FACULTY OF ENGINEERING AND ARCHITECTURE

Innovative Molecular Imaging and Therapy

DEVELOPMENTS IN TOTAL BODY PET SYSTEMS

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GHENT UNIVERSITY

Penn
University of Pennsylvania

University of Pisa

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THE PAST	**PRECLINICAL IMAGING**
THE PRESENT	TOTAL BODY TRANSLATIONAL IMAGING
THE FUTURE	TB MOLECULAR PHARMA AND TREATMENT

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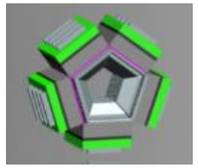
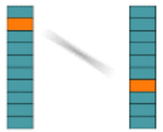
HARDWARE DETECTOR AND SYSTEM DEVELOPMENT IN MEDISIP

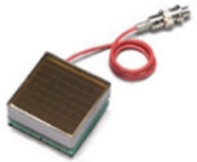


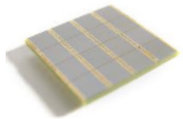


- MEDISIP software experience
  - Iterative reconstruction
  - System design with Monte Carlo simulations

- Infinity lab
  - Direct access to phantom animal and tracer
  - Strengths and limitations of current imaging systems

- MEDISIP systems
  - High resolution detectors
  - Compact design
  - Iterative reconstruction





- MEDISIP high res detectors
  - Electronics
  - Silicon photomultipliers
  - Positioning algorithms
  - Collimator production

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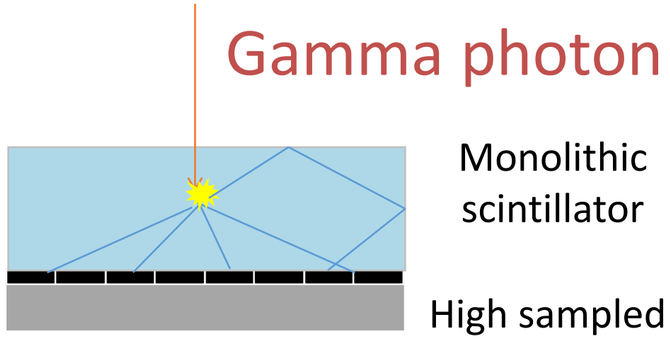
BASIS = HIGH RESOLUTION MONOLITHIC DETECTORS

Monolithic detectors with light spreading and ML positioning

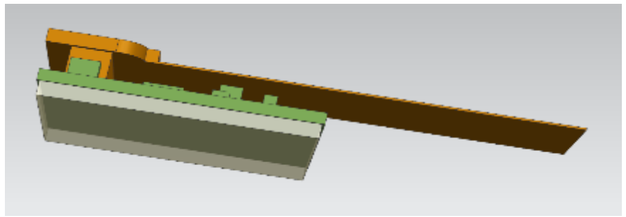


SPECT version based on CsI and PS-PMTs

0.7 mm intrinsic spatial resolution

Thin detector

PET version based on LYSO and Silicon photomultipliers



0.6 mm intrinsic spatial resolution

Detector with 4-6 layer DOI

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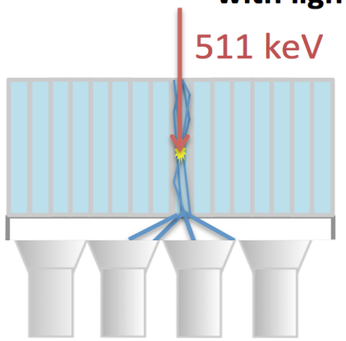
Evolution of detectors in PET

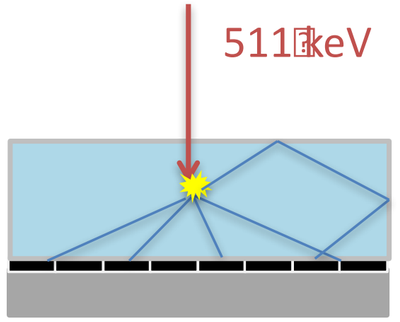
Pixelated detector blocks with light spreading



Expensive for very small pixels (< 1mm)

Depth of Interaction challenging

Monolithic detectors with light spreading and ML positioning



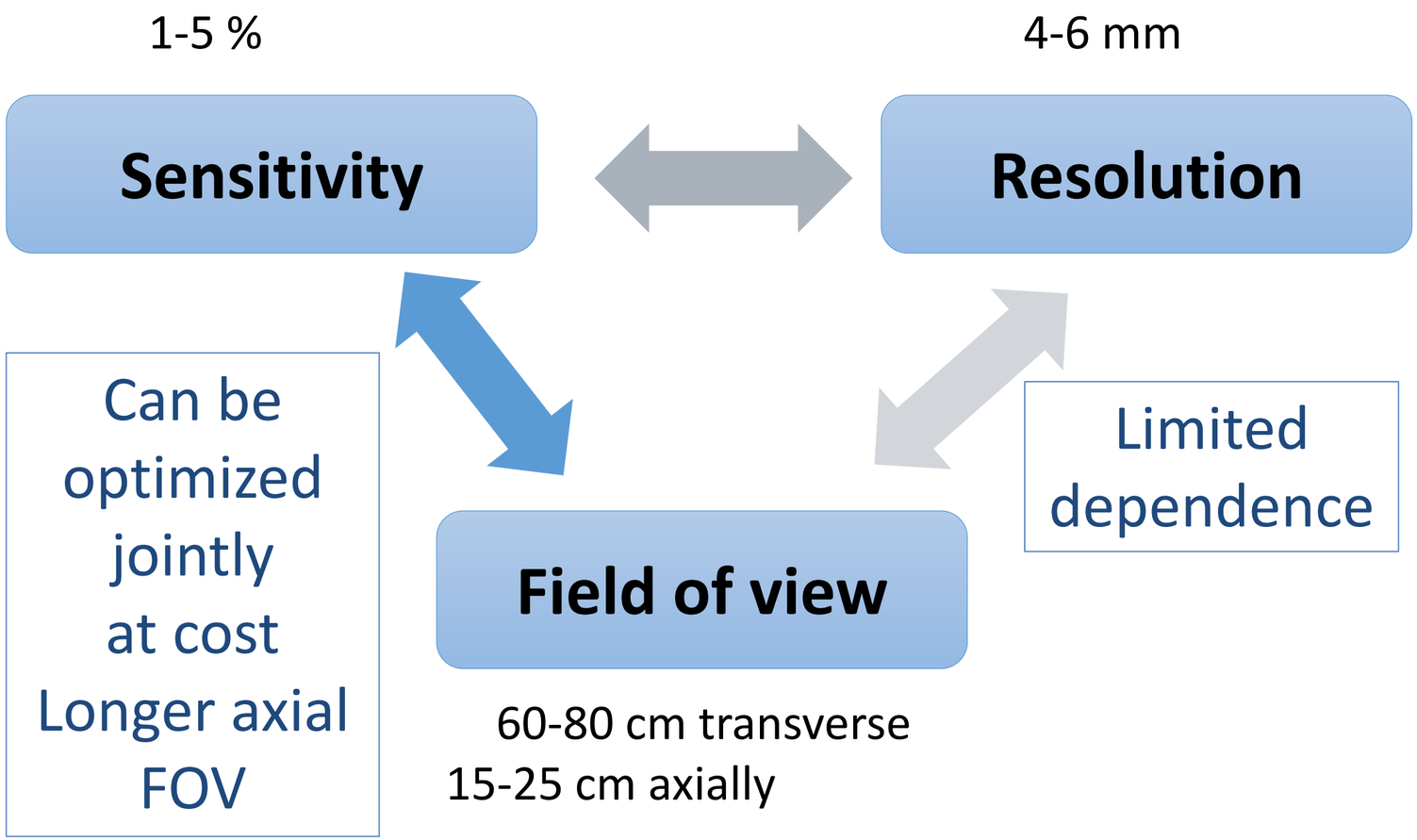
Requires SiPM or PSPMT

Excellent spatial resolution for thin crystals

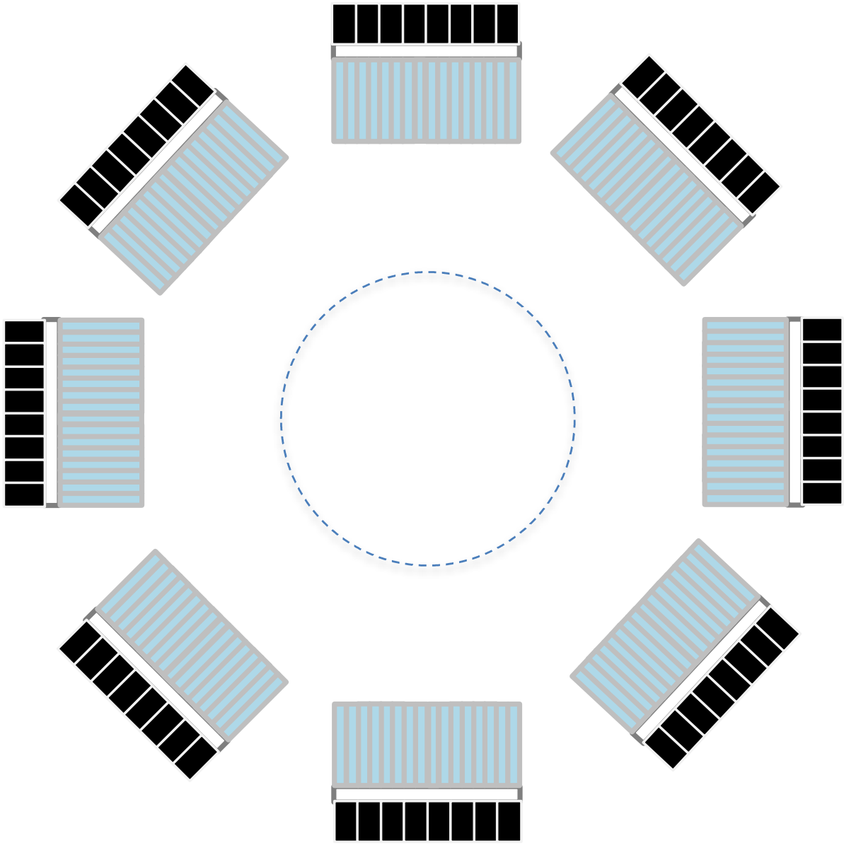
Free Depth of Interaction

FPGA + ML
ML= Most Likely
ML= Max Likelihood
ML=Machine Learning

(Pre)Clinical PET system design



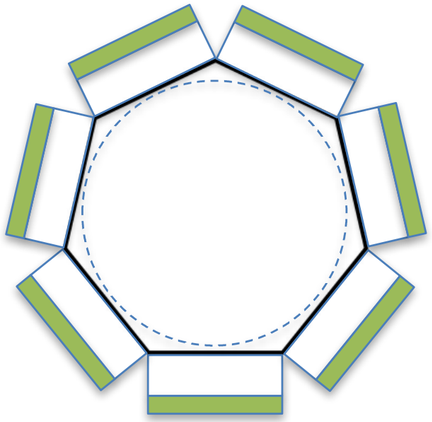
Potential of High resolution detectors with DOI for microPET



15-20 cm diameter detectors

7-10 cm FOV, no DOI

Expensive pixelated detectors



7-8 cm diameter detectors

7 cm FOV due to DOI

Cheaper monolithic detectors

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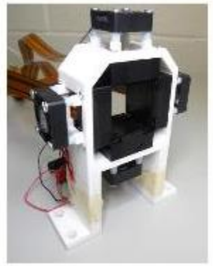
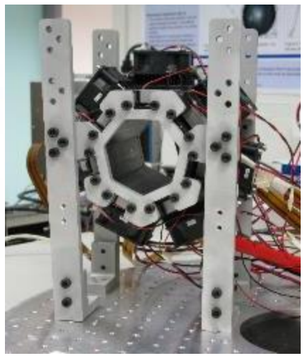
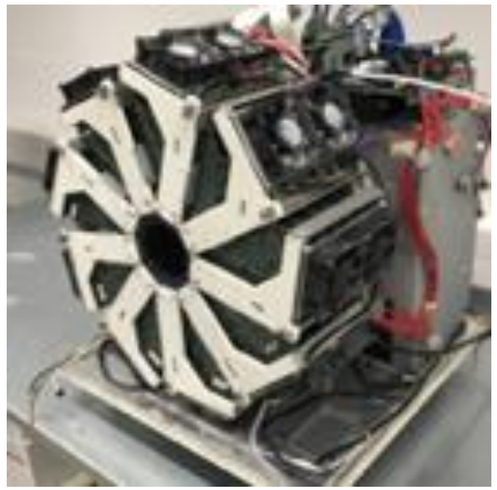
MICRO PET DEVELOPMENT IN GHENT



2014
DigiPET v1

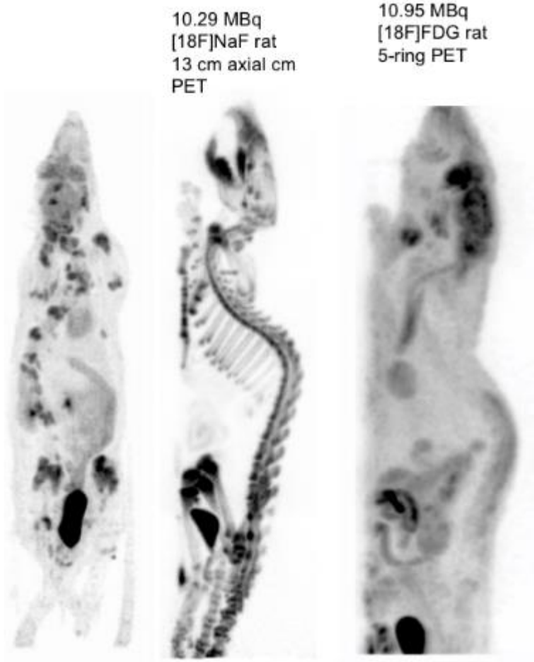


2015
DigiPET v2



2016
Beta Cube v1

2017
Molecubes Beta + X Cube
8 mm thick LYSO
13 cm axial FOV
still sub mm



FIRST PET-CT installed in February 2017

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THE PAST PRECLINICAL IMAGING

THE PRESENT **TOTAL BODY TRANSLATIONAL IMAGING**

THE FUTURE TB MOLECULAR PHARMA AND TREATMENT

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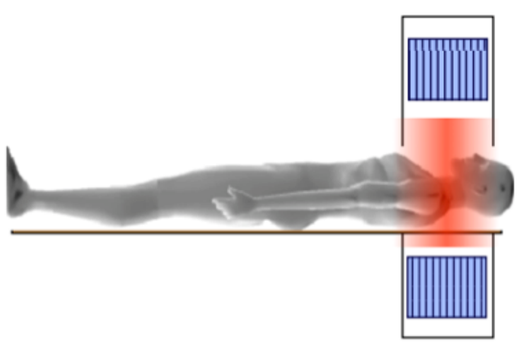
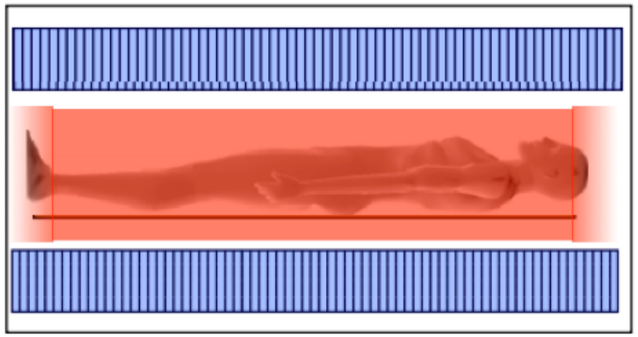
TOTAL BODY PET CONCEPT

From current 15-25 cm to 1-2 m long PET





Courtesy of Simon Cherry

Point peak Sensitivity: 4-6%	X 3-5 →	Point peak Sensitivity: 12-24 %
Body imaging sensitivity (NECR): 7-21 cps/kBq	X 30-50 →	Body imaging sensitivity (NECR): 200-500 cps/kBq
Acquisition time for total body 20 min	20-40 x faster →	Acquisition time for total body 0.5 min

Options

Quality

NEW

Improved images (reduce Poisson noise)

Dynamic imaging (multiple images after each other)

Reduce dose to patients and cost of tracer production

Faster imaging more patients on same day

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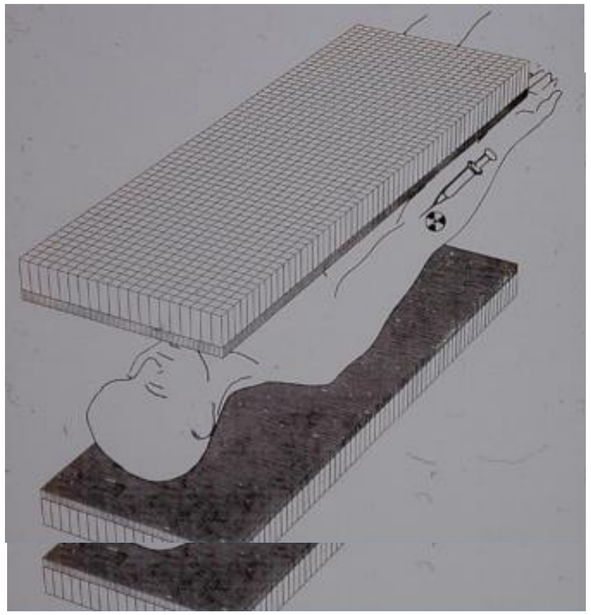
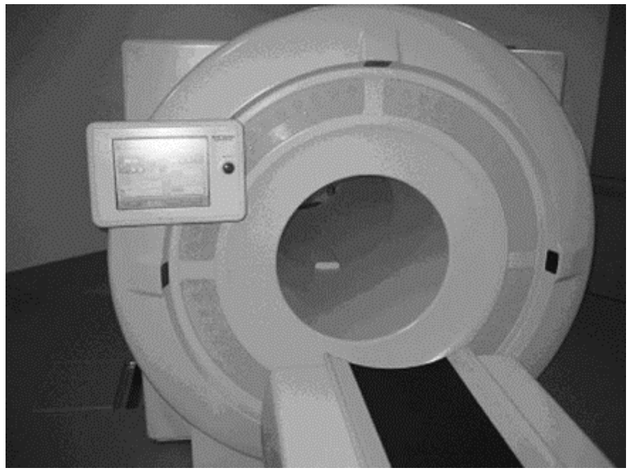
WHY NO EARLIER TOTAL BODY PET ?



Terry Jones, IEEE, 1990



68 cm Axial FOV – BGO (Hamamatsu SHR-92000) M. Watanabe, et al., IEEE Trans. Nucl. Sci. NS51: pp. 796–800, 2004

2018 Explorer-UCDavis

PET	BGO/NaI	Septa	Coincidence
↓	↓	↓	↓
PET-CT	L(Y)SO	Fully 3D	Time-of-Flight

Improvements in iterative recon and scatter correction

Increase in computing power, memory and storage

Funding for large projects

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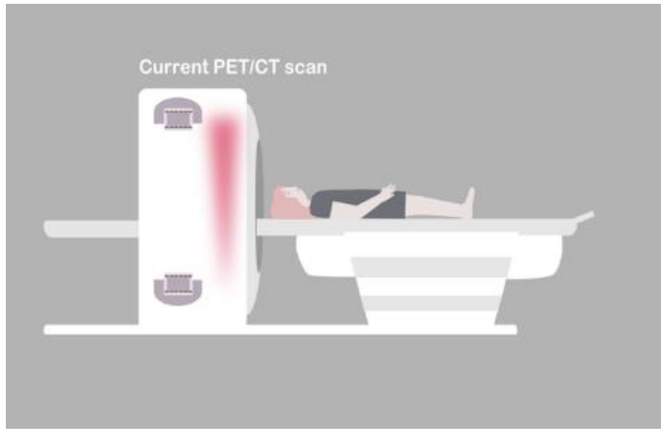
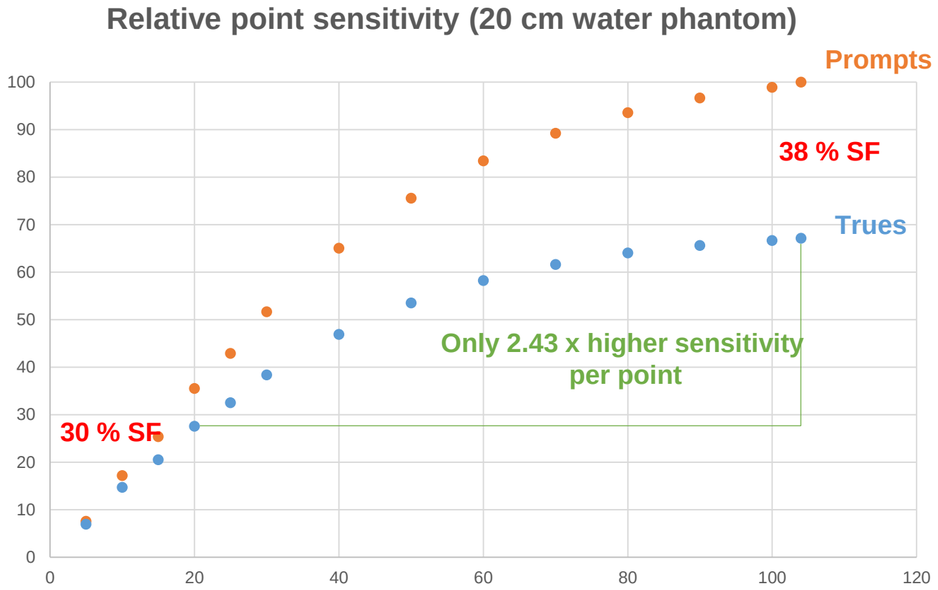
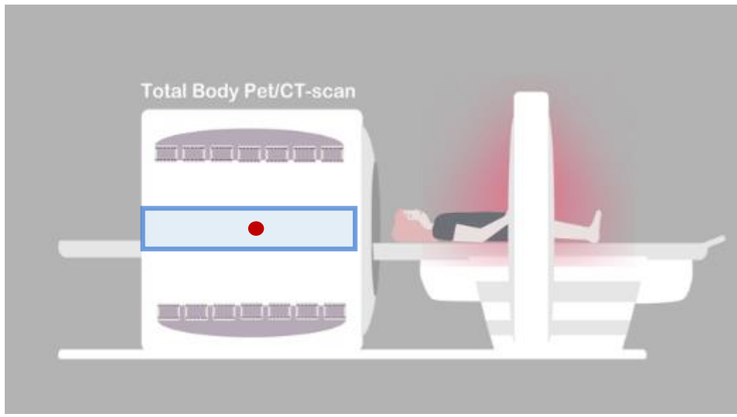
POINT SENSITIVITY VERSUS AXIAL LENGTH

20 cm axial FOV





100 cm axial FOV

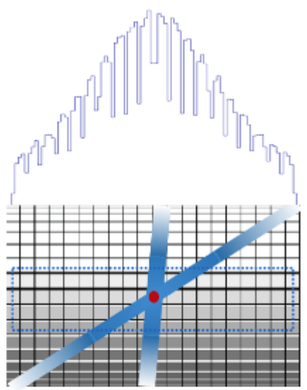


5 x axial length gives only 2.43 x higher efficiency

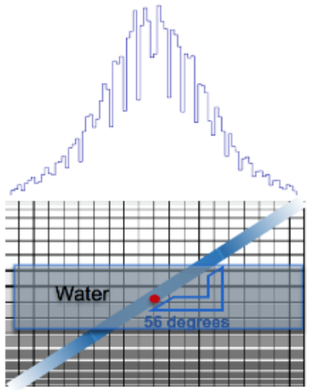
Total body PET is not for imaging short objects

40-60 cm axial length is better choice for this

Oblique LORs: less gain due to smaller solid angle per detector and much more attenuation



Solid angle reduces significantly with obliqueness due to larger distance to detector



56 degrees
36 cm path through
20 cm phantom

511 kev
20 cm path: 14 %
36 cm path: 3.1 % of photon pairs are not attenuated

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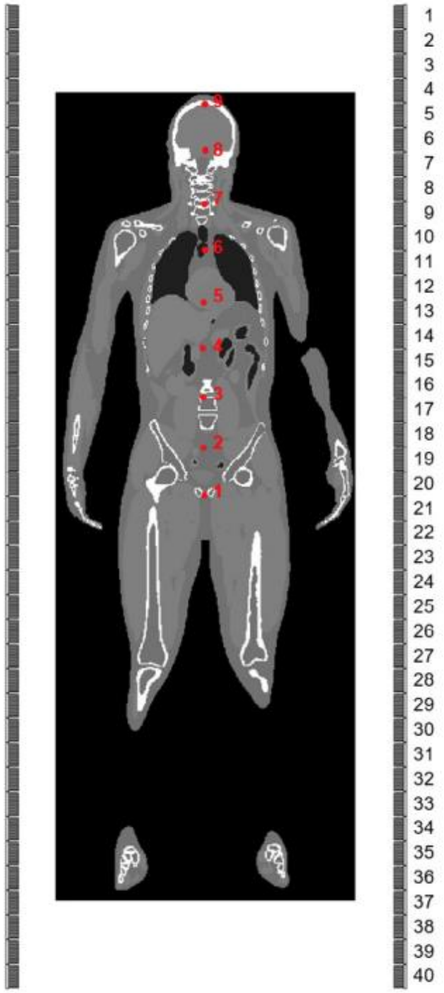
POINT SENSITIVITY GAIN

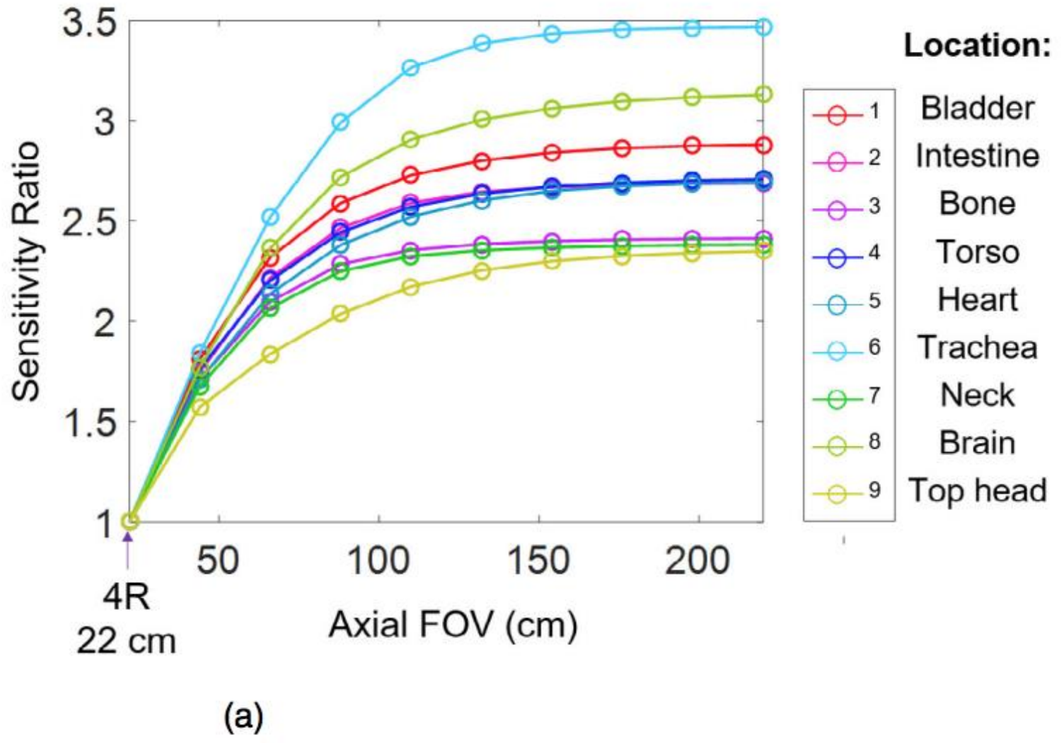
Physics in Medicine & Biology

PAPER

Theoretical study of the benefit of long axial field-of-view PET on region of interest quantification

Xuezhu Zhang[1], Ramsey D Badawi[1,2], Simon R Cherry[1,2] and Jinyi Qi[1]





(a)

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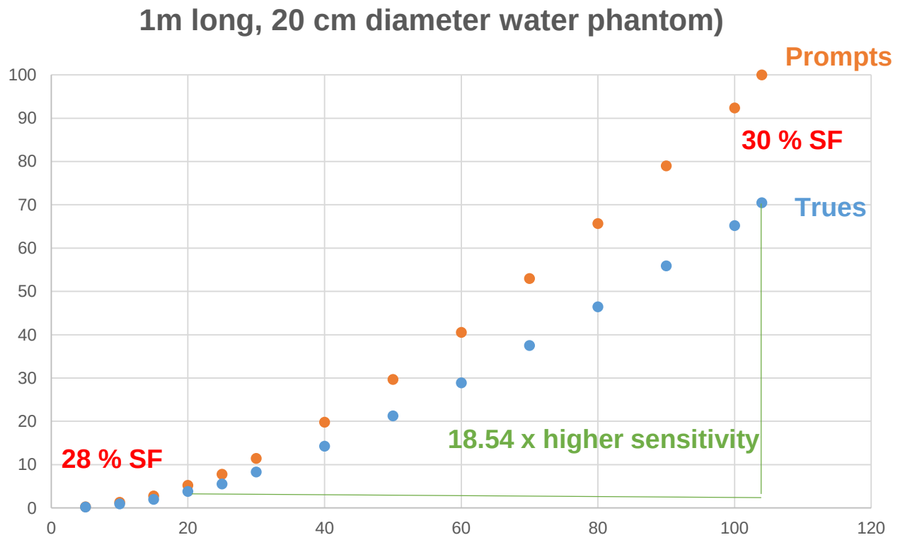
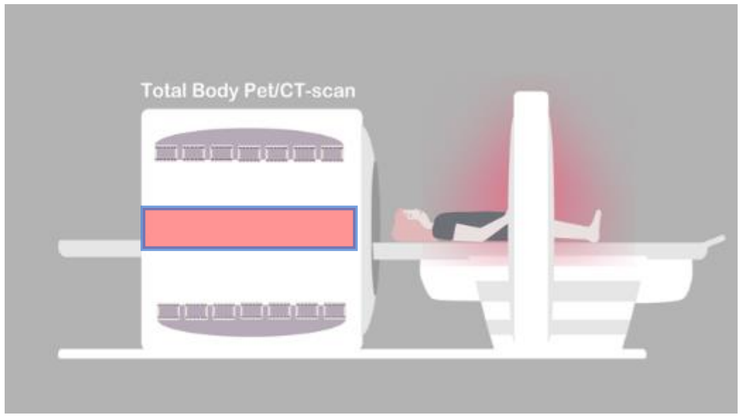
VOLUME SENSITIVITY VERSUS AXIAL LENGTH





5 x axial length gives 18 x higher efficiency

Total body PET is for imaging longer objects
Gain for single organ imaging (eg brain, heart) is limited

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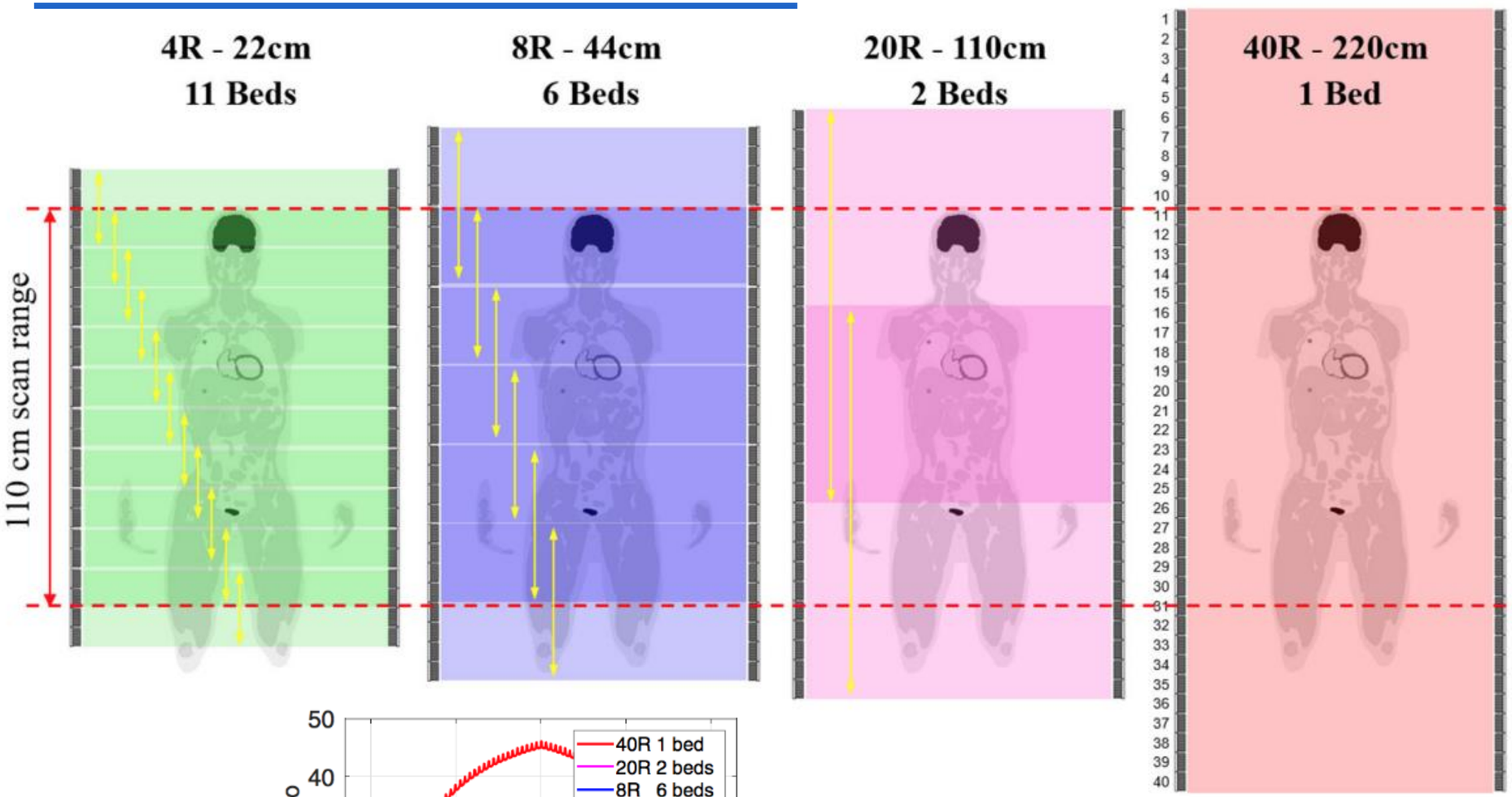
BODY SENSITIVITY

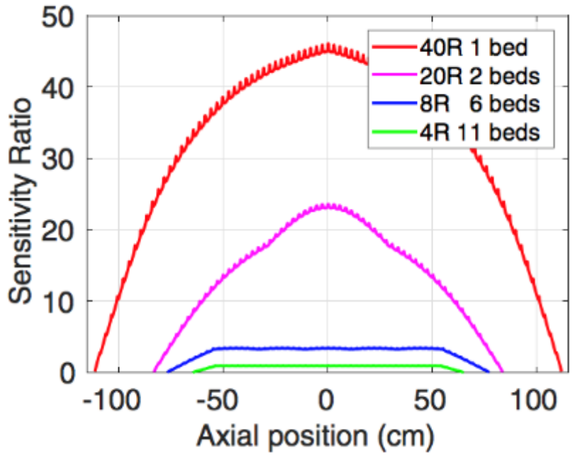
Physics in Medicine & Biology

PAPER

Theoretical study of the benefit of long axial field-of-view PET on region of interest quantification

Xuezhu Zhang[1], Ramsey D Badawi[1,2], Simon R Cherry[1,2] and Jinyi Qi[1]





For a 110 cm scanning range
Gain of 20 x higher for a 1 m long scanner (2 bed positions)
Gain of 40 x higher for a 2 m long scanner (1 bed position)
compared to a 22 cm long scanner (11 bed positions)

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The EXPLORER Project

Penn

UC DAVIS
UNIVERSITY OF CALIFORNIA

MiniEXPLORER-I

- Applications prototype
- Non-human primate imager
- Siemens technology platform

MiniEXPLORER-II

- Technology prototype
- Companion animal/human brain imager
- UIH technology platform

PennPET EXPLORER

- High TOF resolution (close to 200 ps)
- Torso imager
- Philips technology platform

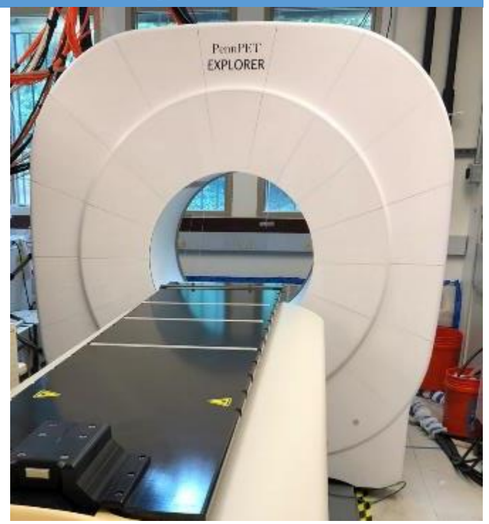
uEXPLORER

- High spatial resolution
- Total-body imager
- UIH technology platform

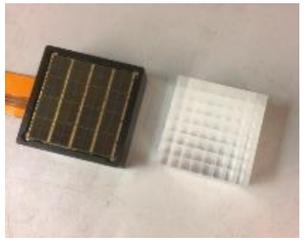
Slide courtesy of Joel Karp, UPENN

PennPET EXPLORER

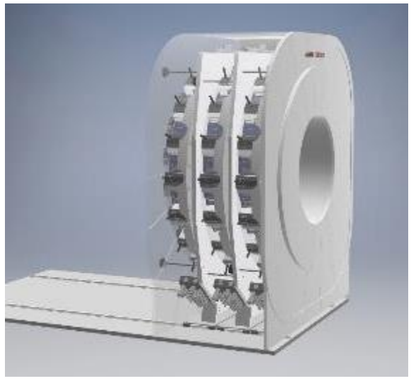
3 rings completed May 2018



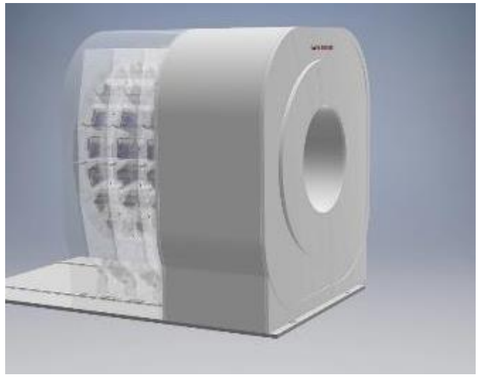
3.86 x 3.86 x 19 mm^3 LYSO
Philips DPC digital SiPM
(64 channels)



70 cm

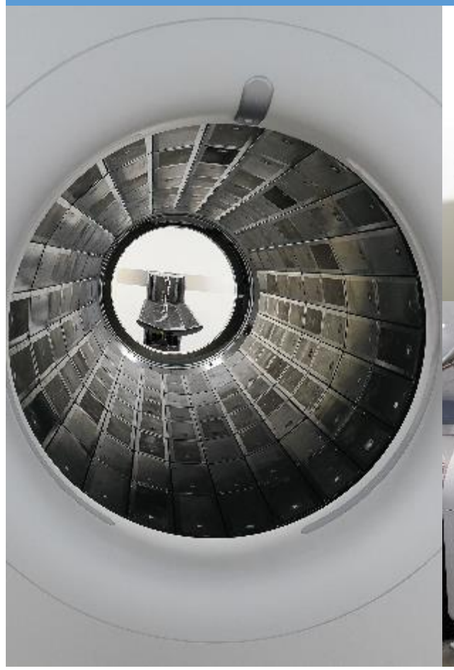


140 cm



UCDavis EXPLORER

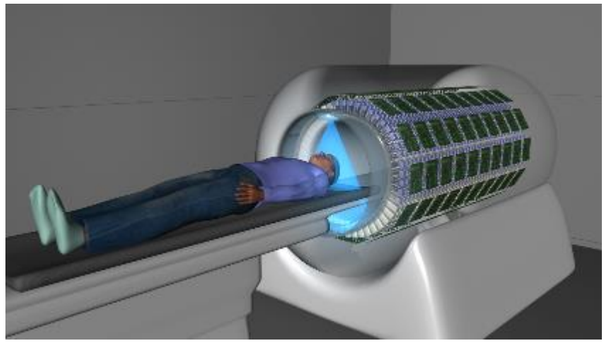
Scanner completed April 2018

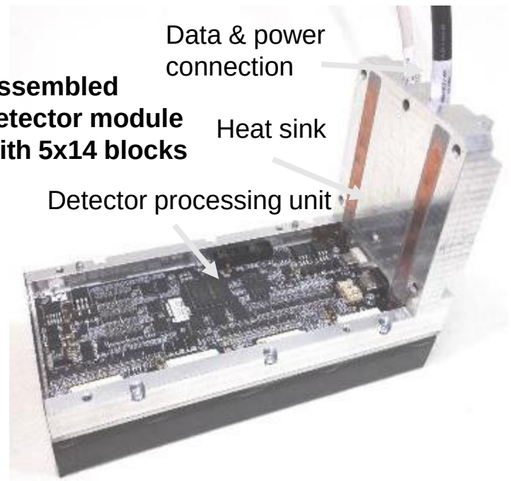


UNITED IMAGING

Crystals: 2.76 x 2.76 x 18.1 mm LYSO
Array: 7 (transaxial) x 6 (axial)
SiPMs: 4 - Sensl 6 mm J-series

200 cm





Measurements : *Count-rate Performance 70 cm PENN PET*

Siemens mCT- 22 cm aFOV

NECR peak ~ 180 kcps
TOF 540 ps

14-24 x effective gain

GE discovery MI- 20 cm aFOV

NECR peak ~ 180 kcps
TOF 385 ps

10-17 x effective gain

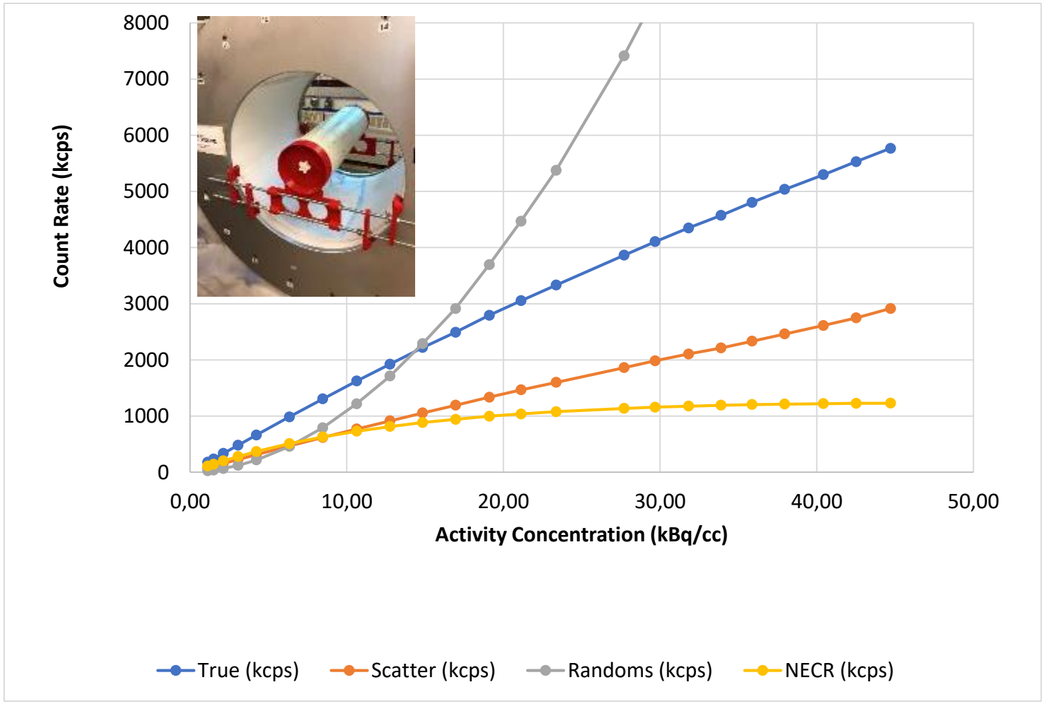
Biograph Vision-26.3 cm aFOV

NECR peak ~ 300 kcps
TOF 214 ps

3.4-5.7 x effective gain

- Trues linear over wide range
- Scatter fraction 32%
- **NECR peak ~ 1200 kcps**
- **TOF 250 ps**
- **28 % of ring not yet active !**

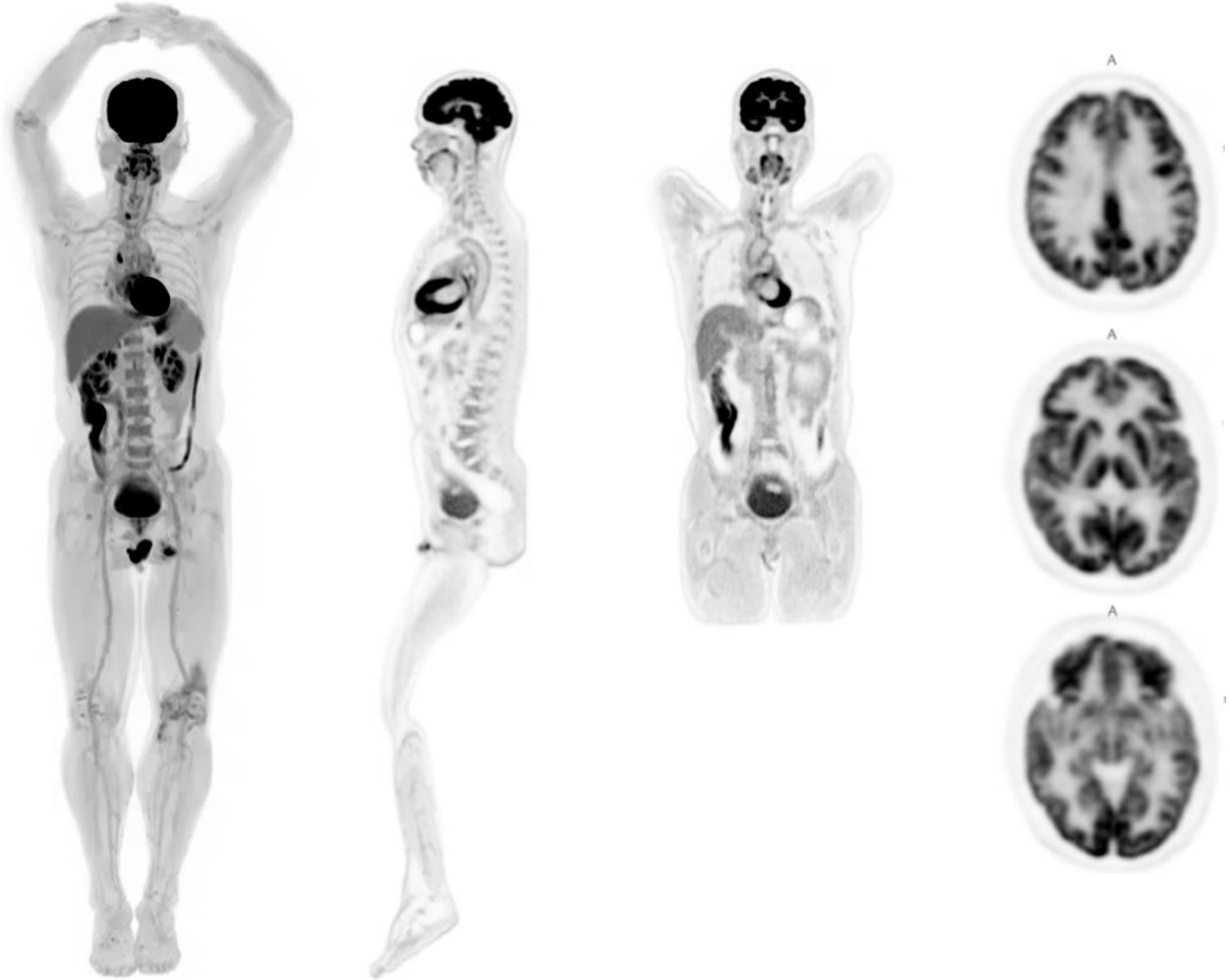
→ **final config > 2000 kcps NECR peak**



ref. Siemens mCT, Rausch et al , Discovery MI, Hsu, JNM, 2017, Biograph Vision B. Bendriem

Penn PET results courtesy of JS.Karp, UPENN

EXPLORER: First Human Images



7.8 mCi FDG
65 kg subject
20 minute scan
1 bed position
90 mins post-injection
OSEM with PSF and TOF
20 subsets, 5 iterations
1x1x1.425 mm^3 voxels

Courtesy of
UC Davis
United Imaging
Zhongshan Hospital

Check Youtube: Simon Cherry Explorer for movies

Explorer.ucdavis.edu/Media

FIRST SET OF CLINICAL RESULTS CONFIRMS OR EXCEEDS EXPECTATIONS

https://youtu.be/JaszDkmgfMY

JNM
The Journal of Nuclear Medicine

First Human Imaging Studies with the EXPLORER Total-Body PET Scanner*

Ramsey D. Badawi[1,2], Hongcheng Shi[3], Pengcheng Hu[3], Shuguang Chen[3], Tianyi Xu[4], Patricia M. Price[5], Yu Ding[4], Benjamin A. Spencer[1], Lorenzo Nardo[1], Weiping Liu[4], Jun Bao[4], Terry Jones[1], Hongdi Li[4] and Simon R. Cherry[1,2]

Image faster

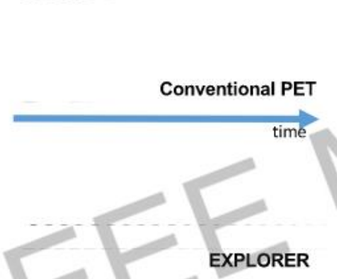
- **Total-body PET in 15-30 secs**
- Reduce respiratory motion
- Higher resolution

61-yo male, 65 kg; 164 cm; 7.8 mCi; 82 min p.i.; 20 min acq.
Credit: Zhongshan Hospital; Shanghai

20 min | 18.75 sec | uMI 780

Image longer

- Image for 5 more half lives
- Reveal kinetics inaccessible currently



56 kg female; 6.7 mCi injected activity; 14 min acquisition

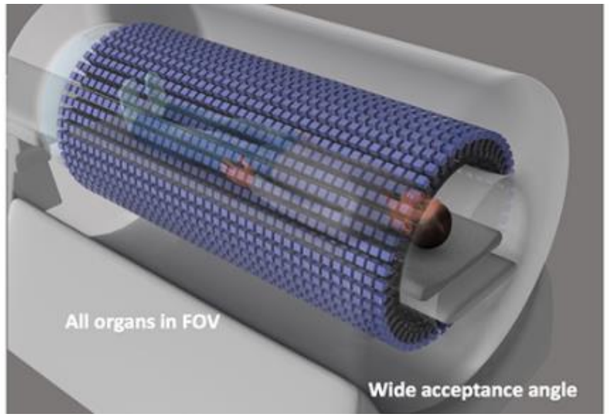
1 hour | 3 hours | 8 hours | 10 hours

NEXT STEPS: TOF, SPATIAL RESOLUTION AND DOI

Improve effective sensitivity by better TOF

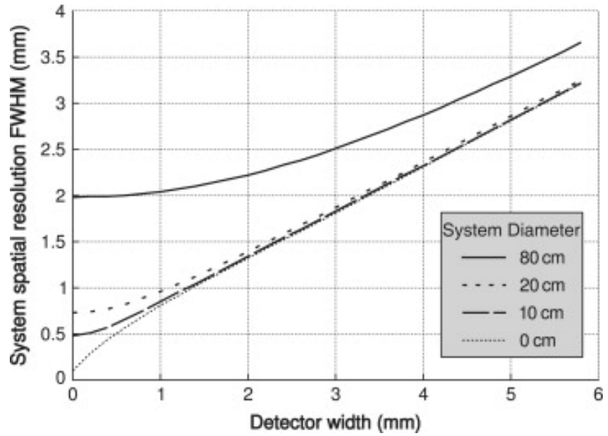
PennPET Explorer
250 ps

Siemens Biograph Vision
214 ps



Full body coverage → geometric sensitivity maximal
About 400 ps TOF
2.8 mm crystals
no DOI

Towards the 2mm limit of spatial resolution in clinical PET



The promise of nuclear medicine technology: Status and future perspective of high-resolution whole-body PET,Physica Medica, Klaus P.Schäfers

Transverse and axial DOI in TB-PET

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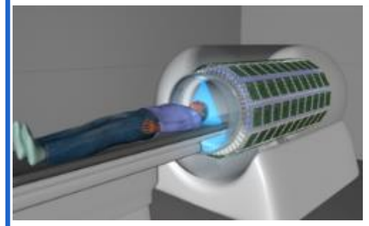
EXPLORER

Penn
University of Pennsylvania



15.5 M US$

Advancing the Potential and Promise of Total-Body PET Imaging
NIH, National Cancer Institute, Apr 7 2017

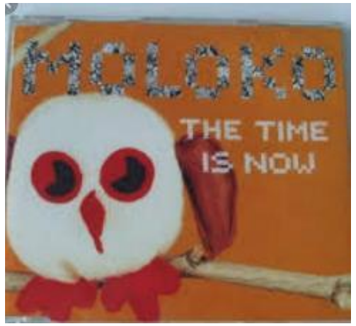
Neue Einblicke ins Körperinnere [New insights into the inner body]
Deutschlandfunk [Germany-Radio], Mar 31 2017, [Article only in German]

World's first full-body PET scanner could aid drug development, monitor environmental toxins
Science AAAS, Mar 17 2017, Get the journal article here

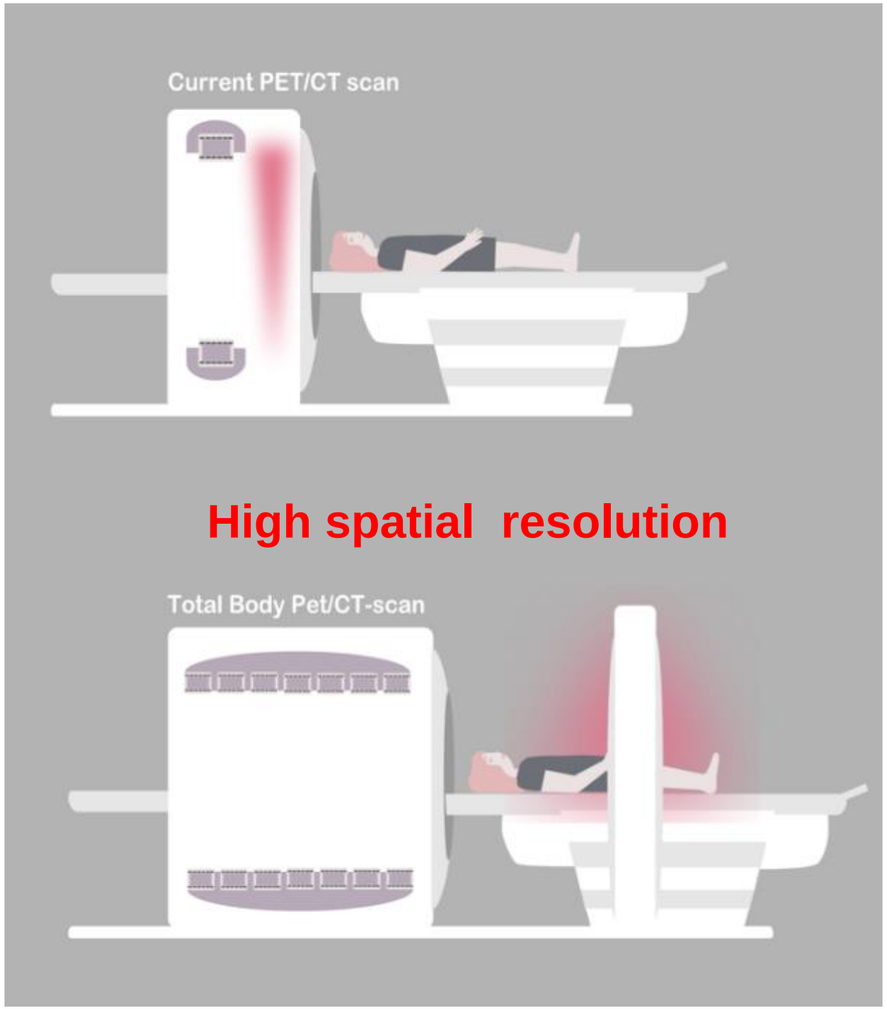
First Total Body PET Scanner Could Change Biomedical Research
Bioscience Technology, Mar 16 2017

NIH
National Institutes of Health

University of California, Davis
Project Title: EXPLORER: Changing the Molecular Imaging Paradigm with Total Body PET
Grant ID: R01-CA-206187



PET 2020
EUROPEAN EXPLORER IN GHENT



Medical cyclotron map Europe

Belgium = heart of Europe

Unique HR PET tech in Ghent

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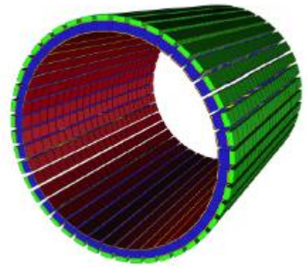
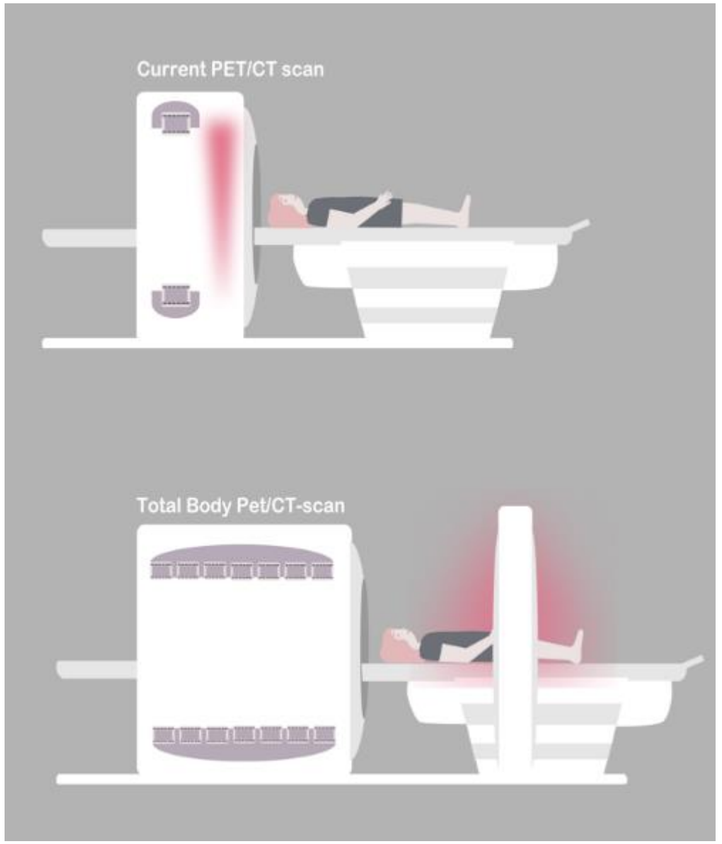
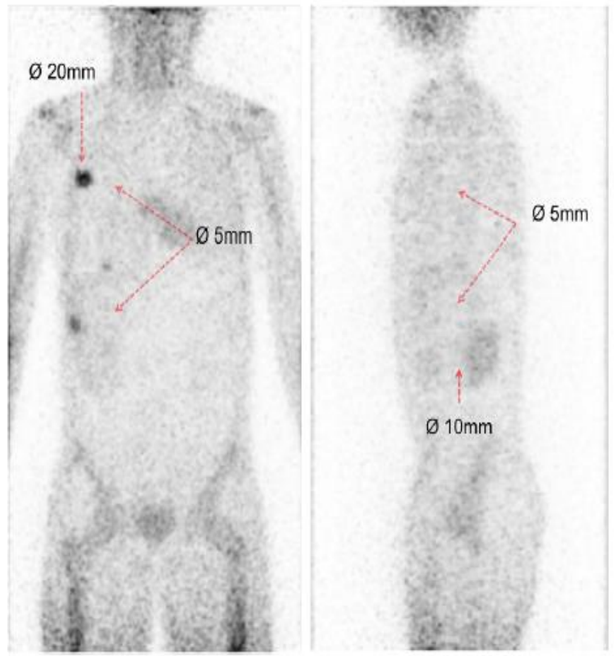
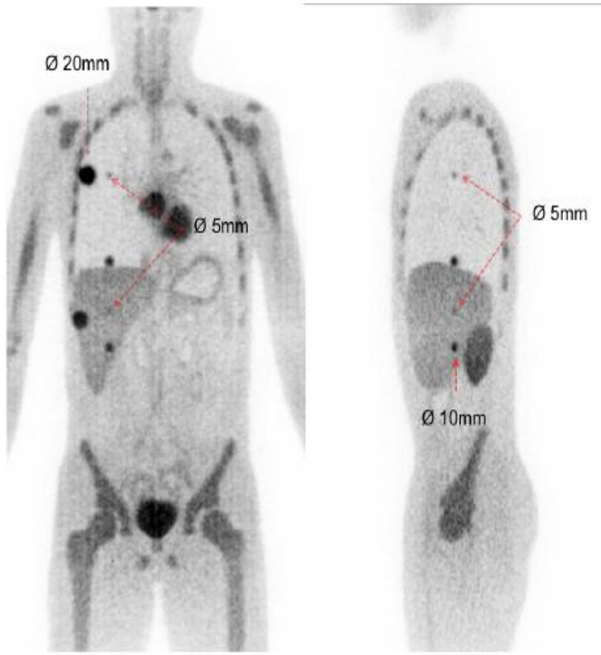
Slides courtesy of Stefaan Vandenberghe, Boudewijn Brans, Simon Cherry, Joel Karp

2019-2022: TOTAL BODY PET DEVELOPMENT BASED ON PRECLINICAL MONOLITIC DETECTOR TECHNOLOGY









Reconstructed distribution of a Monte Carlo simulation of a realistic FDG distribution in a 10 year old boy in 2 systems. Total dose was 40 MBq and acquisition time 3 min, data was reconstructed with same TOF reconstruction code.

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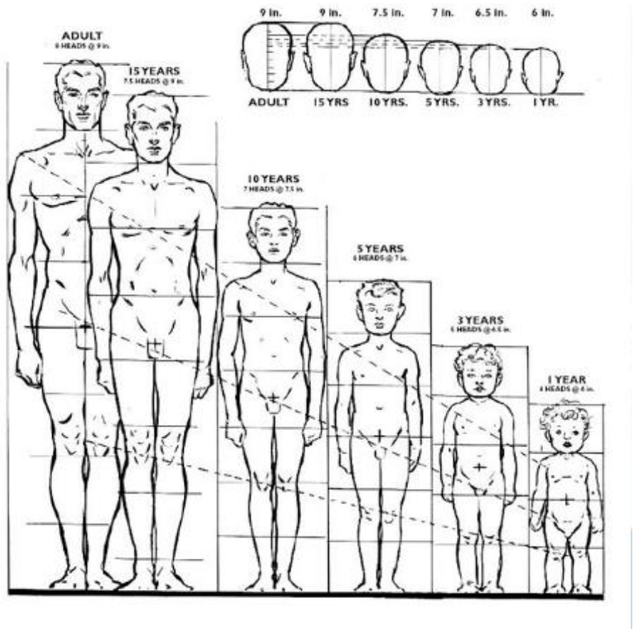
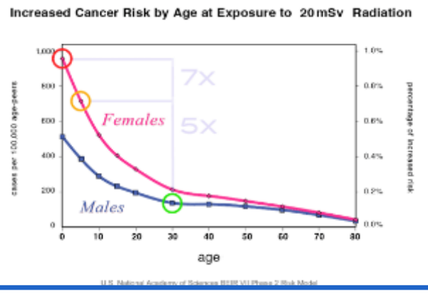
PET 20.0 AS A UNIQUE TOOL FOR PAEDIATRIC ONCOLOGY, NEUROLOGY AND CARDIOLOGY



Children more sensitive to radiation → Lower dose allowed

Spatial resolution needs to be improved due to reduced size

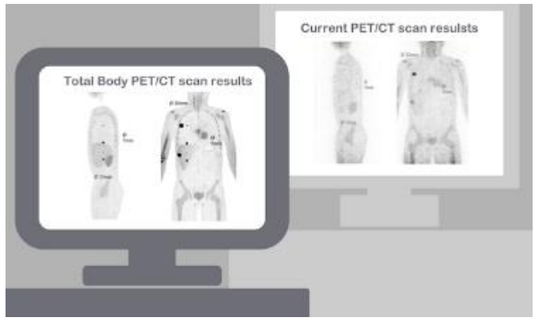


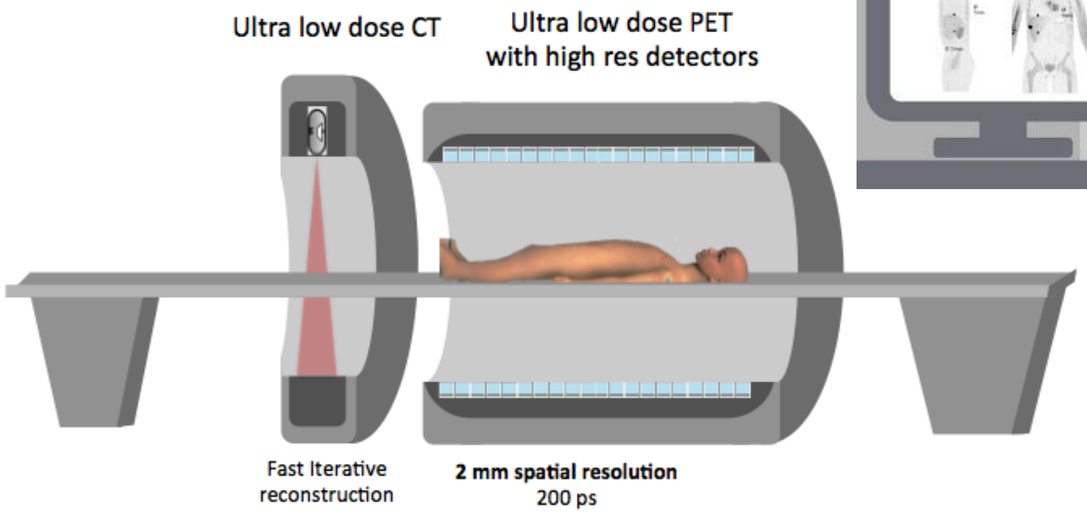
BARCO Visibly yours

Adaptive child friendly ambient room

MOLECUBES MODULAR BENCHTOP IMAGING

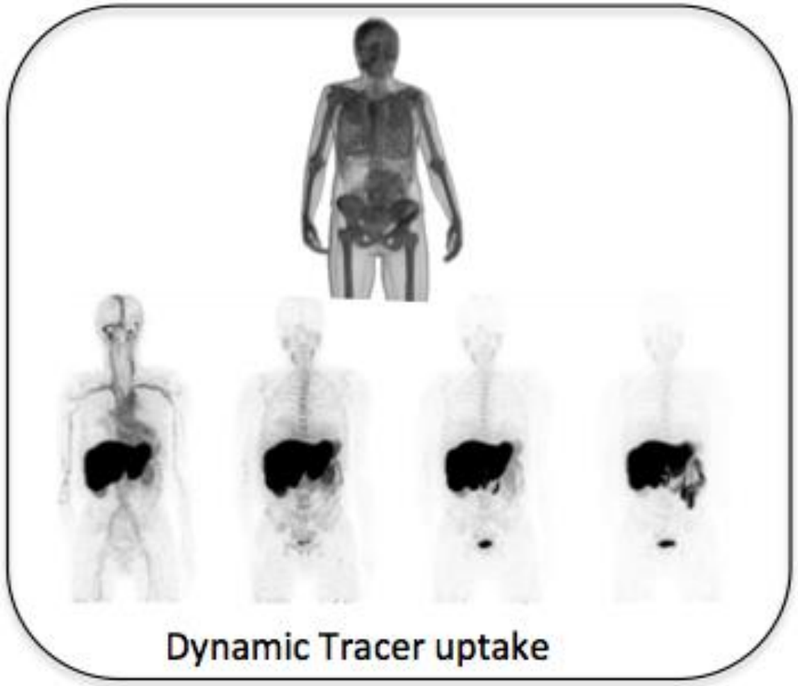
Bringing preclinical resolution to the clinic



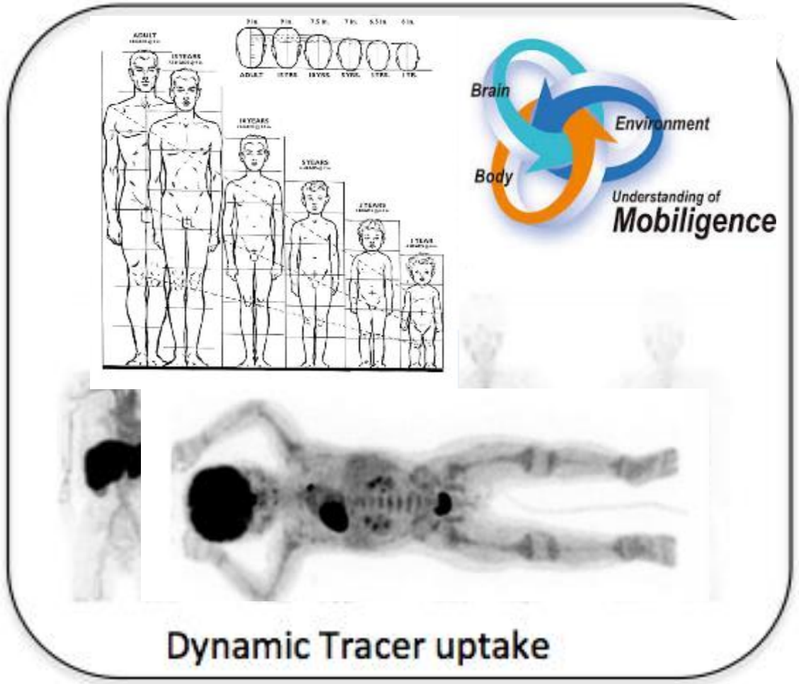


PET 2020 : 4D MOLECULAR IMAGING PHARMA

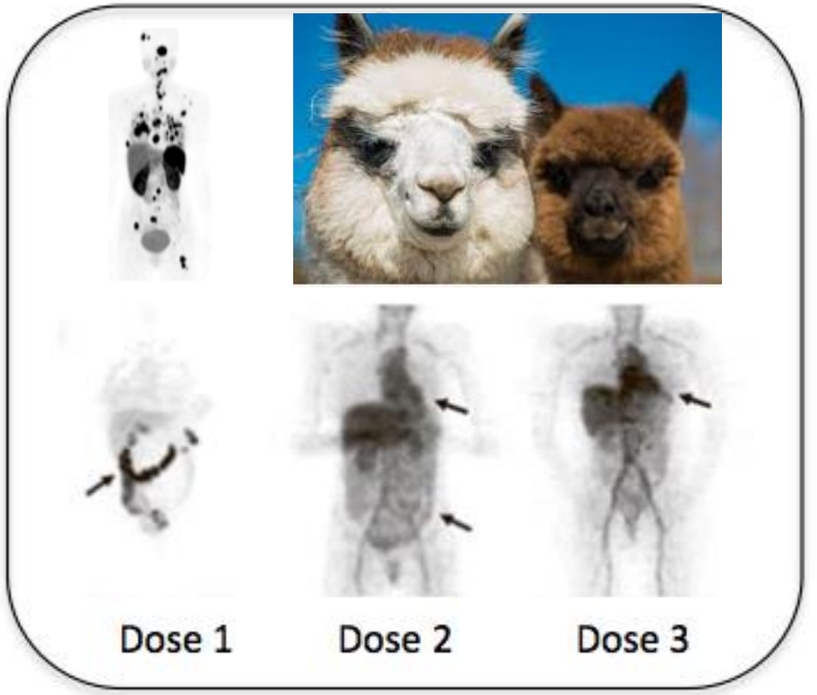
New tracers



Faster lower dose
Total body



Theranostics Therapy
Drug dosing



INSTITUT
JULES BORDET
INSTITUUT

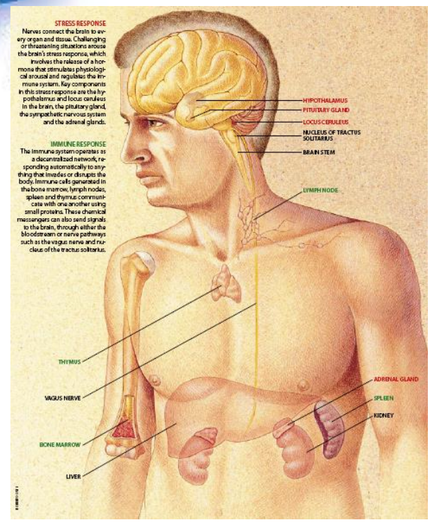
GHENT
UNIVERSITY

Vrije
Universiteit
Brussel

Evaluation at ultra low dose
Dynamic Imaging

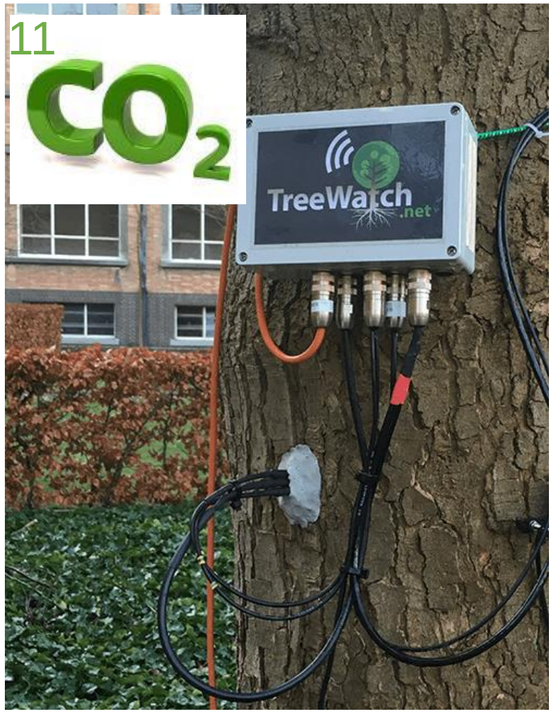
PET 20.0 AS A FUNDAMENTAL SCIENCE TOOL

Brain-body interaction



Larger animals

Plants



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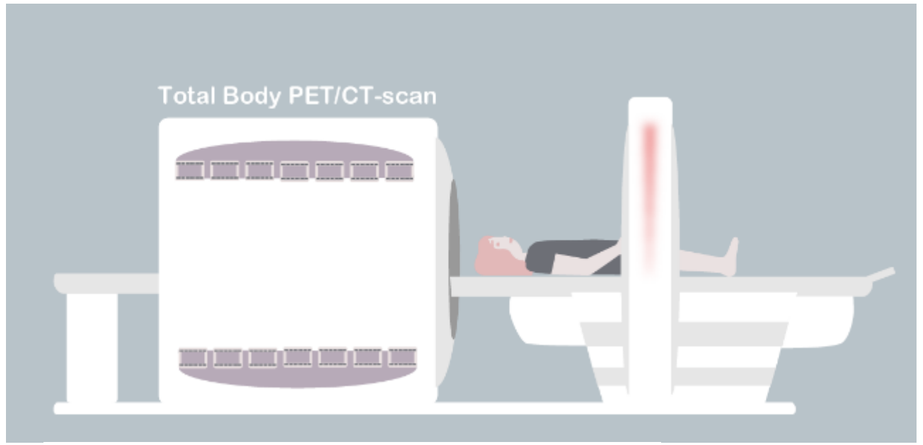
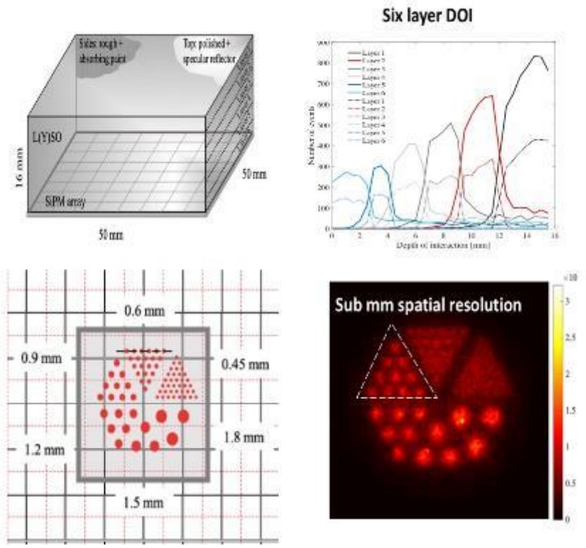
PET-2020





16 mm thick LYSO
6 layers DOI
Submm resolution
1Mcps

Detector

Monolithic 16 mm thick LYSO

Readout by analog SiPMs

Detectors have **sub mm intrinsic spatial resolution**

Light sharing + fine sampling + Advanced positioning

6 layer DOI

Cost effective base geometry

70 cm long - 70 cm bore

System performance

2-2.5 mm system spatial resolution over whole FOV

3-4 times faster for single organ imaging

9-10 x faster for routine clinical FDG body PET imaging

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Submitted to PMB, Mariele Stockhoff, PhD Ugent

GE discovery MI 4-ring- 20 cm

Pixelated
25 mm thick LYSO
20 cm long - 85 cm bore
13 Liter-94 kg LYSO

0.5 m² SiPM

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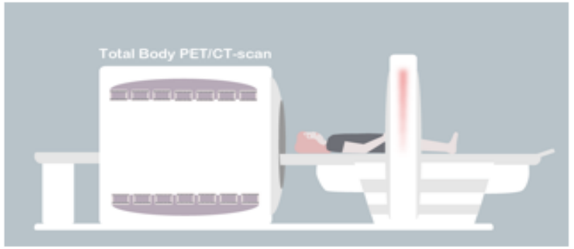
1.9 x more Scintillator

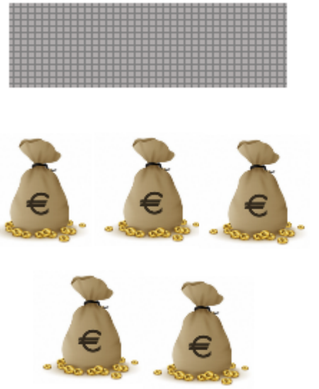
3x more Light Detector

PET-2020



Monolithic
16 mm thick LYSO
70 cm long - 70 cm bore
25 Liter-180 kg LYSO *

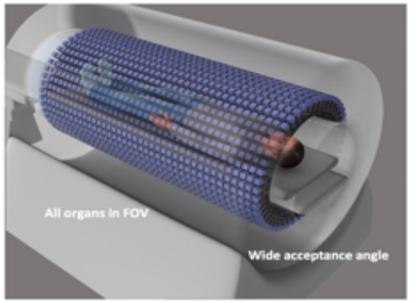
1.5 m² SiPM



3.5 x more Scintillator

1.5-3.3x more Light Detector

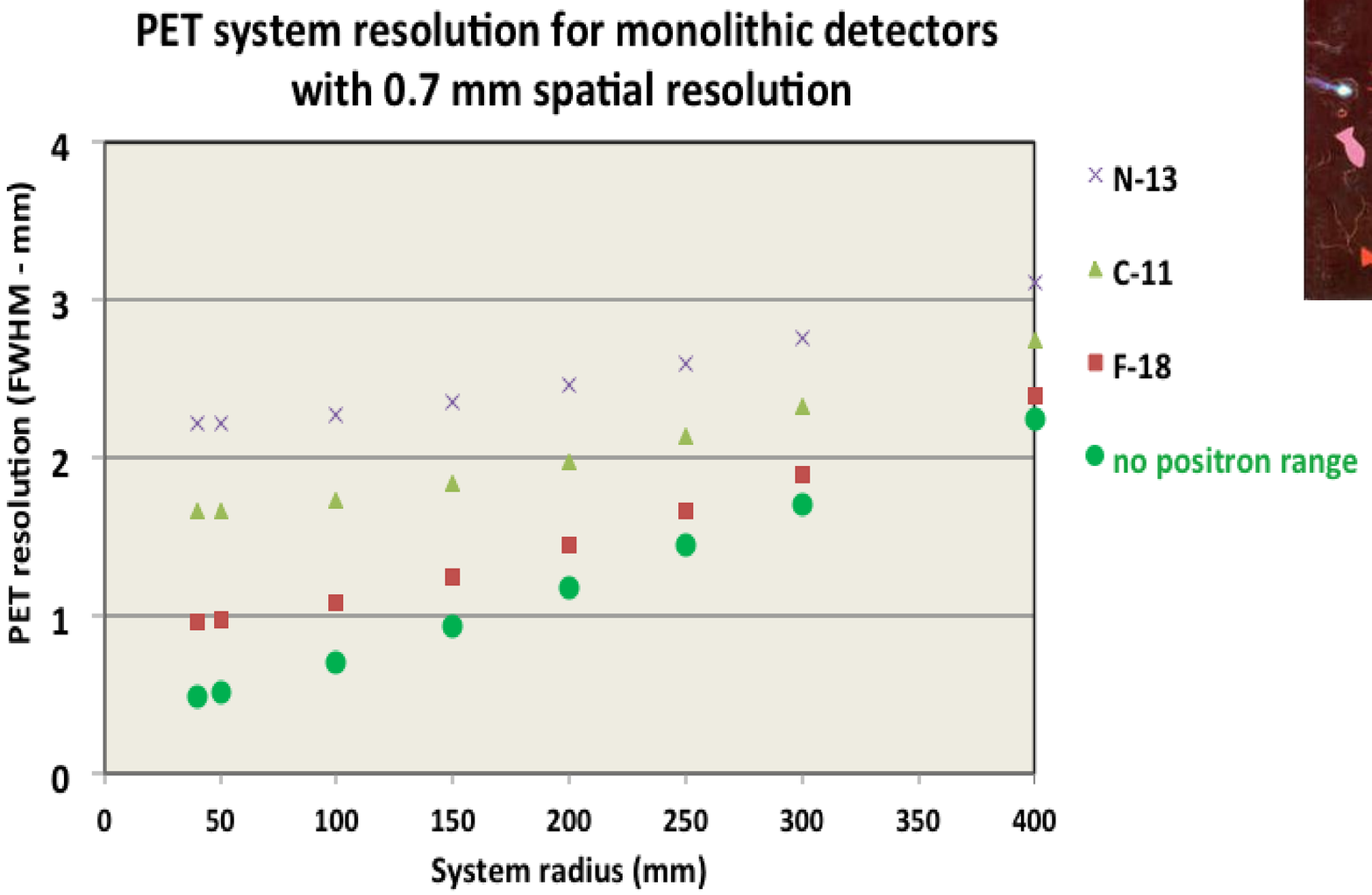
Explorer



Pixelated
18 mm thick LYSO
198 cm long – 78.6 cm bore
88 Liter-624 kg LYSO

5 m² SiPM **

ACOLINEARITY DOMINATES CLINICAL PET IN THE LIMIT



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VERITON: DESIGNED FOR SPECT IMAGING

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SPECTRUM DYNAMICS MEDICAL

ADAPTIVE RESEARCH MODE: **PET2020 HRS** (HIGH RESOLUTION SENSITIVITY)

- Starts from base configuration
- **No additional detectors**
- Requires only additional **mechanics and software**

- Adapts to objects between
  - Transverse: 35 cm-70 cm diameter (but still circular)
  - Axially max 140 cm (dynamic mode)

- Increases performance (resolution + sensitivity) for most objects

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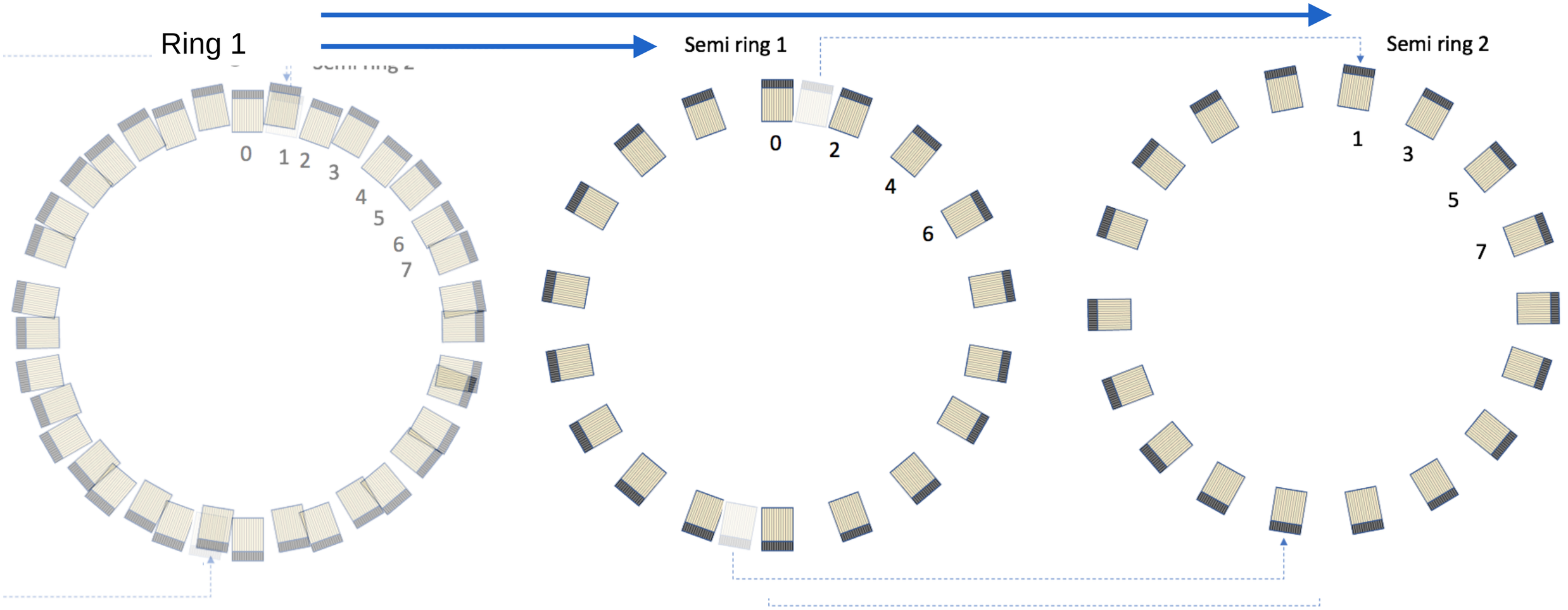
ONE RING IS/ARE TWO SEMI-RINGS BY AXIAL SPLITTING



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High sensitivity single organ imaging
Fast continuous static body scans
Easier access

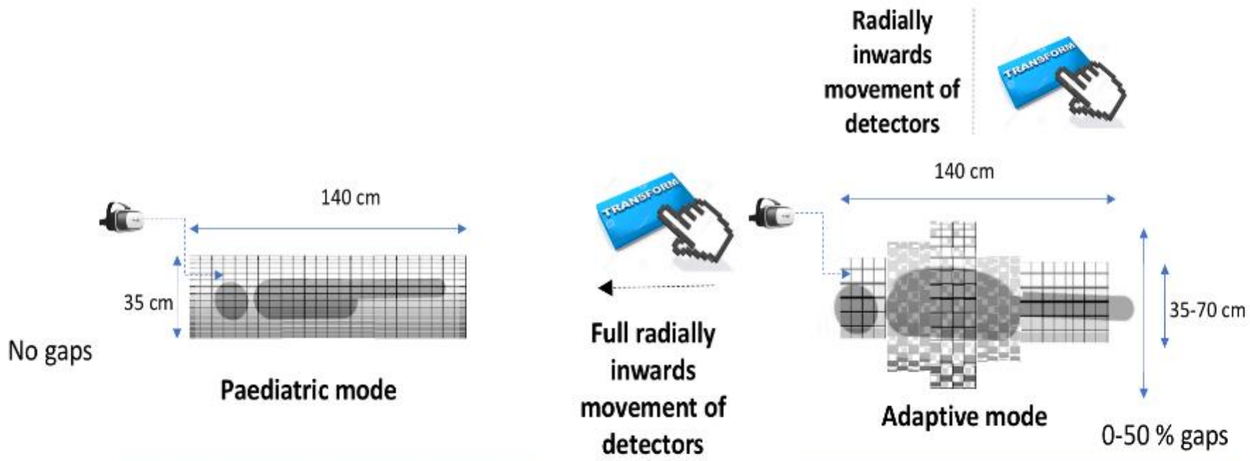
Speed vs 20 cm
9-10x faster (for body imaging)
3-4 for single organ imaging

Spatial resolution of 2 mm
with monolithic

Total body imaging
Fast continuous body scans
Long axial FOV

Speed vs 20 cm
9-10x faster (for body imaging)

Spatial resolution of 2 mm
with monolithic



Total body imaging of small object (paediatric)
Fast dynamic scans

Speed vs 20 cm
30-40 x faster (for body imaging)

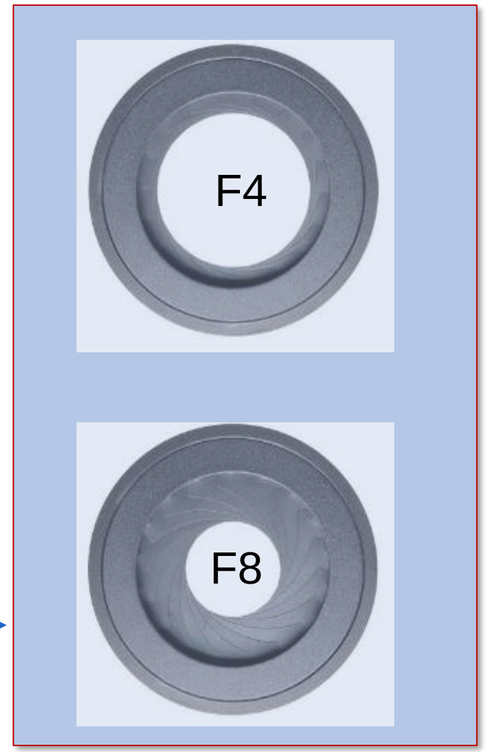
High spatial resolution with 1 mm monolithic
+ 6 layer DOI
→ < 1.5 mm

Adapts to patient body
Fast dynamic body scans
Brain body interactions

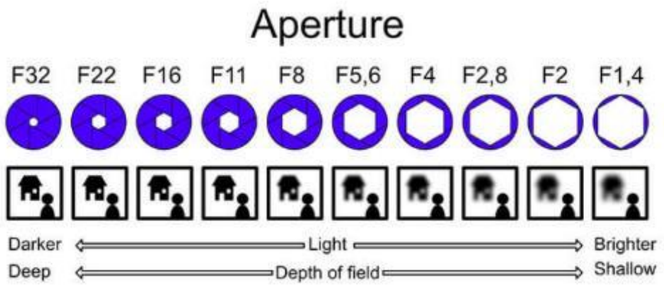
Speed vs 20 cm
15-25 x faster (for body imaging)

High spatial resolution with 1 mm monolithic
+ 6 layer DOI
--> < 1.5 mm

Adaptive per ring based on one motor and camera aperture principle

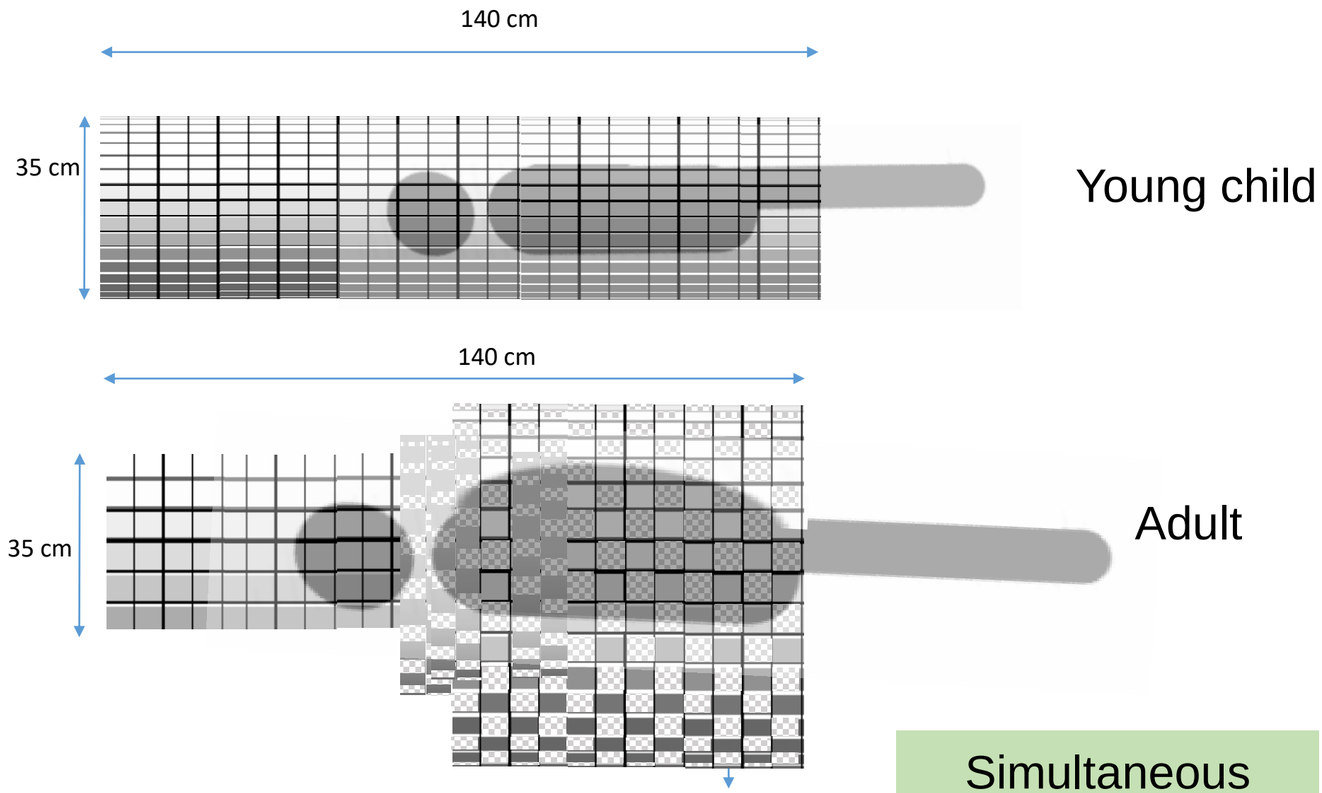


Penn
University of Pennsylvania



ADAPTIVE HIGH SENSITIVITY BRAIN + TORSO MODE

Almost complete solid angle coverage above head for all patients



Simultaneous Input function from blood/aorta

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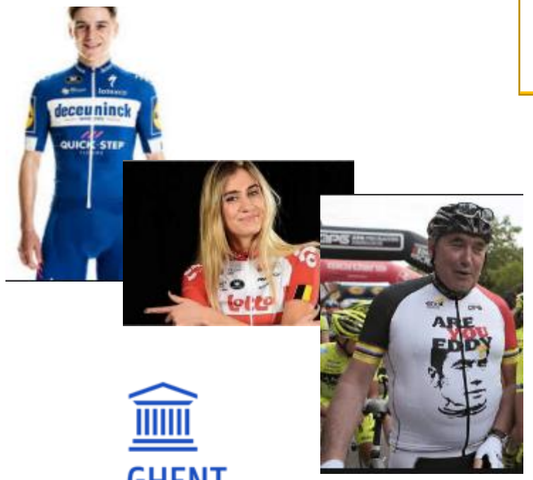
ADAPTIVE APERTURE PET



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Small bore ?

Hypothyroid in cats

Please, no CAT scan again

I better fit in here !

Lion Columbus zoo, Ohio imaging center, refurbished GE LightSpeed 16-slice CAT scanner

FACULTY OF ENGINEERING AND ARCHITECTURE

INTRO	MOLECULAR IMAGING WITH PET AND SPECT
THE PAST	PRECLINICAL IMAGING
THE PRESENT	TOTAL BODY TRANSLATIONAL IMAGING
THE FUTURE	**TB MOLECULAR PHARMA AND TREATMENT**

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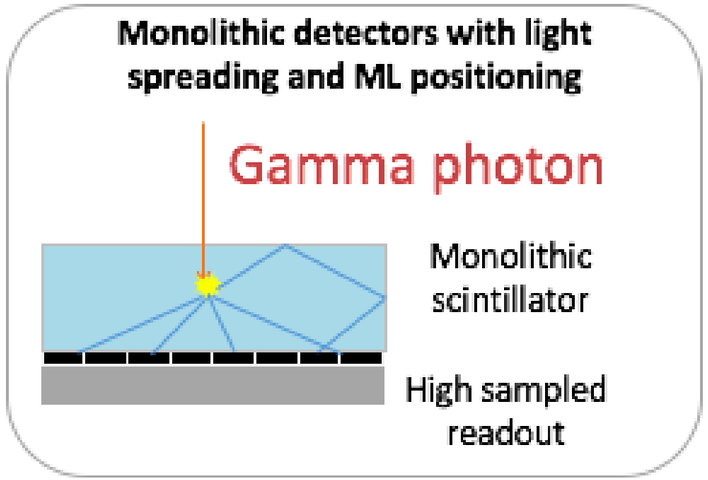
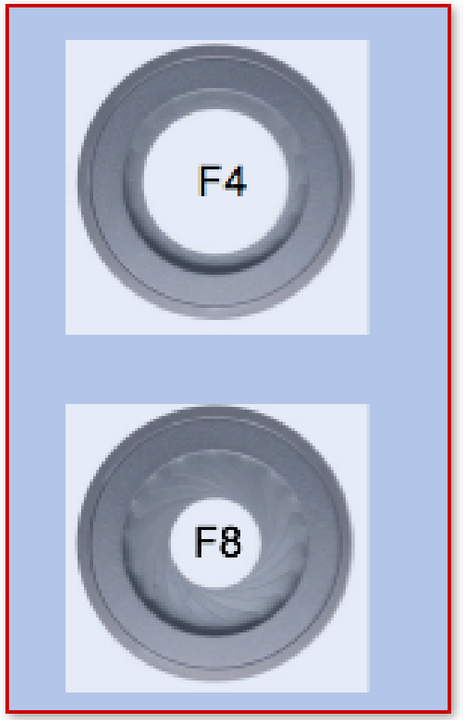
PET2020 IS VERY STRONG COST-EFFECTIVE COMBO

3D detector



Compact parallel computing

Simple Adaptive Mechanical design



Real time positioning

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3D listmode TOF acquisition and reconstruction

University of Pisa

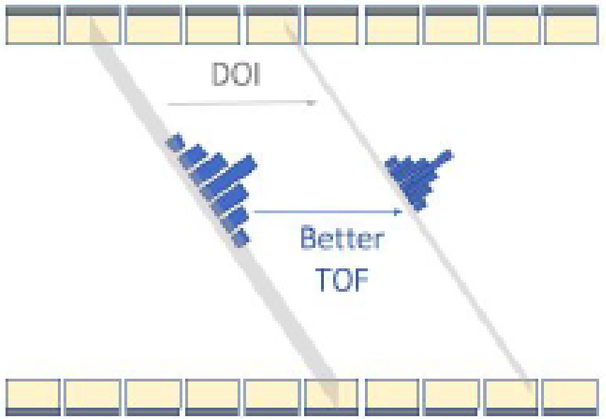
https://www.labworld.it/utofpet-sviluppera-nuove-tecnologie-per-rivelatori-pet/

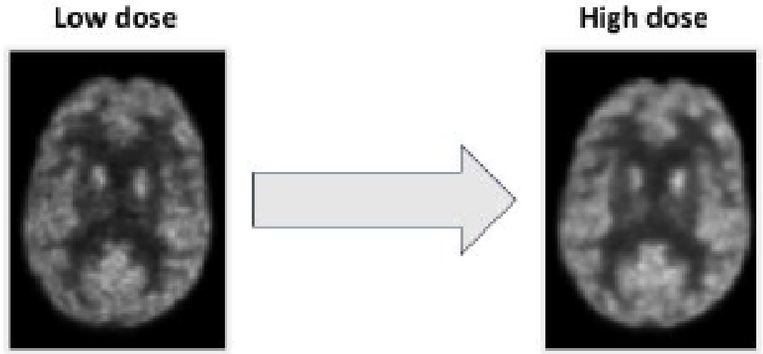
DEEP LEARNING (WELL DEFINED TASKS) AT DIFFERENT LEVELS

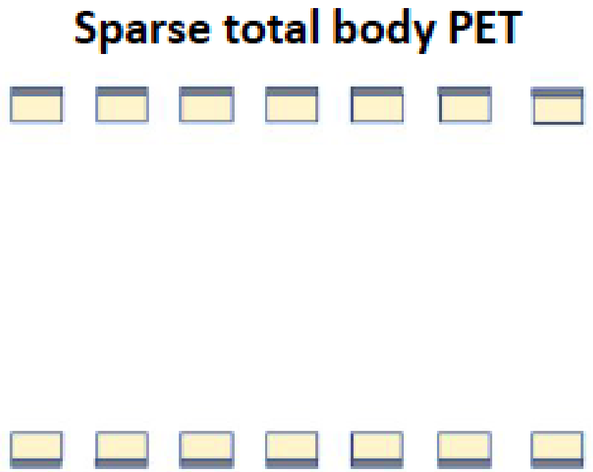
ACQUISITION

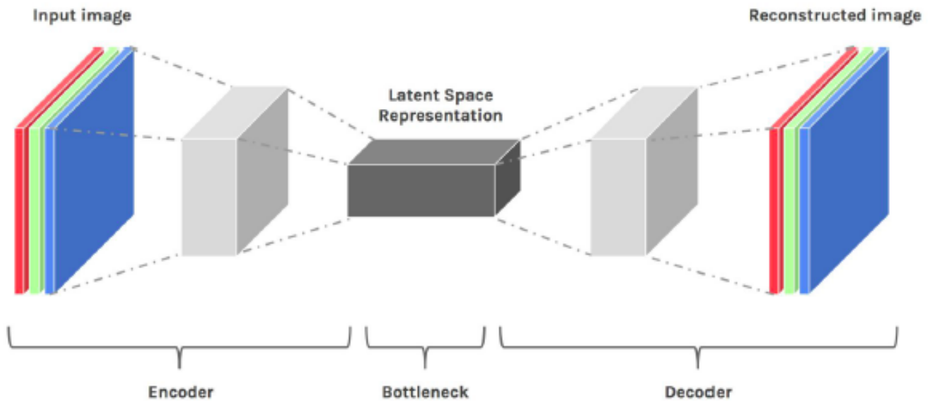
LOW NOISE RECONSTRUCTION

SYSTEM DESIGN









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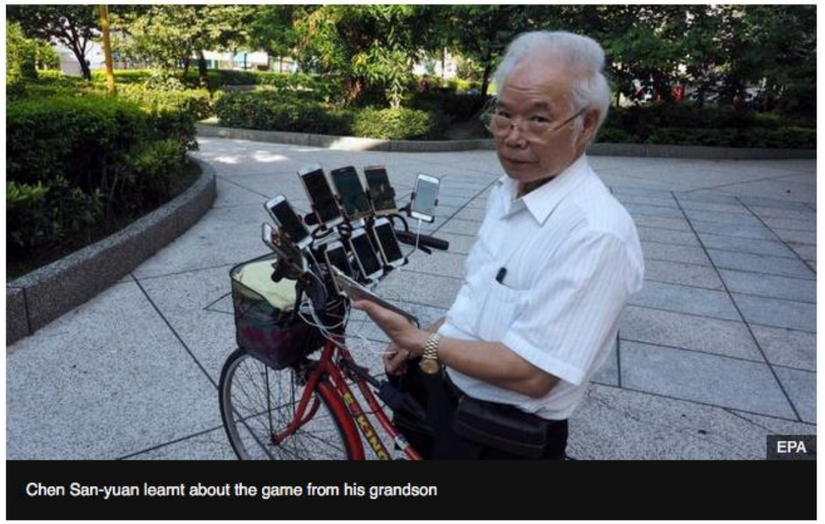
PET2020 WILL USE THE BEST CRYSTAL DOUBLE DOPING (LEGAL ☺)

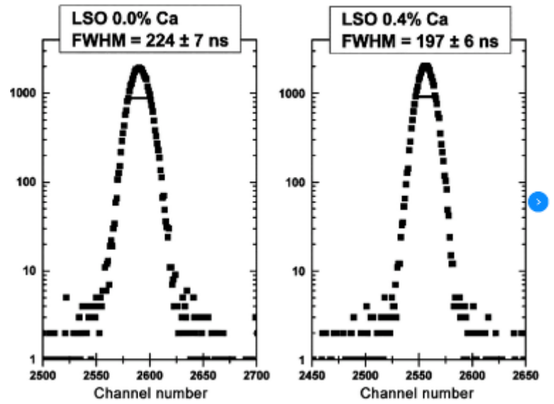
Taiwan man rigs bike with 11 phones to play Pokemon Go

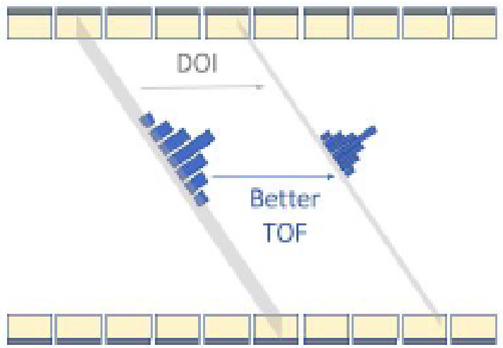
9 August 2018 Share



Chen San-yuan learnt about the game from his grandson

If you're going to catch them all, you need to have the right kit.





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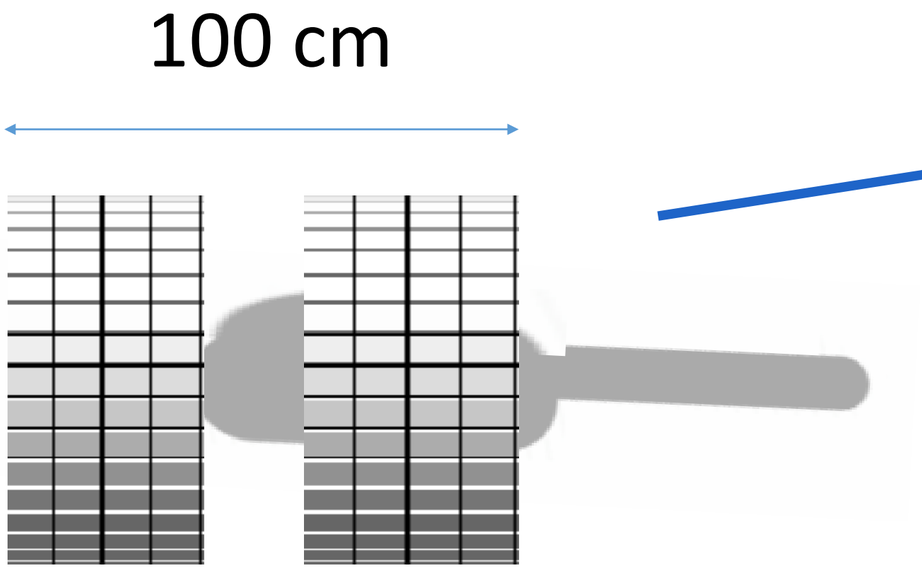
HIGH SENSITIVITY IN-BEAM IMAGING

3D information with simultaneous beam



FDG imaging while treating

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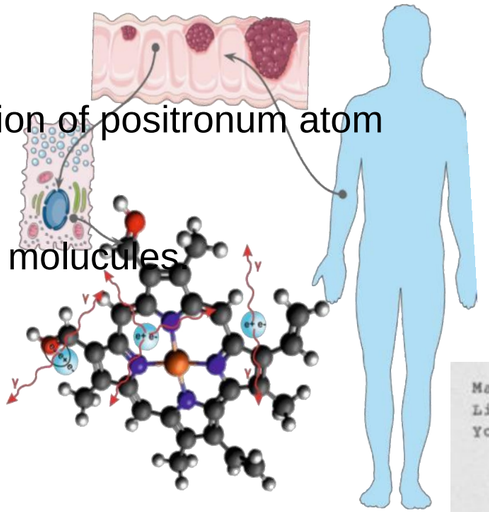
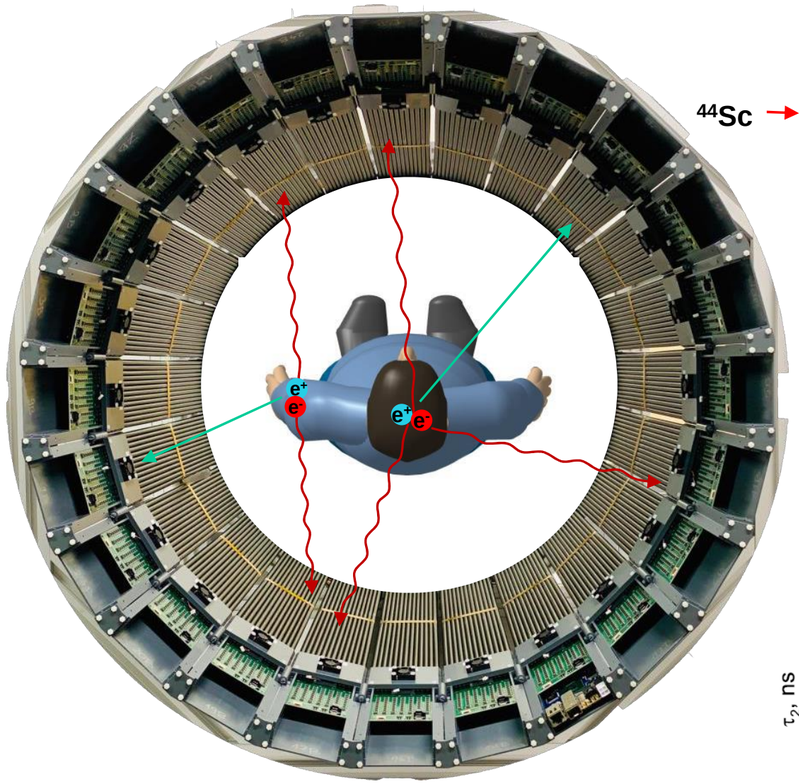
POSITRONIUM LIFETIME IMAGING

Positronium Imaging (P. Moskal et al., Phys. Med. Biol. 64 (2019) 055017)

Combination of metabolic and morphometric imaging

In about 35% cases e+e- annihilation proceeds in the body via formation of positronium atom
Due to the interaction with the electrons from surrounding atoms
mean life-time and ratio of 2γ to 3γ dacay rate of positronium
depend on the nano-structure of cells and concentration of bio-active molucules.
Ortho-positronium mean lifetime changes from 142 ns in vaccum
to 1.8 ns in water.





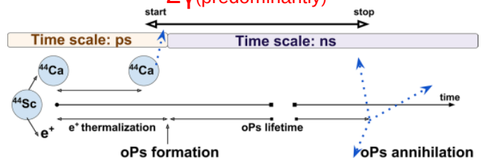
J-PET modular scanner

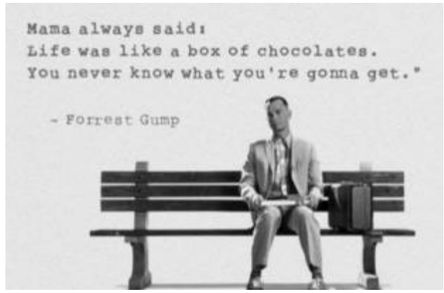
$^{44}Ca^* \rightarrow {}^{44}Ca + \gamma$ (promt gamma)

$^{44}Sc \rightarrow {}^{44}Ca^* + e^+ + \nu_e$

$e^+e^- \rightarrow Ps \rightarrow 2\gamma, 3\gamma$

2γ (predominantly)

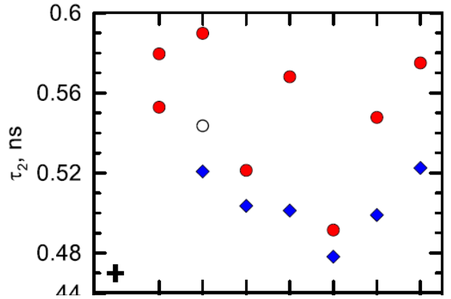


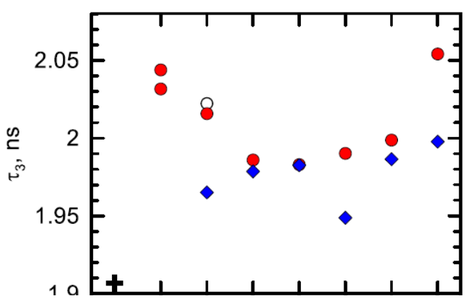


GPS reconstruction:
A. Gajos et al.,
Nucl. Instr. Meth. A **819 (2016)** 54

In-vitro studies comparing the positronium properties in cancerous and healthy tissues suggest that the ortho-positronium mean lifetime is correlated with the grade of development of metabolic disorders in cancer cells.

B. Jasińska et al., Acta Physica Polonica B 48 (2017) 1737





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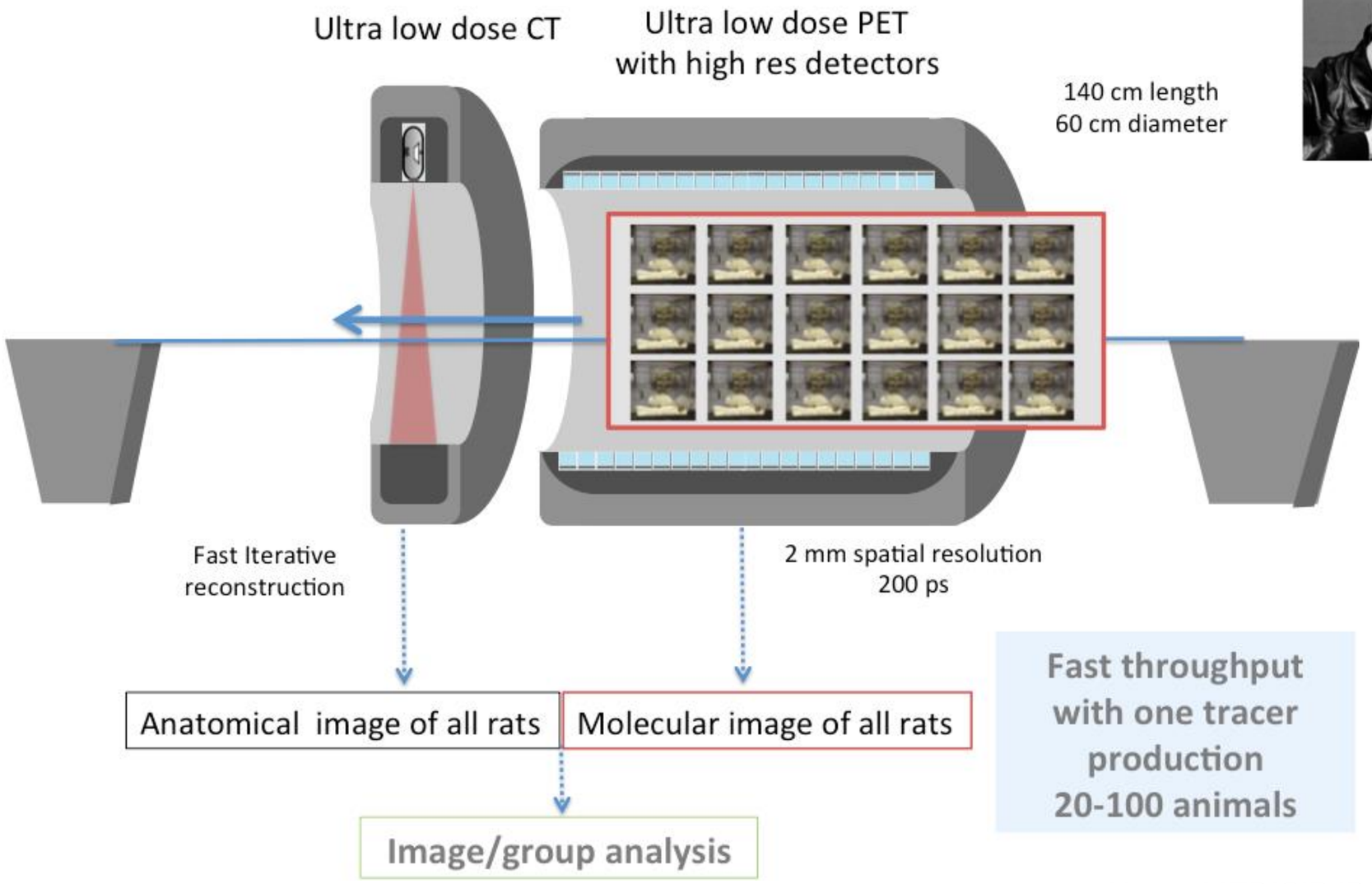
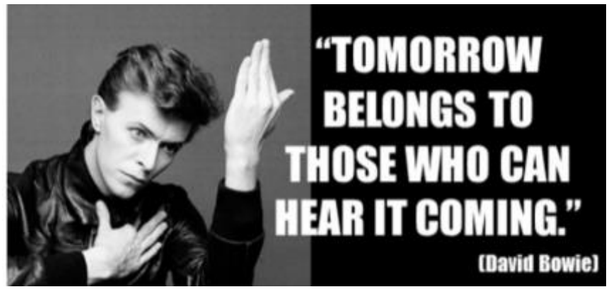
PET 20.0 AS A TOOL FOR PHARMA RESEARCH

Animal hotel imaging on total body PET-CT





One pharma study in one day

Fast throughput with one tracer production 20-100 animals

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Ugent-MEDISIP IDF to be filed in April 2017

SUMMARY

1. High resolution detectors (sub mm intrinsic) are the basis of this innovative Total Body system
2. Unique high resolution (2 mm)
3. Optimal length for routine PET imaging (90 % of studies are FDG body)
4. Fast throughput for routine imaging
5. Adapts in a simple mechanic transformation to smaller or longer objects
6. Cost-effective (only 2-3 x detector material of current PET-CT)
7. Adapts to a wide range of subjects-One PET fits all
   - axially: standard 70 cup to 140 cm axial lenght
   - transverse to subjects of 35 to 70 cm diameter

Future projects

- In-beam imaging
- Lifetime Positronium imaging
- Molecular guided pharmacy
- Molecular guided interventions

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TOTAL BODY PET 2020: FIRST ANNOUNCEMENT

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Penn

UCDAVIS
UNIVERSITY OF CALIFORNIA

THE UNIVERSITY OF EDINBURGH

FACULTY OF ENGINEERING AND ARCHITECTURE

Thank You!

INTERESTED IN COST EFFECTIVE TOTAL BODY PET

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☎ 0032 93325854

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GE discovery MI 4-ring- 20 cm

GE discovery MI

Pixelated

25 mm thick LYSO

20 cm long - 85 cm bore

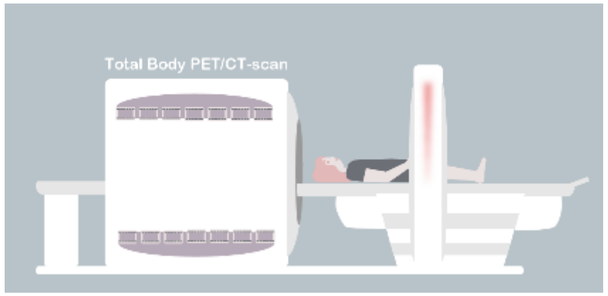
13 Liter-94 kg LYSO

0.5 m² SiPM

1.9 x more Scintillator

3x more Light Detector

PET-2020



Monolithic

16 mm thick LYSO

70 cm long - 70 cm bore

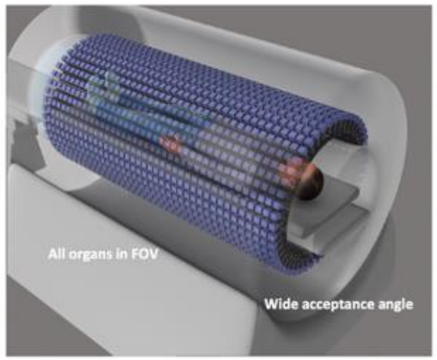
25 Liter-180 kg LYSO *

1.5 m² SiPM

3.5 x more Scintillator

1.5-3.3x more Light Detector

Explorer



Pixelated

18 mm thick LYSO

198 cm long – 78.6 cm bore

88 Liter-624 kg LYSO

5 m² SiPM **

* Monolithic LYSO about 12 % more expensive for same volume than pixelated 4x4 mm

** area reduced by the staggered SiPM approach

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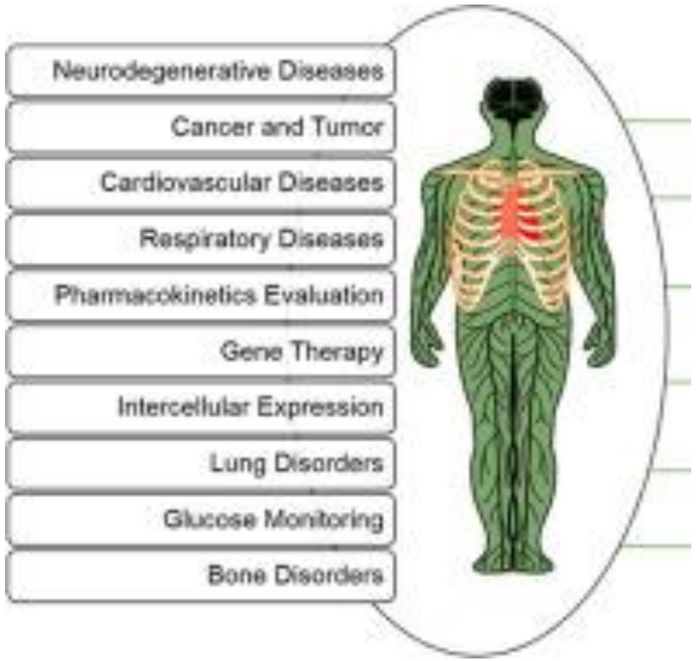
WHY MOLECULAR IMAGING ?



RX and CT are visualizing anatomical structure via density

Very useful for diseases with clear changes in density: stroke, fractures, kidney stones, ….

These changes happen quite late in other diseases: Cancer, Alzheimer,…

Molecular imaging for early detection and disease and treatment monitoring and for pharmacology

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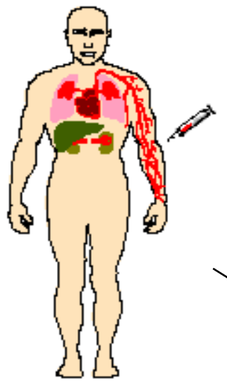
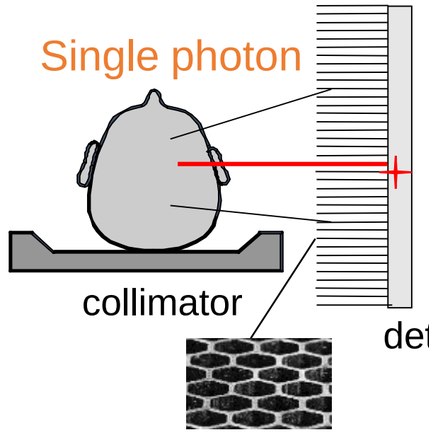
SPECT VERSUS PET

Injection of radioactive Labelled molecule (single photon or positron emittor)



Single Photon Emission CT (SPECT)

Single photon



collimator

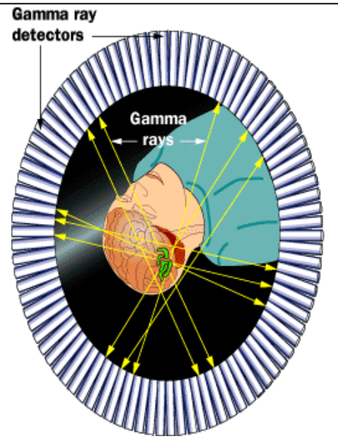
detector

511 keV foton

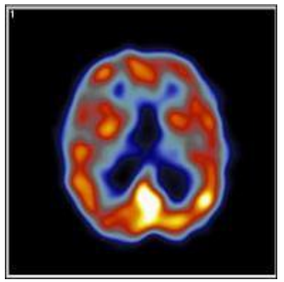
positron

annihilation positron with elektron

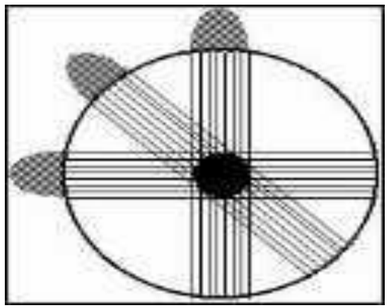
511 keV foton

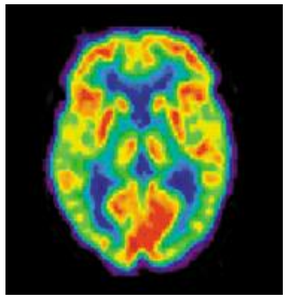


Positron Emission Tomography (PET)



Reconstruction





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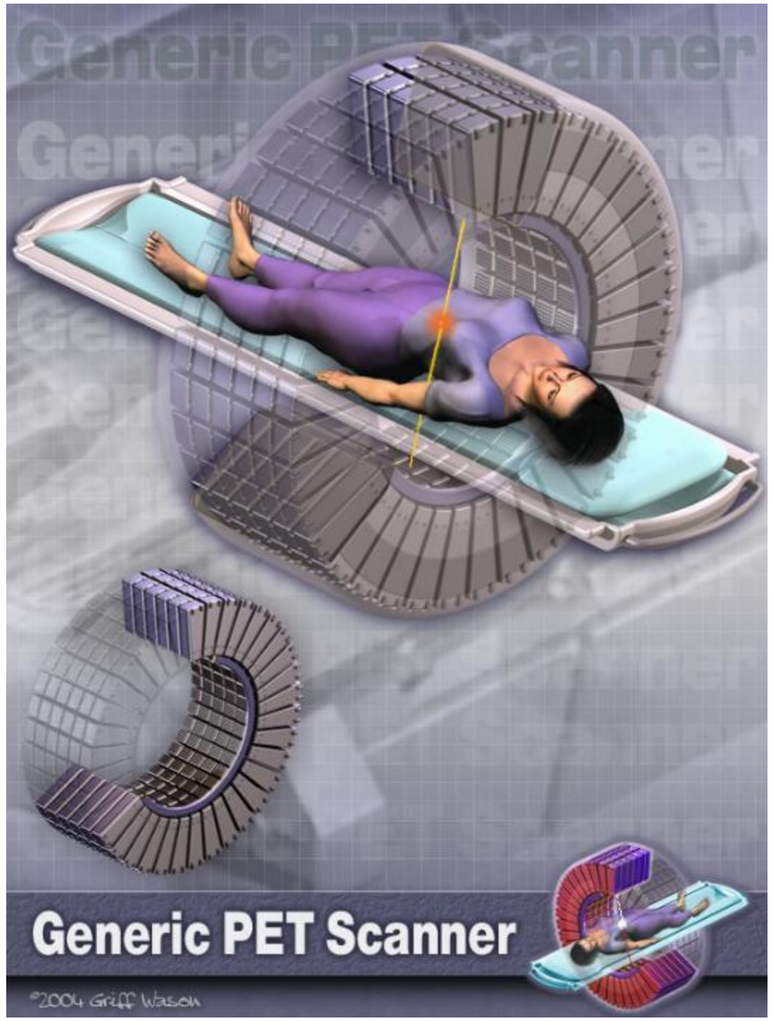
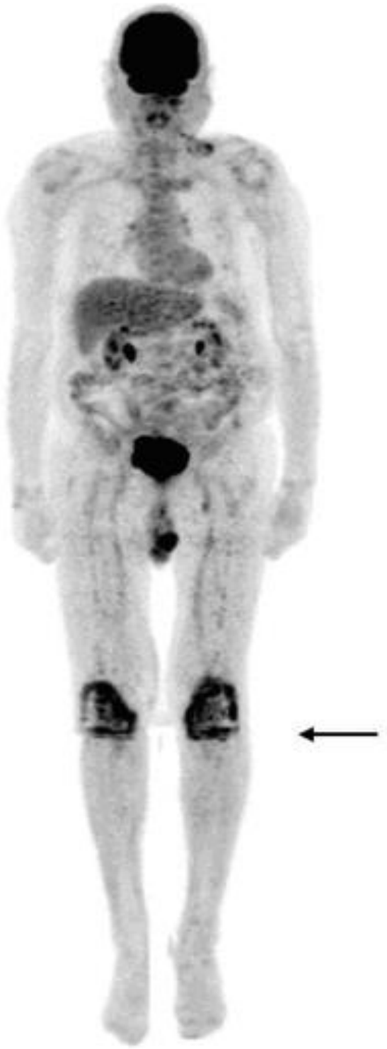
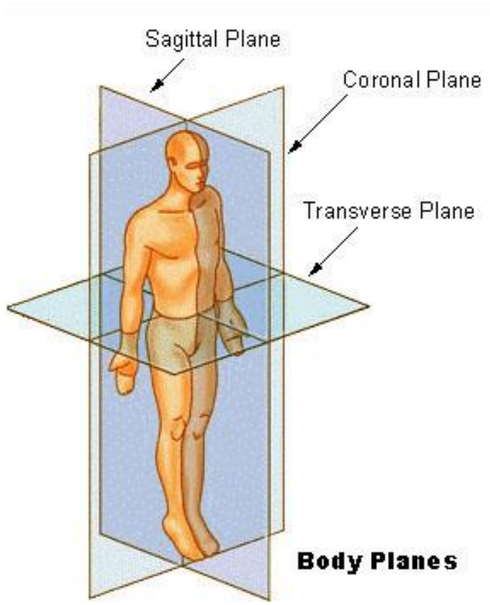
PET IS A STATIONARY TOMOGRAPHIC SYSTEM WITH HIGH SENSITIVITY





10-20 minutes for a total body PET-CT scan



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200 YEARS
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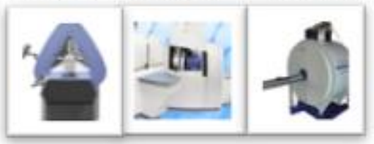
Molecular imaging Gent 2016

IMIT - Innovative Molecular Imaging and Therapy consortium

Imitghent.be

Preclinical imaging

SPECT-CT PET-CT 7T MRI



US Radiotherapy Optical

Veterinary imaging

SPECT

Open MRI

CT

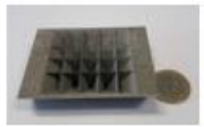
Clinical imaging

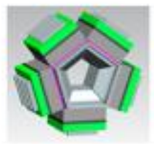
SPECT-CT

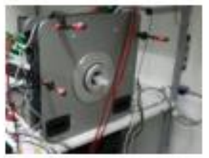
Flemish TOF PET-MR@UZ Leuven

SPECT

TOF PET-CT







New molecular imaging systems
Expertise in image processing

18 MeV Cyclotron

Hot lab + cells

PET and SPECT tracer production

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20.0
A HISTORY FOR THE FUTURE

Gent at center of Belgium EU Ghent-Gand-Gante-Ganda

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