Application of Physics to Medicine

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Danube School on Instrumentation in Elementary Particle & Nuclear Physics

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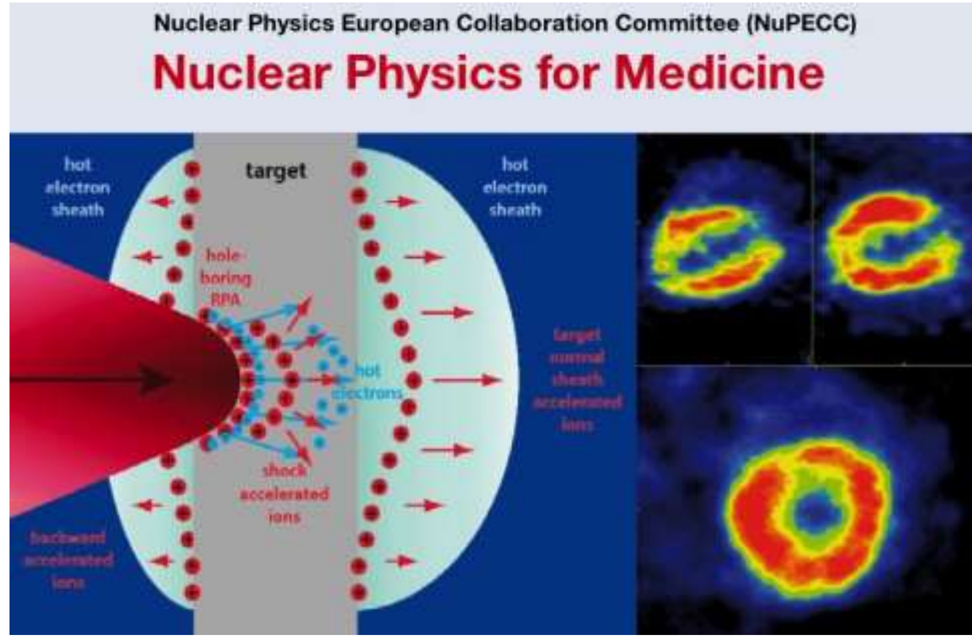
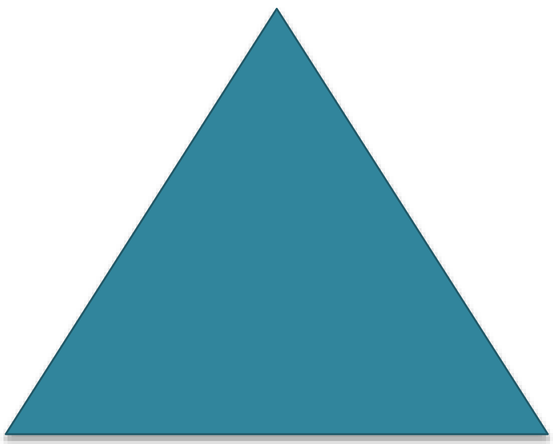
Nuclear Physics for Medicine
NuPECC 2014



http://www.nupecc.org/pub/npmed2014.pdf

Medical Imaging



Radioisotopes

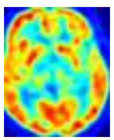
Particle Therapy

Overview

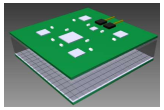
✧ browse the developments in Medical Physics applications?

✧ **select some examples and try and give some insight**

Radioisotopes

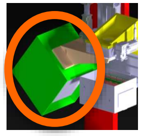


PET Imaging

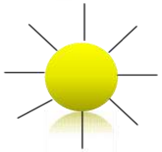


Innovative PET detectors

Hybrid imaging technologies (PET/MRI/EEG)



PET detectors application in particle therapy monitoring



Nanotechnologies + particle therapy

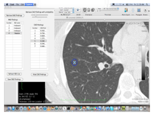


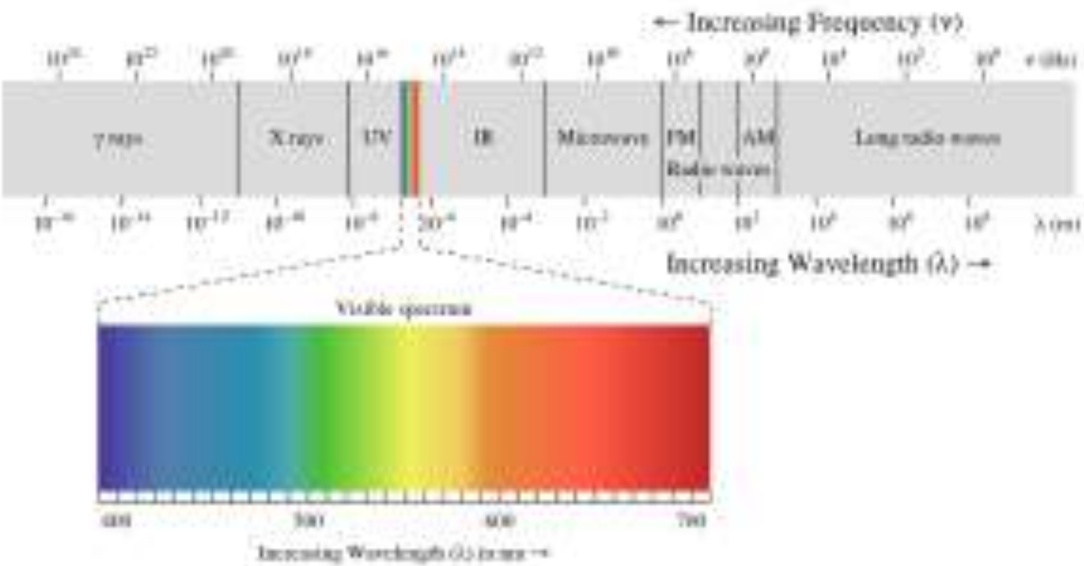
Image Processing

0

Medical Imaging

Medical Imaging

Physics and Medicine have been tightly bound by Medical Imaging technologies for more than a century…



Medical Imaging can be…
… morphological (e.g., CT)

X-rays!!! (Roentgen, 1895)

Medical Imaging

X-rays are absorbed by the target (i.e., the human body)

Absorption is related to the density via the Lambert-Beer law

$$I(z) = I(0)\ \exp(-\mu(\rho)z)$$

$$\rho = \rho(z)$$

By measuring I, μ can be evaluated!

And the body local density, with an amazing resolution…

Let's take a look at a CT scan…

Medical Imaging

Spatial Resolution: ~ 100 μm

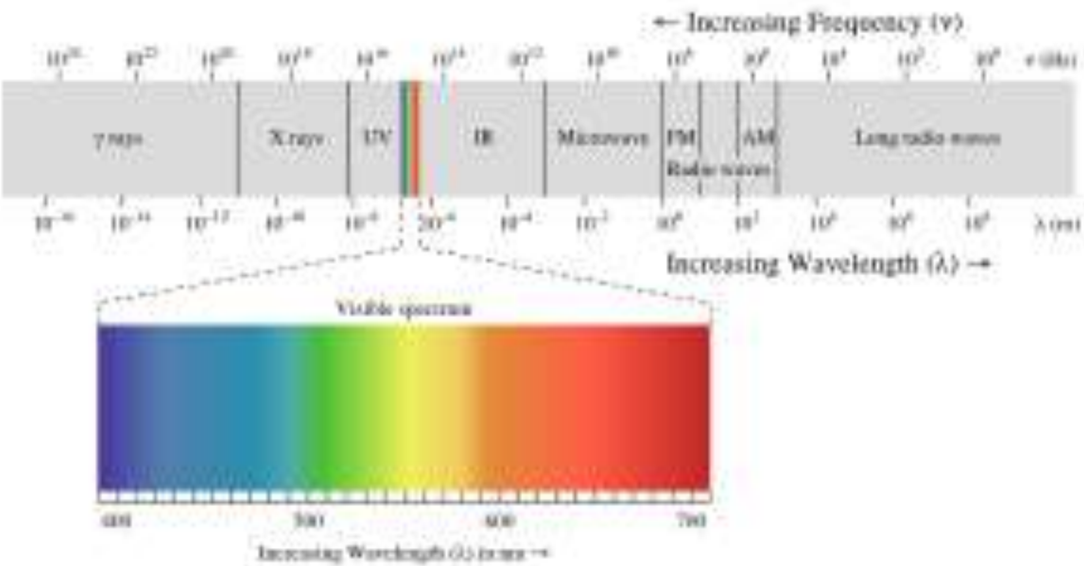
Time Resolution: irrelevant

Energy Resolution: irrelevant

is morphological information enough for diagnosis, staging, follow-up of a disease?

Medical Imaging

Physics and Medicine have been tightly bound by Medical Imaging technologies for more than a century…



Medical Imaging can be…

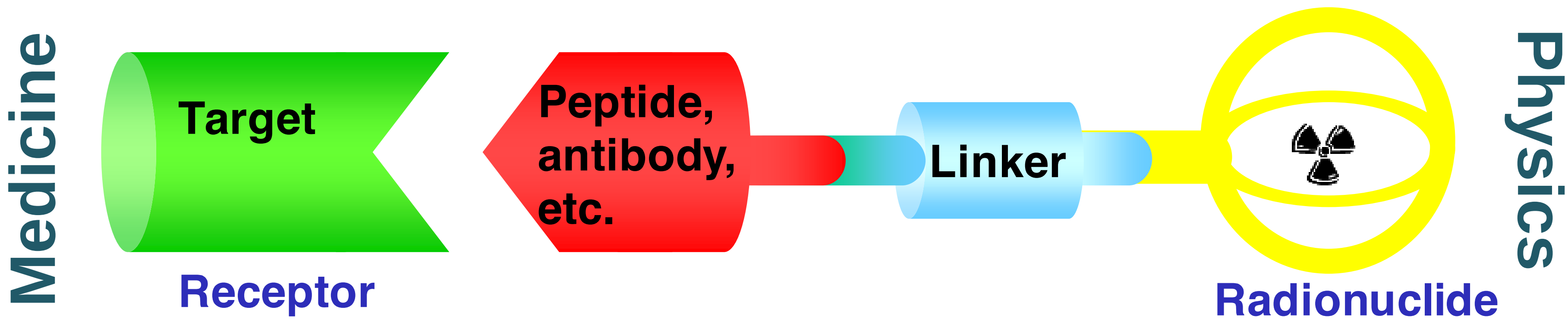
… morphological (e.g., CT)

… functional (e.g., PET)

X-rays!!! (Roentgen, 1895)

Nuclear Medicine

… is multi-disciplinary!



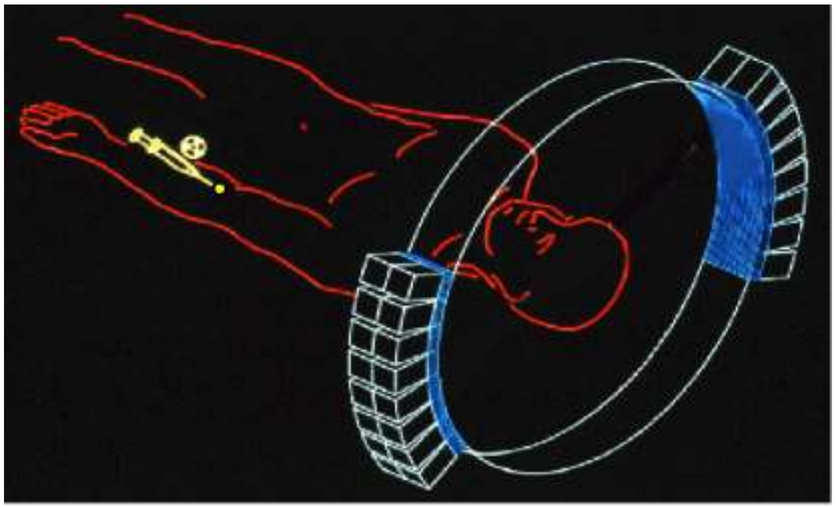
Immunology
Structural biology

Coordination chemistry

Nuclear physics and radiochemistry

Should the peptide/antibody be specific or not?
It depends on the target…

Nuclear Imaging: Ingredients



Nuclear Imaging is functional!

1) a radioisotope bound to 'functionally-relevant' molecules

the emitted particle must be (in)directly detected

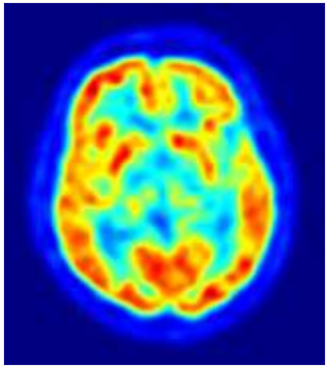
2) a detector

generates information about energy, position, time of the interaction

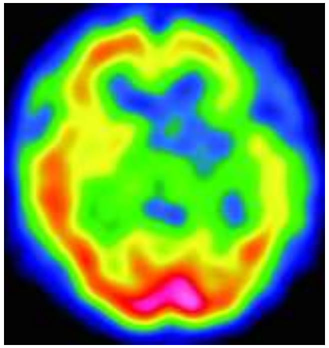
3) Reconstruction software

provides a 2D/3D activity map

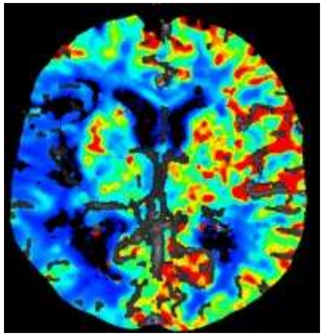
Functional Imaging: Modalities



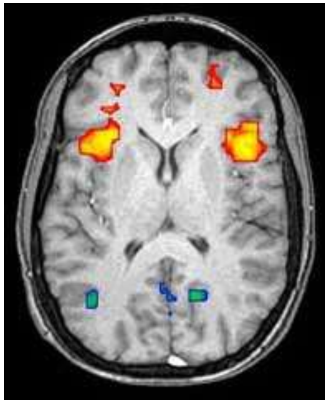
Positron Emission Tomography (PET)



Single Photon Emission Computed Tomography (SPECT)

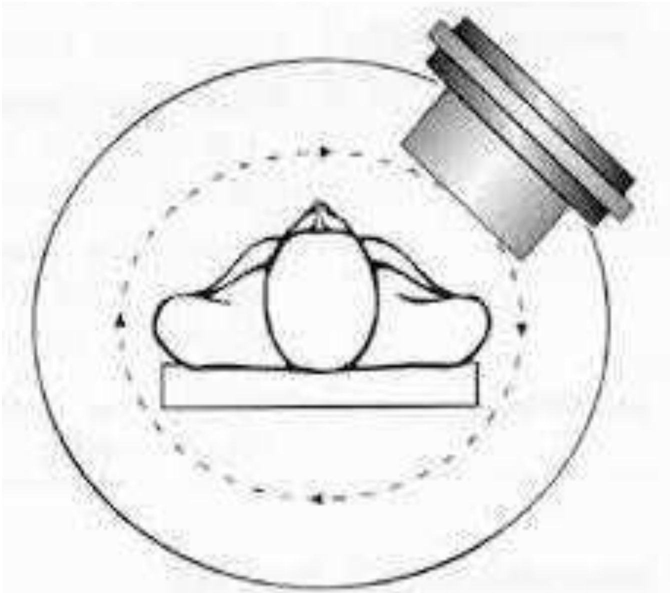


Computed Tomography Perfusion Imaging (CT)



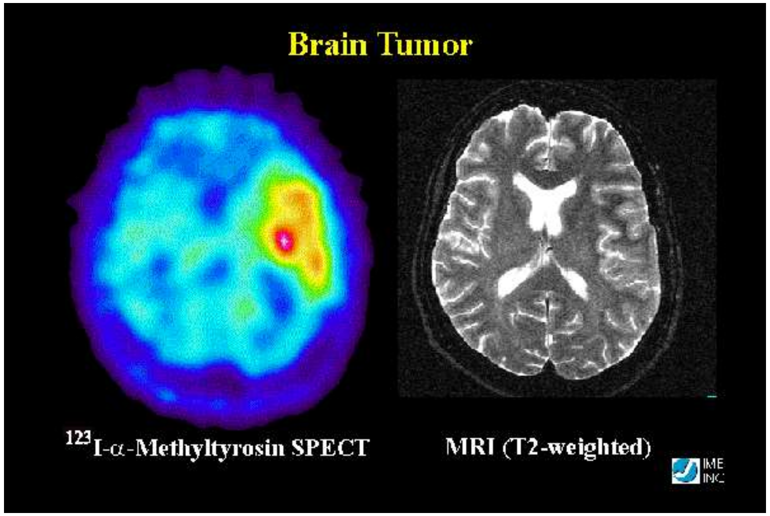
Functional Magnetic Resonance Imaging (fMRI)

SPECT Imaging: ingredients



1) A **γ emitting isotope** bound to ‘functionally-relevant’ molecule

the emitted photon must be in the 70 -300 keV energy range



2) a photon detector

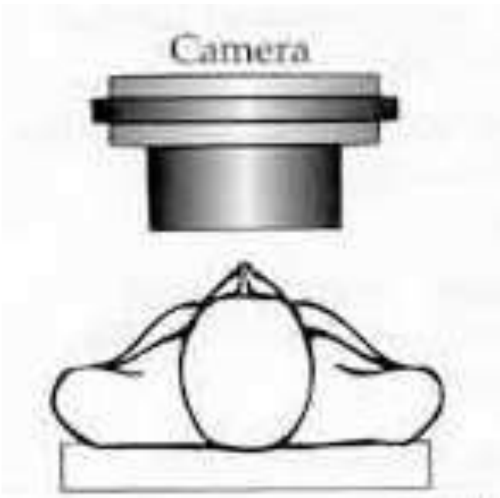
gamma camera + collimator

3) Reconstruction software

provides a 2D/3D activity map

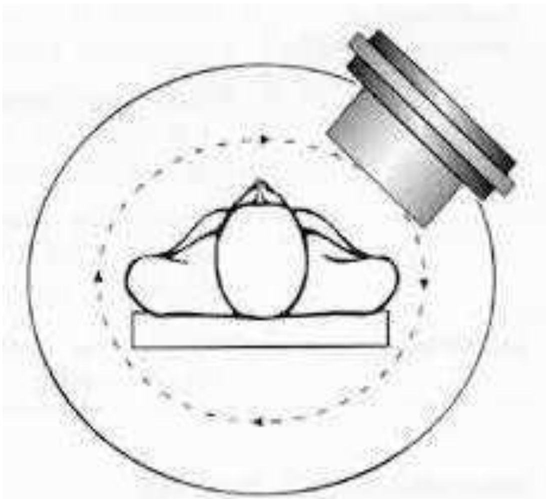
SPECT Imaging: ingredients

Gamma camera

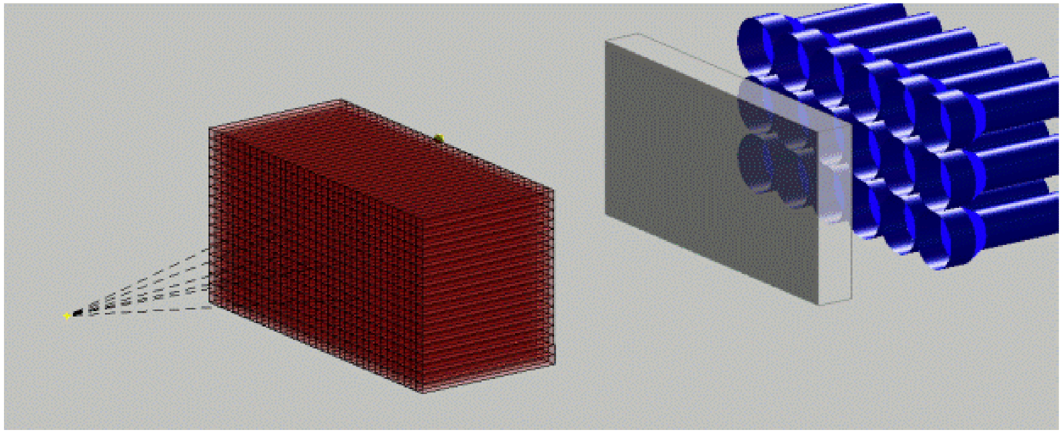


2D: planar scan

SPECT



3D: SPECT: Single Photon Emission Computer Tomography



$E_\gamma >$ 70 keV

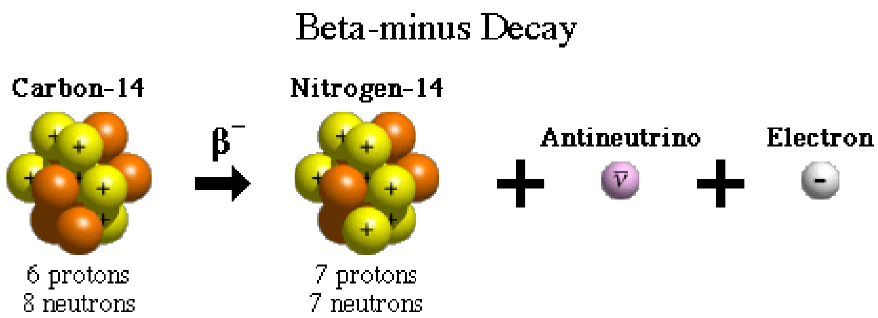
absorption in body

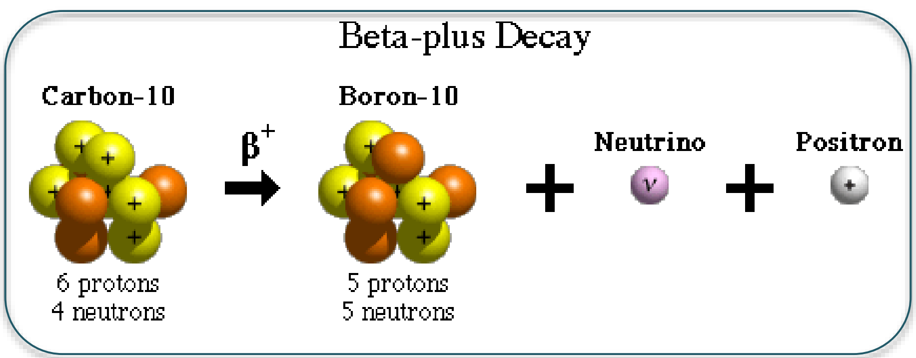
$E_\gamma <$ 300 keV

efficient collimation and detection

PET Imaging: Ingredients

β-decay

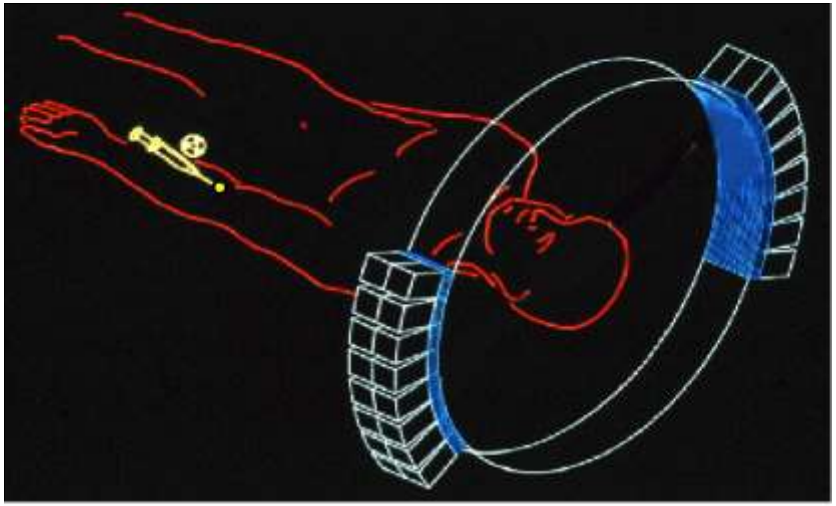


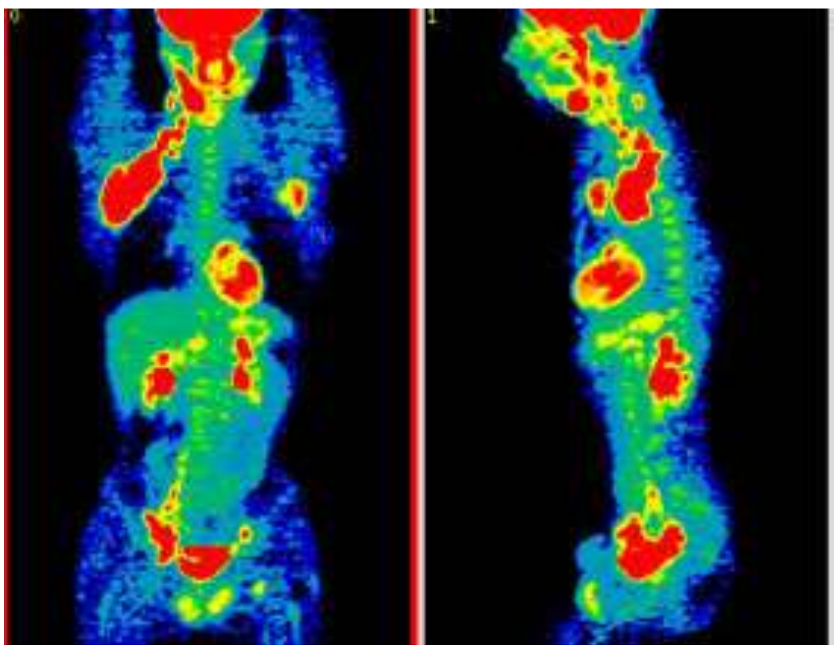


Annihilation

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

PET Imaging: Ingredients





1) a **β+ decaying isotope** bound to 'functionally-relevant' molecule

the emitted e+ annihilates (almost at rest) close to the emission point into a (nearly) back-to-back 511 keV photon pair

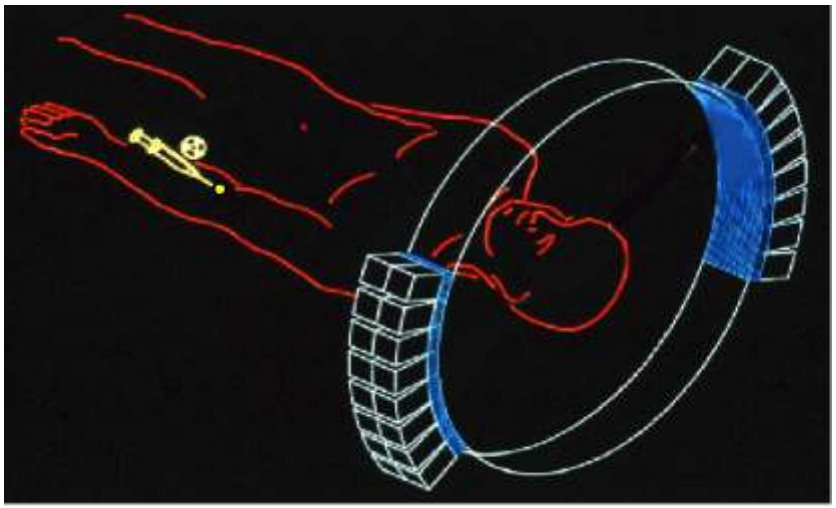
2) a photon detector (typically a crystal)

generates a list of Lines Of Response (LOR)

3) Reconstruction software

provides a 3D activity map

SPECT/PET Imaging: Operations



0) Choose Radiotracer

1) Synthesize Radiotracer

2) Inject Radiotracer

3) Wait (about 60 min)

4) Scan patient

How do you select and produce a Radiotracer?

1

Radioisotopes

Radioisotopes

… the fuel of Nuclear Medicine

What is the optimum isotope for an application ?

Are we using today the optimum isotopes?

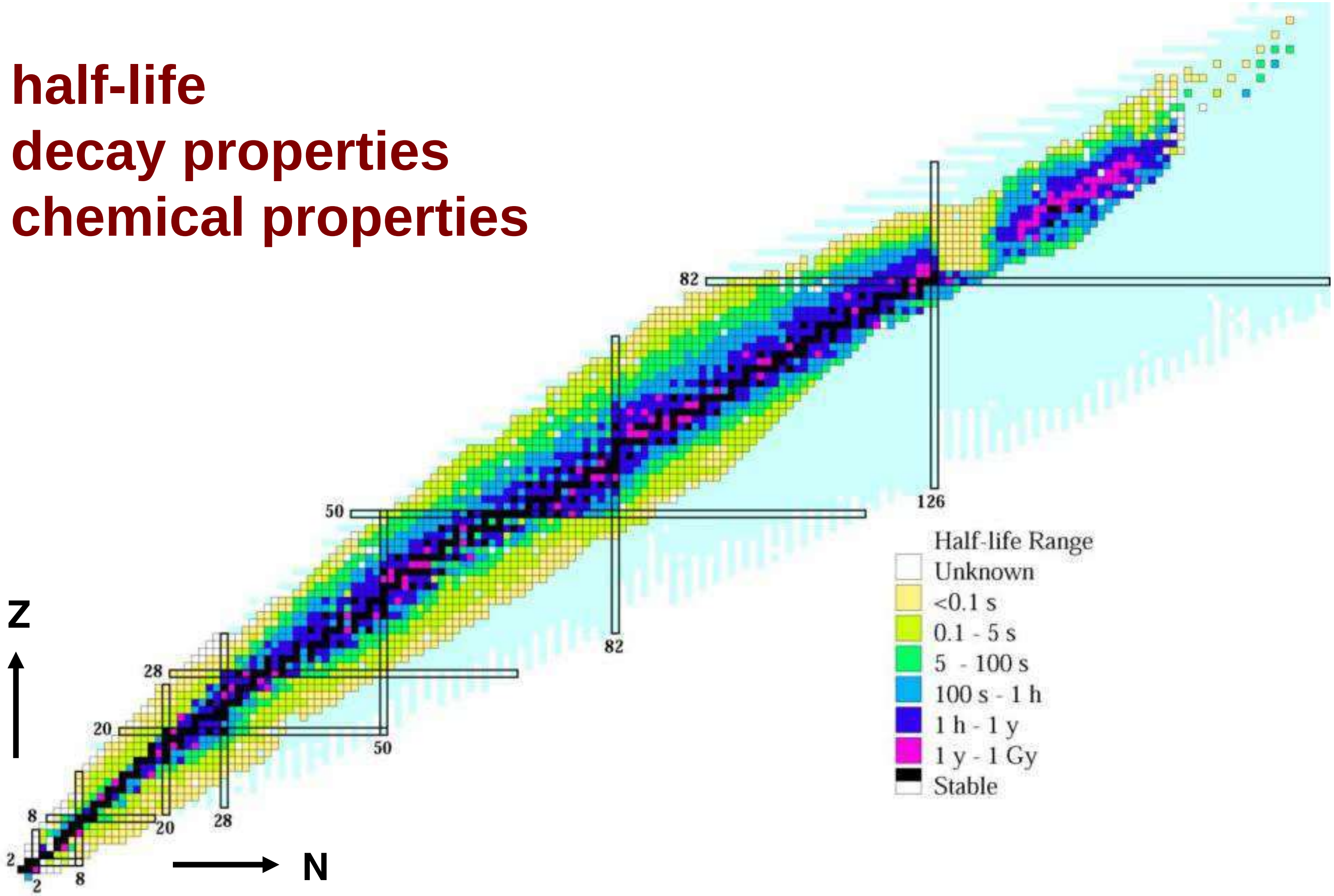
Is there sufficient supply of isotopes at reasonable cost?

How reliable is the isotope supply ?

Radioisotopes

more than 3000 known radioisotopes…

half-life
decay properties
chemical properties

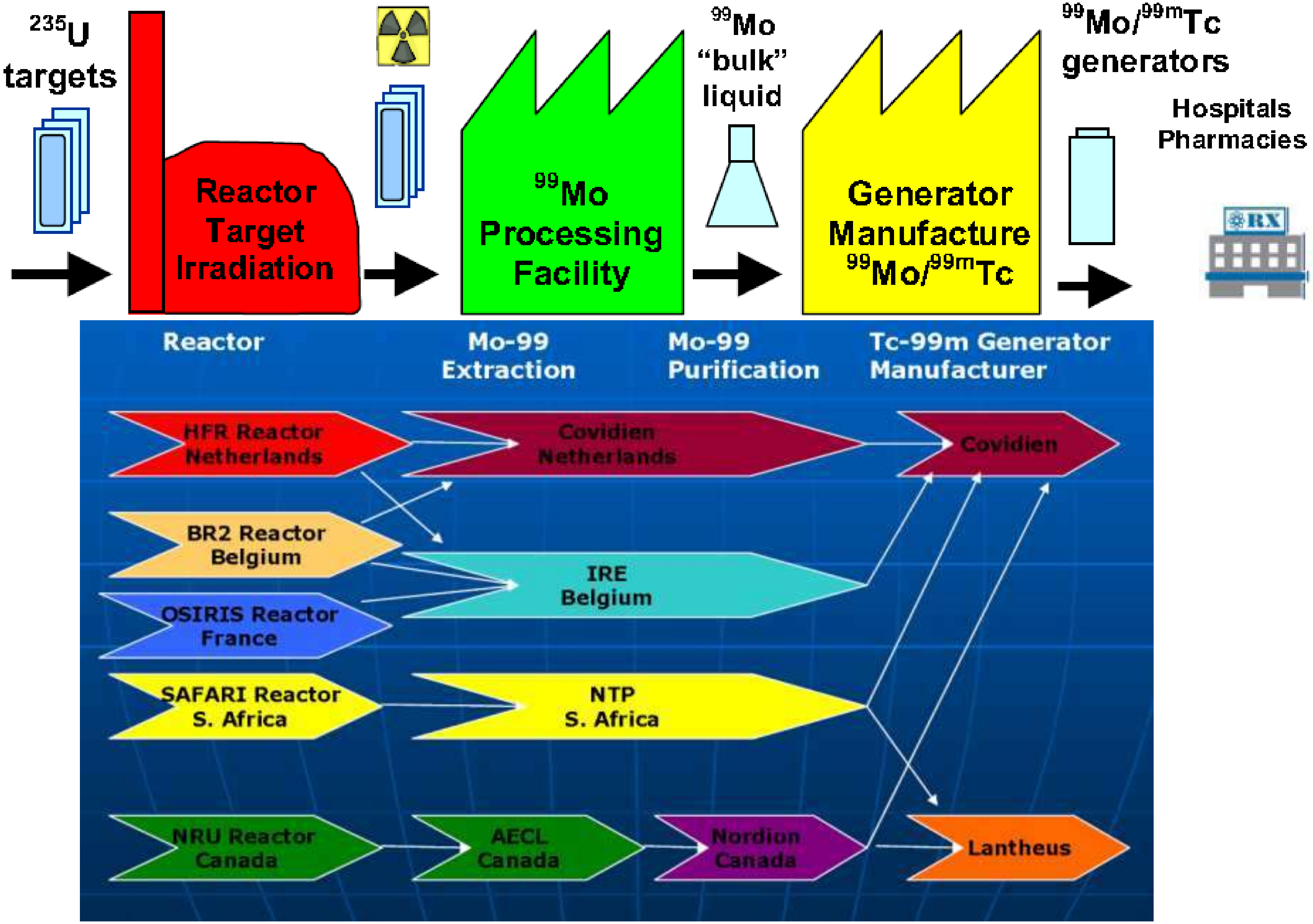


SPECT Radioisotopes: γ emitters

Isotope	Half Life	Energy in KeV	Common Applications/Strengths
Technetium–99m [^{99m}Tc]	6 hours	140.5	Most common clinical SPECT isotope; bone imaging
Iodine–123 [^{123}I]	13.2 hours	159.0	Neuro–Imaging
Indium–111 [^{111}In]	2.8 days	171.3, 245.4	Biodistribution
Gallium–67 [^{67}Ga]	3.3 days	93.3, 184.6, 300	Translatable to [68Ga] PET radiotracer
Lutetium–177 [^{177}Lu]	6.73 days	113, 210	Radiotherapy
Thallium–201 [^{201}Tl]	12.23 days	135, 167	Cardiac Imaging
Tin–117m [^{117m}Sn]	14 days	158.6	Long term Biodistribution
Iodine–125 [^{125}I]	59 days	27 to 32	Iodination

Radioisotopes supply chain

The traditional supply chain of $^{99}Mo/^{99m}Tc$

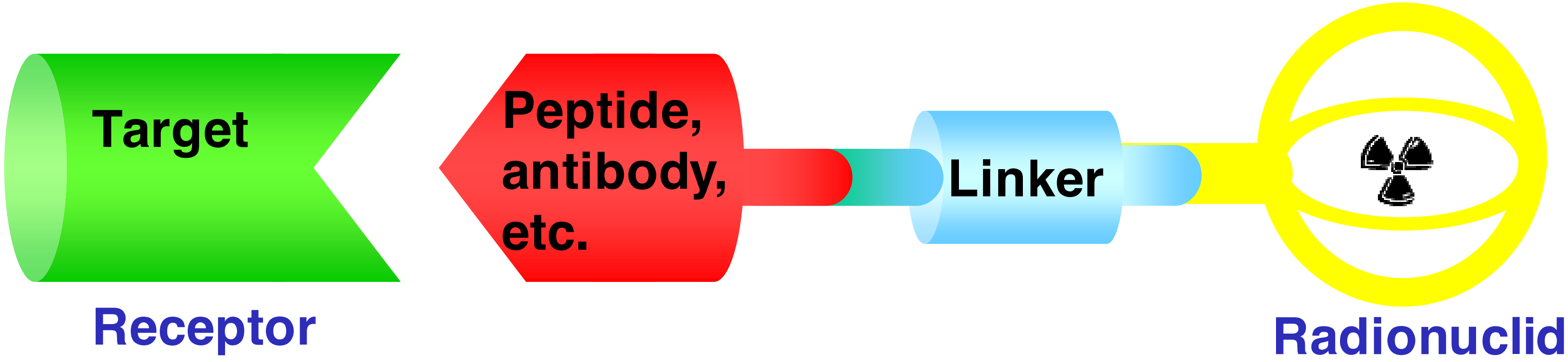


PET Radioisotopes: β+ emitters

PET Isotope	Half Life	Common Applications
Fluorine-18 [^{18}F]	1.8 hours	FLT, FDG
Copper -64 [^{64}Cu]	12.7 hours	Short term tracking of small molecules and peptides; imaging of disease state adn efficacy using targeted biologics
Yttrium-86 [^{86}Y]	14.7 hours	Analog of [90Y] radiotherapy isotope that can be used for imaging studies
Cobalt-55 [^{55}Co]	17.5 hours	Characterization of tissue infarct regions
Iodine-124 [^{124}I]	4.2 days	Iodination labeling of proteins
Zirconium-89 [^{89}Zr]	3.27 days	Biodistribution

Therapy with Radioisotopes

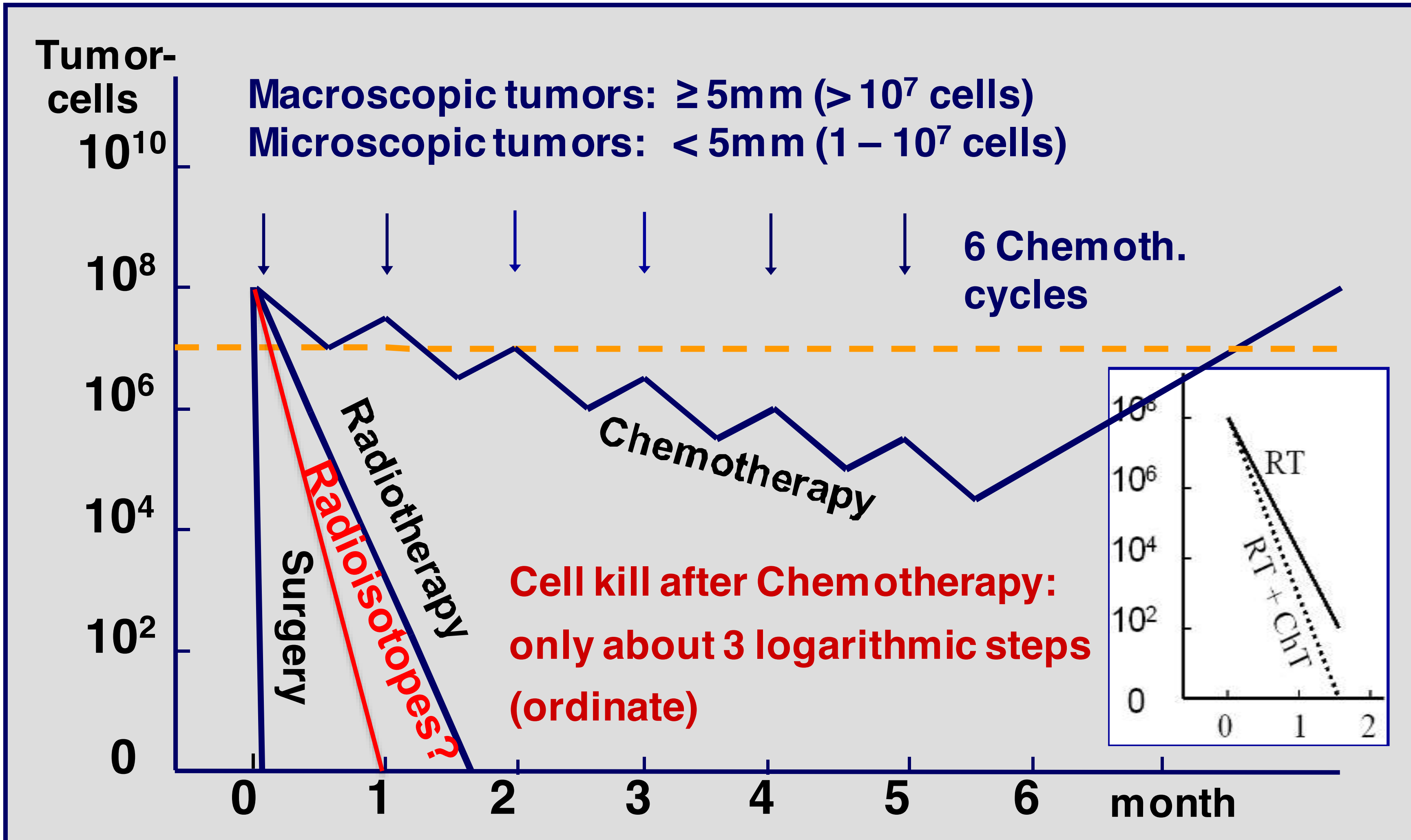
Not only imaging!



Immunology Structural biology	Coordination chemistry	Nuclear physics and radiochemistry

- the peptide/antibody MUST be VERY specific
- half-life: delivery and washout

Tumor therapy comparison



(Molls, TU München; according to Tannock: Lancet 1998, Nature 2006)

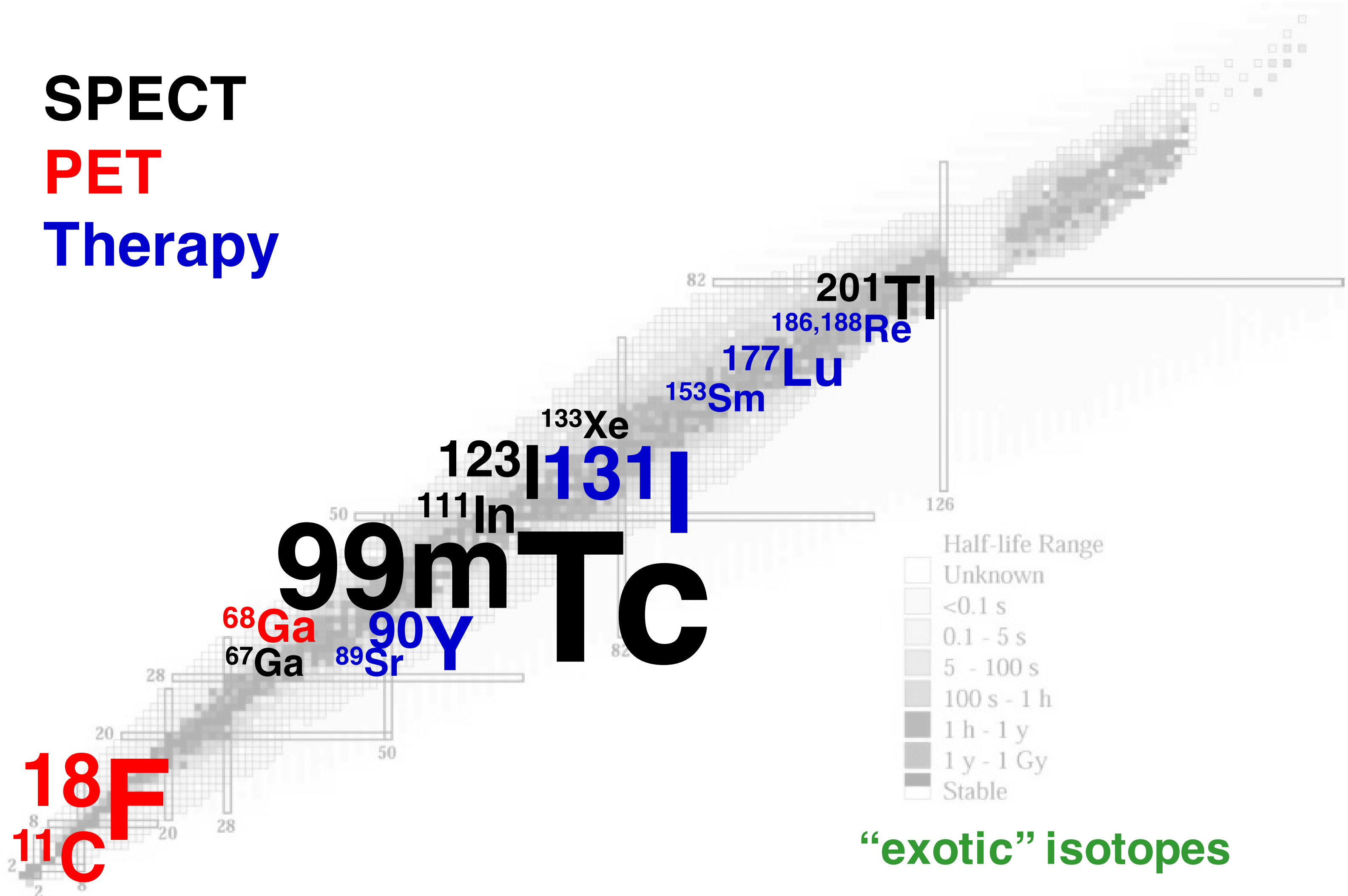
Therapeutic Radioisotopes

Radio-nuclide	Half-life (d)	E mean (keV)	Eγ (B.R.) (keV)	Range	
Y-90	2.7	934 β	-	**12 mm**	**Established isotopes**
I-131	8.0	182 β	364 (82%)	**3 mm**	
Lu-177	6.7	134 β	208 (10%) 113 (6%)	**2 mm**	**Emerging isotope**

… I would expect new developments in the field…

Chart of Radioisotopes

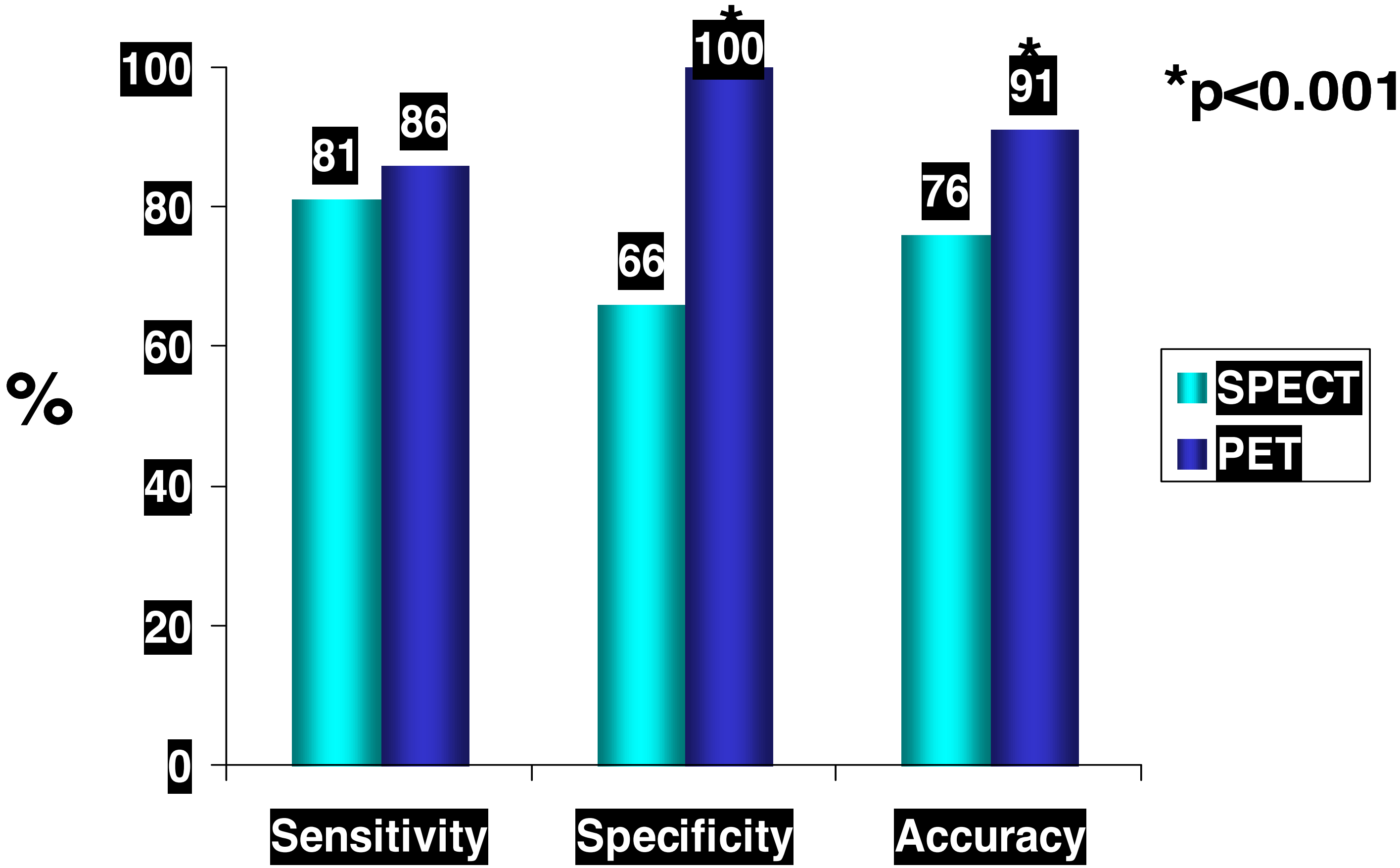
SPECT
PET
Therapy



2

PET Imaging

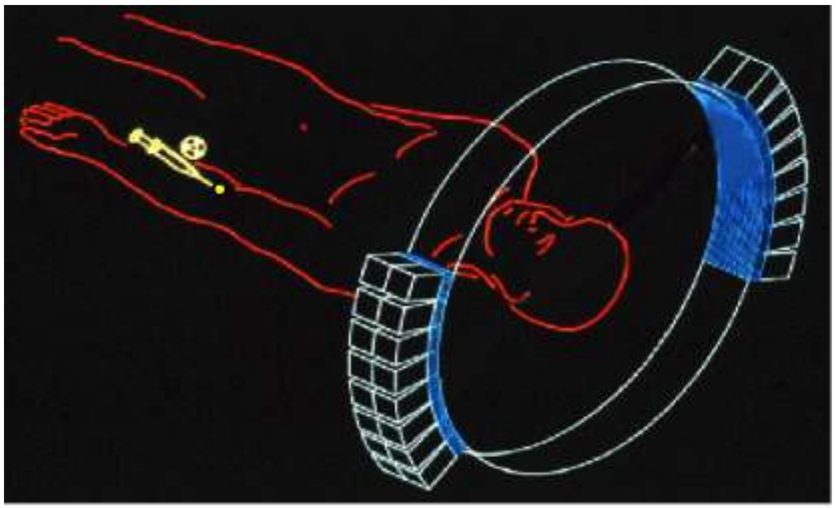
Diagnostic Accuracy: PET vs. SPECT



D. Le Guludec, ICTR-PHE2012

Bateman et al, J Nucl Cardiol 2006

PET Imaging



Operations

1) Synthesize Radiotracer
2) Inject Radiotracer
3) Wait (about 60 min)
4) **Scan patient**

How do you design a PET system?

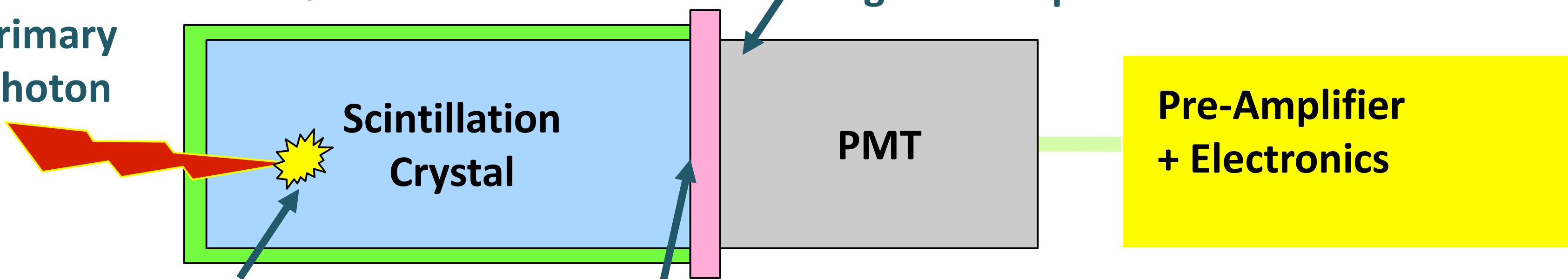
PET Imaging

Conventional PET detector

light is converted to an electrical signal & amplified

Optical reflector

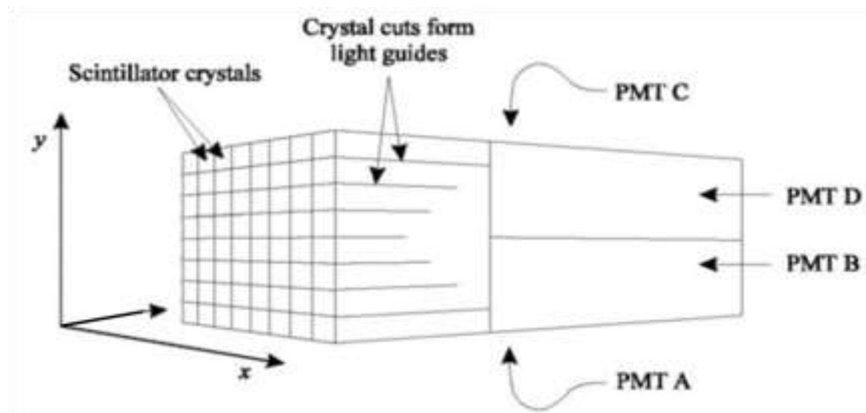
Primary Photon



photon converts to optical (secondary) photons (number proportional to gamma energy, typ. 1000's)

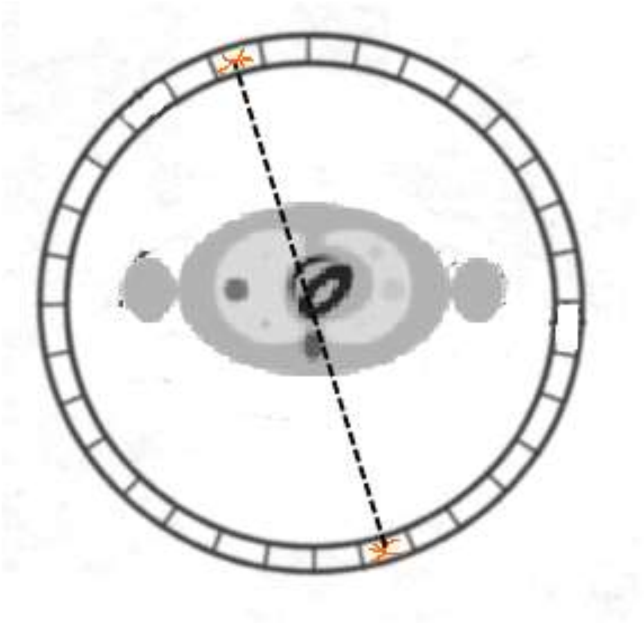
photons are collected at the end of the crystal

Front-end electronics: signal processing

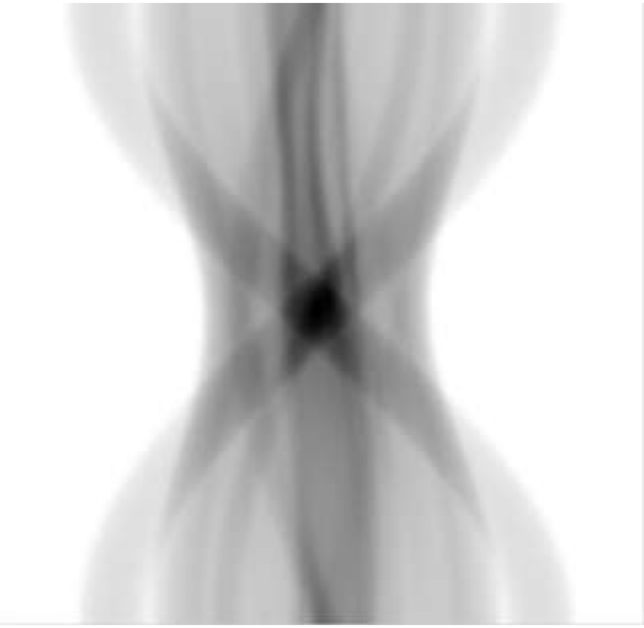


PET Imaging

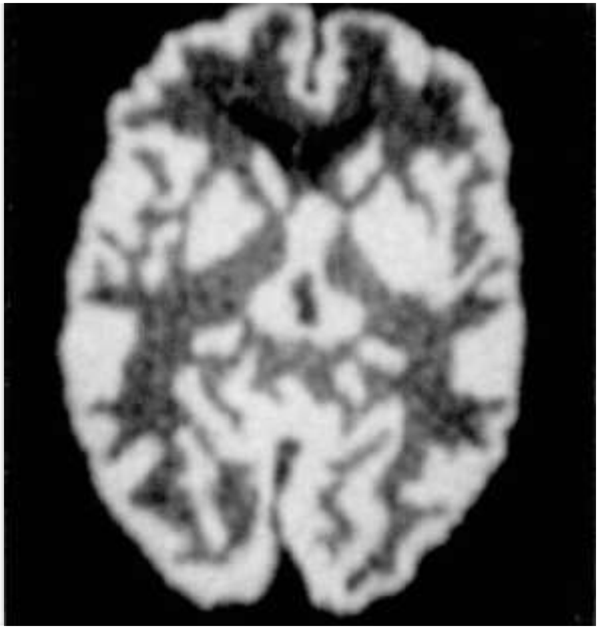
Line of Response



Sinogram



Image



What are the critical parameters of a PET system?

PET Imaging parameters

Field Of View

Photon detection efficiency

Energy resolution

- Compton scattering vs. photopeak

Spatial Resolution

- positron path
- depth of interaction
- time of flight

Time Resolution

- Annihilation point along the LOR

PET Imaging: detection efficiency

Detection efficiency

(aka sensitivity, stopping power)

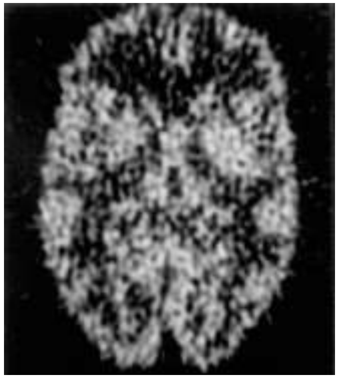
Reduces noise from counting statistics

Reduces dose

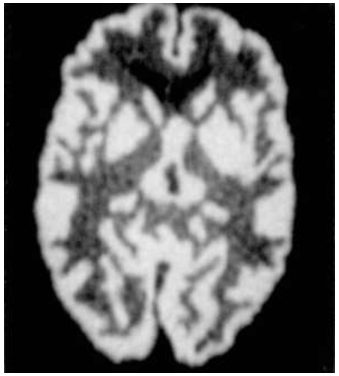
Example: 2cm of LSO

~ 82% (singles)

~ 67% (coincidences)

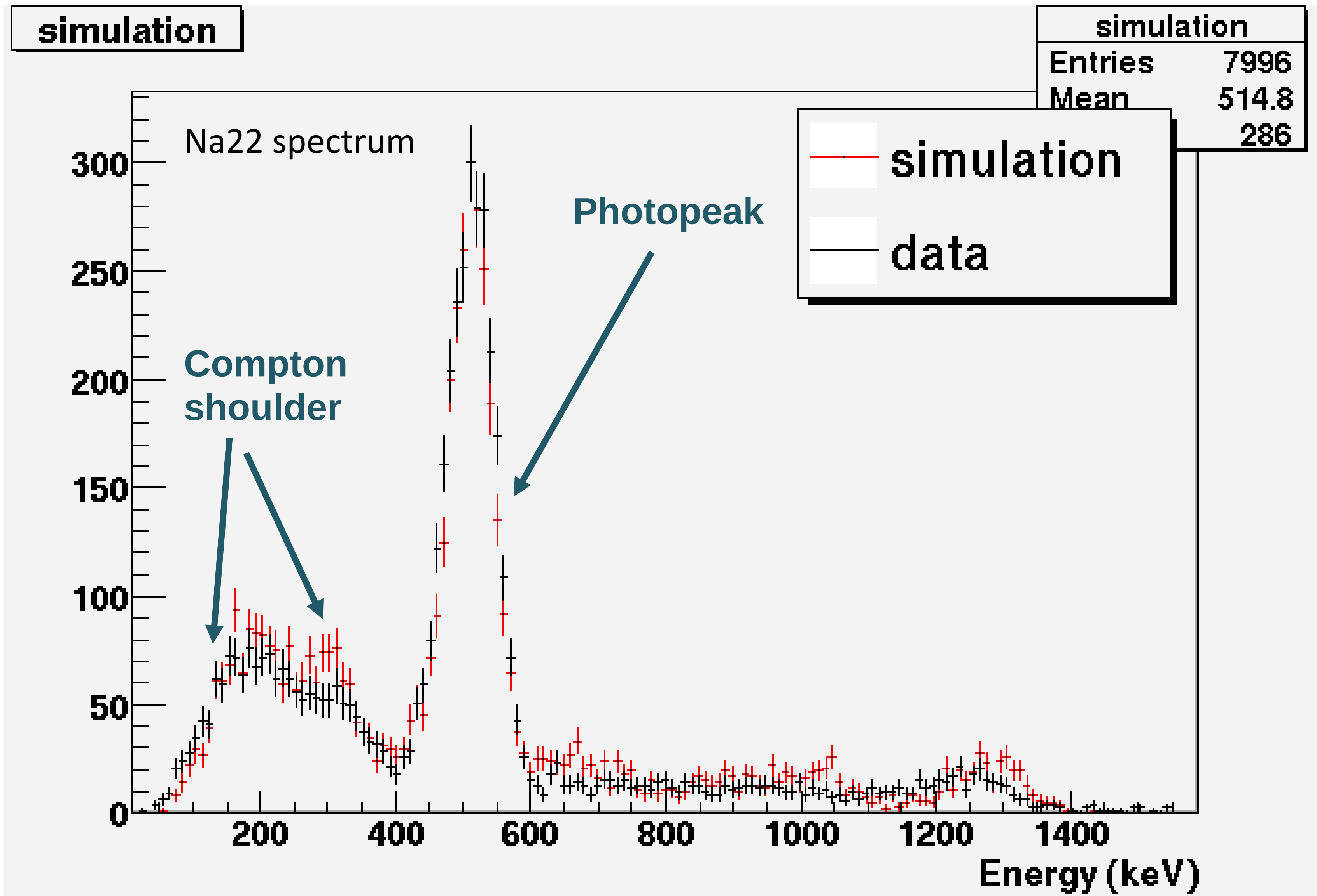


1M Events



55M Events

PET Imaging: Energy Spectrum



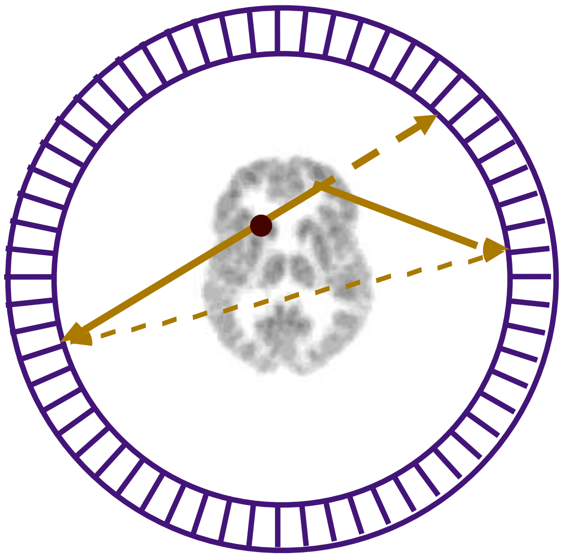
PET Imaging: Compton background

Energy resolution

Scattered photons change direction
AND lose energy

Affects acceptance of scattered
coincidences

Currently ~ 15 - 20%



Deadtime / Rate

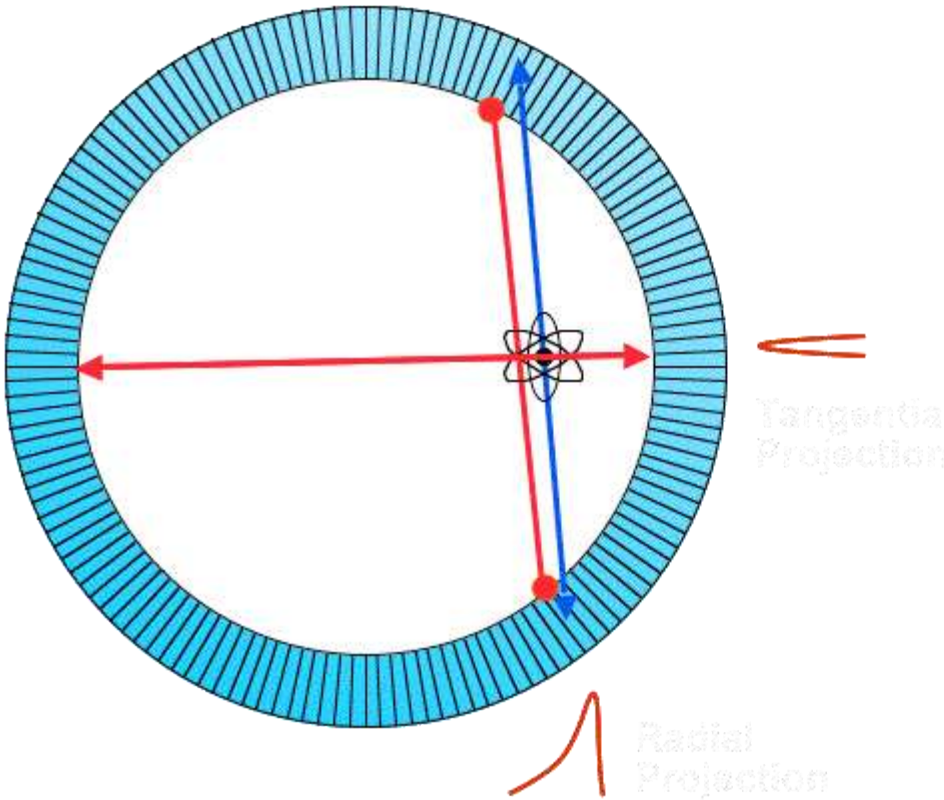
single channels must handle
MHz count rates!

multiple coincidences rejection

PET Imaging: Depth of Interaction

Depth Of Interaction

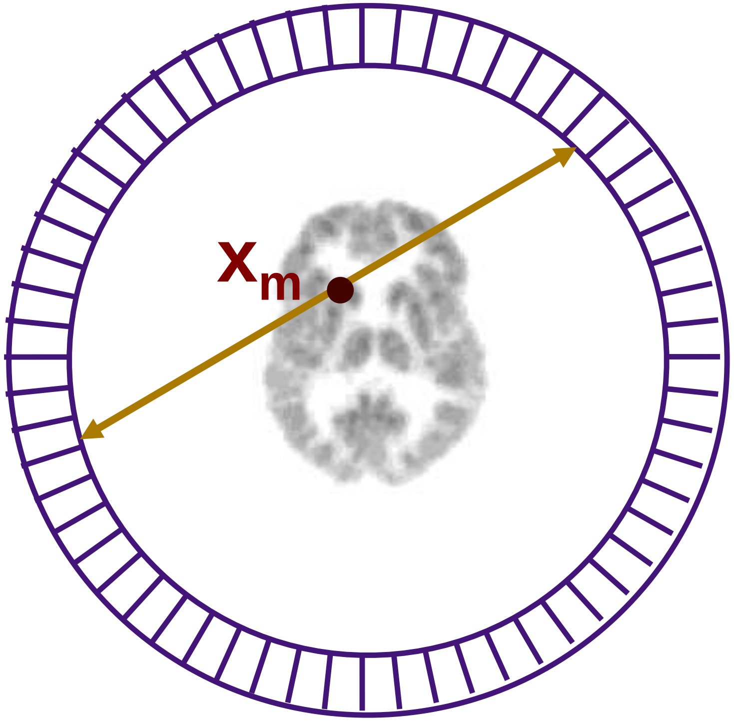
- parallax error
- goal ~ 1 mm



PET Imaging: Time of Flight

Time Of Flight

- more information on LOR
- less background
- Detection Quantum Efficiency
- present intrinsic limit: ~ 100 ps



$P(x) \sim \exp(-(x - x_m)/2\sigma^2)$

$$\frac{\sigma(S/N_{tof})}{\sigma(S/N_{non-tof})} = \sqrt{\frac{2D}{c\Delta t}}$$

Can PET performance be improved? Why should it?

- Better image quality and/or Lower dose
- Better sensitivity & specificity in disease detection
- Quantitative PET analysis
  - that also requires protocol standardization
- Shorter Exam Time / Lower Cost

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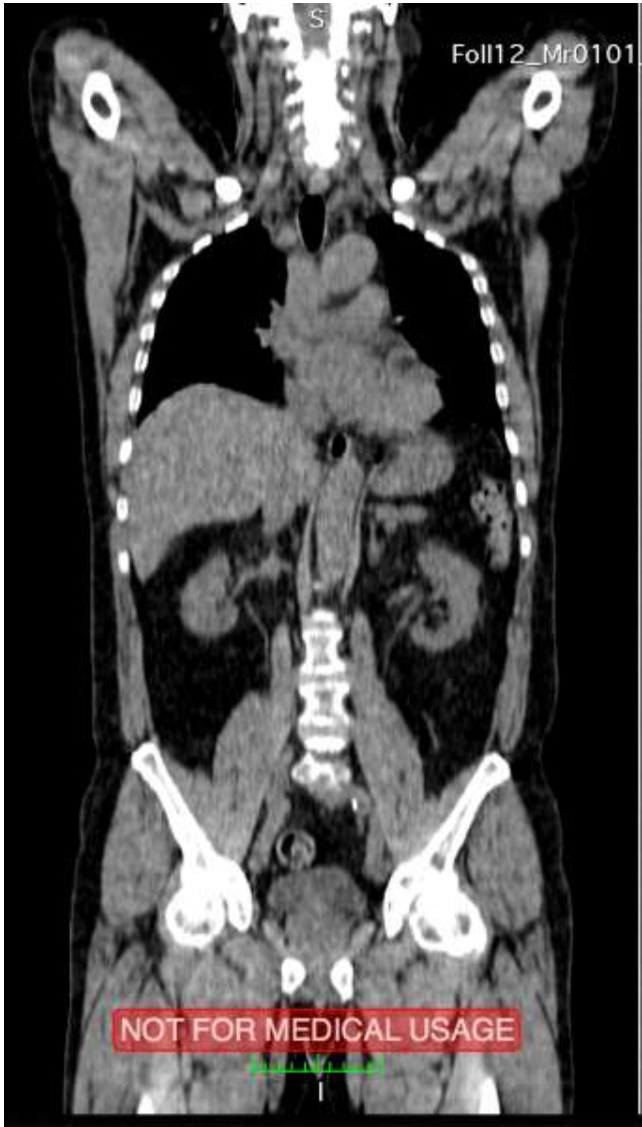

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3

PET detectors

How to improve PET performance?

- 4D detectors with new design
  - **Depth of Interaction**
    - Parallax error
  - **Time Of Flight**
    - Weighted Line Of Response
  - **MR compatibility**
    - PET/MR Hybrid Imaging
  - **Compactness**
    - In-beam PET in HadronTherapy
  - **Cost & Scalability**

How to improve PET design?

- Scintillators
- Photon Detectors
- Front-End Electronics
- System Design & Integration

Scintillators

	NaI	BGO	GSO	LSO	LYSO	LGSO	LuAP	YAP	$LaBr_3$
Light yield 10^3 ph/MeV	38	9	8	30	32	16	12	17	60
Primary decay time	250	300	60	40	41	65	18	30	16
$\Delta E/E$ (%) at 662 keV	6	10	8	10	10	9	15	4.4	3
Density (g/cm^3)	3.67	7.13	6.71	7.35	7.19	6.5	8.34	5.5	5.08
Effective Z_{eff}	50	73	58	65	64	59	65	33	46
$1/\mu$ @ 511 keV (mm)	25.9	11.2	15.0	12.3	12.6	14.3	11.0	21.3	22.3
PE (%) at 511 keV	18	44	26	34	33	28	32	4.4	14

Photon Detectors

Detector	PMT	APD	(d)SiPM	UFSD
Gain	10^5	50-1000	~ 10^6	5-15
Rise Time (ns)	~ 1	~ 5	~ 1	~ 0.1
QE @ 420 nm (%)	~ 25	~ 70	~ 25-75 (PDE)	~ 75
Bias (V)	> 1000	300-1000	30-80	100
Temperature sensitivity (%/K)	< 1	~ 3	1-8	Negligible
Magnetic filed sensitivity	Yes	No	No	No

Front-End Electronics

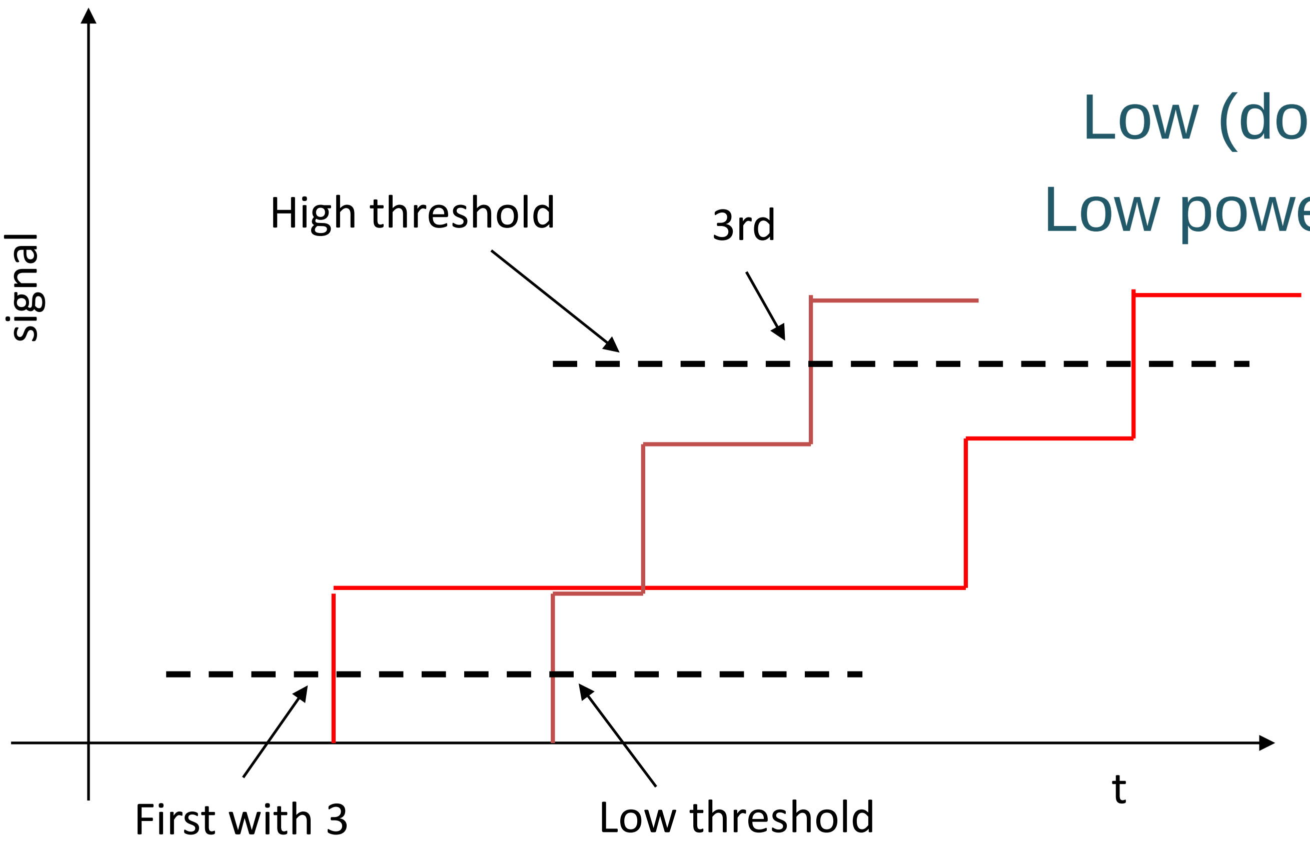
- **“Catch the first de-excitation photon”**

Speed

Low Noise

Low (double) threshold

Low power consumption



System Design

- **Segmented vs. Monolithic crystal**

  Axial

  Block

- **Time measurement strategy**

  Single secondary photon detection

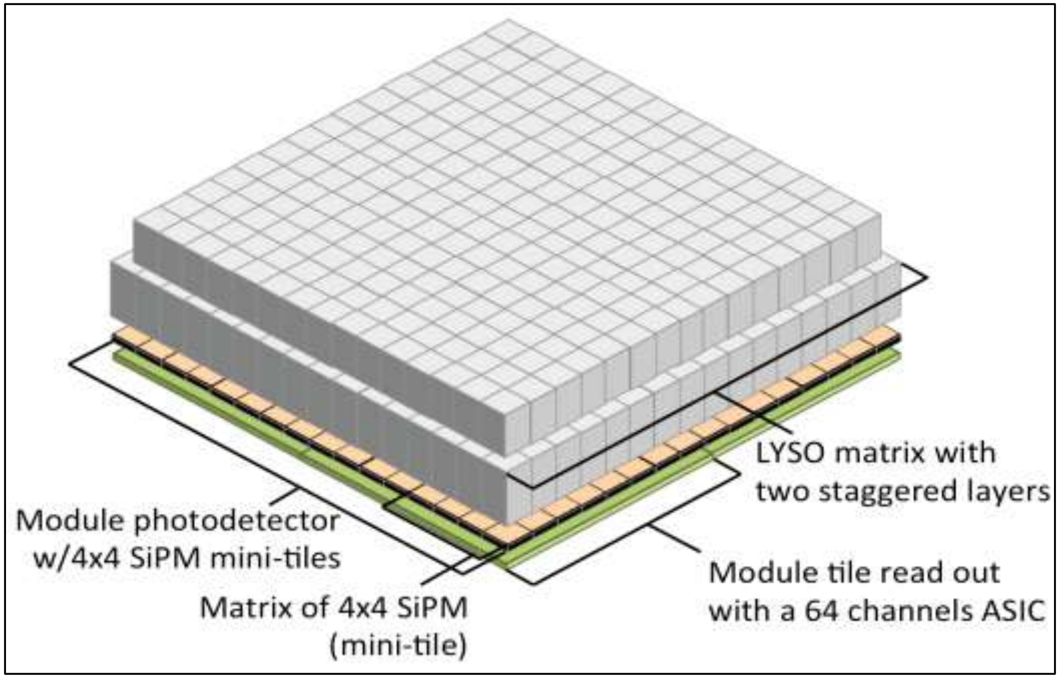
  - noise

  - dark counts

Some Examples…

- Apologies in advance to all the projects that I will not mention
  - **4DMPET**
  - **AXPET**
  - **SpadNet**

The "standard"

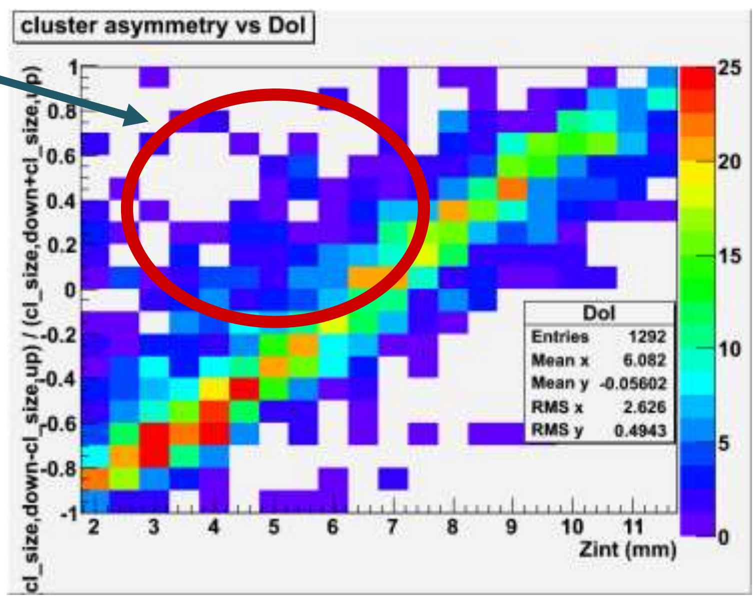


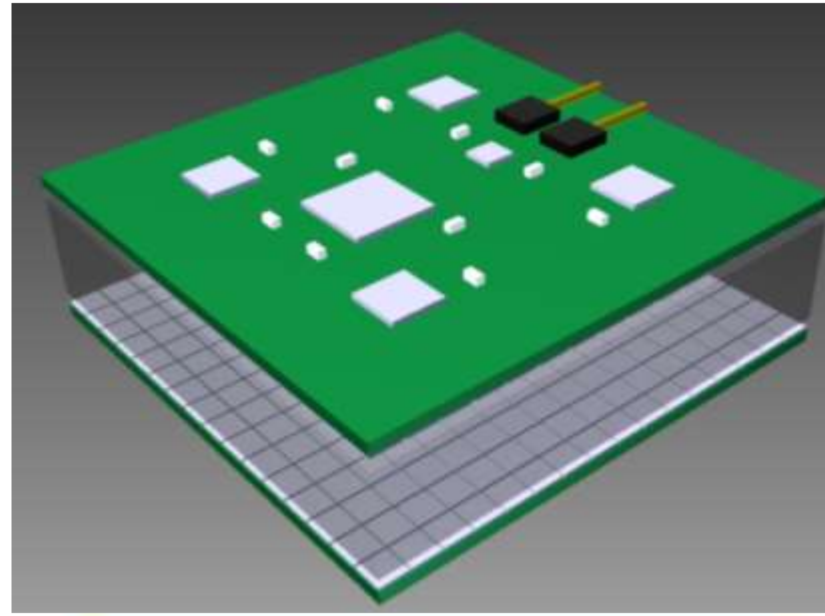
4DM-PET Detector Layout

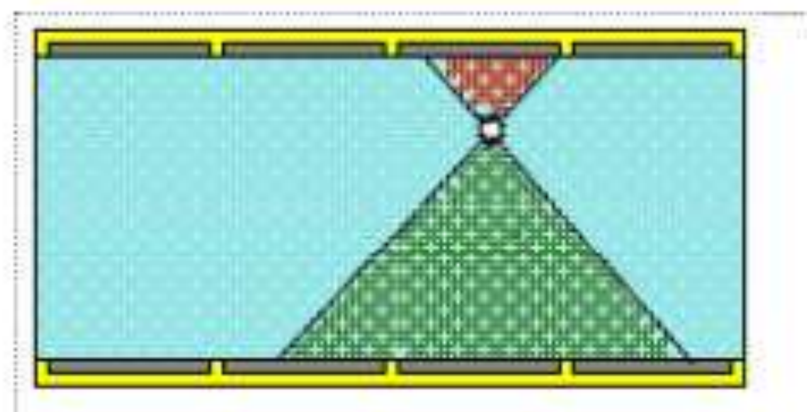
A. LYSO scintillator slab Size: $48 \cdot 48 \cdot 10\ mm^3$
B. Top / bottom SiPM layers
   - 16x16 square pixels, 3mm pitch
C. Independent identical readout boards

- Depth Of Interaction
  - Size Asymmetry: (t - b)/(t + b)
  - Simulated FWHM: 1.0 mm

Compton effect





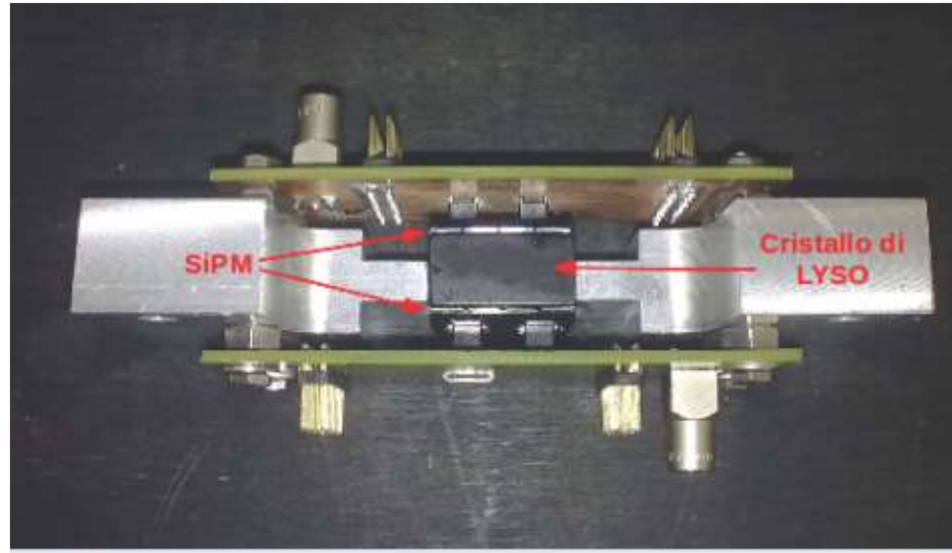


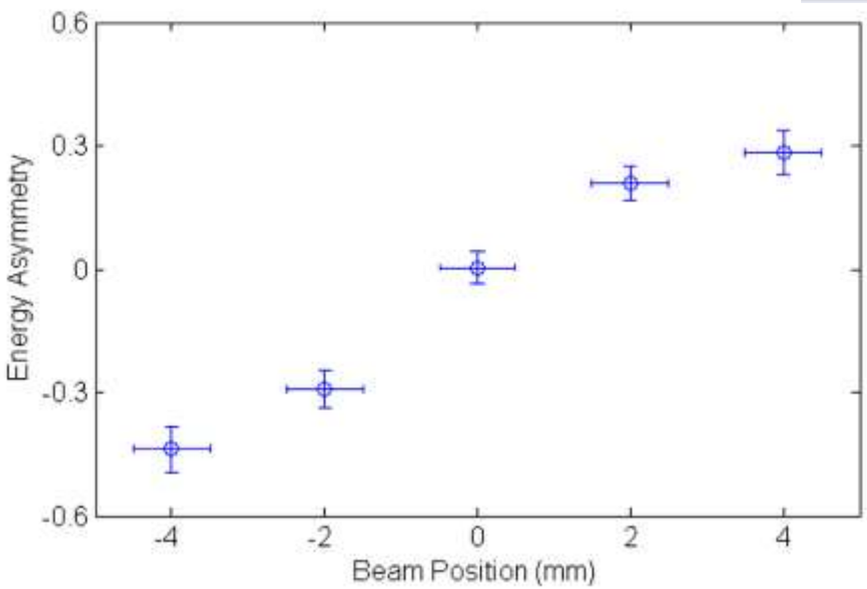
Courtesy of the 4DM-PET Collaboration

4DM-PET DOI measurement

Preliminary DOI measurement on a 5x5 mm^2 detector with 4x4 channels

- **“worst case scenario”**
- **2 mm FHWM**



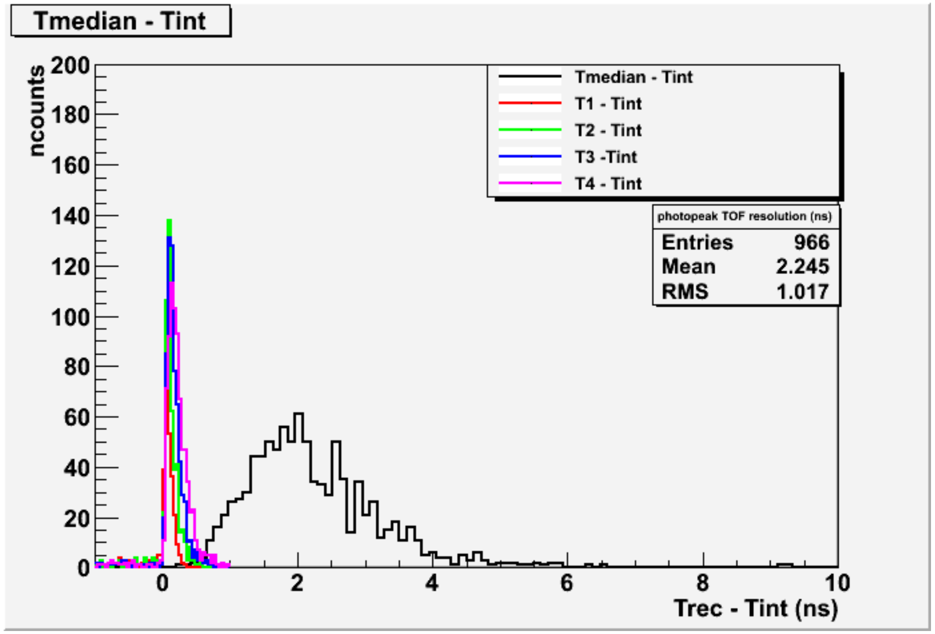


16x16 module with TOF capabilities under construction

Courtesy of the 4DM-PET Collaboration

4DM-PET TOF simulation

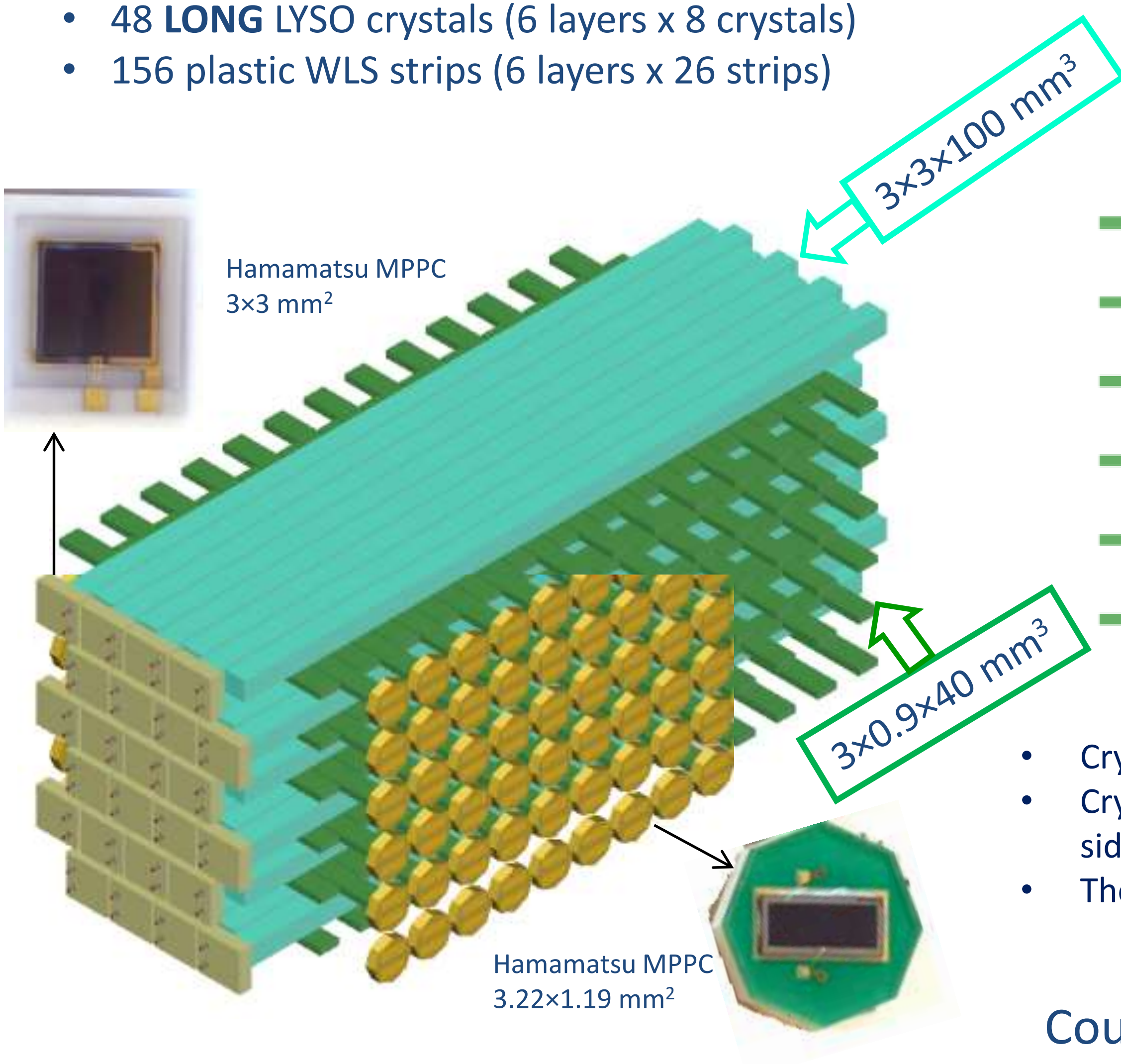
- **Time Resolution**
  - Cluster timing is affected by single pixel dark counts
  - A cluster is defined by N times that sample the crystal decay profile
    - take as cluster time the second minimum pixel time!
  - T_2 RMS: 230 ps, FWHM: 100 ps

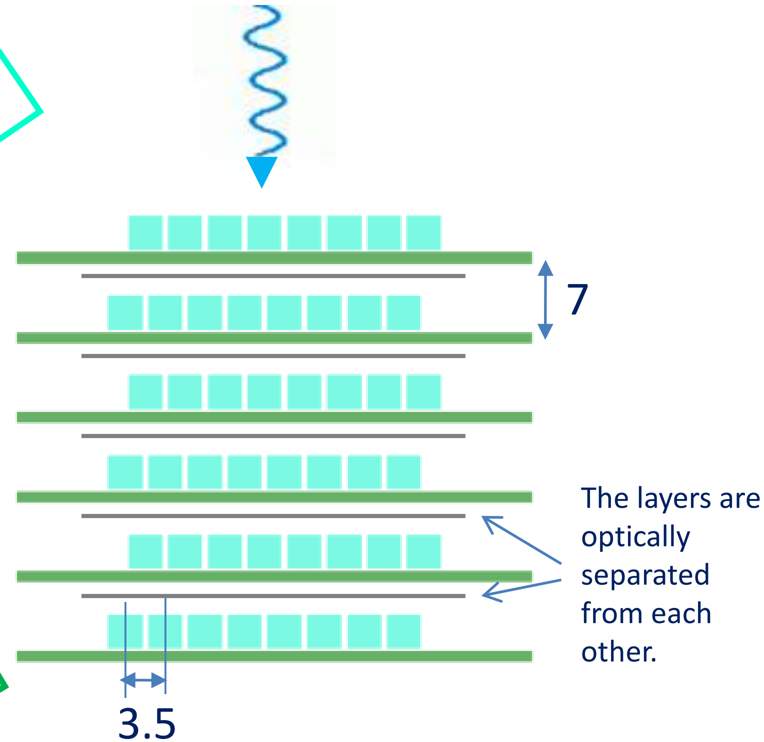


Courtesy of the
4DM-PET Collaboration

The AX-PET Demonstrator

It consists only of **two camera modules**
- 48 **LONG** LYSO crystals (6 layers x 8 crystals)
- 156 plastic WLS strips (6 layers x 26 strips)



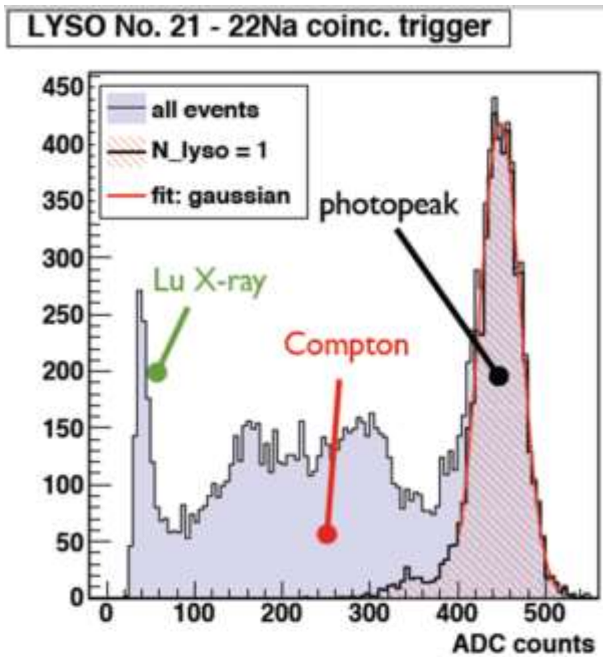


- Crystals are staggered by 2 mm.
- Crystals and WLS strips are read out on alternate sides to allow maximum packing density.
- The other side is Al-coated, i.e. mirrored.

Courtesy of the AXPET Collaboration

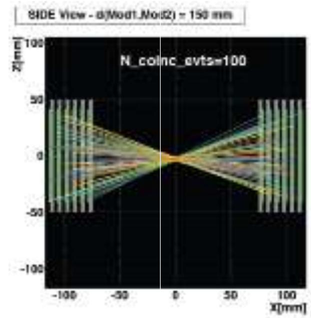
AxPET Performance

Yield LYSO: ~1100 pe / 511 keV
Yield (2-3) WLS: ~100 pe / 511 keV

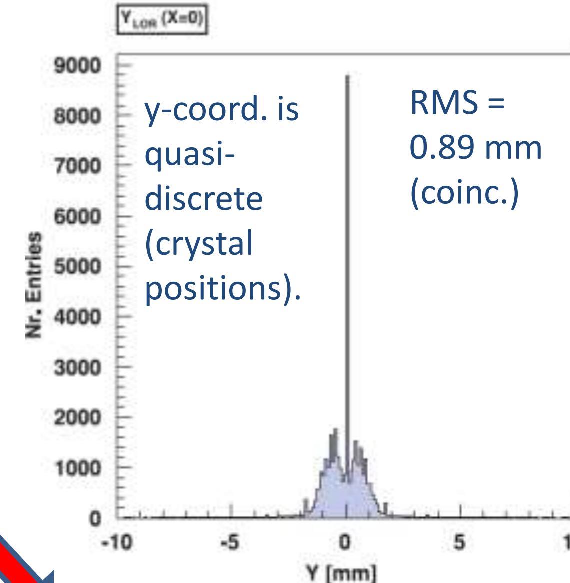


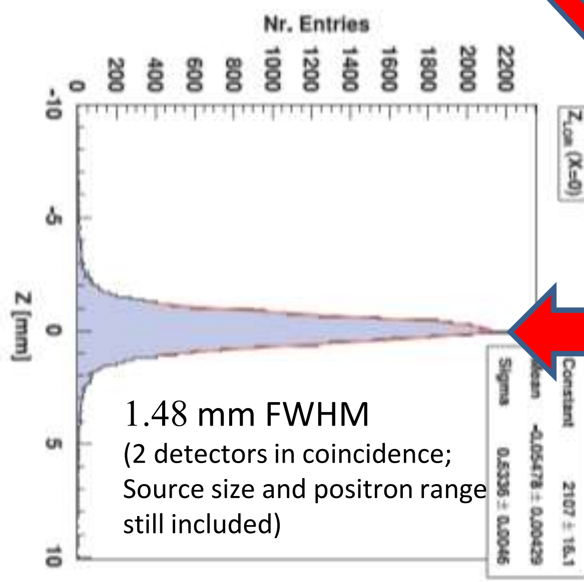
$\langle R_E \rangle_{511} = 11.7\ \%$ (FWHM)

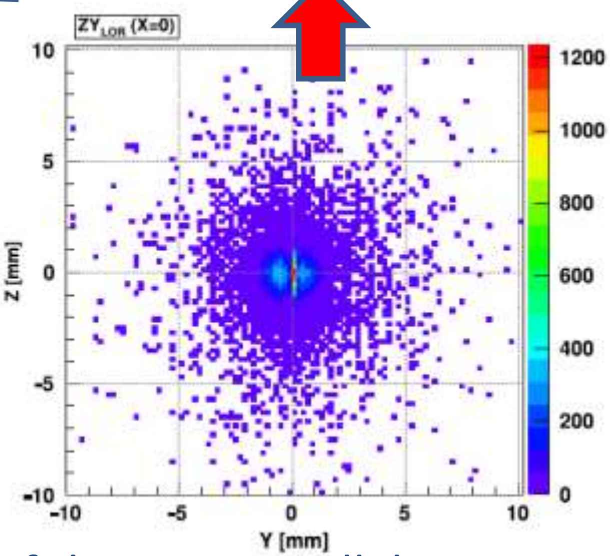
Calibrated and averaged over all crystals.



Look at the YZ distribution at x=0 ("confocal reconstruction")



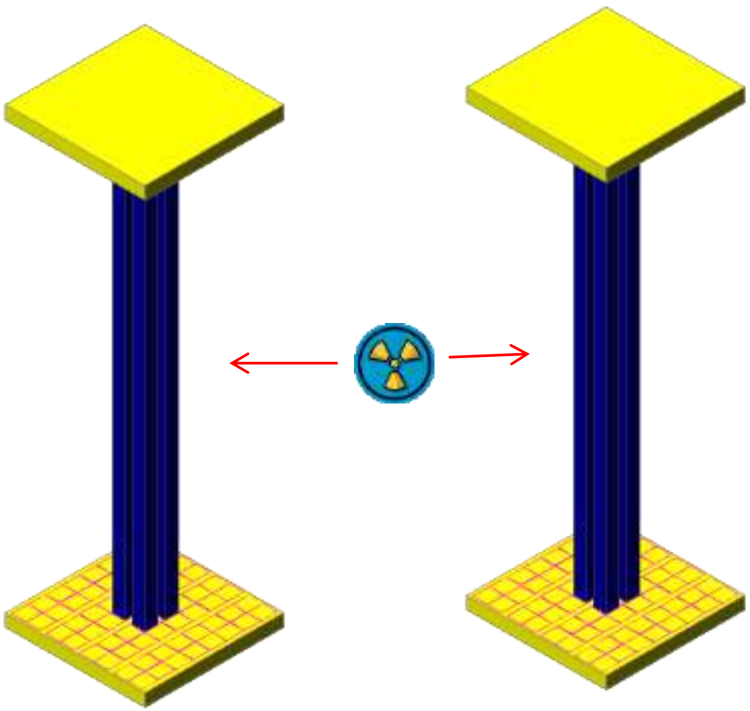


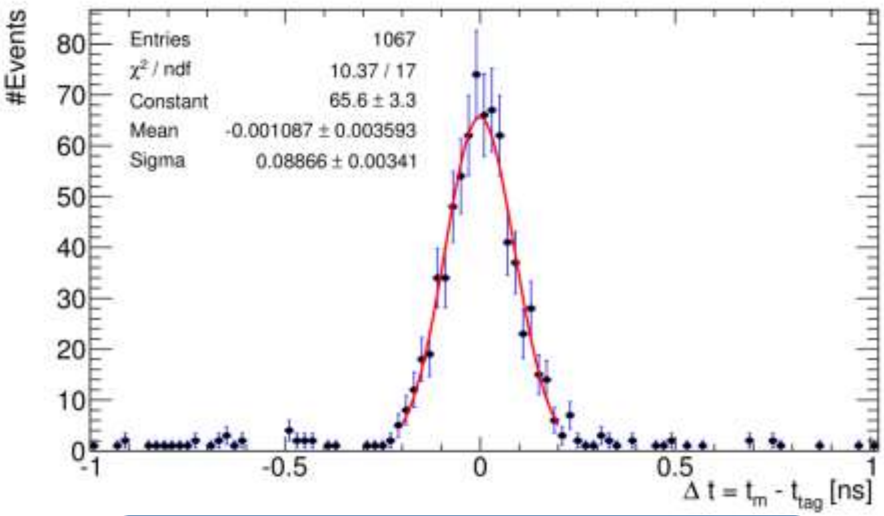


Courtesy of the AXPET Collaboration

AX-PET 2.0. Mini set-up

Dual-sided readout with dSiPMs





Consider dual-sided readout of long crystals to get rid of propagation delays.

Modules coincidence
CRT = **211 ps FWHM**
(~ 6 cm)

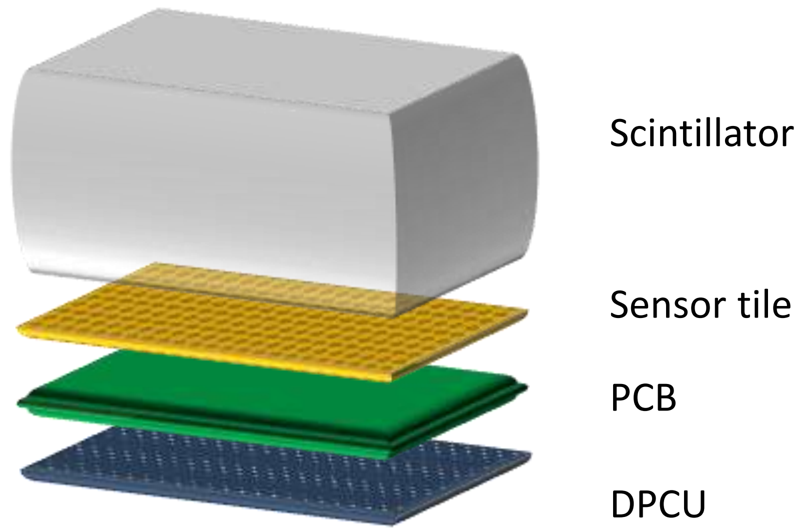
Single module time resolution
211/√2 = **149 ps FWHM**

Courtesy of the AXPET Collaboration

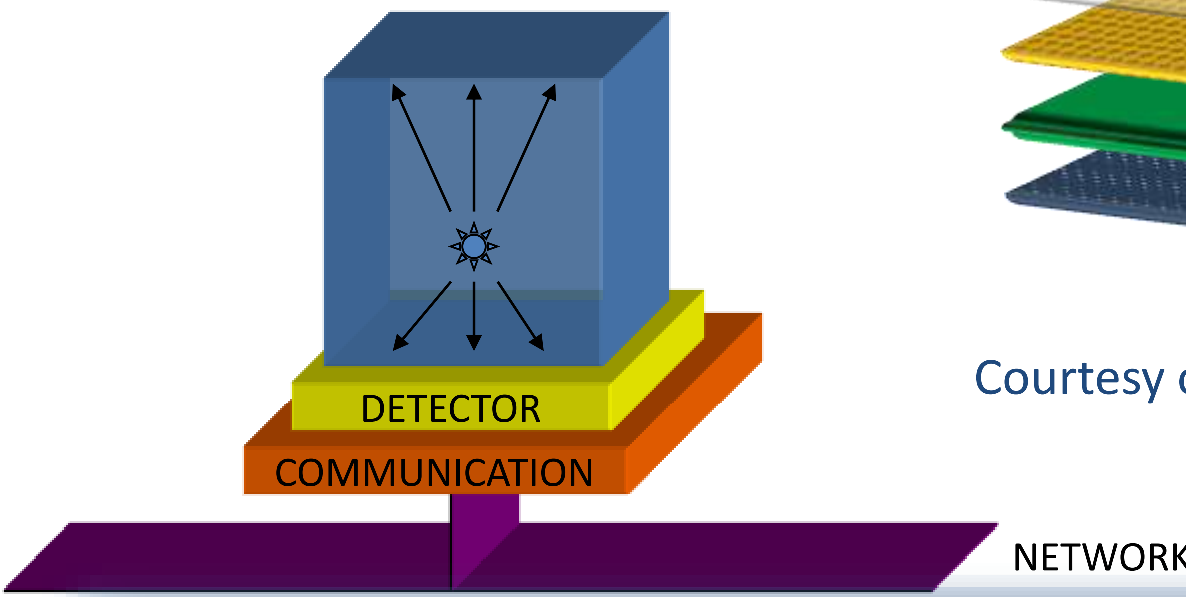
SPADnet: Deferred Coincidence

Photonic Module:

- Scintillator (LYSO)
- Sensor (SPAD)
- Network (Gbps)

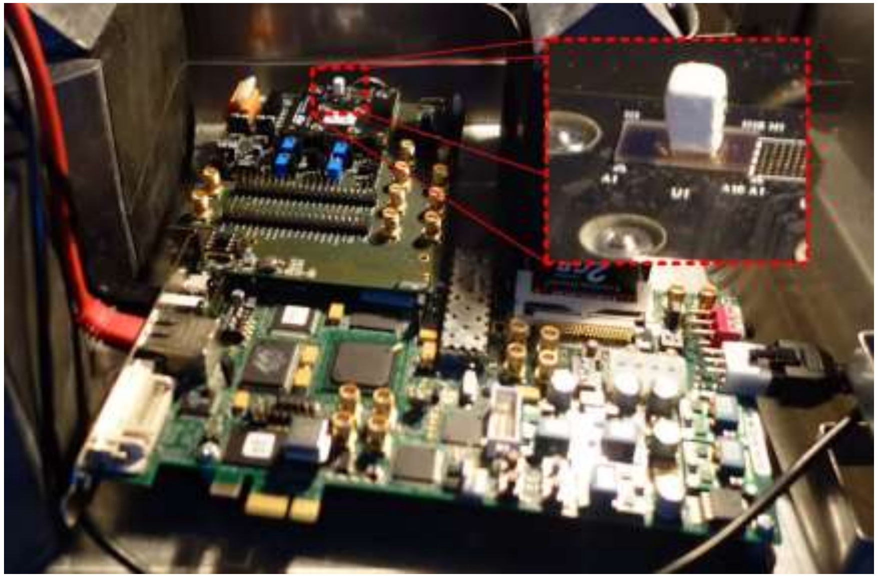


Courtesy of the SpadNET Collaboration



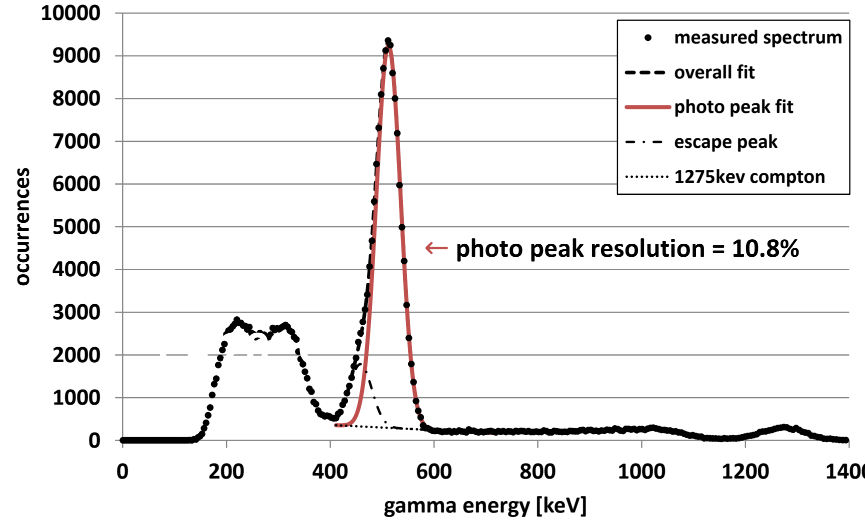
Digital, scalable, networked Photonic Module

SPADnet



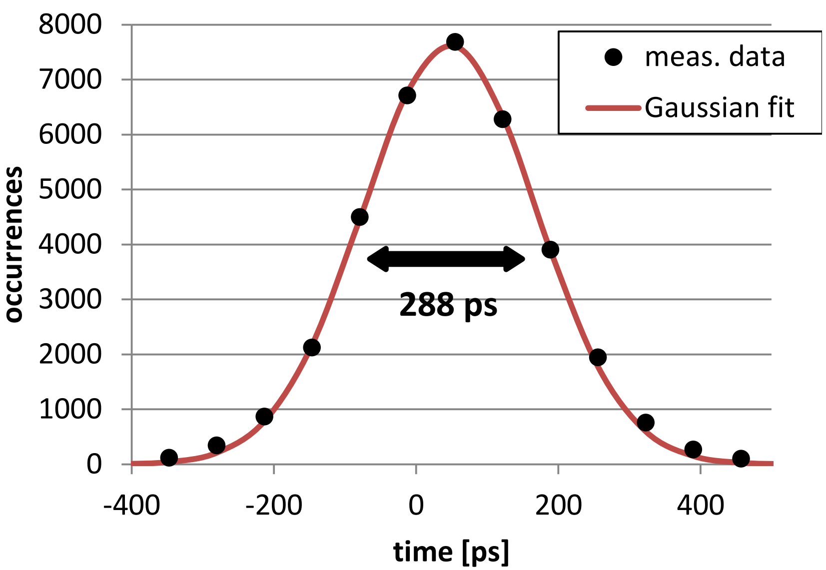
(^{22}Na, 370kBq)

Energy Spectrum



Braga *et al.*, ISSCC 2013

Coincidence Timing Resolution



Courtesy of the SpadNET Collaboration

Status of PET detectors

- (d)SiPM-based Magnetic compatible 4D detectors will soon be available
- PET 3D resolution will reach its intrinsic limit
- **TOF is the key to further improvements**
  - **But can we push it towards 10 ps (3mm)?**
- PET imaging will be a milestone for molecular imaging and personalized medicine

new PET detectors

TOF-PET: crucial

real “phase transition”:
time resolution ~ 10 - 20 ps

the challenge lies in the detector
rather than the electronics…

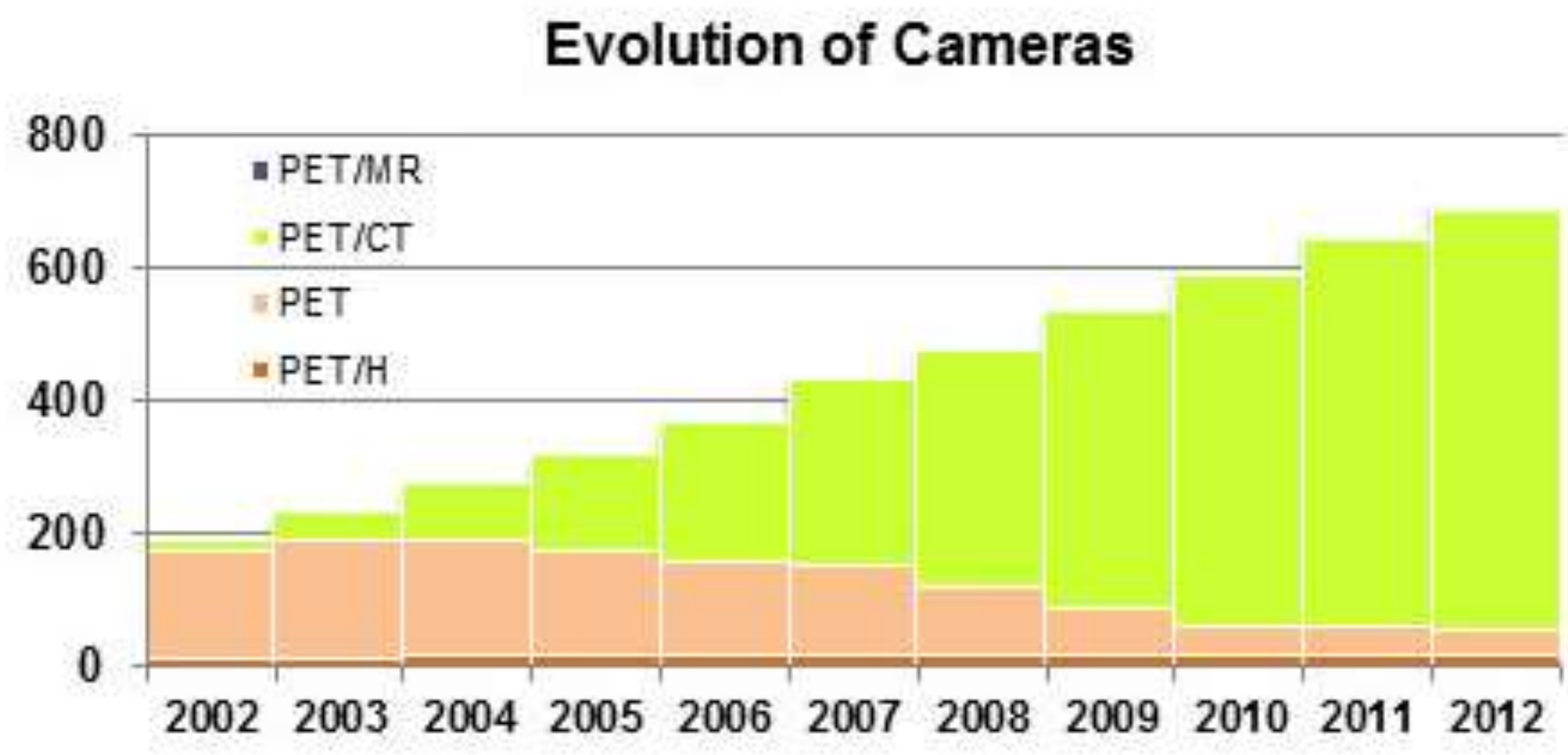
Any idea?

4

Hybrid Imaging

Hybrid Imaging

morphological + functional



Hybrid Imaging

- **PET/CT Hybrid Imaging**

  virtually available anywhere

  Clinical routine in cancer staging, therapy assessment

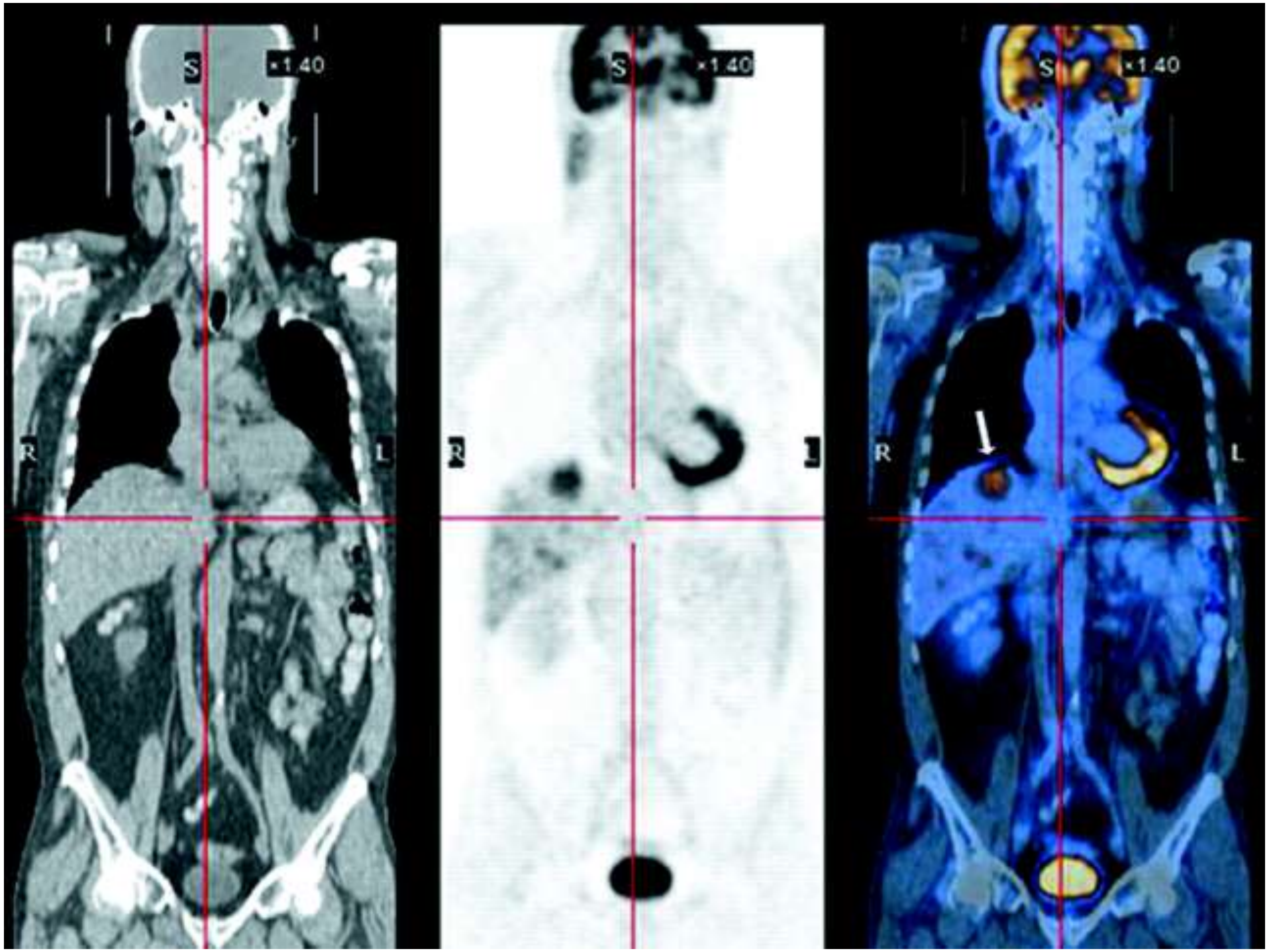
- **PET/MRI Hybrid Imaging**

  … on its way

- Excellent performance

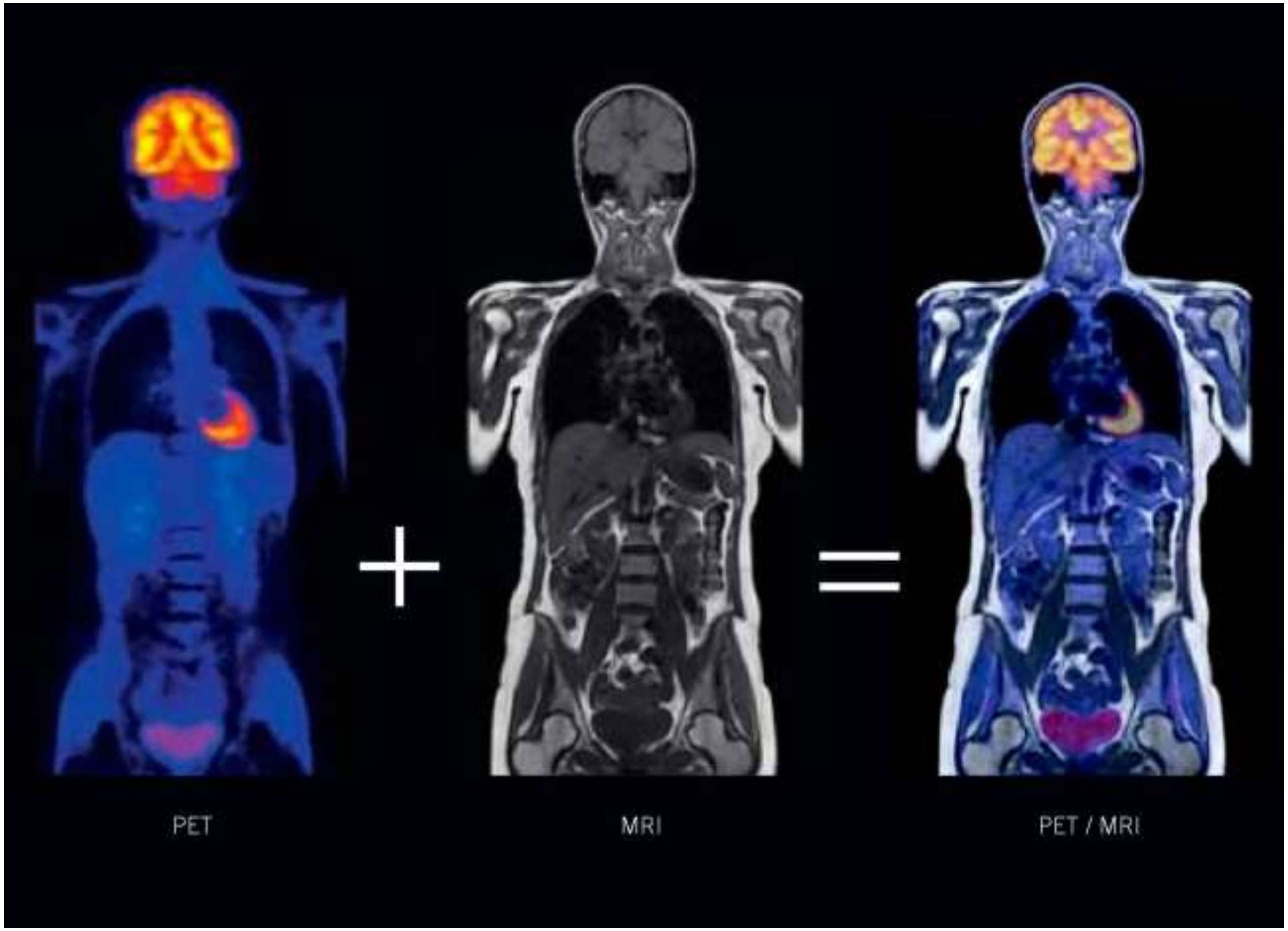
Hybrid Imaging

PET/CT: technological evolution, medical revolution



Hybrid Imaging

PET/MR: technological revolution, medical evolution



PET

MR

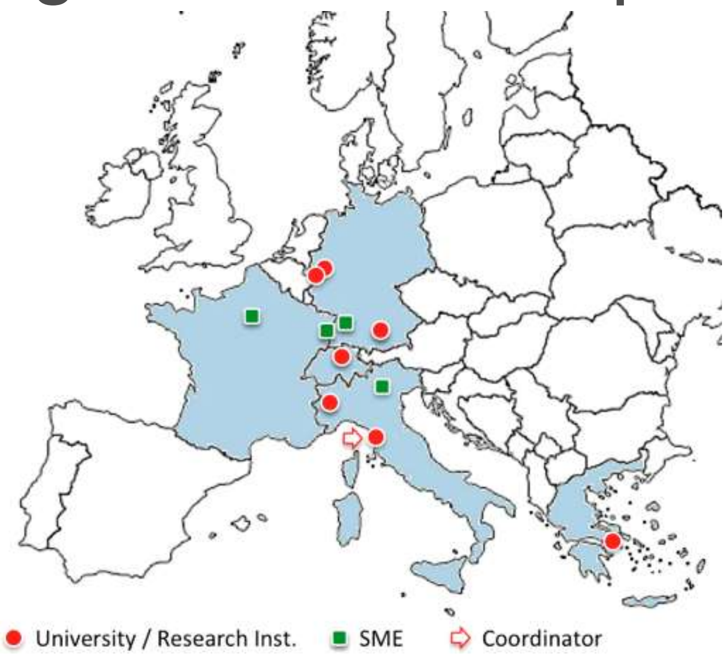
EEG

TRImage

"An optimised trimodality (**PET/MR/EEG**) imaging tool for schizophrenia"

11 Partners

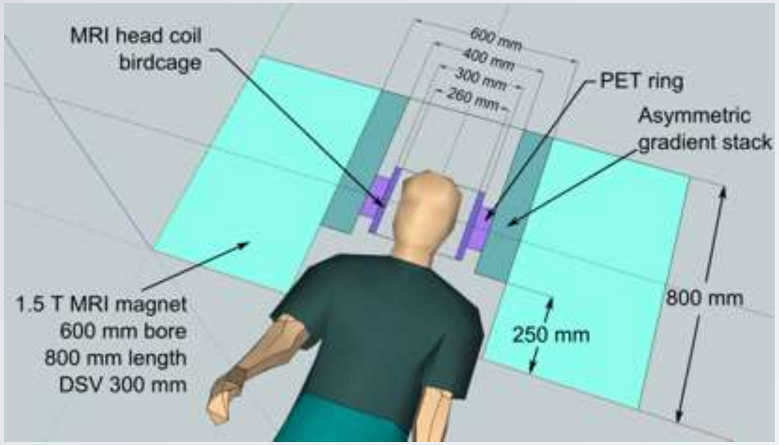
3 Italy
4 Germany
2 France
1 Greece
1 Switzerland

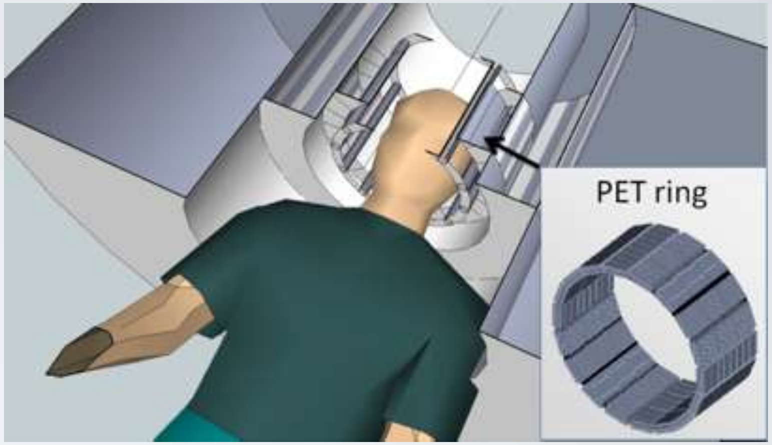


OBJECTIVES

- find new biomarkers and define a suitable multimodal paradigm that provides clinical evidence on the feasibility of advanced schizophrenia diagnosis
- construct and test an optimized cost-effective trimodality imaging instrument (brain PET/MR/EEG) for diagnosis, monitoring and follow-up of schizophrenia disorders.
- validate the trimodal imaging device with regard to the results and the clinical data obtained from objective 1

A closer LOOK at the TRIMAGE detector





Dimensional outline (left) and artistic view (right) of the dedicated brain PET/MR/EEG system (the EEG cap is not shown).

MR CRITICITY

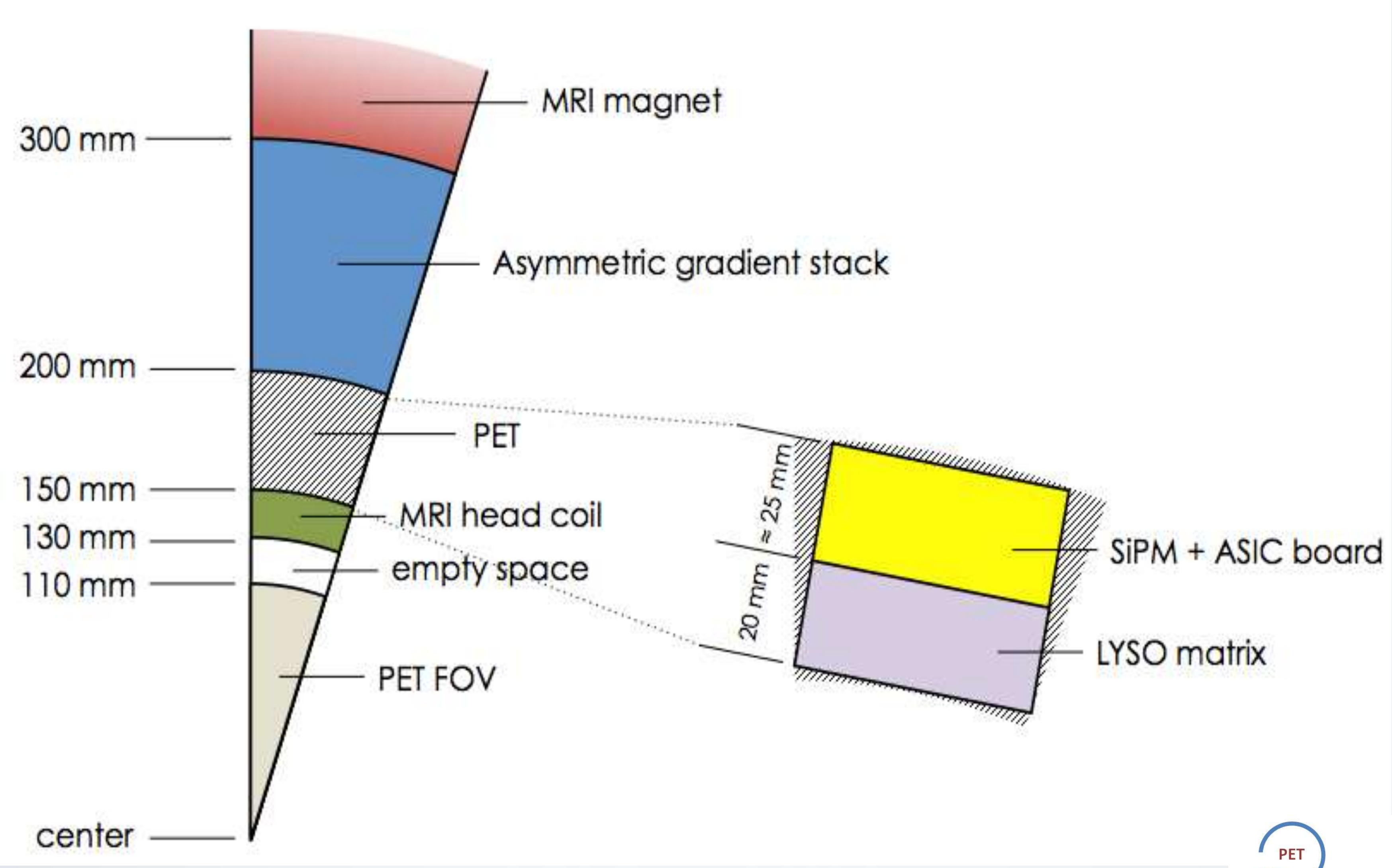
-800 mm bore
- Asymmetric gradient
- low field 1.5 T

PET CRITICITY

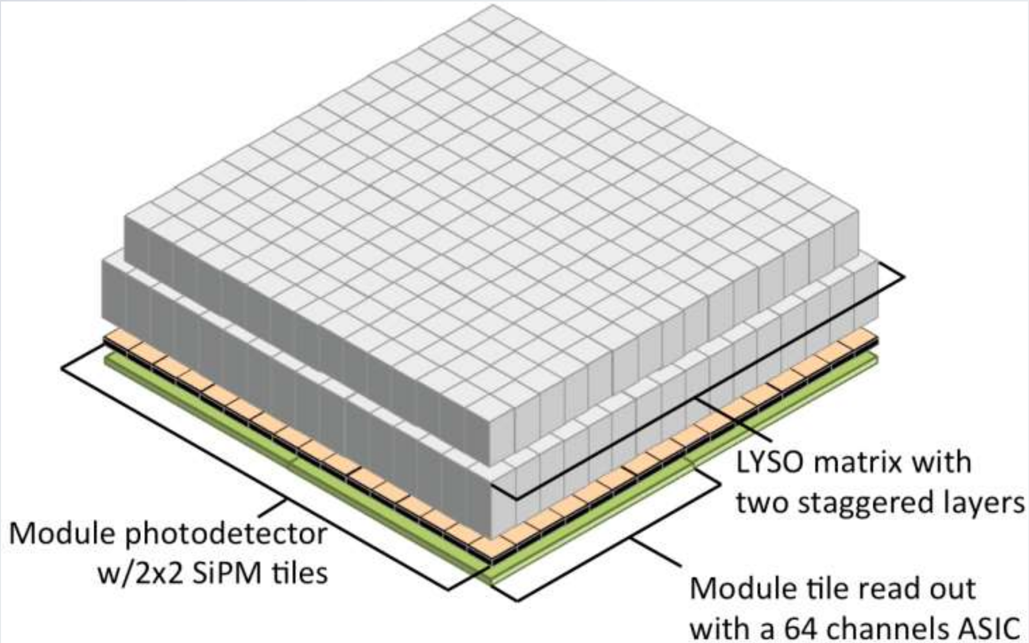
- sp res 2mm (DOI)
- high efficiency
- axial FOV

low-cost is important!!!

The TRIMAGE PET detector



The TRIMAGE PET detector



256 SiPMs

on an array of 2×2 tiles

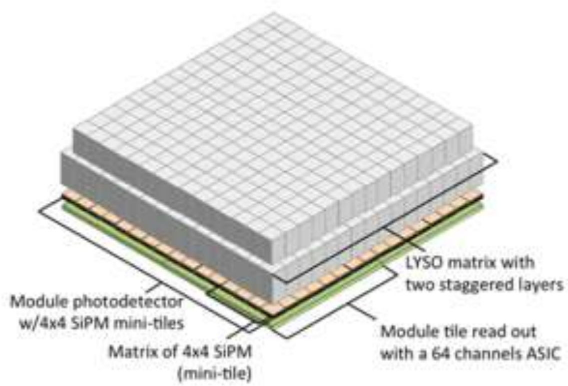
Tile: matrix of 8×8 SiPMs

SiPM size: 3 mm, pitch: 3.125 mm

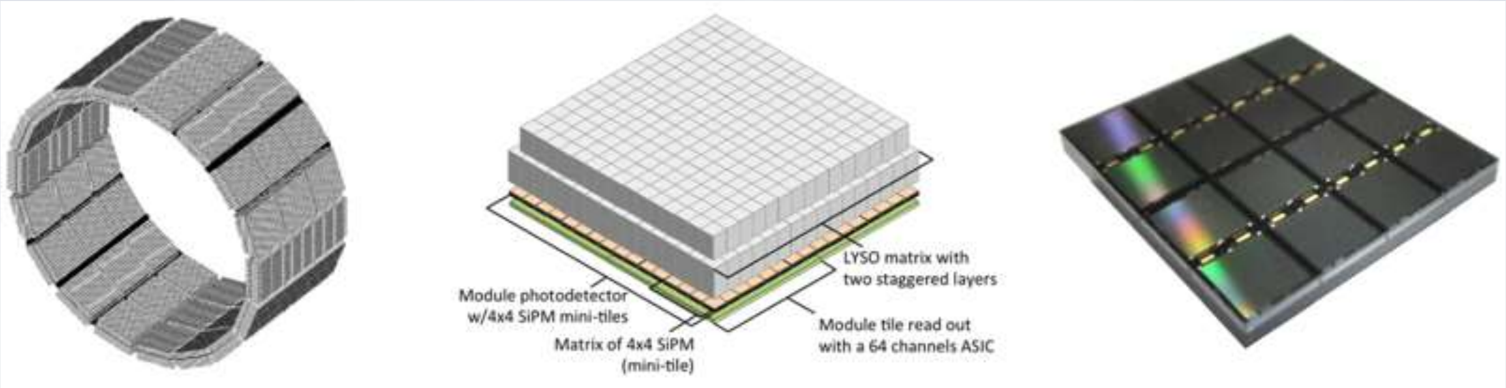
Total module area:

50 mm × 50 mm

18 modules x 3 rings



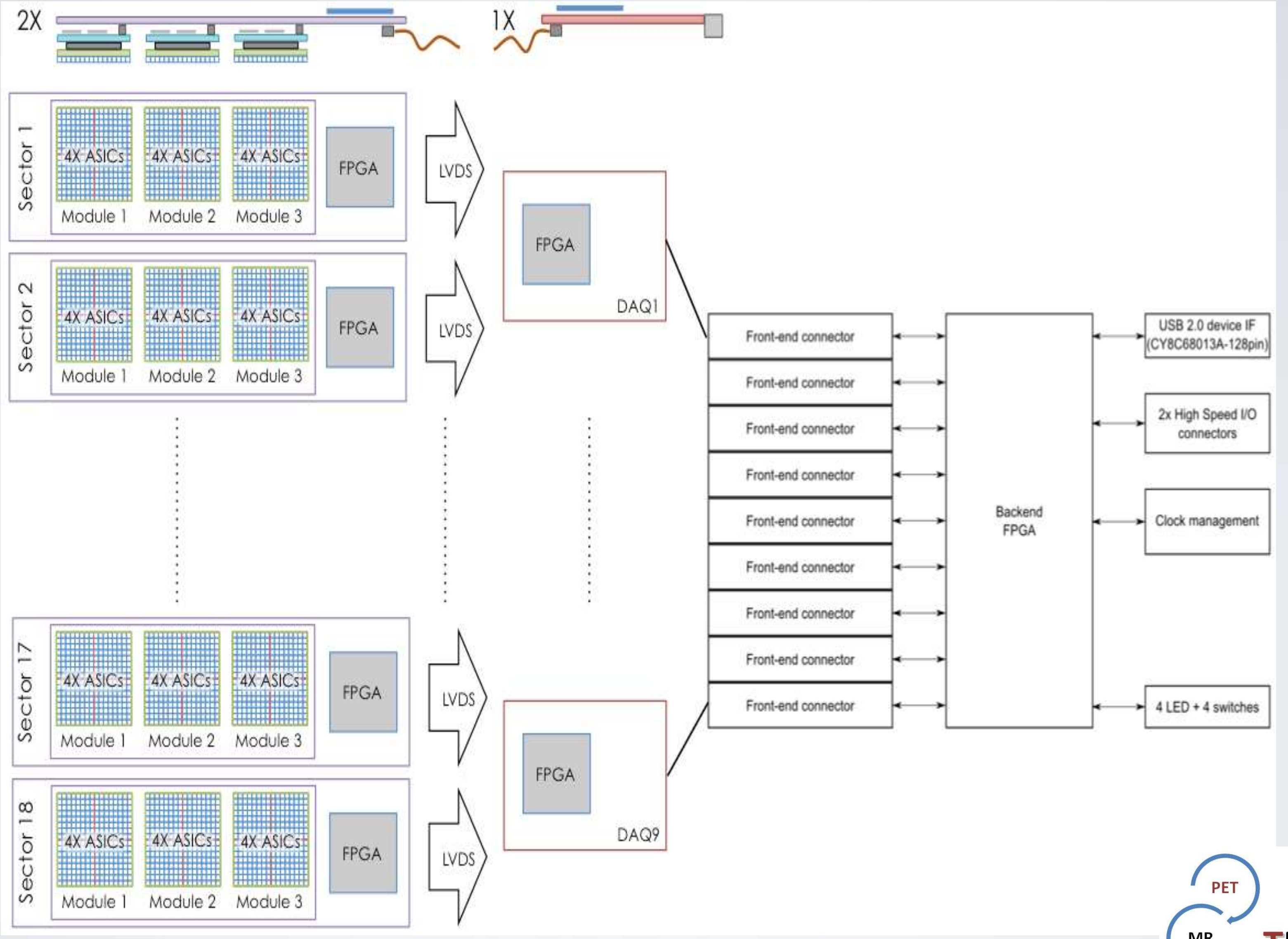
The TRIMAGE PET detector



Expected PET performance

18 modules x 3 rings
Axial field of view: 150mm
Transaxial field of view = 110 mm radius
Efficiency: 67% at the center (2 cm LYSO)
Spatial resolution: 2mm (FWHM)

The TRIMAGE PET detector



The TRIMAGE PET detector

The PET/MRI challenge

a standard PET system is expected to:

- Work well in a magnetic field
- **Heavily affect the MRI performance**

  (eddy currents)

The TRIMAGE PET detector

Custom magnetic compatible design must be developed:

- ASIC / connectors / boards / FPGA
- Mechanical structure (cooling!)
- MR shielding (copper, carbon fibre)

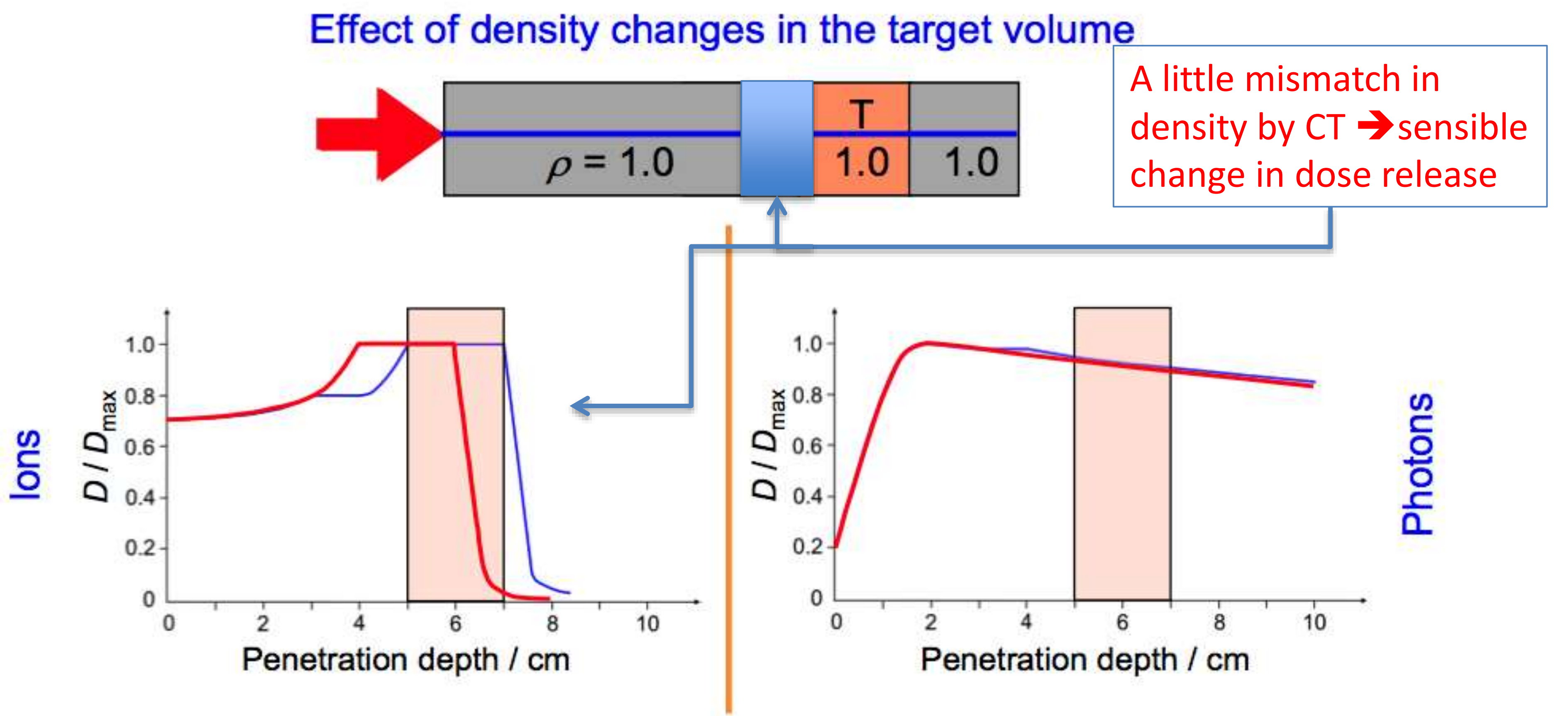
5

Range Monitoring in hadrontherapy

Range verification in HT

AAPM 2012: proton therapy to become mainstream?

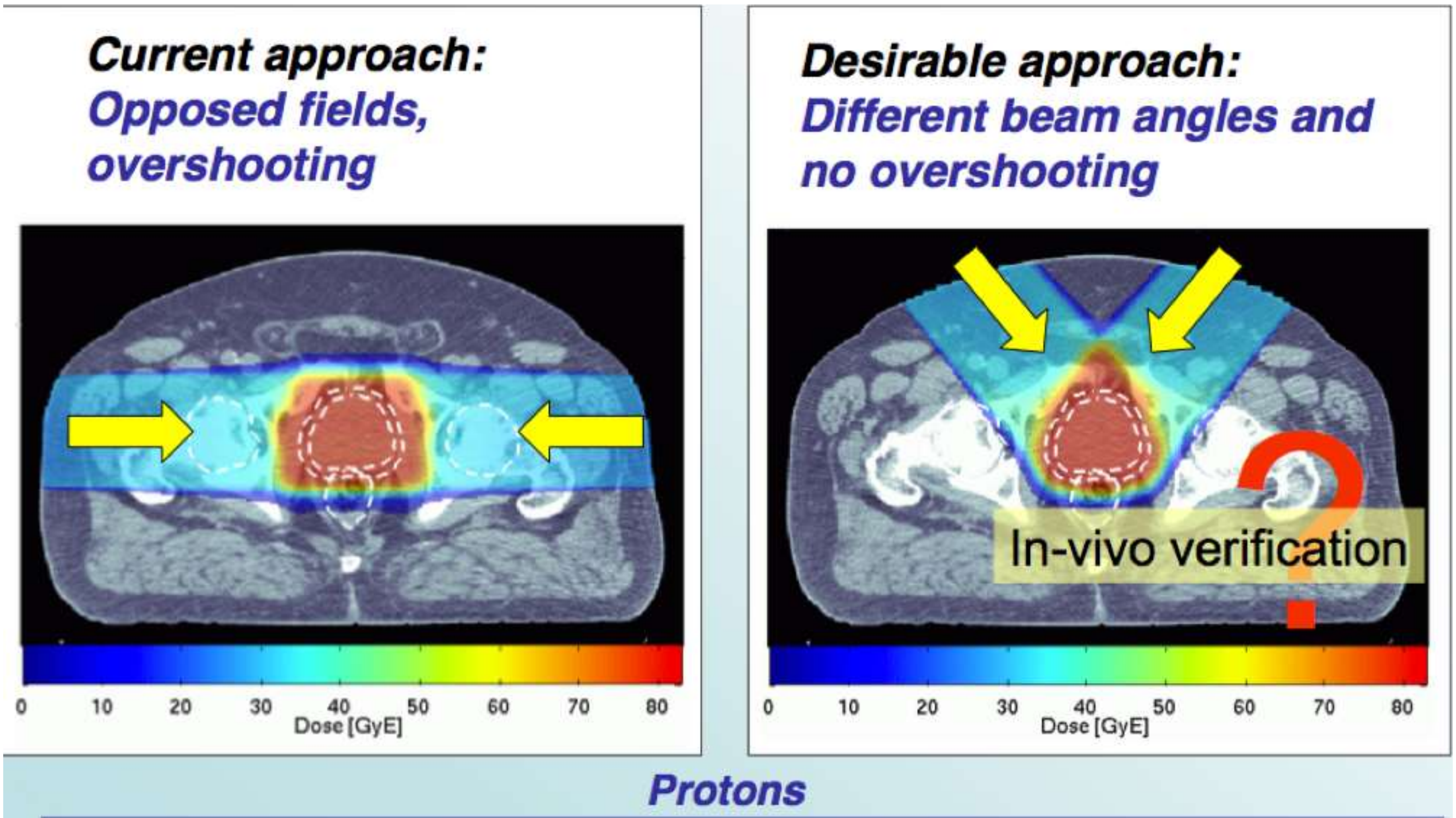
- 35 % unproven clinical advantage of lower integral dose
- **33 % range uncertainties**
- 19 % never become a mainstream treatment option



Particle Therapy: error sources

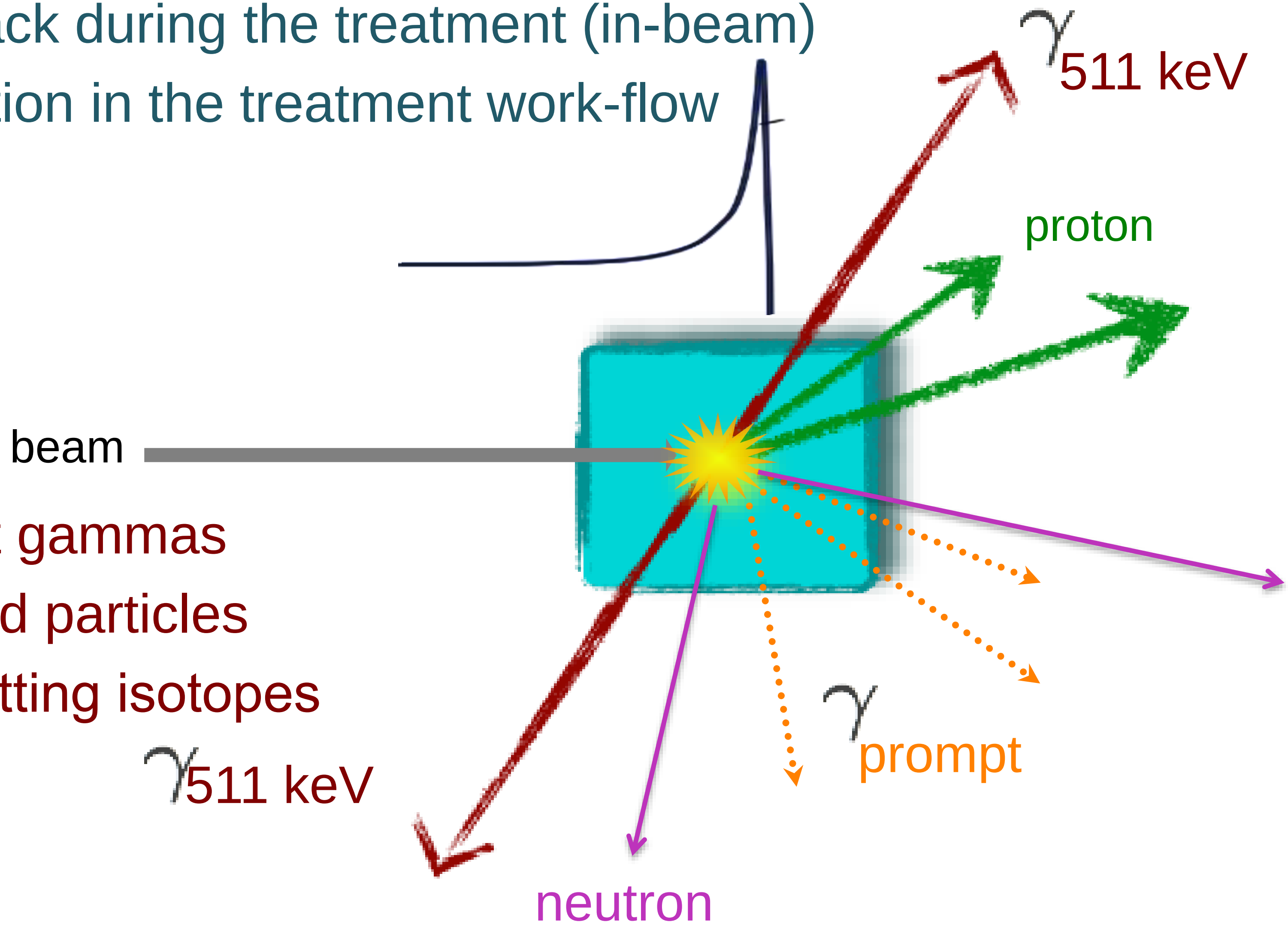
– Treatment Planning uncertainties

– Treatment delivery



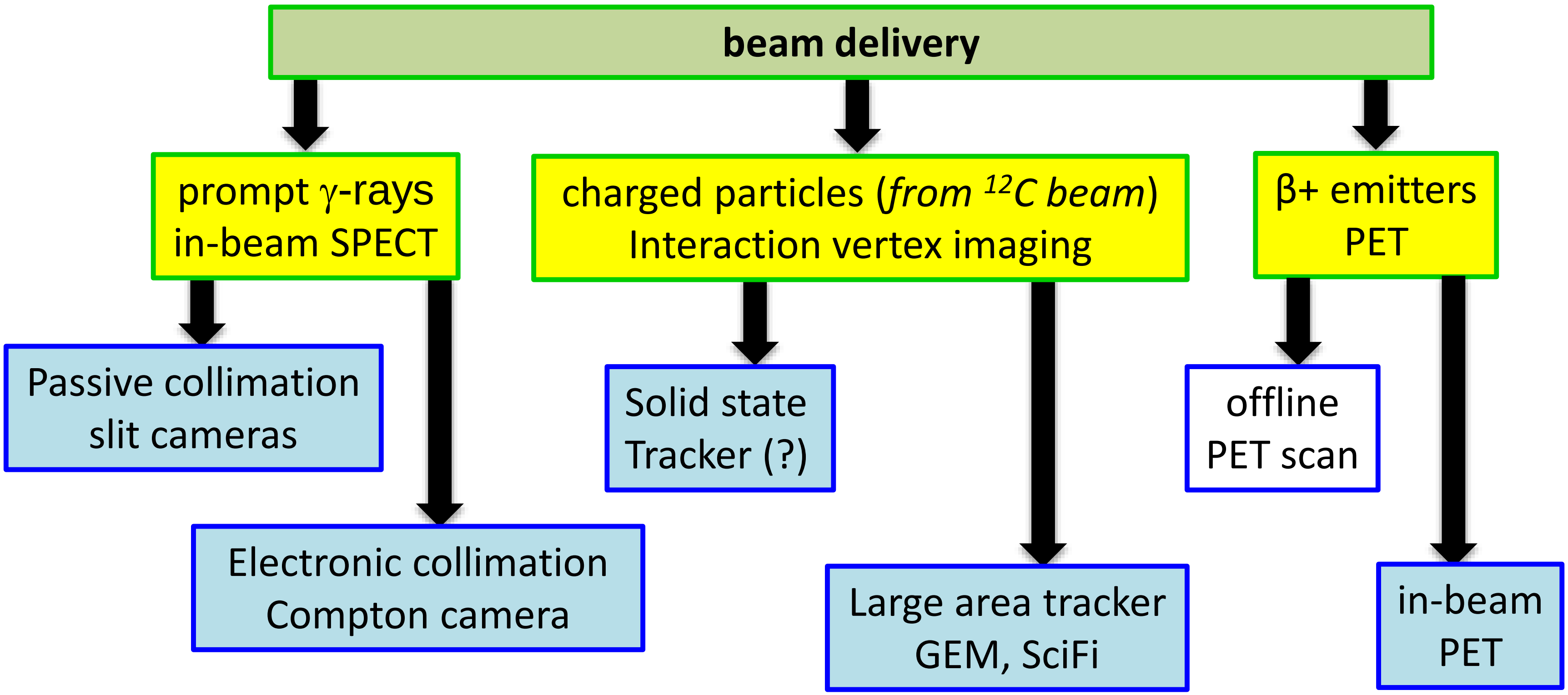
Secondary particles: a SIGNAL!

- check of dose release shape
- feed-back during the treatment (in-beam)
- integration in the treatment work-flow



- prompt gammas
- charged particles
- β+ emitting isotopes

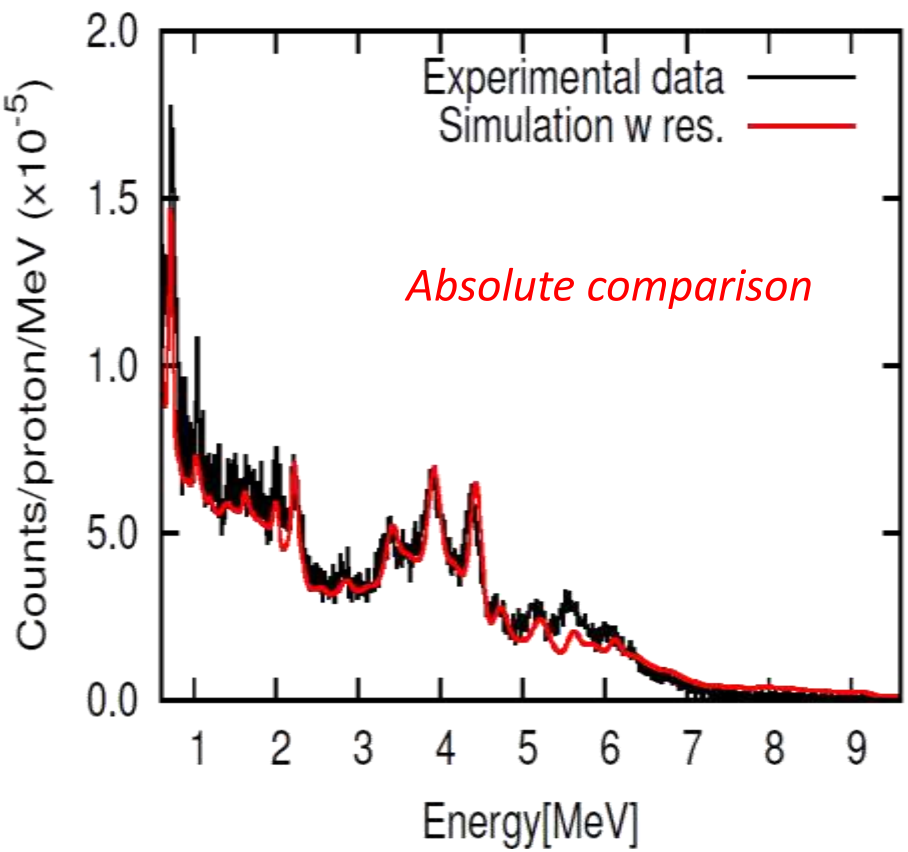
Secondary particles: a SIGNAL!

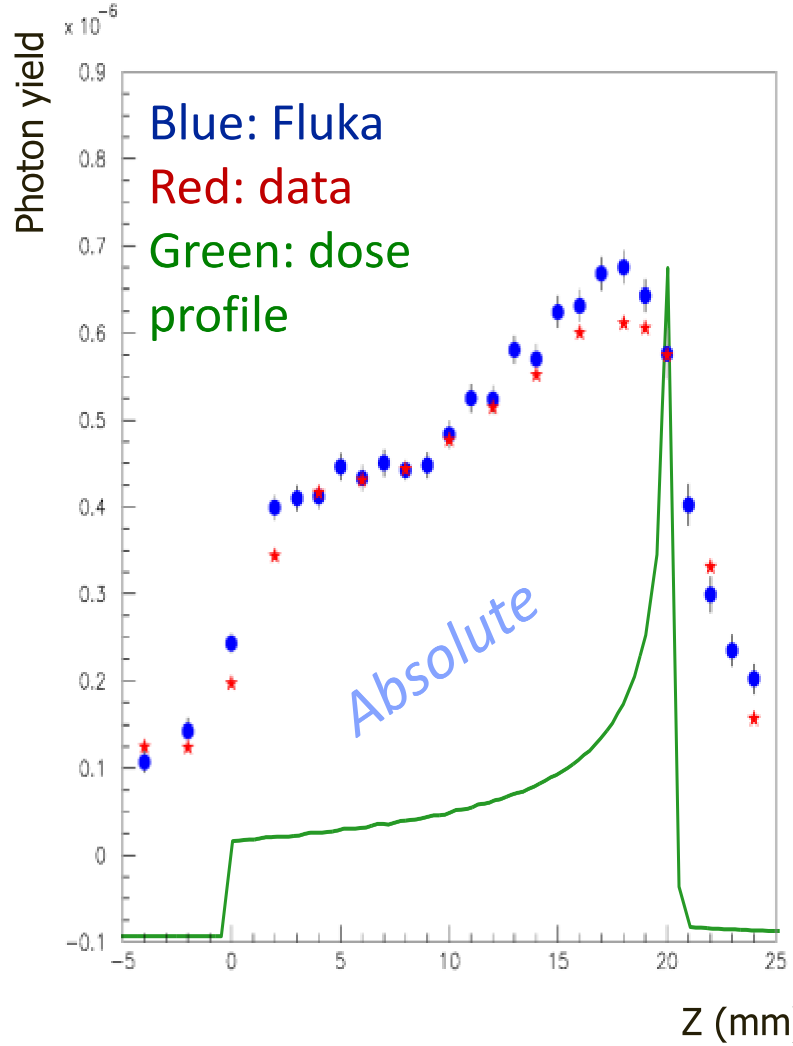


Prompt photons

160 MeV proton beam
Energy spectrum of prompt “photons”
(J.Smeets et al., IBA)

Courtesy
Alfredo Ferrari

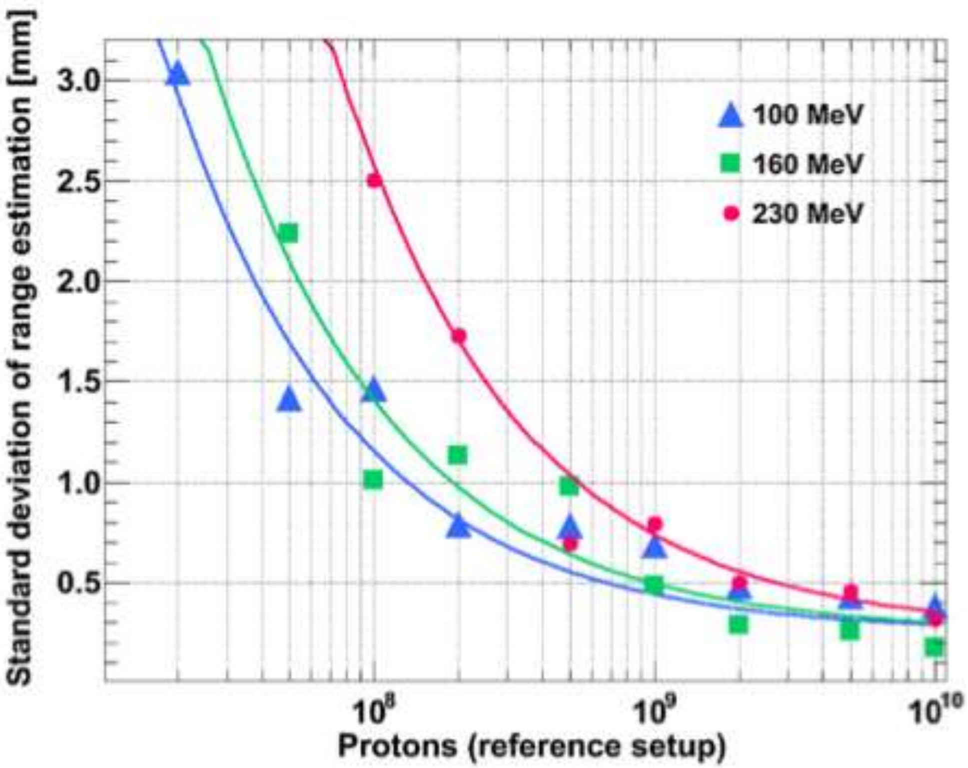


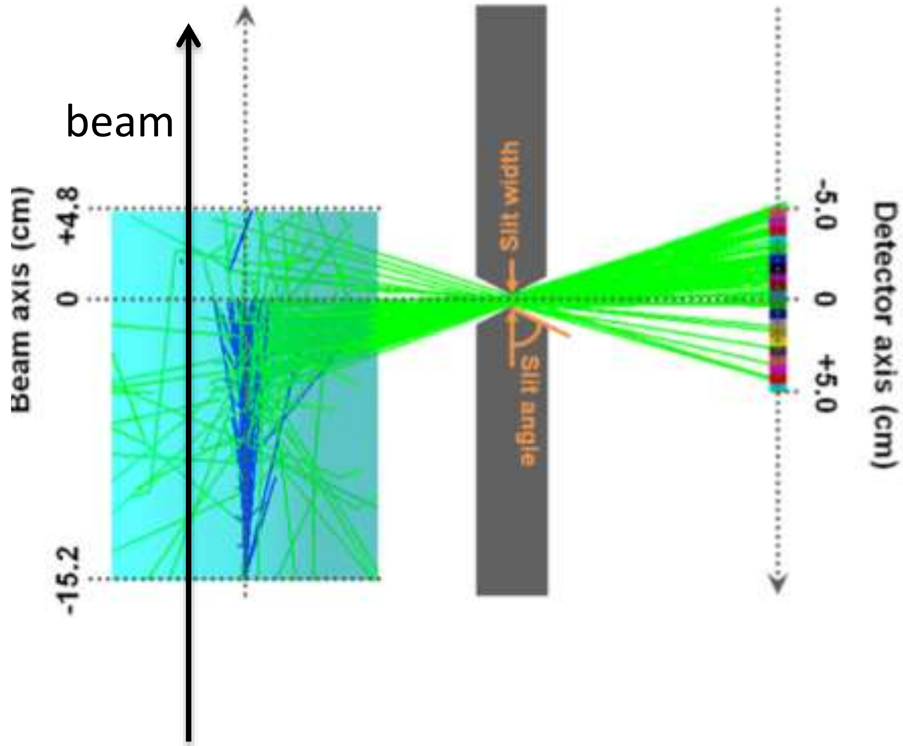


The energy spectrum is in the 1-10 MeV range

Prompt photons: slit camera by IBA

- Simple geometrical concept
- Optimized for range measurement on proton beam

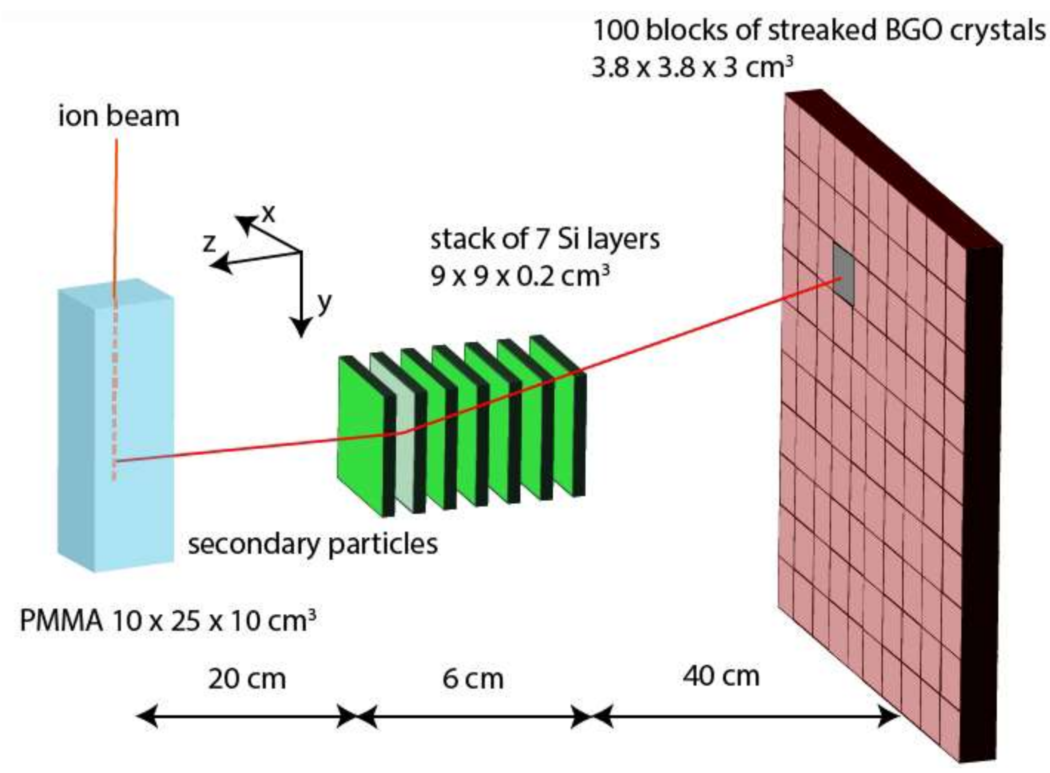


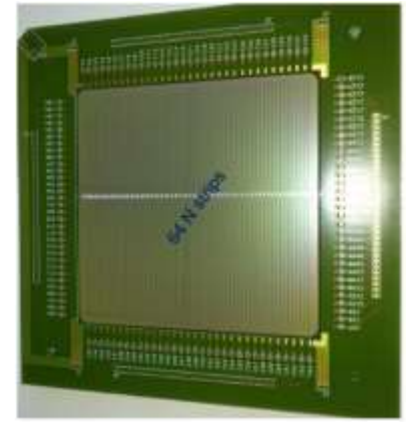


J Smeets et al. Phys. Med. Biol. **57** (2012) 3371

Prompt photons: Compton camera

$$\cos\varphi = 1 - m_0 c^2 \left(\frac{1}{E_{\gamma'}} - \frac{1}{E_\gamma} \right)$$





CNRS,
UCB Lyon

Absorber: Scintillator

- BGO 35 × 38 × 30 mm^3
- 4 PMT

Scatterer: double-sided Si strip detectors

- Large size detector bonded on PCB
- Dedicated
  low-noise ASIC

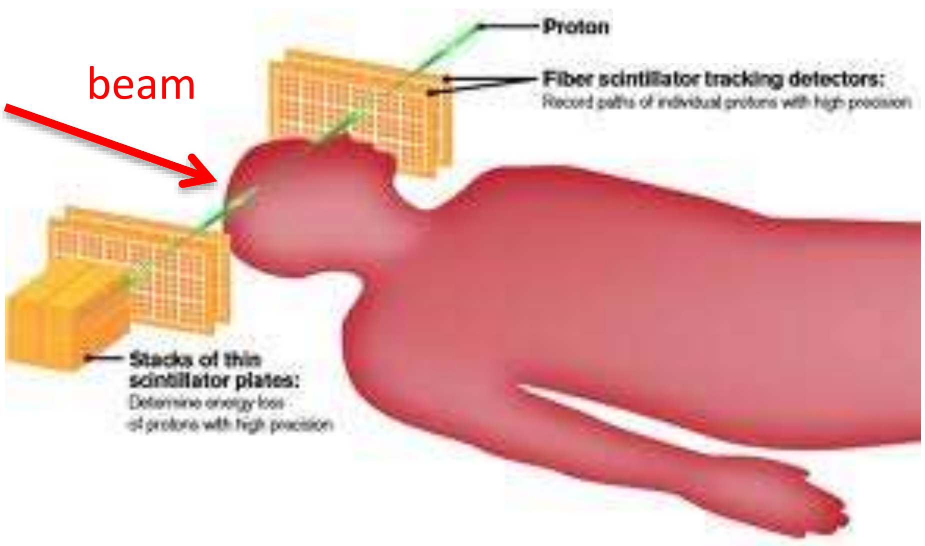
ENVISION

Charged particles

- detection efficiency ~ 100%
- easily back-tracked to the emission point
  - correlation to the beam profile as for β^+ activity

but…

- Low emission rate
- Escape energy threshold ~ 50-100 MeV
- multiple scattering inside the patient -> 6-8 mm on single track back-pointing resolution

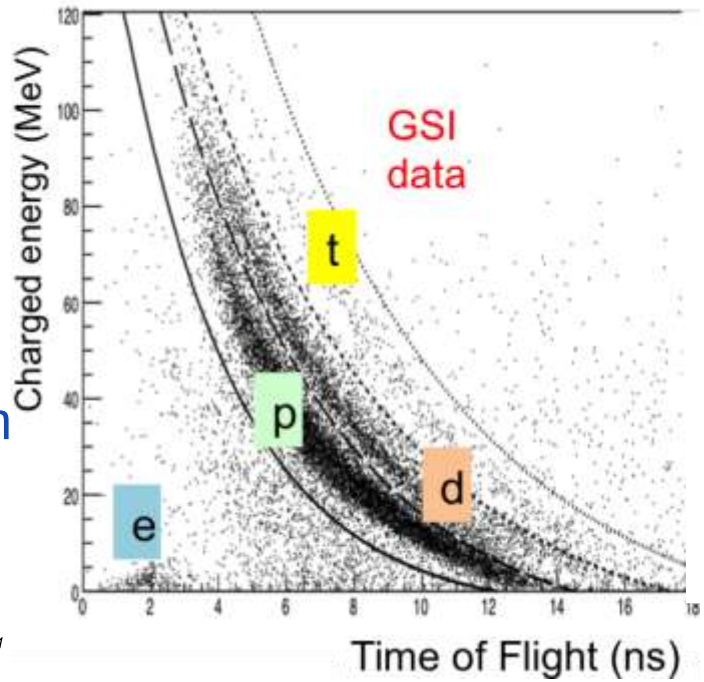


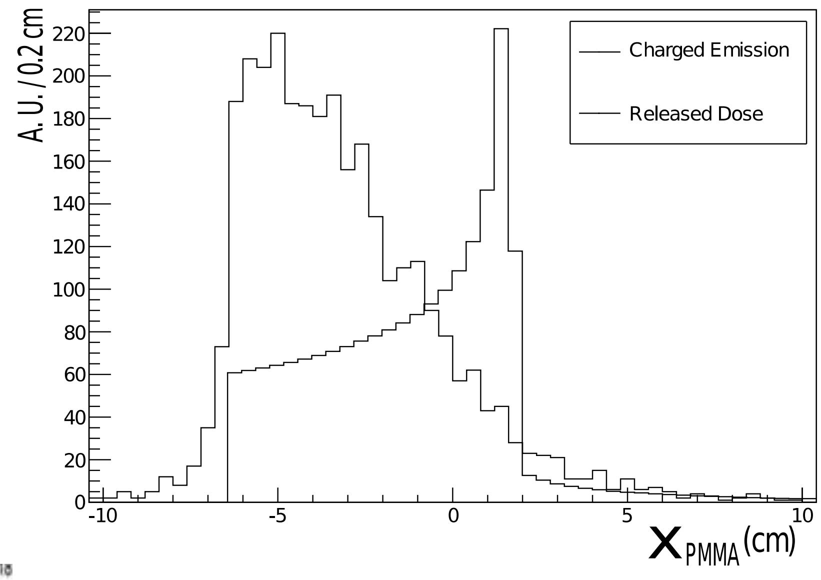
~ 10^3 events required to achieve desired accuracy on the emission point distribution: detector size matters!

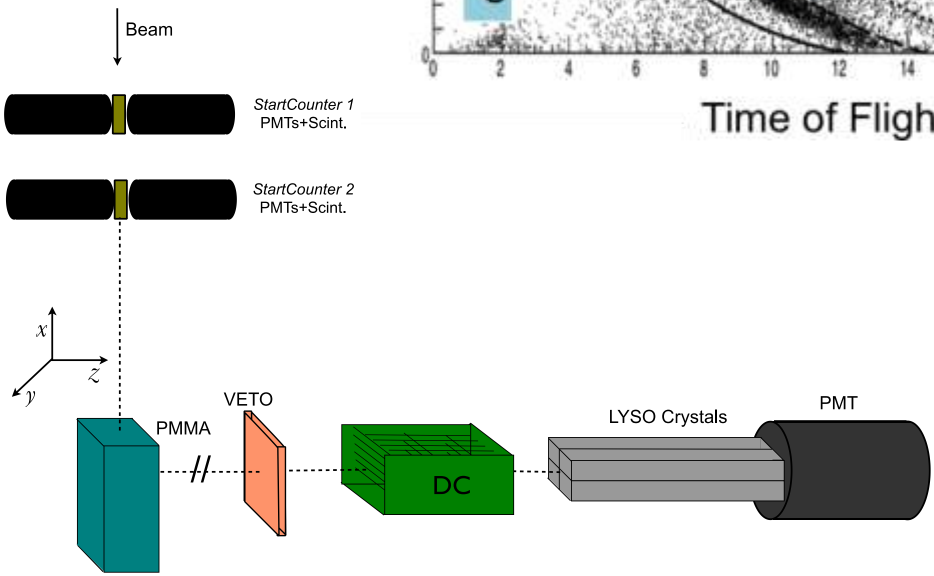
Charged particles

L.Piersanti et al. PMB **59** (2014) 1857

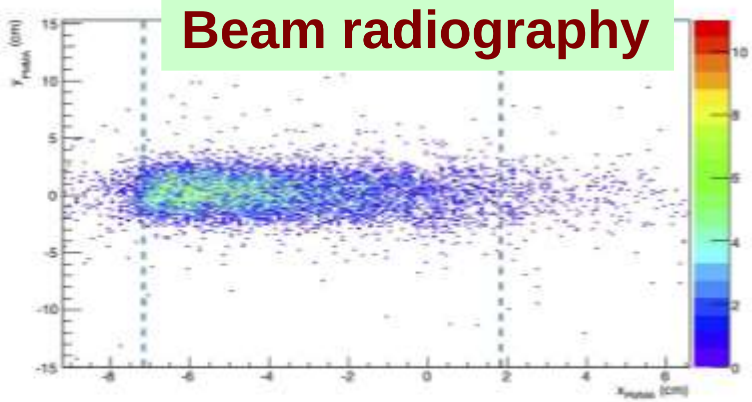
Charged secondaries produced at 90^0 wrt the beam from PMMA target on 220 AMeV ^{12}C beam at GSI





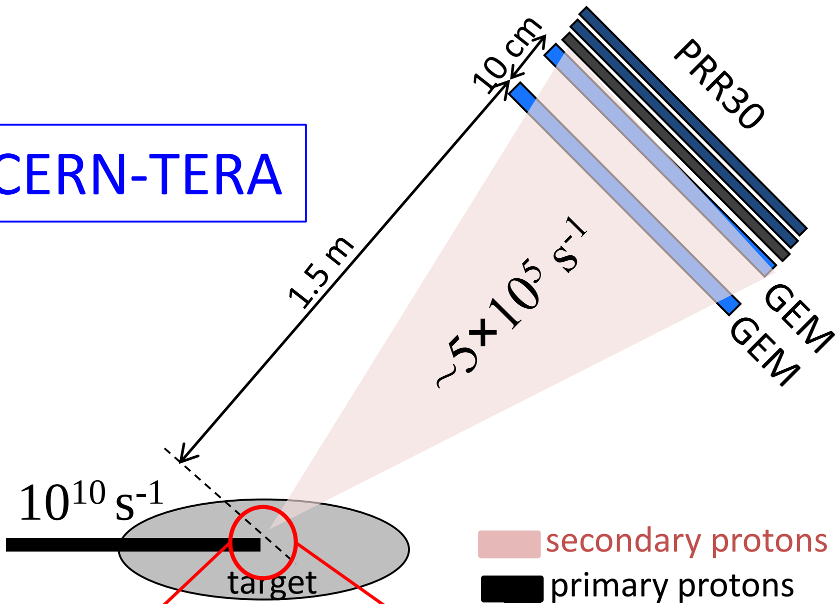


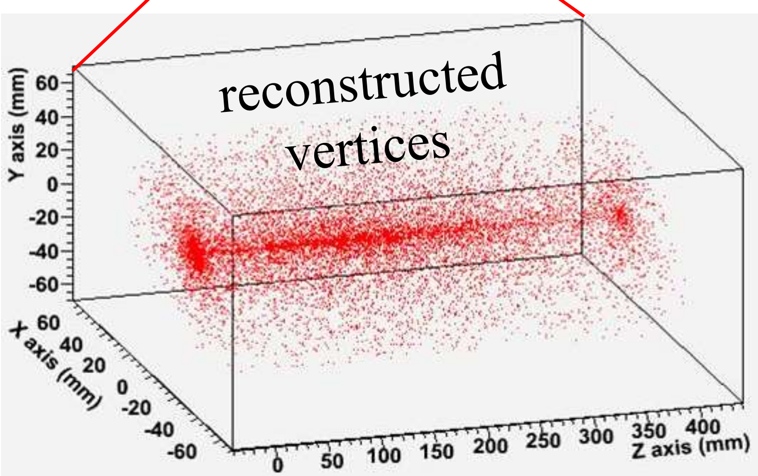
Beam radiography



Charged particles: GEM tracker

CERN-TERA





- Large area gas (!) detector
- Acceptable solid angle even far away from the patient
- No need for TOF

Expected performance

$\sigma_{\text{GEM-spatial}} \cong 400\mu m$

$\sigma_{\theta} \cong 6mrad$ Angular resolution

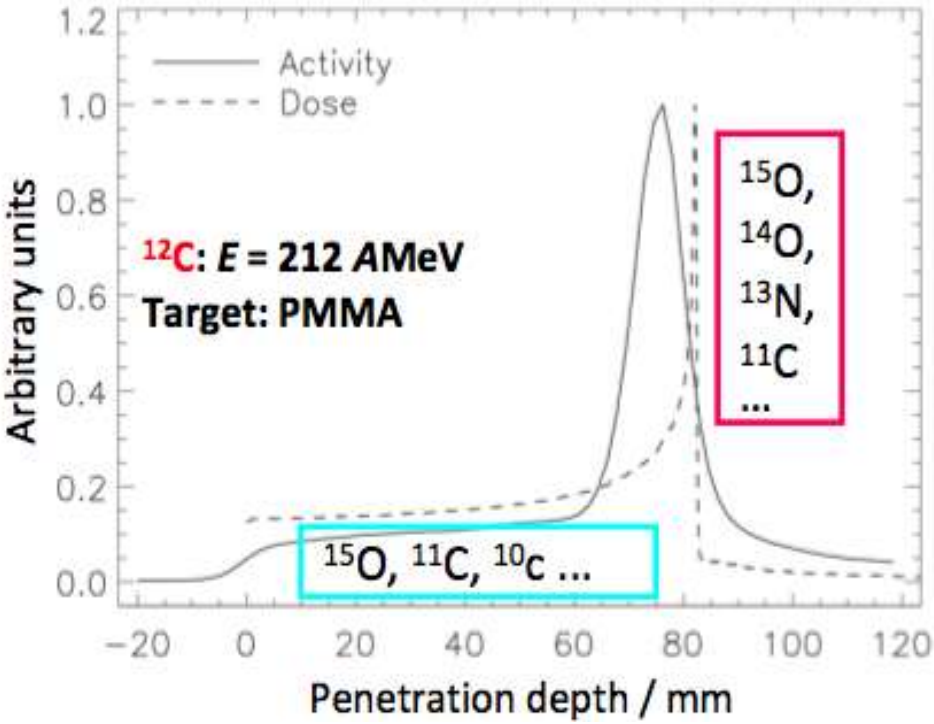
Ω~0.3% (0.04 sr) Solid angle

Courtesy of TERA- Foundation

β^+ activity and dose: correlation

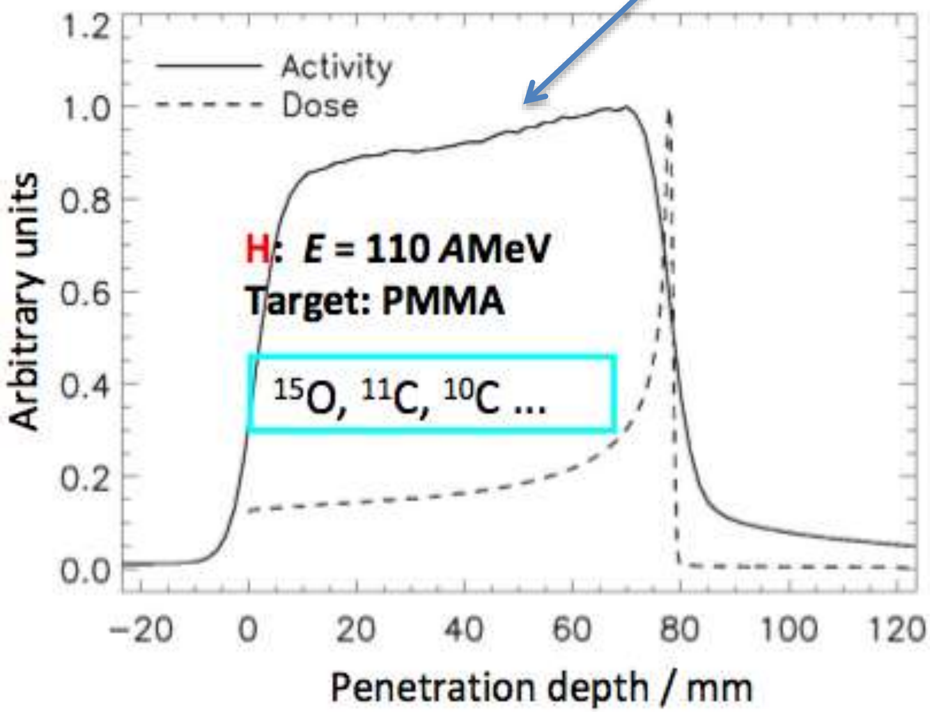
Therapy beam	^{1}H	^{3}He	^{7}Li	^{12}C	^{16}O	Nuclear medicine
Activity density / Bq cm^{-3} Gy^{-1}	6600	5300	3060	1600	1030	$10^4 - 10^5$ Bq cm^{-3}

Projectiles & target fragmentation

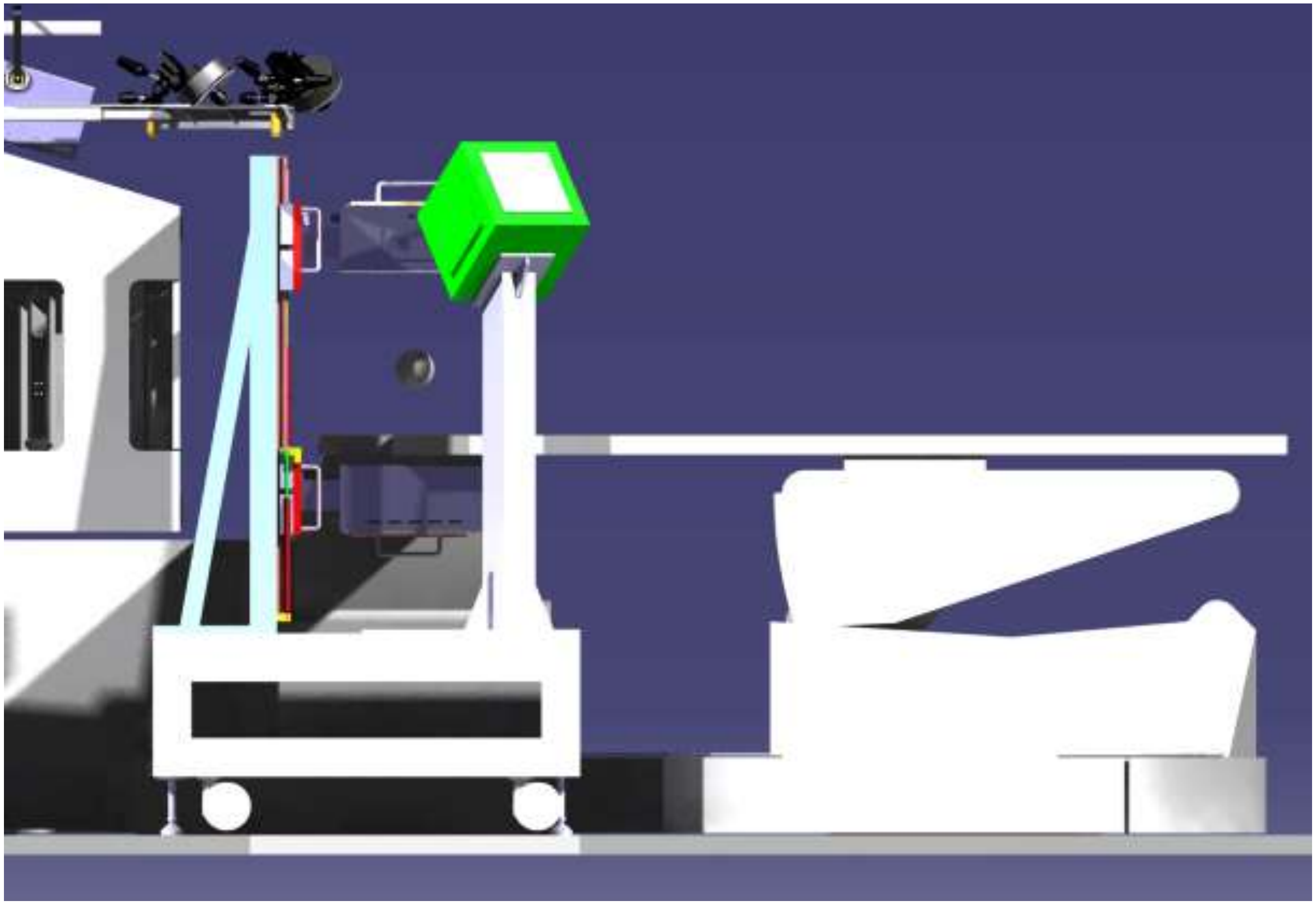


Target fragmentation

measured



Charged particles & in-beam PET



INSIDE

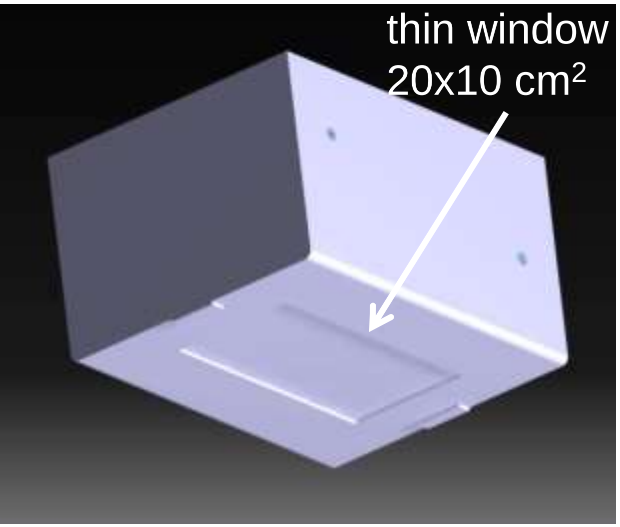
in-beam, multimodal dose profiler for hadron-therapy at CNAO

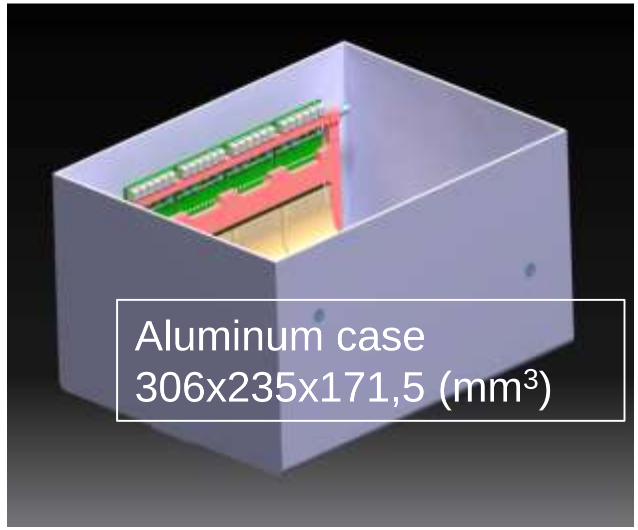
detection of:

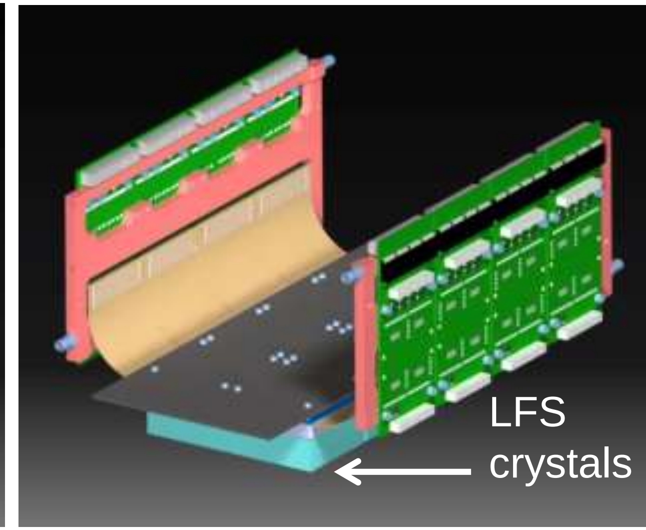
- **β+ decaying isotopes (PET)**
- **charged secondaries & (?) prompt photons (Tracker)**

the PET detector

^{15}O, ^{11}C

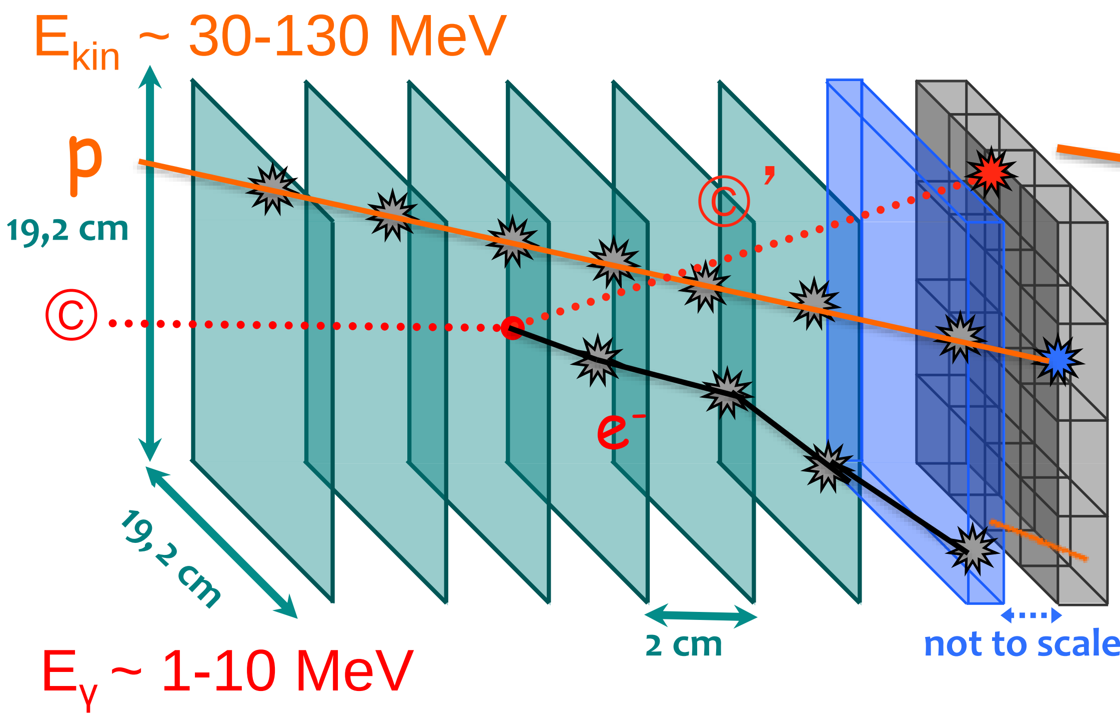




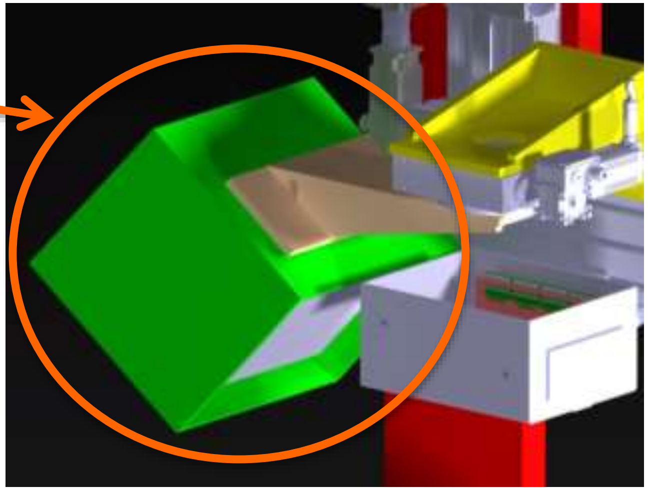


- 2 planar panels 10 cm x 20 cm^2 , each made by 2 x 4 detection modules
- Each module is composed of a 16 x 16 pixelated LYSO (or LFS) scintillator matrix (3x3 mm^2 crystals, 3.1 mm pitch, for a total sensitive area of 5x5 cm^2) coupled to a SiPM array

the Tracker



prompt γ, p

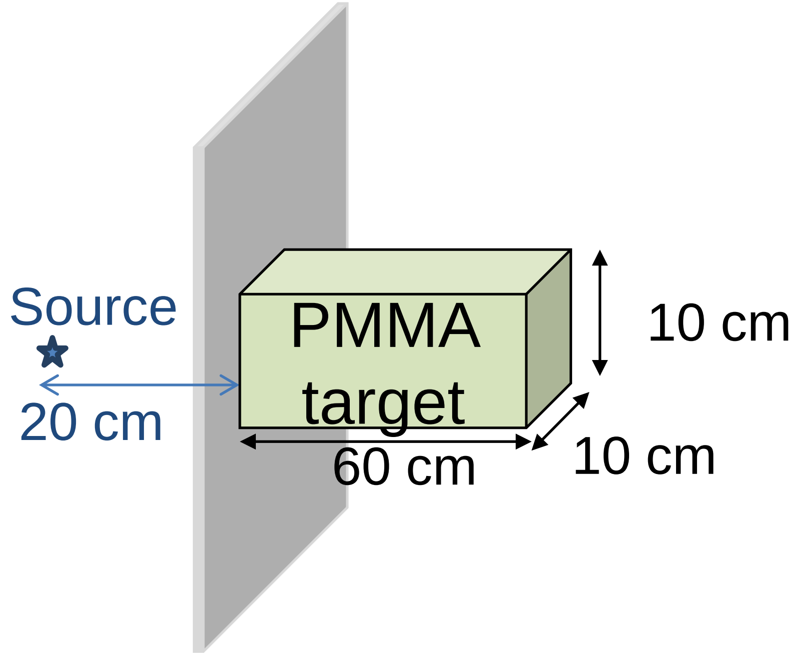


- 6 XY planes, with 2 cm spacing, made of 2 stereo layers of 192 0.5x0.5 mm^2 square scintillating fibers, read out by Hamamatsu 1mm^2 SiPM : S12571-050P
- 1 pad with 4x4 LYSO pixelated crystals (50 x 50 x 16 mm^3), with 1.5 cm thick Plastic absorber in front to screen electrons, read out by 64 ch Hamamatsu MultiAnode

Simulations

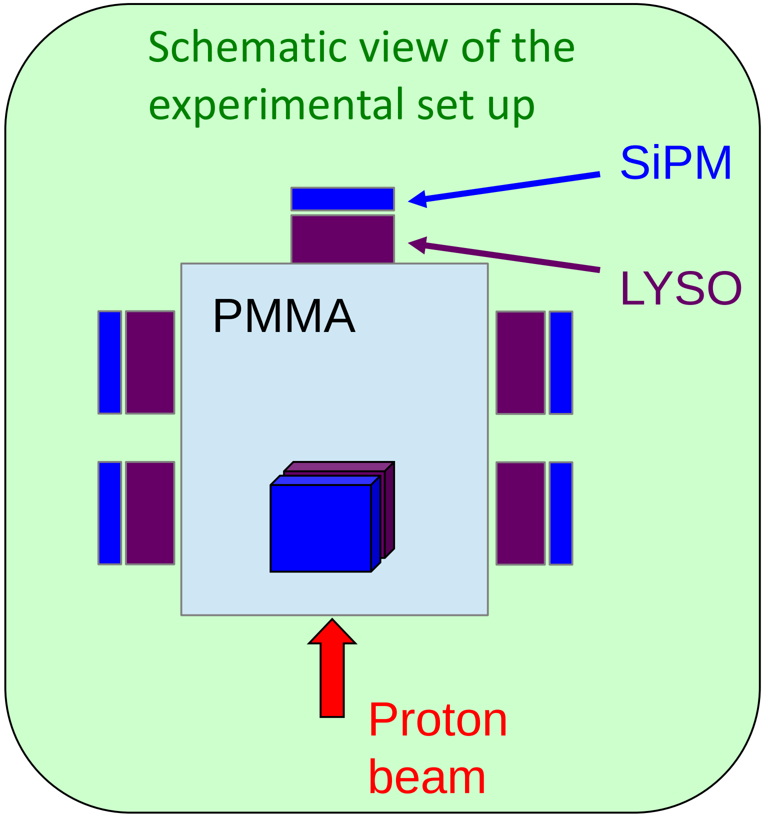
- based on FLUKA + ROOT
  - Detailed detector description
  - Signal generation and reconstruction with readout features
  - Geometry and material description (electronic board, mechanical structures)
- extensively used for the detector design optimization
- **now being exploited for further optimization and beam test validation**
- will be used on INFN-cloud computing facilities to provide input to optimize the reconstruction and analysis

Primaries: 10^8 protons
Energy: 134 MeV
Time: **2 ms beam on**, 300 s beam off
Rate: $5*10^{10}$ pps, scaled down to $5*10^9$ pps



Test of PET system "prototype"

- **Beam**
  - **Energy: 95 Mev**
  - **Intensity2*10^9 p/s**
- **Detectors**
  - **LYSO crystal 3 x 3 x 10 mm^3**
  - **RGB SiPM from AdvanSid 3x3 mm^2**
  - **Front-end ASIC: TOFPET - LIP Lisbon/INFN Torino**
  - **64 input channels, 100 kHz/chn**
  - **Dyn range 200 pC**
  - **SNR 20 dB**
  - **Time resolution 500ps FWHM**
  - **Power consumption 10 mW/chn**

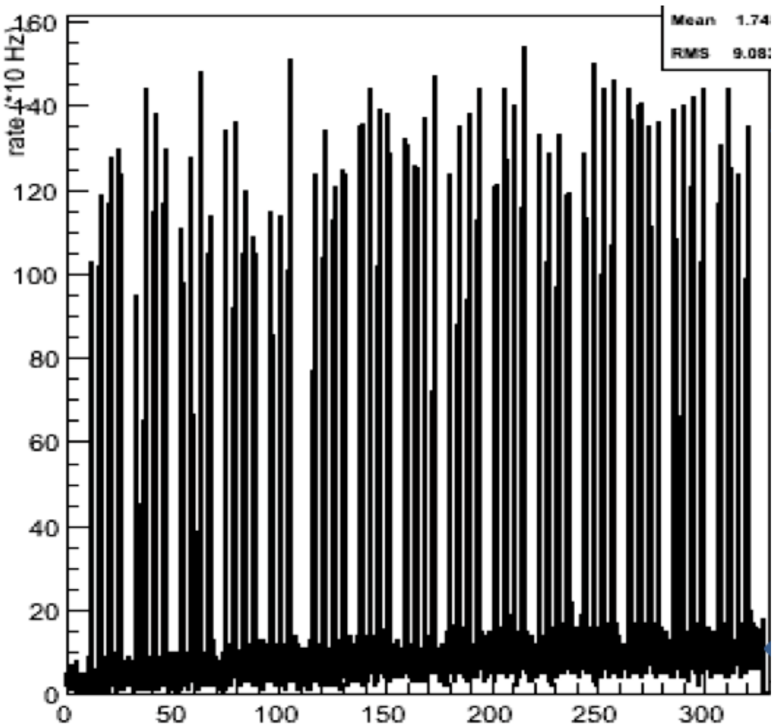


PMMA phantom

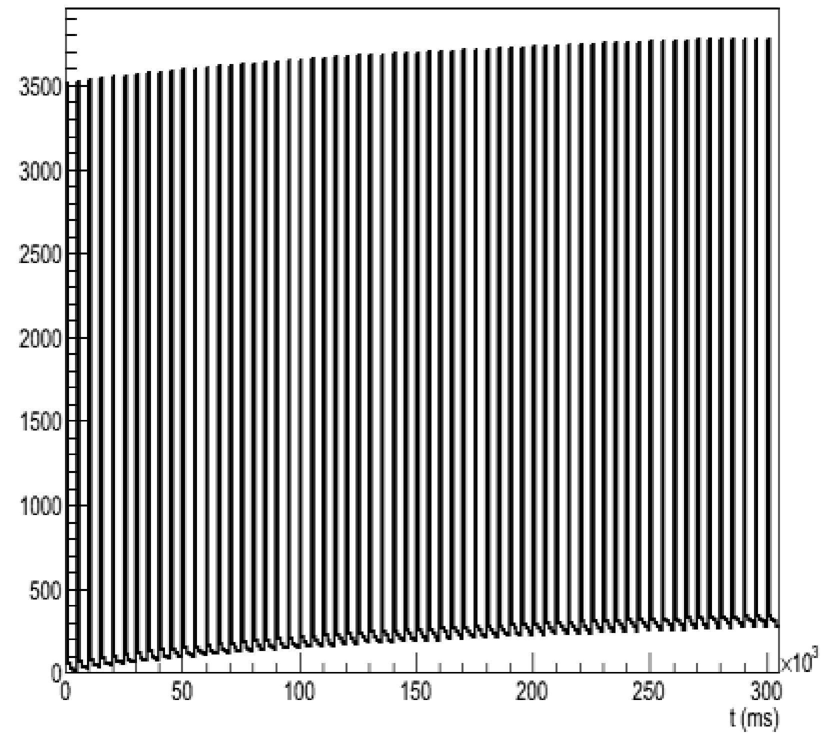
(5 x 5 x 7 cm^3)

PET Single Trigger Rate

Raw Data



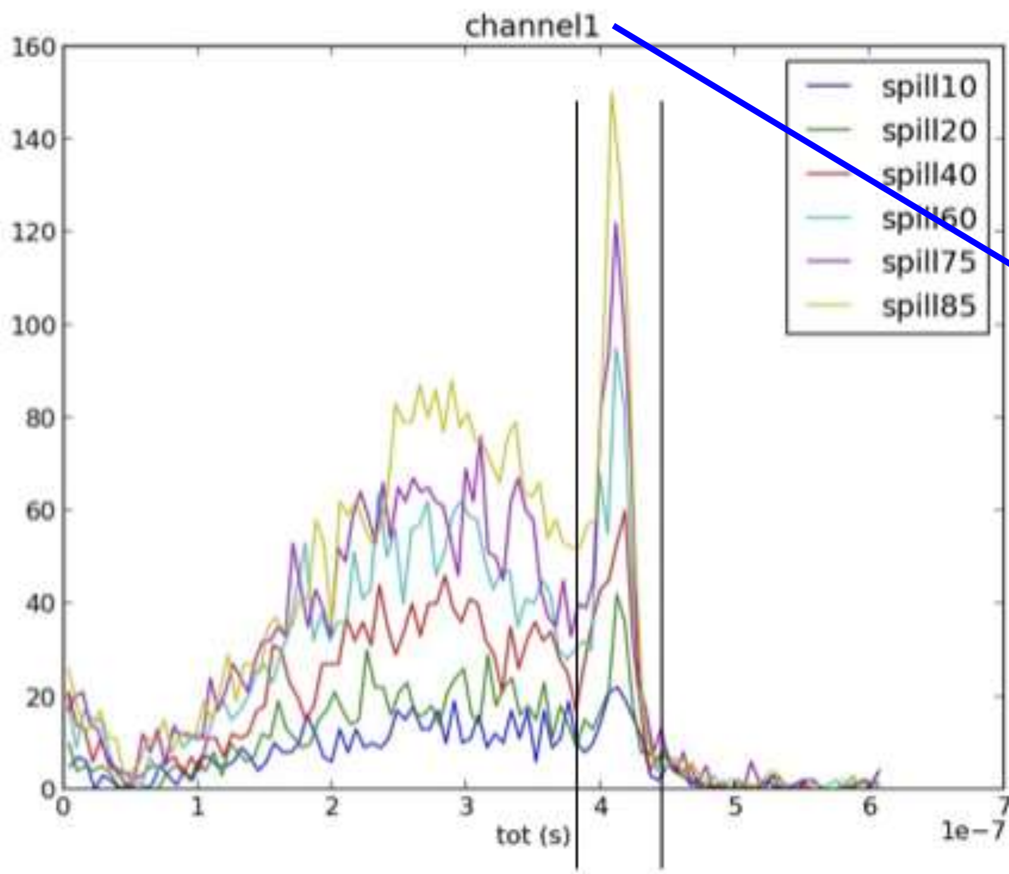
Simulation



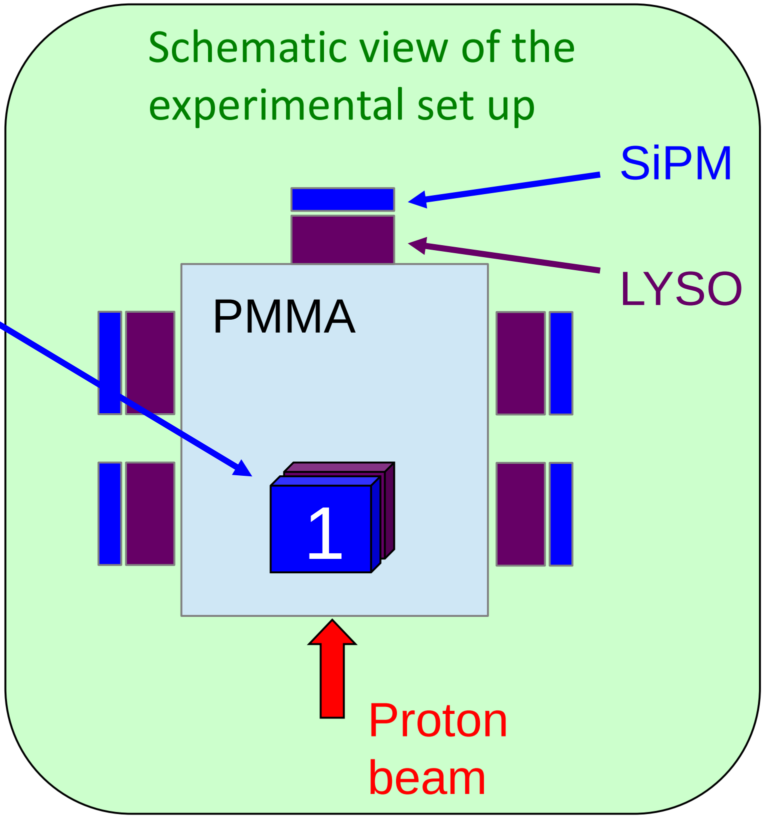
Peak to valley: ~ 15 (Raw Data), ~ 16 (Simulation)

DAQ Rate and full beam/in beam structure under control

Photopeak position (singles!)

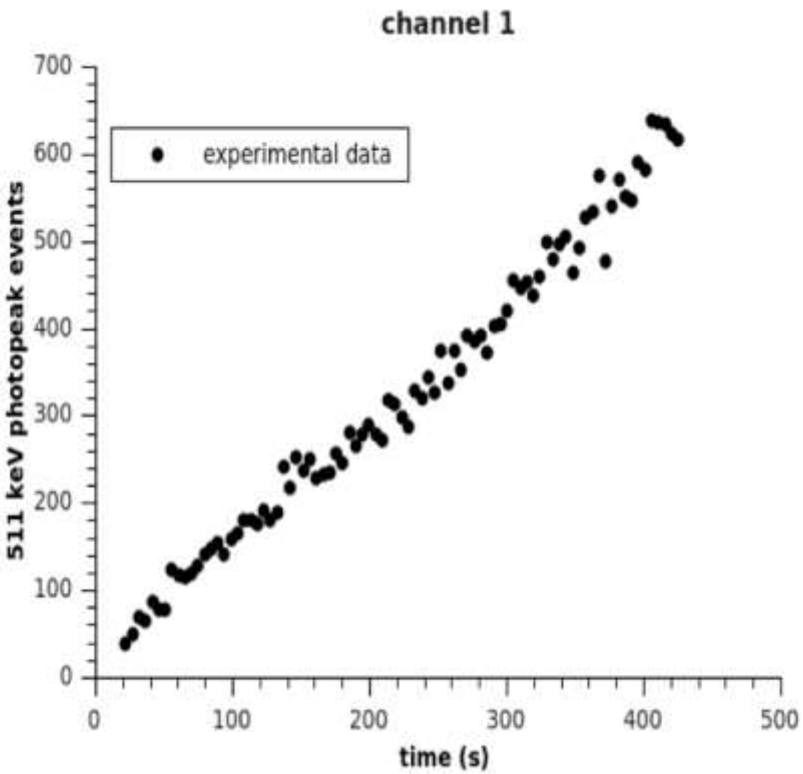


511 keV photopeak events

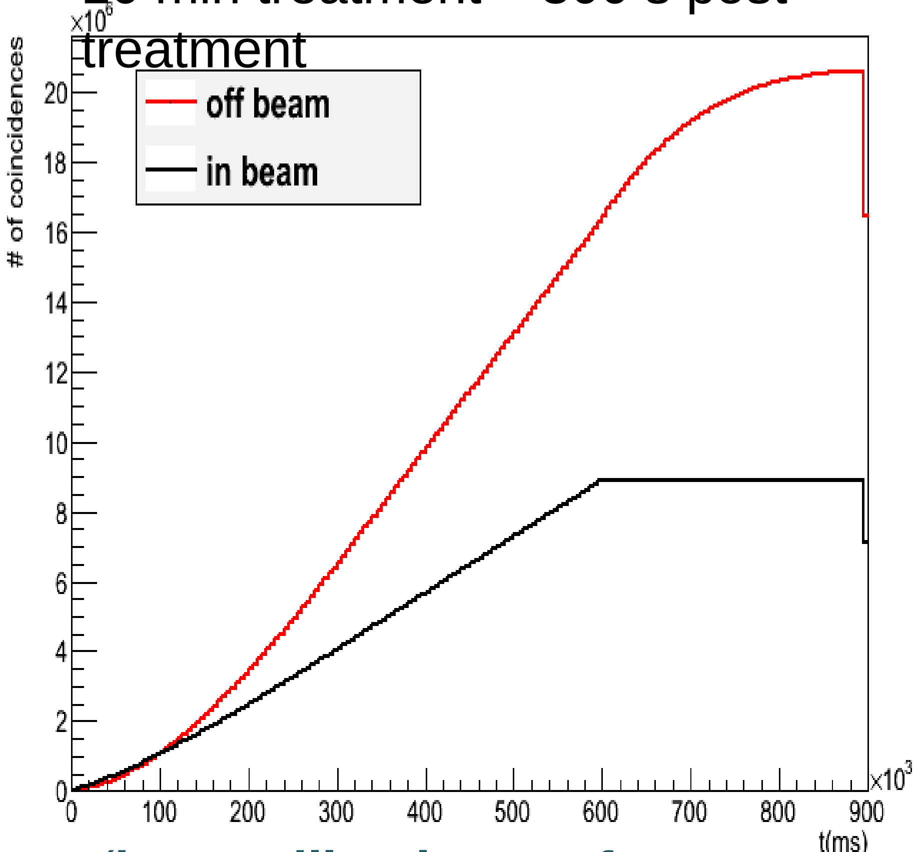


Number of events

Integrated "single" photopeak triggers on channel 1 during beam test



Total number of coincidences with beam on and off, $5 \cdot 10^9$ pps, 10 min treatment + 300 s post-treatment

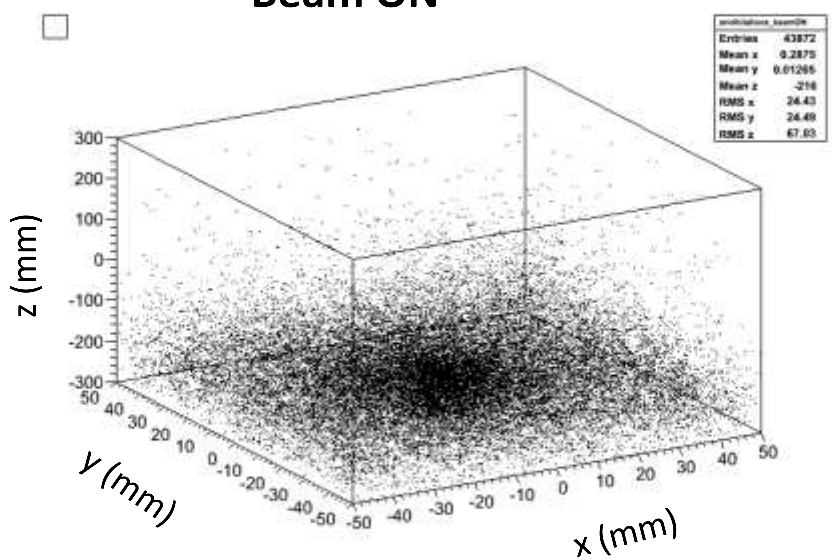


Expected number of **coincidences** (**interspill only, no after treatment acquisition**) evaluated on an **input treatment plan**, taking the detector acceptance/efficiency into account: **$3.09 \cdot 10^5$**

Annihilation position

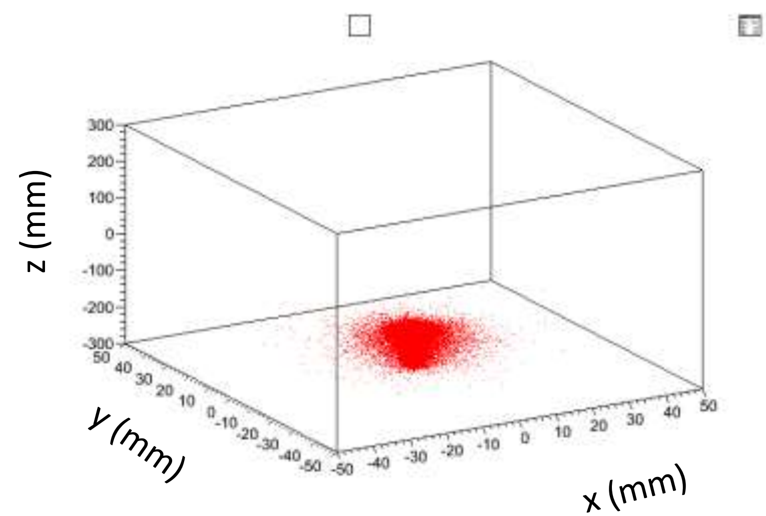
- **Simulation of the annihilation position :**
  - 2 ms beam on + 300 s beam off
  - Plot of the **(known!!!)** annihilation positions

Beam ON



prompt annihilations
& β^+ decays

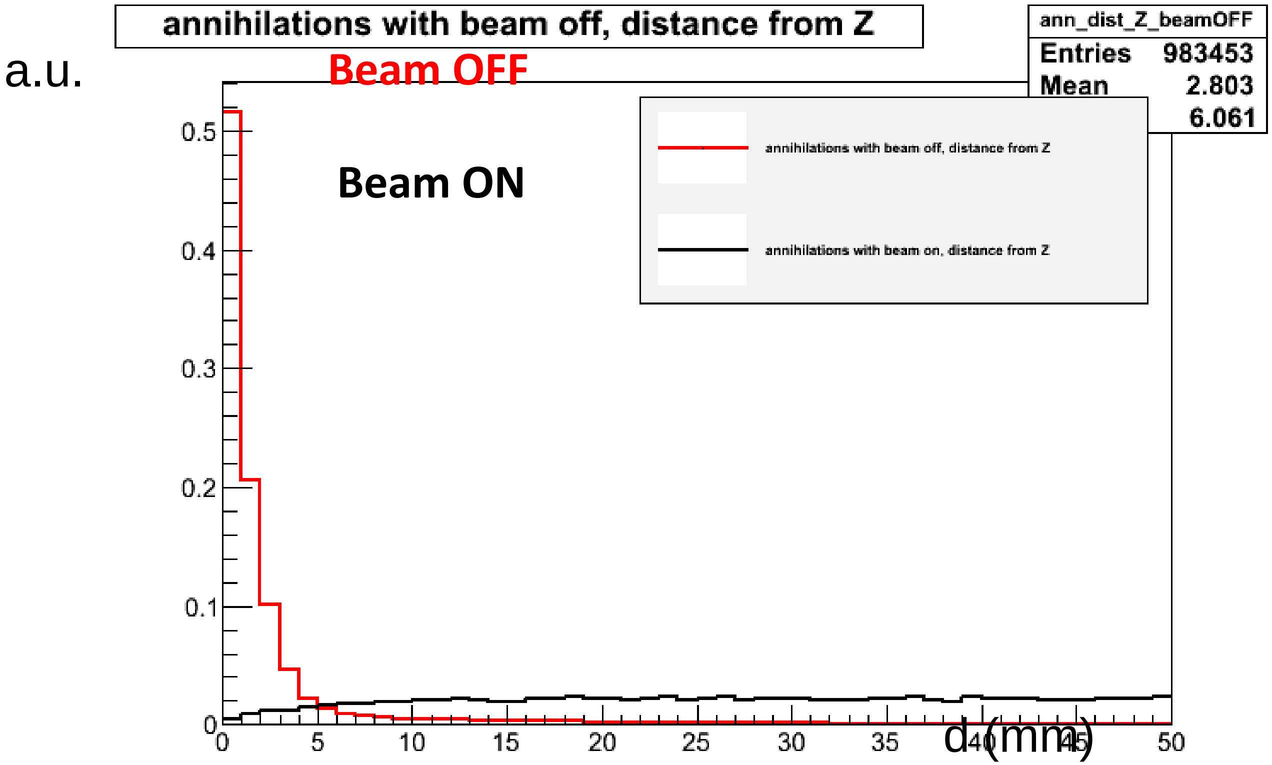
Beam OFF



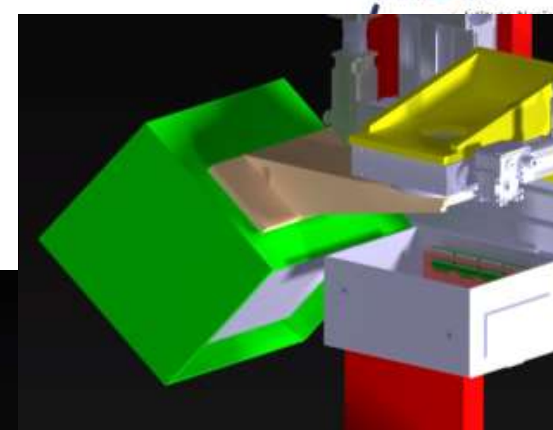
β^+ decays only

Annihilation position

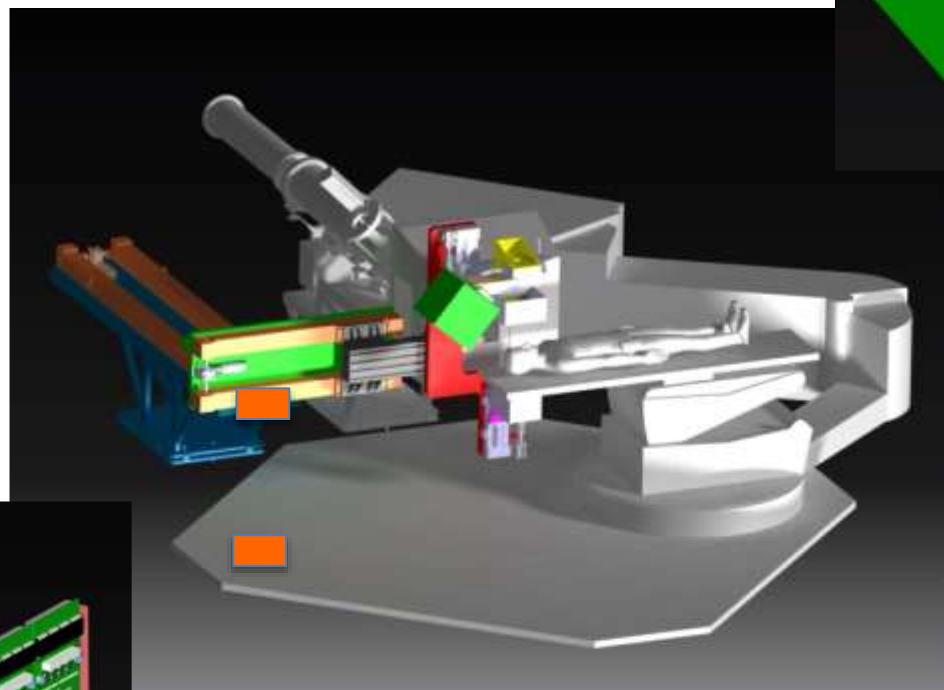
- **Simulation of the annihilation position :**
  - 2 ms beam on + 300 s beam off
  - Plot of the **(known!!!)** annihilation positions

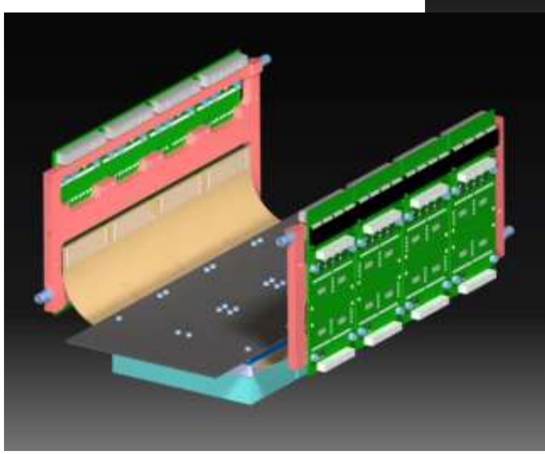


INSIDE



2014 construction





2015 commissioning

Opportunity: correlate PET and Tracker information in the data analysis

PT Monitoring: summary

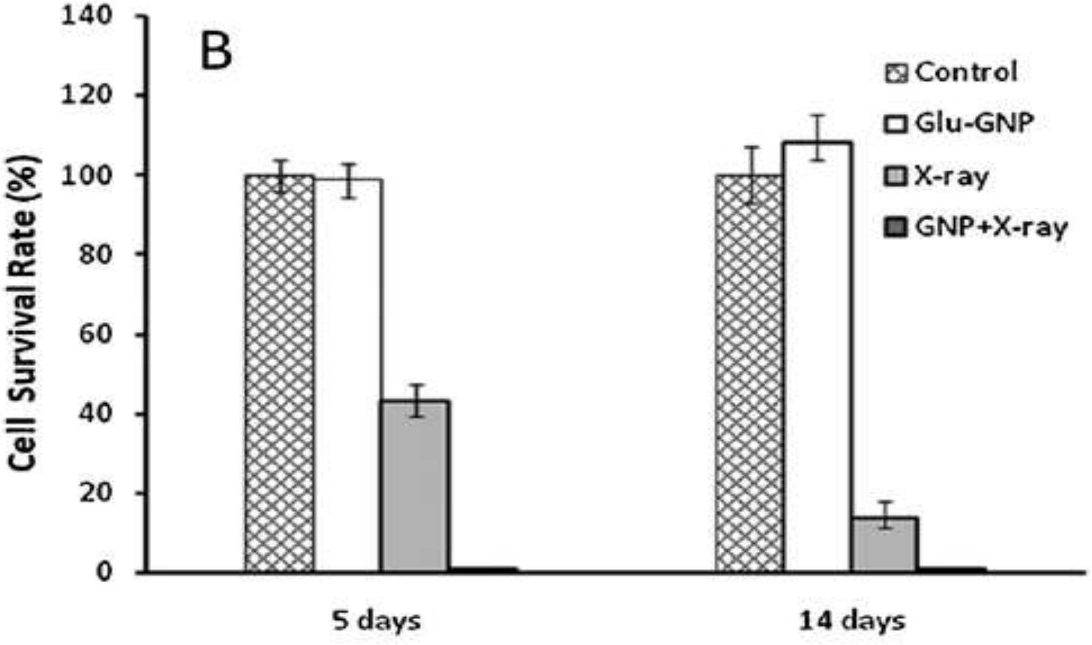
- The dose monitoring problem is a key issue to improve Quality Assurance in Particle Therapy
  - **in beam-PET**: metabolic wash-out and difficulty in quick feedback are clear limitations
  - **prompt gamma**: can suffer from the presence of a huge neutral background
  - **light charged particles**: statistics should balance the absorption and scattaring in the patient body

6

Nano-particles

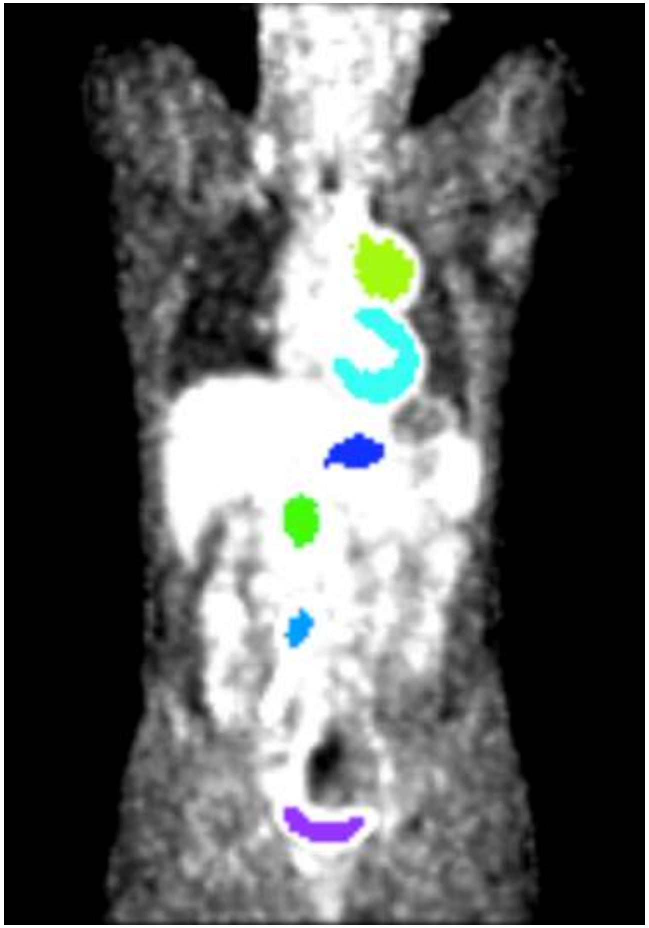
RDH/nATT project

- Intra-venous injection of nanoparticles increases the effect of radio- and hadron-therapy



What are the physical processes that cause the additional damage?

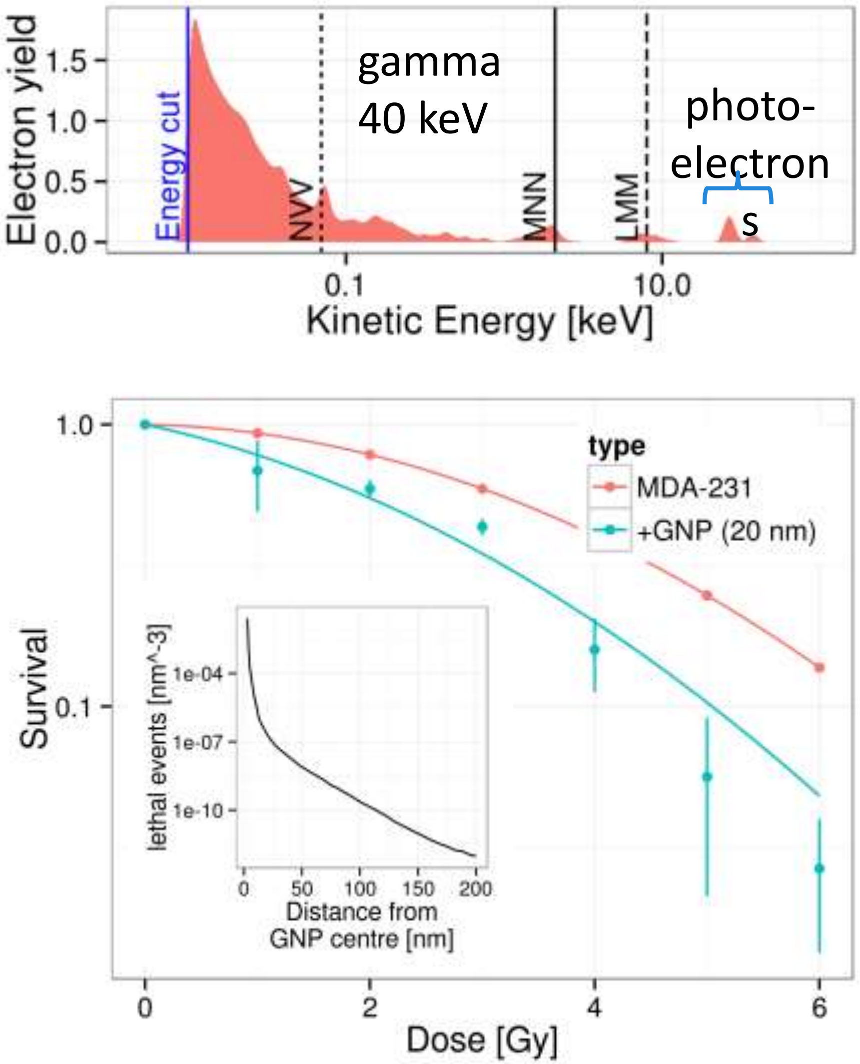
RDH/nATT project



FDG-bound nanoparticles were proposed as a way to concentrate nanoparticles in the tumor volume and observe functional features with morphological imaging

Why not using biomarker-tagged nanoparticles to selectively amplify the therapy effect?

Damage mechanisms

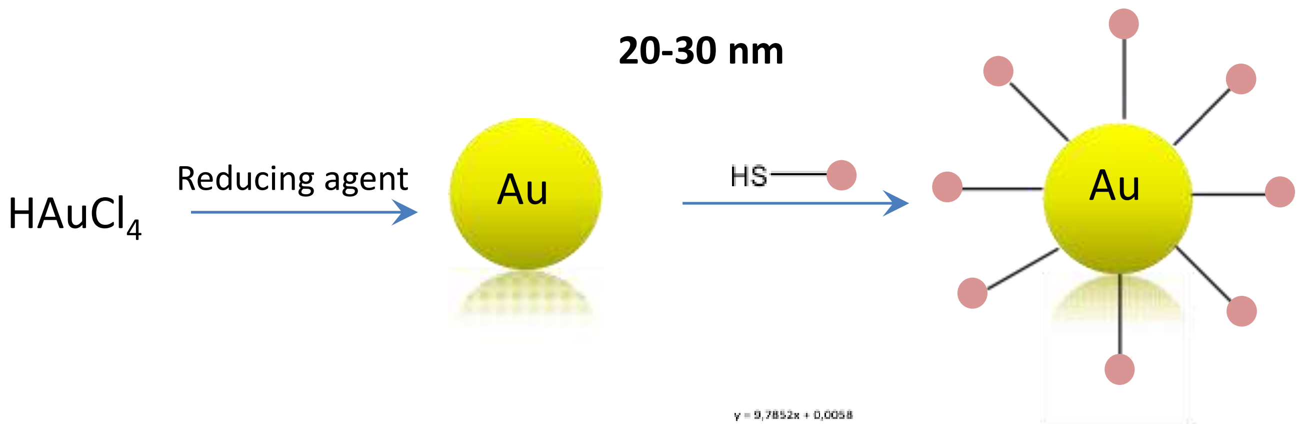


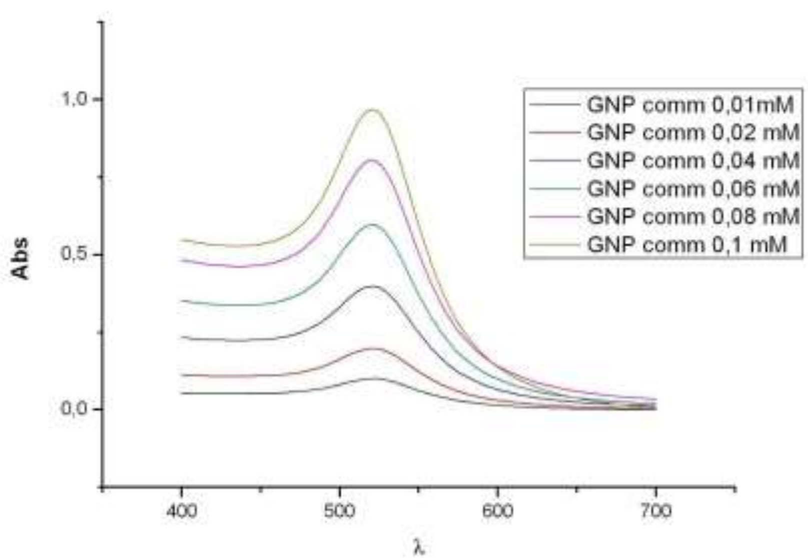
The biological outcome is related to the structure of the energy deposition nearby the GNP. A set of MC simulation were performed:

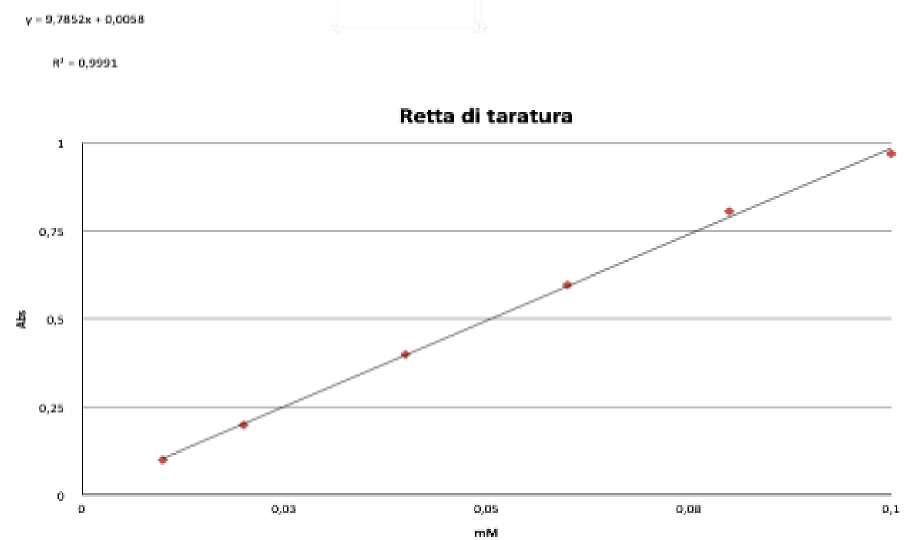
- GNP: 10, 20 and 50 nm radius
- Primary particles: gamma @ (40 keV, 160 keV, 6 MeV, 15 MeV), proton @ (50, 100 and 150 MeV).
- A computational model based on the LEM is being studied to evaluate the biological effect.

GNP Production & Characterization

- GNP produced and characterized with spectrophotometry
- GNP functionalized (57% efficiency) with18F-FDG

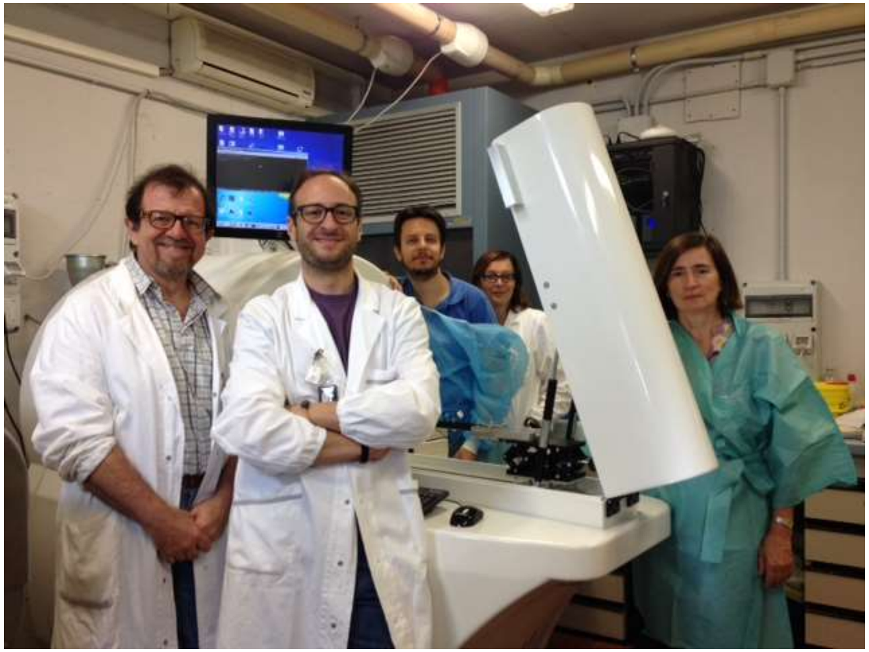


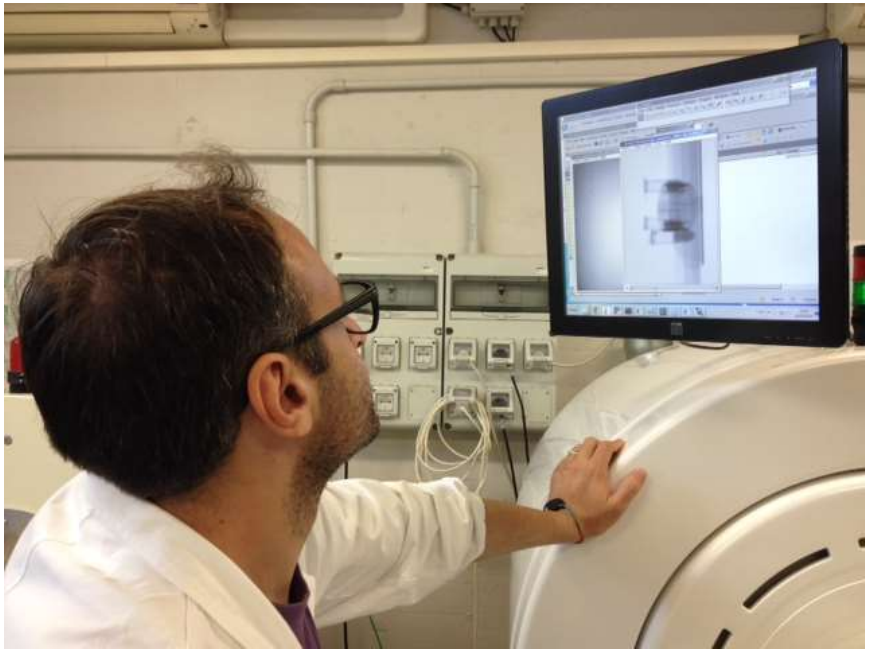




in-vivo microPET/CT measurements

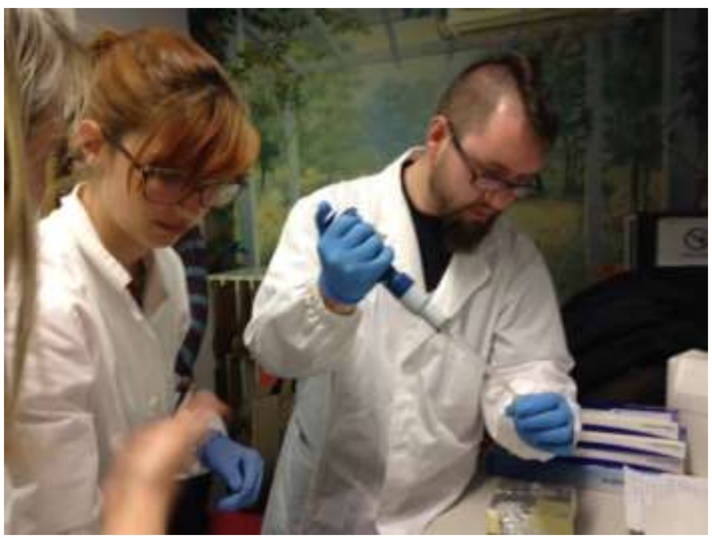
- Protocol submission for measurements with small animals submitted (May 2014)
  - Waiting for the approval
  - Measurements likely will start by the end of September
- in vitro test of the protocol (Jul 1st)

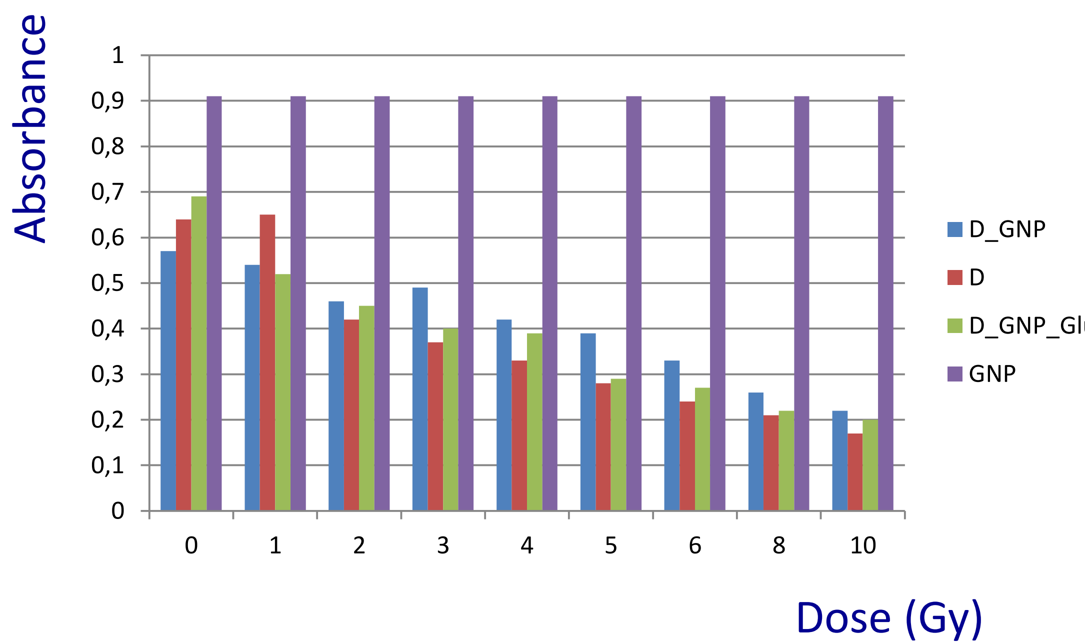




in-vitro test on GNPs

- Reactive Oxygen Species production tests started (Istituto Tumori, Milano; Ospedale Mauriziano, Torino)
  - 6 MV photons
  - DPBF as oxygen quencher (to be replaced in new measurements)





Piergiorgio Cerello (cerello@to.infn.it)

7

CAD Software

Software

Data Acquisition

Reconstruction

Image Processing: Computer Assisted Detection

the ‘Lazy consistency model’

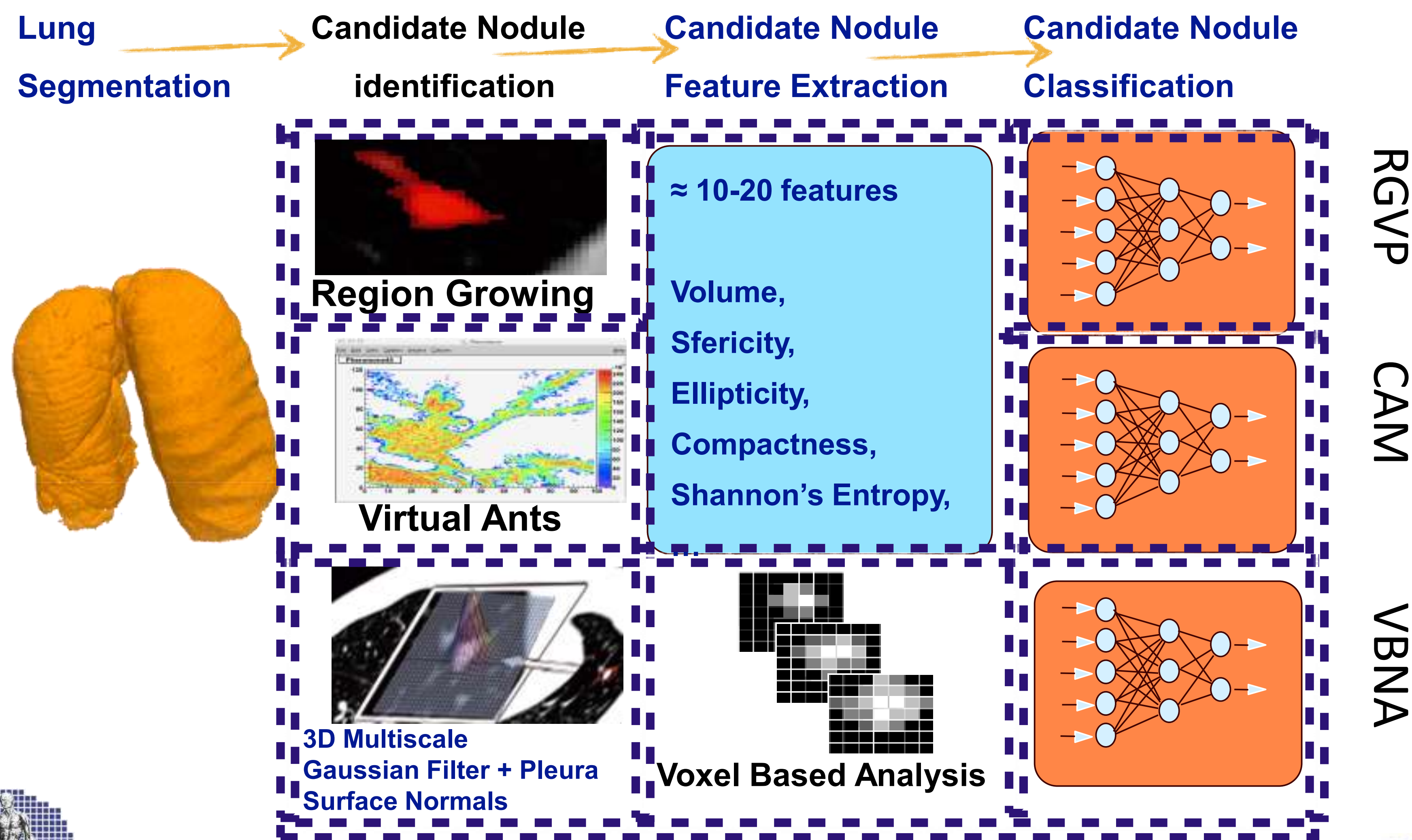
a suggestion

the first rule of debugging

Computer Assisted Detection

A multi-thread WEB-based CADe system for nodule detection on chest multislice CT scans

the M5L algorithms

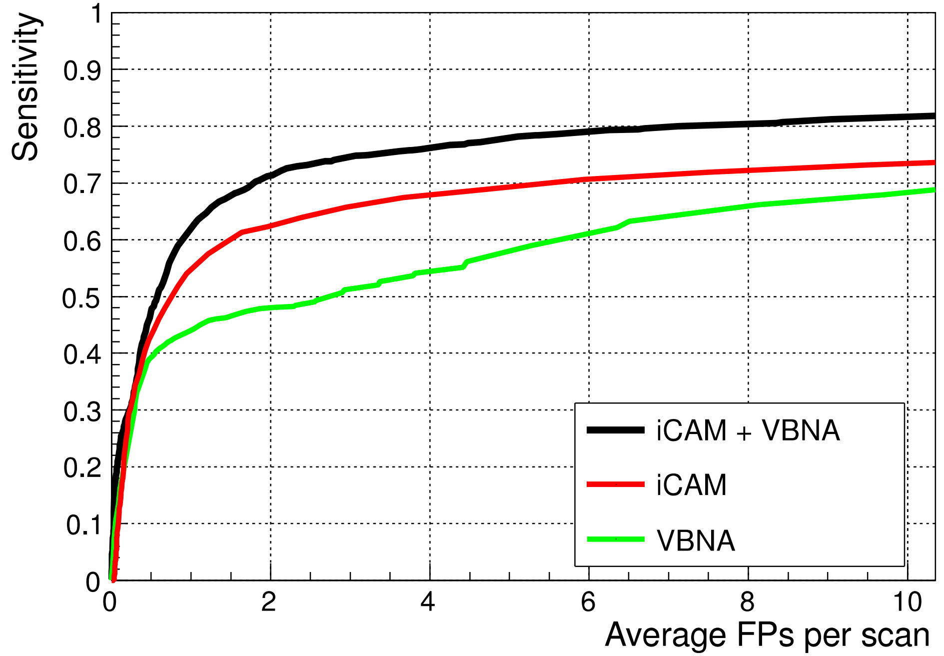


M5L validation

LIDC Public Database

- **Annotation by 4 radiologists**
- **Slice thickness: 0.5-3mm**
- **Gold standard: set of nodules with at least 2 annotations**

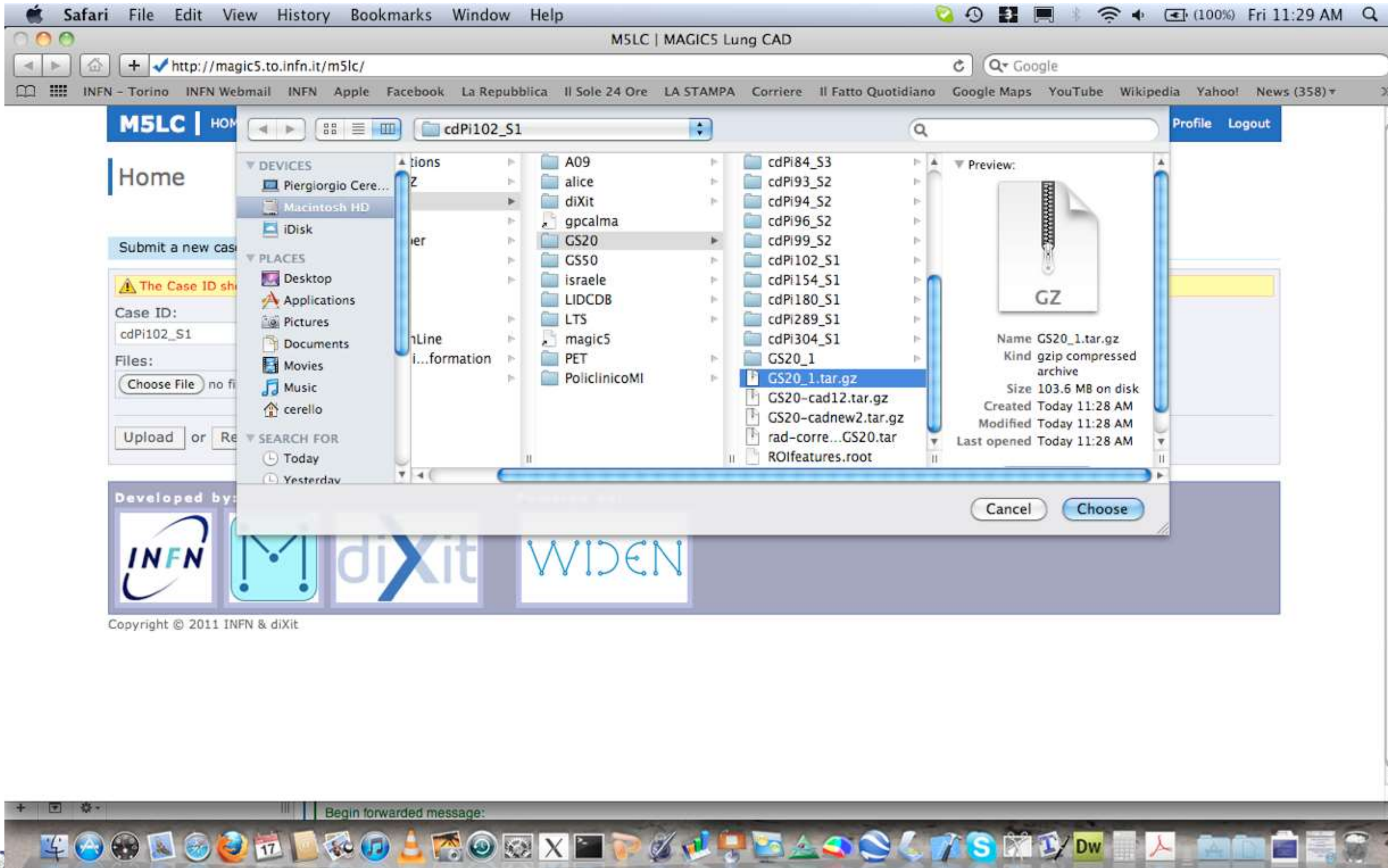
Training: 94 CTs
Validation: 949 CTs



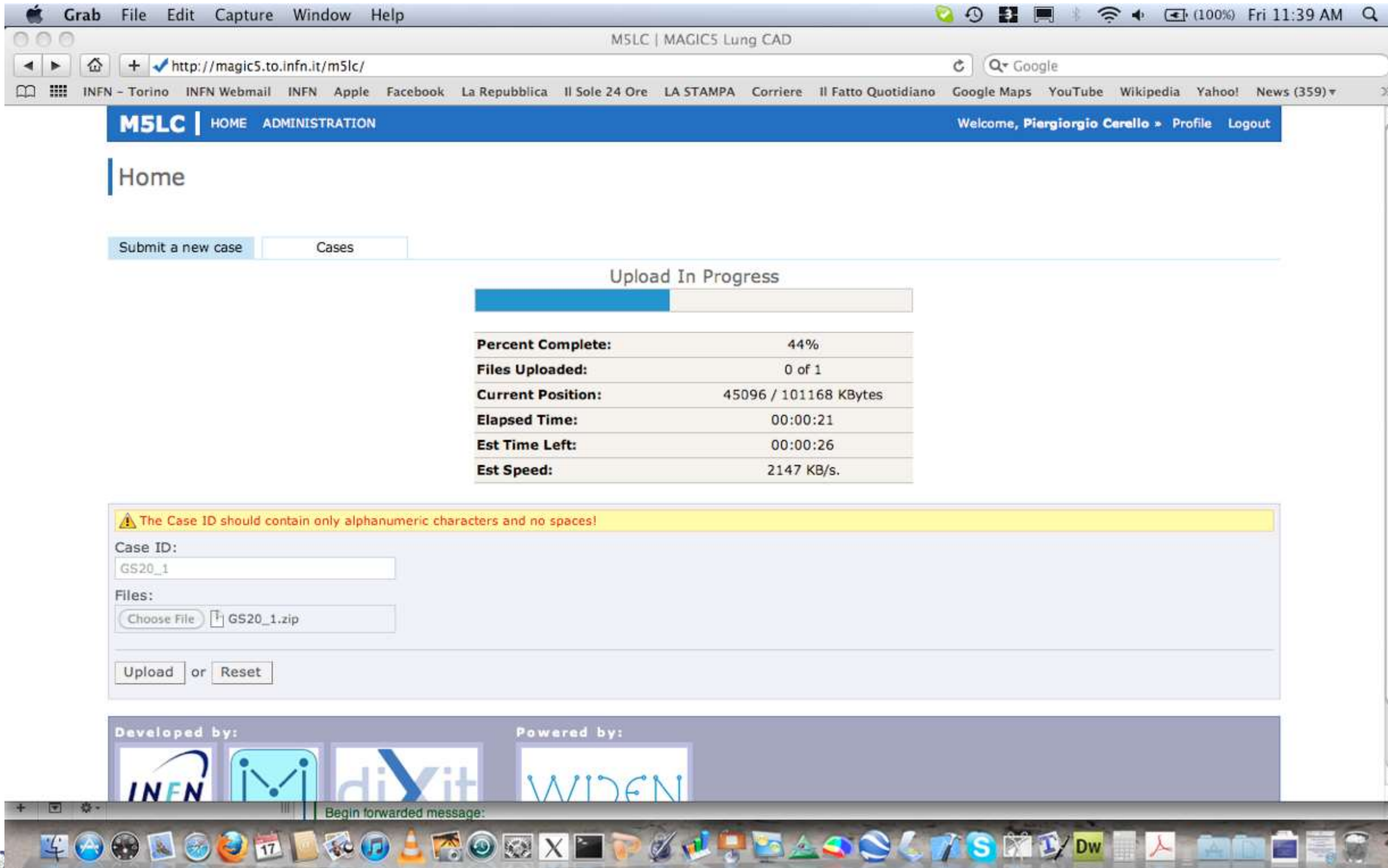
E. Lopez Torres et al,
"Large scale validation of the M5L lung CAD on heterogeneous CT datasets"
submitted to Medical Physics

the WEB-based M5L

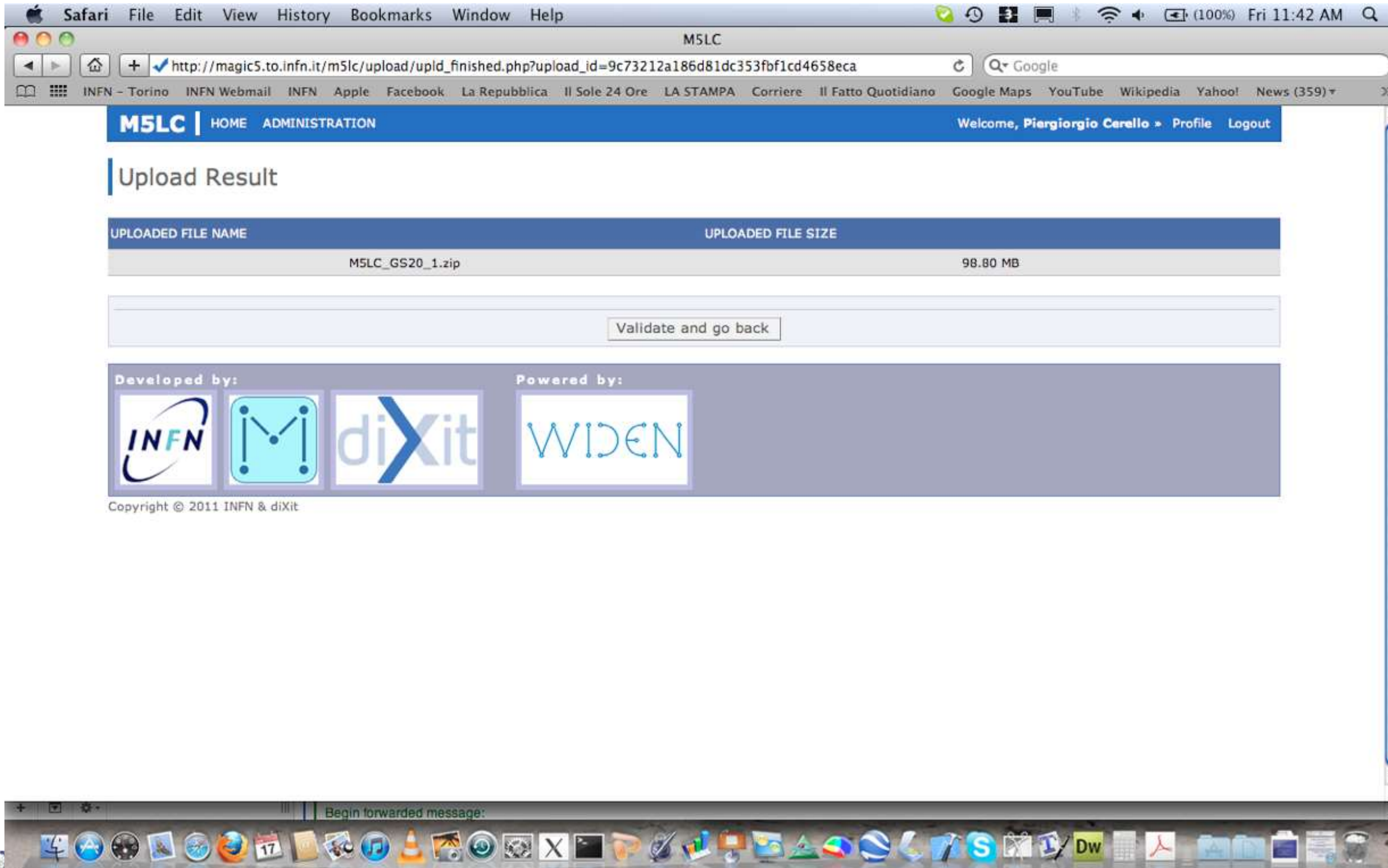
the WEB-based M5L



the WEB-based M5L



the WEB-based M5L

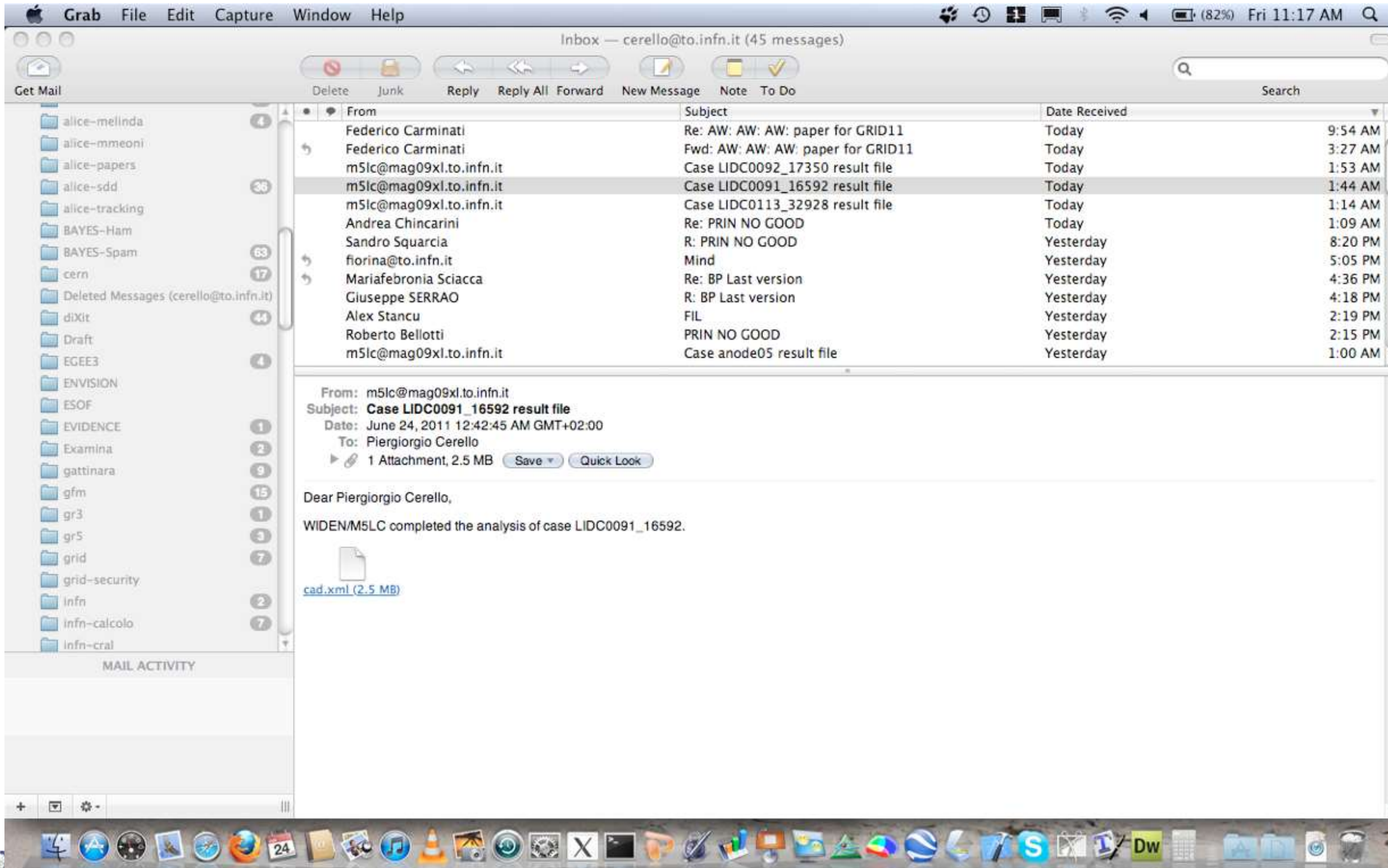


the WEB-based M5L

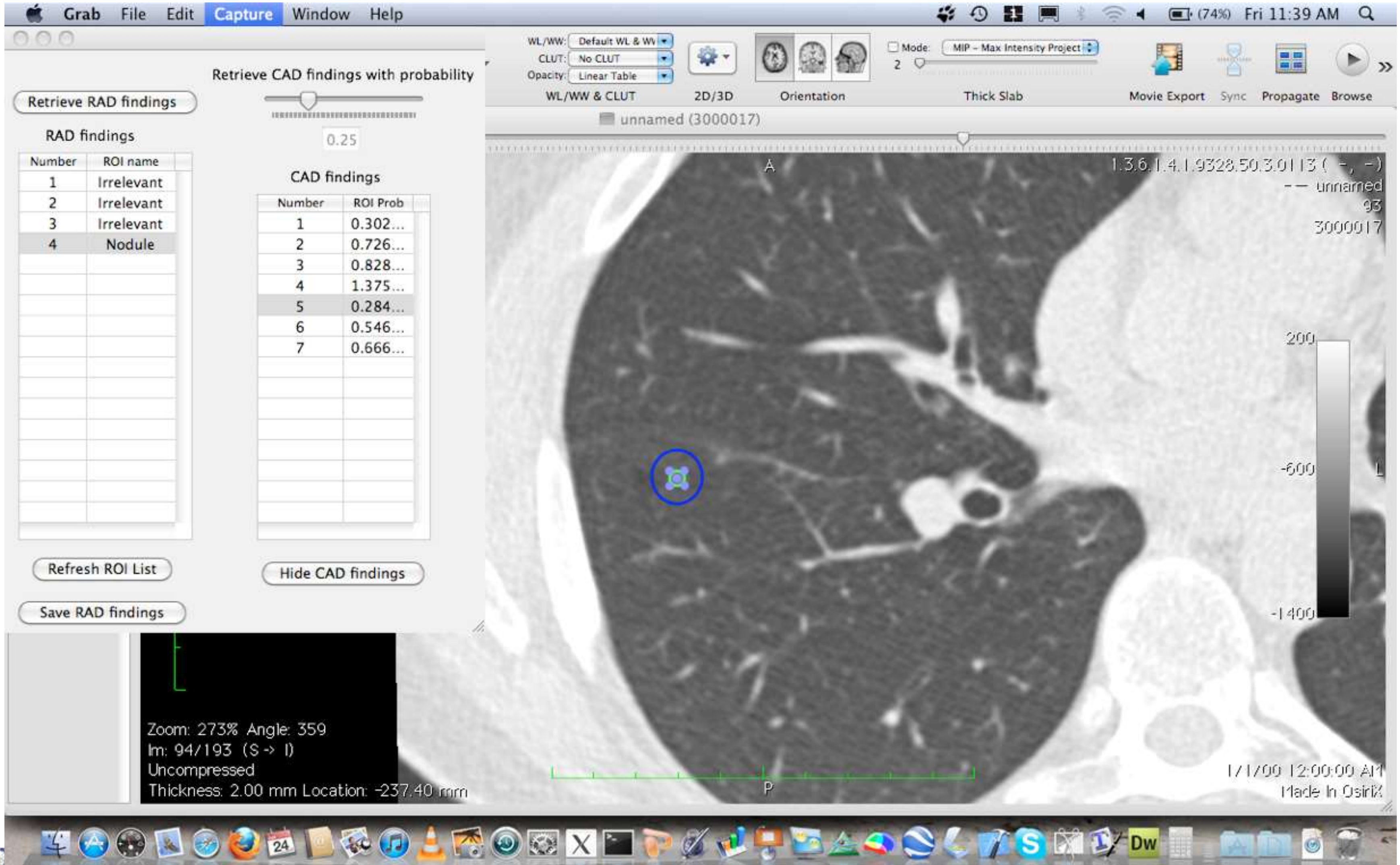
- sit back and relax...
  or do something else

- ... but something is going on in the OpenNebula Cloud at INFN-Torino

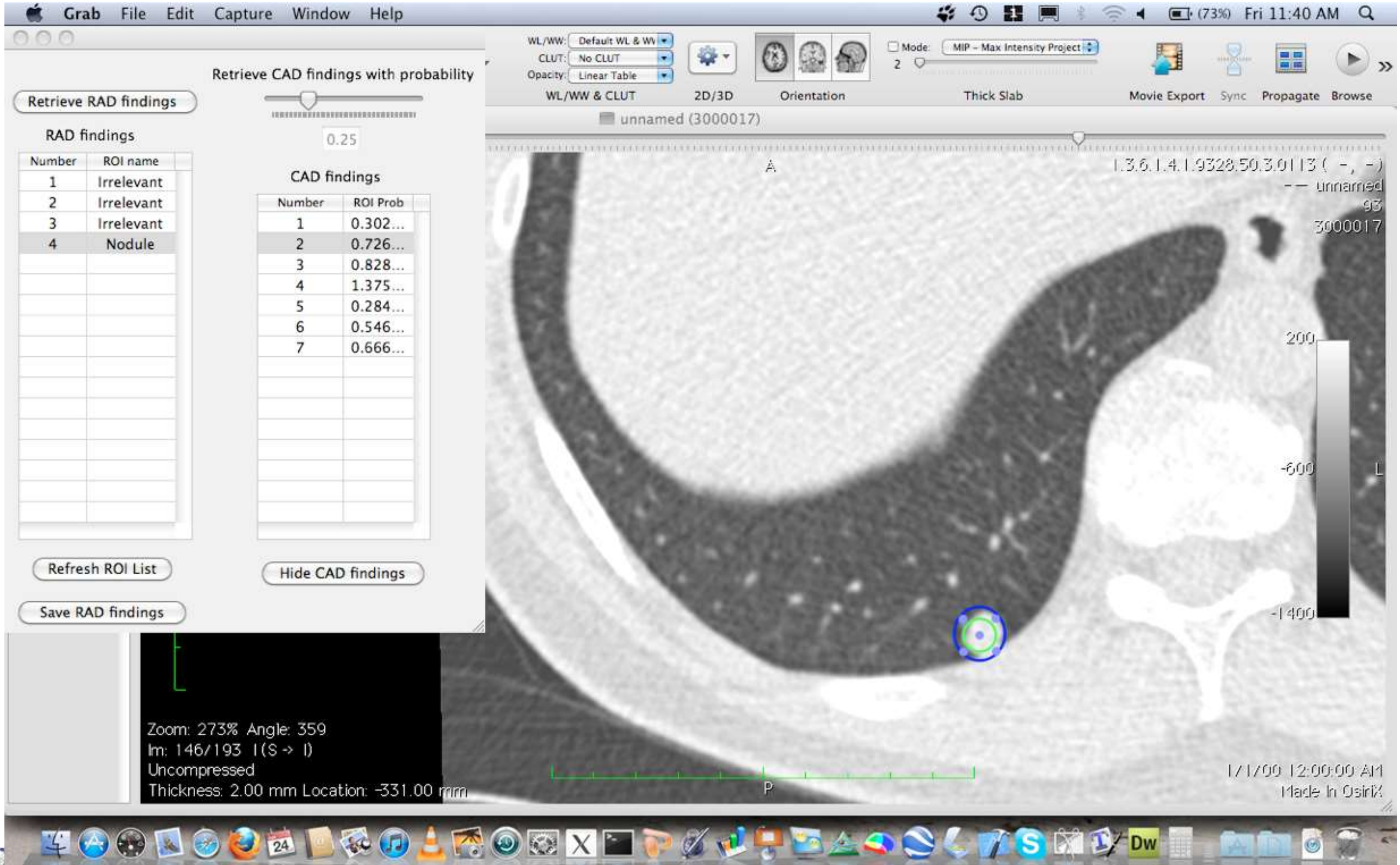
the WEB-based M5L



the WEB-based M5L



the WEB-based M5L



Can physics help?

INFN Istituto Nazionale di Fisica Nucleare

Cancer and efficiency of treatments

At time of diagnosis	Primary tumor	With metastases	Total
Diagnosed	58%	42%	100%
Cured by:			
Surgery	22%		
Radiation therapy	12%		
Surgery+radiation therapy	6%		
All other treatments and combinations incl. chemotherapy		5%	
Total cured	40%	5%	45%
Fraction cured	69%	12%	45%

Per year over one million cancer deaths in the EU.

⇒ improve early diagnosis

⇒ improve systemic treatments

… probably yes

Medical Imaging

will PET/CT replace CT as the standard in oncology?
what will the evolution of PET/MR be?
how far can we push the PET Time Of Flight resolution?

Particle therapy

how will it scale?
real-time range monitoring?
use of nanoparticles as amplifiers?

Radioisotopes

the key to molecular imaging…

Computer Assisted Detection

large scale validation?
cloud-based deployment?