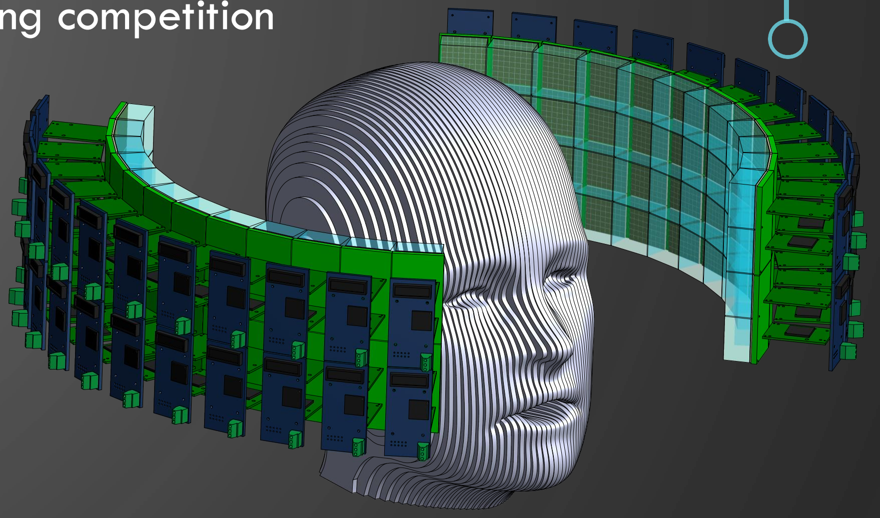
- **Anatomy changes** may perturb dose distributions to a significantly greater extent for protons than for photons
- **High gradients in proton dose distributions** are very sensitive to anatomy motion and changes, and to set up variations
- **Gaps in the knowledge** of relative biological effectiveness (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

A successful 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)

From Radhe Mohan, PhD

THE TPPT PROJECT: INCEPTION



- 3 years ago we formed a consortium to compete in the UTAustin - Portugal funding competition
- The consortium includes
  - **U. of Texas MD Anderson Proton Therapy Center**

    Sahoo Narayan, Falk Poenisch, David R. Grosshans
  - **U. of Texas at Austin**

    Karol Lang, Marek Proga, +
  - **PETsys Electronics**

    Vasco Varela, João Varela, Stefaan Tavernier, Ricardo Bugalho, Luis Ferramacho, Miguel Silveira, Carlos Leong, Jose da Silva
  - **LIP, Laboratorio de Instrumentação e Fisica Experimental de Particulas (Coimbra)**

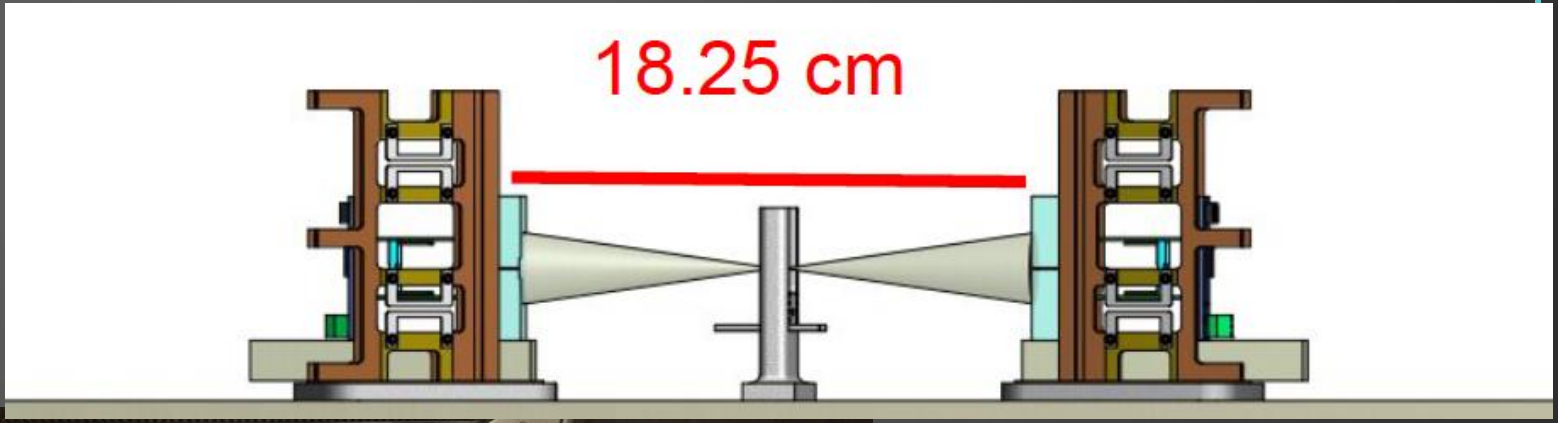
    Paulo Crespo, Mario Pimenta, Patricia Goncalves, Hugo Simões, Andrey Morozov
  - **Centro de Ciências e Tecnologias Nucleares (C^2TN), Instituto Superior Técnico (Lisbon)**

    António Paulo, Fernanda Marques, Paula Raposinho, Joana Guerreiro , Filipa Mendes, Salvatore di Maria, Maria Paula Campello
  - **Instituto de Ciências Nucleares Aplicadas à Saúde (ICNAS), Universidade de Coimbra**

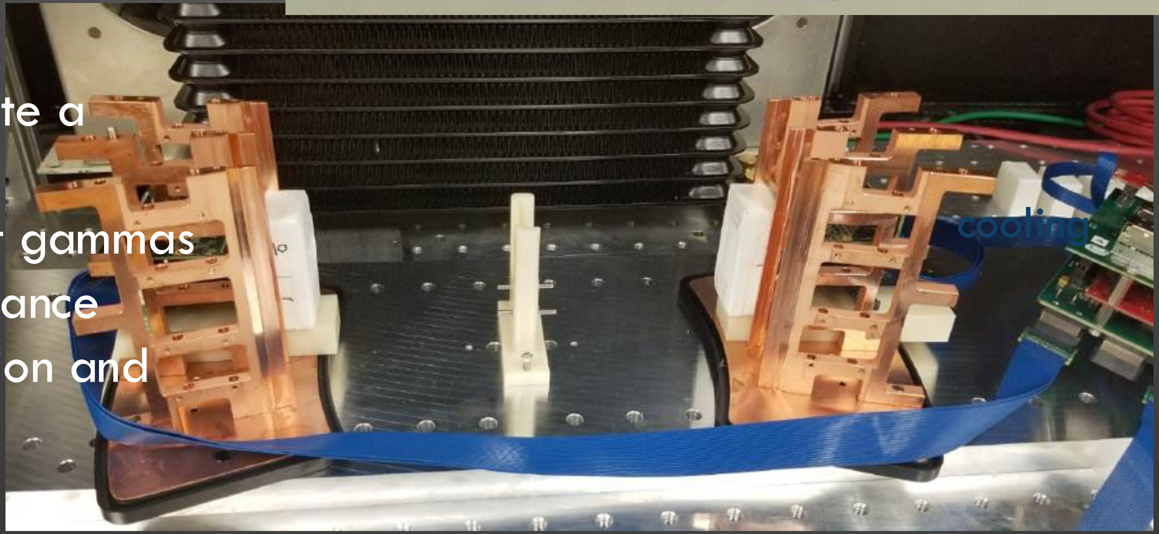
    Nuno Ferreira, Francisco Caramelo, Antero Abrunhosa
- We proposed a "feedback" PET scanner to register nuclides activated in proton irradiations:
  - C-11 ($T_{1/2}$=20min), N-13 ($T_{1/2}$=10min), O-15($T_{1/2}$=123sec)

UTAustin Portugal

THE TPPT PROJECT: MINI-PET

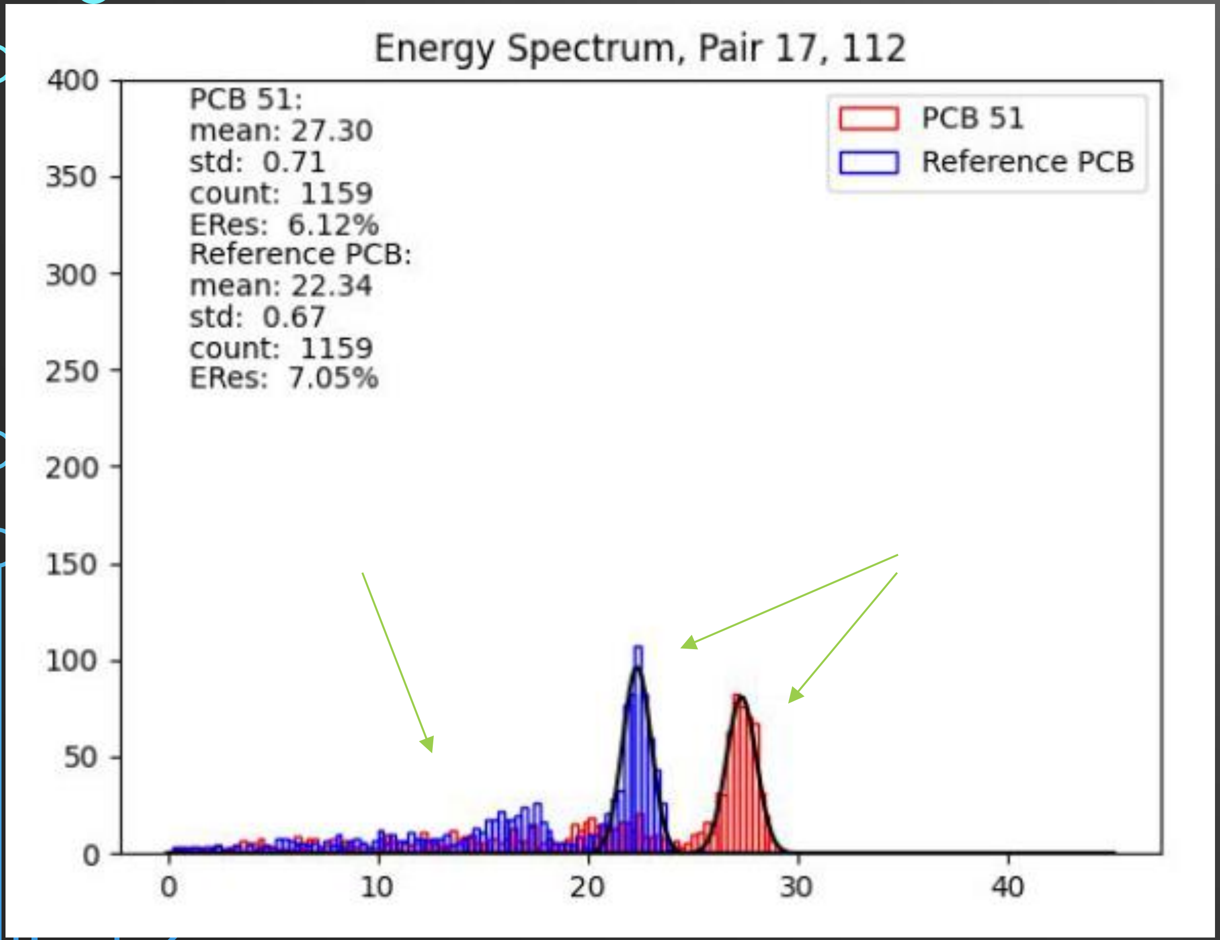


- Characterization and evaluation of all modules after gluing
  - Quality assurance
- Each module placed opposite a reference module
- Na-22 source for coincident gammas
- Extraction of early performance parameters (energy resolution and coincidence time resolution)
  - Next slides

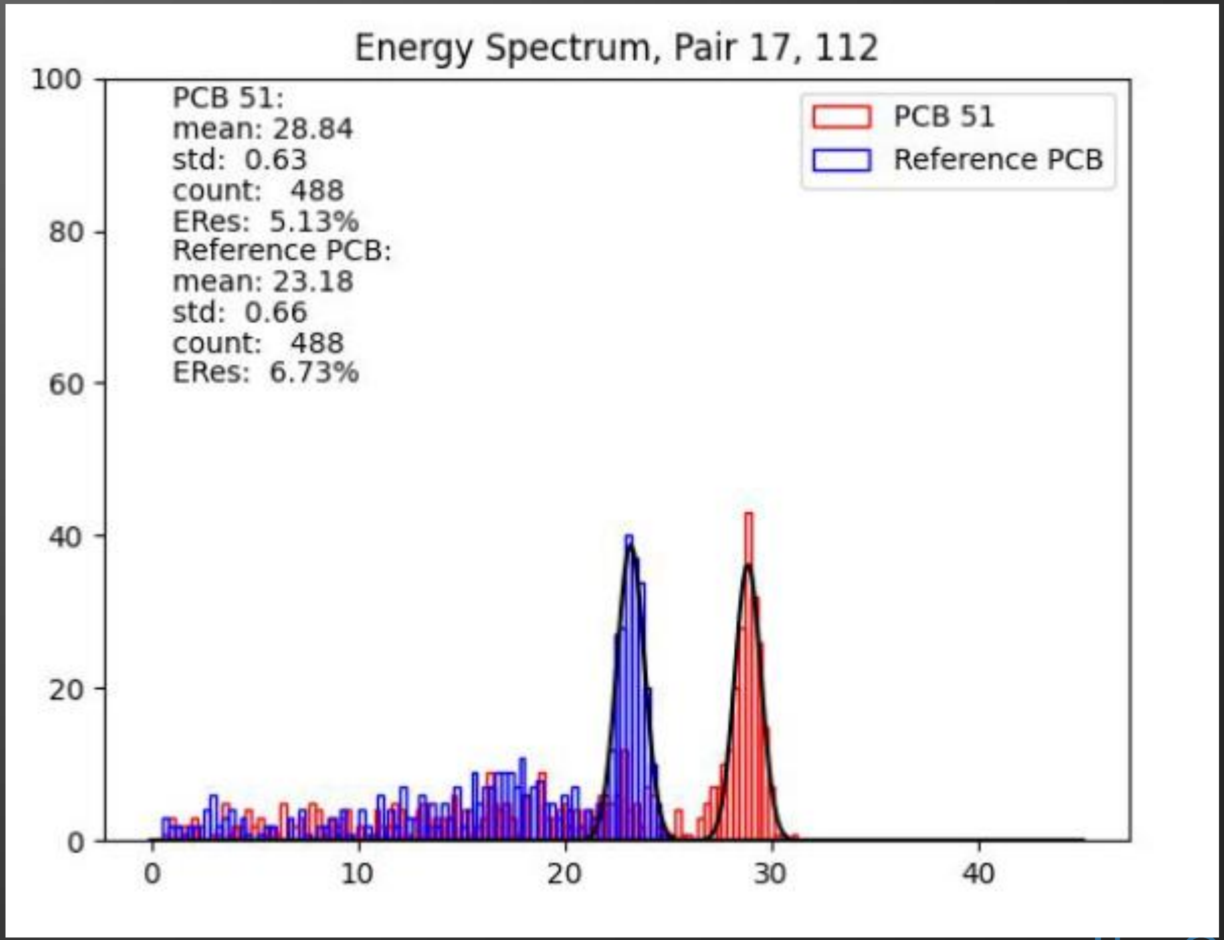


THE TPPT PROJECT: MINI-PET EVALUATION

Na-22

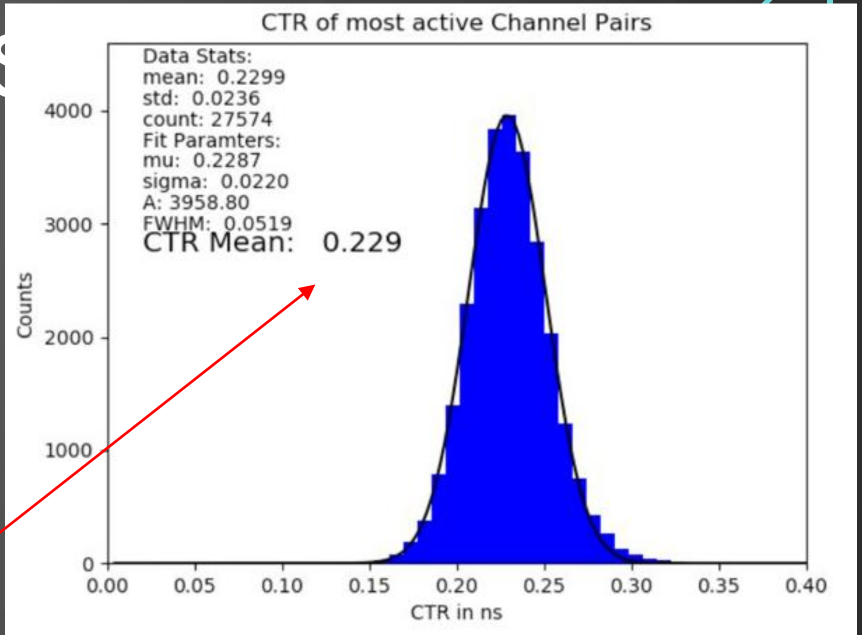


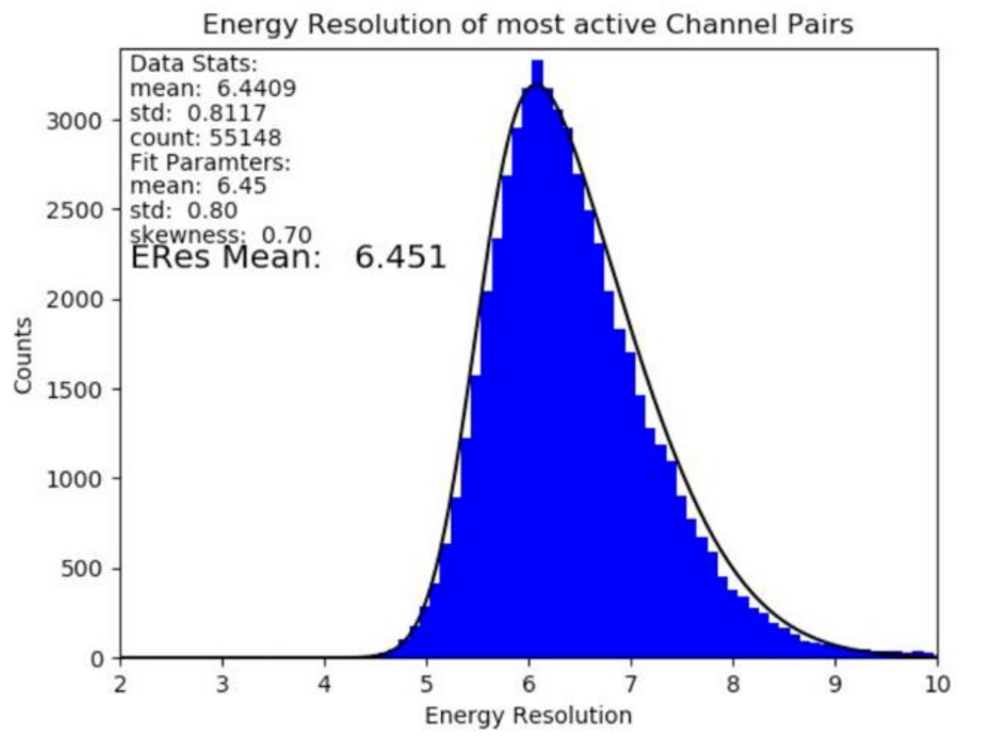
Ge-68



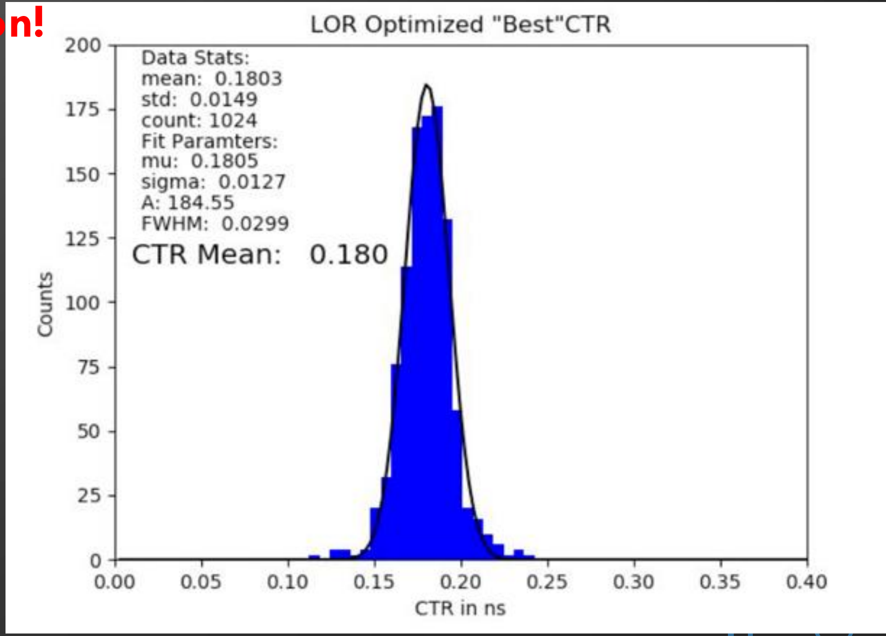
THE TPPT PROJECT: MINI-PET RESULTS

- Select photopeak events from previous energy spectra
  - Estimate energy resolution across pairs of channels
  - Coincidence time resolution (CTR) calculated from time difference between photopeak gammas



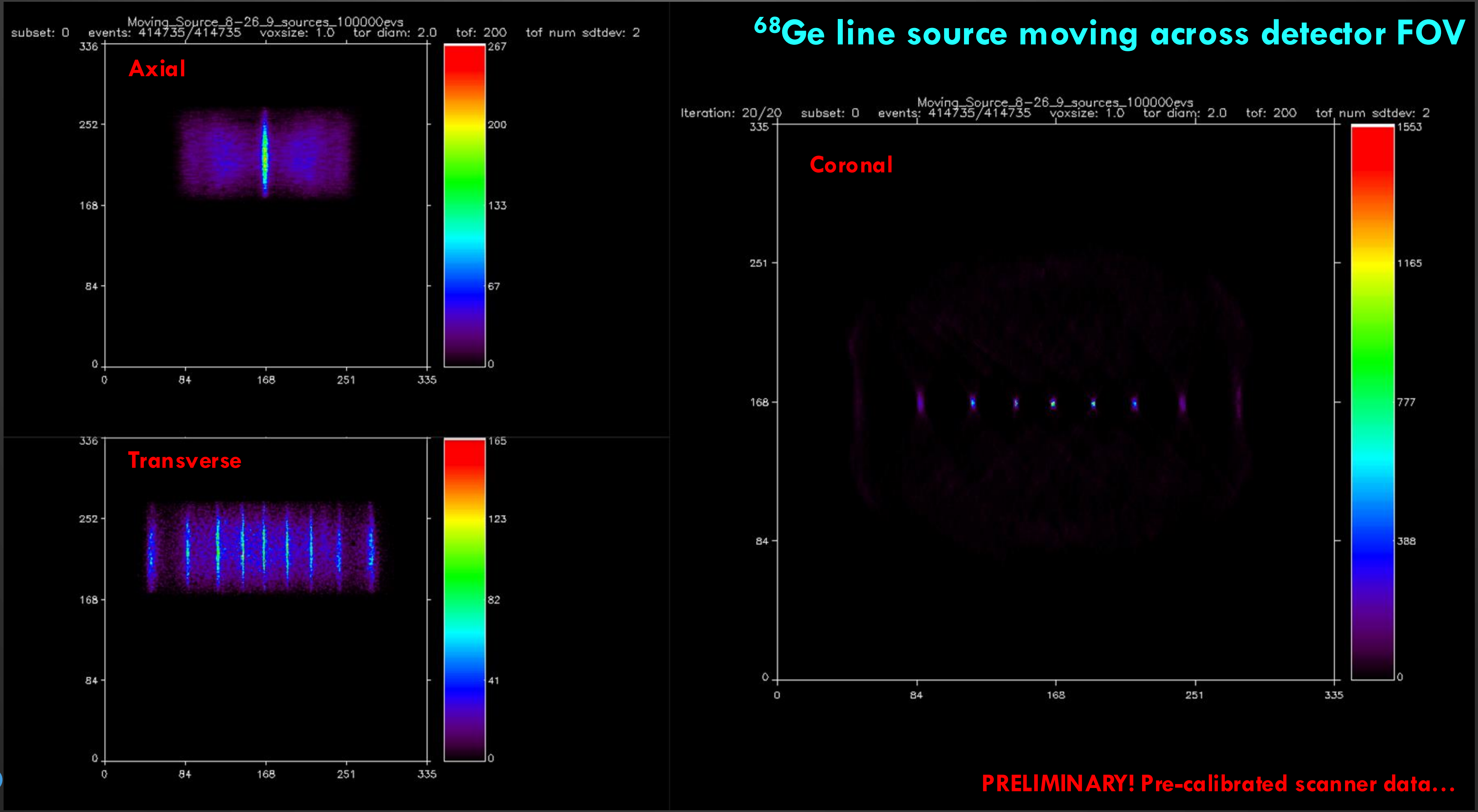


230 ps ToF resolution!

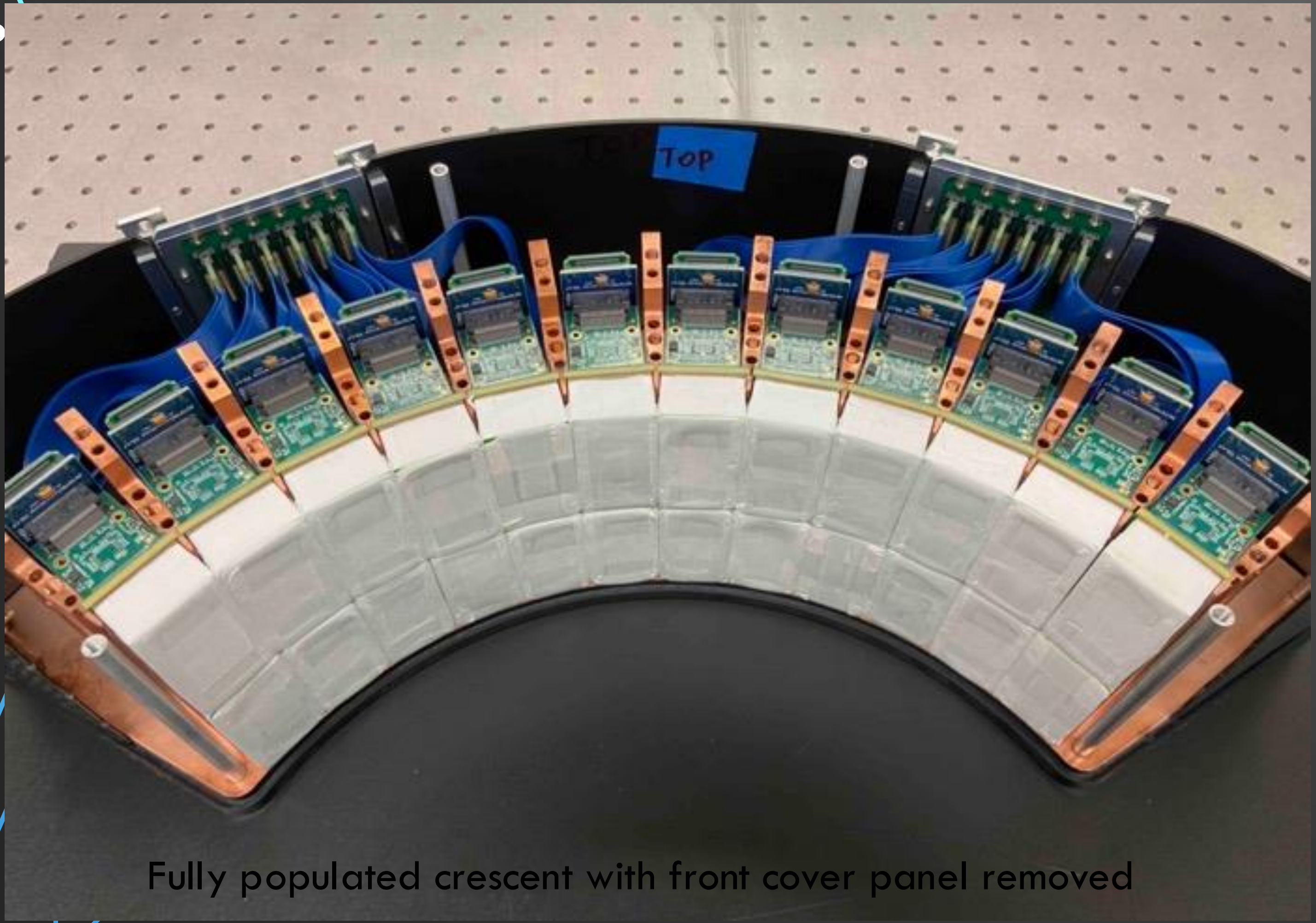


Even better when looking at most optimal lines of response…

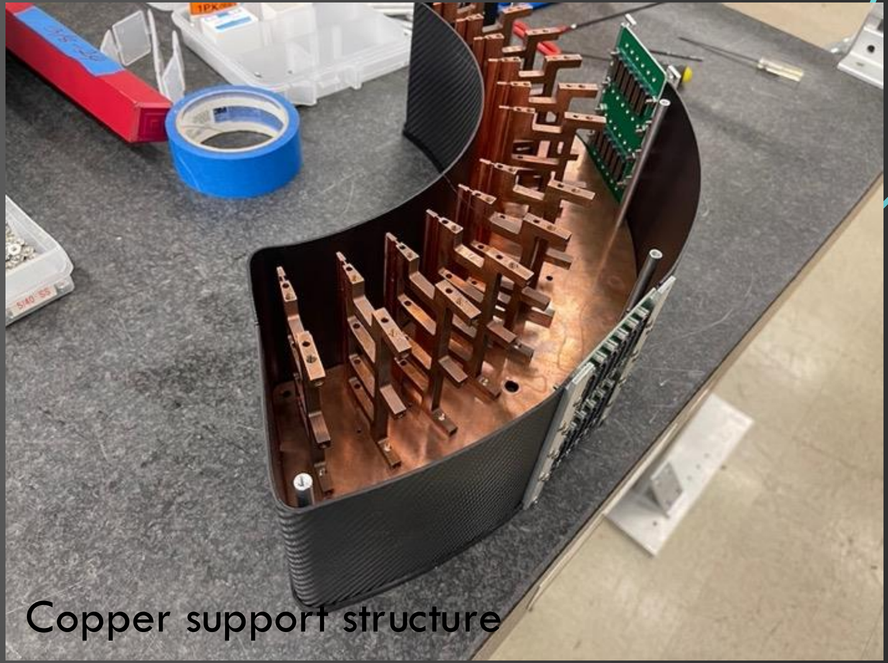
THE TPPT PROJECT: FIRST RECONSTRUCTED IMAGES!



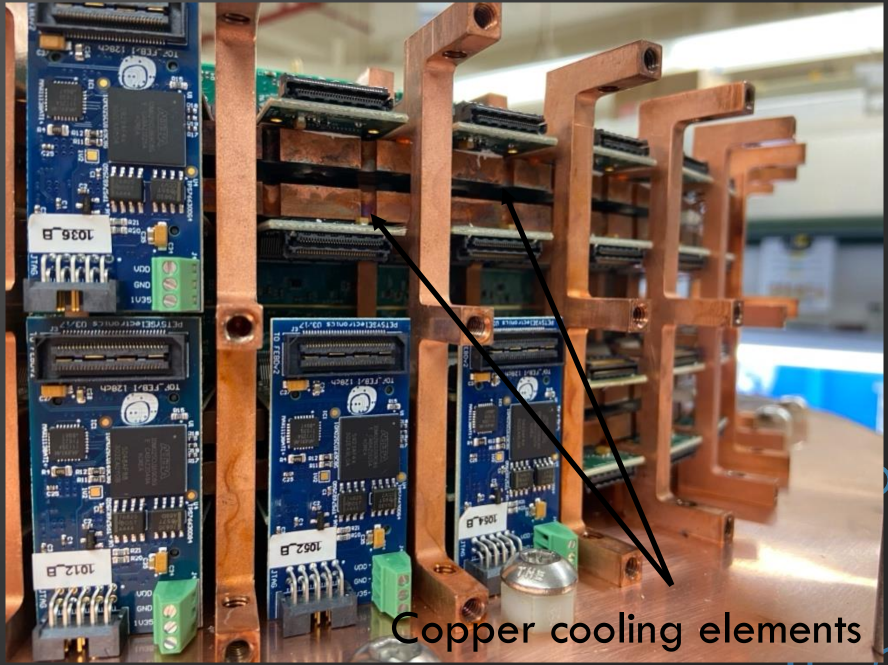
THE TPPT PROJECT: ASSEMBLY



Fully populated crescent with front cover panel removed

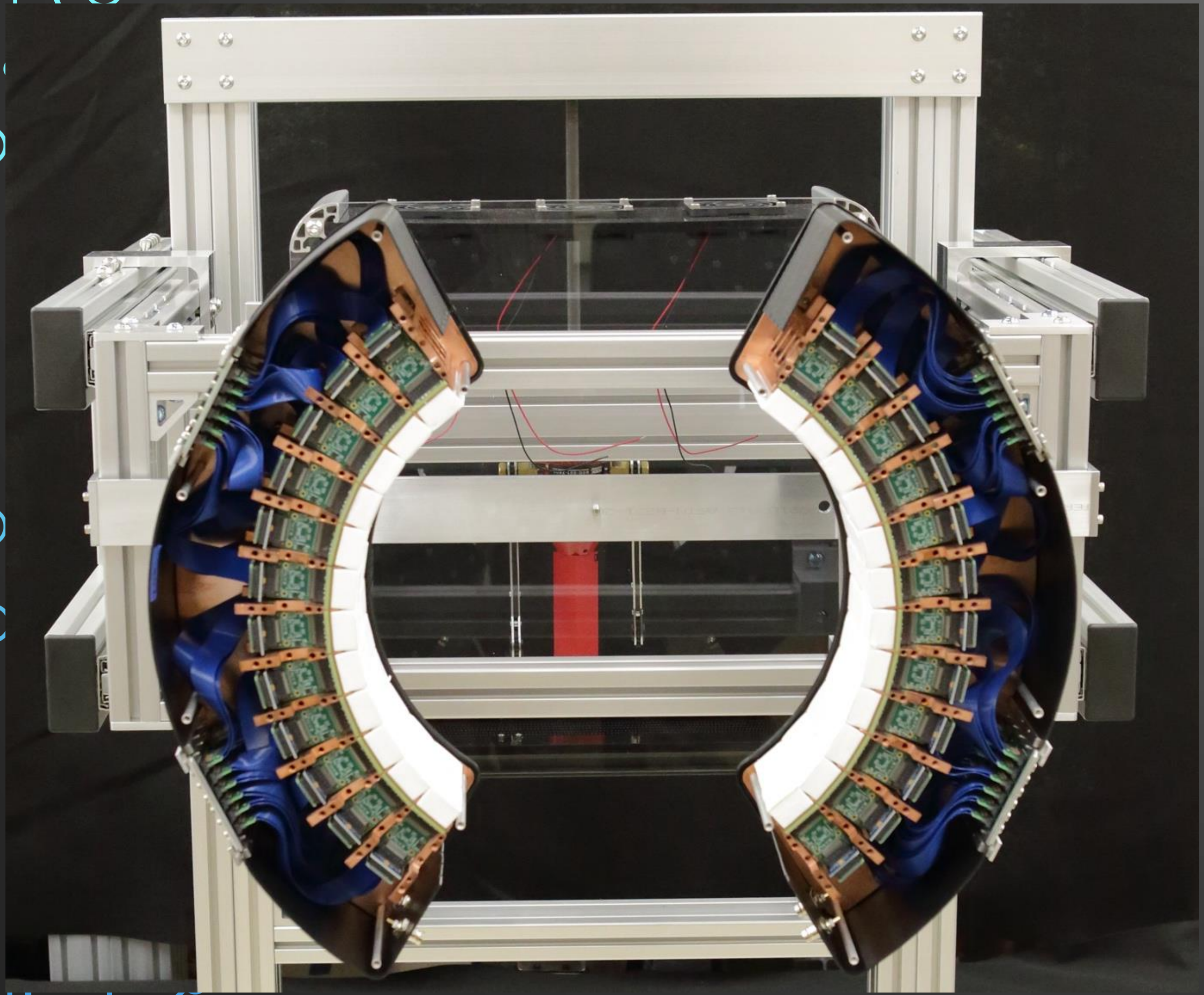


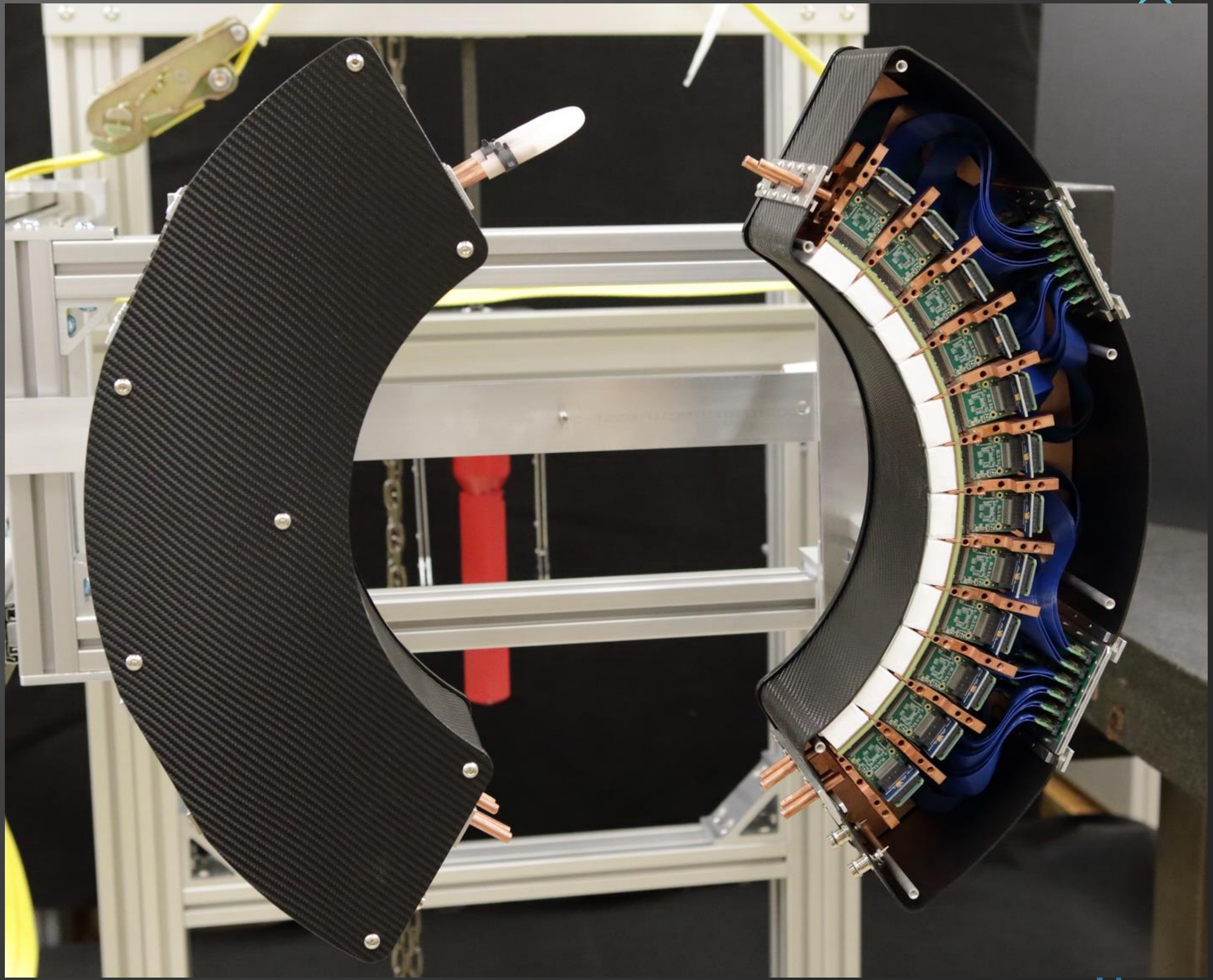
Copper support structure



Copper cooling elements

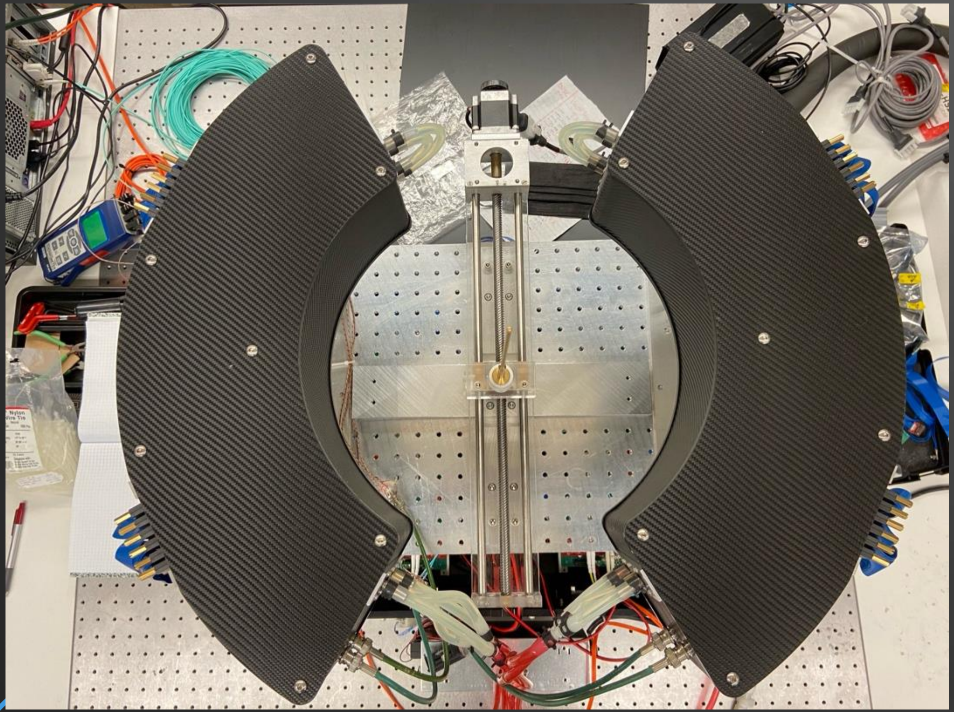
THE TPPT PROJECT: FULL SCANNER ON GANTRY

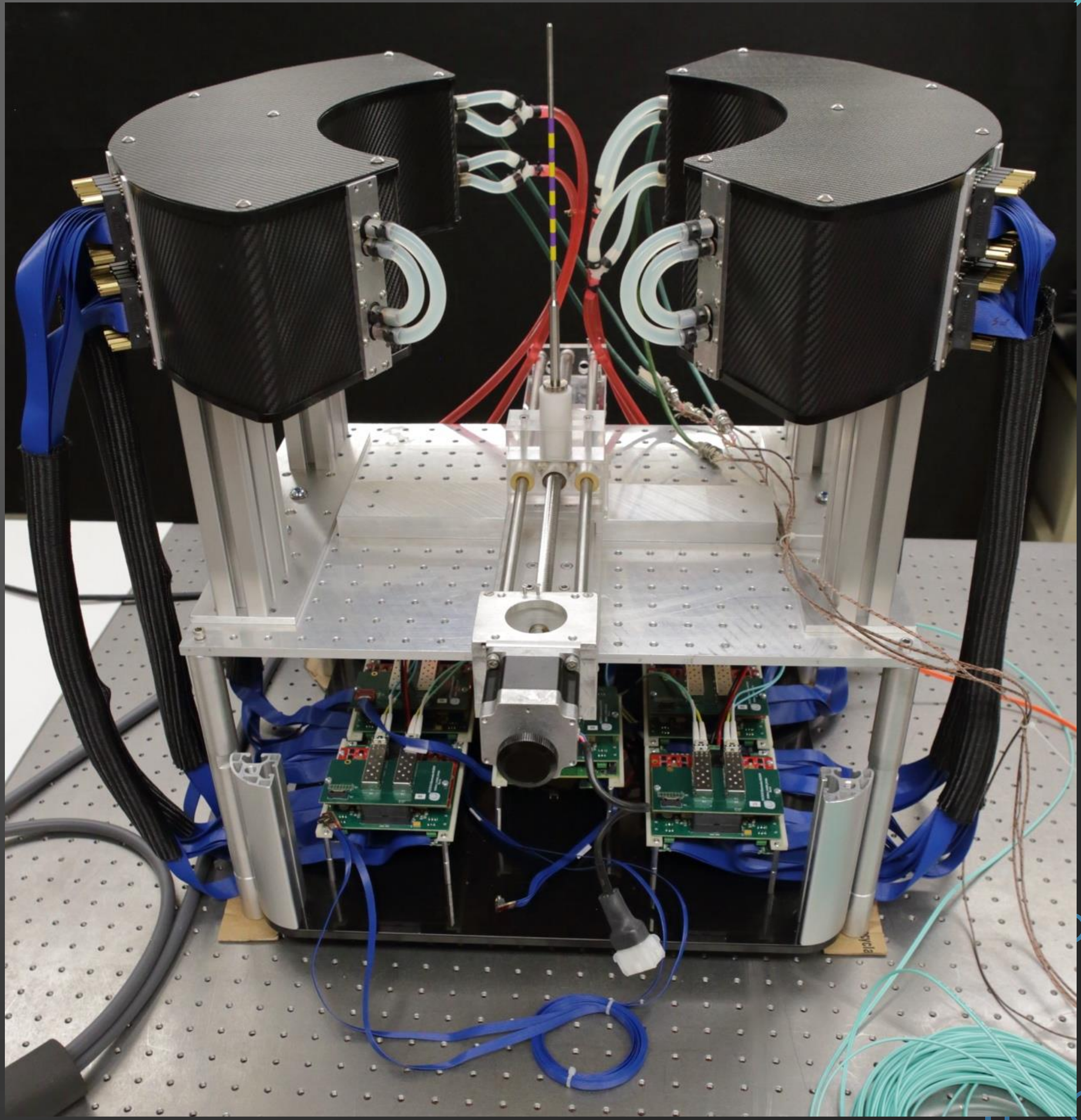




THE TPPT PROJECT: THE COMPLETE SCANNER

- Various calibrations performed (or in the process):
  - SiPM OV and ASIC threshold scan
  - Normalization + Time alignment
    - Requires moving line source (^{68}Ge)
  - Cooling studies
  - DAQ stress testing
  - Image reconstruction debugging





LYSO VS BGO CRYSTAL PROPERTIES

Table 1.

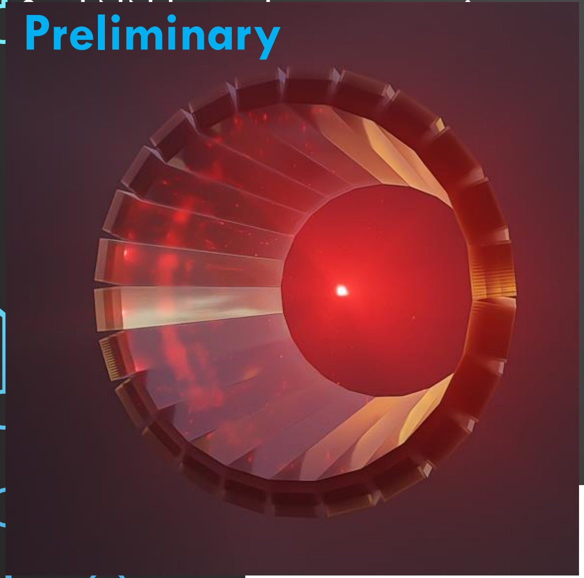
Properties of LYSO and BGO (from Saint-Gobain 2014, 2017).

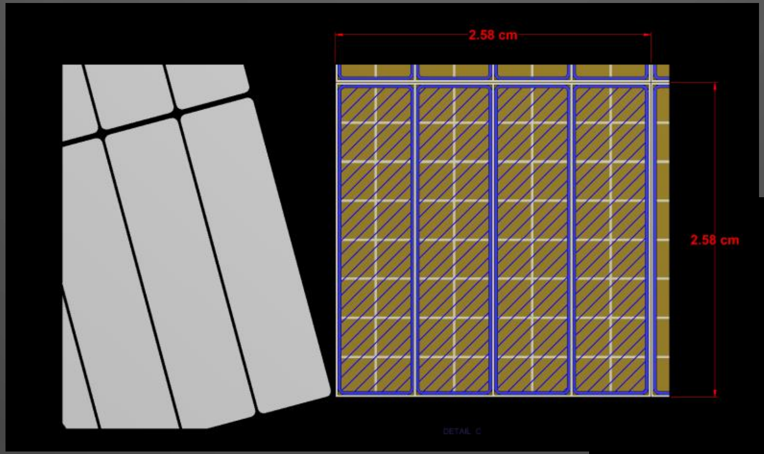
	LYSO	BGO
Effective atomic number (Z_{eff})	60	74
Density (g cm^{-3})	7.1	7.13
Attenuation length for 511 keV (cm)	1.2	1.0
Light yield (photons MeV^{-1})	8000–10 000	30 000
Decay time (ns)	37–45 ns	300
Peak wavelength (nm)	420	480

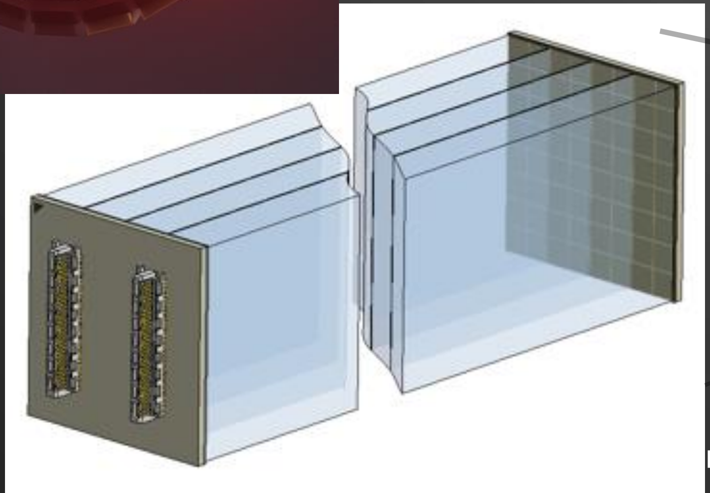
Image courtesy of doi: 10.1088/1361-6560/abc365

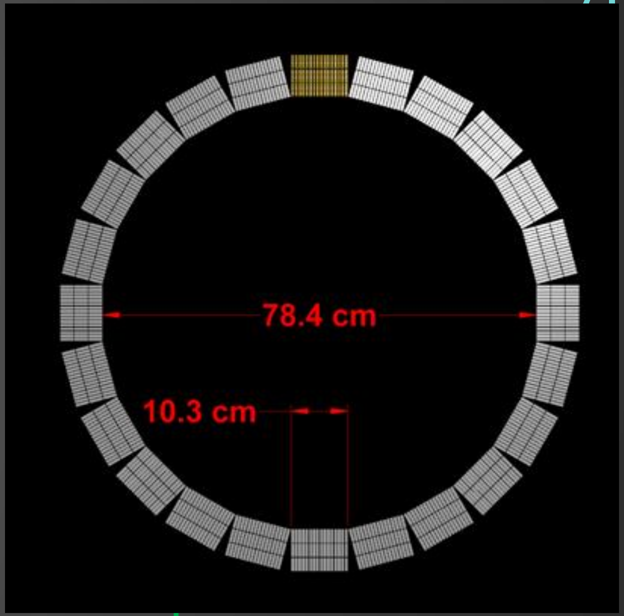
FUTURE IDEAS: FULL BODY PET

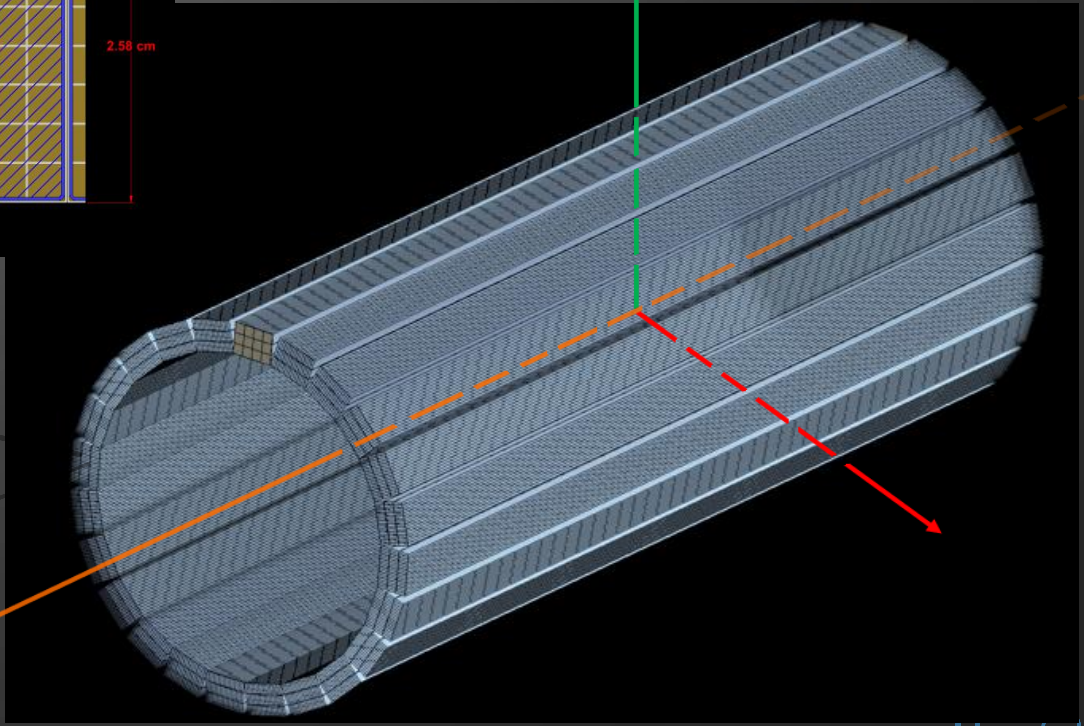
- 1m long barrel PET (2.54 x 0.62 x 100cm scintillator)
- 1152 plastic scintillator strips and 576 SiPMs.



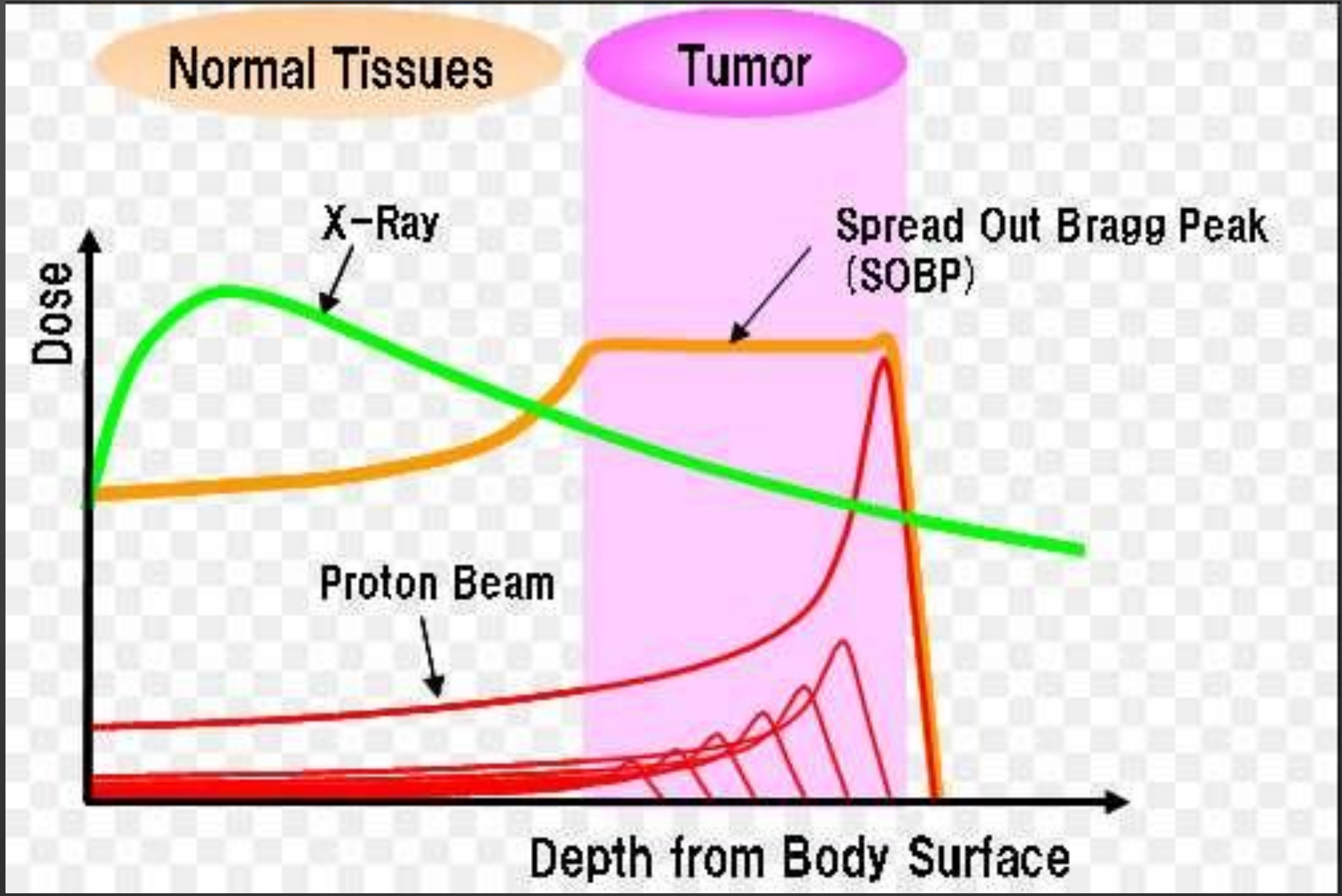




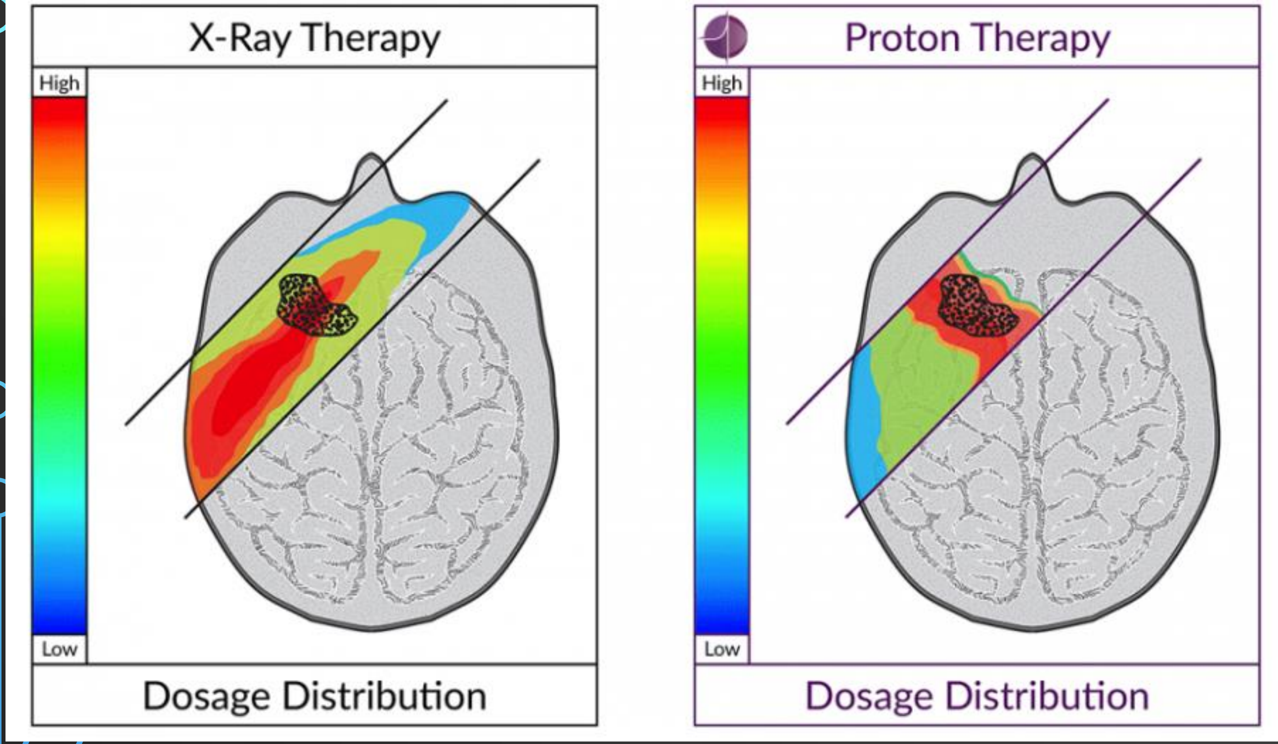


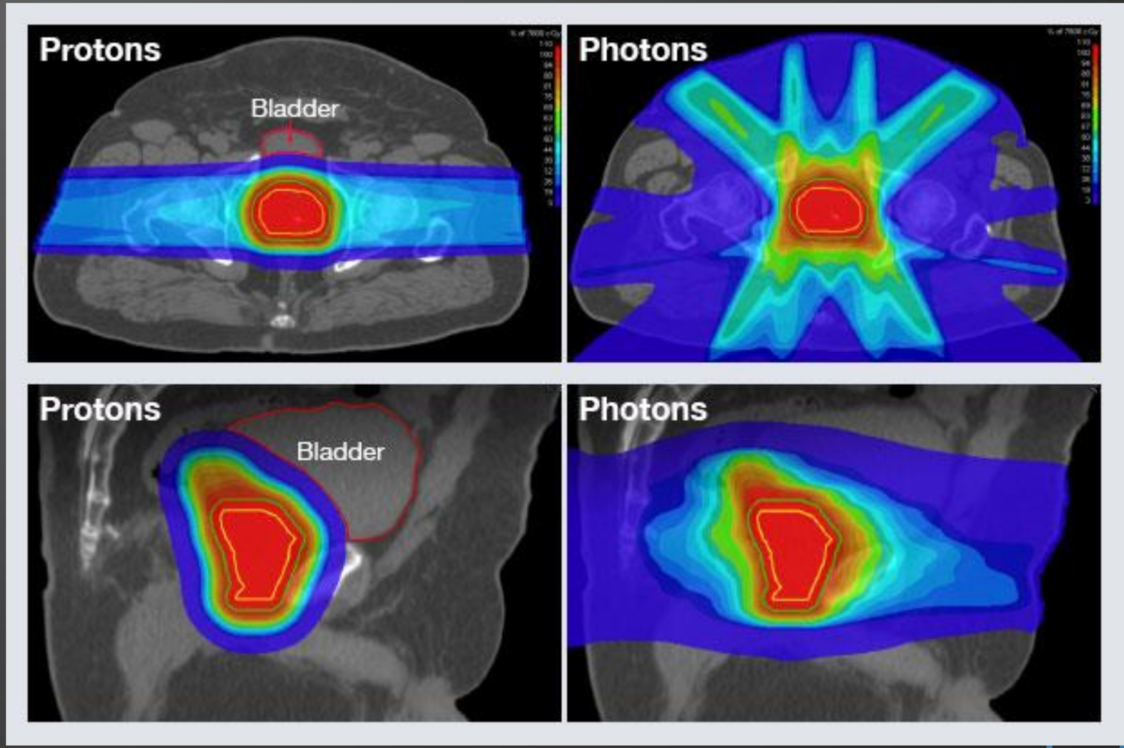


IMPT
(INTENSITY MODULATED PROTON THERAPY)

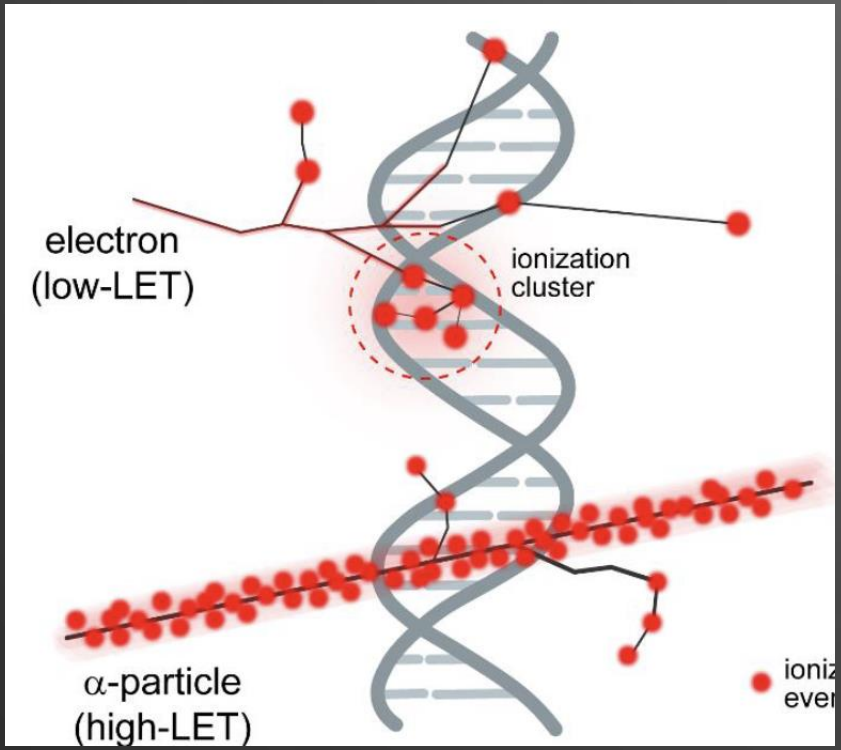


IMRT VS IMPT

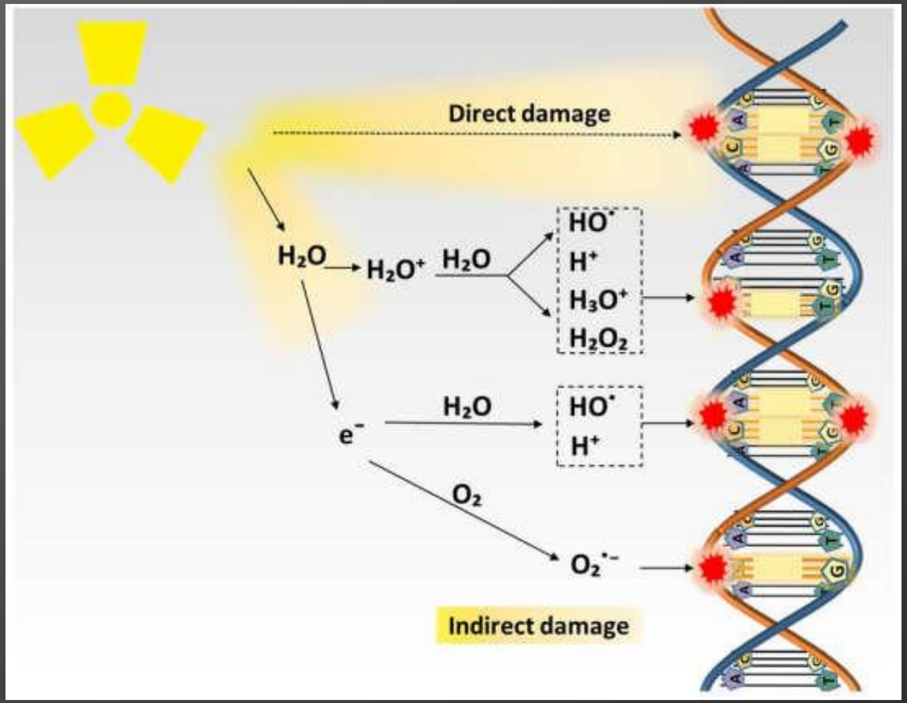

X-Ray Therapy
High
Low
Dosage Distribution
Proton Therapy
High
Low
Dosage Distribution


Protons
Bladder
Photons
Protons
Bladder
Photons

DESTROYING CANCER OR IMPEDING ITS GROWTH

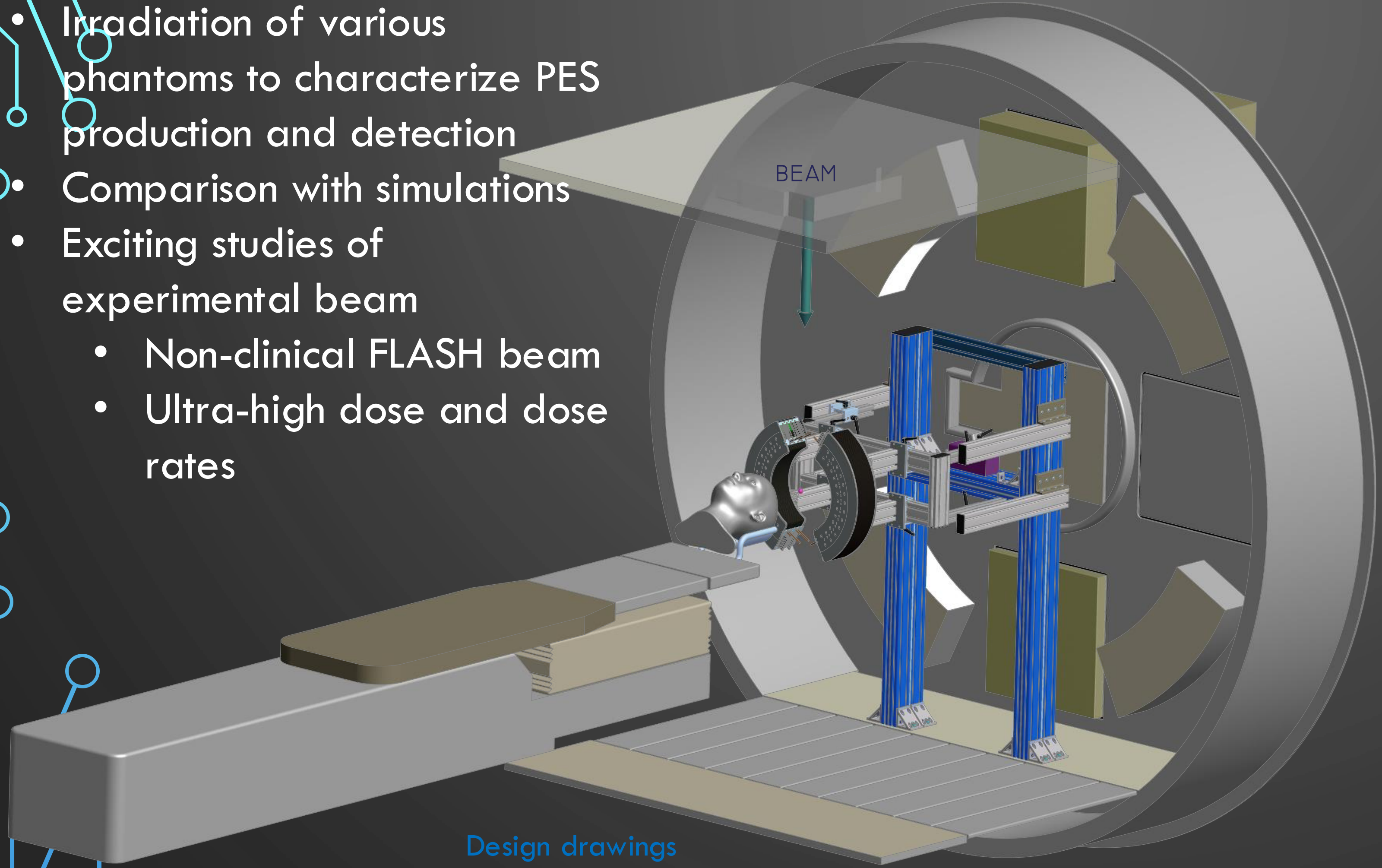


oxygen radicals ...



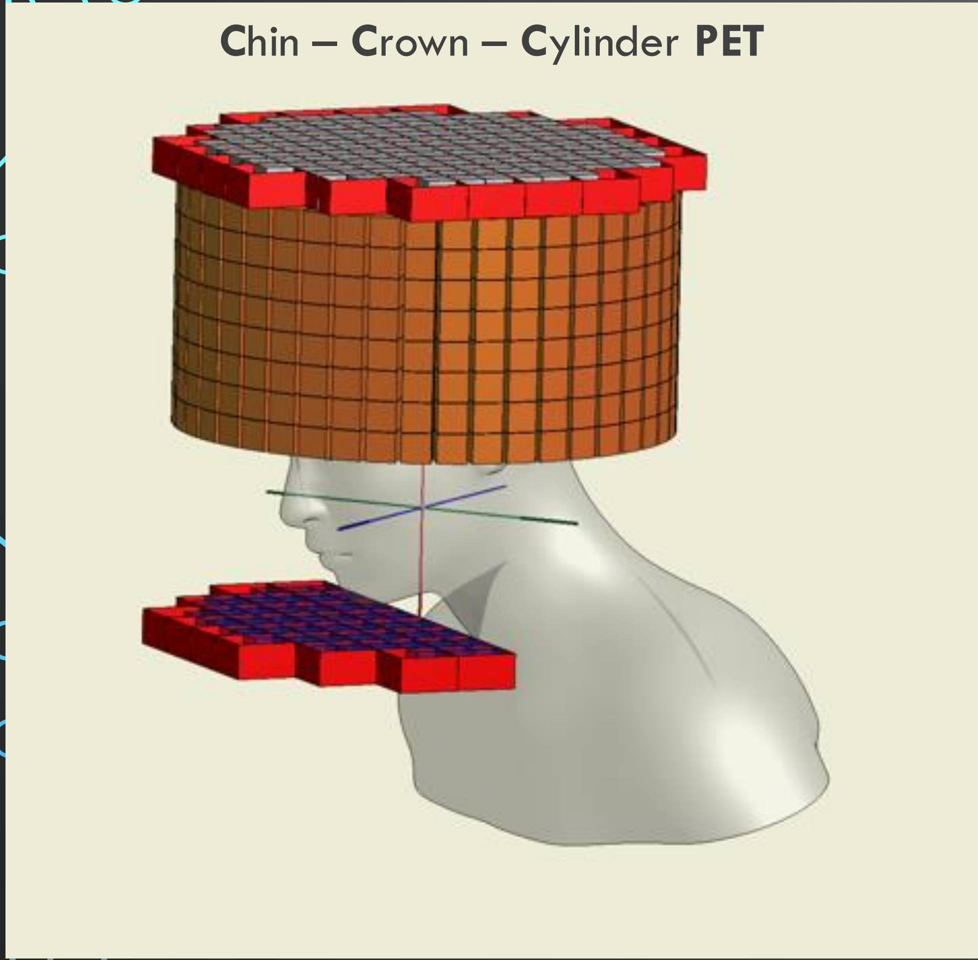
THE TPPT PROJECT: THE NEAR FUTUR

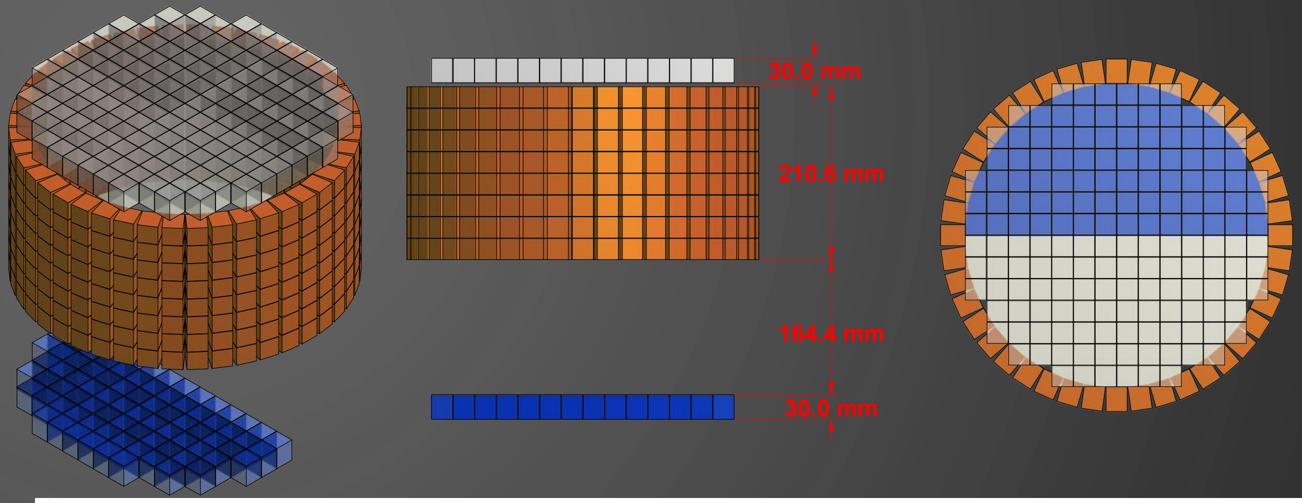
- Live in-beam tests at MDACC
- Irradiation of various phantoms to characterize PES production and detection
- Comparison with simulations
- Exciting studies of experimental beam
    - Non-clinical FLASH beam
    - Ultra-high dose and dose rates



Design drawings by Marek Proga

FUTURE IDEAS: C^3-PET





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]

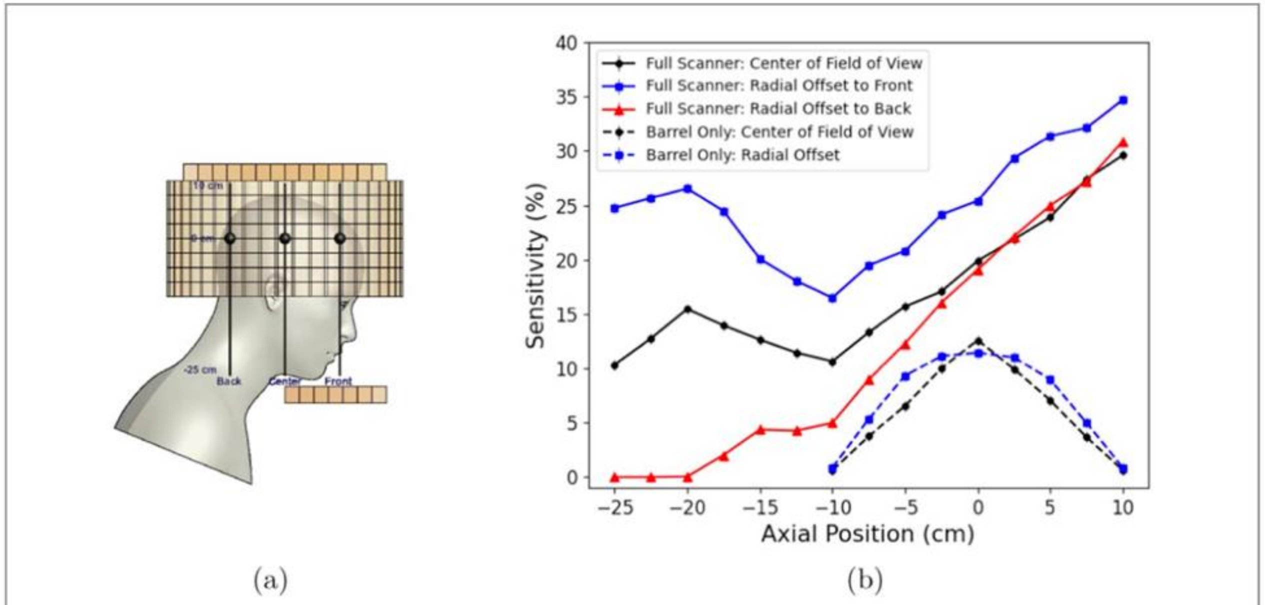


Figure 3. (a) Positions of line sources used for sensitivity predictions. (b) Absolute sensitivities for point sources placed along the line sources, for both the full scanner and barrel module alone, at the center of the radial field of view and at 10 cm radial offsets.