EndoTOFPET-US

a novel multimodal tool for endoscopy and positron emission tomography

Standort Bahrenfeld
(Physikalische Institute)

Erika Garutti

Universität Hamburg

on behalf of the EndoTOFPET-US collaboration

Outline

- The EndoTOFPET-US Project
  - Endoscopic Detector
  - External Detector Plate
- Tracking
- Image Reconstruction
- Full System Simulation
- Conclusion

This work has been partly funded by the European Union 7th Framework Program (FP7/2007-2013) under Grant Agreement No. 256984 EndoTOFPET-US, and supported by a Marie Curie Early Initial Training Network Fellowship of the European Union 7th Framework Program (PITN-.-GA-.-2011-.-289355-.-PicoSEC-MCNet)

The EndoTOFPET-US project

©DESY / Stuhrmann

Endo = Endoscopic

TOF = Time of Flight

PET = Positron Emission Tomography

US = Ultrasound

The EndoTOFPET-US project

©DESY / Stuhrmann

The tool

- Endo = Endoscopic
- TOF = Time of Flight
- PET = Positron Emission Tomography
- US = Ultrasound

The goals:

1) development of biomarkers for prostate and pancreas tumor
2) intra-operative imaging of prostatic and pancreatic lesions (guided surgery / biopsy)

The EndoTOFPET-US project

©DESY / Stuhrmann

The tool

- Enhanced resolution due to proximity
- Combination with biopsy needle

Endo = Endoscopic

TOF = Time of Flight

PET = Positron Emission Tomography

US = Ultrasound

The goals:

1) development of biomarkers for prostate and pancreas tumor

2) intra-operative imaging of prostatic and pancreatic lesions (guided surgery / biopsy)

The EndoTOFPET-US project

The tool

- Enhanced resolution due to proximity
- Combination with biopsy needle

Endo = Endoscopic

TOF = Time of Flight

PET = Positron Emission Tomography

US = Ultrasound

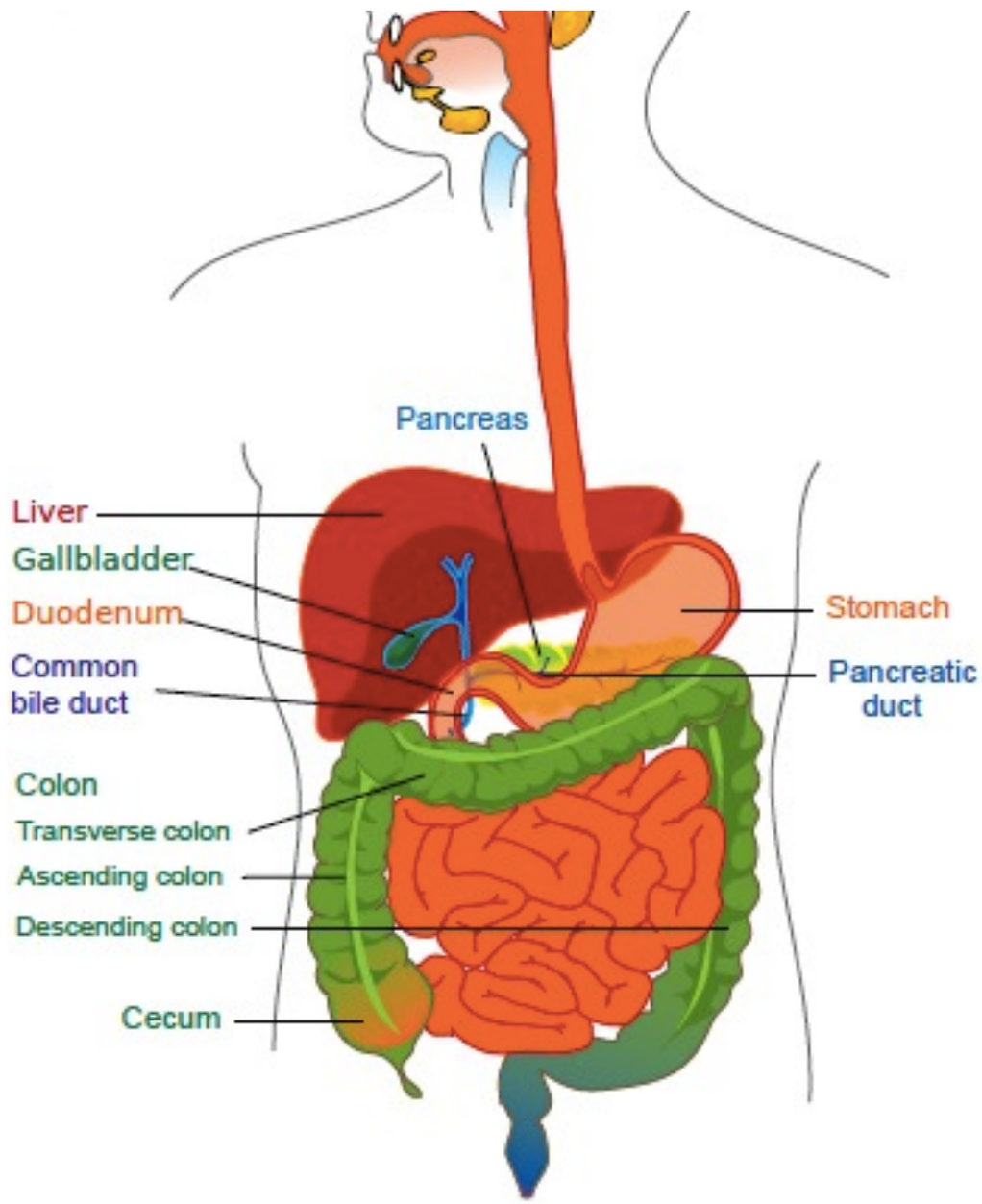
Multi-modal instrument:
high resolution metabolic imaging (PET)
plus anatomical imaging (US)

The goals:

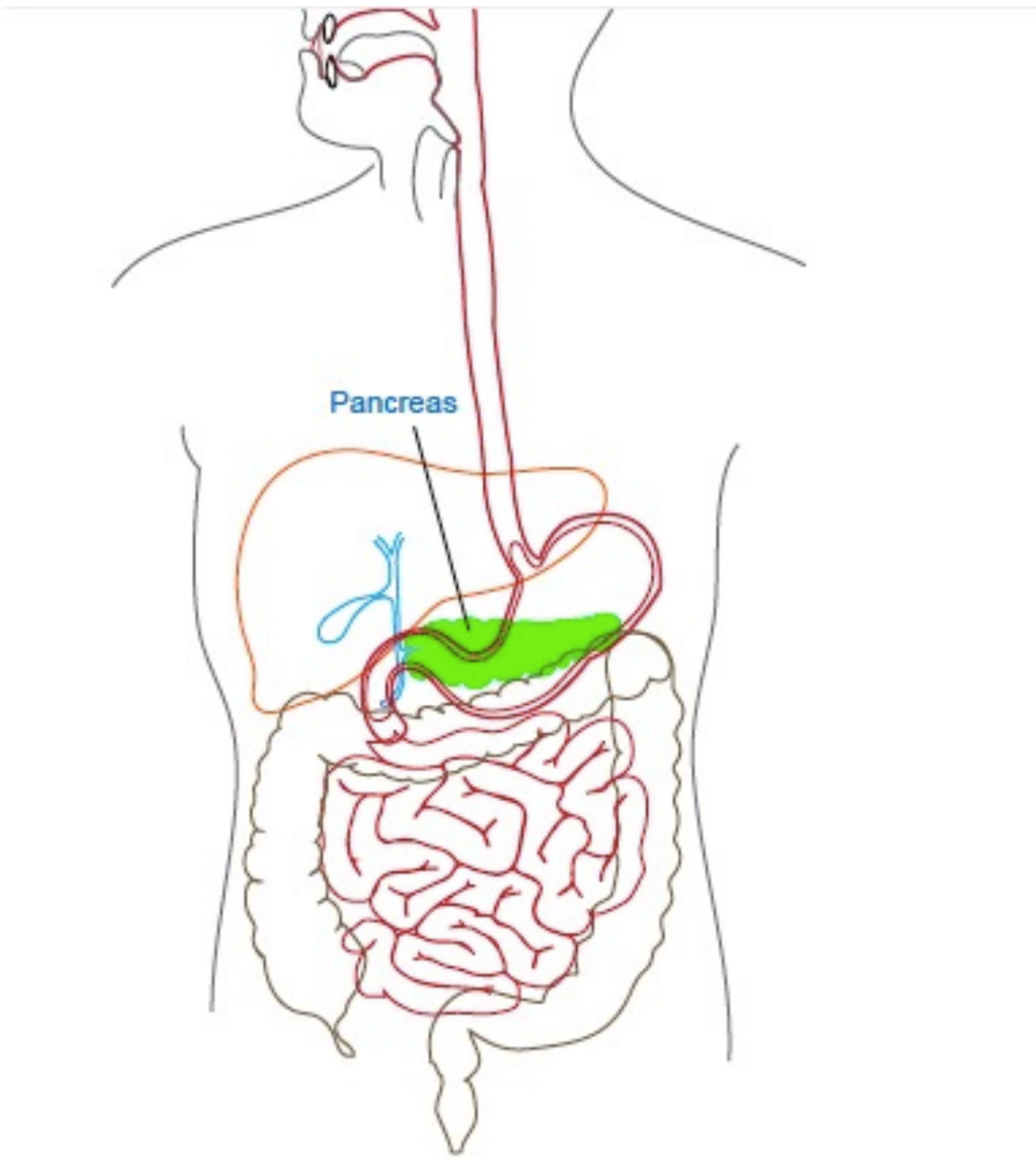
1) development of biomarkers for prostate and pancreas tumor

2) intra-operative imaging of prostatic and pancreatic lesions (guided surgery / biopsy)

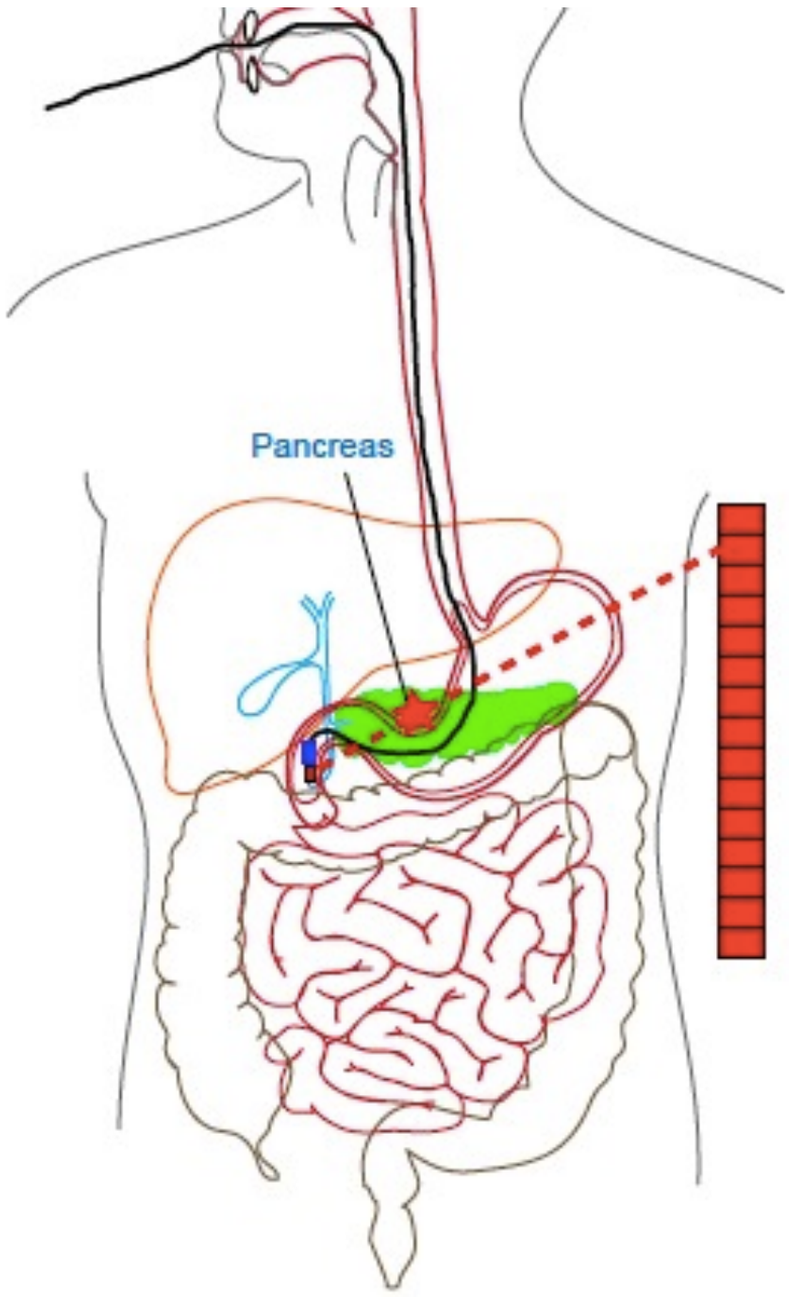
How does endoscopic PET work?



How does endoscopic PET work?

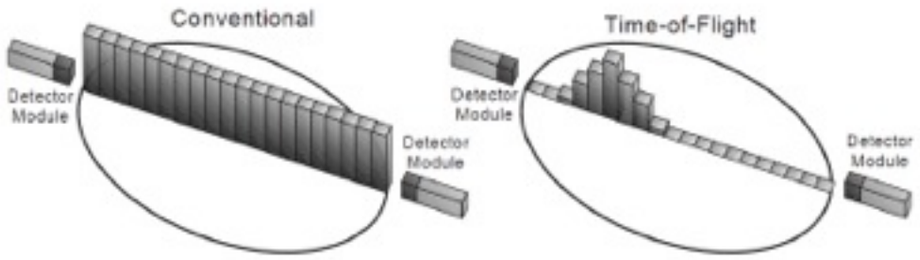


How does endoscopic PET work?



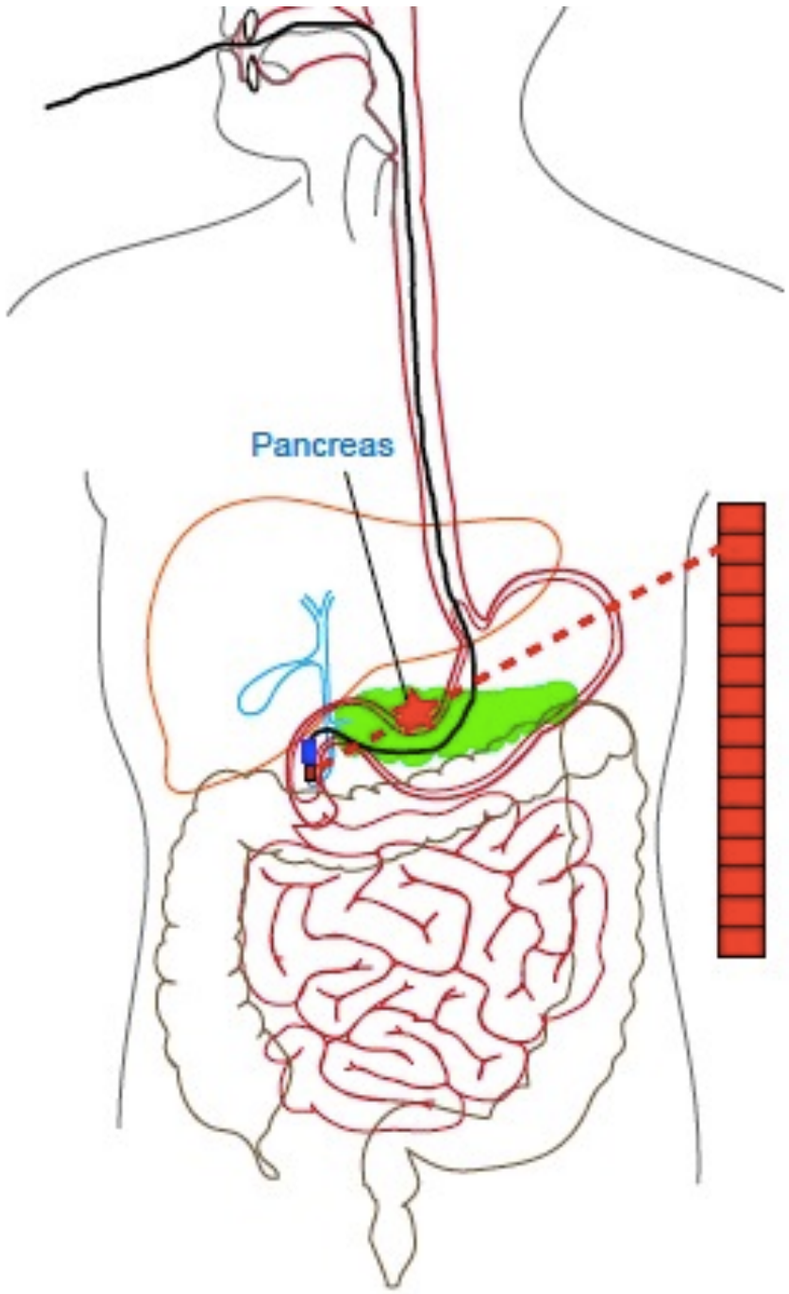
PET image from the line of response obtained between two detectors in coincidence

1) External detector plate
2) Endoscopic detector head mounted on the tip of an US transducer



Time of Flight: to reject false coincidences from near by organs.

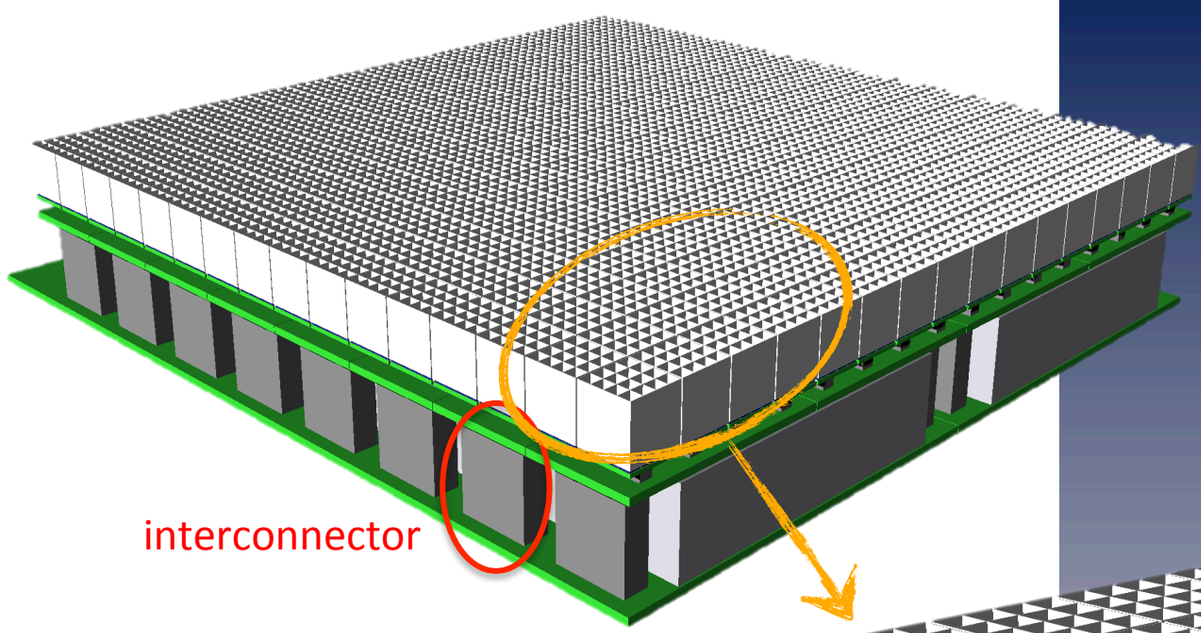
How does endoscopic PET work?

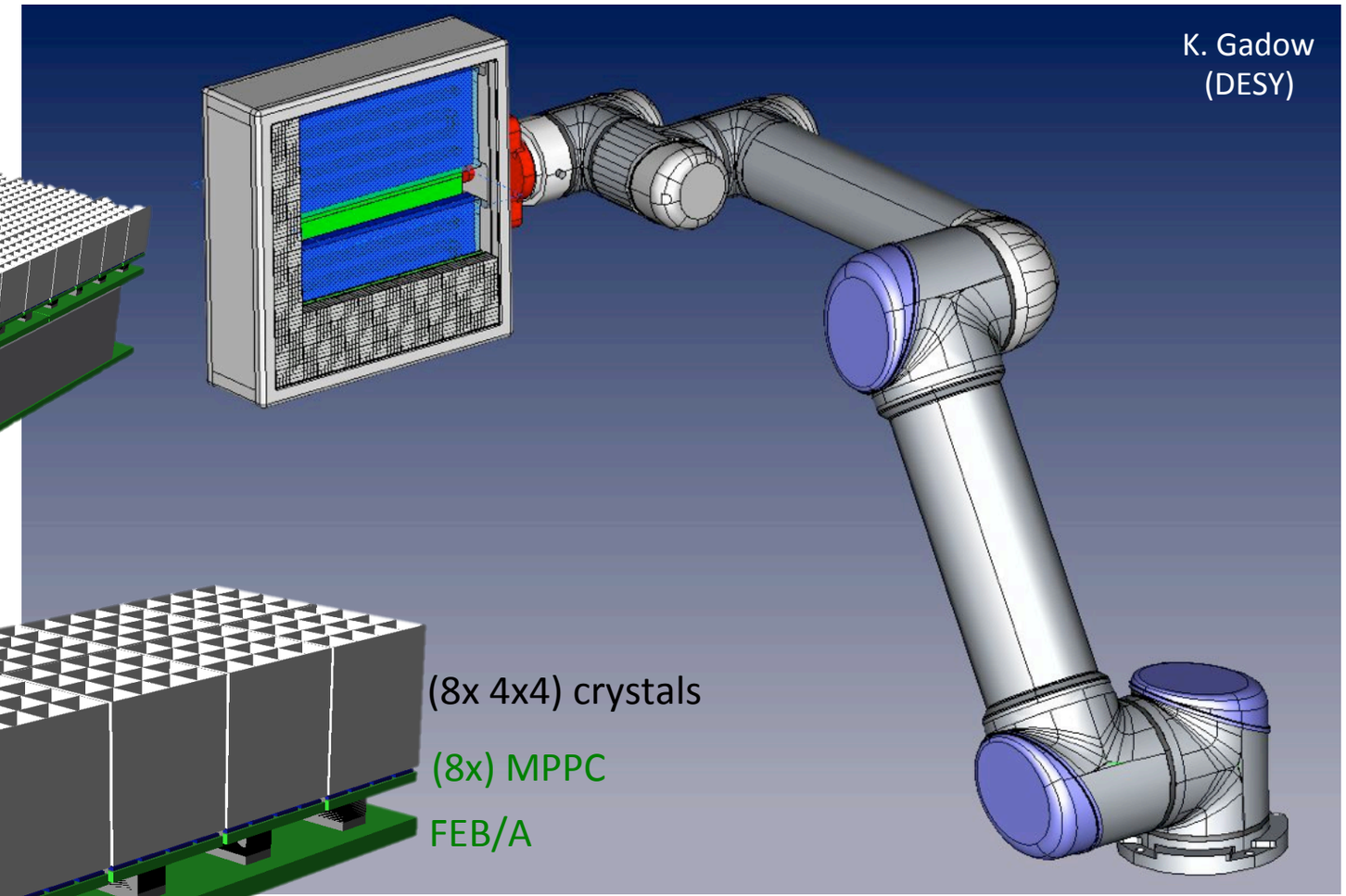


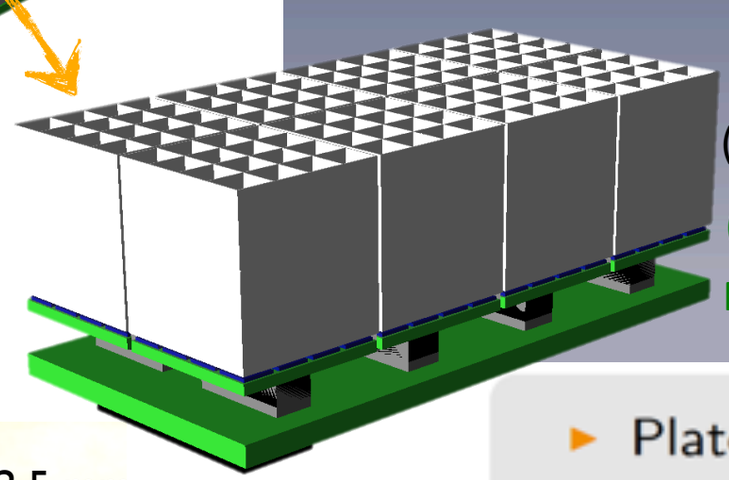
Technical Challenges:

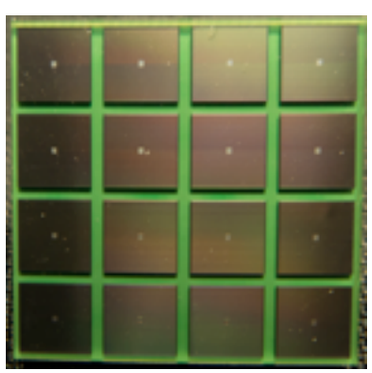
- Extreme miniaturization
- Coincidence time resolution 200 ps FWHM (~3cm background rejection)
- Fast crystals & ultra-fast photo-detection
- Image reconstruction for free-hand imaging,
- O(mm) spatial resolution ➔ tracking
- Fusion of US and PET images

External PET plate - detector design





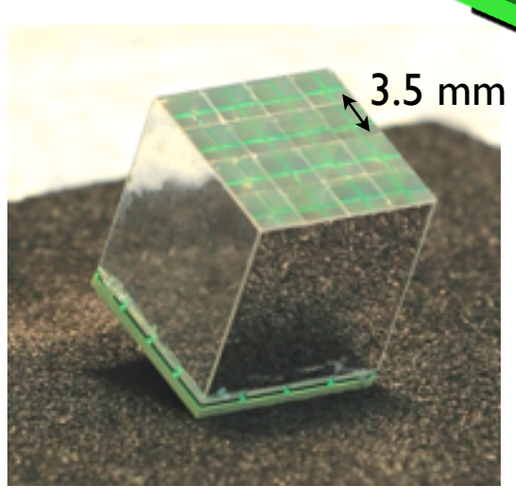




MPPC

+

LYSO



- Plate area: 23×23 cm^2
- 4096 LYSO crystals à $3.5 \times 3.5 \times 15$ mm^3
- Coupled to SiPMs (Discrete Through-Silicon Via MPPC arrays from Hamamatsu)
- Dedicated fast 64-channel ASIC & cooling plate embedded in detector housing
- Mounted on moveable arm

ENDO TOFPET US
Endoscopic TOFPET & Ultrasound

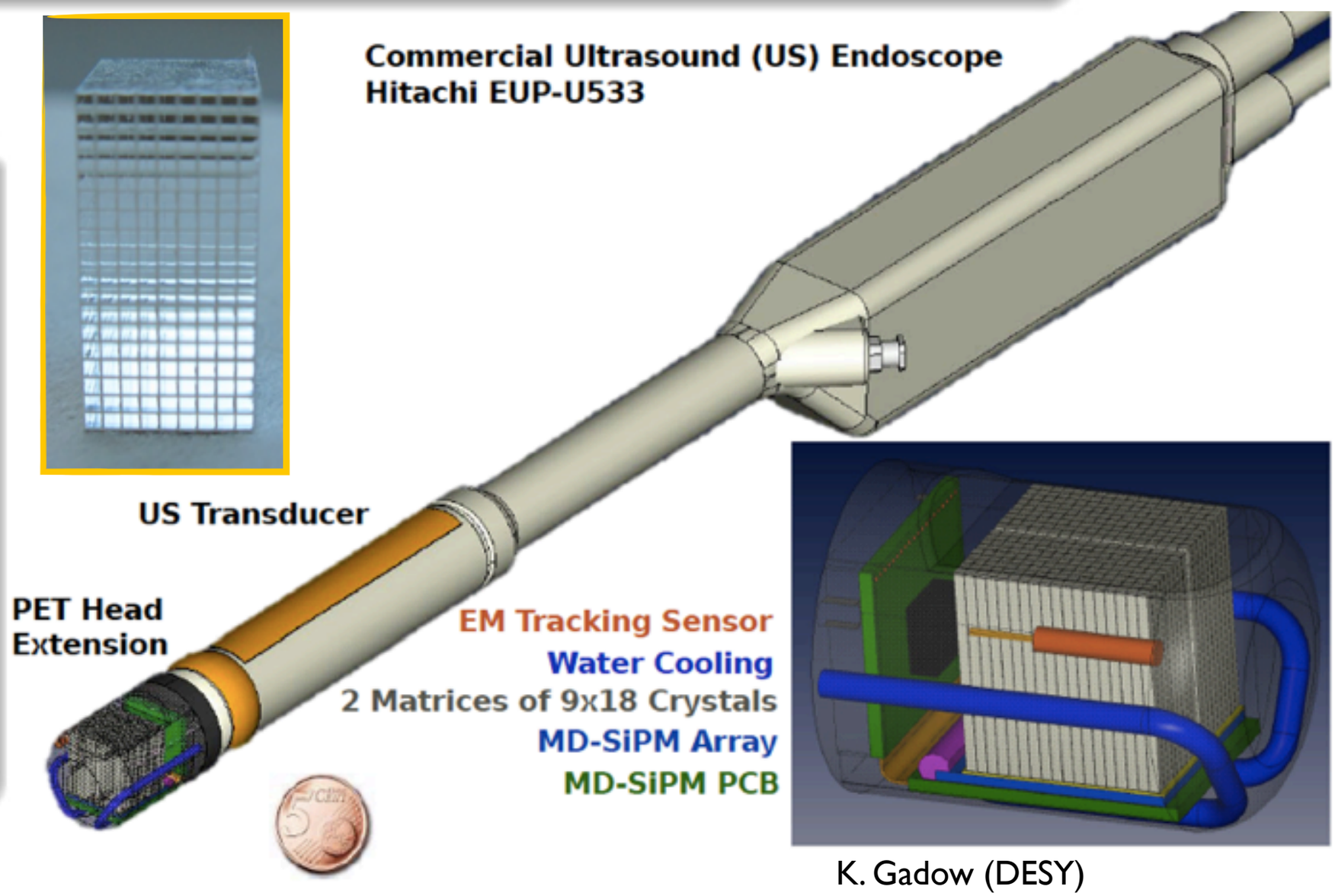
erika.garutti

Internal PET head - detector design

Endoscopic PET Detector

- PET extension mounted on a transrectal US endoscope
- Clamped on endoscope head without alterations of the endoscope
- PET head volume: $23 \times 23 \times 40$ mm^3

- 2 matrices of 9×18 crystals $0.71 \times 0.71 \times 15$ mm^3
- High granularity for excellent spatial resolution
- Coupled to Multichannel -Digital SiPMs (MD-SiPM)
- Readout: digital output of SPADs via interconnection PCB to DAQ
- Cooling via water pipes



K. Gadow (DESY)

ENDO TOFPET US
Endoscopic TOFPET & Ultrasound

erika.garutti@desy.de

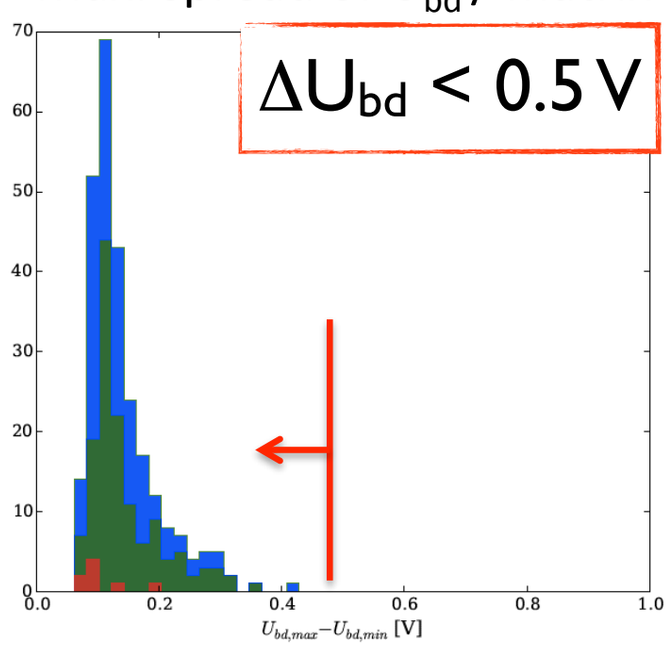
External PET plate - Photo-detector - SiPM

- 276 MPPC-matrices tested (> 4400 single photo-detectors)
- EachMPPC: 3600 pixels, pixel size 50 x 50 um^2

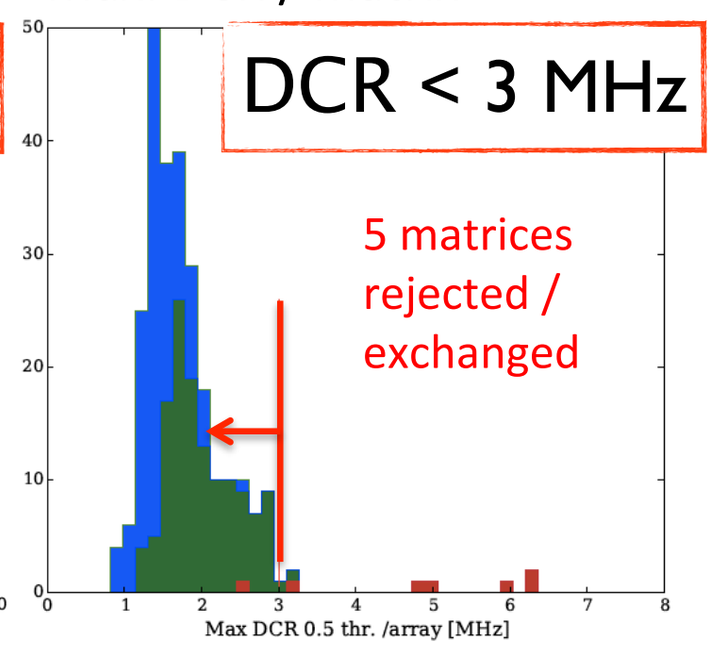
Verify producers parameters:

- Gain: 2% reproducibility error,
- DCR: 10-20% absolute error,
- breakdown V: 50 mV error,
- breakdown V spread in one matrix (16 MPPC)

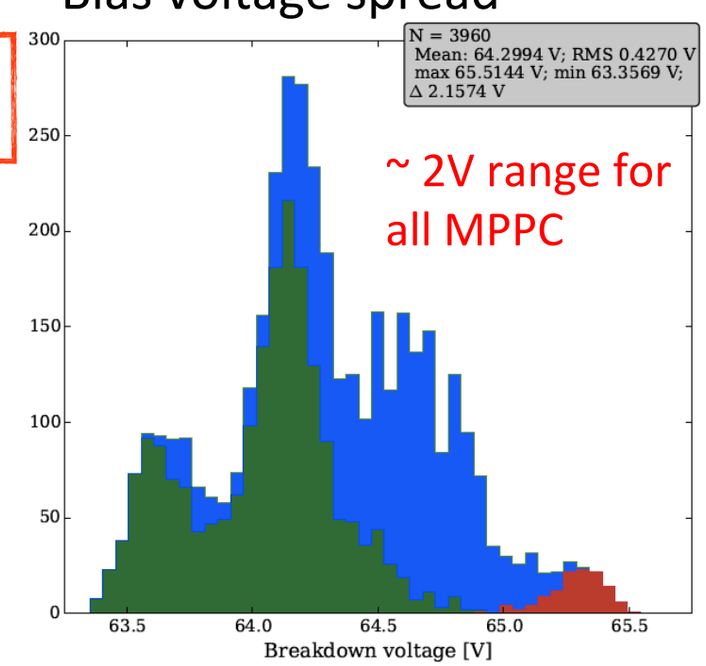
Max. spread of U_{bd} / matrix



Max. DCR / matrix



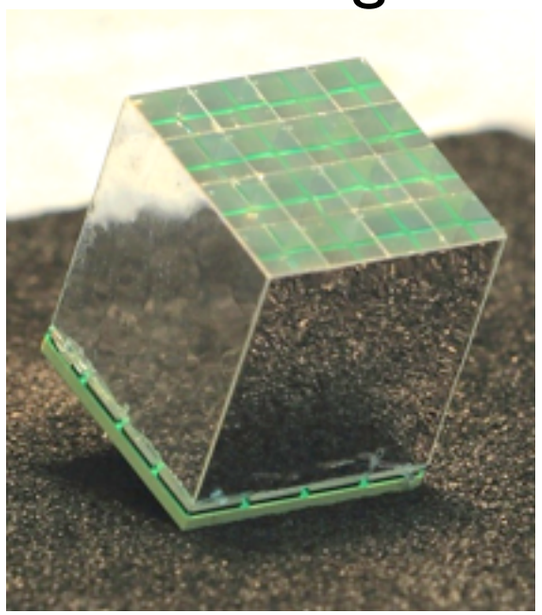
Bias voltage spread



External PET plate - Scintillator crystals

Light yield calibration

Glueing



Coating

Crystals:

- LYSO, 3.5 x 3.5 x 15 mm^3

Light yield:

- Time resolution scales with light yield
- Measure with a photomultiplier tube; correct for air gap, glue & wrapping,
- Average LY = 32 200 ph/MeV
- σ_E/E ~13% (similar for PET head crystals)

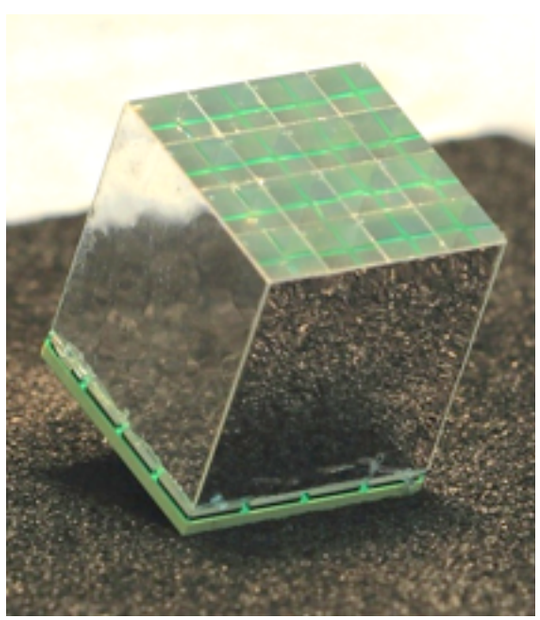
Gluing & wrapping:

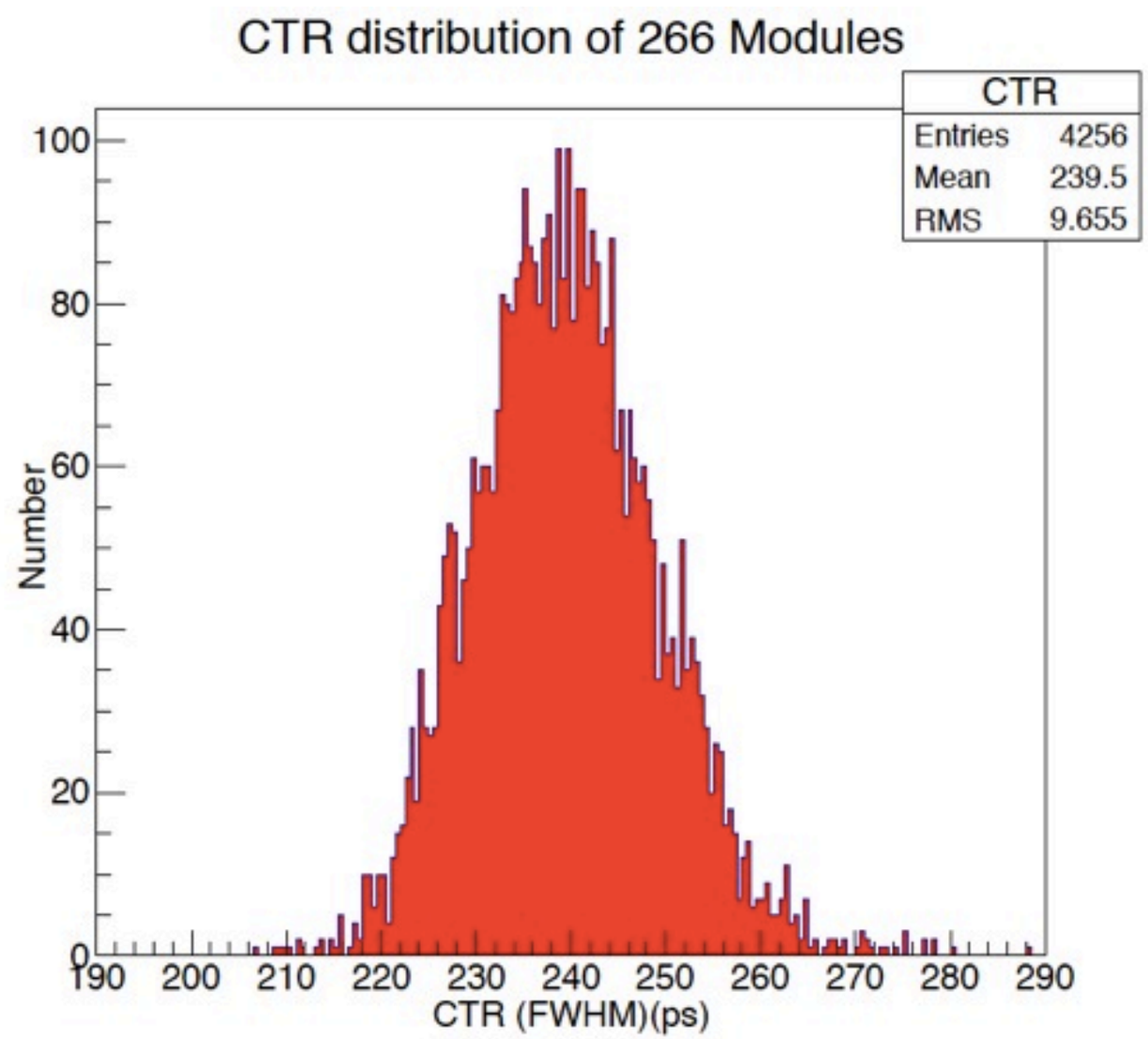
- Automated alignment + visual inspection
- Reflector foil (ESR by 3M) + Teflon cap

External PET plate - time performance

- All matrices of MPPC + LYSO crystals tested using NINO amplifier & HPTDC
- Average Coincidence Time Resolution (FWHM):

$$\text{CTR} = 239.5 \pm 10 \text{ ps}$$



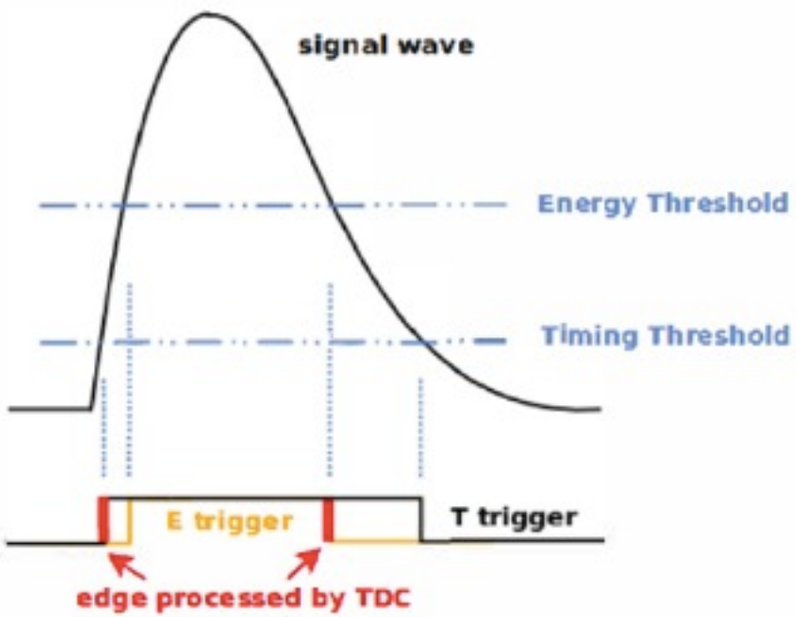


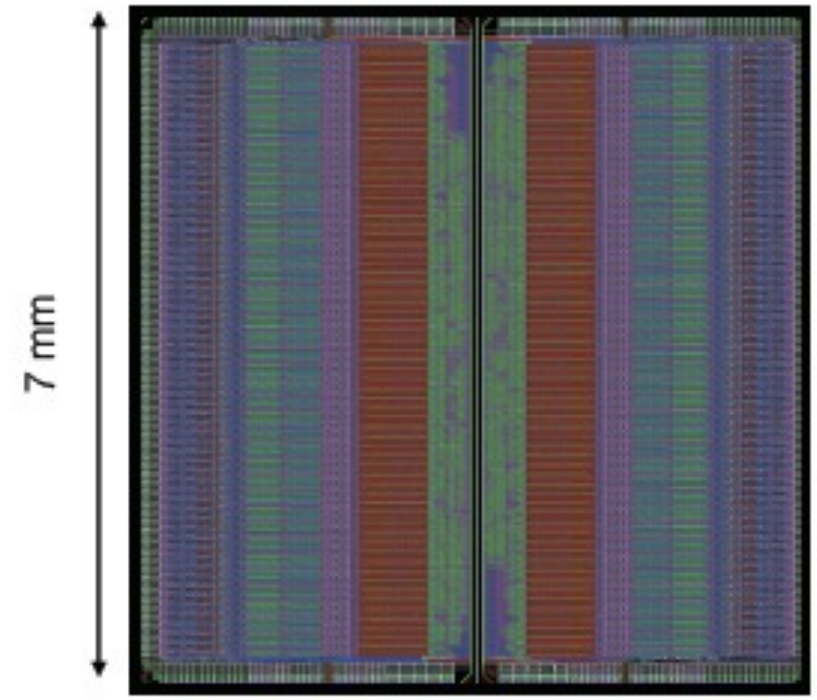
Two dedicated fast SiPM r/o ASICs

Measure time and energy information

Timing via leading-edge technique

Energy using time-over-threshold method

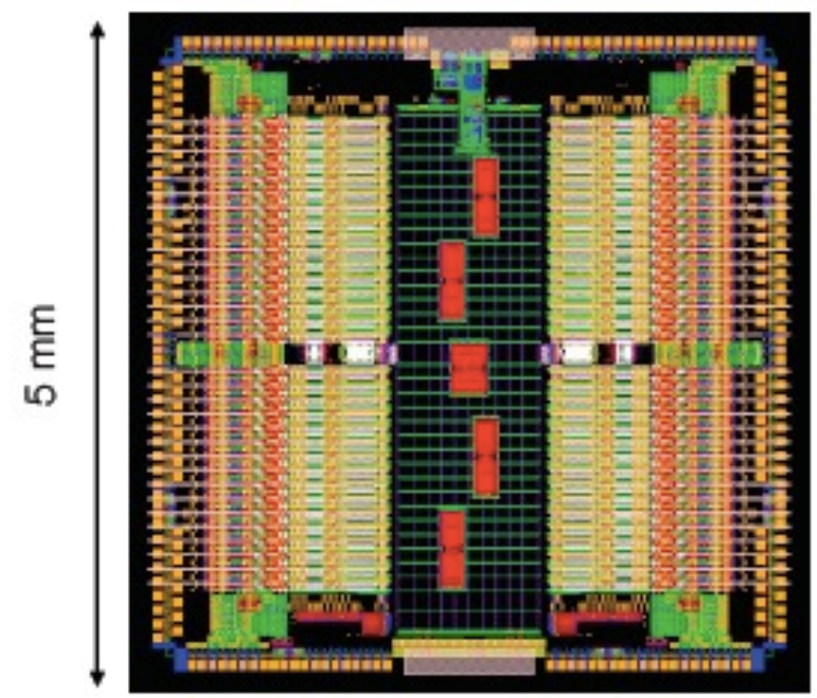




ToFPET ASIC

128 channels

[LIP]



STiC 3.0 ASIC

64 channels

[KIP]

Large channel density

4000 channels within 20 x 20 cm^2

Low noise, low timing jitter

Aim: smaller 30 ps ...

Low power consumption

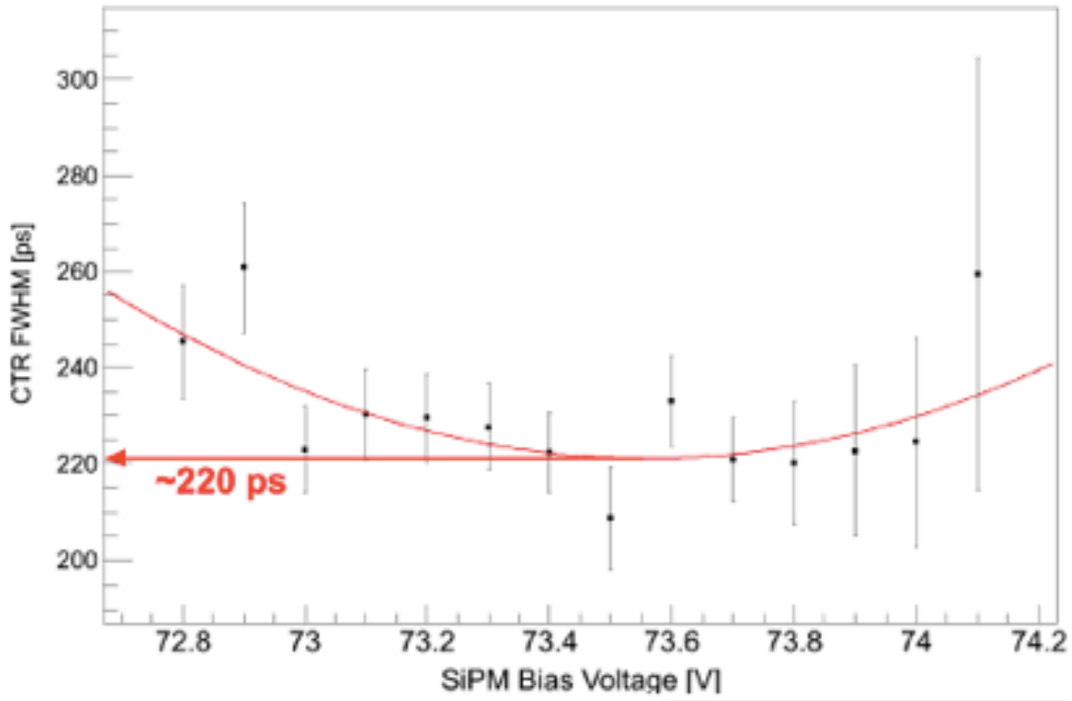
Aim: smaller 10-20 mW/channel ...

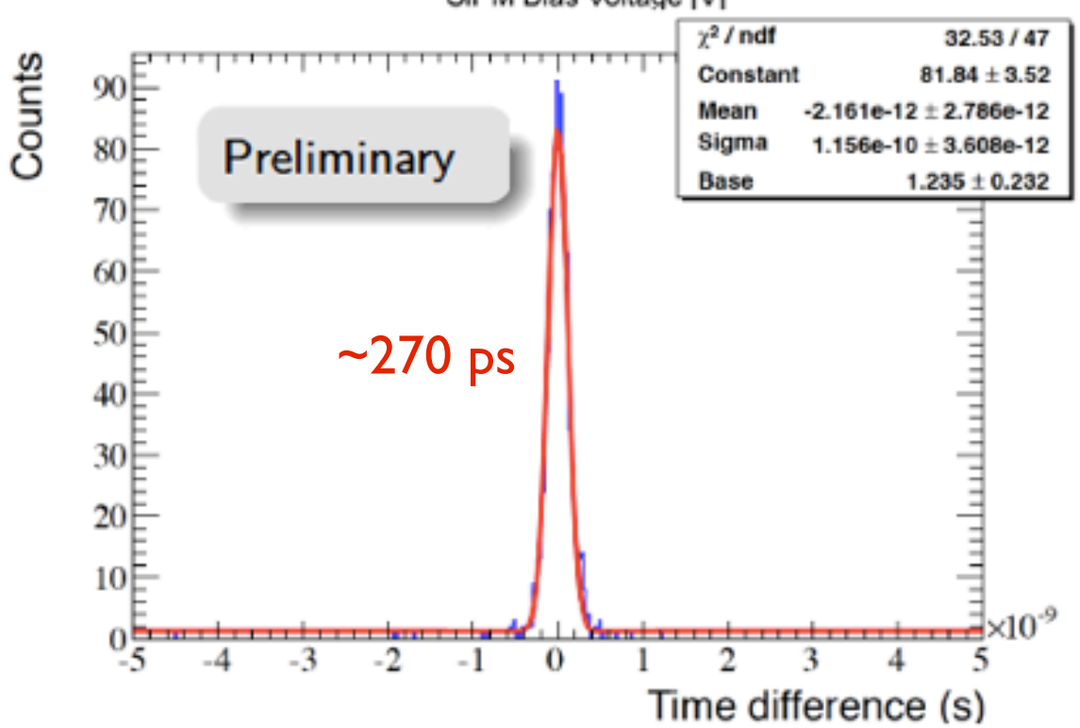
SiPM bias tuning

Adjustment range: 500 mV

erika.garutti@desy.de

ASICs characterization





16-channel STiC Chip

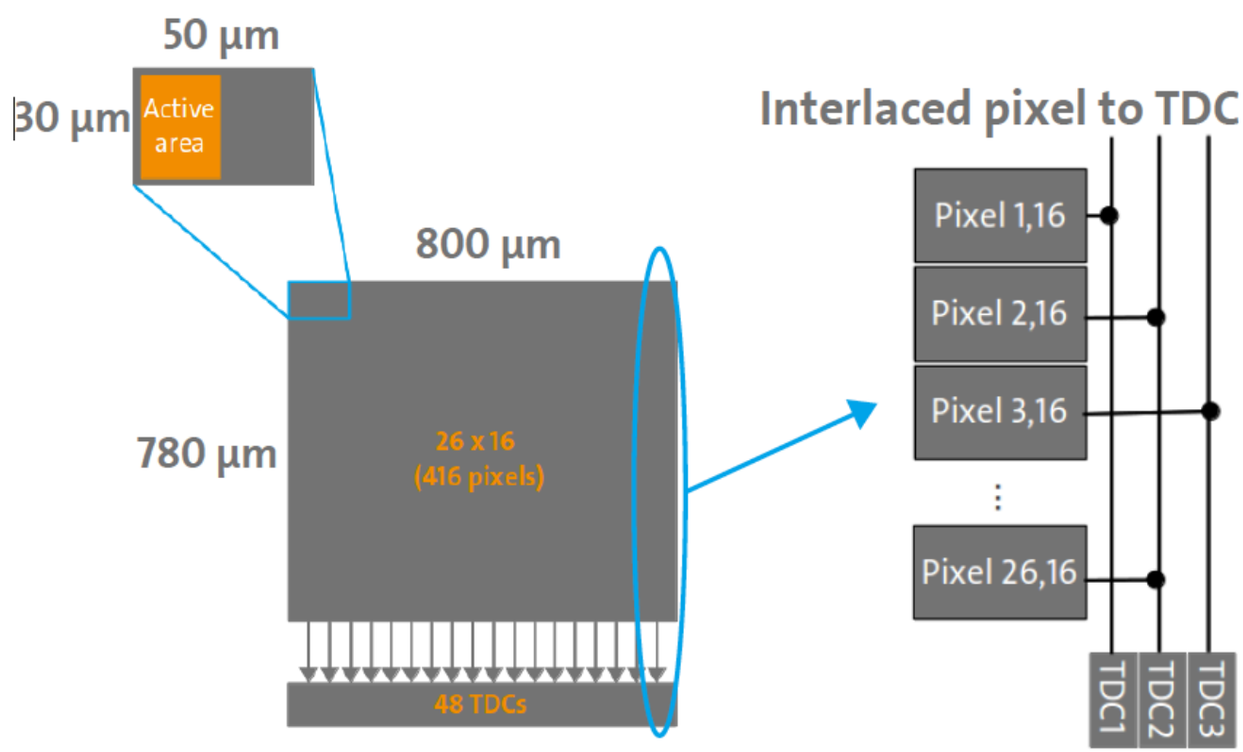
- ^{22}Na source, 3.1x3.1x15 mm LYSO crystals coupled to MPPC
- Connected to STiC chip using differential readout
- Energy resolution of 511 keV peak is $\approx 12\%$
- Measured CTR at optimal HV-settings is 220 ps FWHM
- 64 channel STiC chip delivered, tests ongoing

64-channel TOFPET Chip

- ^{22}Na source, 3.1x3.1x15 mm LYSO crystals coupled to MPPC
- Connected to TOFPET chip using single-ended readout
- Measured CTR: 270 ps FWHM (preliminary)

Inner PET head - Photo-detector - MD-SiPM

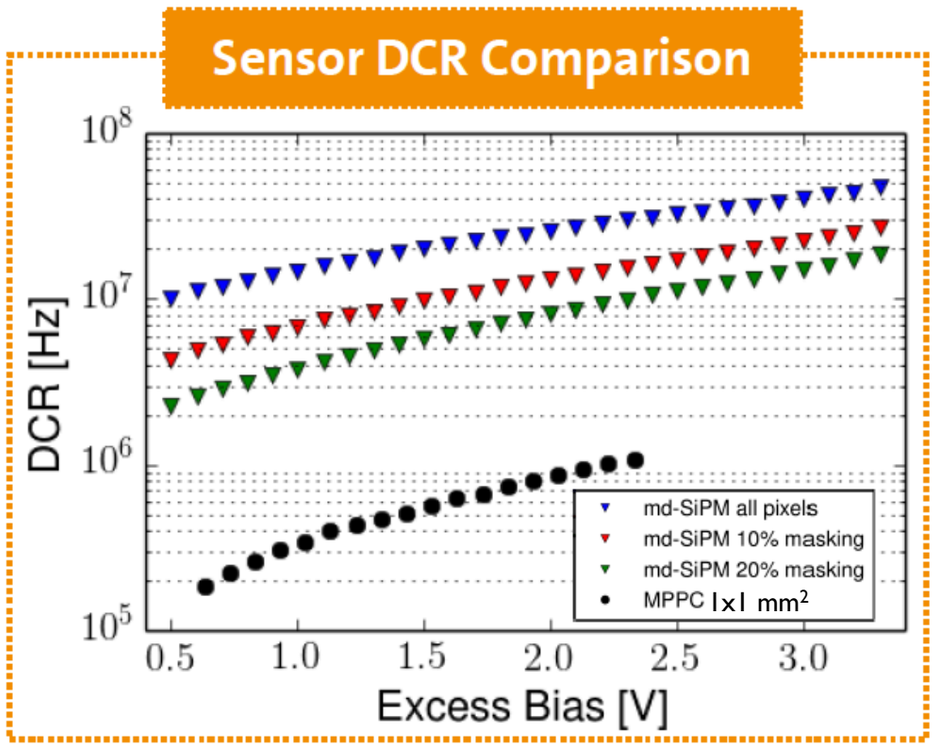
- **TU Delft's MD-SiPM prototype specification:**
  - 30x50 μm^2 pixel size with 57% fill factor
  - 416 SPAD pixels (26x16) per cluster
  - 780x800 μm^2 cluster size
  - Photon Detection Efficiency (PDE) up to 17%
  - 48 column-wise shared TDC
  - 45 ps per TDC bin



Courtesy of E. Charbon, Delft

MD-SiPM - dark count rate

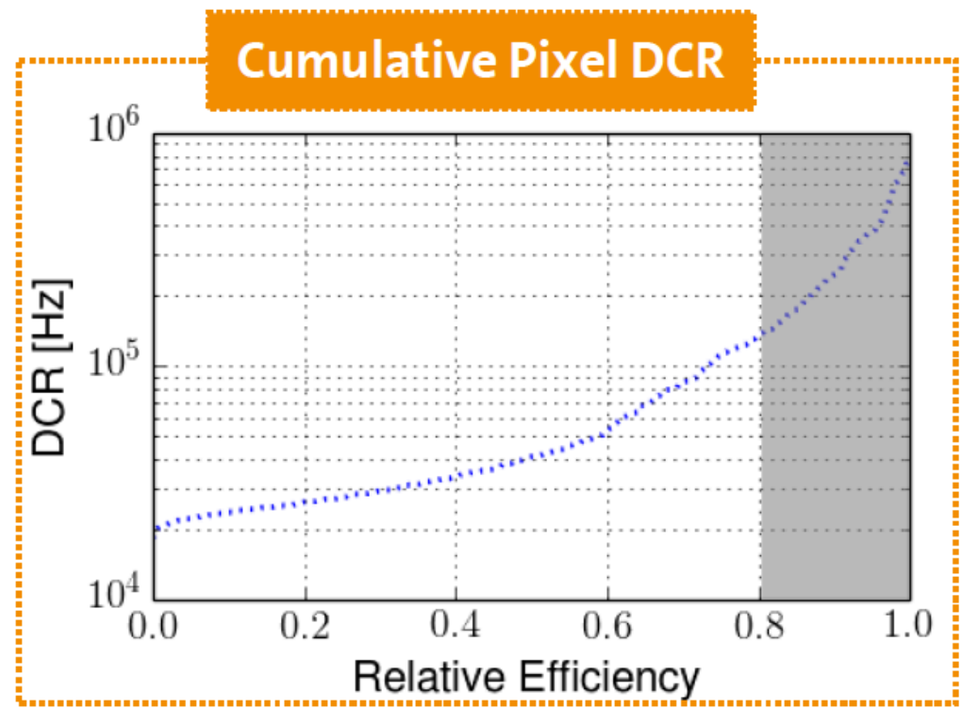
- **Compare to MPPC**



- **DCR per μm² of the two sensors at nominal operating voltage, room temperature**

MPPC	MD-SiPM
~ 1 Hz/μm²	~ 50 Hz/μm²

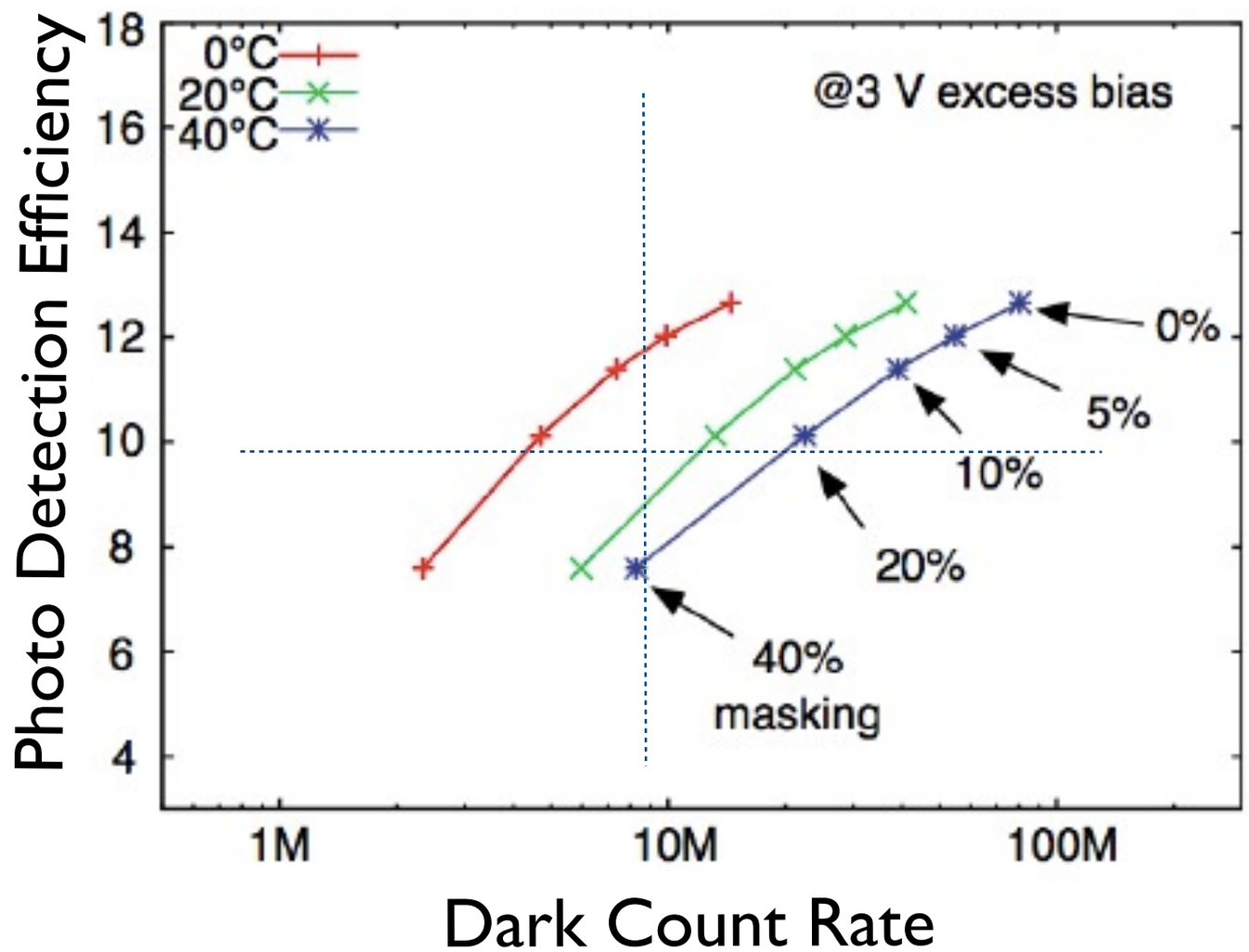
- **DCR Suppression:**
  - **Cool the sensor**
  - **Turn noisy pixel off (lost in efficiency)**



- Room temperature
- 2.5 V excess bias
- Readout frame of 100 ns

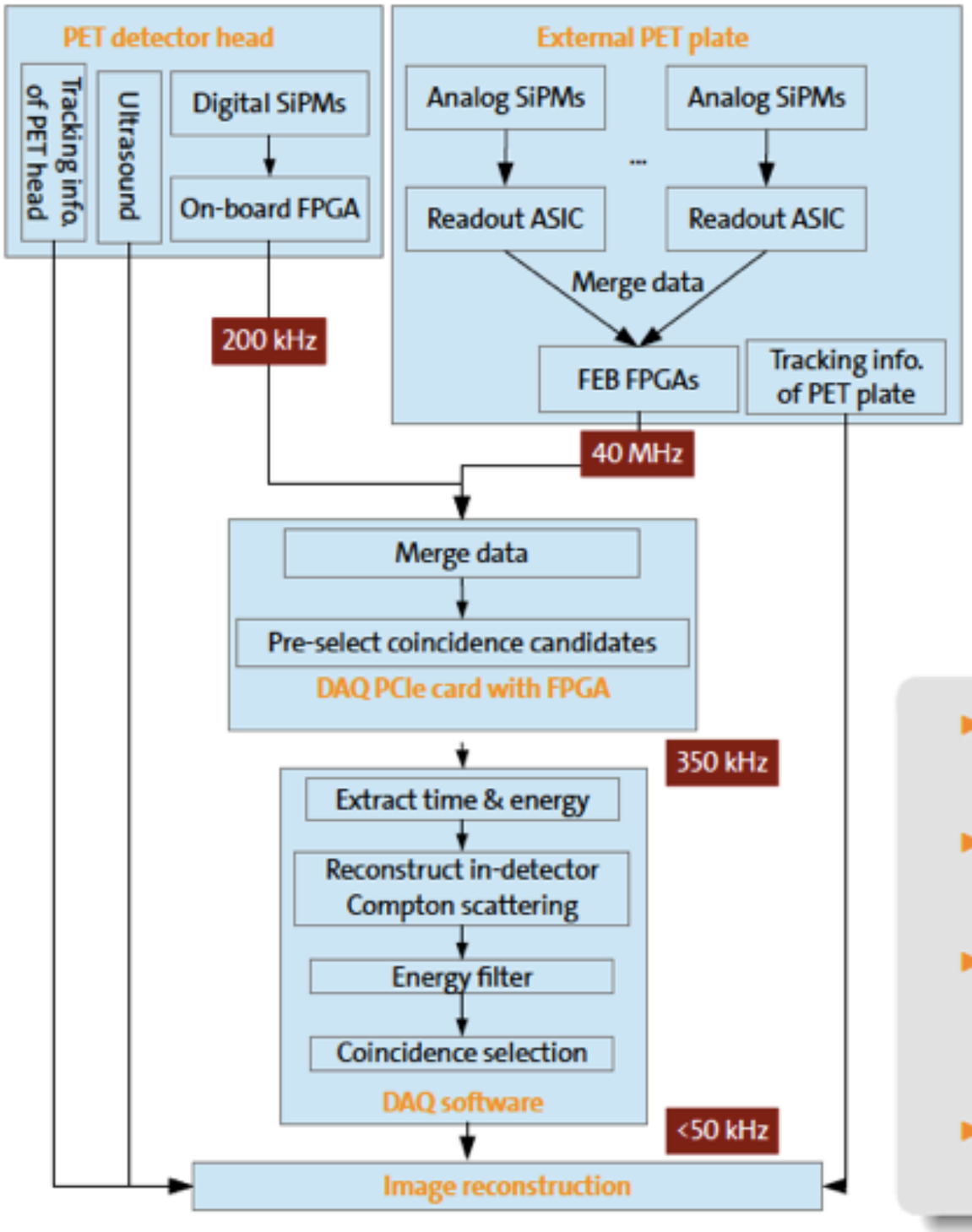
MD-SiPM - cooling requirement

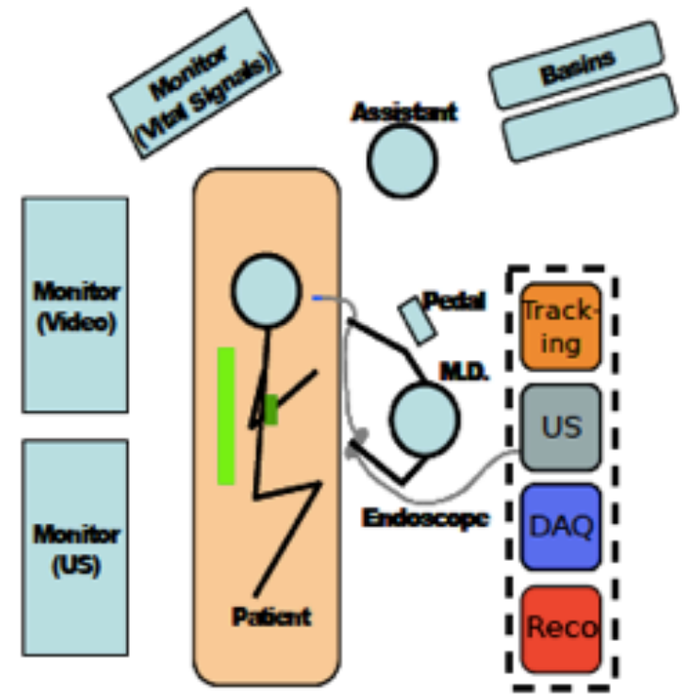
Design goal: 200 ps coincident time resolution
Requirement: PDE > 10% & DCR < 10 MHz



→ reachable only with sensor cooled < 20 °C

Data acquisition



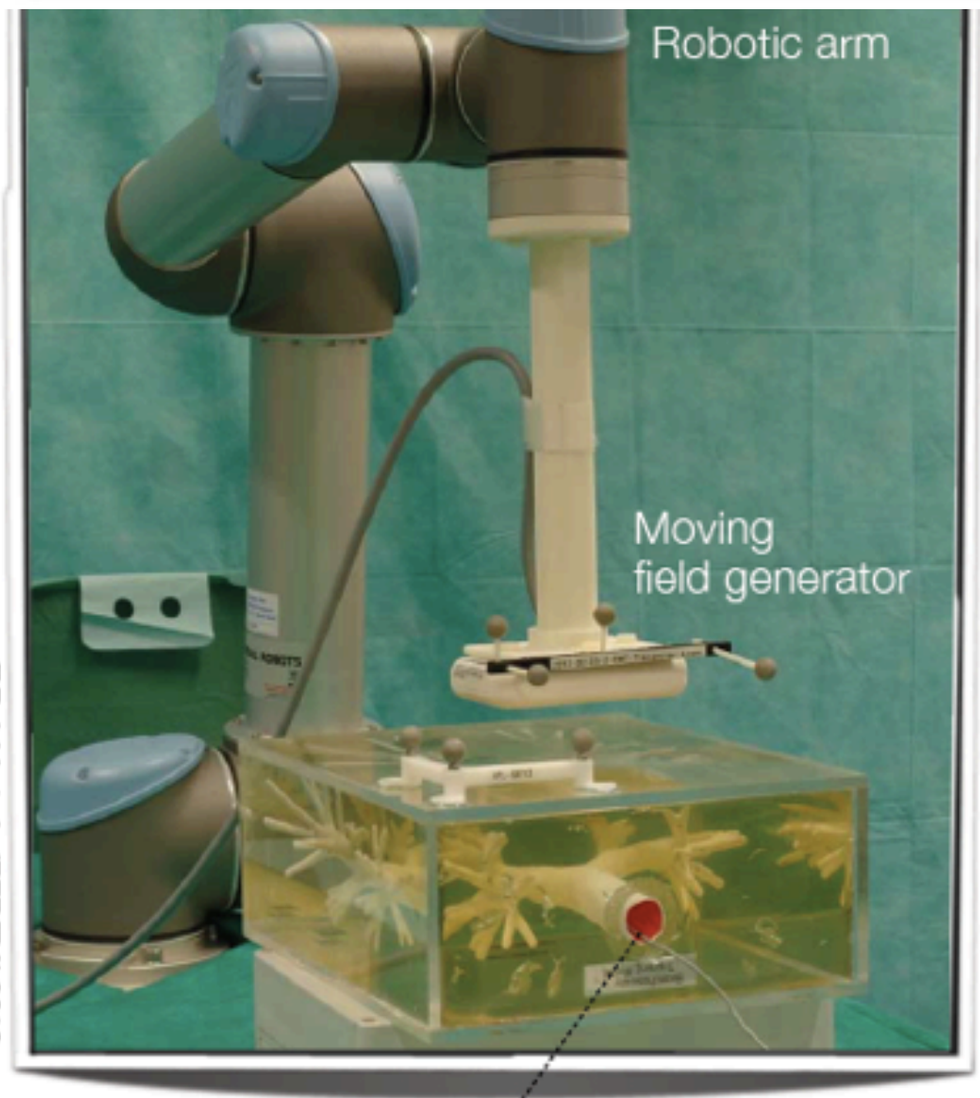


- DAQ backend implemented in PCI-e board interfacing to DAQ PC
- Firmware to communicate with ASIC and probe developed and tested
- Medical data communication framework (control communication between multiple imaging & tracking devices)
- Graphical user interface, incl. PET/US fusion

Electromagnetic tracking system

Tracking Precision

- Electromagnetic: $\approx 3 - 4$ mm
- Optical: $\approx 0.1 - 0.5$ mm
- Mechanic: $\approx 50\,\mu m - 0.1$ mm



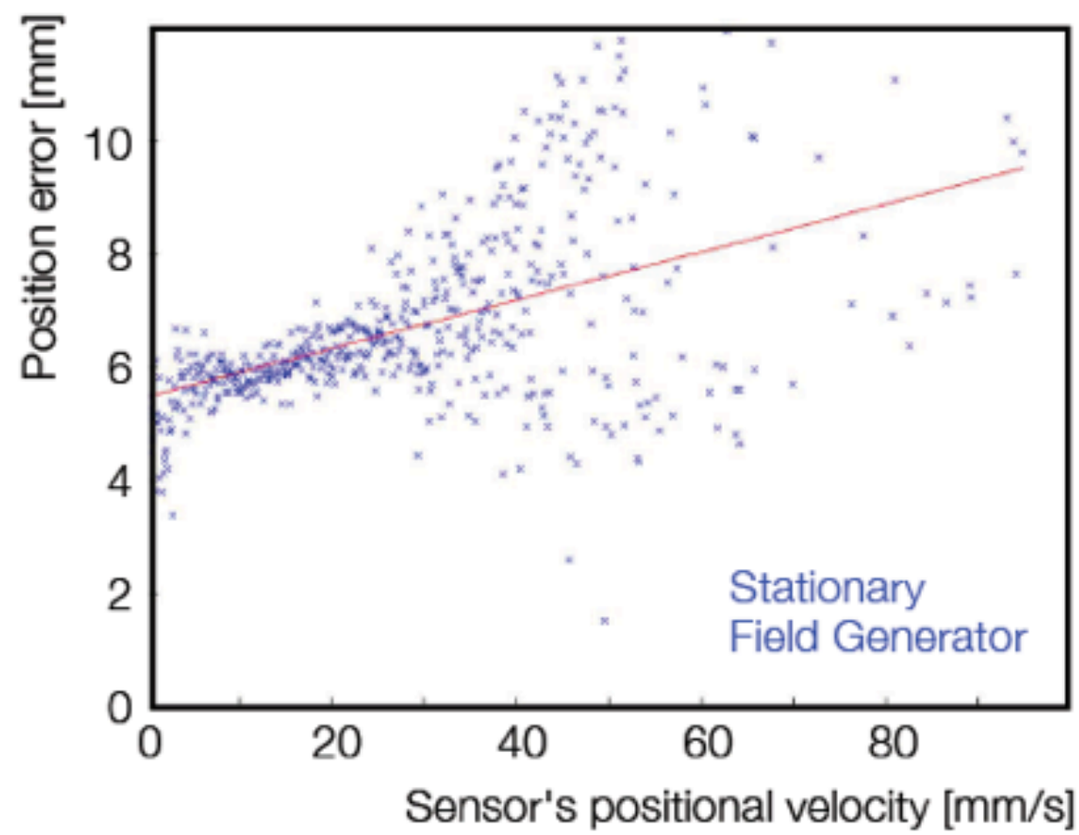
T.Reichl et al., IEEE TMI 2013

Moving sensor
[within bronchoscopy training phantom]

Calibration of EM tracking system in motion:

	Position Accuracy	Orientation Accuracy
Dynamic, stationary FG	6.64 ± 7.86 mm	2.70 ± 1.56 °
Dynamic, moving FG	3.83 ± 6.43 mm	1.34 ± 0.52 °
Static acquisition	1.55 ± 0.62 mm	1.46 ± 1.07 °

Reichl et al., IEEE 2013



T.Reichl et al., IEEE TMI 2013

Electromagnetic tracking system

Tracking Precision

- Electromagnetic: $\approx 3 - 4$ mm
- Optical: $\approx 0.1 - 0.5$ mm
- Mechanic: $\approx 50\,\mu m - 0.1$ mm

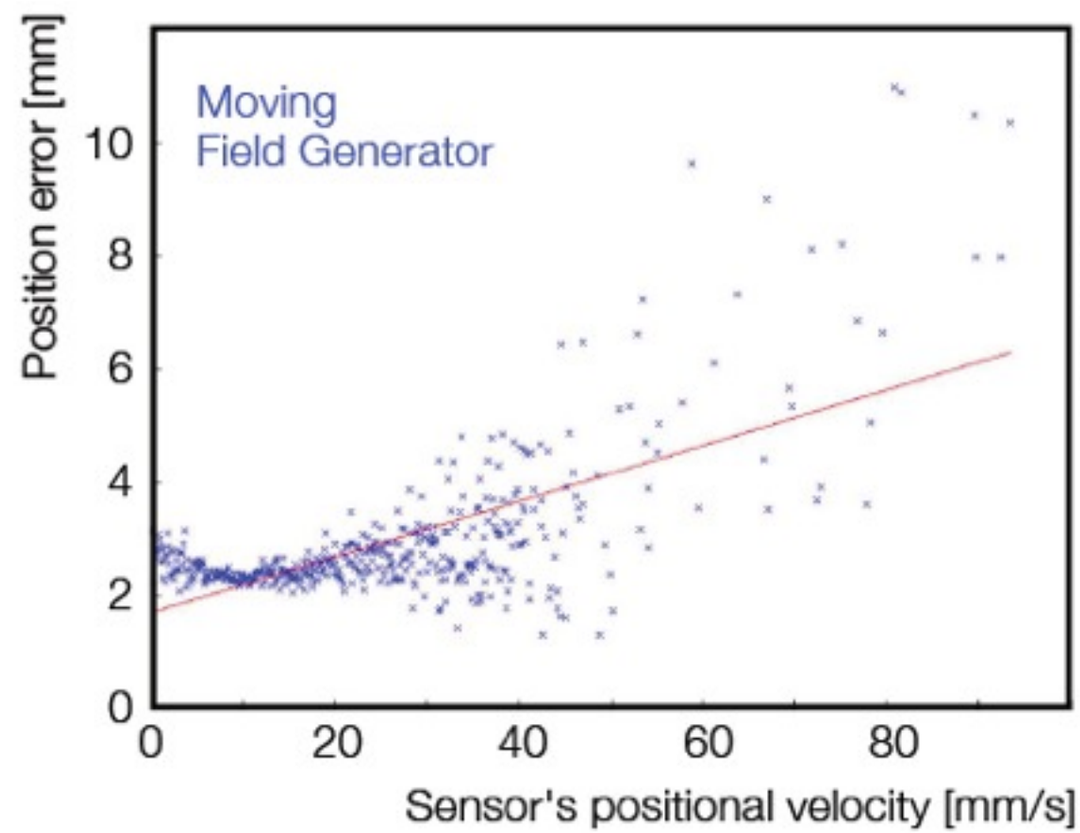
T.Reichl et al., IEEE TMI 2013

Moving sensor
[within bronchoscopy training phantom]

Calibration of EM tracking system in motion:

	Position Accuracy	Orientation Accuracy
Dynamic, stationary FG	6.64 ± 7.86 mm	2.70 ± 1.56 °
Dynamic, moving FG	3.83 ± 6.43 mm	1.34 ± 0.52 °
Static acquisition	1.55 ± 0.62 mm	1.46 ± 1.07 °

Reichl et al., IEEE 2013

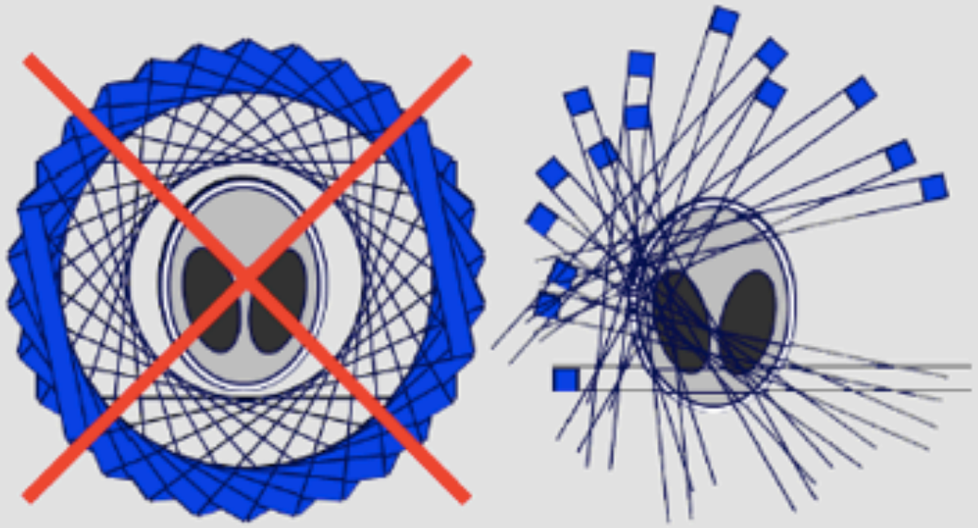


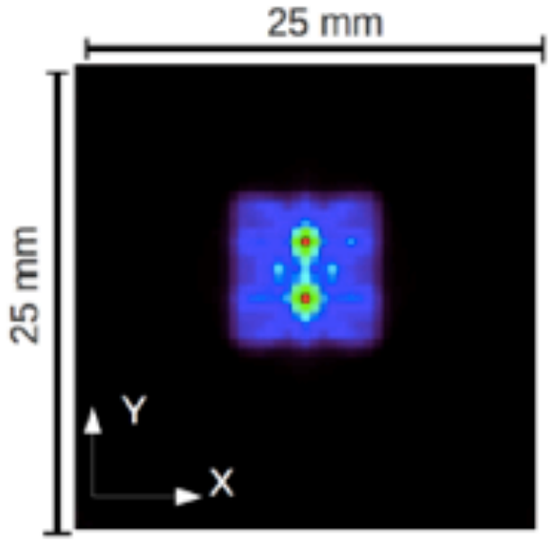
T.Reichl et al., IEEE TMI 2013

PET image reconstruction

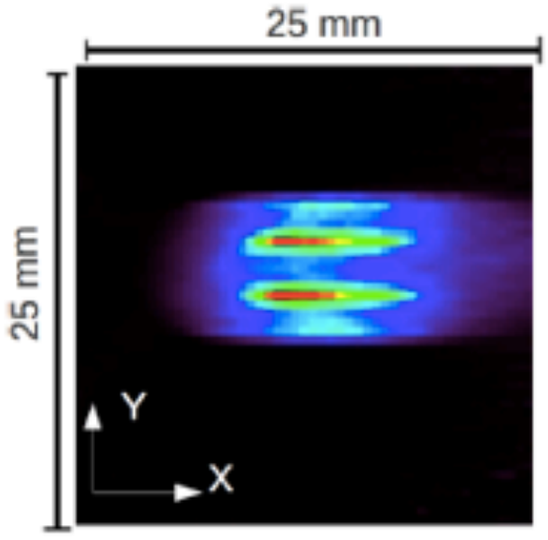
Challenges

- Time of flight (TOF)
- Limited angle problem
- Freehand
  → undefined volume of interest
- Low sensitivity, high noise
- Reconstruct the image on-line to provide guidance for the physician





Full Rotation



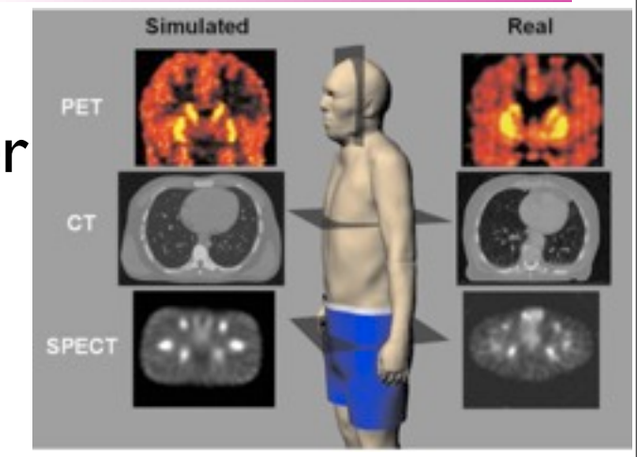
Limited Rotation

- Use a Maximum Likelihood Expectation Maximization iterative reconstruction running on GPUs
- Image reconstruction possible in O(min.)
- Effect of asymmetric detector

Full body simulation with GAMOS

Geant4-based Architecture for Medical-Oriented Simulation

- Allows asymmetric detectors → use in-built coincidence sorter
- Possibility to import whole body phantom (i.e. visible human)

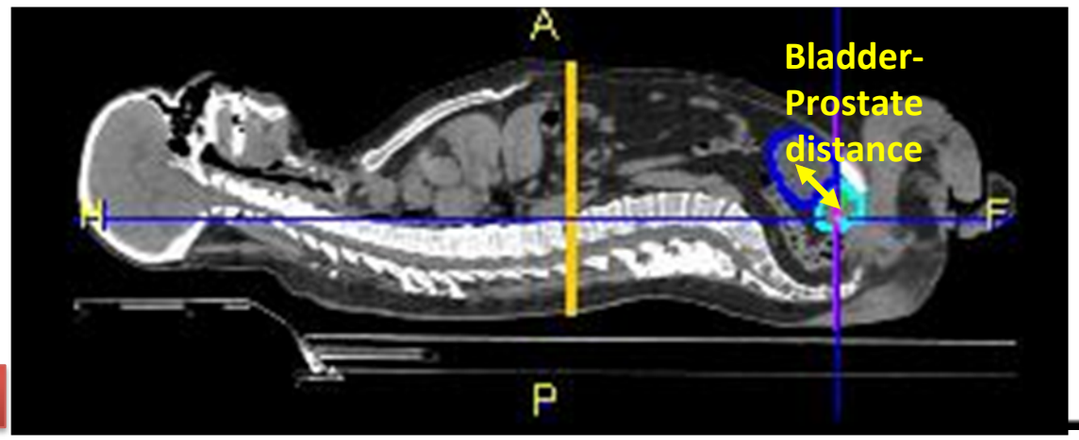


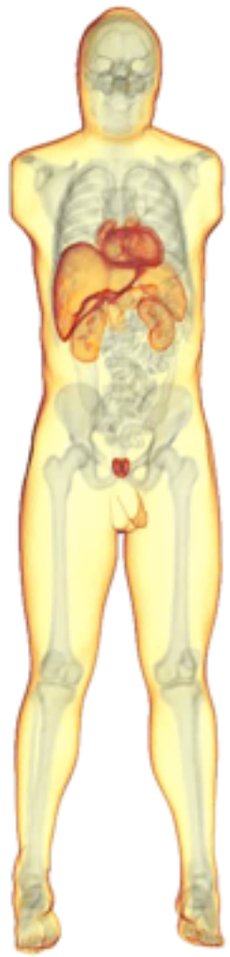
- Ability to tune all parameters according to patient data

Number Patient Examination Date0	Patient 1 27.10.2011	Patient 4 17.03.2010
Prostate Volume	96 ml	75 ml
Bladder Volume	232 ml	121 ml
Thickness of Pelvis Bone (at the prostate level)	2.3 cm	2.4 cm
Uptake Prostate (average)	1.9 kBq/ml	1.9 kBq/ml
Uptake Bladder (average)	1.4 KBq/ml	1 kBq/ml
Uptake of prostatic lesions (average)	3.3 kBq/ml	6.7 kBq/ml
Volume of prostatic lesions	8.5 ml	3.4 ml

Signal / Background ~ 1/10 – 1/20

- Anonymous databank of measured prostate lesions from CHUV, Lausanne
- Possibility to import directly clinical data from PET/CT





erika.garutti@desy.de

Conclusions

EndoTOFPET-US ...

... a novel multimodal endoscopic ToFPET/US imaging system
for improved prostate and pancreas tumor diagnostics

... requires frontline research concerning

- Novel Photosensors
- Ultra-fast readout electronics
- Scintillating crystals & optical systems
- Tracking and image reconstruction
- Biomarkers

... entails knowledge transfer between HEP and medicine ...

Time Schedule:

System Integration: Spring 2014
System Commissioning/Validation: Summer 2014
Delivery to medical hospital: Autumn/End 2014

Project motivation

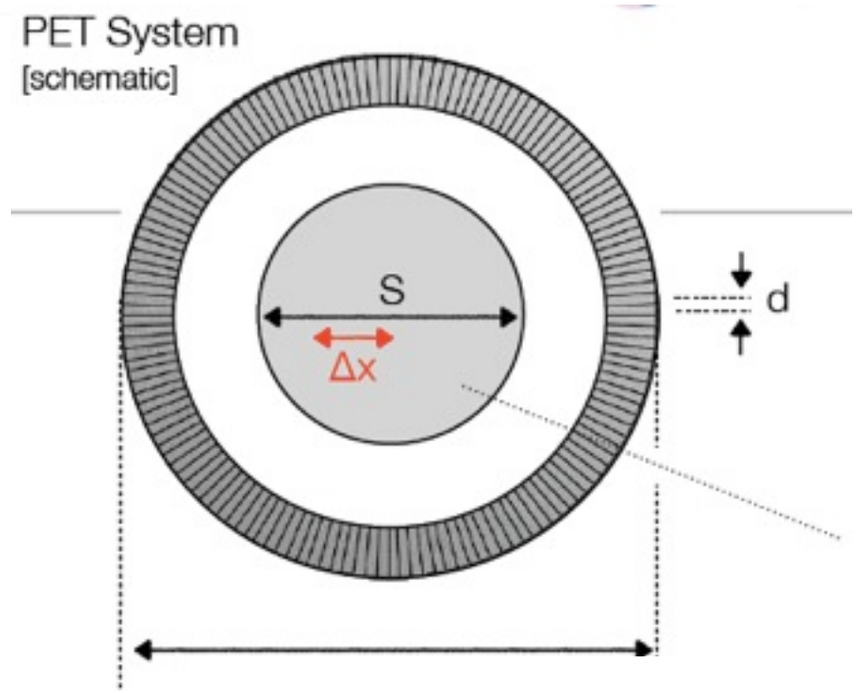
Why Endoscopic?

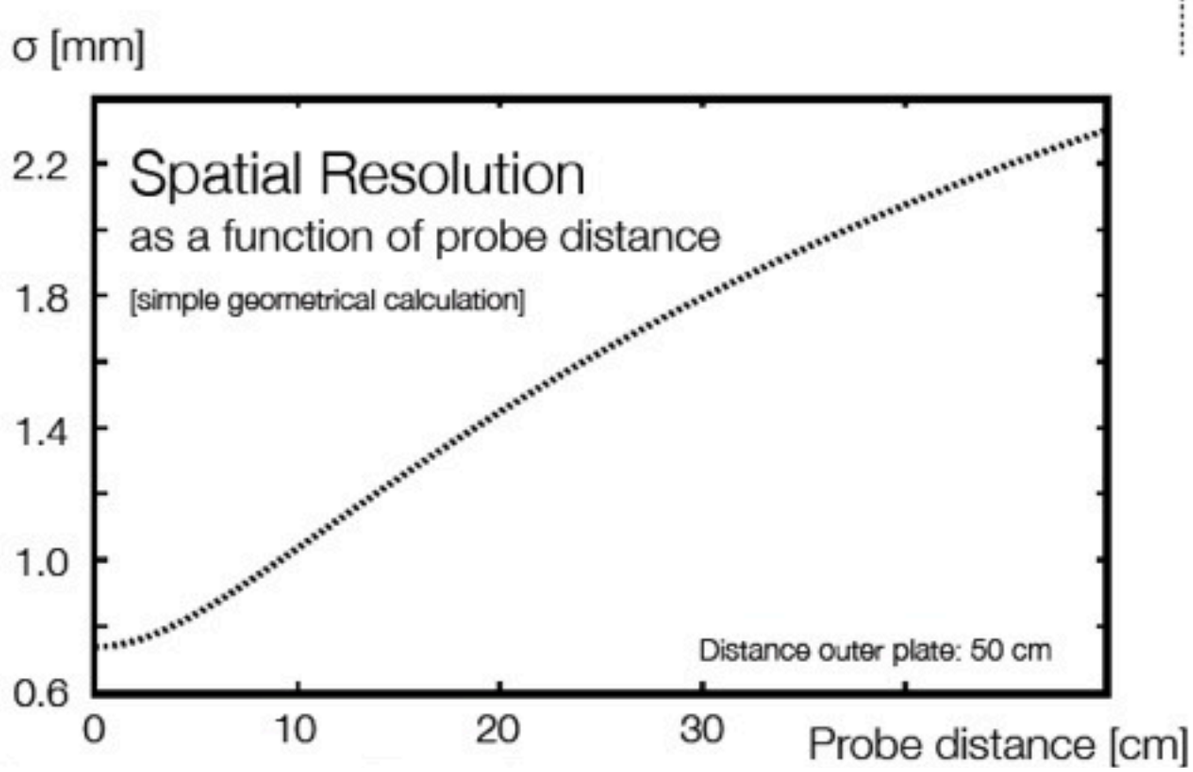
PET image resolution:

$$\sigma^2 \propto r^2 + (d/2)^2 + (.0022D)^2$$

r : Positron range [ca. 0.5 mm]
d : Detector size [ca. 1.0 mm; inner probe]
D : Detector distance

[see e.g. R.Lecomte, NIM A 526]
[zero position decoding error]





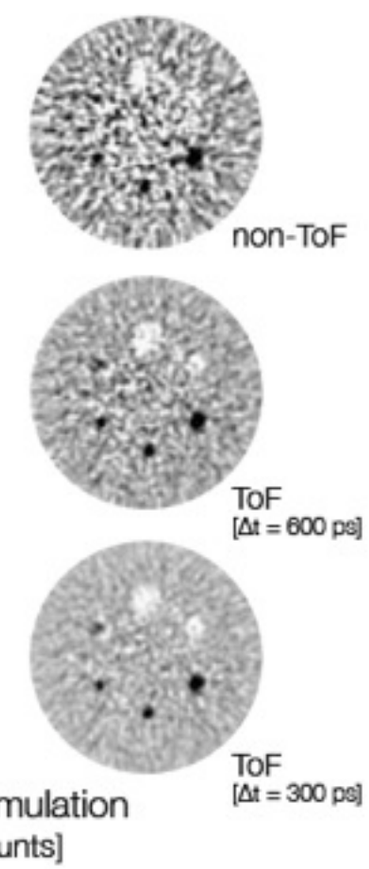
Why Time-of-Flight?

Sensitivity improvement:

$$SNR^2_{TOF} \propto \frac{S}{\Delta x} \times SNR^2_{non\text{-}TOF}$$

S : Size of patient
Δx : Source localization using ToF

[M.Conti, Eur. J Nucl. Med Mol. Imag. 38 ...]

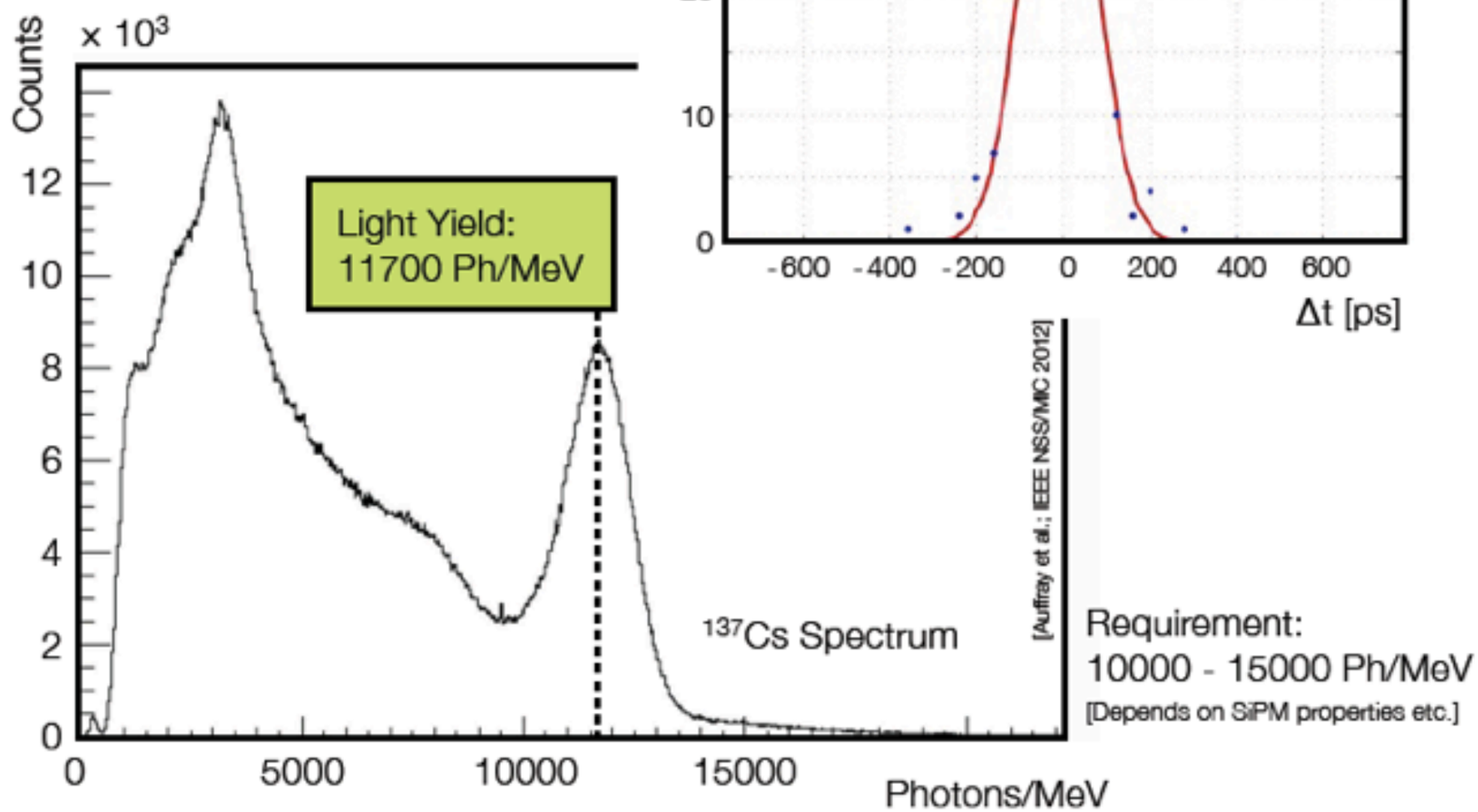


MC Simulation
[10^7 counts]

Inner PET head - Scintillator crystals

Crystal Matrix – Inner Probe

Scintillator : LYSO; ESR reflector by 3M;
Photosensor : Hamamatsu 1x1 mm^2 MPPC [CTR meas.]
Photonics PMT [LY meas.]
Electronics : Nino Chip + HPTDC

[Note: dry contact to photosensor]

LYSO matrix [Proteus]
9x18 crystals; each: 0.71x0.71x15 mm^3