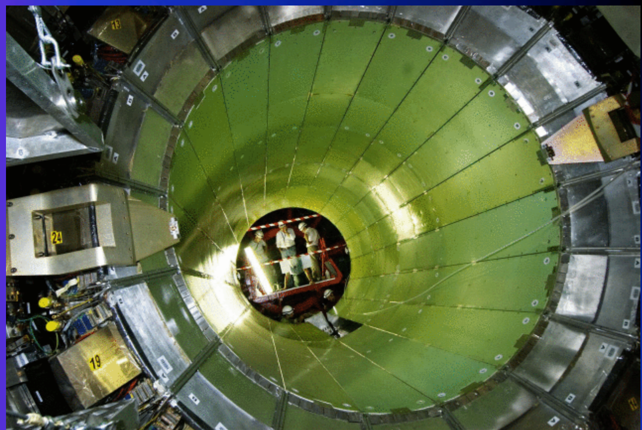
Endo-TOFPET-US

FP7 Project, Call Health 2010

A Multimodal Ultrasonic Probe Featuring Time of Flight PET in Diagnostic and Therapeutic Endoscopy



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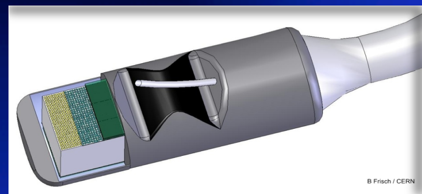
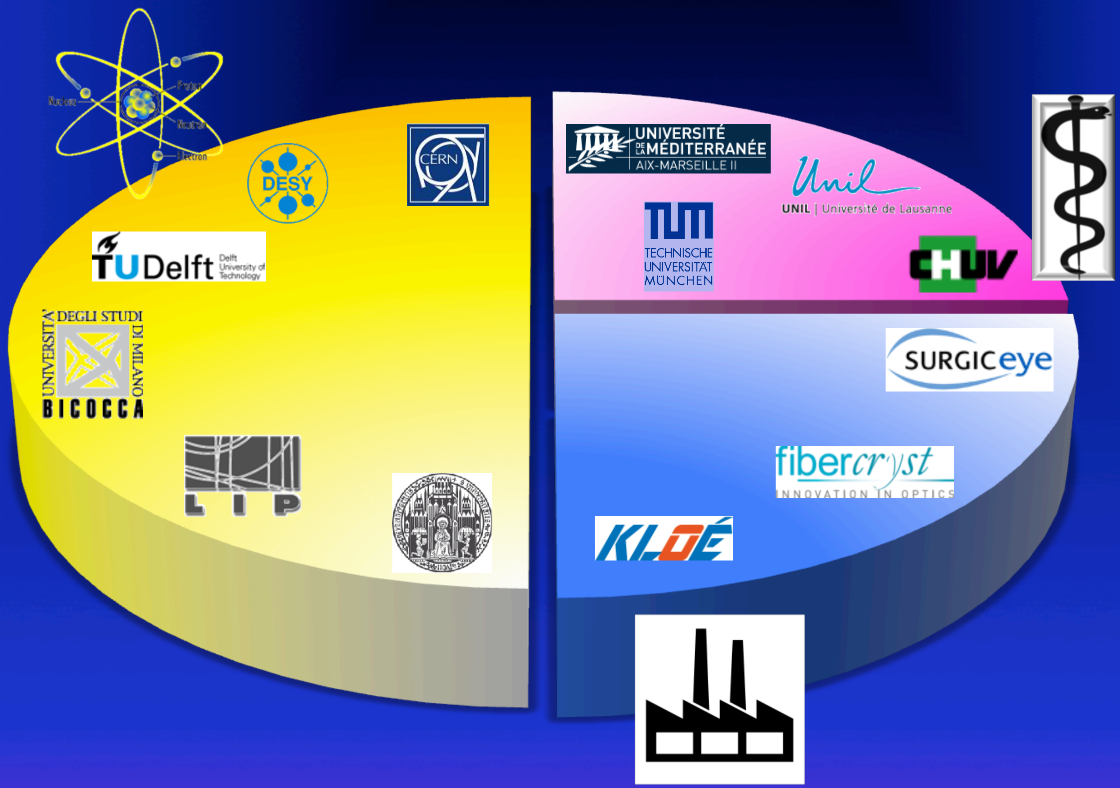


"The research leading to these results has received funding from the European Union Seventh Framework Program (FP7/2007-2013) under Grant Agreement No. 256984. This research is also supported by the Marie-Curie Actions ITN: PicoSEC-MCNeT under Grant Agreement No. 289355."

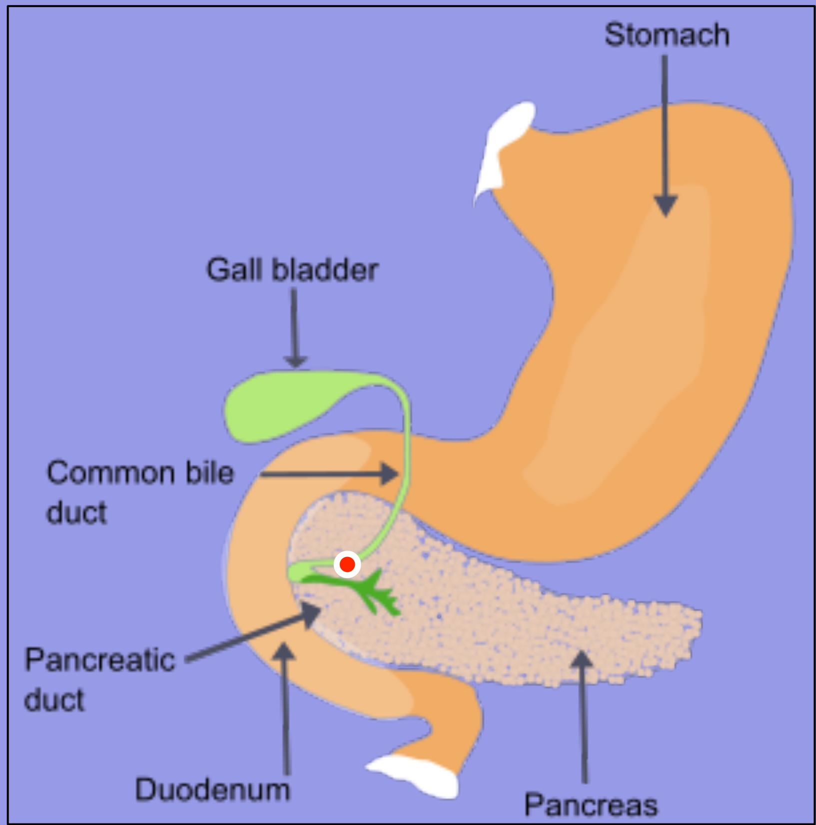
Thomas C. Meyer, CERN, Geneva
On behalf of the EndoTOFPET-US Collaboration

The Consortium

Partners in this project:



EndoTOFPET-US: The Principle



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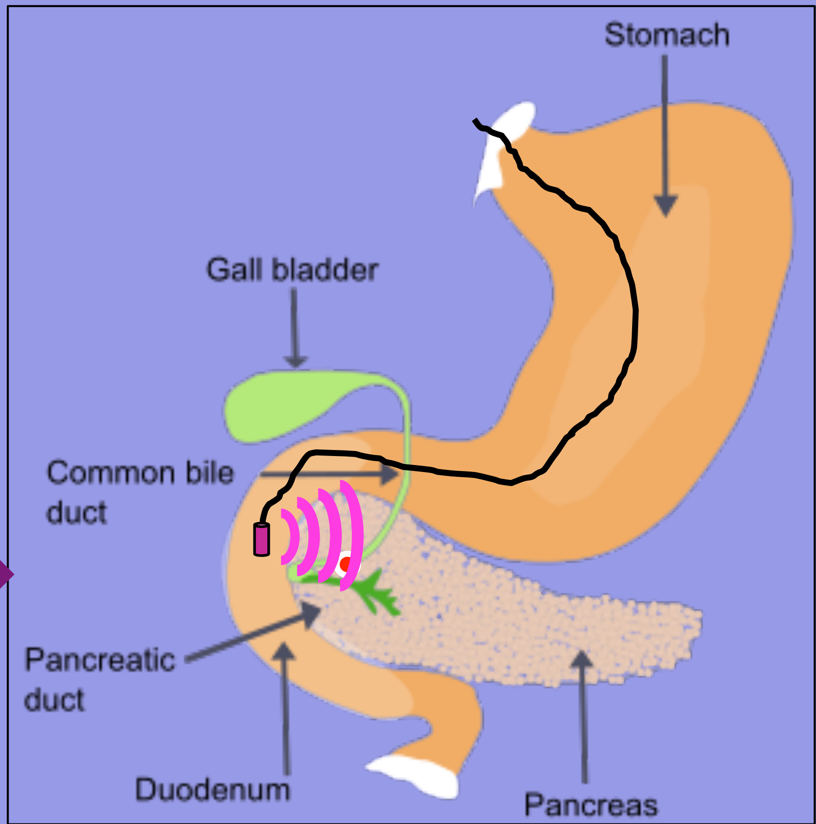

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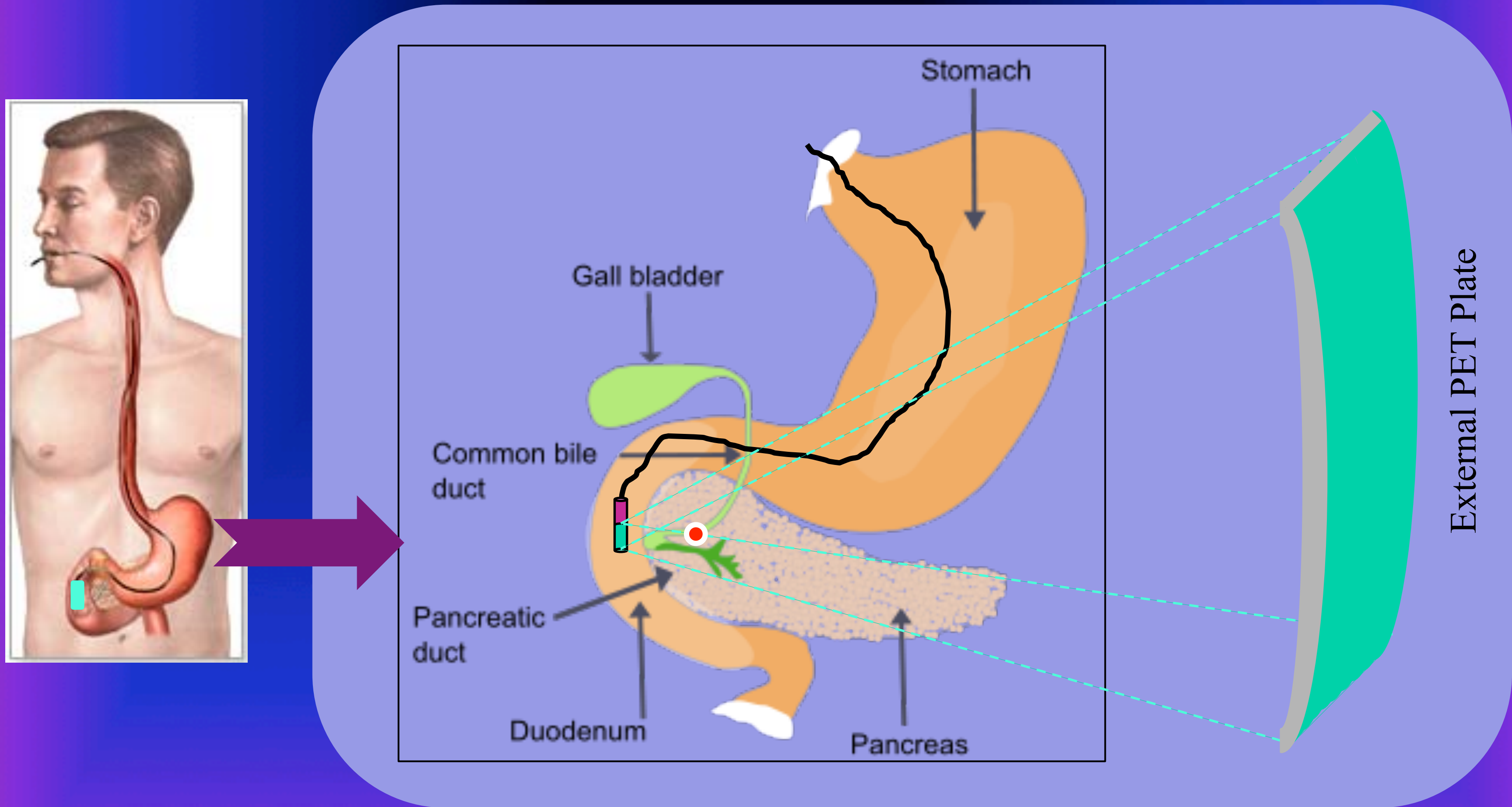

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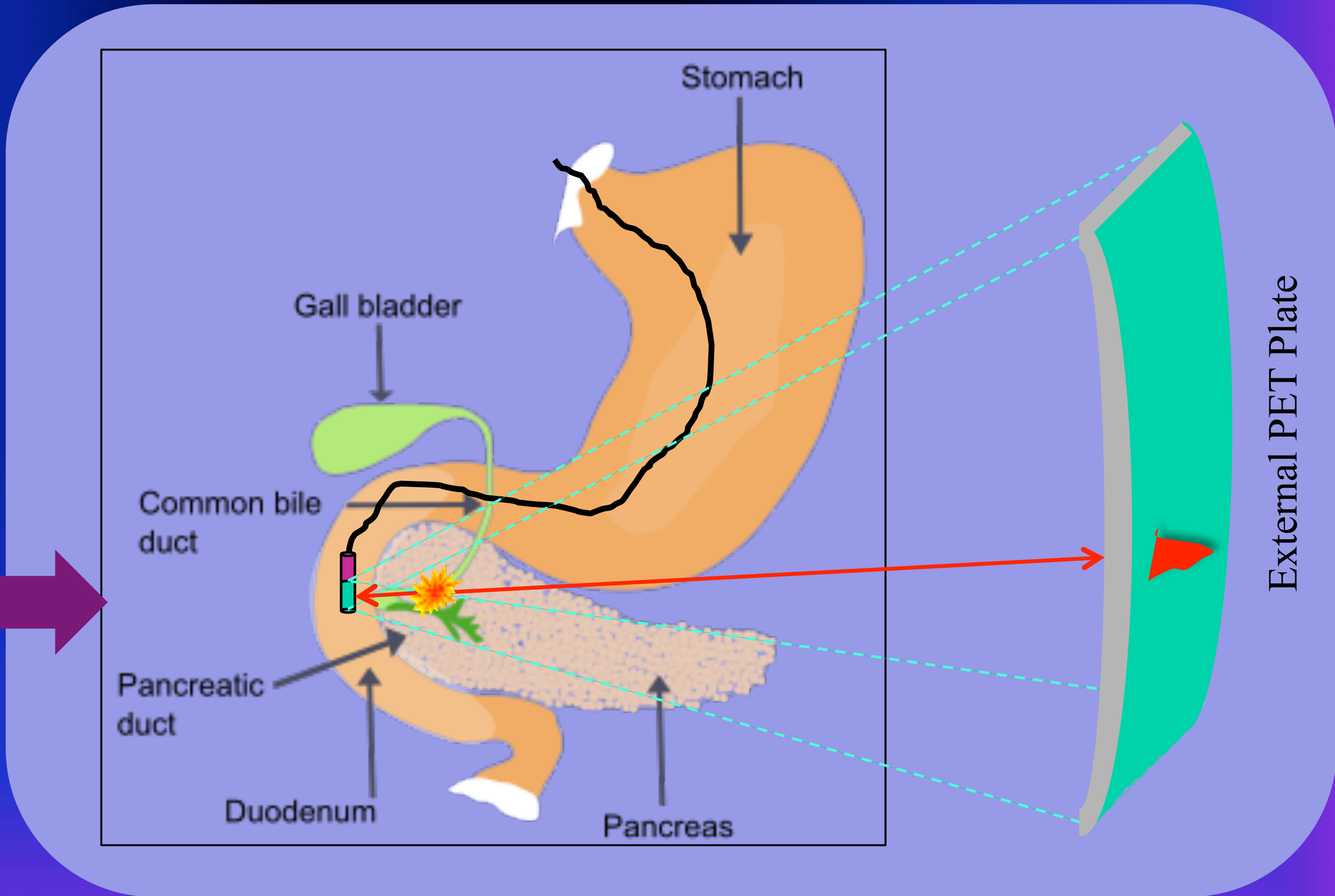

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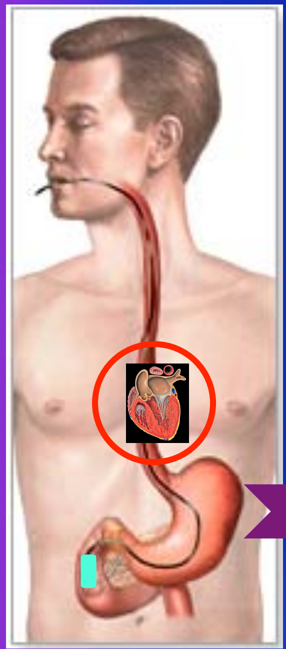

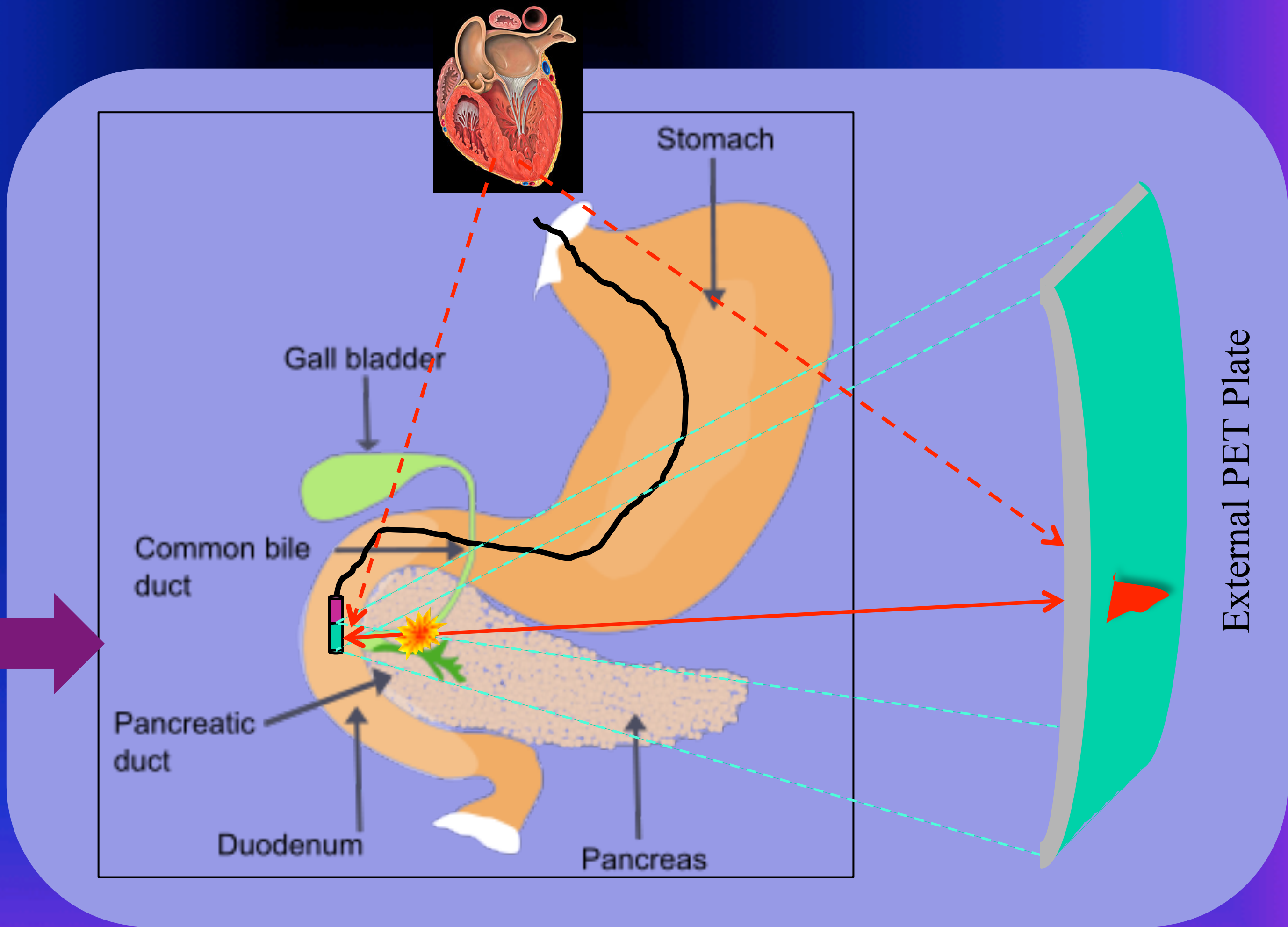

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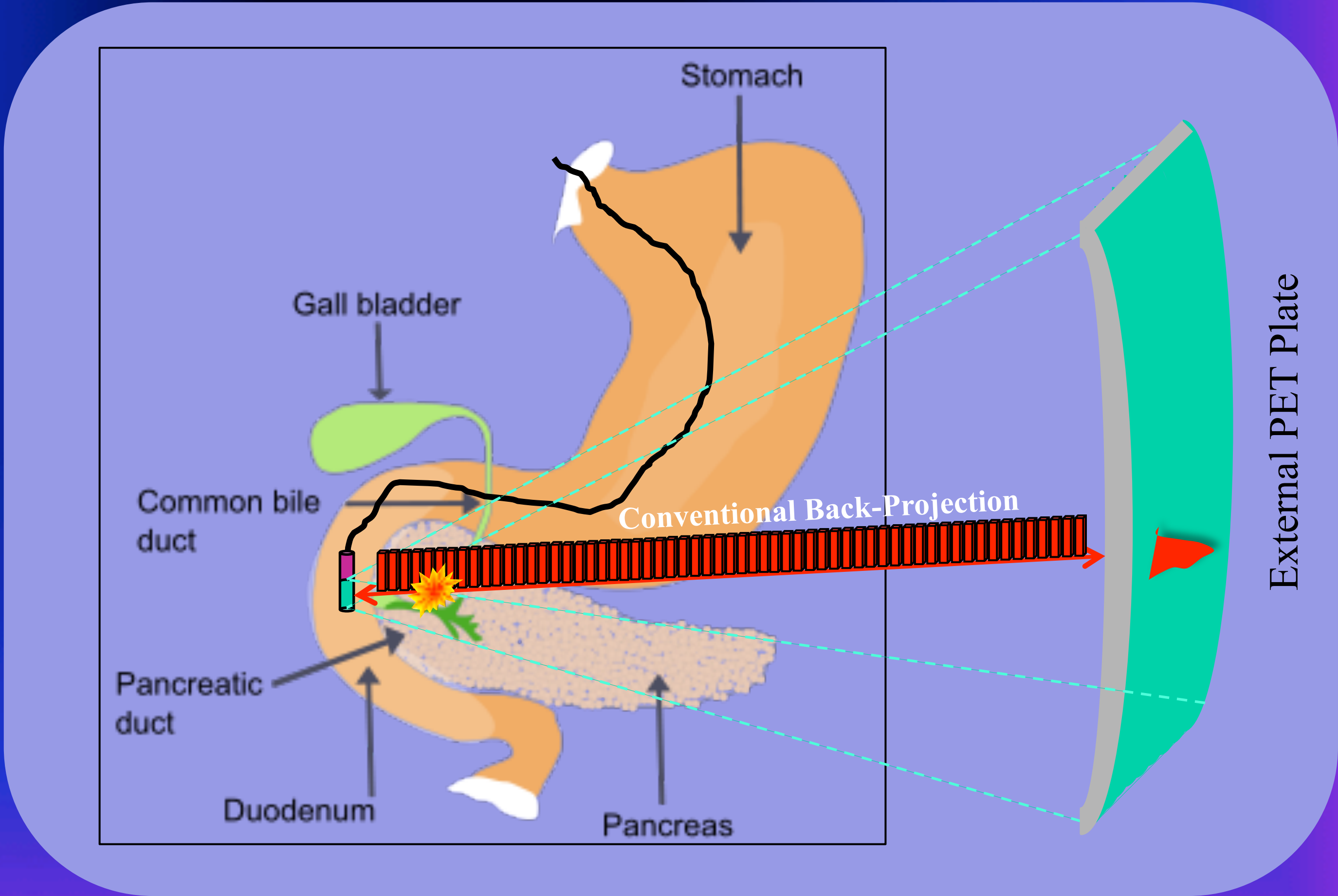
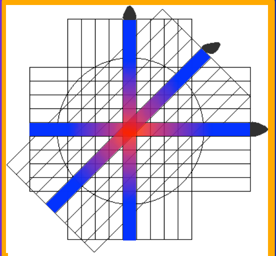


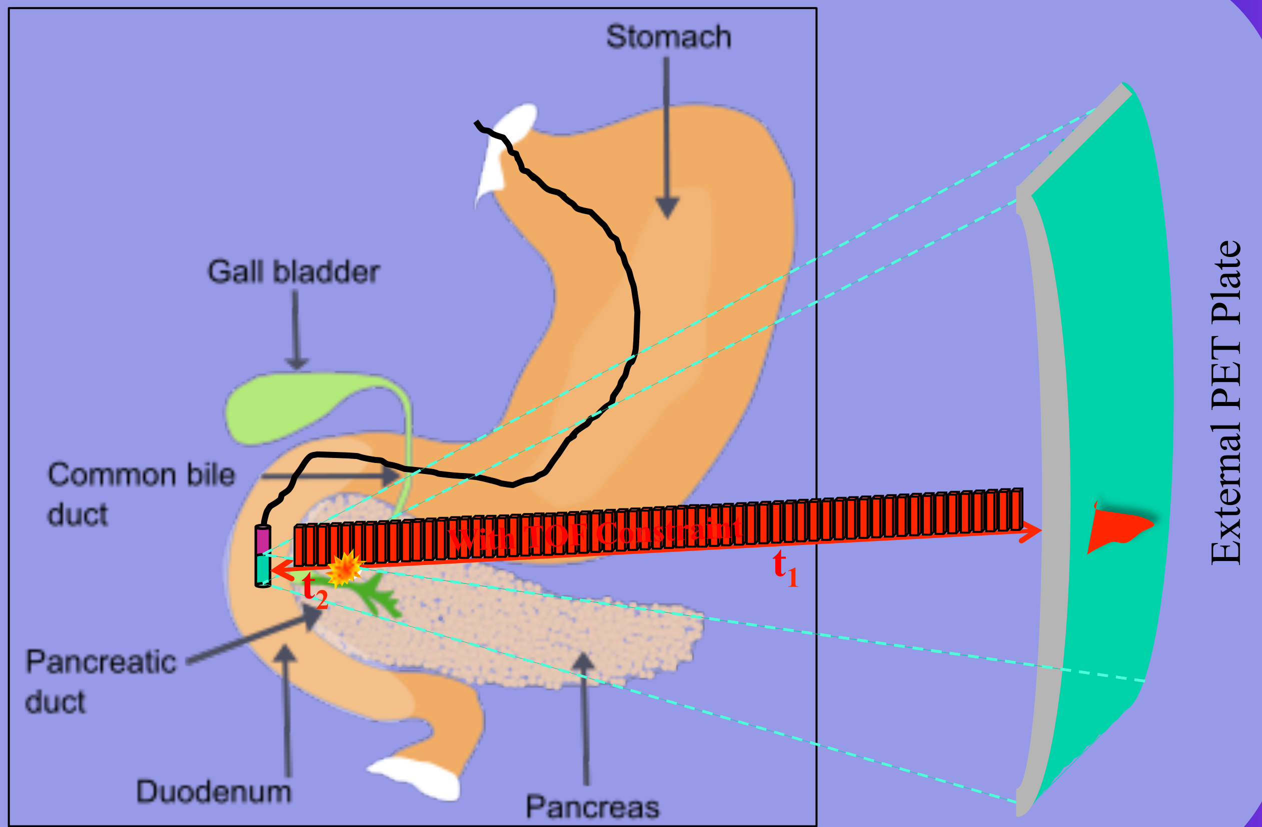
EndoTOFPET-US: Why TOF?



$$\Delta z = \left|\frac{t_2 - t_1}{2}\right| \times c$$

Target CTR: 200ps

→ 30mm *FWHM*



Project Objectives

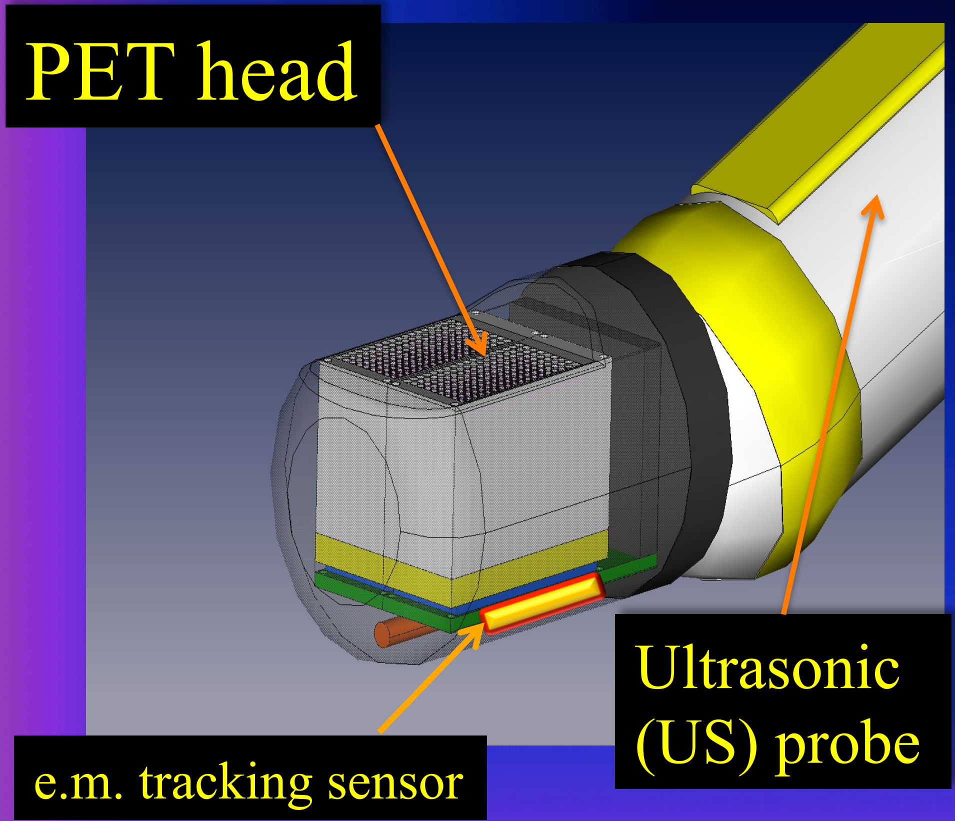
- Development of new biomarkers;
- First clinical targets: pancreatic & prostatic cancers;
- Develop a dual modality PET-US endoscopic probe with...
  - *Spatial* resolution: 1mm;
  - *Timing* resolution: 200ps *FWHM* coincidence;
  - High *sensitivity* to detect 1mm tumors in a few minutes;
  - *Energy* resolution: sufficient to discriminate against Compton events .

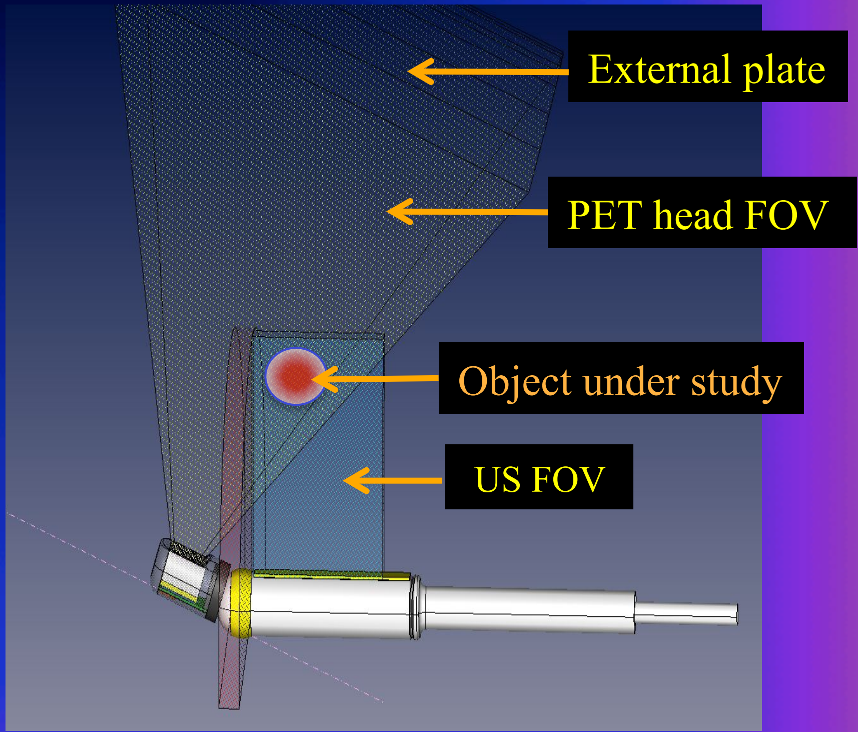
PET Configuration

- Asymmetric:
  - One PET detector close to ROI
    - incomplete (non-2π) projections;
    - → Simulation and reconstruction challenge.

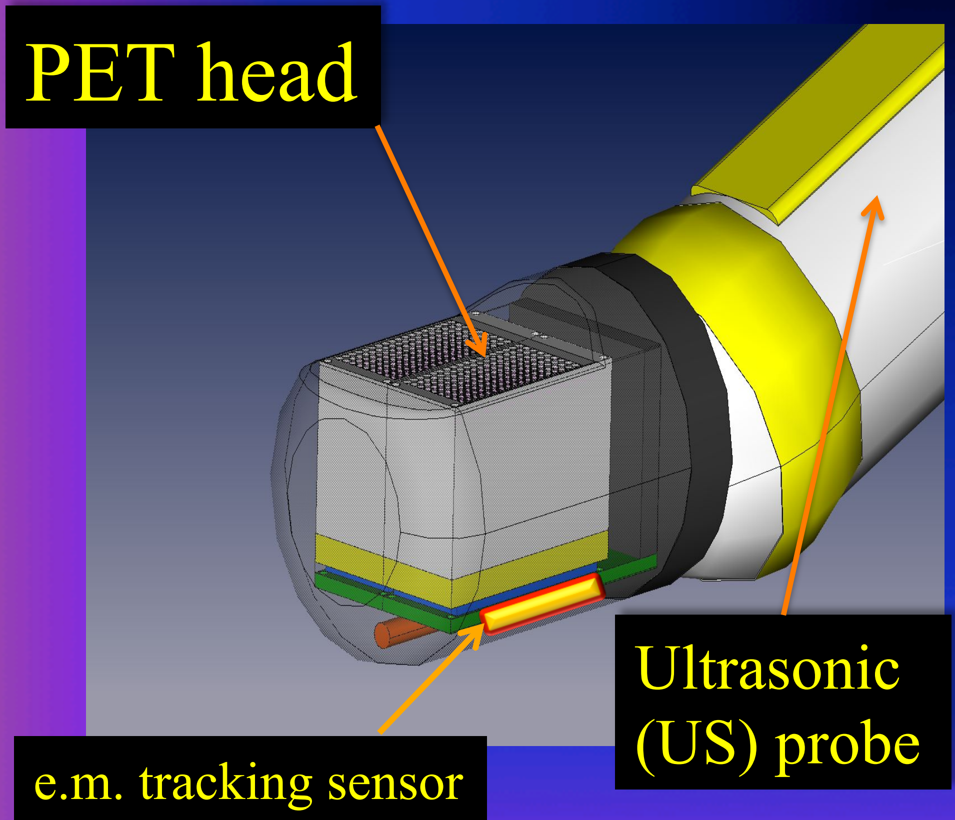
- Endoscopic:
  - One PET head inside the body
    - → Extreme miniaturization;
    - → Background from close organs (e.g. heart, bladder);
    - →Varying geometry (body & organ motion)

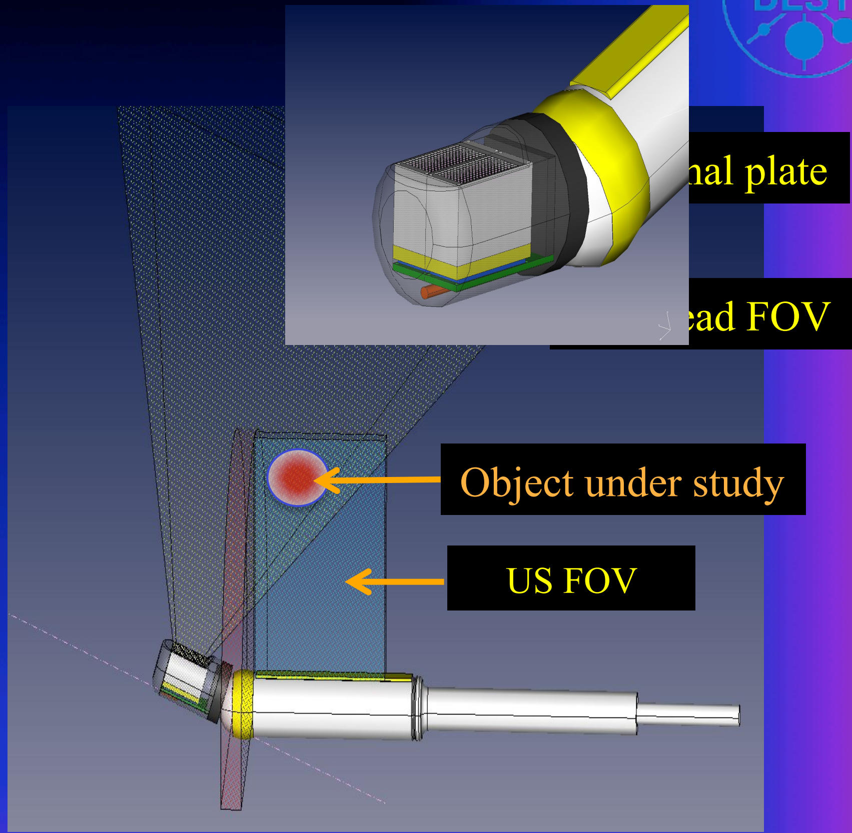
The Endoscopic Probe





Two Different Probes...





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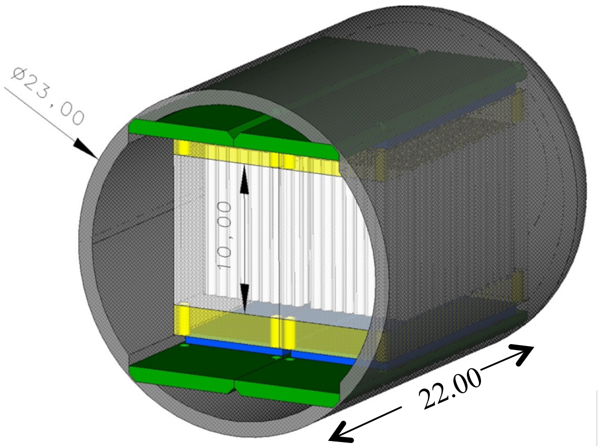
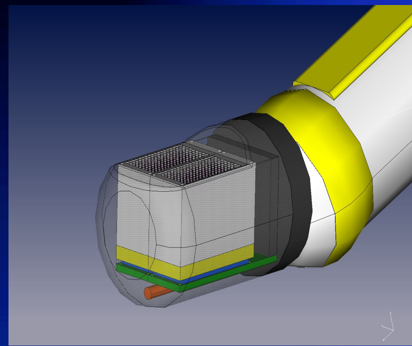
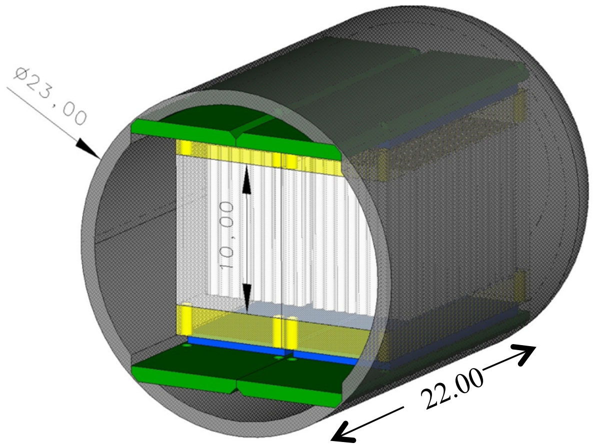


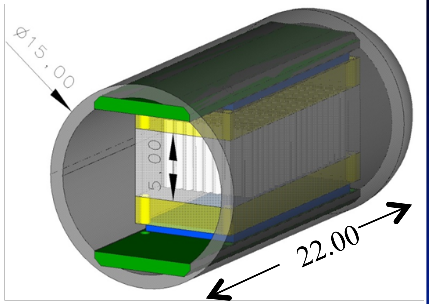
Option 1: prostate

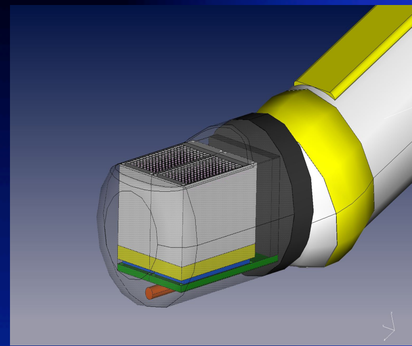


		Prostate
Crystal Matrix	[mm^2]	14 x 15
Fiber length	[mm]	10
Fiber pitch x/y	[µm]	780/800
# Fibers in x/y		18x18 (324)
Diffractive optics	[mm]	2
SPAD array thickness	[mm]	0.75
PCB thickness	[mm]	1
# Readout layers		1
Total thickness	[mm]	18
Diameter of detector	[mm]	23
Length of detector	[mm]	22

Two Different Probes...





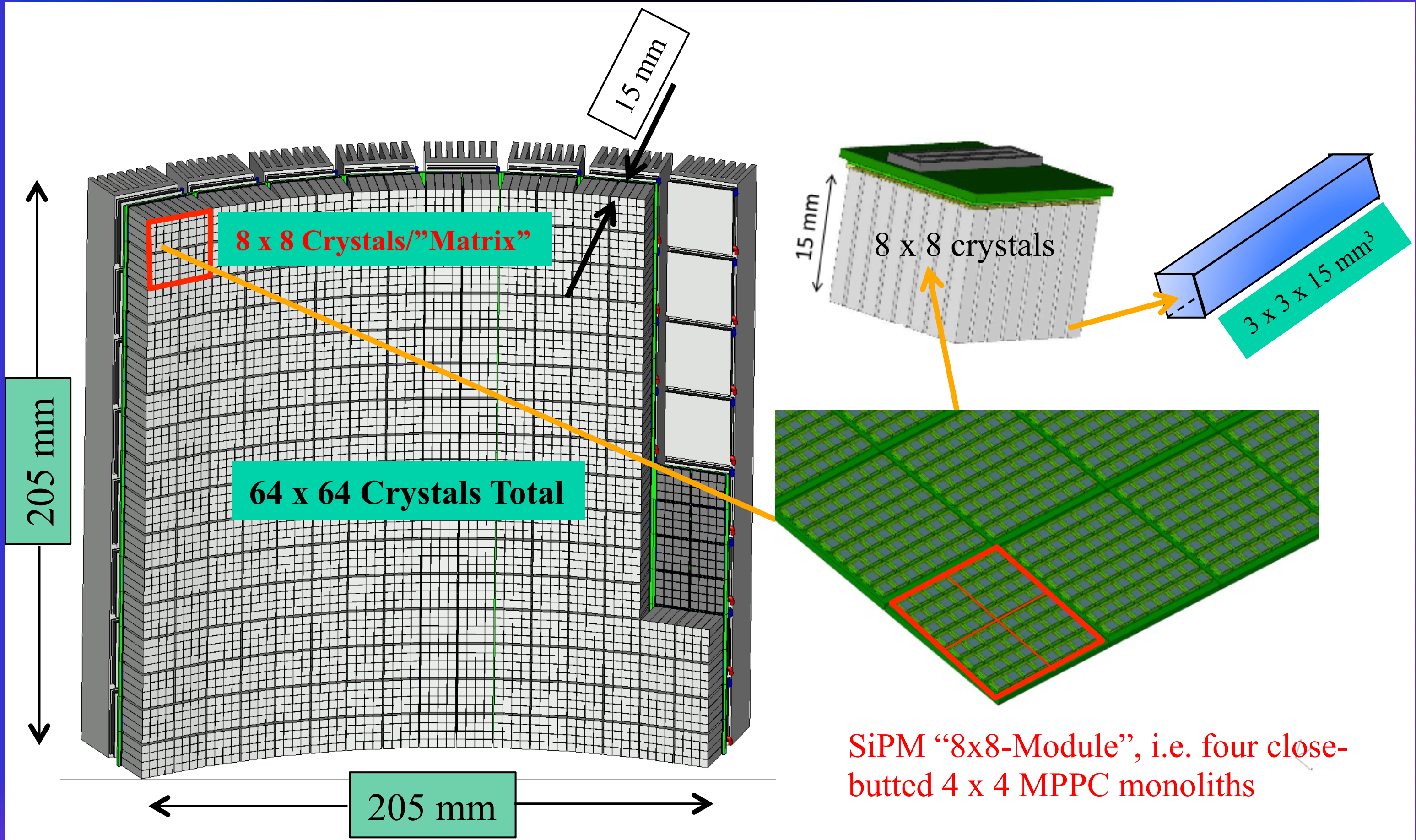


Option 1: prostate

Option 2: pancreas

		Prostate	Pancreas
Crystal Matrix	[mm^2]	14 x 15	7 x 15
Fiber length	[mm]	10	5 (9)
Fiber pitch x/y	[µm]	780/800	780/800
# Fibers in x/y		18x18 (324)	9x18 (162)
Diffractive optics	[mm]	2	2
SPAD array thickness	[mm]	0.75	0.75
PCB thickness	[mm]	1	1
# Readout layers		1	1
Total thickness	[mm]	18	13
Diameter of detector	[mm]	23	15
Length of detector	[mm]	22	22

External PET Plate



Technical Challenges

- Calls for innovative solutions
  - Very thin crystal pixels/fibers for the internal probe;
    - for high granularity and sub-millimeter spatial resolution;
  - Temporal collimation with TOF: CTR < 200ps *FWHM;*
    - for background rejection outside ROI of 30mm;
  - Digital light detection: SiPM with single SPAD readout;
    - for single optical photon counting and ultimate timing resolution;
  - Diffractive optics - light concentrators ;
    - for overcoming loss of sensitive area and optimizing light collection;
  - High level of integration for electronics & mechanics;
    - For miniaturization (±5μm precision);

Detector R&D

1.) Photodetectors

- The analog SiPM (*a*-SiPM)
- The digital "Endo-TOFPET" SiPM (*d*-SiPM)

2.) Diffractive Optics

3.) Scintillators

4.) Integration

5.) Readout and Data Acquisition

Detector R&D

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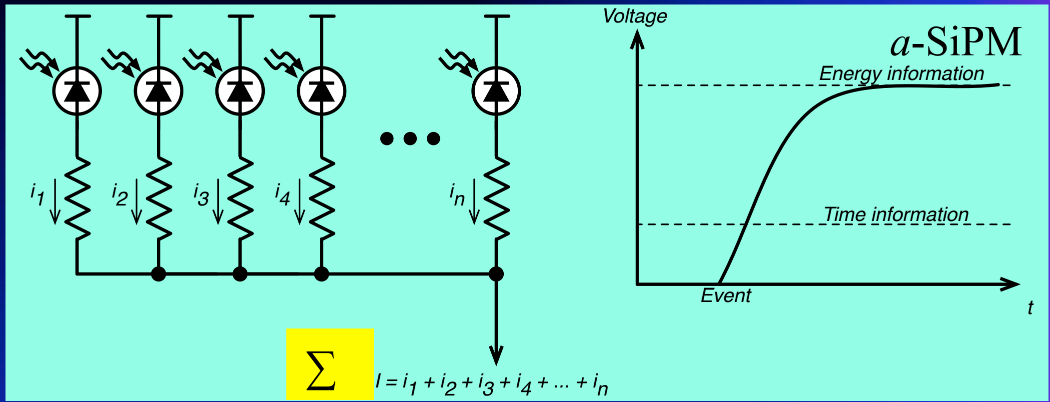
Photodetectors: Choices

The *a*-SiPM:

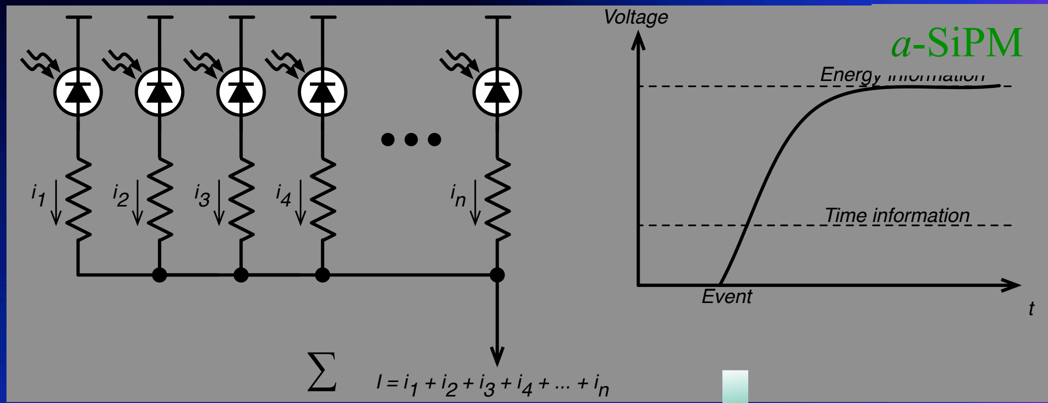
- low rise time;
- high capacitance;
- reasonable fill factor (FF);
- mature technology;
- commercially available
- time over threshold discr.
- standard (HP)TDC readout.



a-SiPM versus d-SiPM

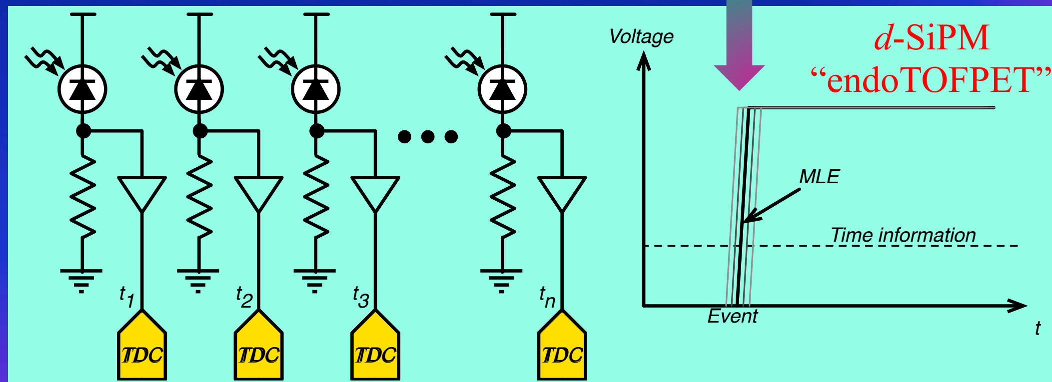
The *a*-SiPM:

- low rise time;
- high capacitance;
- reasonable fill factor (FF);
- mature technology;
- commercially available
- time over threshold discr.
- standard (HP)TDC readout.



The *d*-SiPM:

- very low rise time;
- individual SPAD readout
  - → single photon counting
  - → optimum timing
- high functionality
- ambitious/risky
- novel technology
- optimized for endoscope



Detector R&D

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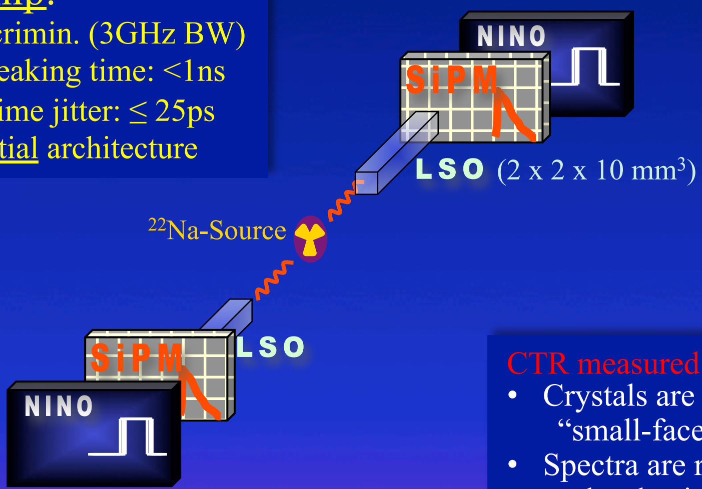
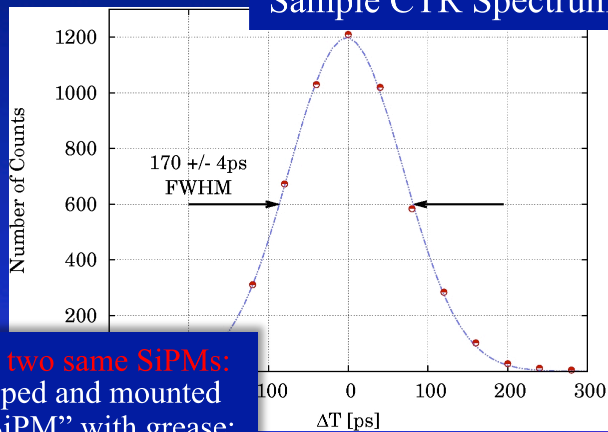
a-SiPM: Test Scenario

- ☛ For an intrinsic SiPM timing evaluation, see poster by Stefan Gundacker/CERN;
- Coincidence time resolution (CTR) measured with scintillating "reference" crystals and the NINO amplifier/discriminator;
- Use high-BW scope (LeCroy DDA 735Zi, 40GS/s) or HPTDC.

NINO chip:
- Fast discrimin. (3GHz BW)
- Signal peaking time: <1ns
- Output time jitter: ≤ 25ps
- Differential architecture



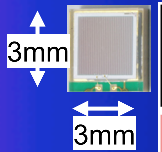
Sample CTR Spectrum



CTR measured with two same SiPMs:
- Crystals are wrapped and mounted "small-face-to-SiPM" with grease;
- Spectra are refined through photo-peak selection.

a-SiPM: Evaluation & Selection

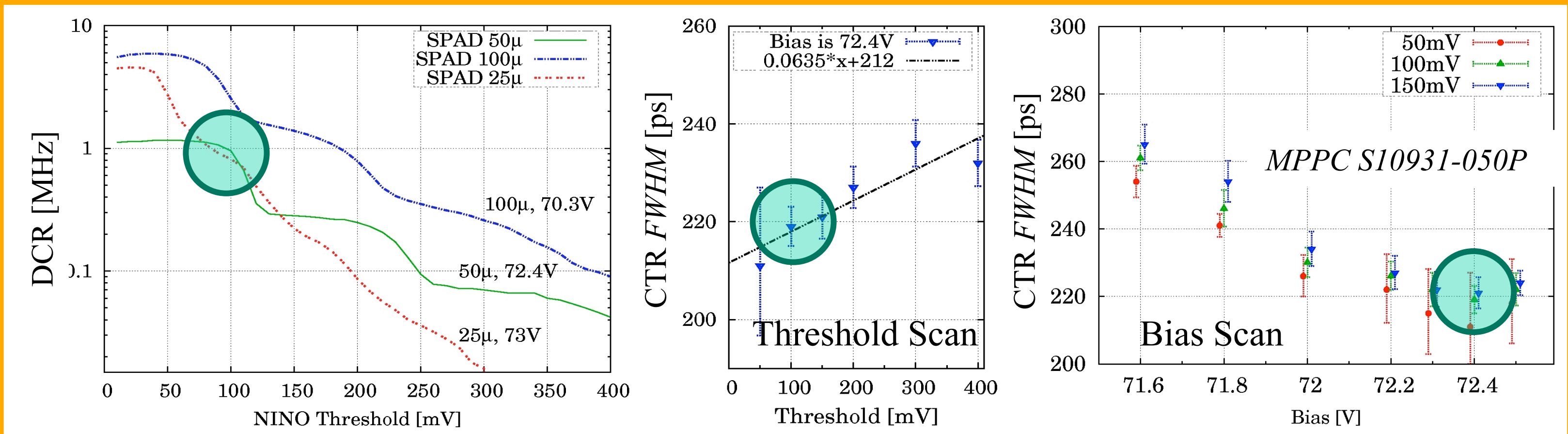
- Suitable SiPMs are commercial MPPCs by Hamamatsu Photonics;
- Evaluation of photodetectors via measurement of the (CTR):



MPPC S10931-	# SPADs	Fill Factor [%]	$V_{Manuf.}$ [V]	$V_{optimum}$ [V]	DCR*) [MHz]	NINO Thr. [mV]	CTR *FWHM* [ps]
-025P	14’400	30.8	71.49 71.44	73.0	3.2	150	340±9
-050P	3’600	61.5	72.11 72.09	72.4	1.1 1.0	100	220±4
-100P	900	78.5	70.81 70.87	70.3	9.0 9.5	300	280±9

***) DCR = Dark Count Rate**

Note: Optimization of SiPMs done with non-optimized crystals.



S. Gundacker et al., “A Systematic Study to Optimize SiPM Photo-Detectors for Highest Time Resolution in PET” (TNS-00225-2011)

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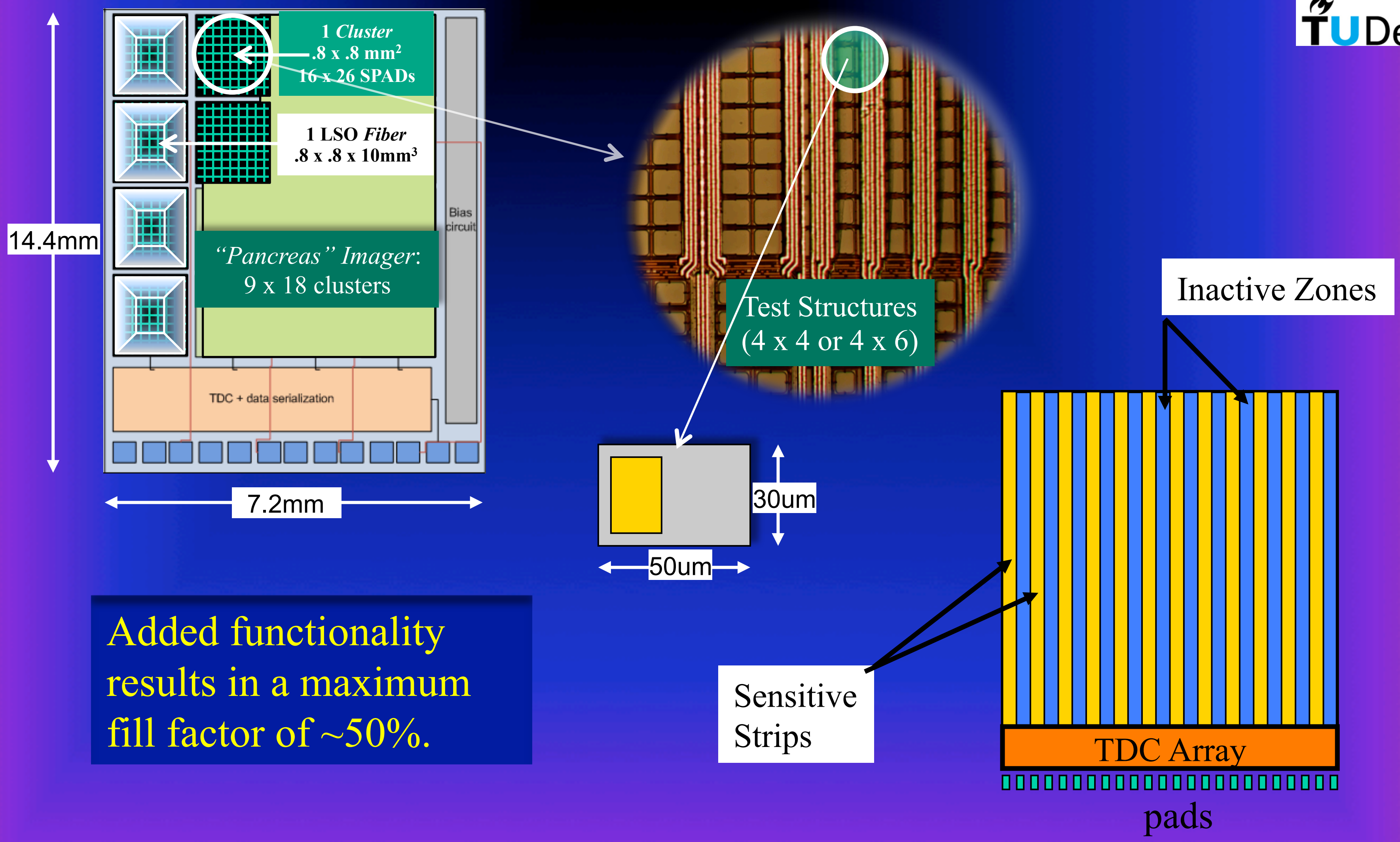
d-SiPM for endo-TOFPET-US

- Capability to gather the statistics of the first individual photons that reach a cluster;
  - Intrinsically best timing performance → attractive for TOF;
- Balance functionality and PDE;
- Design must adapt to process-specific effects:
  - high DCR from tunneling and trap-assisted noise;
  - after-pulsing;
  - lower PDP than with conventional *a*-SiPMs.
- Requires multi-parameter optimization/simulation.

*) M. Fishburn & E. Charbon, “System Tradeoffs in Gamma-Ray Detection Utilizing SPAD Arrays and Scintillators”, IEEE-TNS, VOL. 57, NO. 5, OCTOBER 2010.
S. Seifert et al., “The lower bound on the timing resolution of scintillation detectors”, Phys. Med. Biol. **57** (2012) 1797–1814

d-SiPM: Sensor Floor Plan



Added functionality results in a maximum fill factor of ~50%.

d-SiPM: Characteristics & Results

Characteristic Parameters of *d*-SiPM-"endo-TOFPET-US" Test Structure		Commercial *d*-SiPM
Cluster Pitch [μm]	800	4000
# SPADs/cluster	416	6400
Maximum Fill Factor [%]	50	77
PDP [%] @ 430nm	32	31
PDE [%]	15	24
# TDCs / Cluster Column	48	1
# Time Of Arrivals (TOA) / cluster	48	1
TDC Resolution or LSB [ps]	51.8	-
Clock Frequency [MHz]	25	200

Boost PDE optically!

First evaluation results:

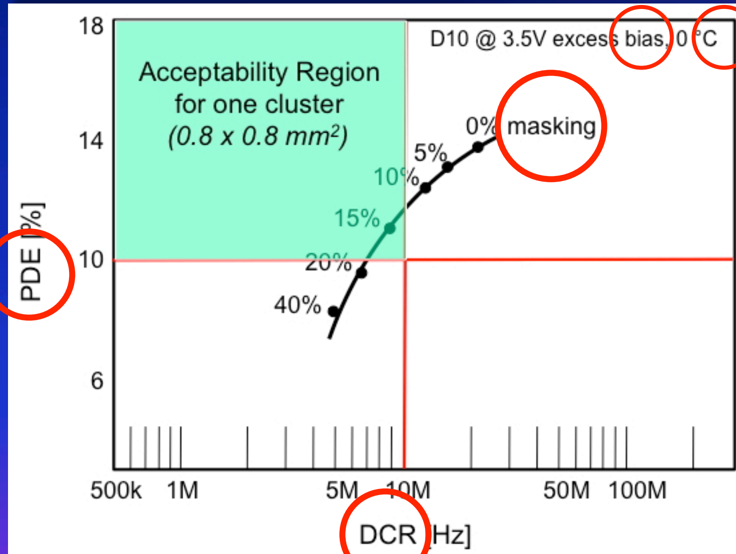
DCR (0 °C): 25kHz/SPAD → DCR (40 °C): 80kHz/SPAD

NEED COOLING OF *d*-SiPM!

Masking of noisy pixels ("screamers"): DCR ↘ but also PDE ↘

Lowering excess bias: DCR ↘ but also PDE ↘

Example of multi-parameter chip optimization:



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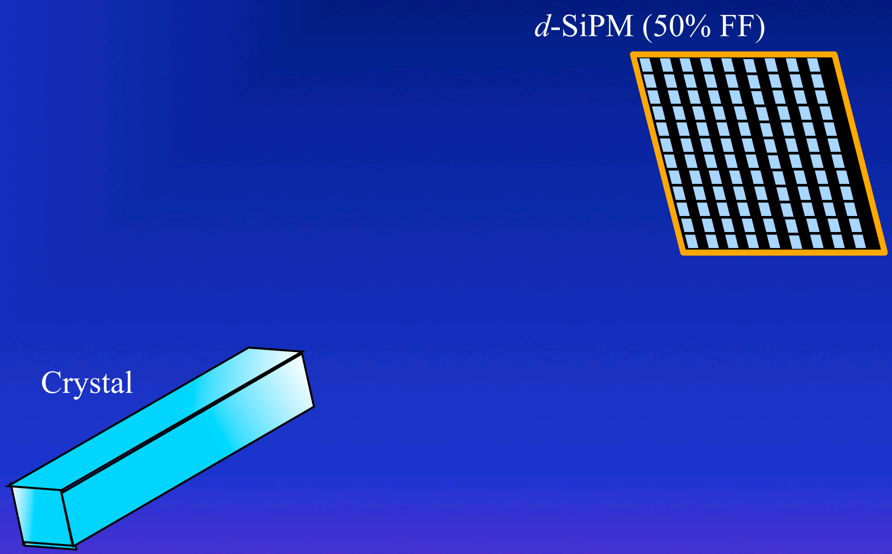
Diffractive Optics: Concept

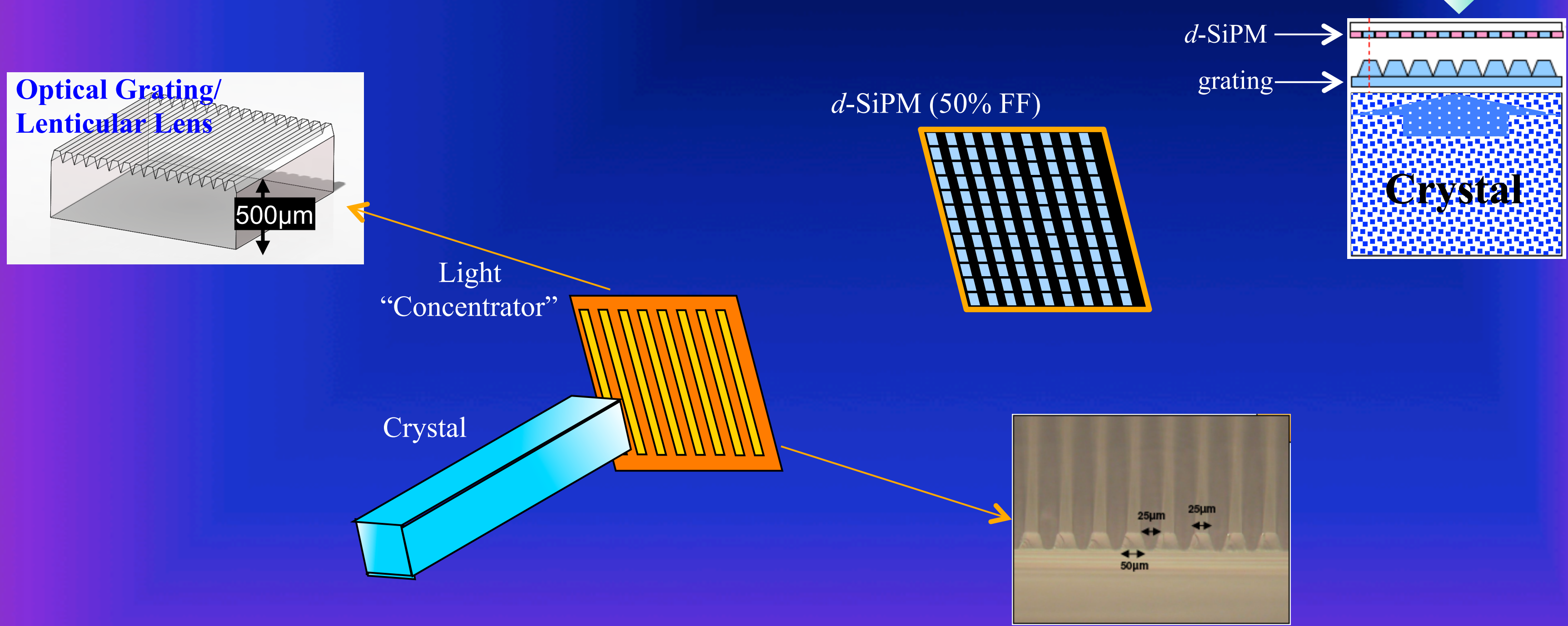
Objective: Recover light lost (50%) in the dead zones of the *d*-SiPM



Diffractive Optics: Concept

Objective: Recover light lost (50%) in the dead zones of the *d*-SiPM

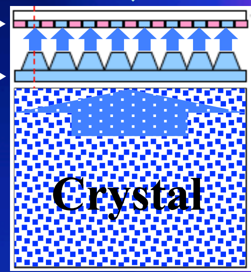
- Glue an optical grating between crystal and photodetector;
- Match pitch of grating with that of *d*-SiPM (50µm);

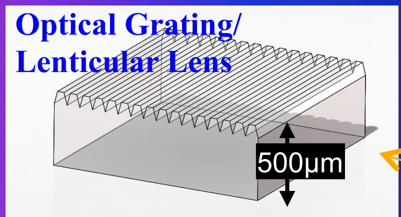


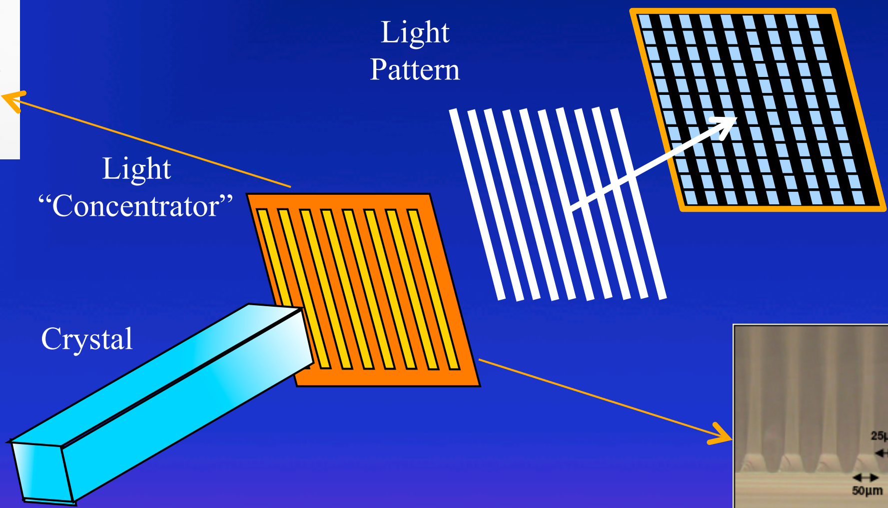
Diffractive Optics: Concept

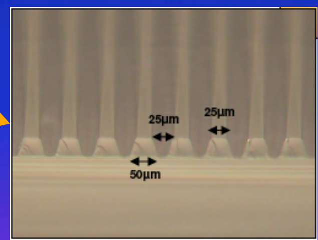
Objective: Recover light lost (50%) in the dead zones of the *d*-SiPM

- Glue an optical grating between crystal and photodetector;
- Match pitch of grating with that of *d*-SiPM (50µm);
- Create ‘differential’ light pattern on the SPAD surface only;
- Expect transmission gain of 1.3 (from simulations).

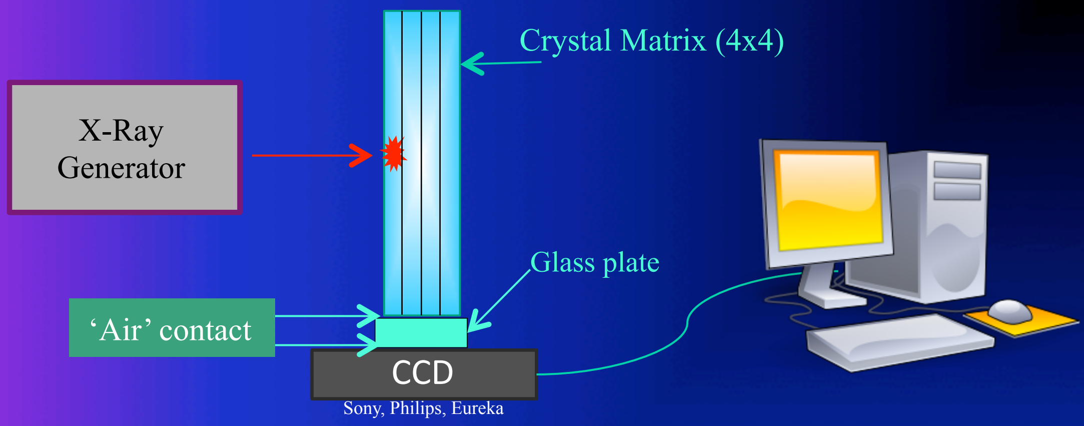


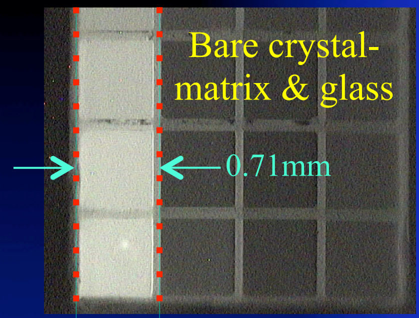






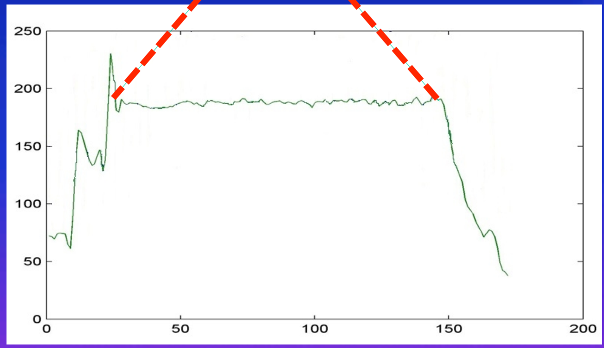
Diffractive Optics: Tests





Tests with Proteus/AGILE crystal matrix:

- interface crystal-grating: air
- interface grating-CCD: air
- all crystals *fully* wrapped (3M-ESR Vikuiti)



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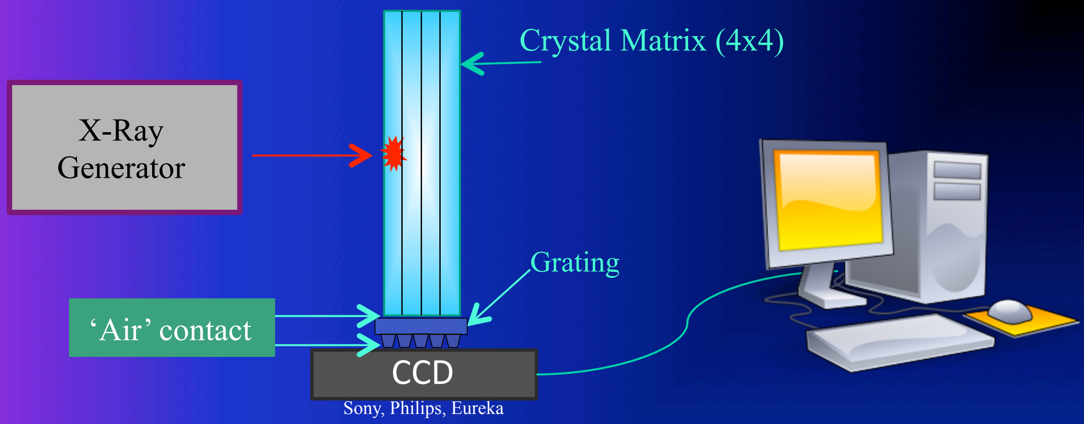

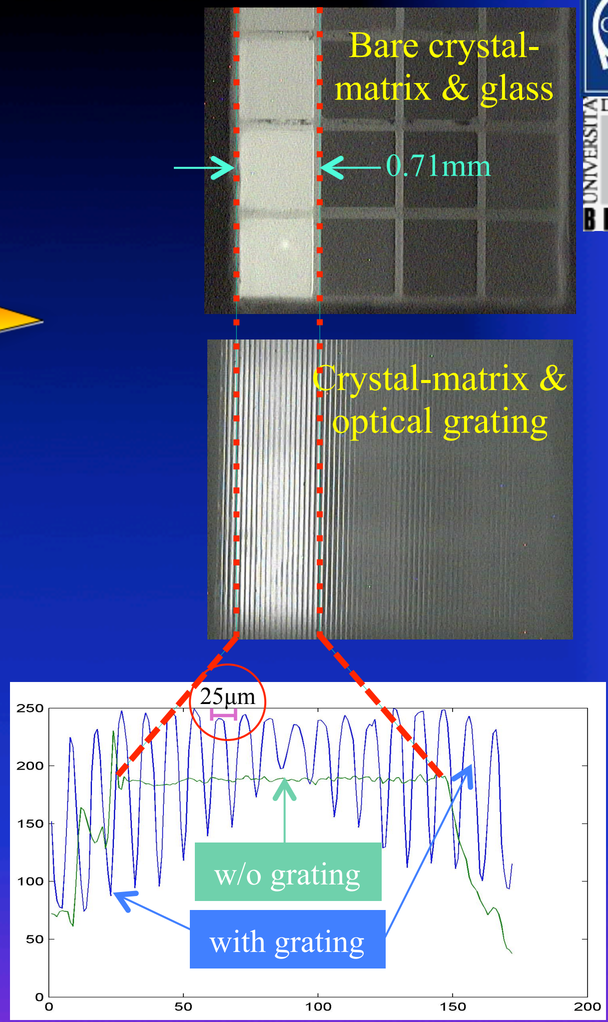

Tests with Proteus/AGILE crystal matrix:

- interface crystal-grating: air
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☛ Average gain in peaks = 1.26

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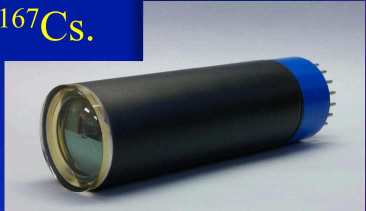
Crystal Performance

Crystal performance is "gauged" by light yield (LY) and coincidence time resolution (CTR):

Crystal	Size [mm³]	Decay Time [ns]	Light Yield [Ph/MeV]	CTR [ps] *FWHM*
LuAG:Ce	2 x 2 x 8	60	15'000	872 ± 50
LuAG:Pr	2 x 2 x 8	20	10'400	672 ± 30

Crystal (2x2x10mm³)	Manufacturer	Decay Time [ns]	Light Yield [Ph/MeV]	CTR [ps] *FWHM*
LGSO:Ce	Hitachi	42.50	19'500	176
LYSO:Ce	SIPAT	42.60	19'000	206
LYSO:Ce	Proteus	41.40	18'000	175
LYSO:Ce	CPI	45.00	17'400	184
LSO:Ce	PML	47.00	16'300	206
LSO:Ce	CTI	43.50	23'000	190
LSO:Ce:Ca	Agile	32.00	15'700	170

Light yield measured with PMT (linear!); crystals wrapped and mounted "small-face-to-PMT" with grease; source: ^{167}Cs.



PMT: Photonis XP 2020 Q

CTR measurements were made with the Hamamatsu MPPC S10931-050P; all crystals were fully wrapped and coupled with grease to the MPPC.

E. Affray et al., Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), 2011 IEEE, 10.1109/NSSMIC.2011.6154402

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slow!

UV!

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LYSO:Ce	CPI	45.00	17'400	184
LSO:Ce	PML	47.00	16'300	206
LSO:Ce	CTI	43.50	23'000	190
LSO:Ce:Ca	Agile	32.00	15'700	170

best!

Light yield measured with PMT (linear!); crystals wrapped and mounted "small-face-to-PMT" with grease; source: ^{167}Cs.

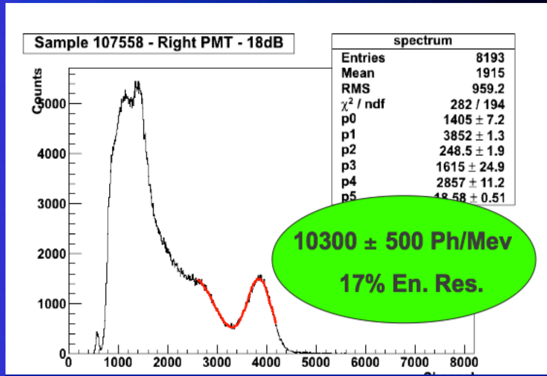
PMT: Photonis XP 2020 Q

CTR measurements were made with the Hamamatsu MPPC S10931-050P; all crystals were fully wrapped and coupled with grease to the MPPC.

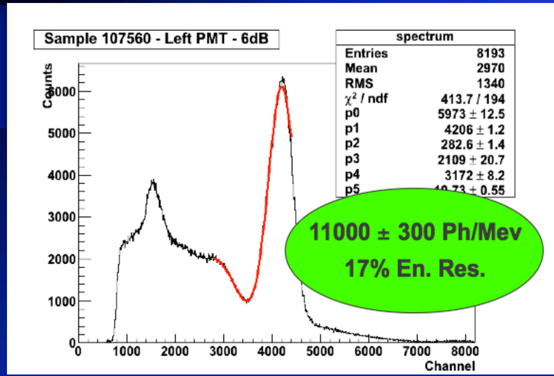
E. Affray et al., Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), 2011 IEEE, 10.1109/NSSMIC.2011.6154402

Small & Large Crystals

0.75 x 0.75 x 10mm^3	Light Yield & E-Resolution	3 x 3 x 15mm^3



Light Yield &
E-Resolution

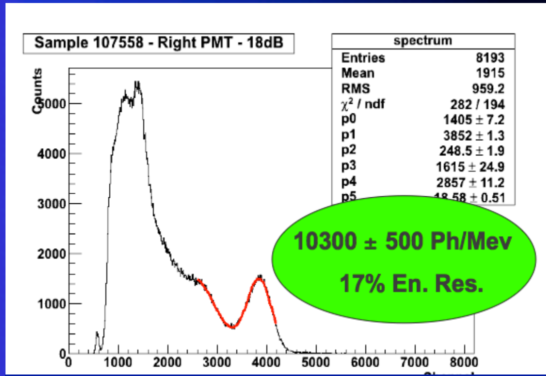


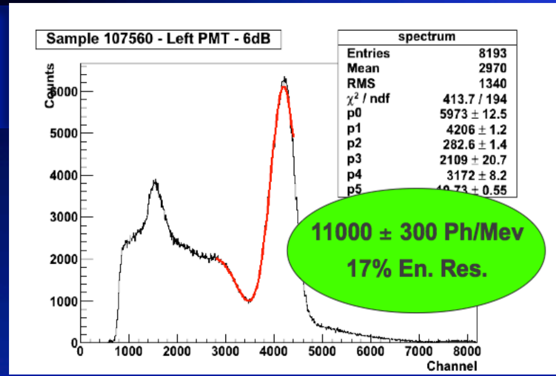
16 LYSO crystals, 4 x 4 matrix; 80μm 3M-ESR Vikuiti wrapping; Uniform irradiation with ^{137}Cs; Dry contact with PMT.

Small & Large Crystals

0.75 x 0.75 x 10mm^3	3 x 3 x 15mm^3

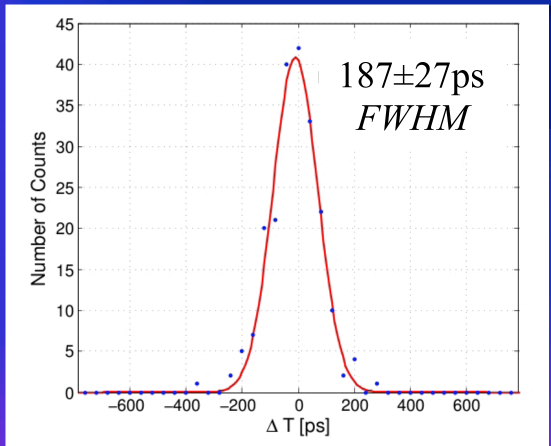
Light Yield & E-Resolution

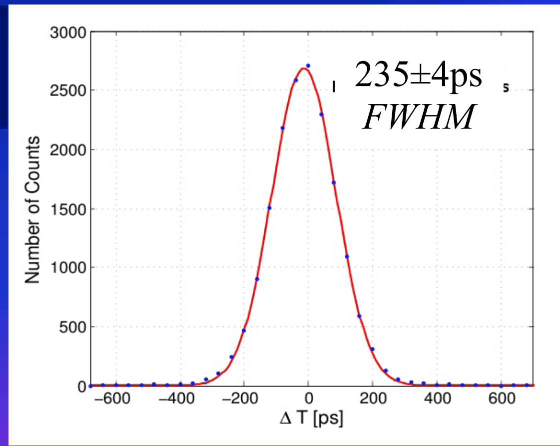




16 LYSO crystals, 4 x 4 matrix; 80μm 3M-ESR Vikuiti wrapping; Uniform irradiation with ^{137}Cs; <u>Dry</u> contact with PMT.

Coincidence Time Resolution

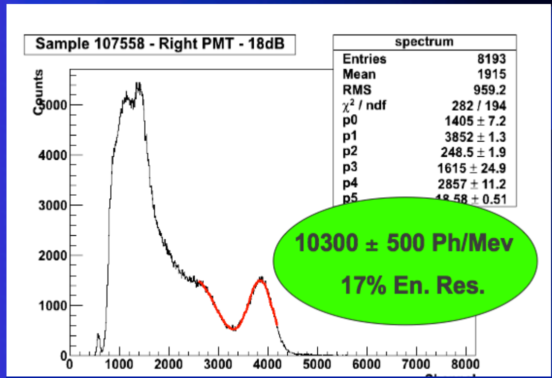


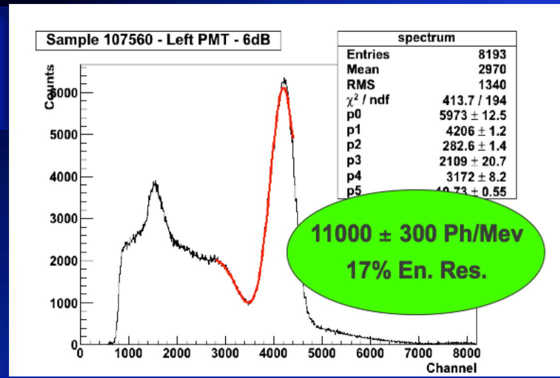


Small & Large Crystals

0.75 x 0.75 x 10mm^3	3 x 3 x 15mm^3

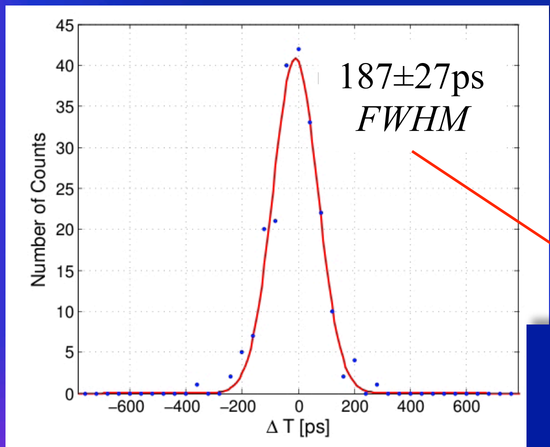
Light Yield & Energy-Resolution

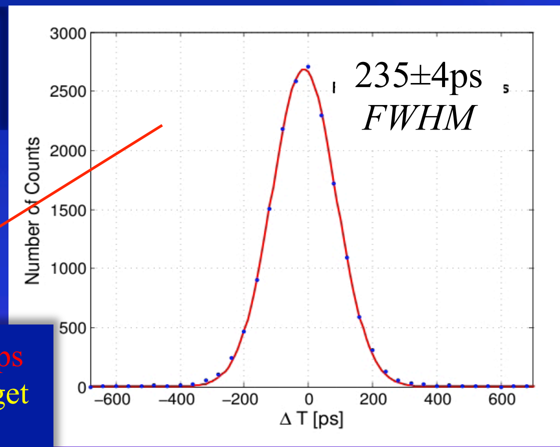




16 LYSO crystals, 4 x 4 matrix; 80μm 3M-ESR Vikuiti wrapping; Uniform irradiation with ^{137}Cs; Dry contact with PMT.

Coincidence Time Resolution





De-convolution yields 212ps *FWHM* small vs. large (target value: 200ps)

Detector R&D

1.) Photodetectors

- The analog SiPM (*a*-SiPM)
- The digital "Endo-TOFPET" SiPM (*d*-SiPM)

2.) Diffractive Optics

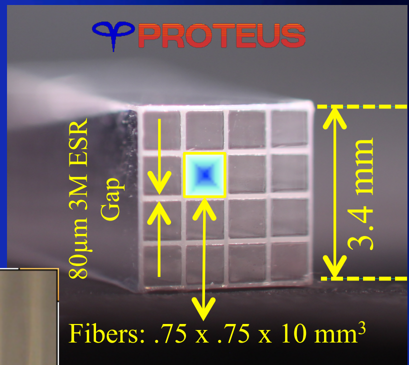
3.) Scintillators

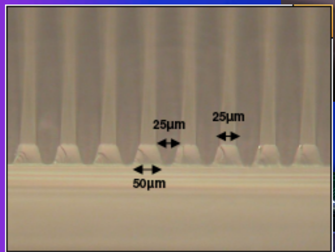
4.) Integration

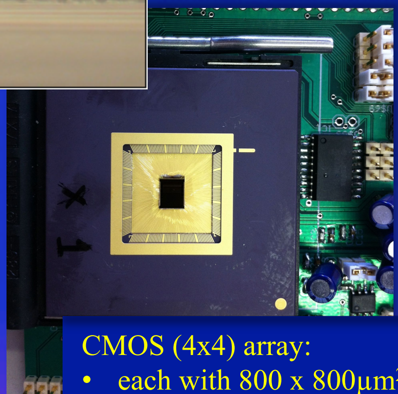
5.) Readout and Data Acquisition

Integration: Crystal Matrices

Endoscope Matrix:

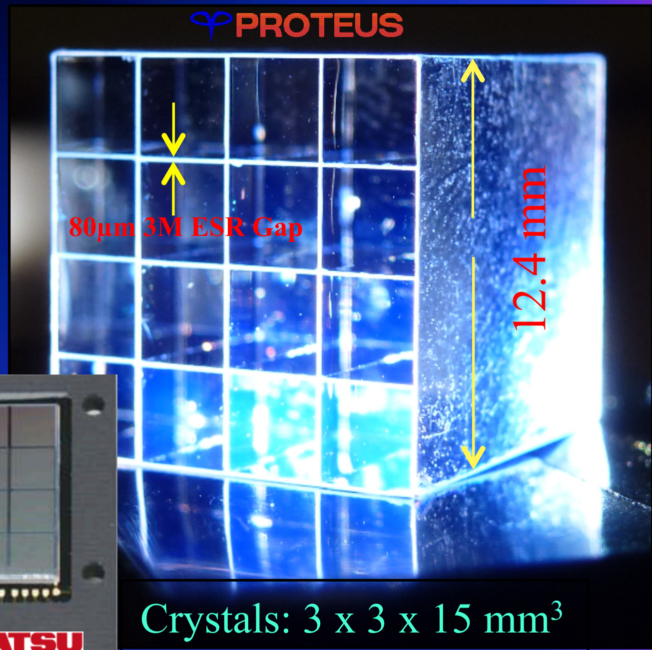






CMOS (4x4) array:
- each with 800 x 800μm^2 area
- SPAD pitch 50µm (x), 30µm (y)
- 192 TDCs total

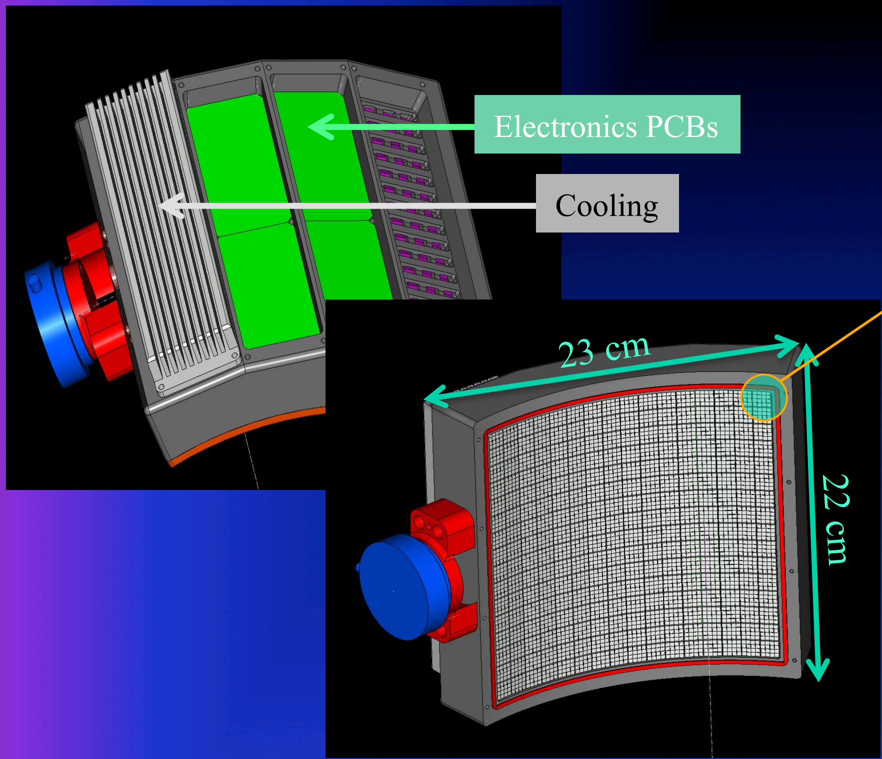
External Plate Matrix:

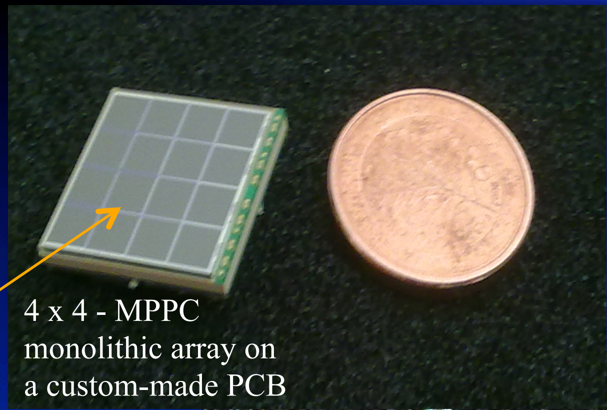


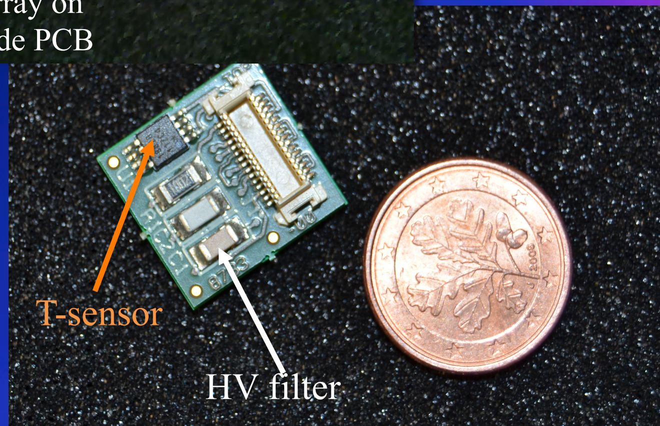
Monolithic (4 x 4) MPPC array:
- each with 3 x 3mm^2 area
- SPAD pitch: 50µm

Photo of MPPCs courtesy of Hamamatsu Photonics

System Integration: External Plate







Sensitive detector: 16 x16 detector units (4096 ch.) with ~100µm gap;
Electronics: dedicated readout chips on PCBs (512 ch./PCB) ;
Cooling: detector stabilized to room temperature via Peltier elements (expected 30mW/ch);
Tracking: detector mounted on a robotic arm for mechanical tracking (6D info, <1mm accuracy);
Curved geometry: facing the organ during diagnose (r = 21cm).

Summary

- Frontline research in the domain of:
  - digital photodetectors;
  - scintillators & optical systems;
  - medical instrumentation.
- Large knowledge and technology transfer between HEP, industry and medicine;
- Defines a roadmap for the development of a new generation of multimodal endoscopic probes.
- Thanks to the endo-TOFET and PicoSEC-Coll.
- We still seek ESR applications for the Marie-Curie ITN
  - Please contact us or our Marie-Curie-Homepage:
  - http://picosec.web.cern.ch/picosec/home.html