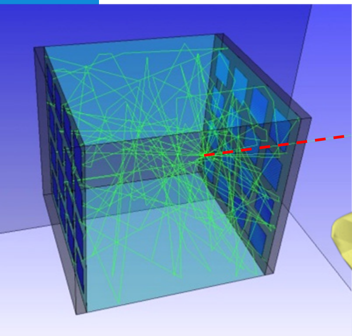
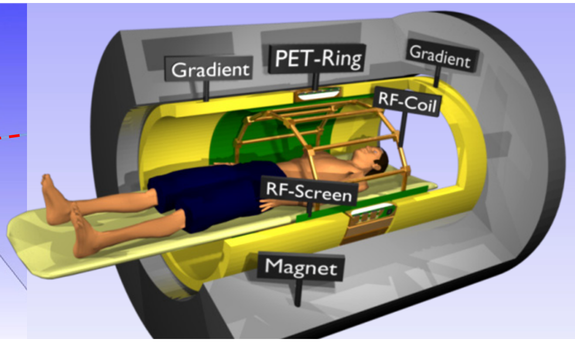
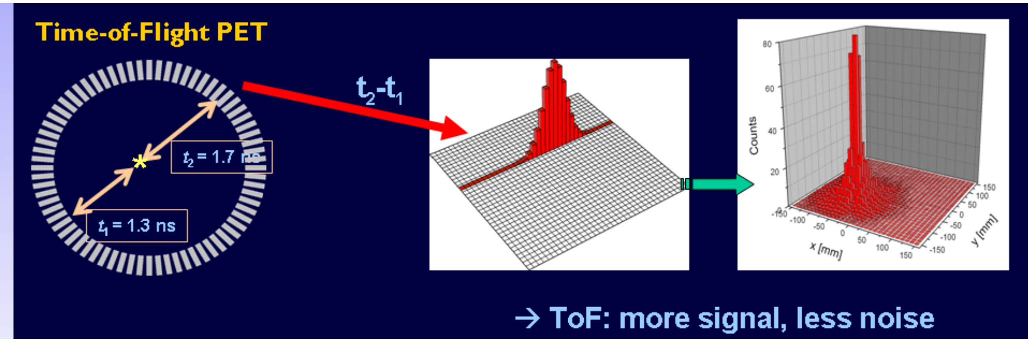






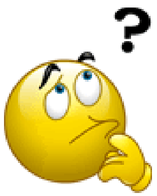
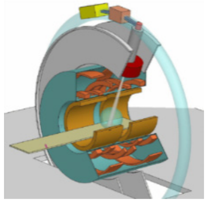
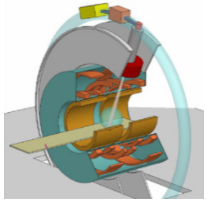
Recent Developments in PET and its Applications in Particle Therapy

Dennis R. Schaart

ENLIGHT Annual Meeting, Utrecht, The Netherlands, September 15-16, 2016

TU Delft
Dennis R. Schaart
Delft University of Technology
d.r.schaart@tudelft.nl

Imaging in radiotherapy

	Diagnosis & Staging	Treatment Planning	In-Situ Verification	Adaptive Radiotherapy	Early Response	Follow-Up
X-rays						
MRI						
PET						

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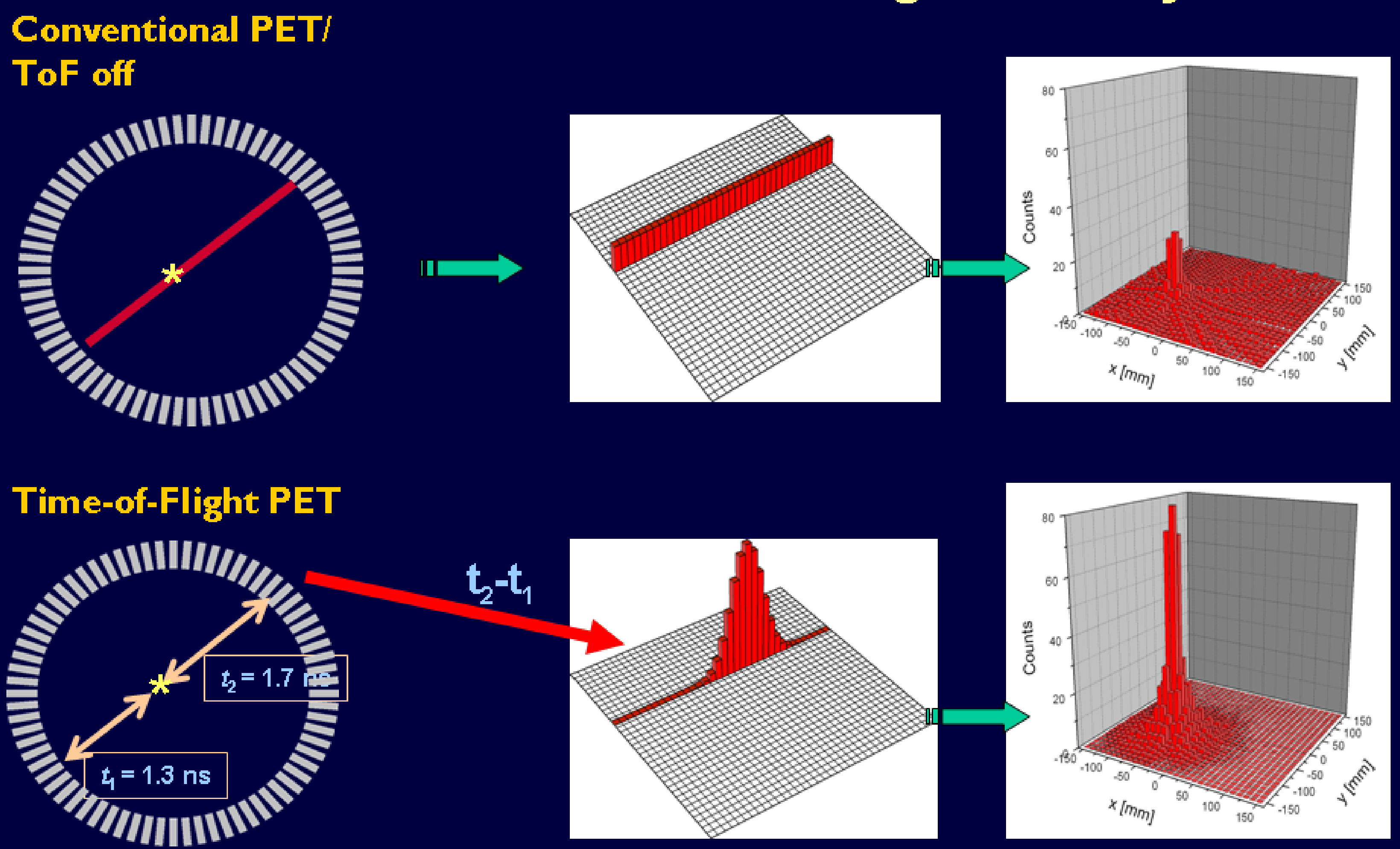
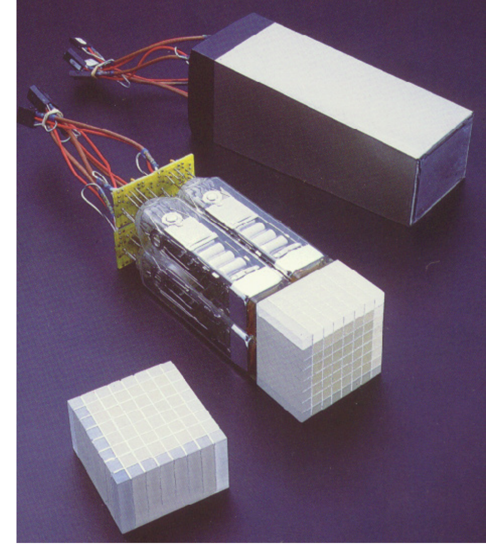
Time of Flight PET Systems



→ ToF: more signal, less noise

First TOF-PET systems

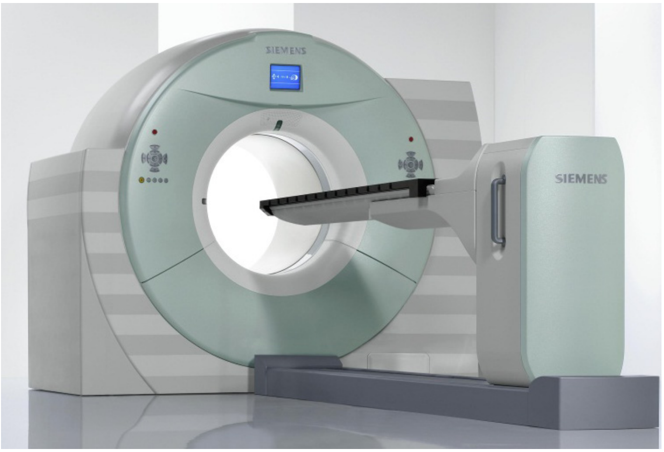
- Commercial TOF PET/CT scanners based on PMTs available from several manufacturers (since 2006)
- Coincidence resolving time (CRT): 500-700 ps FWHM
  ~ 8-10 cm FWHM



PMT-based PET detector

Philips Gemini TF

GE Discovery 690

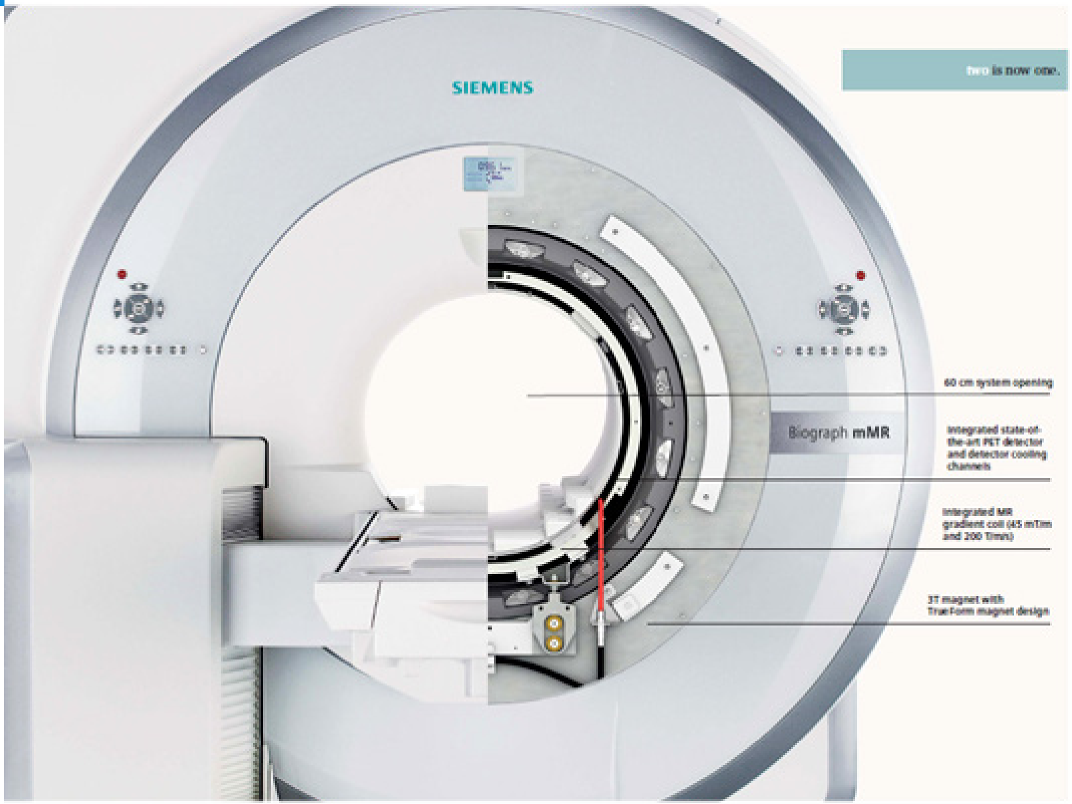


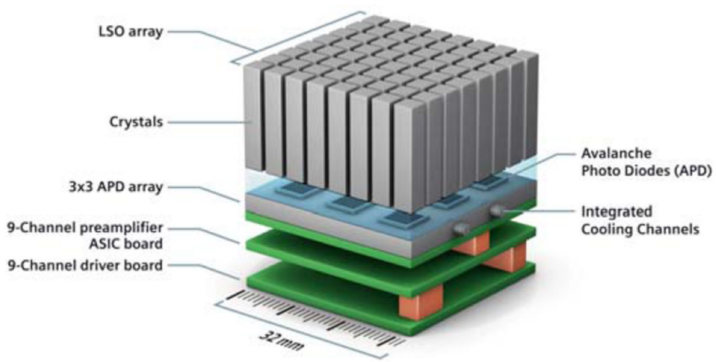
Siemens mCT

Dennis R. Schaart
Delft University of Technology

Integrated PET/MRI system

First clinical PET/MRI system based on avalanche photodiodes (APDs)

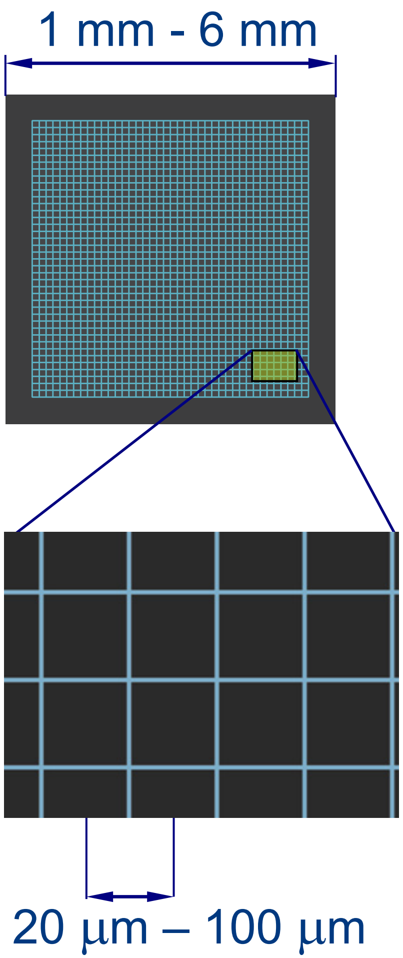




Images: Siemens

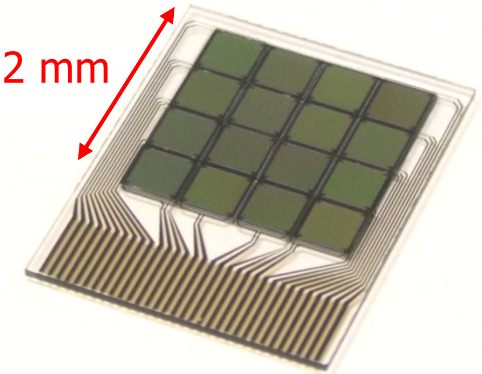
The silicon photomultiplier (SiPM)

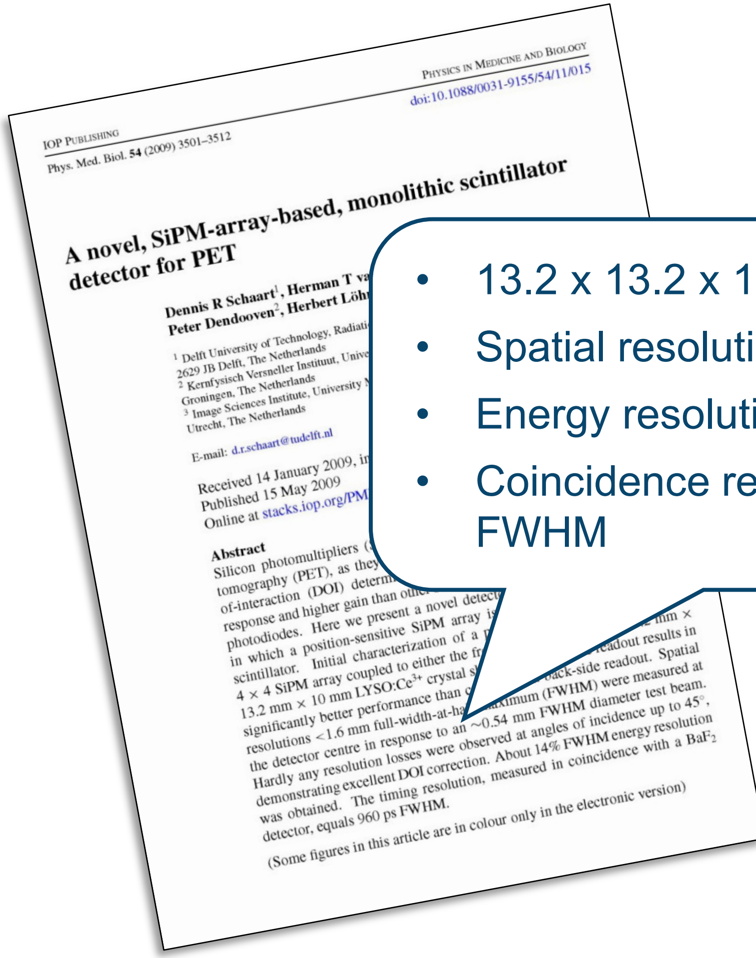
- a disruptive photosensor technology



- Array of many self-quenched Geiger-mode APDs (microcells) connected in parallel
- Increasingly interesting as replacement for PMTs:
  - high gain ($\sim 10^6$)
  - high PDE
  - compact and rugged
  - transparent to γ-photons
  - fast response (ns)
  - insensitive to magnetic fields

First SiPM array based PET detectors (2008)





IOP Publishing
Phys. Med. Biol. 54 (2009) 3501–3512
Physics in Medicine and Biology
doi:10.1088/0031-9155/54/11/015

A novel, SiPM-array-based, monolithic scintillator
detector for PET

Dennis R Schaart[1], Herman T va
Peter Dendooven[2], Herbert Löh

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2629 JB Delft, The Netherlands
[2] Kernfysisch Versneller Instituut, Unive
Groningen, The Netherlands
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Received 14 January 2009, in
Published 15 May 2009
Online at stacks.iop.org/PM

Abstract
Silicon photomultipliers (
tomography (PET), as they
of-interaction (DOI) determ
response and higher gain than other
photodiodes. Here we present a novel detec
in which a position-sensitive SiPM array is
scintillator. Initial characterization of a p
4 × 4 SiPM array coupled to either the fr
13.2 mm × 10 mm LYSO:Ce^{3+} crystal s
significantly better performance than
resolutions <1.6 mm full-width-at-ha
the detector centre in response to an ~0.54 mm FWHM diameter test beam.
Hardly any resolution losses were observed at angles of incidence up to 45°,
demonstrating excellent DOI correction. About 14% FWHM energy resolution
was obtained. The timing resolution, measured in coincidence with a BaF_2
detector, equals 960 ps FWHM.

(Some figures in this article are in colour only in the electronic version)

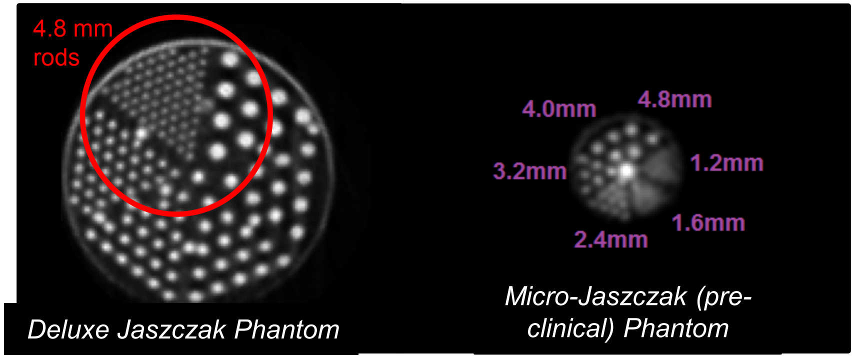
- 13.2 x 13.2 x 10 mm³ LYSO:Ce
- Spatial resolution: 1.6 mm FWHM
- Energy resolution: 14% FWHM
- Coincidence resolving time: 1.4 ns FWHM

One of the first SiPM arrays: SensL SPMarray 3035G16, containing 4 x 4 SiPMs of ~3 x 3 mm² each

D.R. Schaart et al, Phys Med Biol 54, 3501-3512, 2009

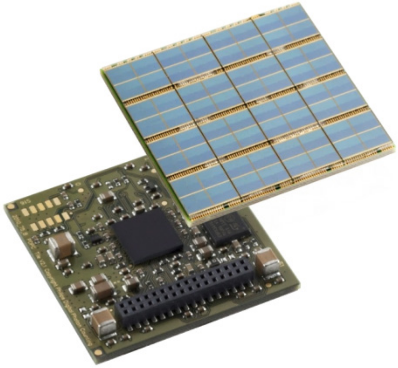
Philips Vereos digital PET/CT system

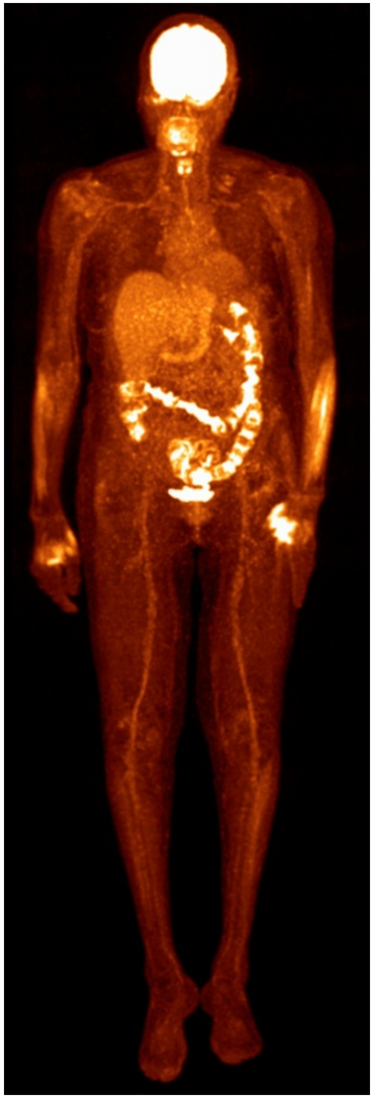
Based on PDPC digital silicon photomultipliers (dSiPMs)



Deluxe Jaszczak Phantom

Micro-Jaszczak (pre-clinical) Phantom



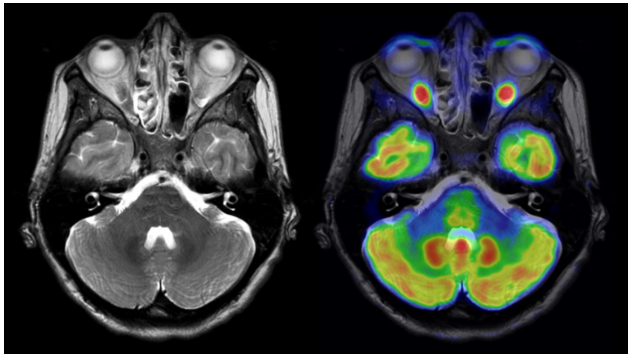


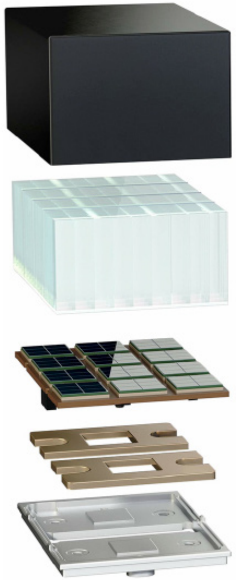
System Performance	
CRT	325 ps FWHM
Sensitivity	22 kcps/MBq
FOV	67.6 x 16.4 cm
Spatial res	4.1 mm
Energy res	< 12%

Images: philips.com

GE Signa SiPM-based PET/MRI system

Based on Hamamatsu silicon photomultipliers (SiPMs)

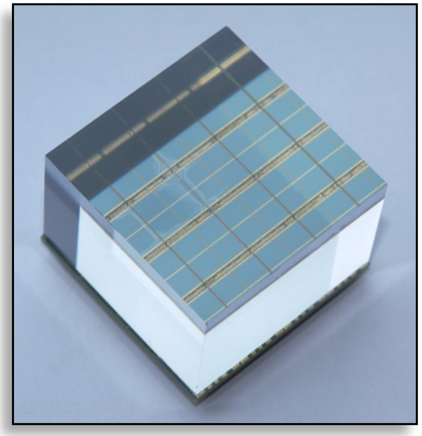




System Performance	
CRT	< 400 ps FWHM
Sensitivity	21 kcps/MBq
FOV	60 x 25 cm
Spatial res	4.1 mm
Energy res	< 12%

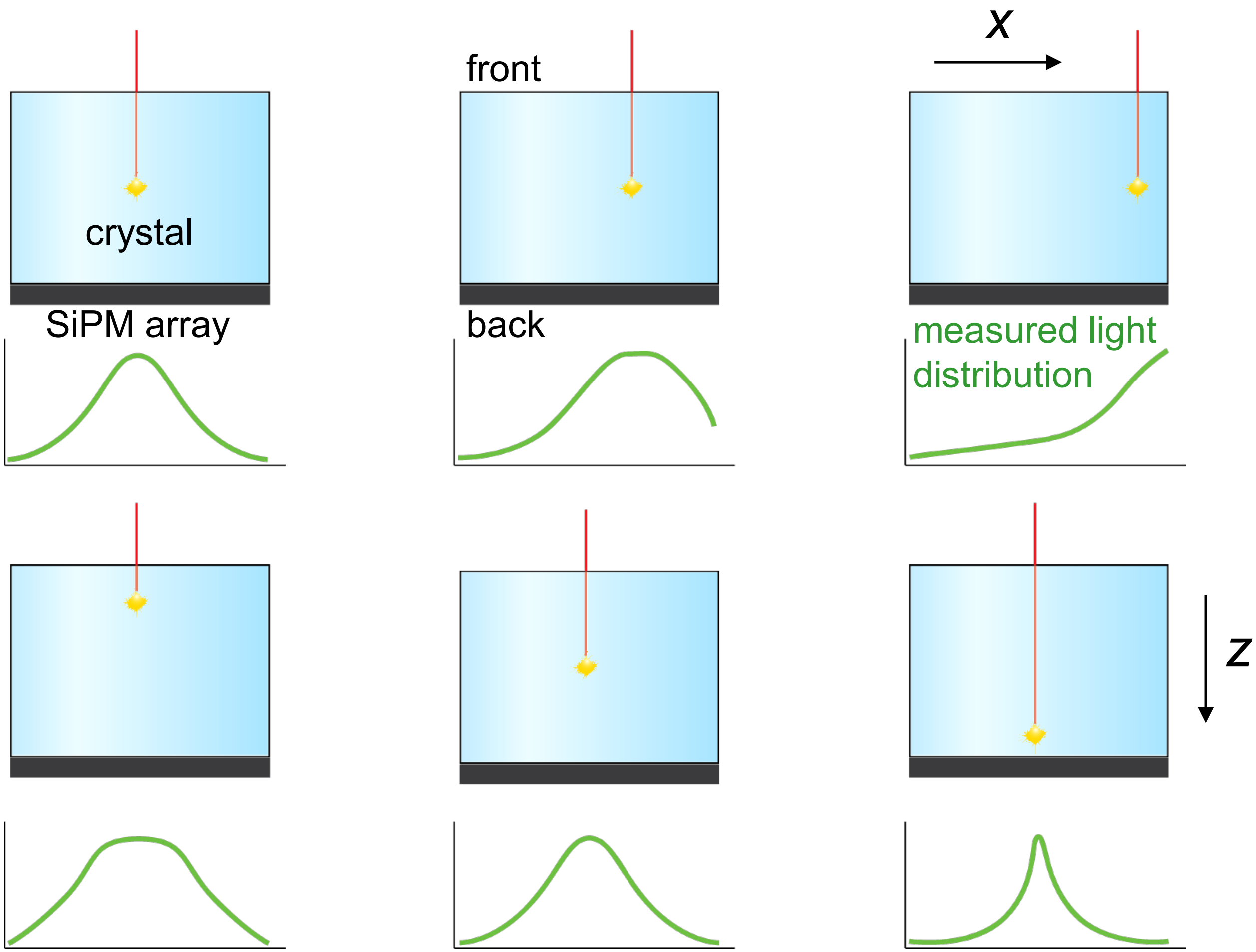
Images: PMB 60 R115, gehealthcare.com

Monolithic scintillator detectors



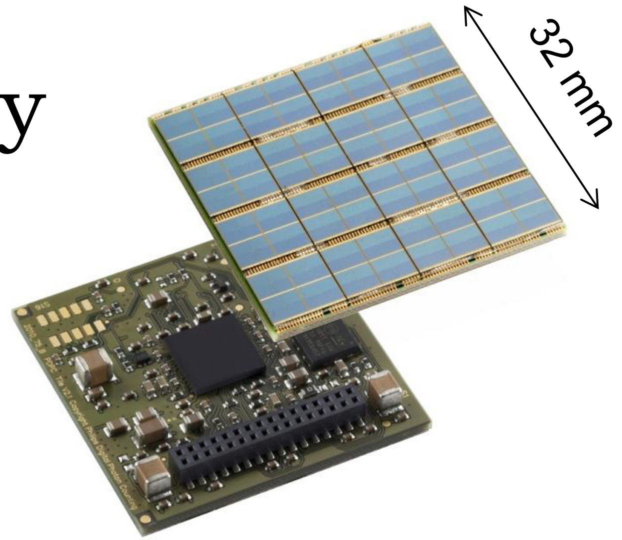
32 mm x 32 mm x 22 mm monolithic LYSO:Ce crystal on digital silicon photomultiplier (dSiPM) array

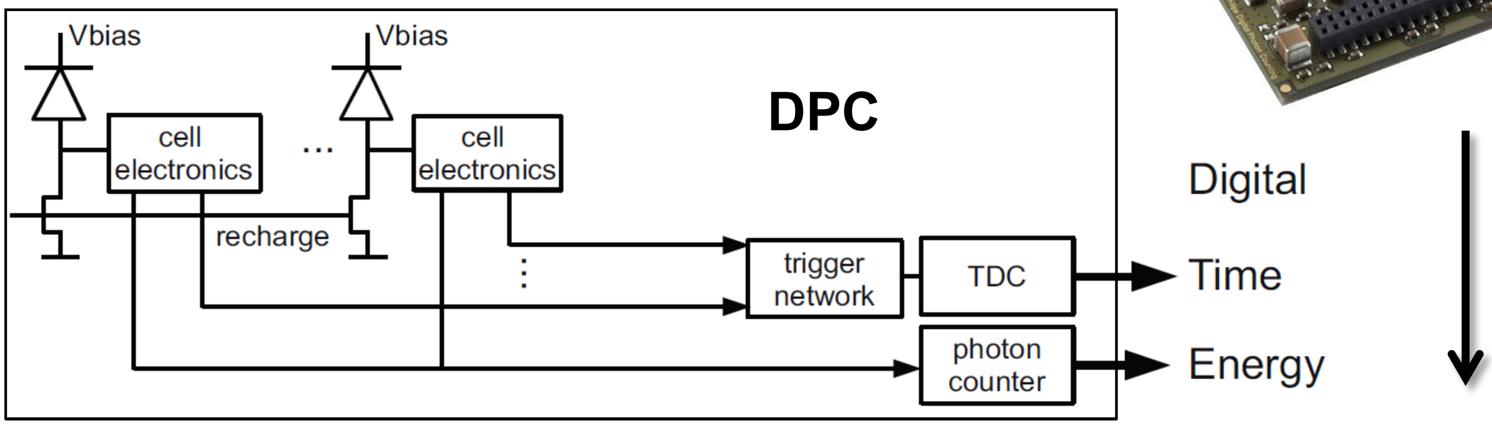
Monolithic scintillator operating principle



See e.g.: - H.T. van Dam et al, Phys Med Biol 58, 3243-3257, 2013
- G. Borghi et al, IEEE Trans Nucl Sc 62, 57-67, 2015

Readout: digital SiPM array





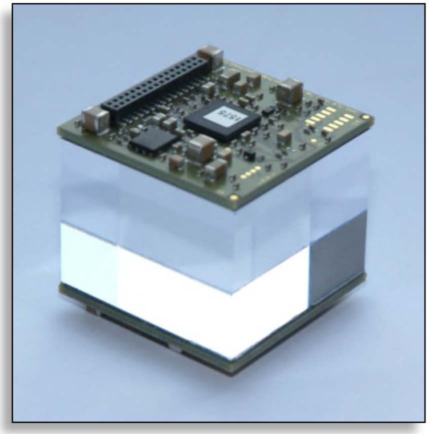
++ small single-photon time jitter
++ negligible noise at the single photon level
++ ~ 30% photon detection efficiency
\+ MR-compatible

16 Si chips (4 x 4)
→ 16 time stamps
→ 64 pixel values (no. of counts)

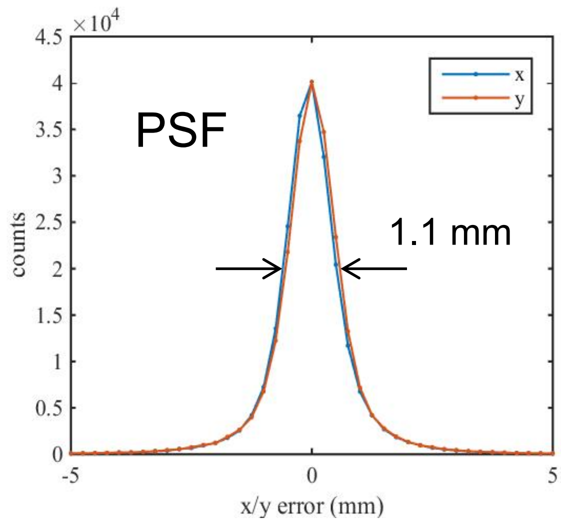
Performance summary

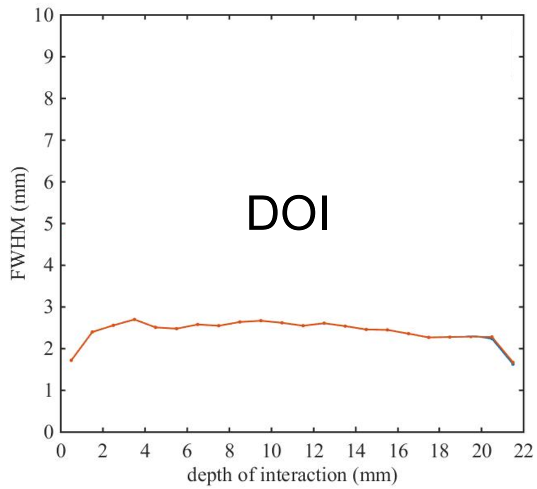
A practical and cost effective detector for PET/CT and PET/MRI with ultrahigh spatial resolution, CRT, and detection efficiency

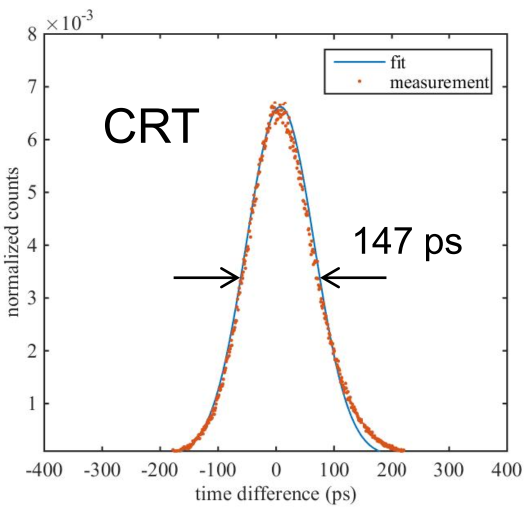
Performance parameter	State of the art	BSR monolithic	DSR monolithic
Energy resolution	< 12%	**~10%**	**~10%**
Spatial resolution	~4 mm	**1.7 mm**	**1.1 mm**
DOI resolution	None	**3.7 mm**	**2.4 mm**
Coincidence resolving time	325-400 ps	**214 ps**	**147 ps**



32 mm x 32 mm x 22 mm commercial-grade LYSO:Ce with double-sided (DSR) dSiPM readout







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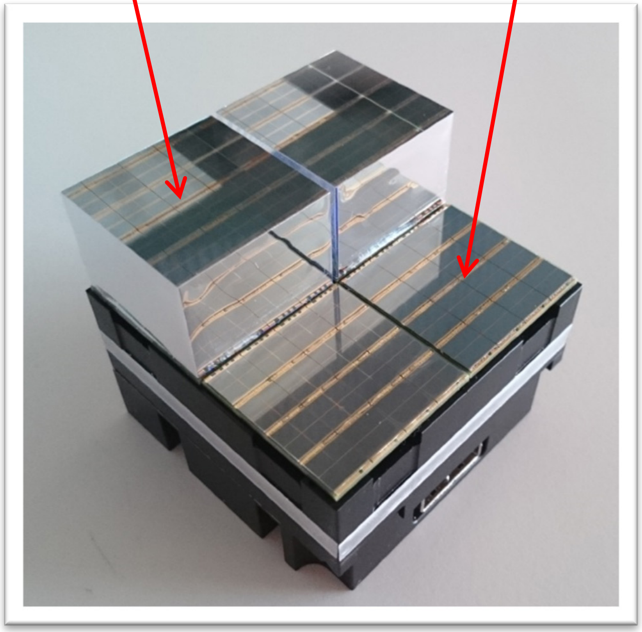
G. Borghi et al, Phys Med Biol 61, 4904–4928, 2016
G. Borghi et al, Phys Med Biol 61, 4929–4949, 2016

Table-top gantry

32 mm x 32 mm x 22 mm LYSO:Ce

DPC 3200-22-44



Detector module with 4 monolithic scintillators (2 mounted)

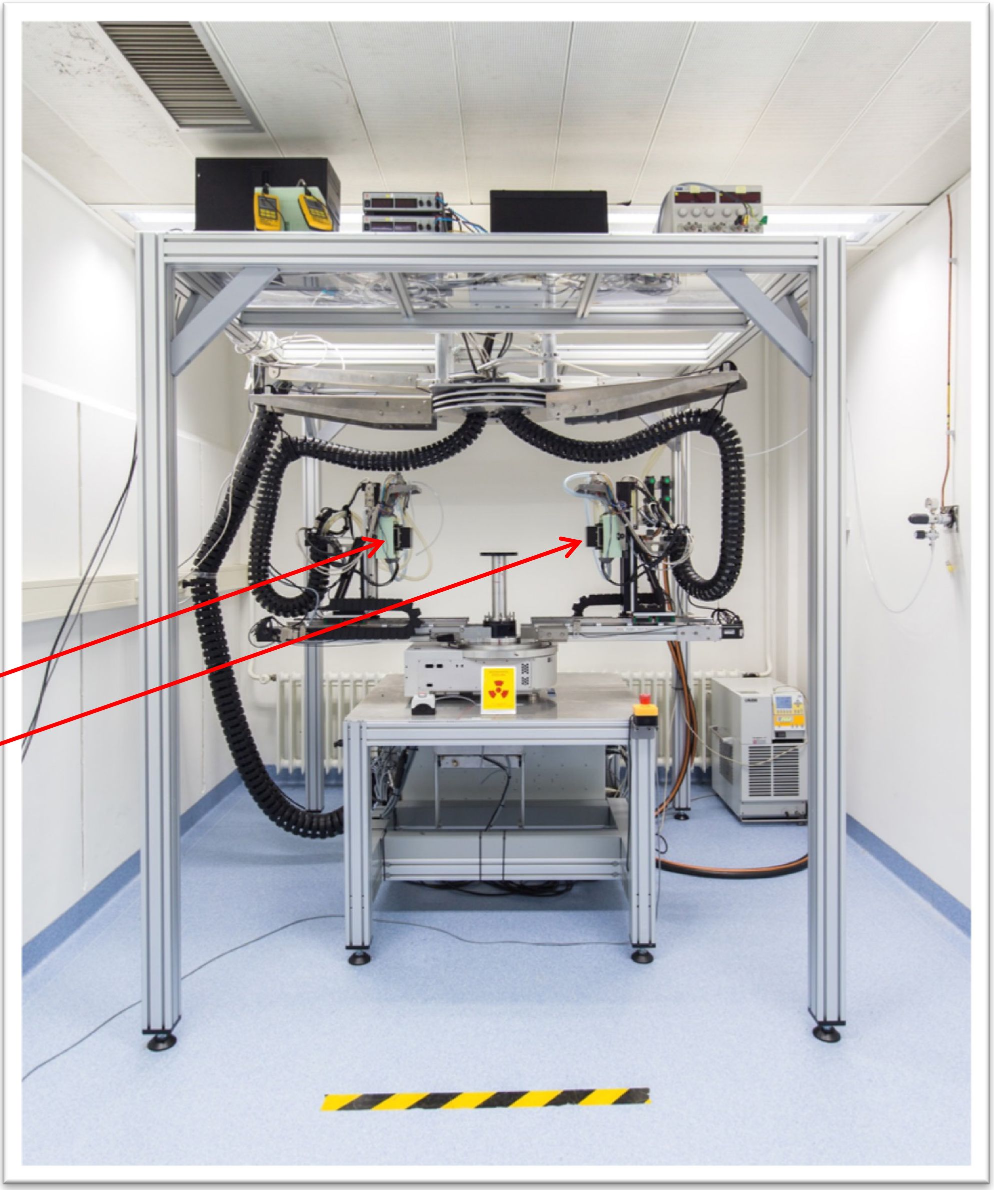
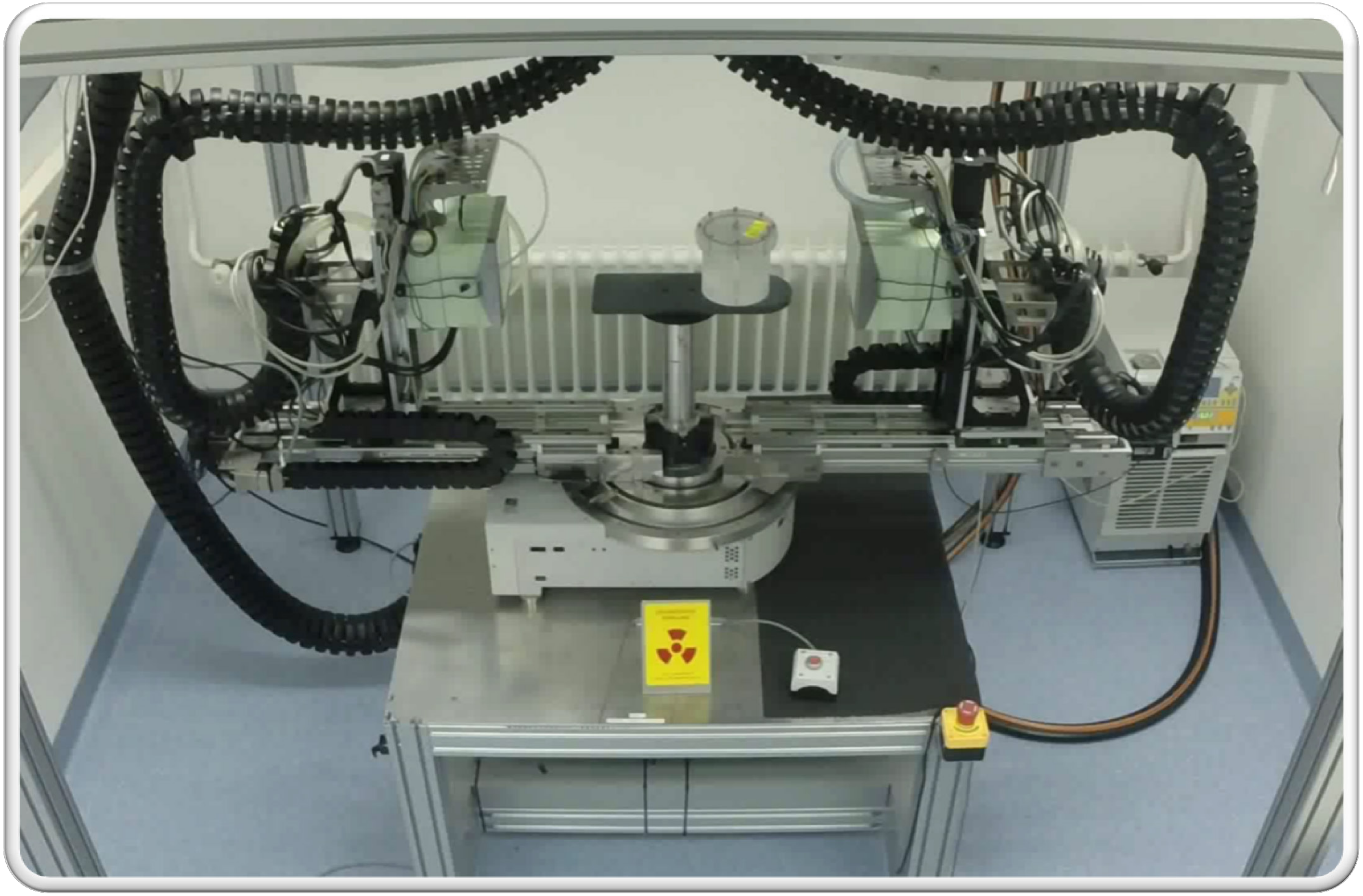
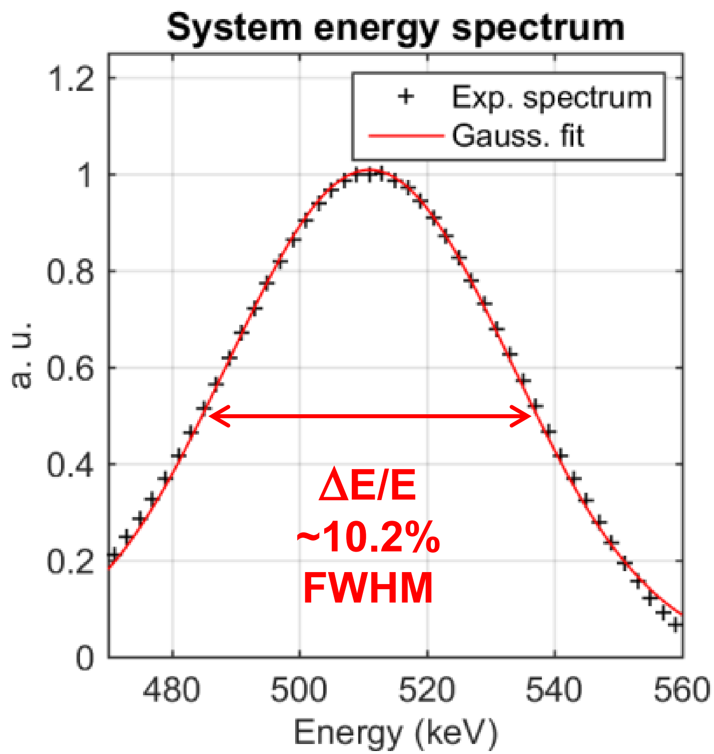


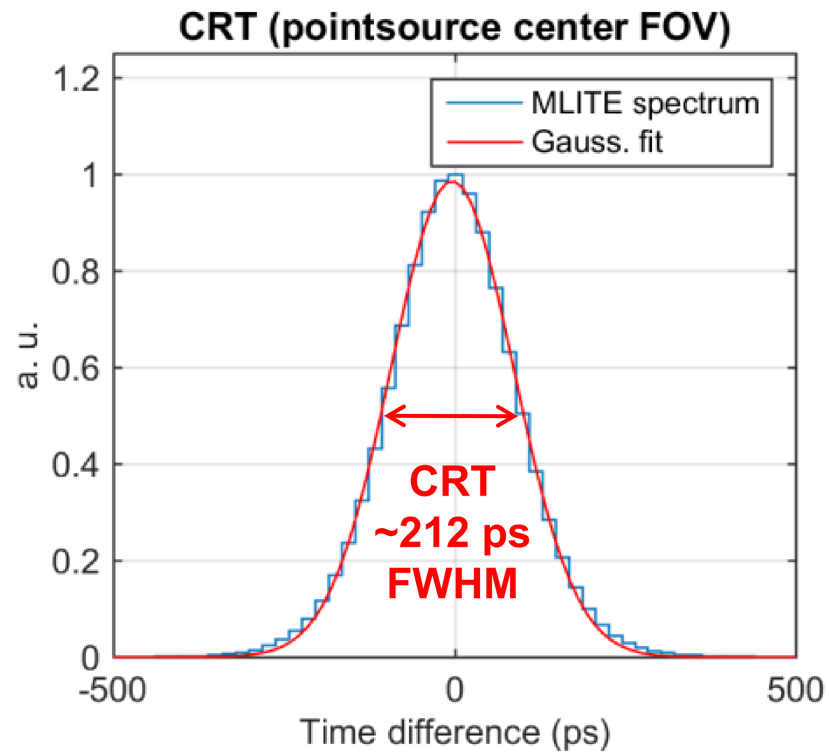
Table-top gantry

Time-lapse: full-ring image acquisition of Na-22 filled Derenzo phantom



Energy and time resolution



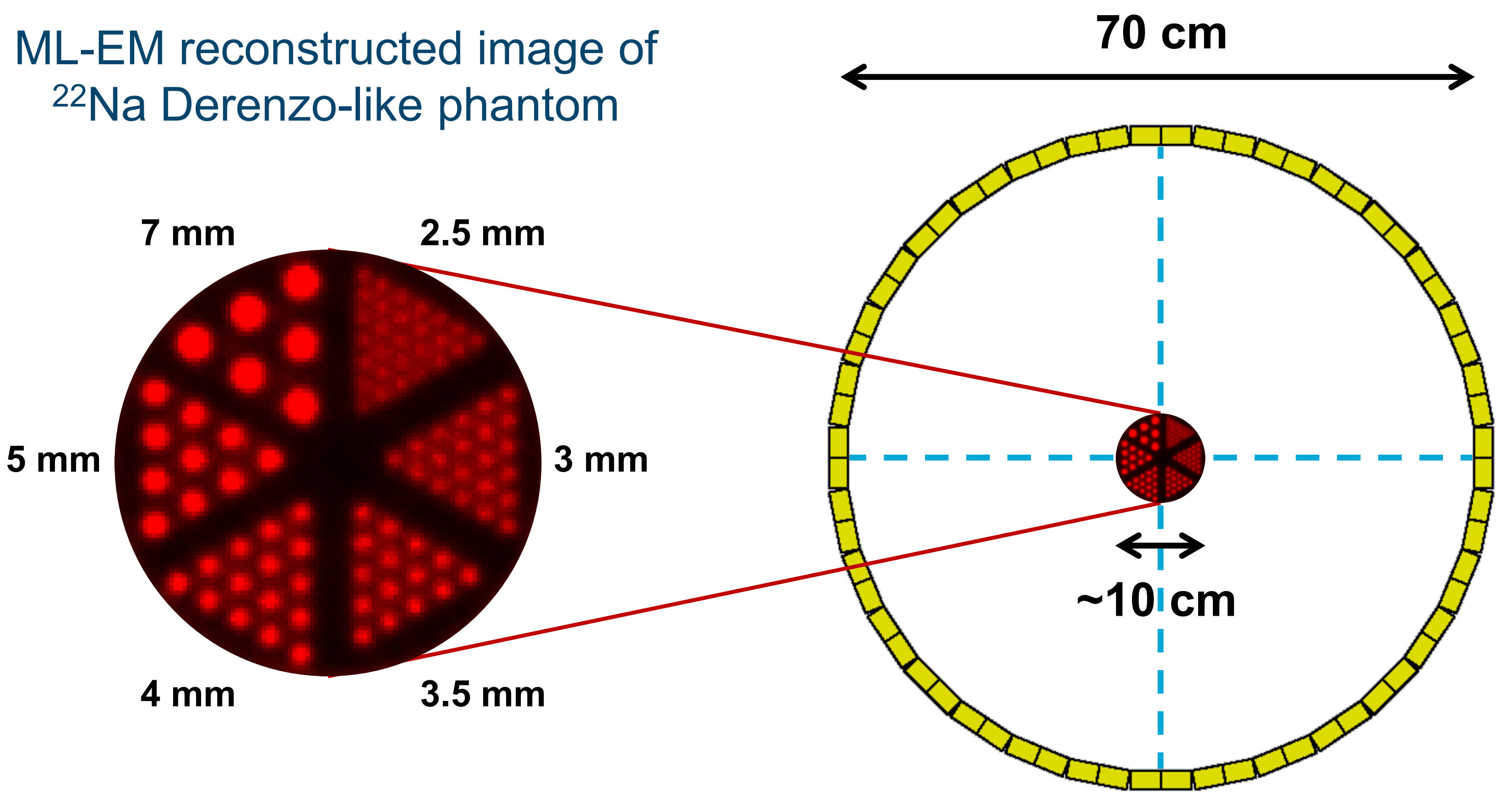


Left: system energy spectrum obtained from a full tomographic acquisition of a ~3 MBq Na-22 point source at the center of the FOV.

Right: coincidence resolving time (CRT) obtained from a full tomographic acquisition of a ~3 MBq Na-22 point source at center FOV. Timestamps were derived using MLITE.

Na-22 filled Derenzo phantom (ML-EM)

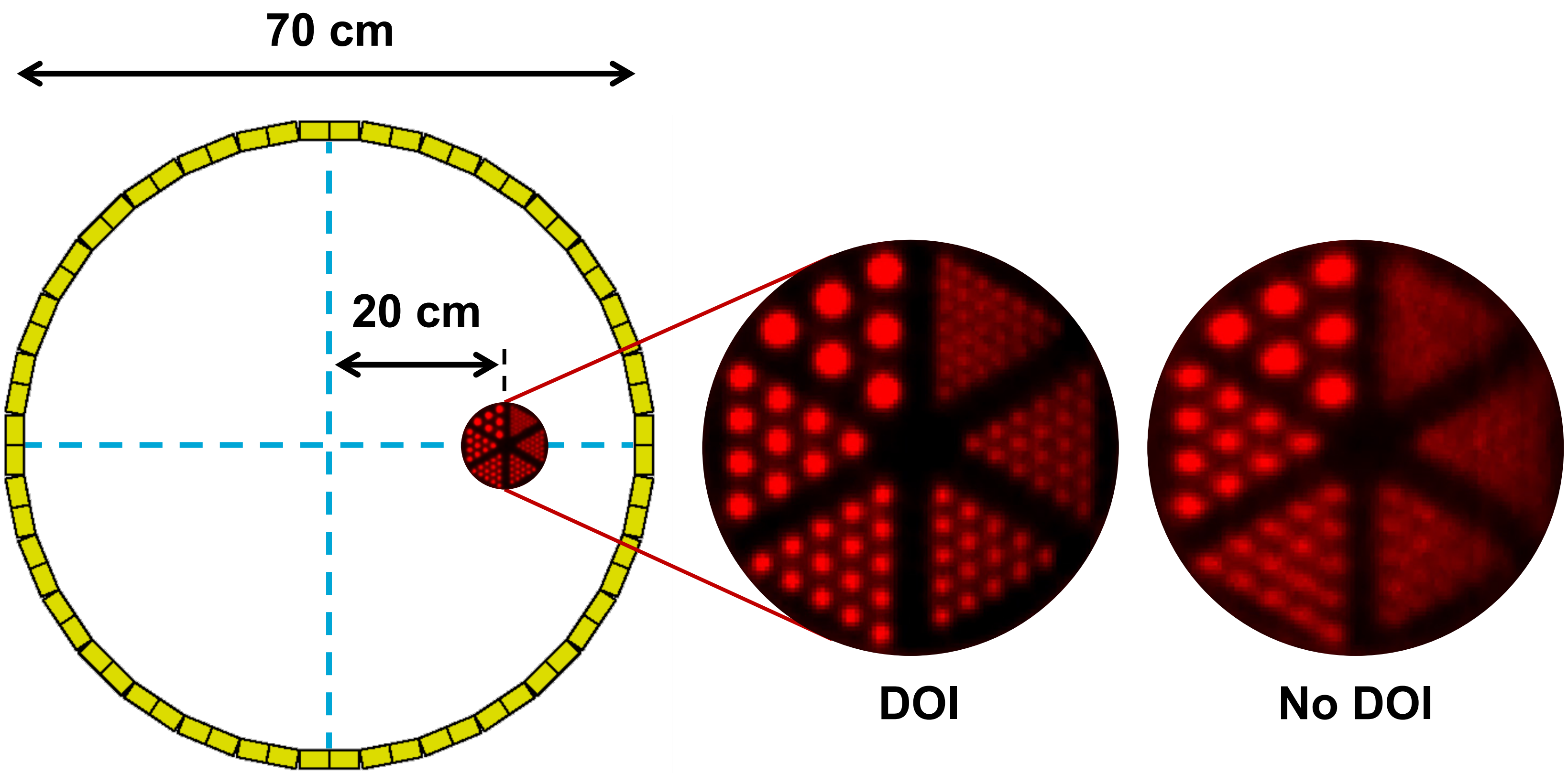
ML-EM reconstructed image of ^{22}Na Derenzo-like phantom



Sub-3 mm spatial resolution & 212 ps timing in a whole-body clinical TOF-PET geometry using monolithic LYSO:Ce scintillators and digital SiPM arrays

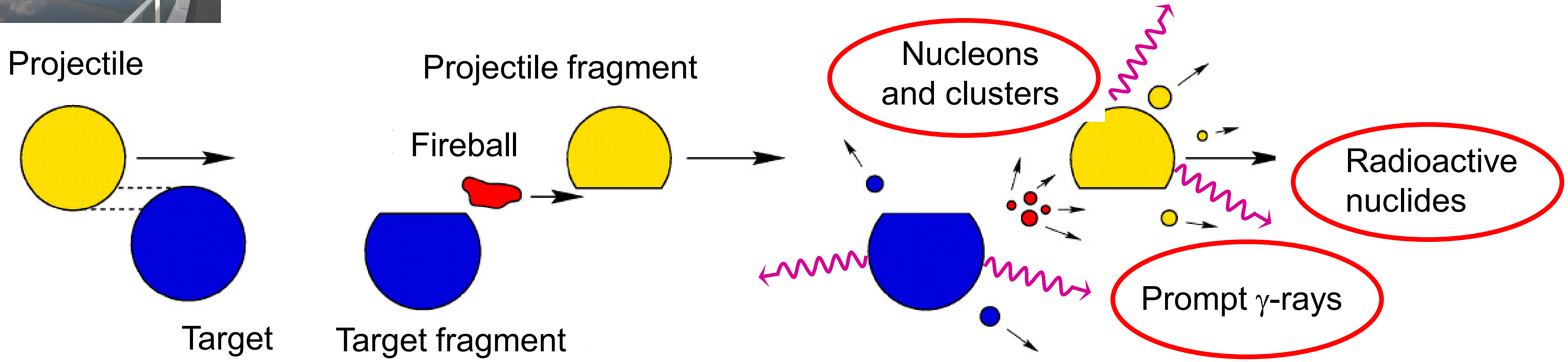
Dennis R. Schaart
Delft University of Technology

Na-22 filled Derenzo phantom (ML-EM)



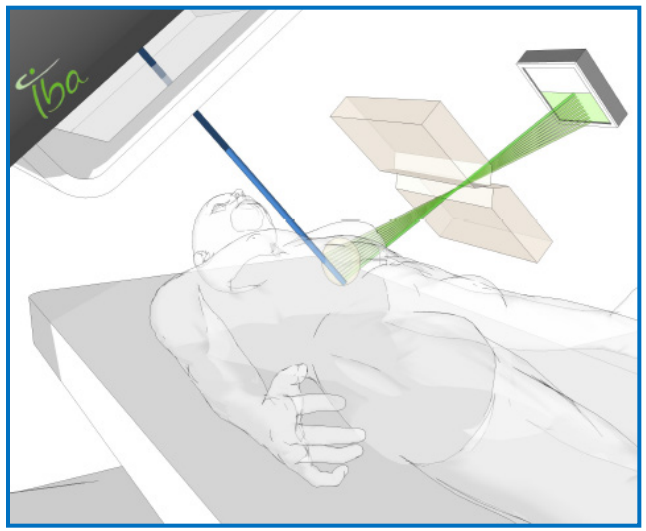
ML-EM reconstructed images of the Na-22 filled Derenzo phantom at 20 cm off-center, with (right) and without (left) depth-of-interaction (DOI) correction.

In-situ treatment verification

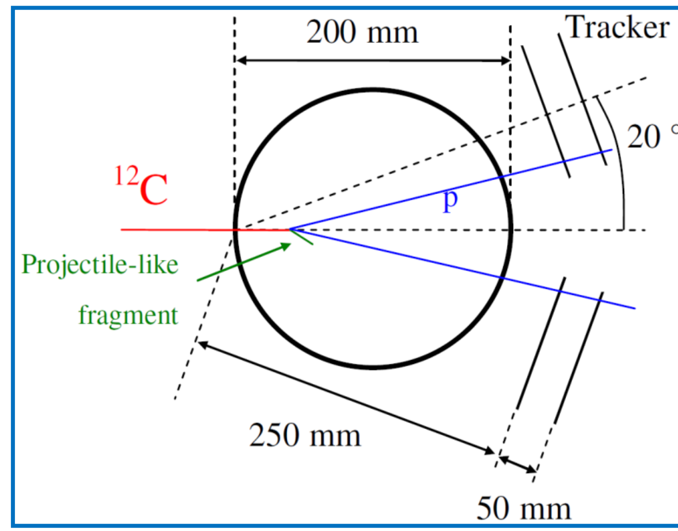


In-situ PET

Prompt γ-ray imaging



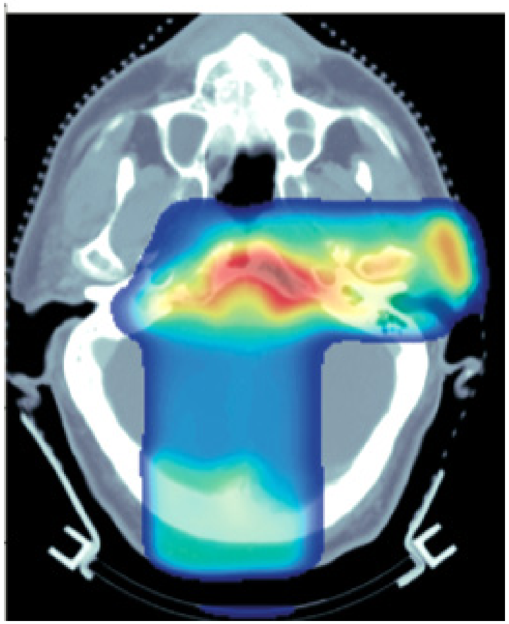
Vertex imaging

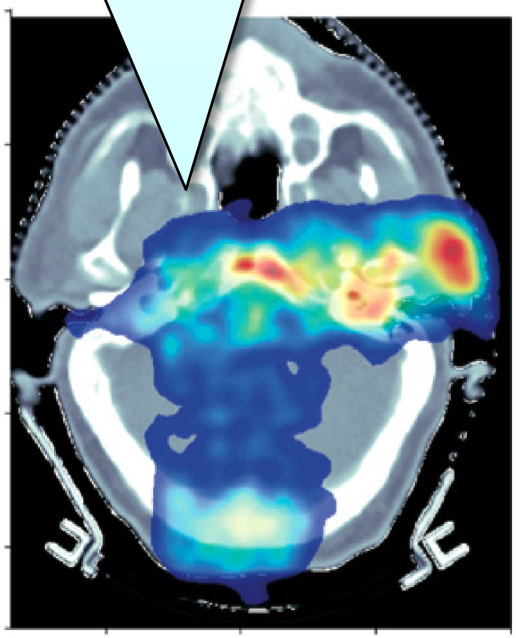


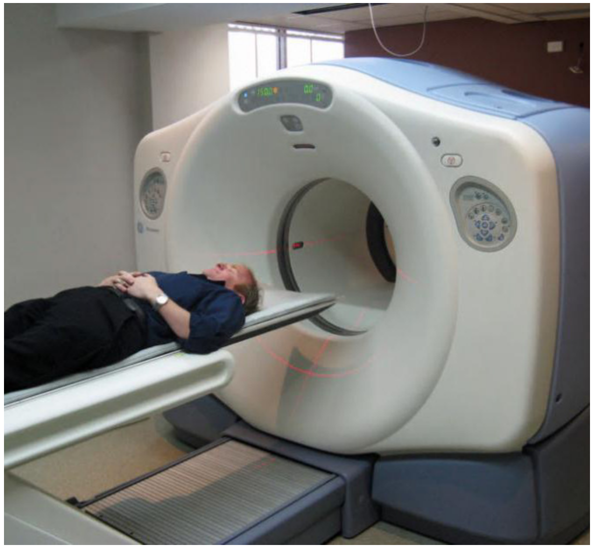
Images: W. Enghardt et al, J. Smeets et al, E. Testa et al

Offline dose imaging

Problem: poor image quality due to rapid decay of radioactivity and biological washout







Commercial PET scanner

Activity distribution after 2-beam proton irradiation at Massachusetts General Hospital.
Left: predicted. Right: measured with PET scanner outside treatment room.

PET images: Katia Parodi (LMU)

medical delta

Erasmus MC Universitair Medisch Centrum Rotterdam

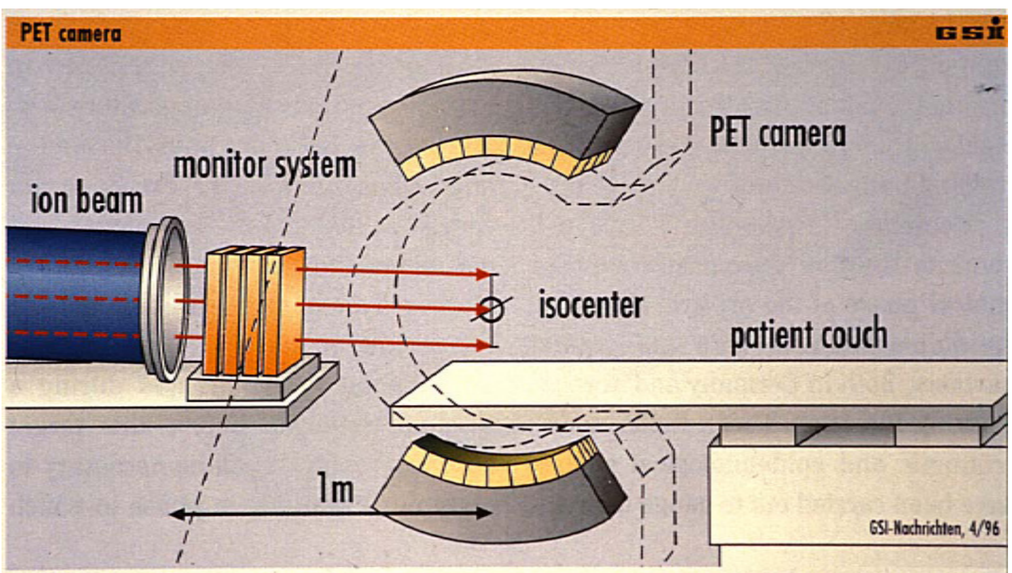
LUMC Leids Universitair Medisch Centrum

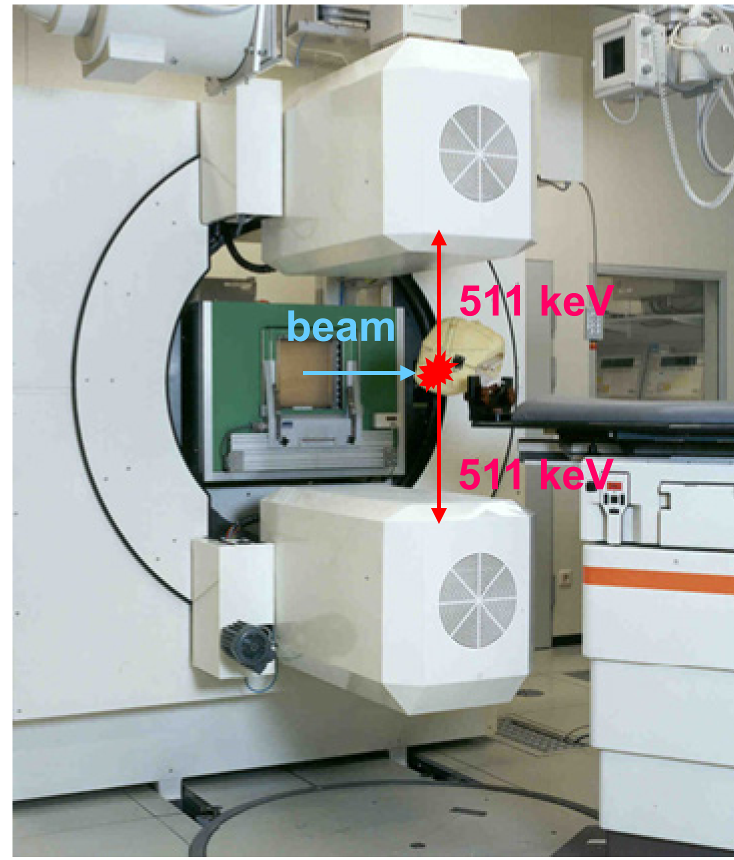
TU Delft

In-situ PET: early work GSI

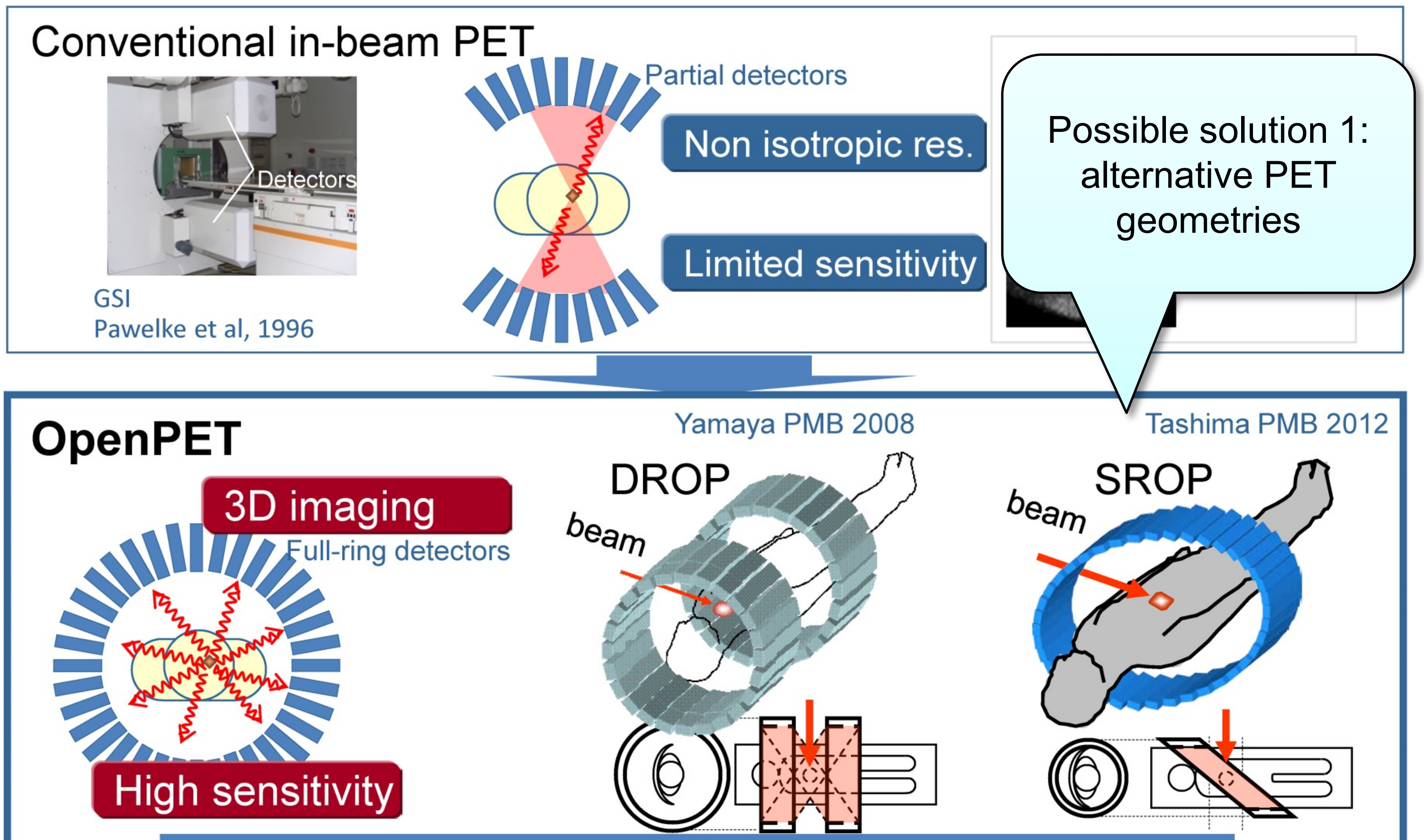
Problem: low angular coverage => insufficient counts & image artefacts

Proof-of-concept
K. Parodi, P. Crespo, et al
GSI Darmstadt / FZ Dresden-Rossendorf





"OpenPET": our idea for 3D in-beam PET

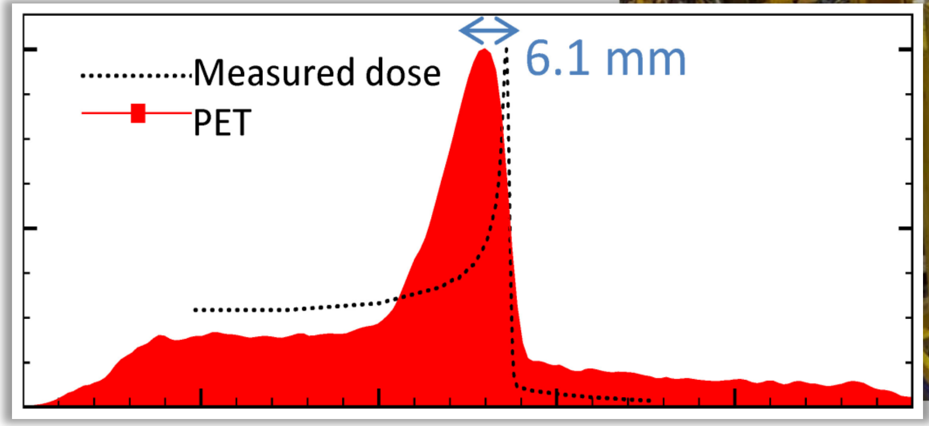


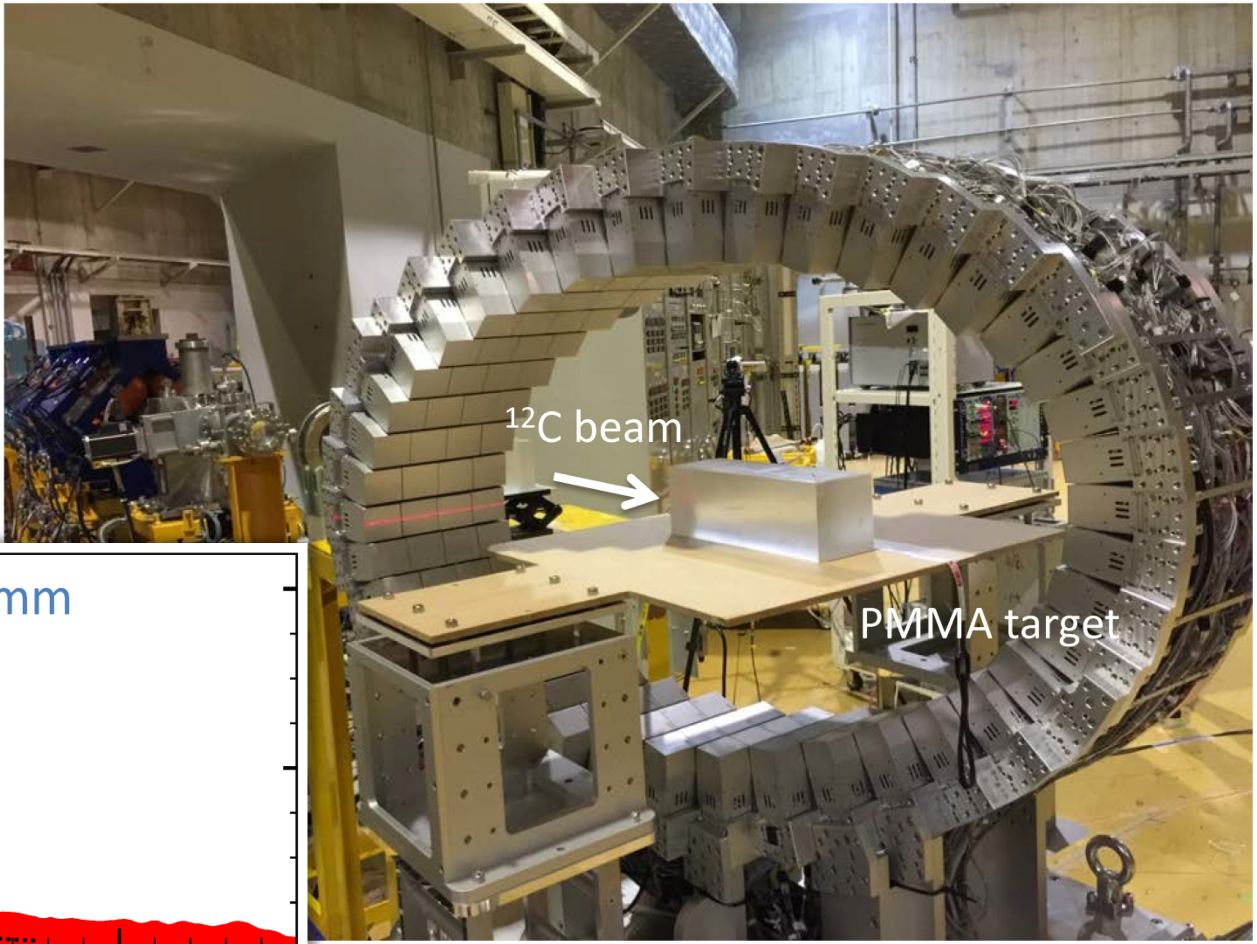
Purpose: experimental comparison of DROP and SROP

Courtesy: Taiga Yamaya (NIRS)

HIMAC test (^{12}C beam)

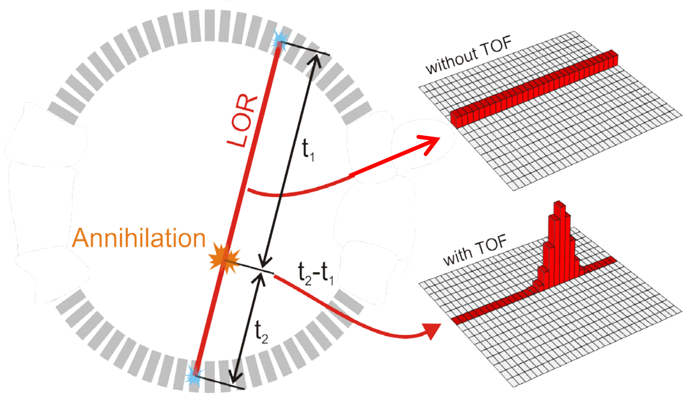
- Beam
  - ^{12}C
  - 3 spill
- PET measurement
  - 23 min
- Target
  - PMMA phantom (10 x 10 x 30 cm^3)



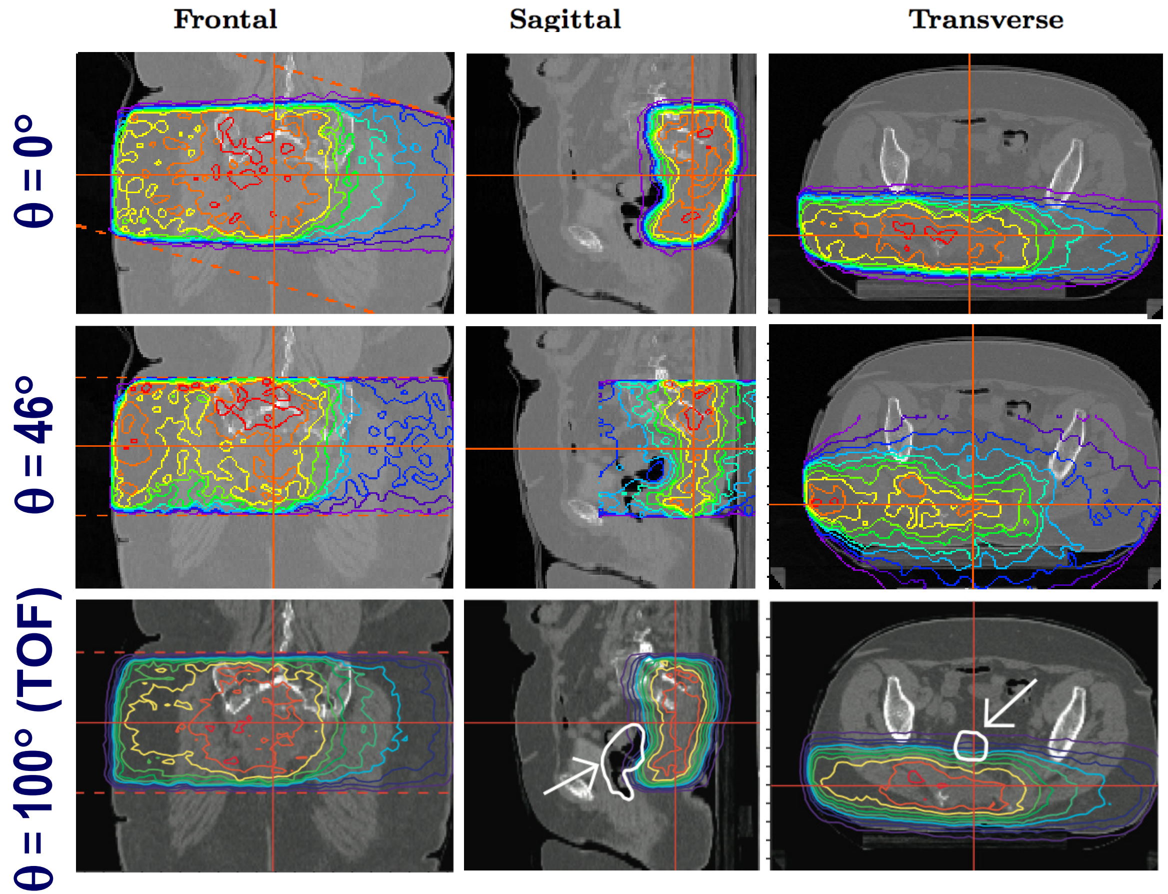


In-situ TOF PET

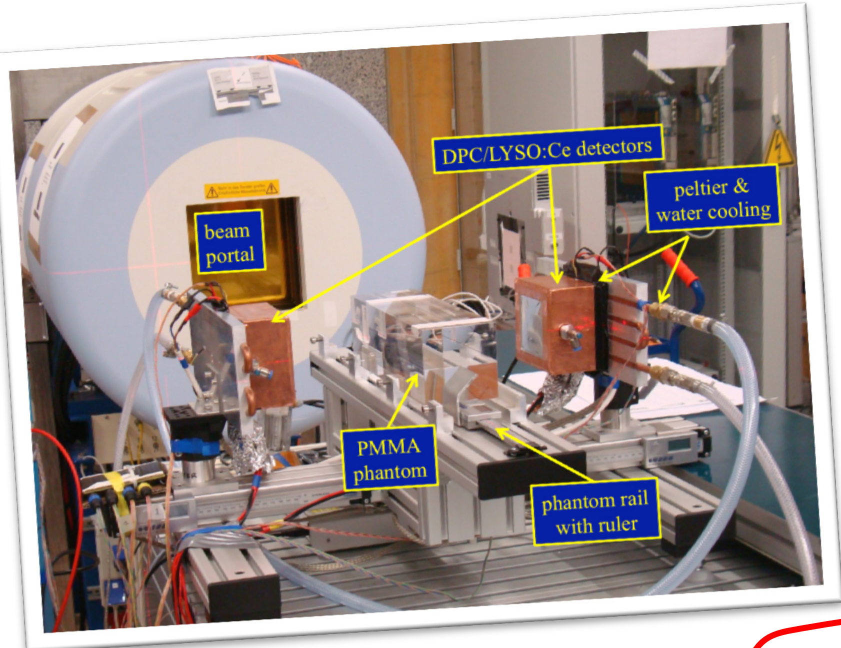
Possible solution 2: TOF-PET
=> less noise & less limited angle artefacts

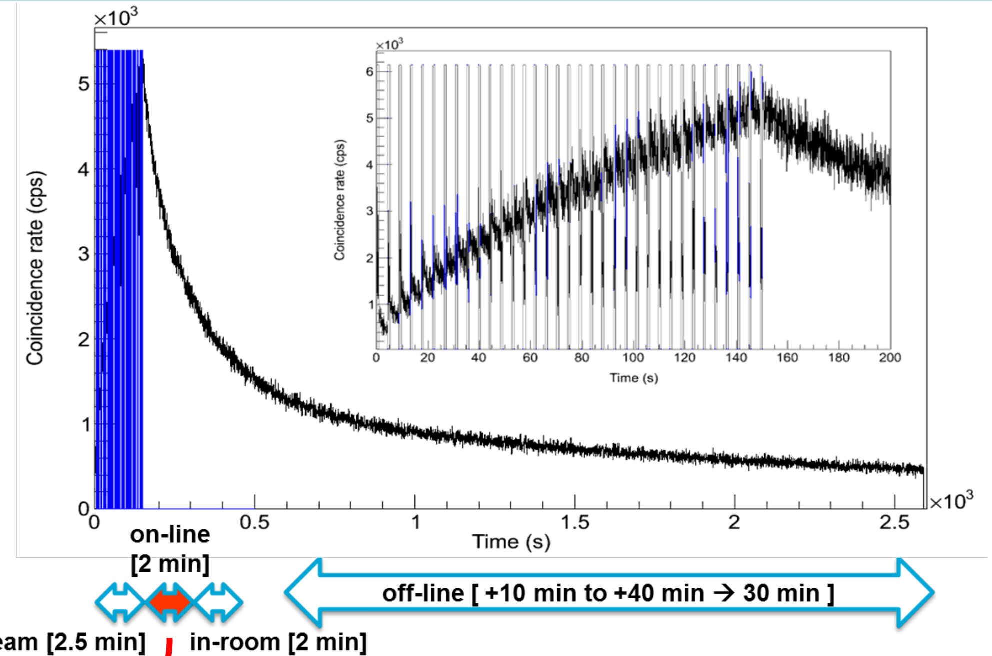


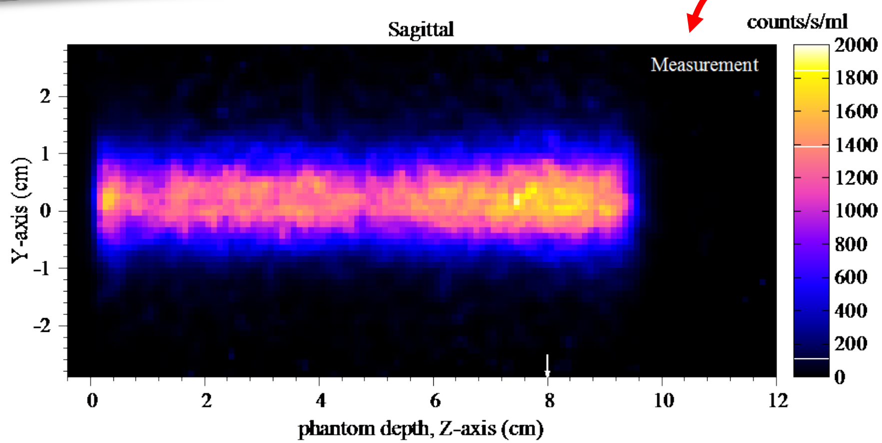
CRT < 200 ps FWHM

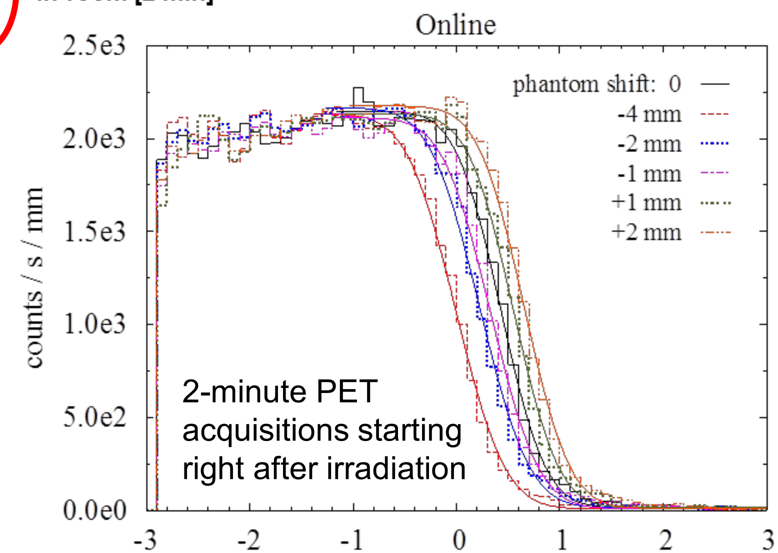


In-Situ TOF-PET







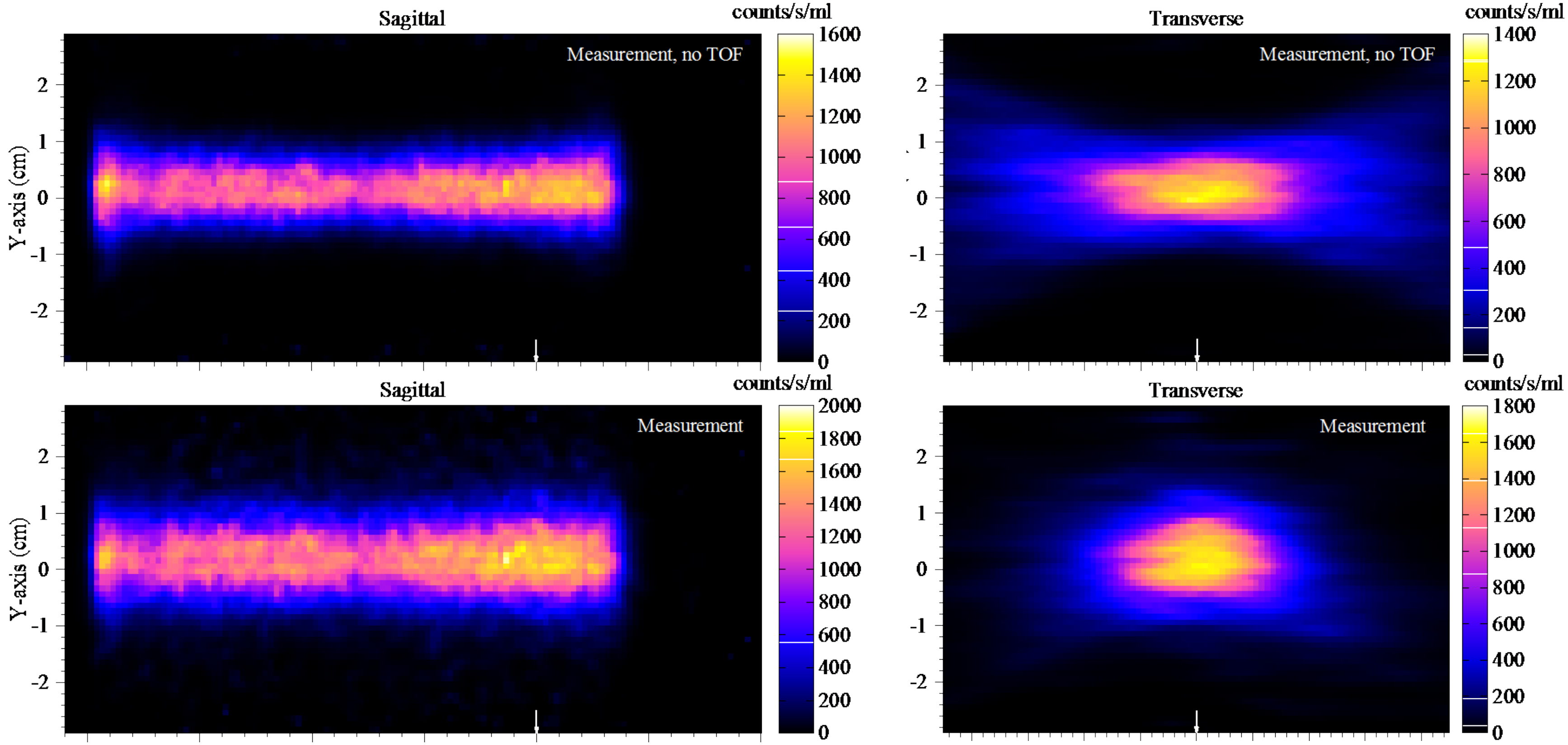


P.C. Lopes et al, "First in-situ TOF-PET study using DPCs for proton range verification," PMB 61, 6203-6230, 2016

TU Delft Delft University of Technology · HIT Heidelberger Ionenstrahl-Therapiezentrum · LIP Laboratório de Instrumentação e Física Experimental de Partículas · UniversitätsKlinikum Heidelberg · PHILIPS · Physics Department Universidade de Coimbra · LMU Ludwig-Maximilians-Universität München

In-situ PET results

Reconstructed images of proton-induced activity in PMMA, without (top) and with TOF information used in the reconstruction (bottom)



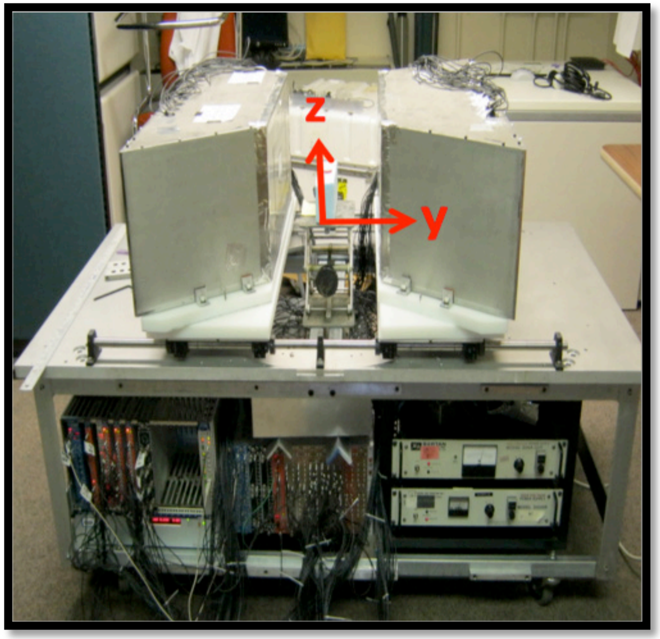
CRT = 382 ps FWHM

P.C. Lopes et al, "First in-situ TOF-PET study using DPCs for proton range verification," PMB 61, 6203-6230, 2016

U Penn prototype partial-ring TOF PET scanner

- Prior simulation* suggests 4 mm wide crystals sufficient to provide ~1 mm accuracy for proton range estimate
- $LaBr_3$ chosen on account of superior TOF capability: CRT = 375 ps FWHM
- 30-mm long crystals for higher sensitivity
- Detector modules: 12 cm along z dir. X 25 cm along x dir.
- Off-the-shelf DAQ components
- Modules separated by ~12 cm
- Angular coverage ~ 2/3

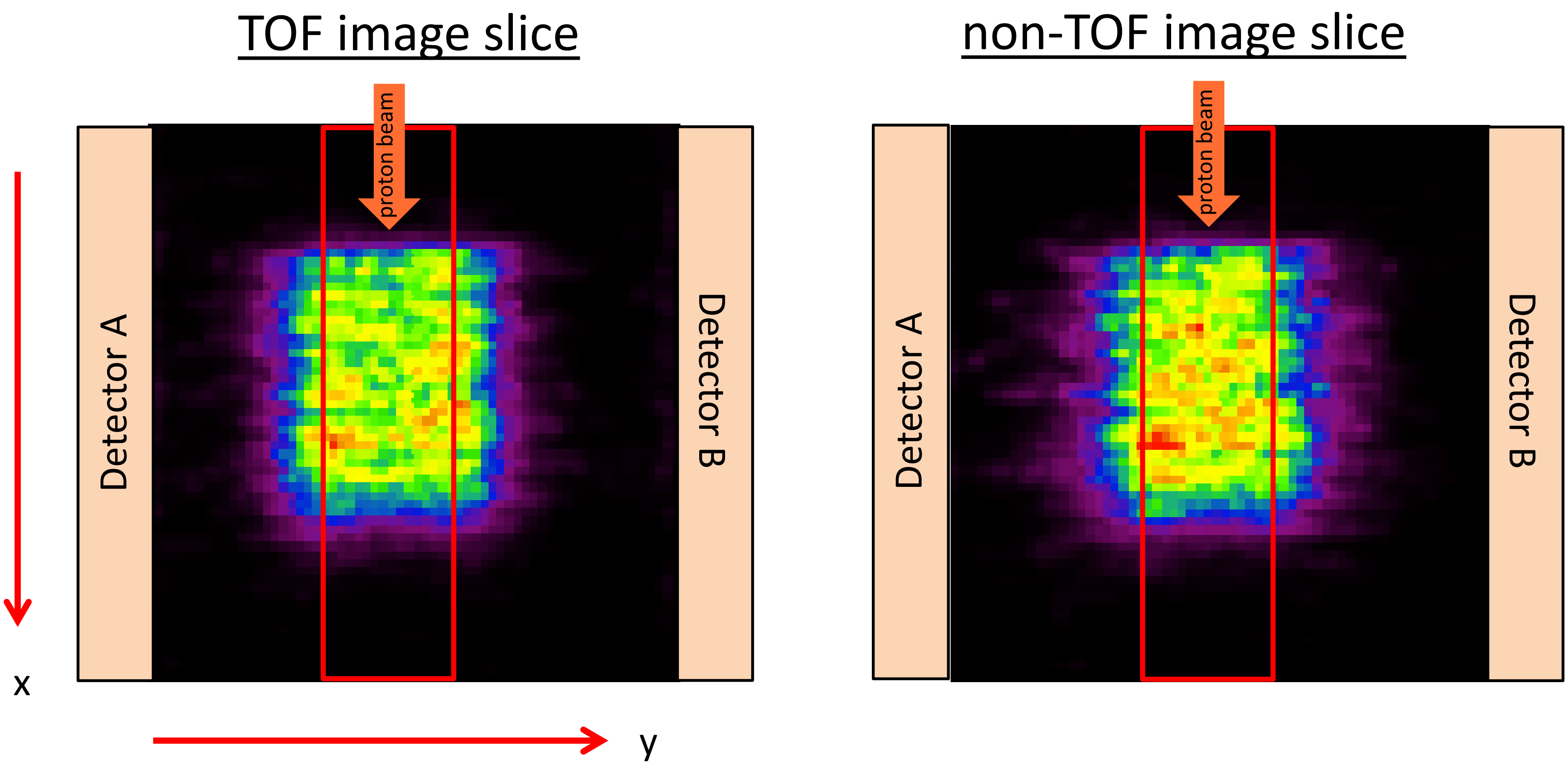
- 92 MeV protons (passive scattering)
- Scanner placed adjacent to proton treatment bed to minimize delay



Courtesy: Suleman Surti (U Penn)

*Surti et al., Phys. Med. Biol., 56 (2011) 2667-85.

Adipose phantom – 92 MeV irradiation



Bias in range ~ 1.0 mm with TOF and 1.6 mm with non-TOF

Courtesy: Suleman Surti (U Penn)

Short-lived isotopes

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Phys. Med. Biol. **60** (2015) 8923–8947

Short-lived positron emitters in beam-on PET imaging during proton therapy

P Dendooven[1], H J T Buitenhuis[1], F Diblen[1,3], P N Heeres[1], A K Biegun[1], F Fiedler[4], M-J van Goethem[2], E R van der Graaf[1] and S Brandenburg[1]

production integrated over the stopping range of 55 MeV protons

Courtesy: Peter Dendooven (KVI-CART)

Production rates

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nuclide	half-life	target	production per proton (± stat. uncertainty)	systematic uncertainty (%)
O-15	2.0 min	water	$8.83 \pm 0.11 \times 10^{-3}$	3
O-14	71 s	water	$7.3 \pm 0.5 \times 10^{-5}$	20
N-12 + O-13	11 / 8.6 ms	water	$< 7 \times 10^{-5}$	12
C-11	20 min	carbon	$8.04 \pm 0.10 \times 10^{-3}$	3
C-10	19 s	carbon	$3.08 \pm 0.08 \times 10^{-4}$	3
C-9	127 ms	carbon	$< 5 \times 10^{-4}$	10
N-12	11 ms	carbon	$7.32 \pm 0.16 \times 10^{-4}$	12
B-8	770 ms	carbon	$1.1 \pm 0.3 \times 10^{-5}$	9
P-29	4.1 s	phosphorus	$1.11 \pm 0.02 \times 10^{-3}$	4
P-30	2.5 min	phosphorus	$5.44 \pm 0.03 \times 10^{-3}$	3
S-30	1.2 s	phosphorus	$1.3 \pm 0.2 \times 10^{-4}$	5
K-38g	7.6 min	calcium	$5.66 \pm 0.06 \times 10^{-4}$	3
K-38m	0.92 s	calcium	$6.38 \pm 0.17 \times 10^{-4}$	8
K-37	1.2 s	calcium	$1.6 \pm 0.2 \times 10^{-4}$	8

Courtesy: Peter Dendooven (KVI-CART)

PET decays from soft tissue

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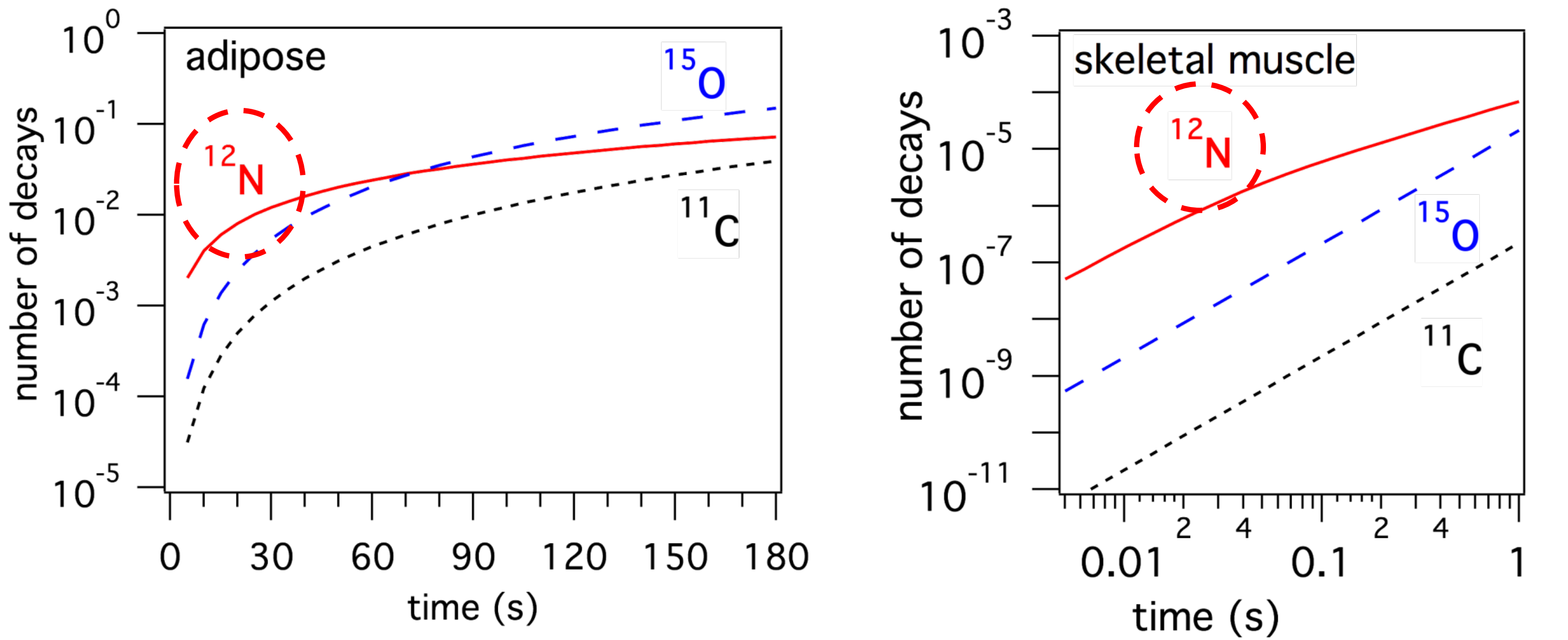

C: 64 w%, O: 23 w% composition C: 11 w%, O: 76 w%

N-12 ($T_{1/2}$ = 11 ms) dominates early on

➔ prompt information ?

Courtesy: Peter Dendooven (KVI-CART)

Positron range blurring

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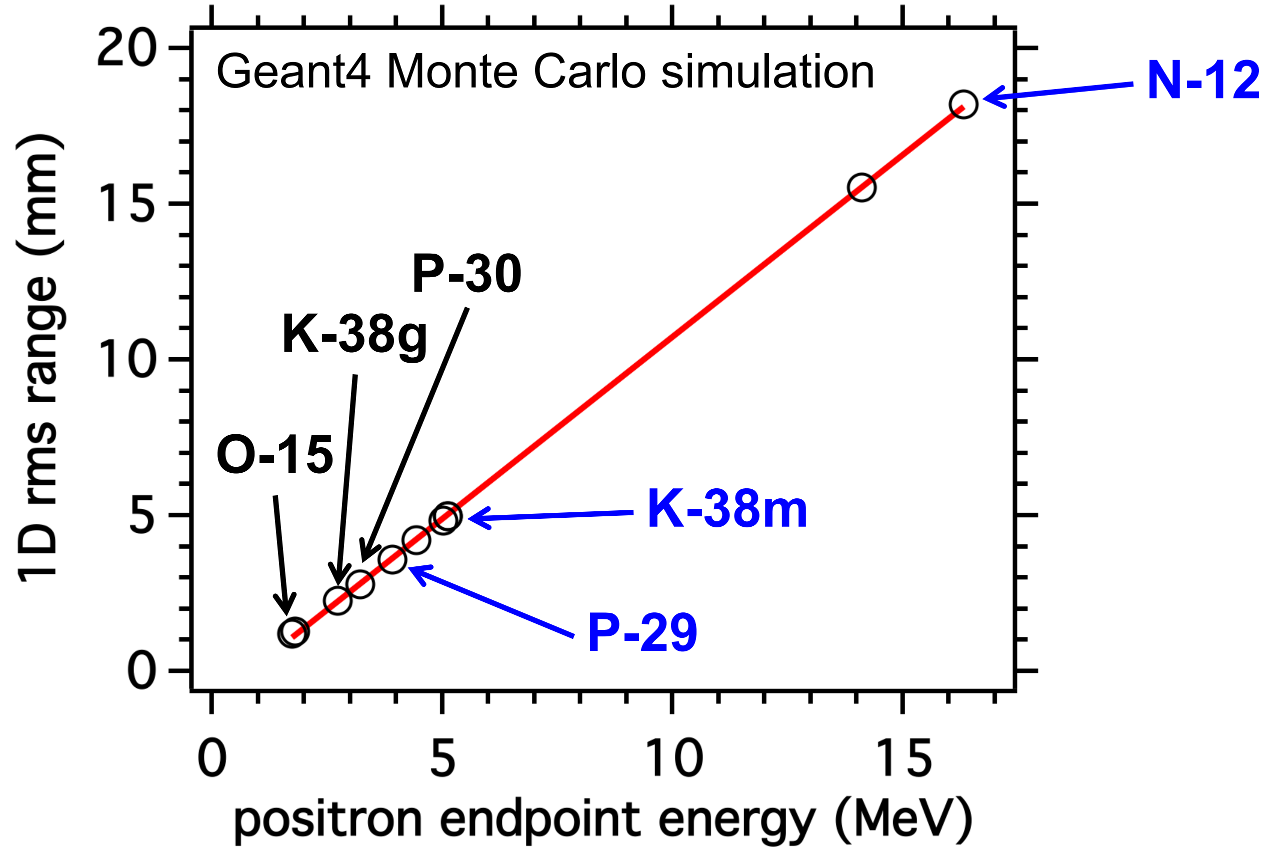
root-mean-square of 1-dimensional projection



N-12: a benefit or a nuisance in beam-on PET ?

Courtesy: Peter Dendooven (KVI-CART)

Beam-on experiment at KVI-CART

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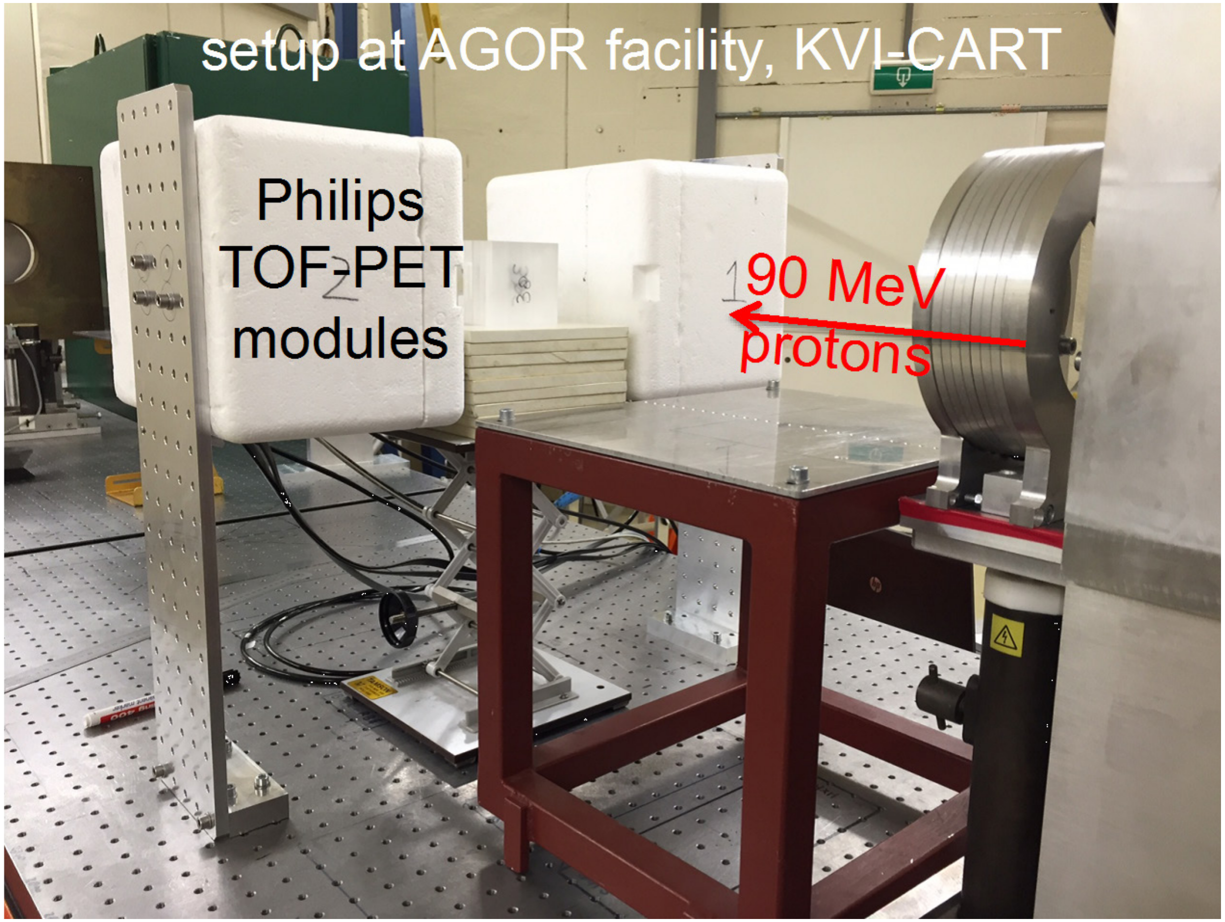

proton **bunches**:
~2 ns full width
23 ns period

proton beam **pulsing**
30 ms on / 59 ms off

Measurements by Tom Buitenhuis & Peter Dendooven

Courtesy: Peter Dendooven (KVI-CART)

Beam-on energy spectra

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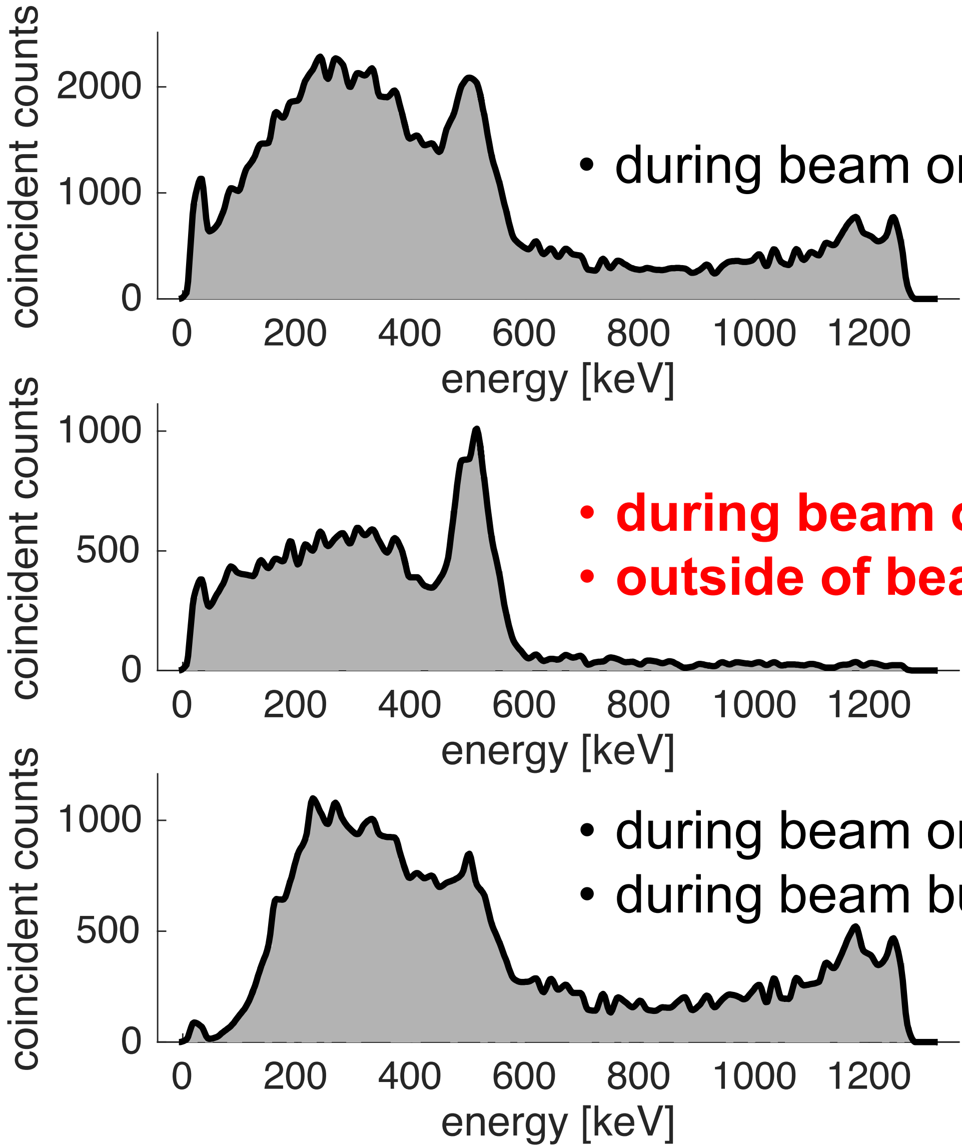
- 120 s irradiation
- ~2 ns p+ bunch width
- 23 ns period
- 10 ns coincidence window



- during beam on

- **during beam on**
- **outside of beam bunches (anticoincidence)**

- during beam on
- during beam bunches

Tom Buitenhuis / Peter Dendooven

Courtesy: Peter Dendooven (KVI-CART)


Thank You
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LAUDA