Medical Physics

Future challenges

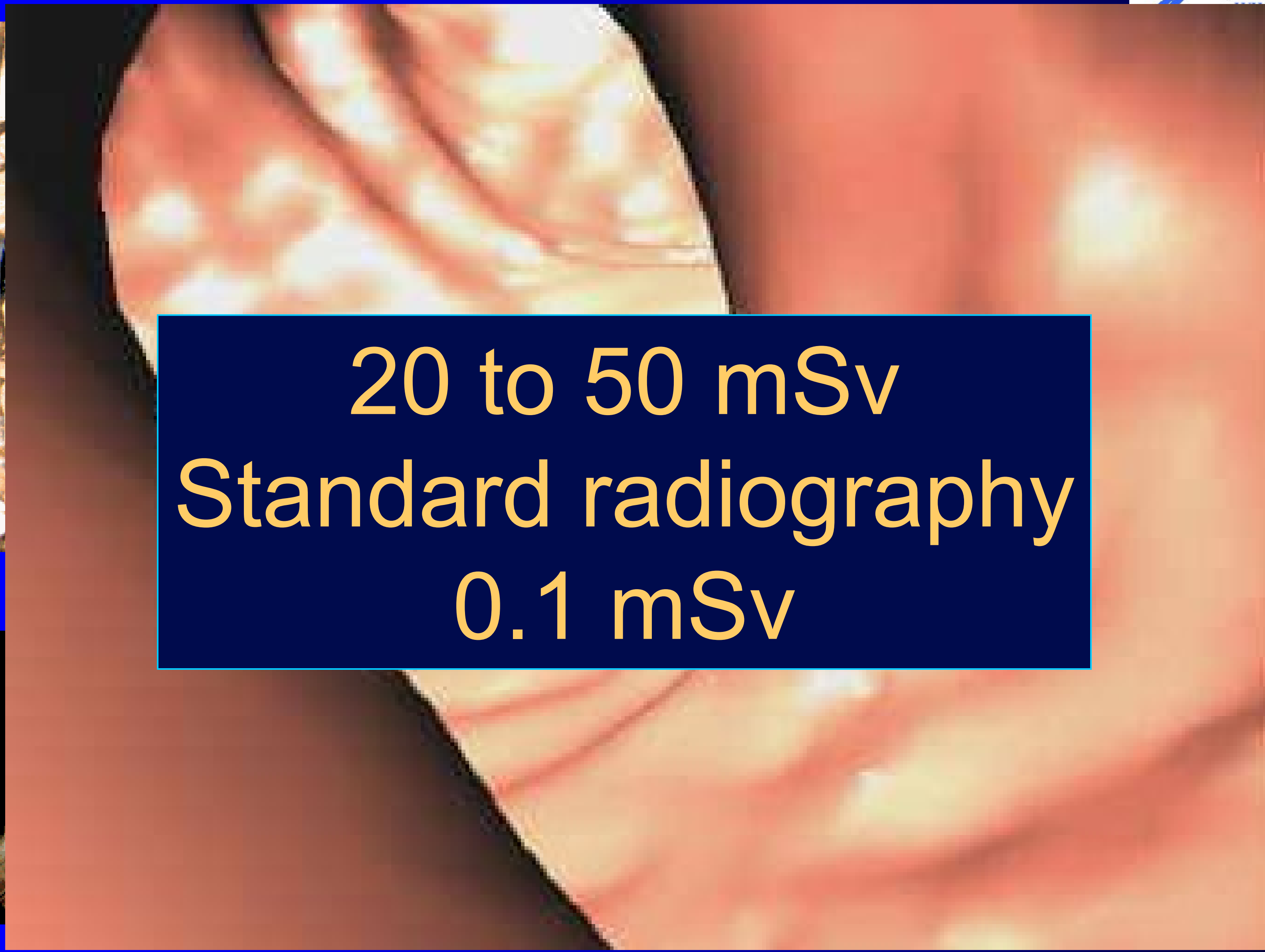
Paul Lecoq
CERN, Geneva

The future Healthcare Mission

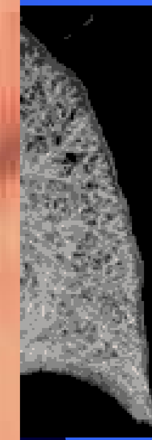
Requires a "new generation" of imaging devices and bioengineering…

Volumetric CT

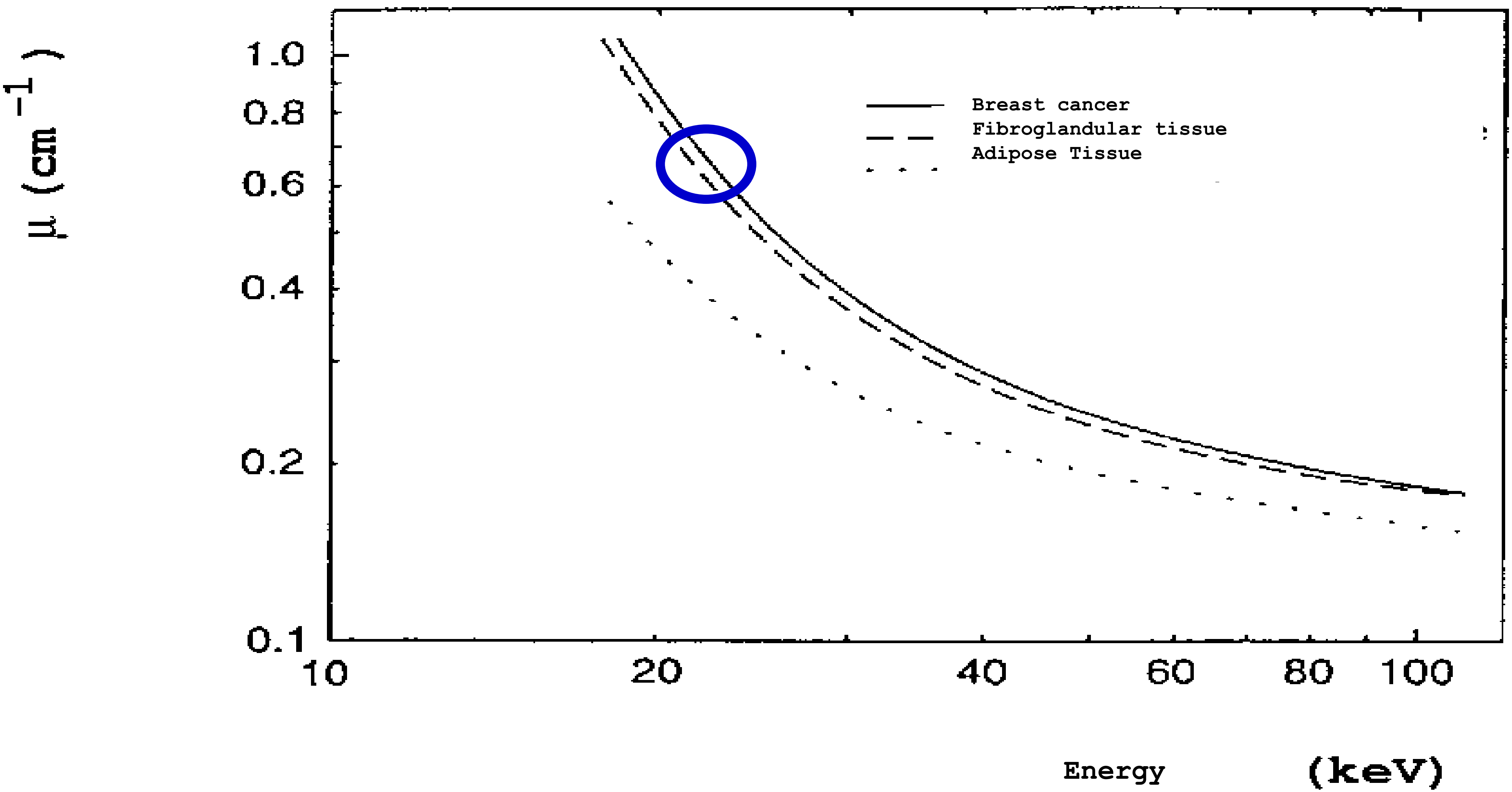
/sec)



20 to 50 mSv
Standard radiography
0.1 mSv



Problem of contrast



Photon counting in CT

Advantages of photon counting CT:

- Each event has equal weight independent of energy
  - ⇒ ***Elimination of weight factor proportional to energy of integration imaging***
  - ⇒ ***Closer to optimal weighting of E^{-3} ****

- Threshold detection allows discrimination of noise and scatter

Requirements :

- Detector: high sensitivity to low-energy X-rays,

  high count rate capability

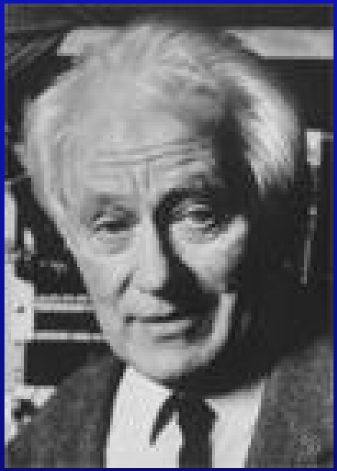
  ⇒ count-rate > 10^6 - 10^7 counts/s/pixel, *the higher the better*

* R.N. Cahn et al., “Detective quantum efficiency dependence on X-ray energy weighting in mammography”, *Med. Phys.* 26 (12), pp. 2680-2683, December 1999.

La chambre proportionnelle Radiographie digitale à faible dose

www.cern.ch/cerimed/

Prix Nobel de Physique 1992



Georges Charpak
Physicien CERN

Hybrid pixel detector
Single photon counting

- **Design in 130 nm CMOS technology, 8 metal layers**
- **~1600 transistors per pixel**

1. Preamplifier

2. Shaper

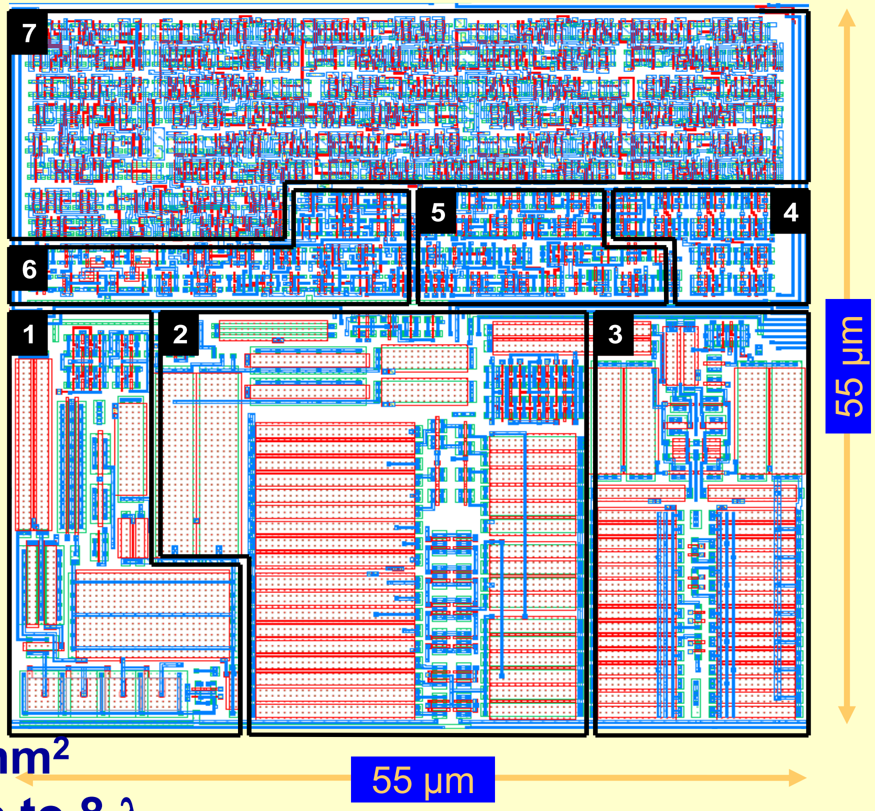
3. Two discriminators with 5-bit threshold adjustment

4. Pixel memory (13-bits)

5. Arbitration logic for charge allocation

6. Control logic

7. Configurable counter

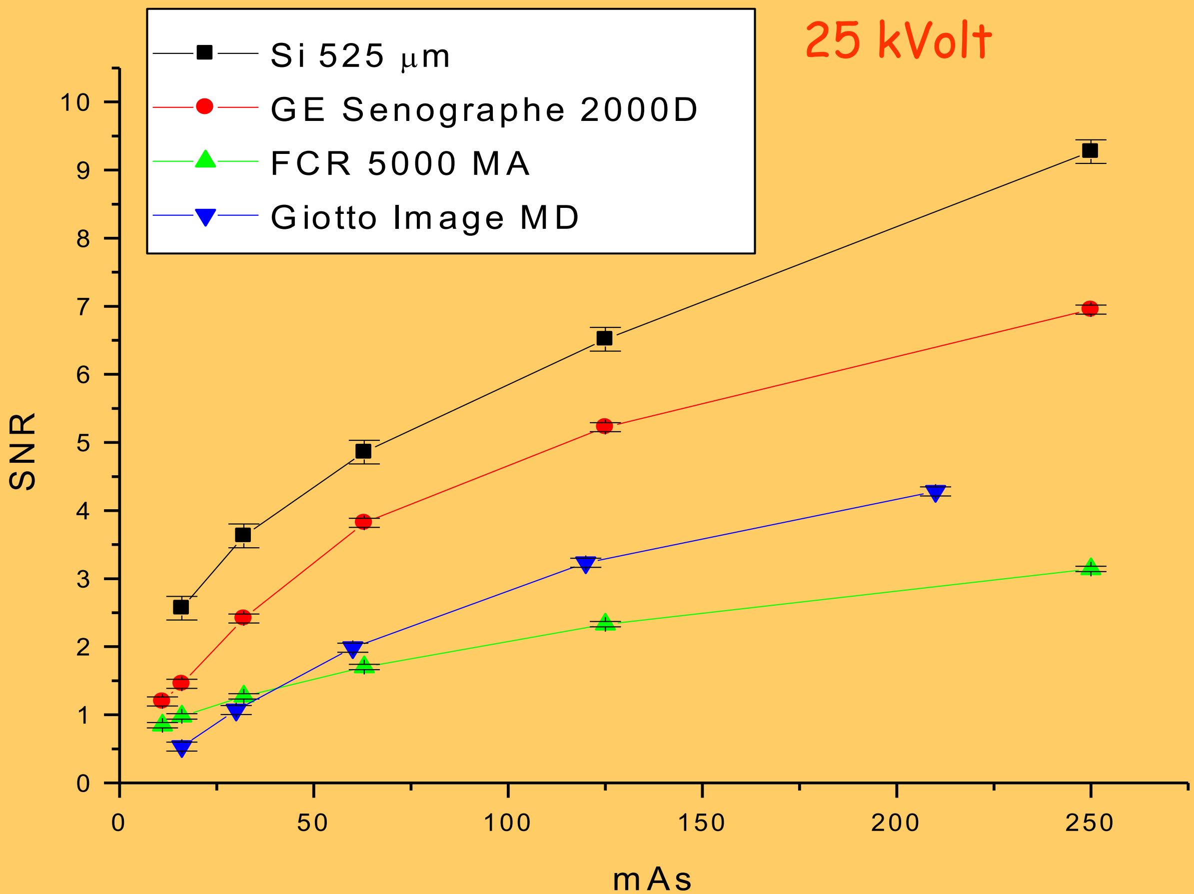


Medipix 3 chip: 256x256 pixels 17.3 X 14.1 mm^2

Pixels summation, Multiwavelength analysis up to 8 λ

Courtesy of M. Campbell

Single photon counting versus integrating digital radiography



- SNR for 2 mm thick tumor mass (RMI 156 phantom)

M. G. Bisogni et al., NIMA 546, 14 (2005)

Combine anatomic and fonctional informations

Patient treated for a colon cancer and revealing under PET/CT scan an additional breast cancer

David Townsend

CERN: 1970-78

Université de Genève

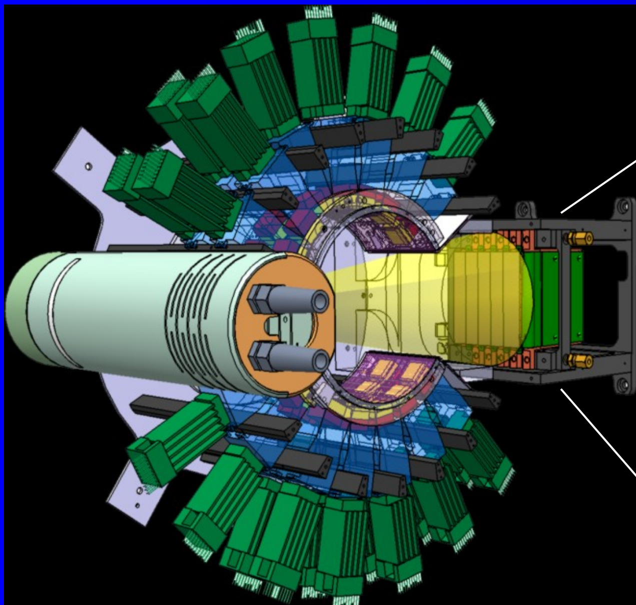
UPSM Pittsburgh

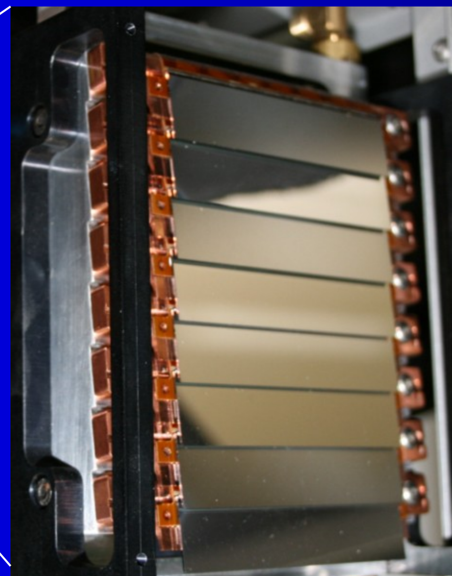
and

Ronald Nutt

(CTS – CTI)

ClearPET-XPAD





ClearPET/XPAD

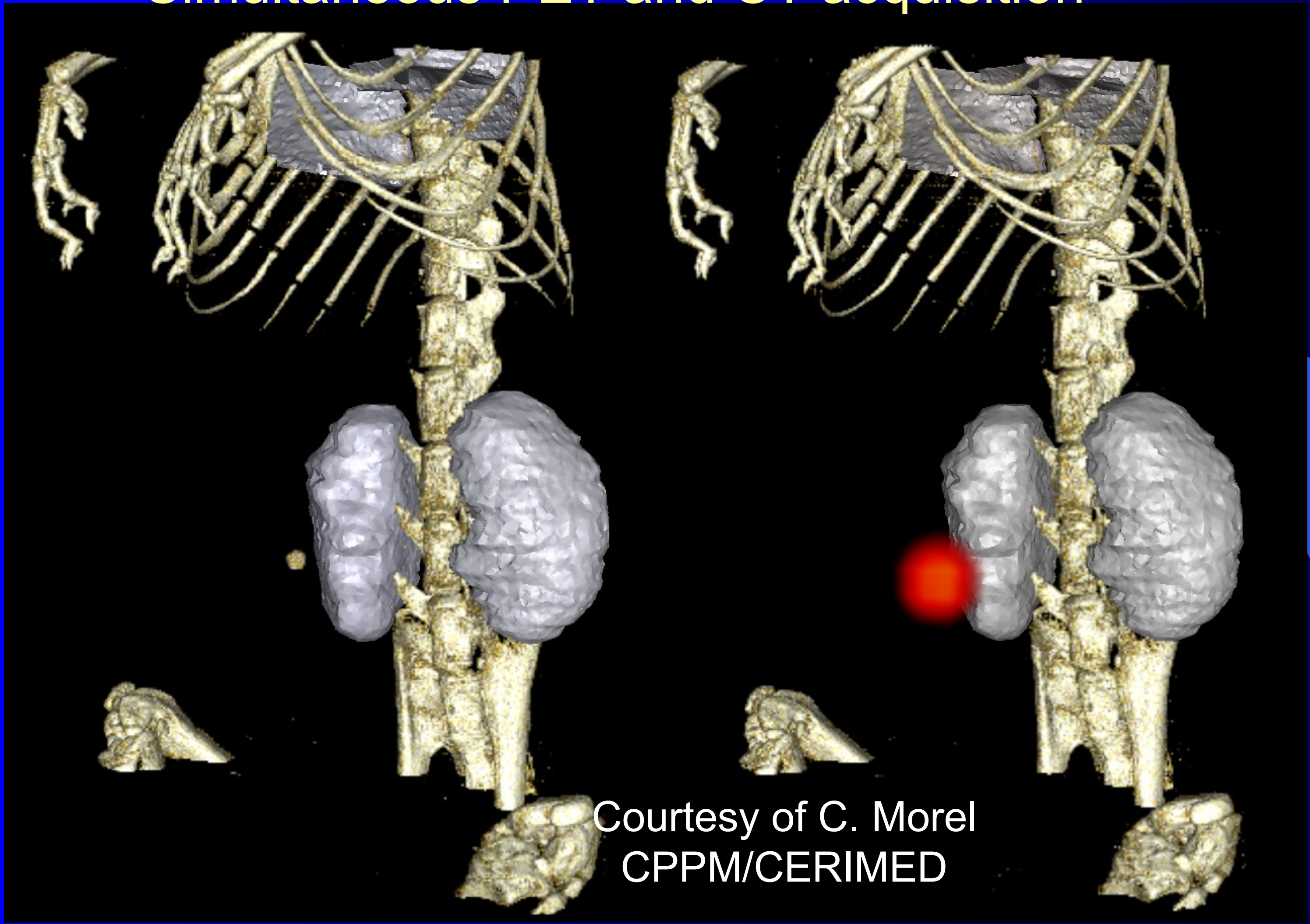
- Simultaneous hybrid PET/CT imaging system

Courtesy of C. Morel
CPPM/CERIMED

- RTW X-ray tube
  - Mo target, 50 µm focal spot size, 50 W
  - Nb/Mo additional filter
  - Collimated 17 keV almost monochromatic
- New Hybrid pixel X-ray camera XPAD3/Si
  - Photon counting mode
  - 500 µm silicon sensor thickness
  - 78 x 75 mm² detector
  - 130 x 130 µm² pixel size
- 36 mm axial FOV
- 35 mm transverse FOV

ClearPET-XPAD

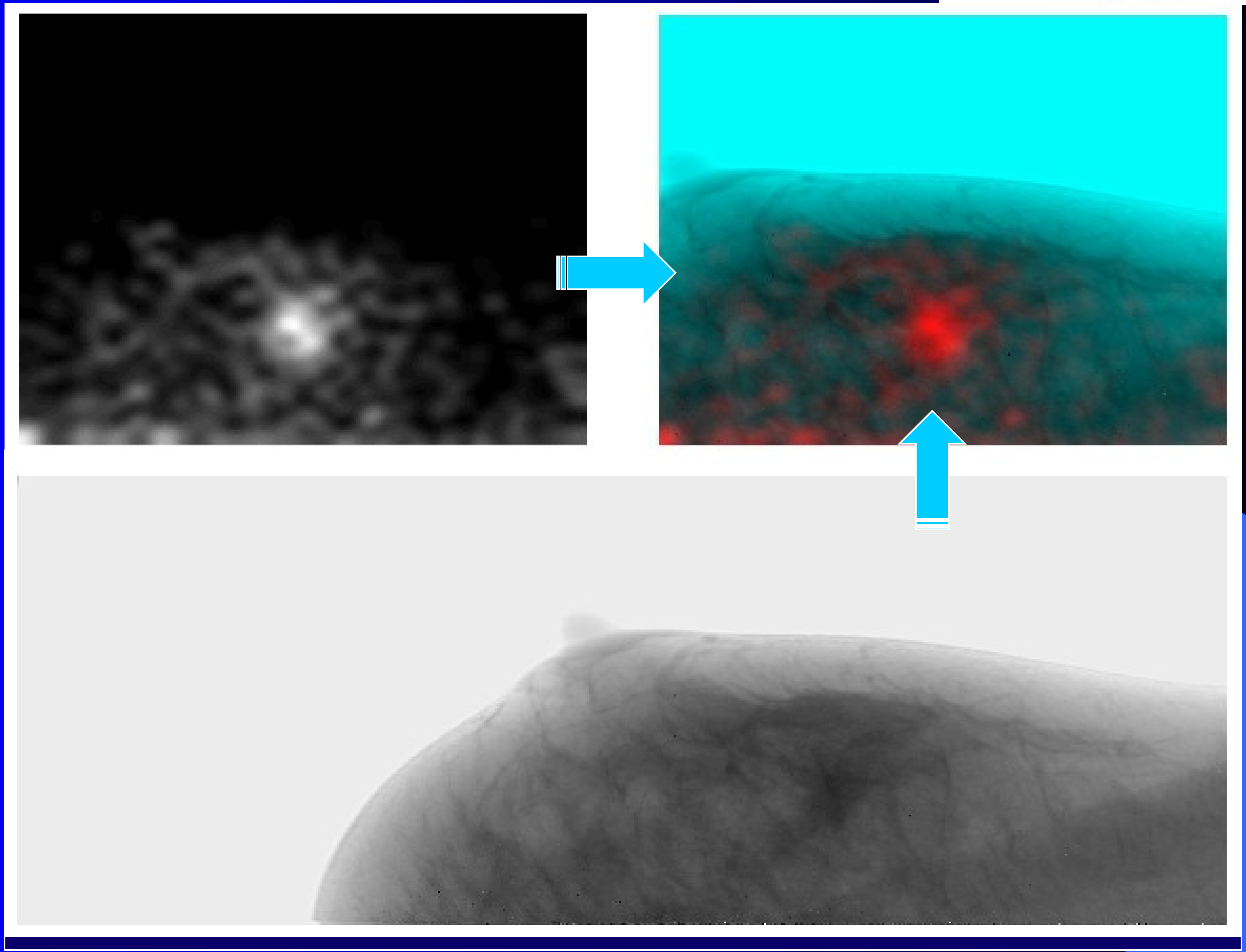
Simultaneous PET and CT acquisition



^{22}Na source surgically inserted in the belly of a dead mouse

Multimodality

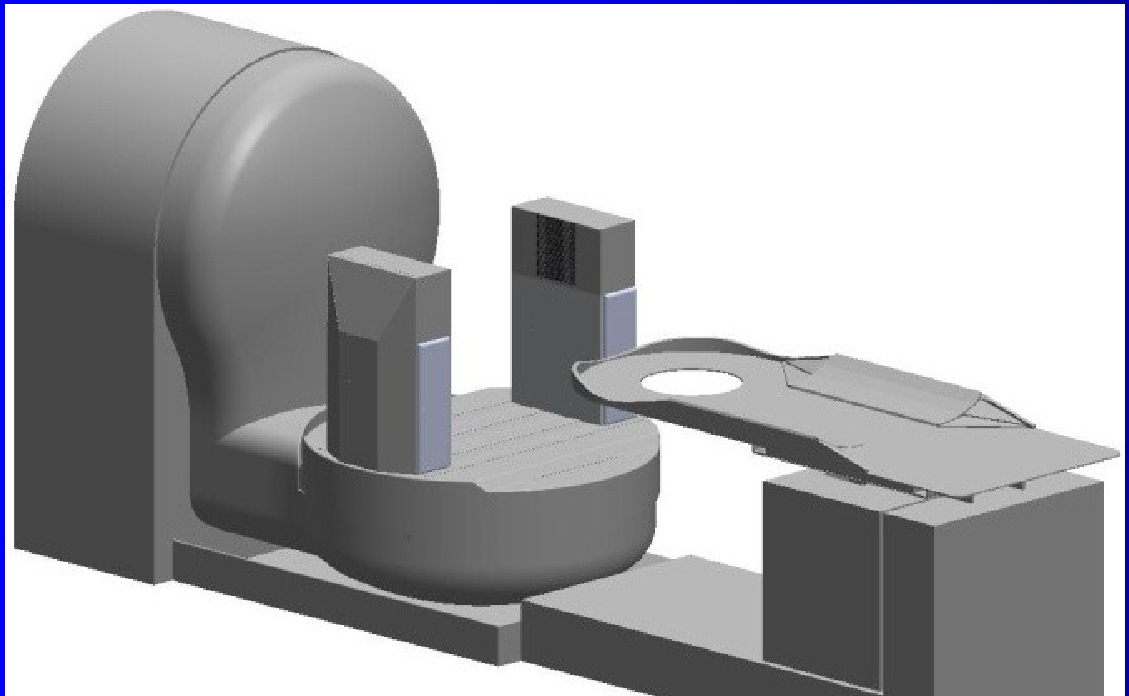
Right breast, mediolateral view.
49 year old
History: 30 mm palpable mass
[BIRADS 5]
Pathology Report: Infiltrating Ductal Carcinoma, moderately differentiated II/III



ClearPEM Imaging System
Crystal Clear Collaboration

ClearPEM-Sonic

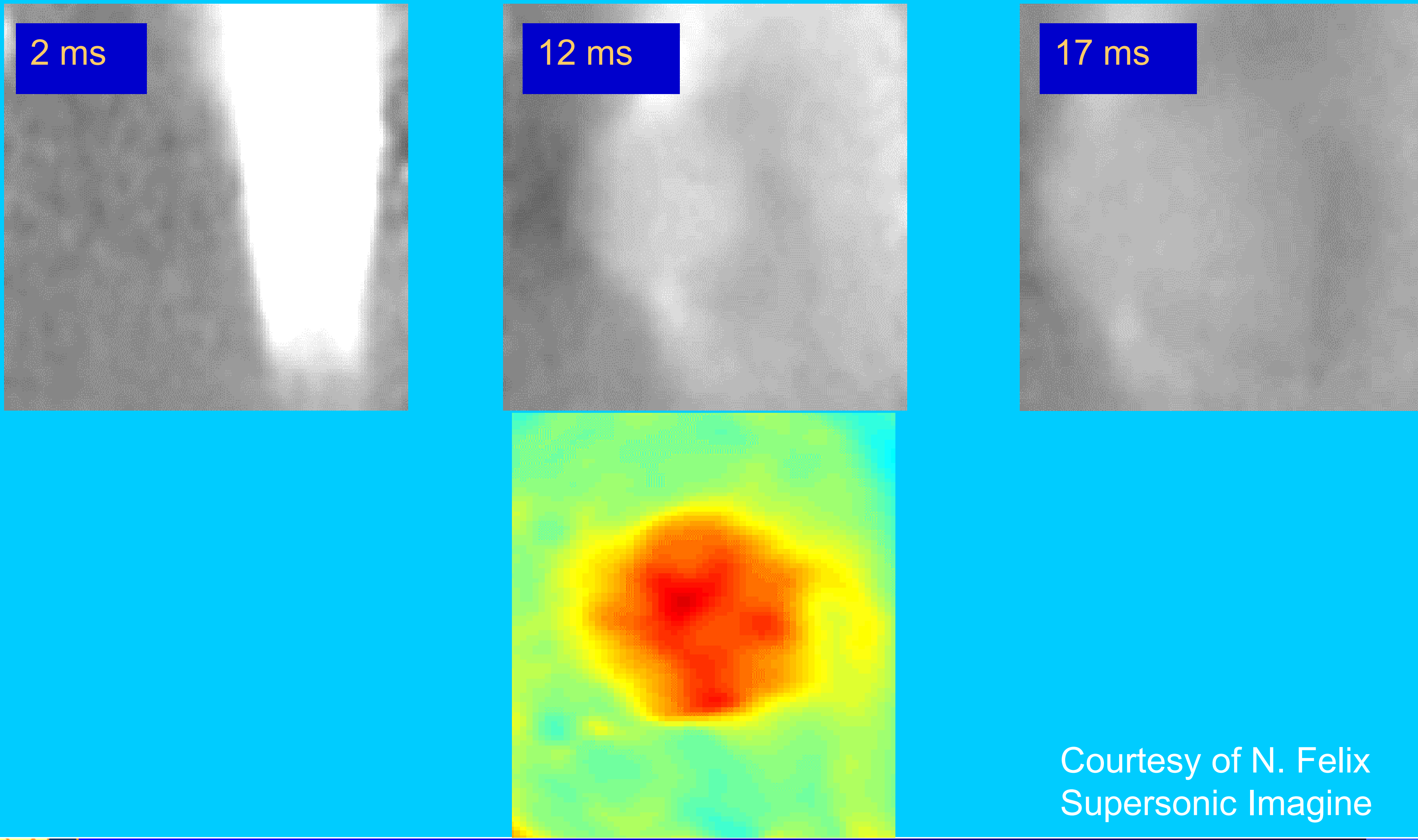
- **ClearPEM-Sonic:** a project in the frame of CERIMED (CERN partner) that combines:
  - a dedicated mammography PET, the ClearPEM from CCC
  - an US transducer working in elastographic mode from SuperSonicImagine



ClearPEM

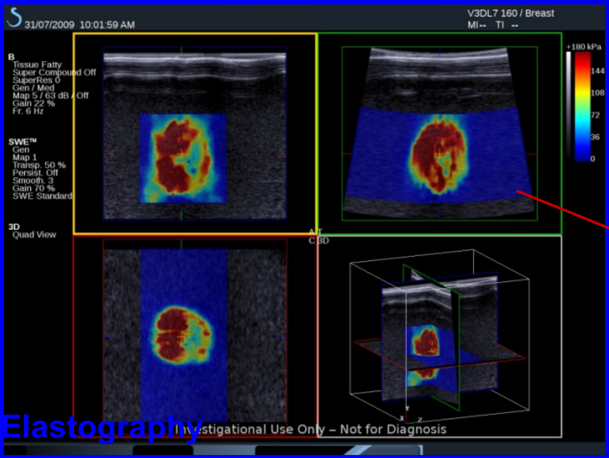
SuperSonic Imagine AIXplorer

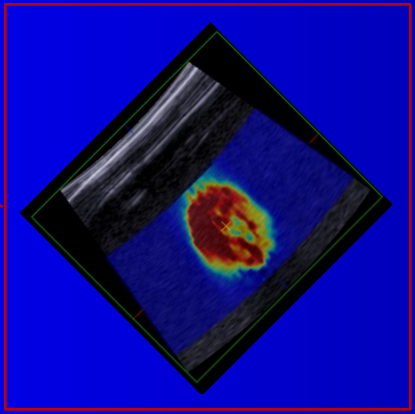
Supersonic shear wave elastography



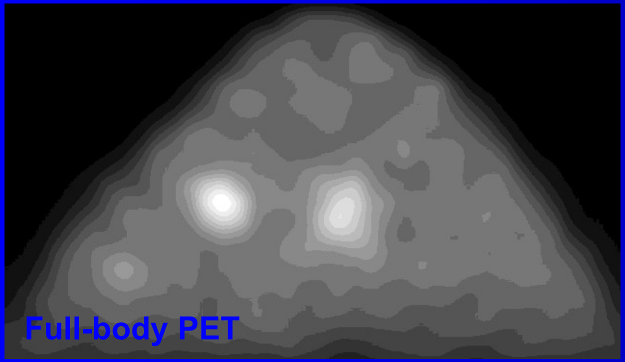
Courtesy of N. Felix
Supersonic Imagine

ClearPEM-Sonic: Proof of Concept

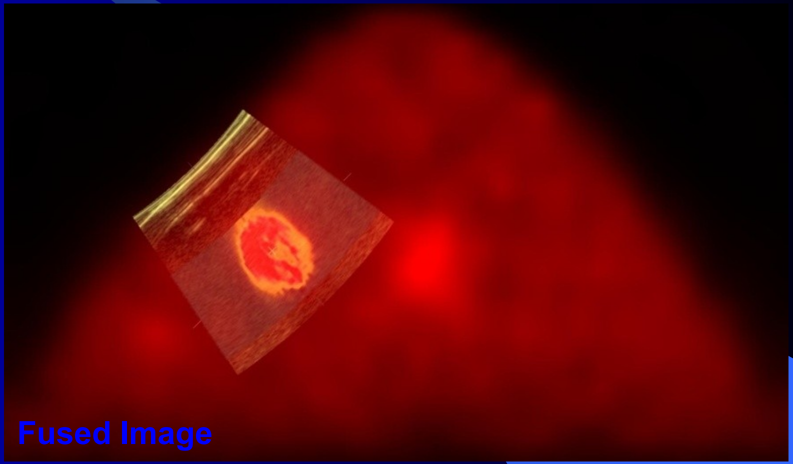




+



=

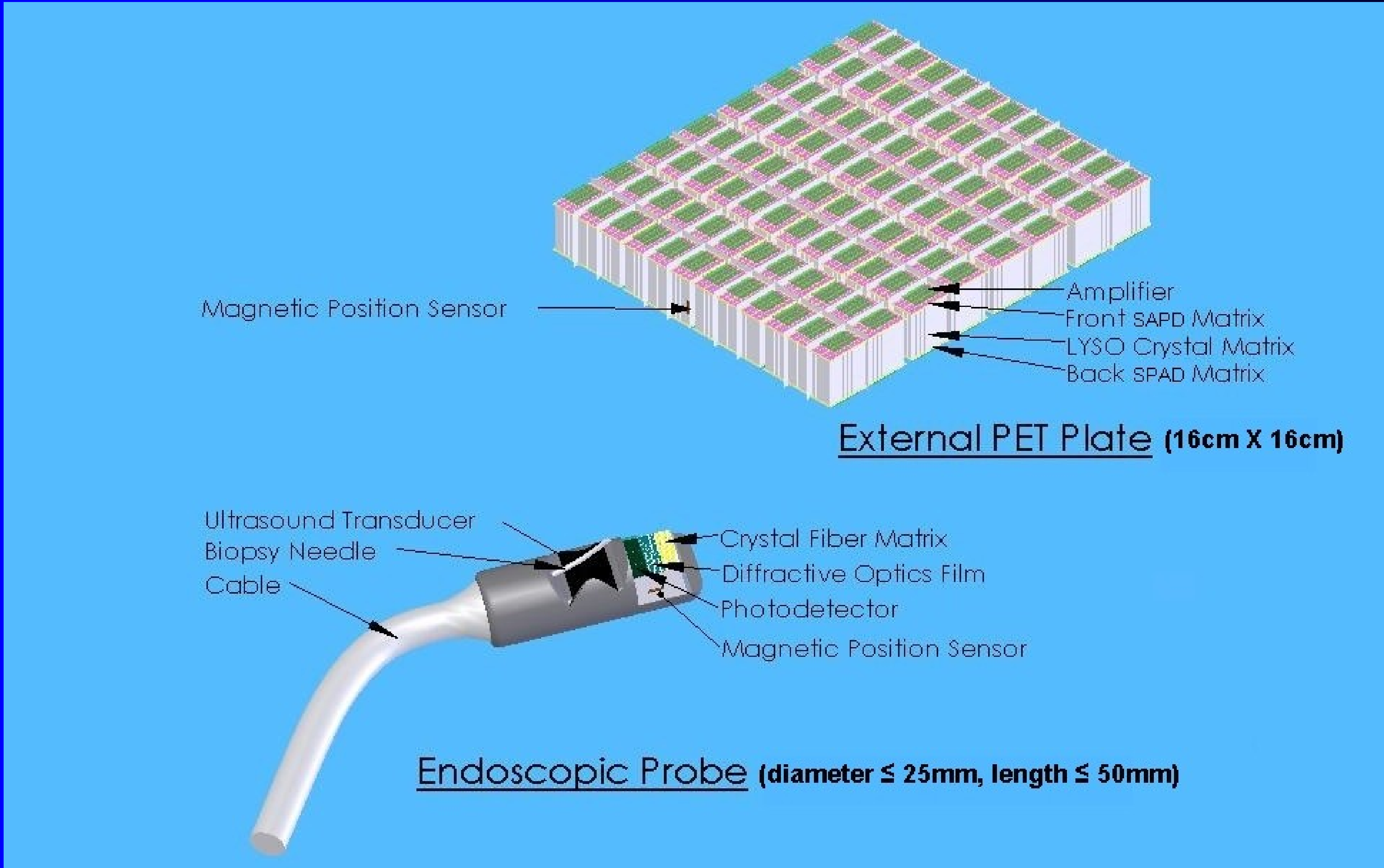


- **Agar-Agar / Gelatin phantom with lesions** (developed by Dang JUN from Brussels University
- First image taken with SSI AIXplorer in **elastographic mode**, second image taken with **full-body PET** (IPO)

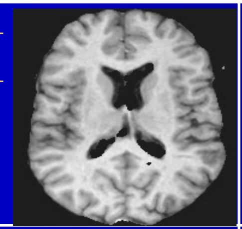
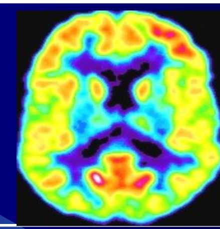
→ **Reconstructed images (courtesy Dang JUN) show it is possible to match both images using fiducial markers and the magnetic positioning system**

Endo TOFPET-US

Novel multimodal endoscopic probes for simultaneous PET/ultrasound imaging for image-guided interventions



Complementary nature of MRI & PET

Parameter	MRI 	PET 
Anatomical Detail	Excellent	Poor
Spatial Resolution	Excellent	Compromised
Clinical Penetration	Excellent	Limited
Sensitivity	Poor	Excellent
Molecular imaging	Limited	Excellent

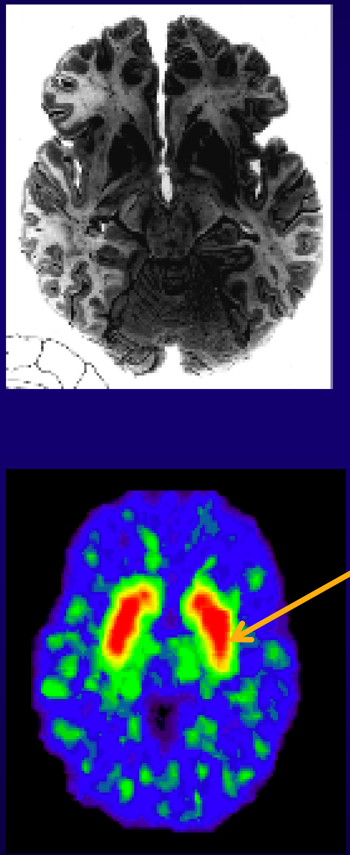
Hence: The Sum of PET and MRI should be excellent and even better

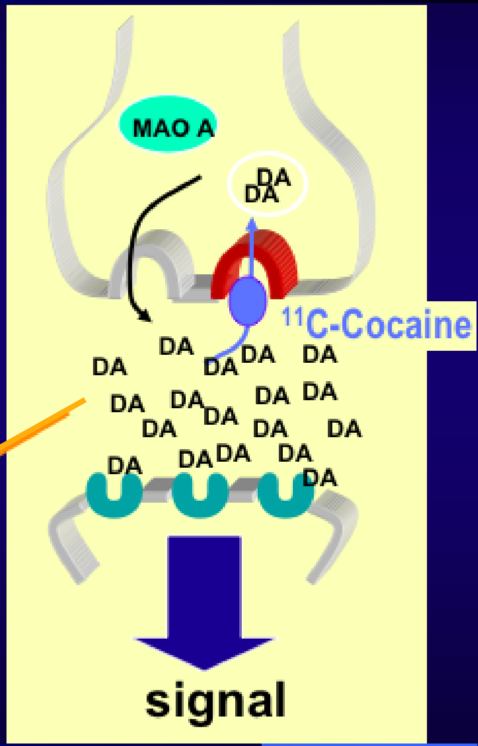
MRI-PET >> MRI + PET

PET-MRI for brain studies

- ❑ Drug addiction
- ❑ Nicotine addiction
- ❑ Alcoholism
- ❑ Attention deficit disorders
- ❑ Obesity
- ❑ Parkinson

These diseases are all related to the dopamine neurotransmitter system and can be studied by PET

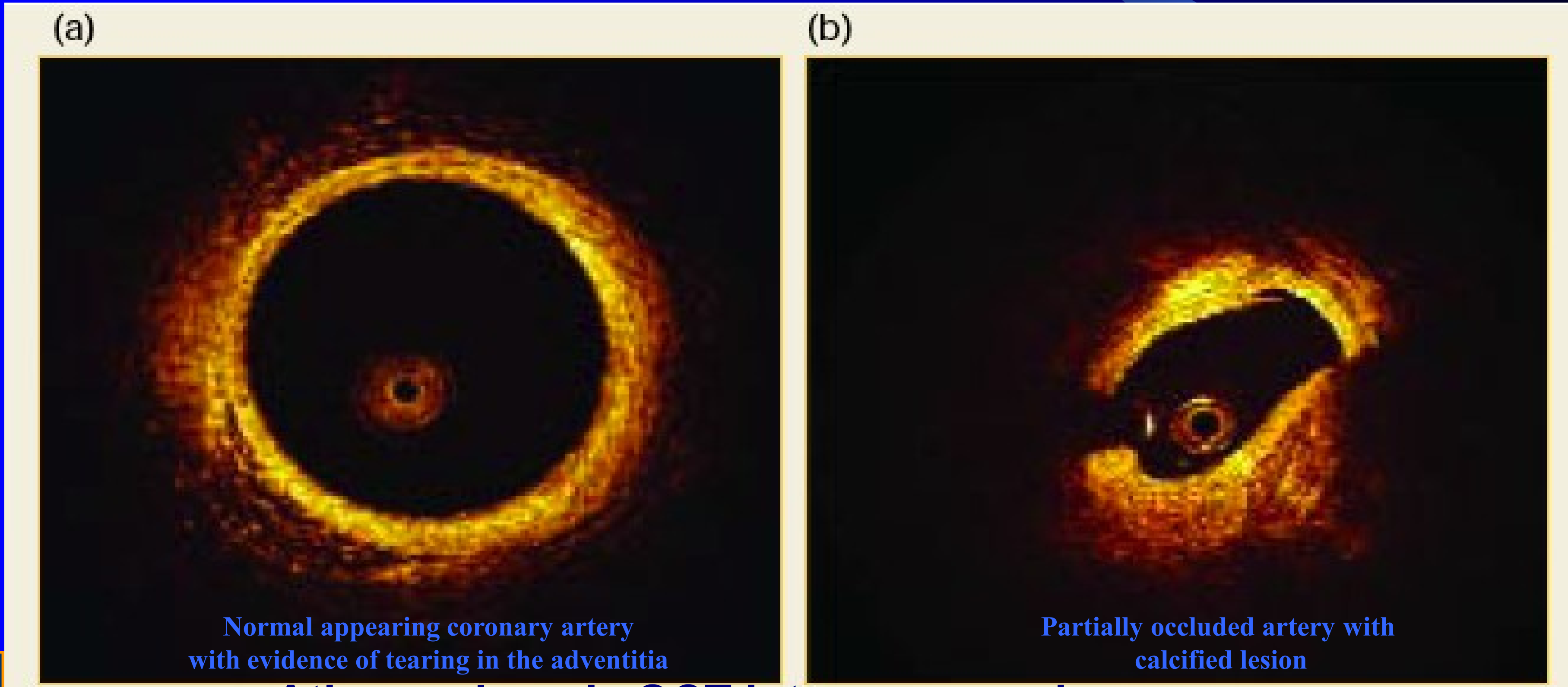




Vulnerable plaque imaging

Source: CERIMED/ISS workshop on cardio-vascular imaging, Rome, Nov06

- A vulnerable plaque is an atherome, an unstable collection of lymphocytes and macrophages (white blood cells) and lipids (including LDL cholesterol) attached to the wall of an artery



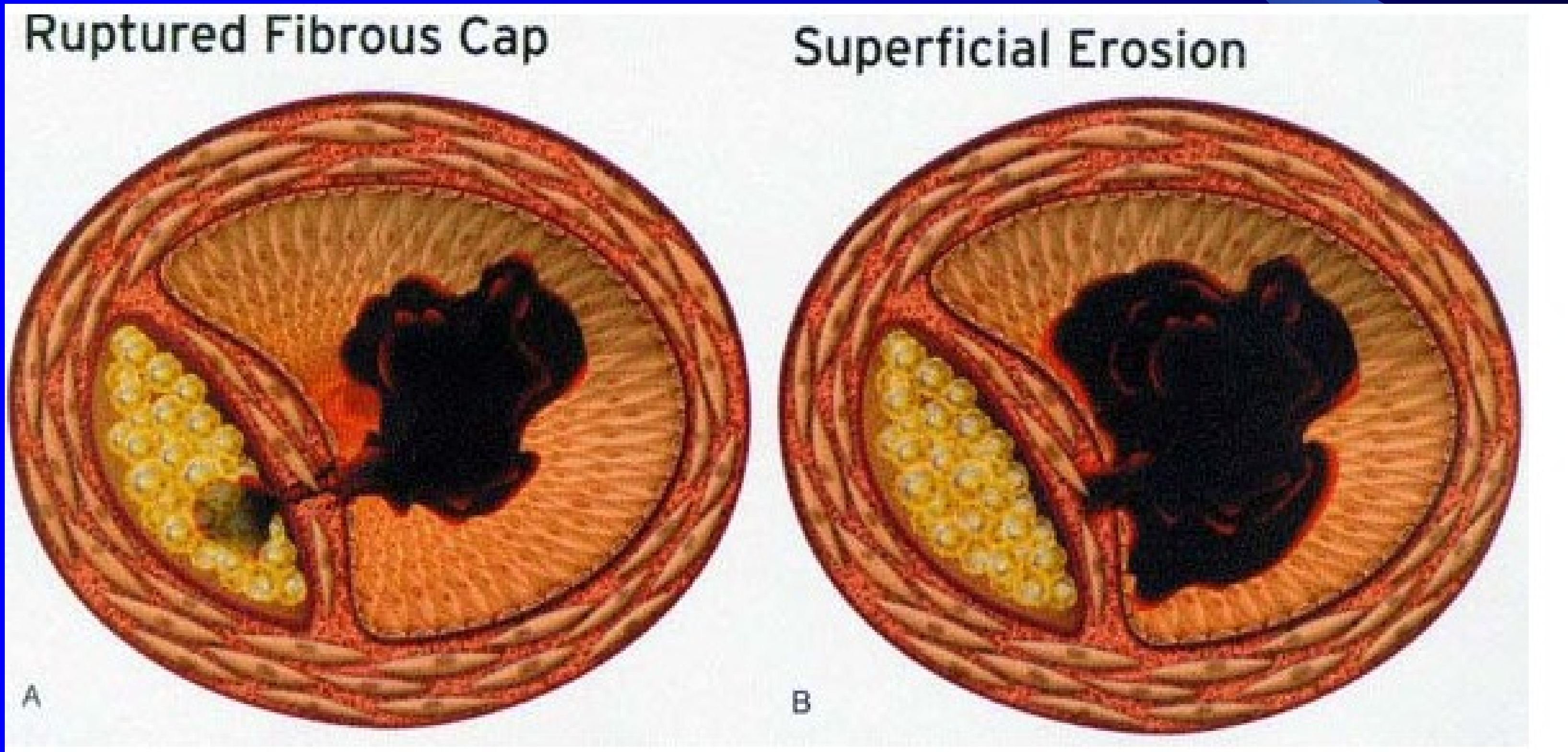
(a) Normal appearing coronary artery with evidence of tearing in the adventitia

(b) Partially occluded artery with calcified lesion

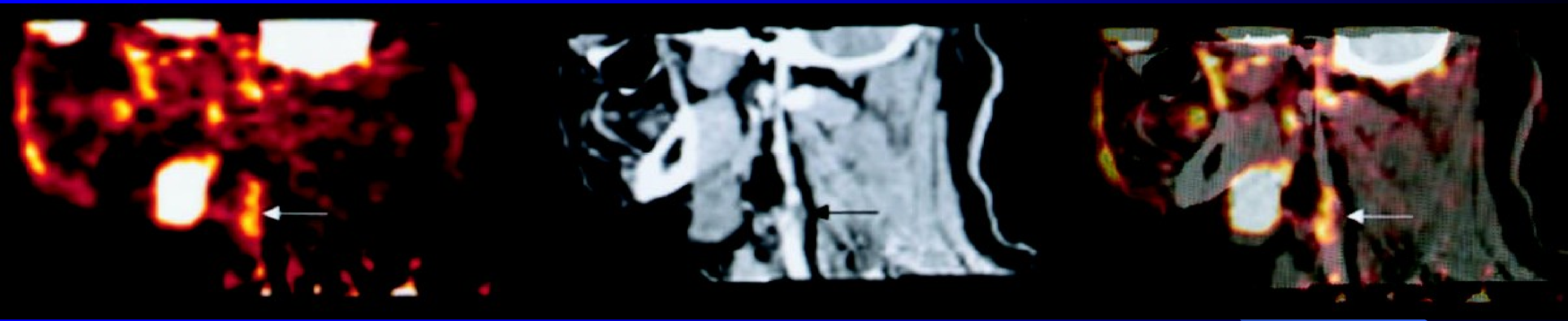
Atherosclerosis OCT intracoronary images

Acute myocardial infarct

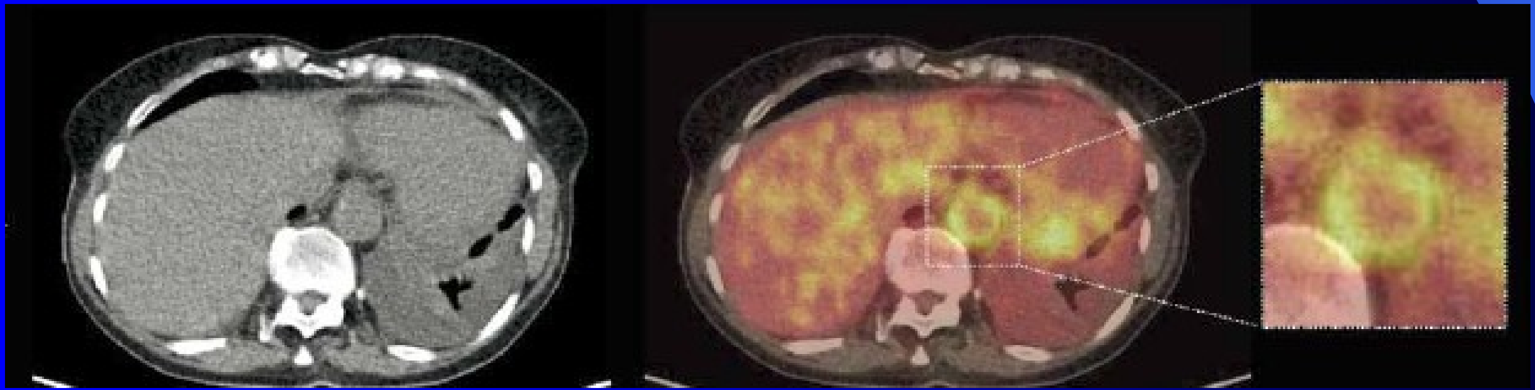
● Both plaque rupture and erosion result in exposure of thrombogenic elements to the blood flowing past the lesion, resulting in thrombus formation. Plaque rupture is seen in ~ 75% of infarcts, erosion in ~ 25%. Erosion is more common in patients 30-50 years old



Imaging of "inflammed plaque" by FDG and PET/CT



"Complicated" carotid plaque in a patient with stroke



Macrophage infiltration in atherosclerotic aorta

Rudd et al Circulation 2002;105:2708

Challenges to Imaging Coronary Atheroma

- Small lesion size
  - Coronary artery is ~ **3mm** internal diameter at the origin
    - A vulnerable plaque may occupy 2x5x0.2 deep (plaque volume $2mm^3$)
    - Gamma camera resolution 6mm
    - PET camera resolution 4mm
- Motion (respiratory and cardiac)
  - Gating of both the CT and the FDG scan (requires sensitivity)
- Background activity in the myocardium
  - Contrast resolution: Concentration in lesion must exceed background
  - Which plaque components are most important?

Need ***either (preferably both)***:

Enhanced spatial resolution

High signal to noise (Target/Background > 30:1)

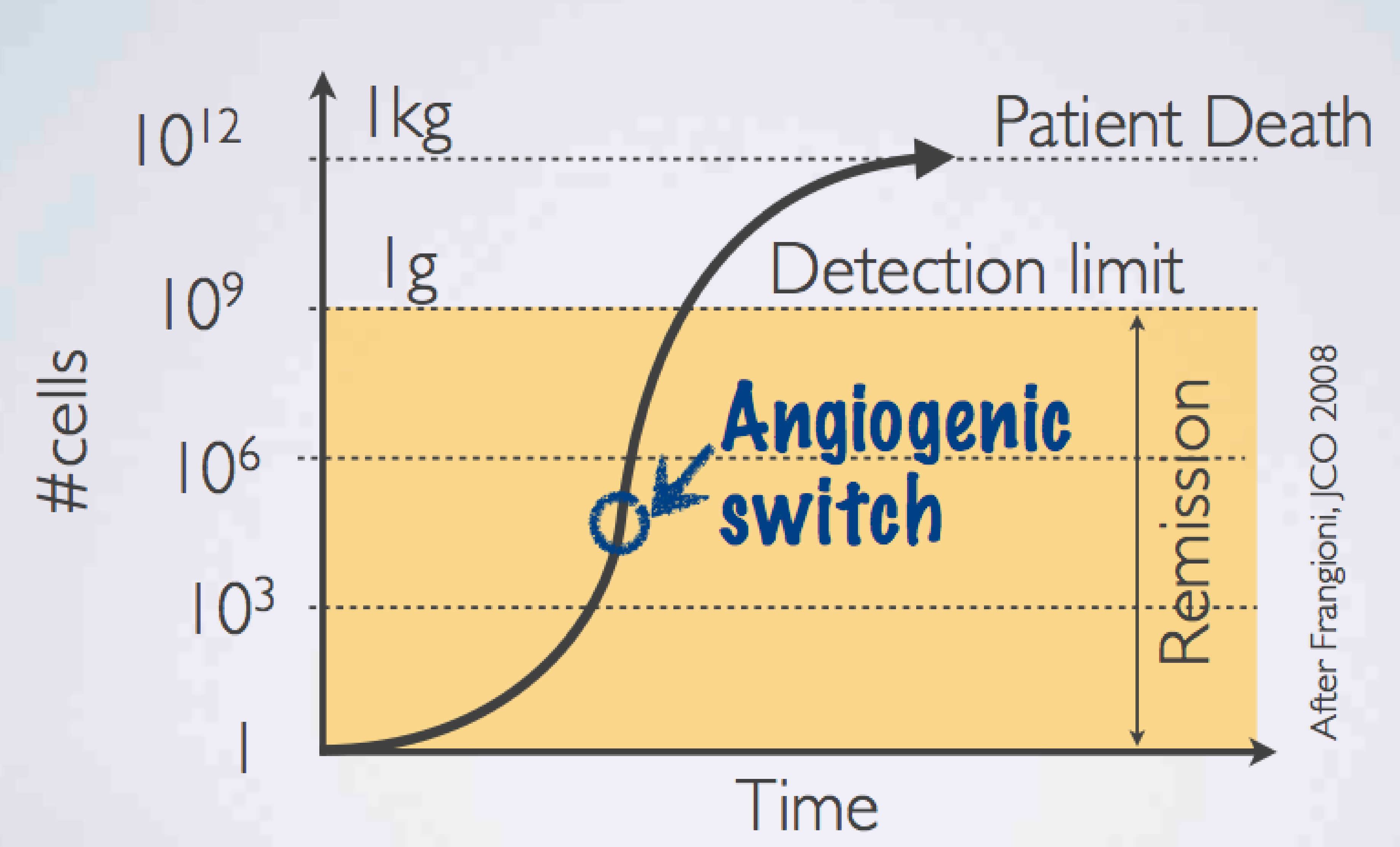
Stem cell imaging & tracking

Source: CERIMED/ISS workshop on Stem Cells imaging, Marseilles, Dec08

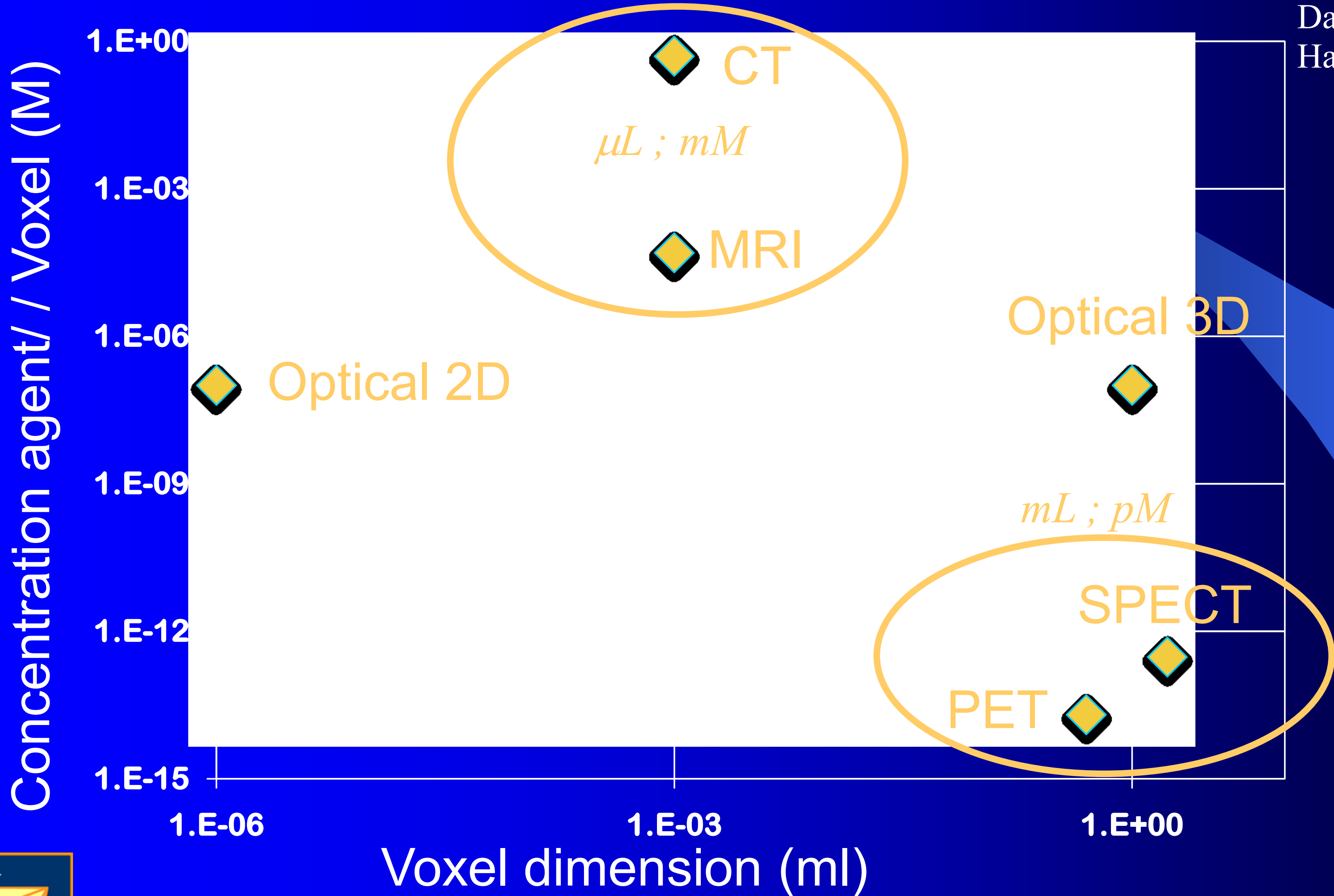
- Rapid increase of reported cases of stem cells being used in cardiology
- Evidence emerging in support of a cancer stem-cell model of carcinogenesis
- Emergence of stem-cell based treatments in cardiology, oncology, immunology, neurology, transplantation

Need for tracking small population of cells in-vivo

PET detection limit today's situation



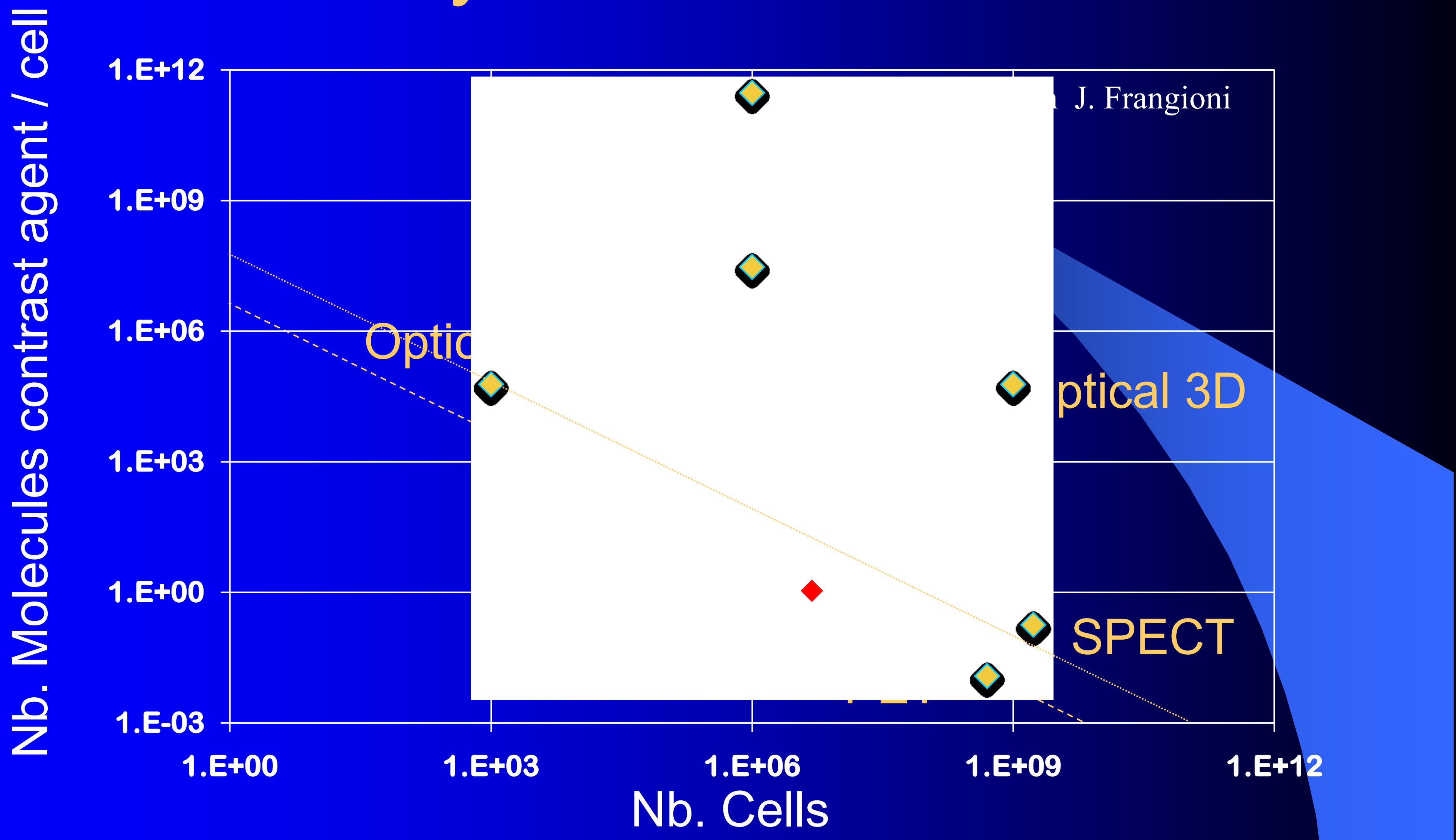
PET detection limit today's situation



Data from J. Frangioni
Harvard Medical School

J. Prior
CHUV Lausanne

PET detection limit today's situation



The future of medical imaging

www.cern.ch/cerimed/

- Faster exams
- Movement correction
  - Breathing
  - Cardiac beating
  - Digestive bolus
- Dynamics
- Quantification
- True multimodality
- Reduce dose to patient

⇒

IMPROVE

- Spatial resolution
- Sensitivity
- Timing resolution
- Signal/Noise ratio

Field of view

Resolution

Time

Artifacts / 3D completeness

Dose

Sensitivity

Scintillating detector is the eye of PET scanner

It needs a 20/20 vision

Spatial Resolution in PET*

$$FWHM = 1.25\sqrt{(d/2)^2 + (0.0022\,D)^2 + r^2 + b^2}$$

d	:	crystal size
D	:	coincident detector separation
r	:	effective source size (including positron range)
b	:	systematic inaccuracy of positioning scheme
1.25	:	degradation due to tomographic reconstruction

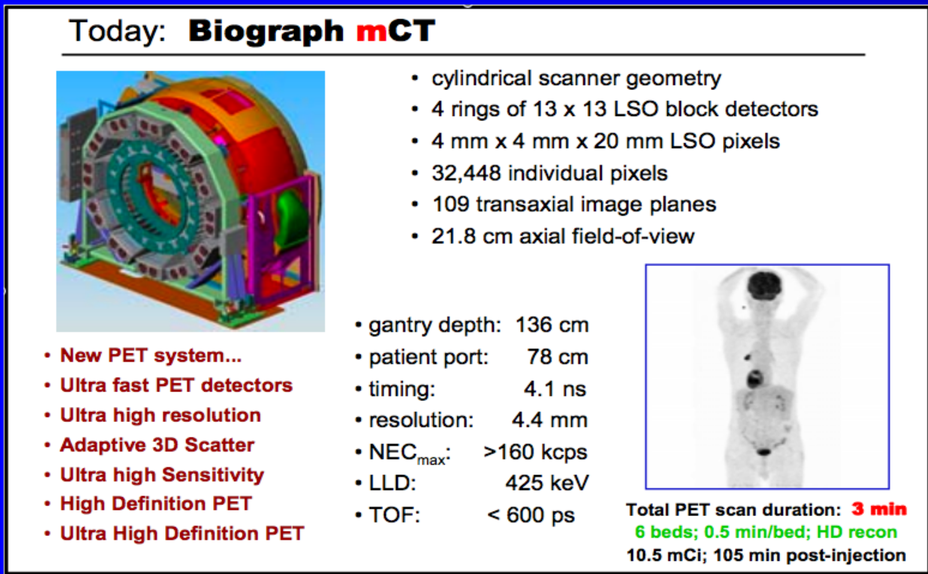
* Derenzo & Moses, "Critical instrumentation issues for resolution <2mm, high sensitivity brain PET", in *Quantification of Brain Function, Tracer Kinetics & Image Analysis in Brain PET*, ed. Uemura et al, Elsevior, 1993, pp. 25-40.

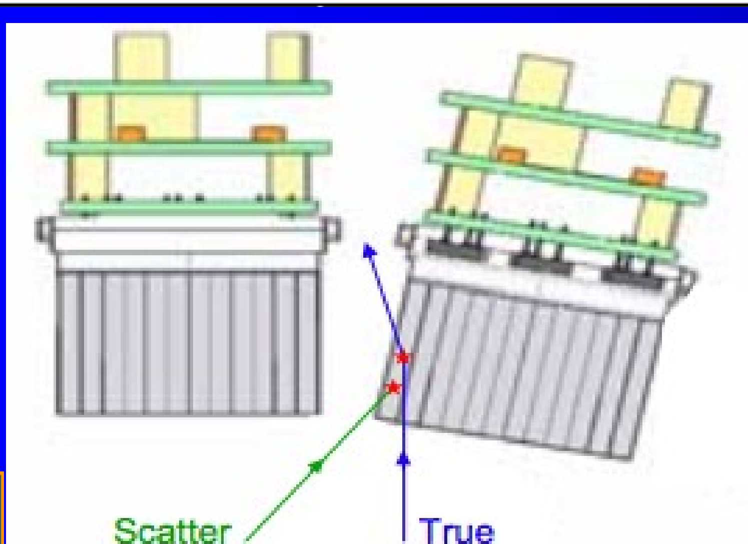
PET sensitivity

$$S \propto \Omega \cdot \eta_{\gamma}^{2}$$

- Improve geometrical acceptance
  - – Dedicated devices
  - – More compact detecting units
- Improve 2γ detection efficiency
  - – Faster electronics
  - – Better use of the complexity of the conversion event
    - Metamaterials
    - UV emiting scintillating glasses doped with quantum dots
- Improve S/N ratio
  - – Better noise rejection (TOF PET)

Improve geometrical acceptance-1





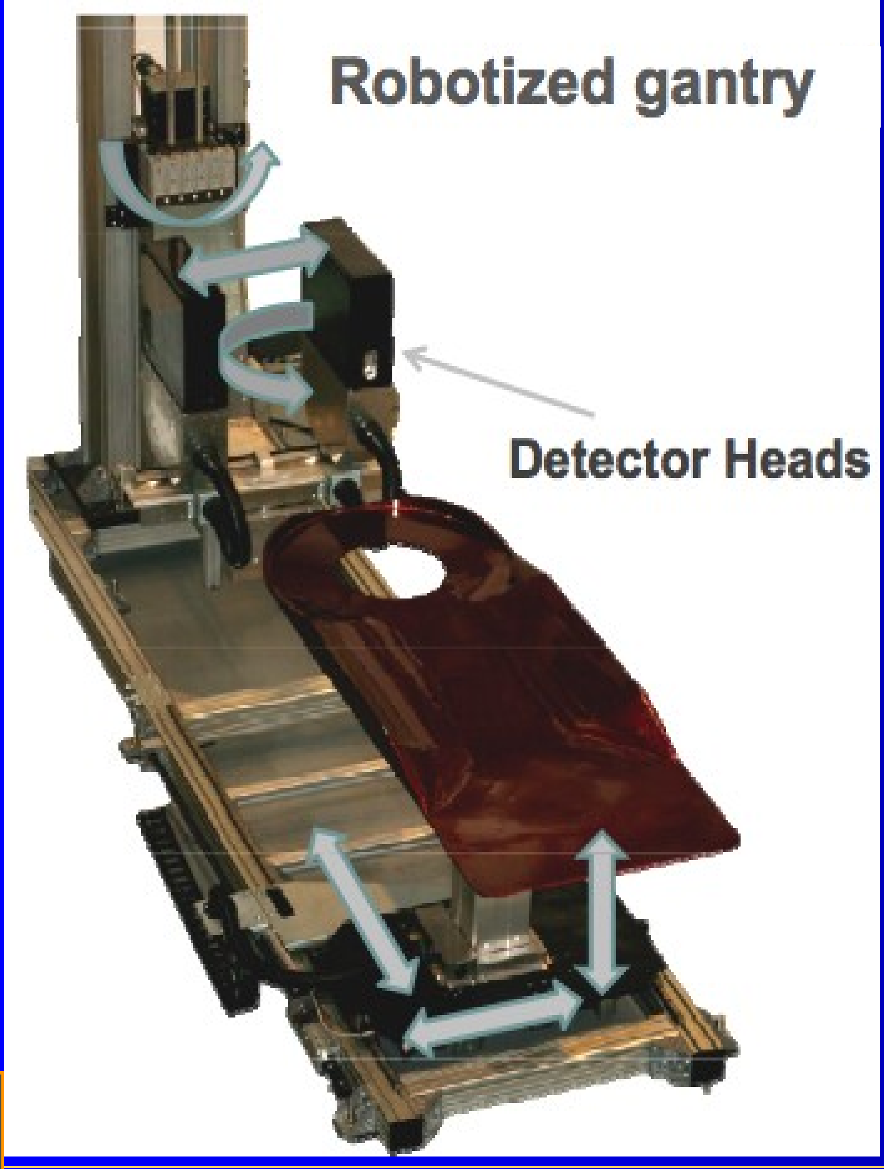
- Commercial WB PETs have a 80cm port and an axial coverage of typically 20cm

$$\Omega \approx 7\%$$

- Crystals are highly segmented with gaps
- This further reduces the acceptance by 50%

$$\Omega_{eff} \approx 3.5\%$$

Dedicated devices

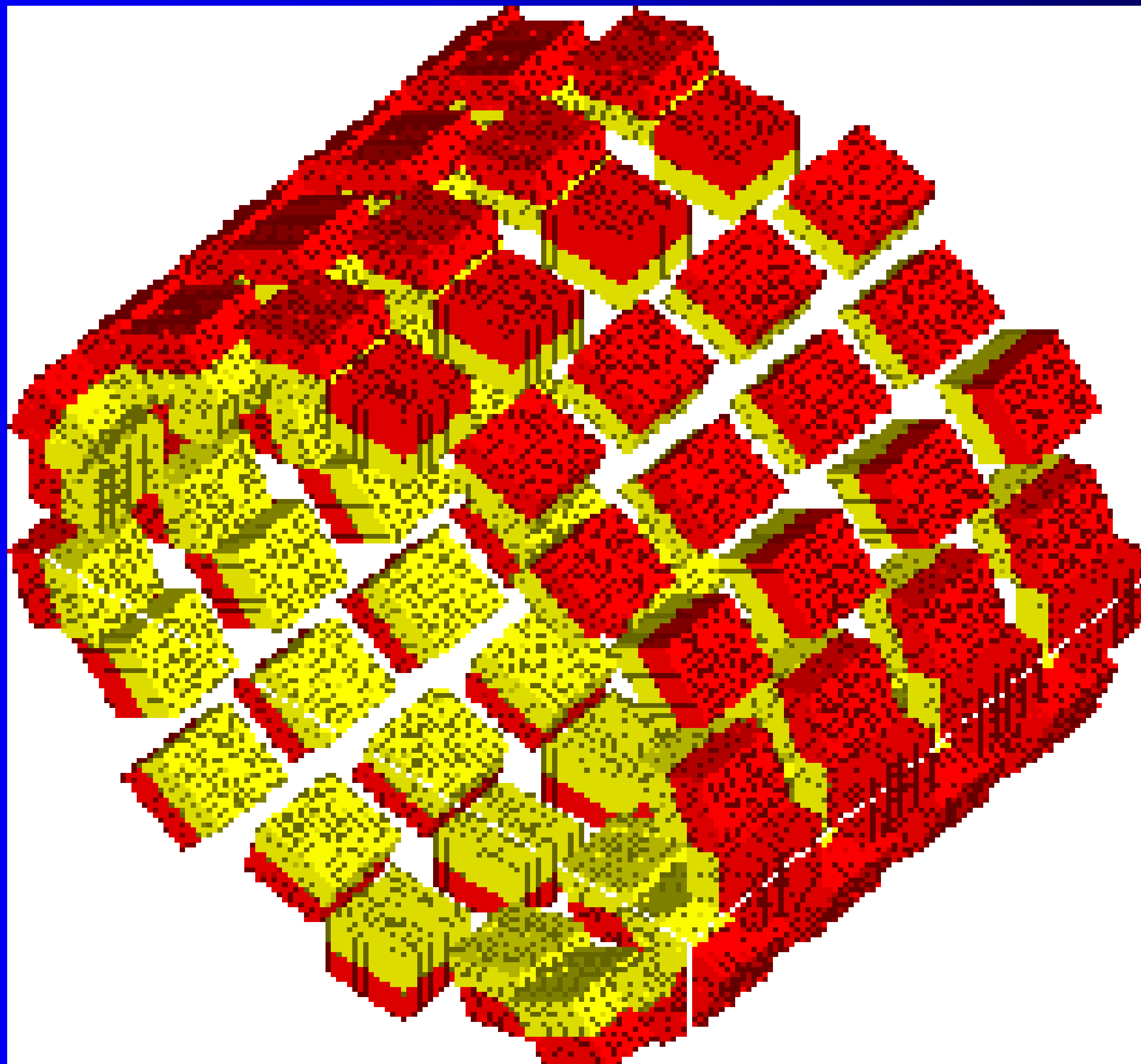


- Exemple of the ClearPEM
- 2 detector plates $15x17cm^2$
- Variable distance between plates
- With 15cm

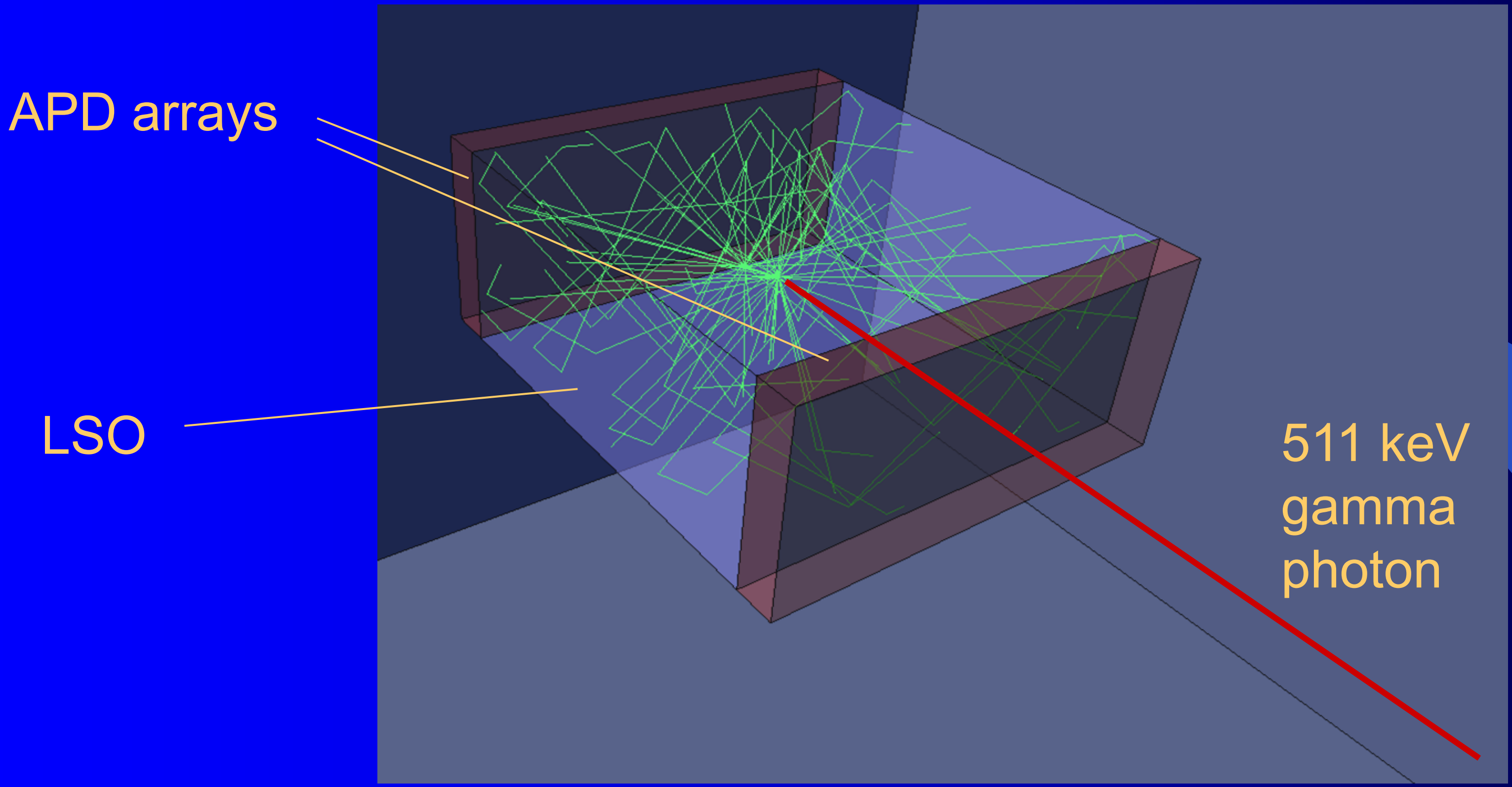
$$\Omega \approx 36\%$$

- 5x improvement
- Can be easily doubled with 4 heads

Improve geometrical acceptance-2



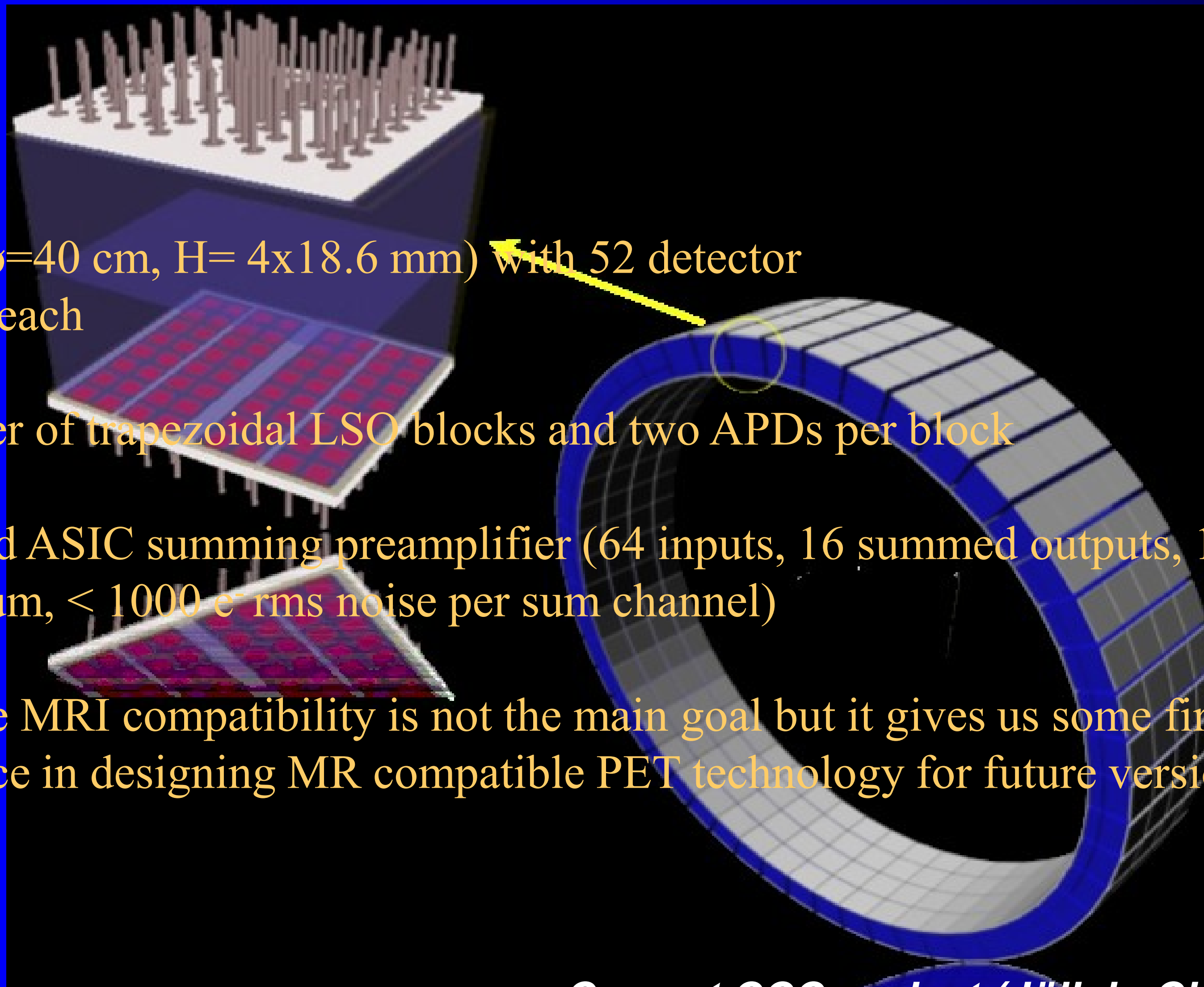
Monolithic scintillation detectors



DOI by light distribution

GEANT4 Monte Carlo simulation of an LSO block read out by two APD arrays. A small fraction of the optical photons produced by the absorption of a 511 keV annihilation photon is shown.

BrainPET insert detectors



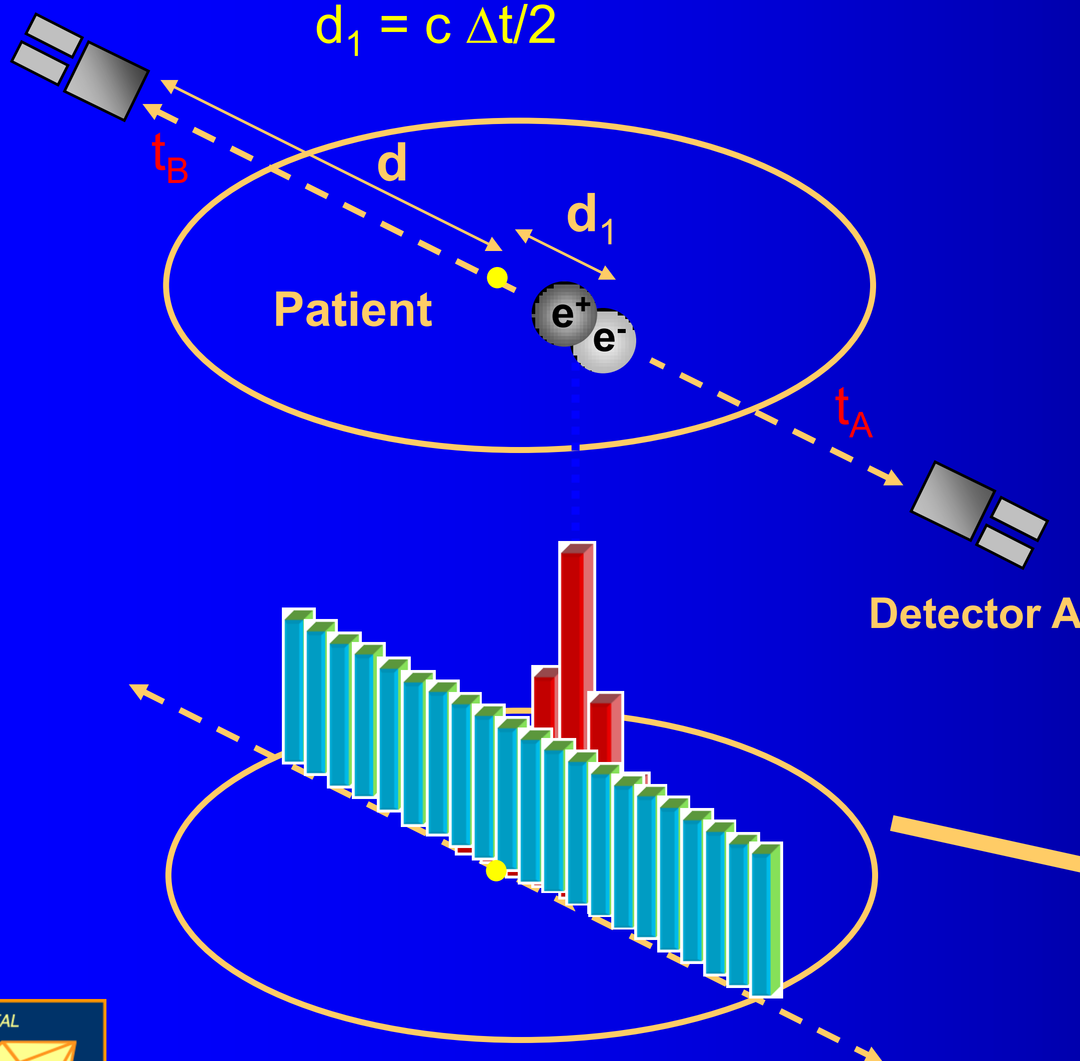
- 4 rings (ø=40 cm, H= 4x18.6 mm) with 52 detector modules each
- Dual layer of trapezoidal LSO blocks and two APDs per block
- Dedicated ASIC summing preamplifier (64 inputs, 16 summed outputs, 1 total energy sum, < 1000 e^- rms noise per sum channel)
- Complete MRI compatibility is not the main goal but it gives us some first experience in designing MR compatible PET technology for future version.

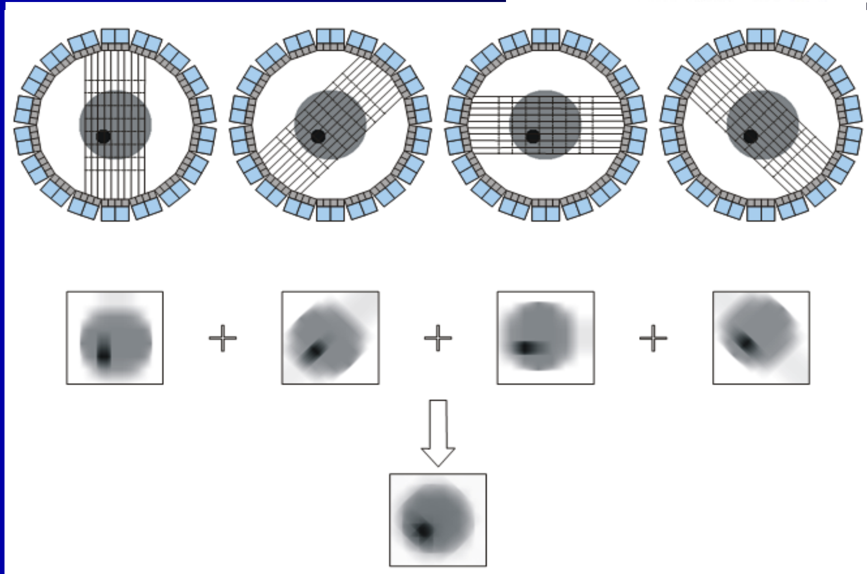
Current CCC project (Jülich, Ciemat, VUB)

Time of Flight PET

$\Delta t = t_A - t_B = [(d+d_1) - (d-d_1)]/c$

$d_1 = c\,\Delta t/2$



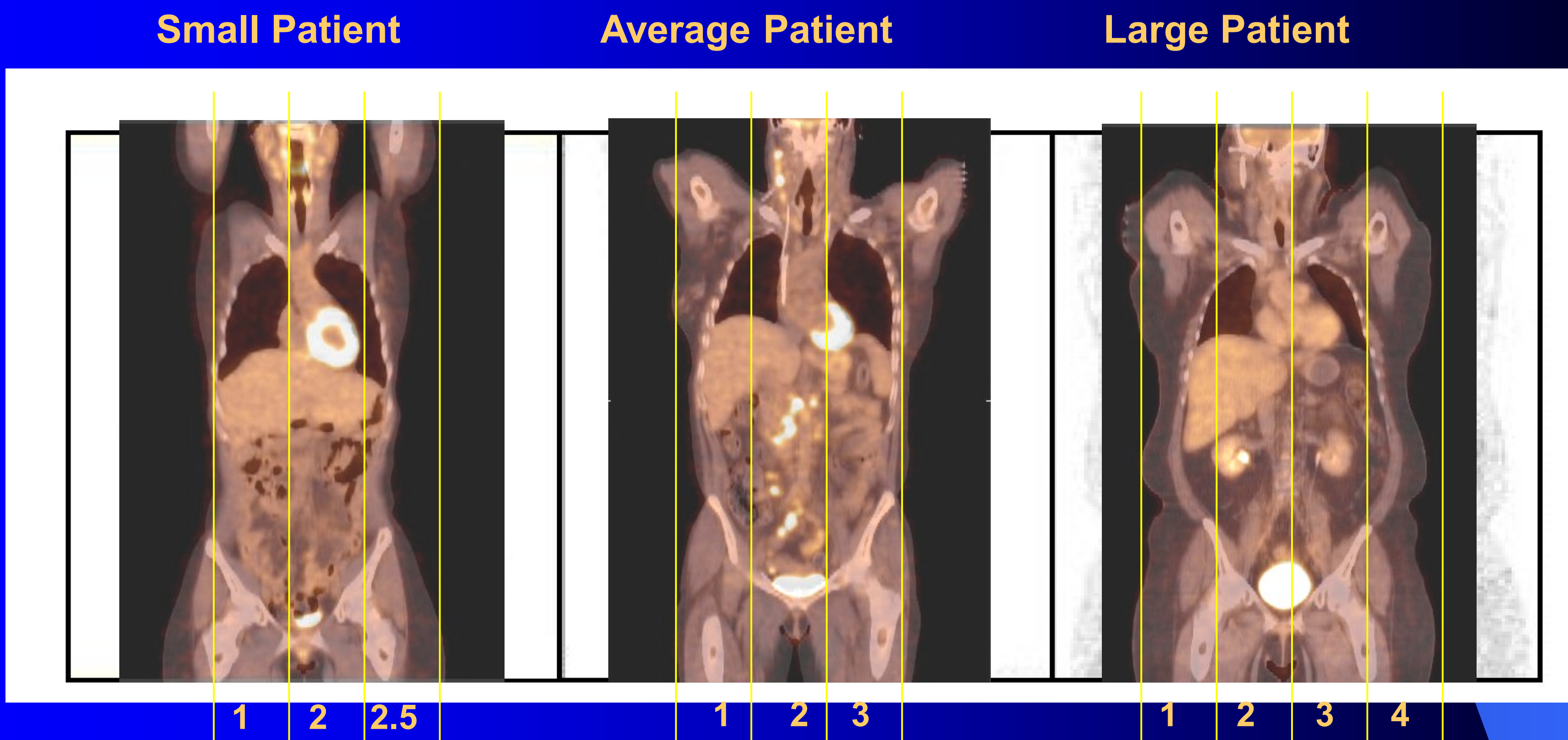


$SNR_{TOF} = \sqrt{(D/\Delta d)} \cdot SNR_{conv}$

δt (ps)	δx (cm)	SNR*
100	1.5	5.2
300	4.5	3.0
500	7.5	2.3
1200	18.0	1.5

** SNR gain for 40 cm phantom*

Technology – Benefit in Patients
PET without TOF



Slim 58 kg
Sensitivity Gain = 2.5

"Normal" 89 kg
Sensitivity Gain > 3.0

Heavy 127 kg
Sensitivity Gain = 4.0

With TOF (650ps): Philips Truefight

Towards Molecular Imaging

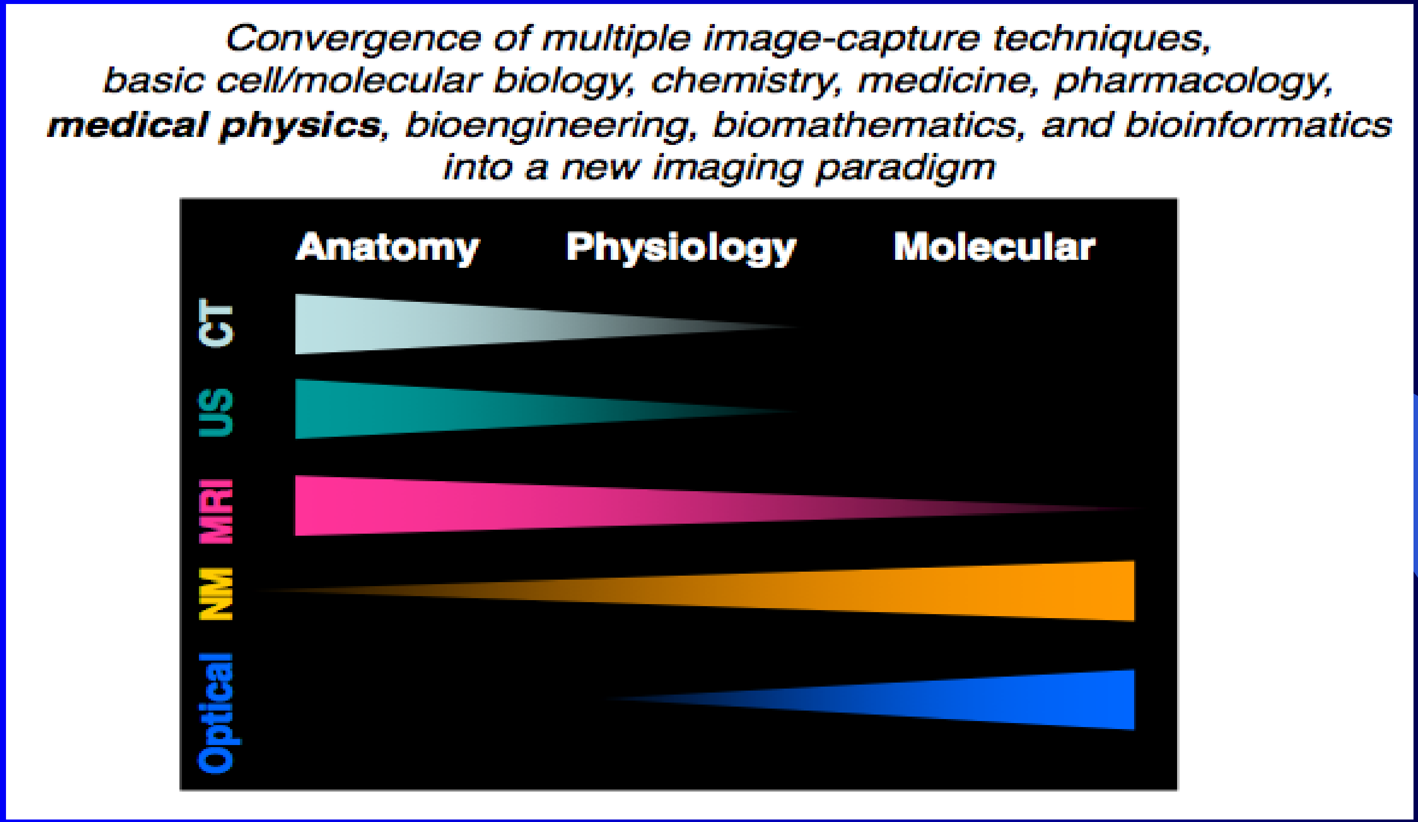
ANATOMICAL IMAGING → **FUNCTIONAL IMAGING** → **MOLECULAR IMAGING**

Visual representation, characterization and quantification of biological processes at the cellular and sub cellular level within living organisms.

- Gene expression (genomics, proteomics, transcriptomics, enzymatic activity, etc…)
- Molecular signal transduction through cell membranes
- Target specific cell receptors that are over-expressed in pathological situations (ex. neo-angiogenesis)
- Multiple imaging capture techniques (Nuclear medicine/PET, MRI, MRS, Optical,…)

MACROSCOPIC → MICROSCOPIC

Molecular Imaging → Interdisciplinariry



Requires specific effort on imaging instrumentation
Sensitivity, Spatial and Temporal resolution

Requires targeting the cellular activity with specific contrast agents


Thank you

CERIMED: a complete and versatile infrastructure

www.cern.ch/cerimed/

Opening in summer 2012