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Next Lecture after Christian Cachard:

• PART 2

The Second part will be devoted to hybrid devices, what complementarities are obvious. What they actually bring as decisive progresses at hospital, what are the main trends in evolution ….
Lecture 2.

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• 6 Image fusion / Hybrids

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Imaging modalities today

Hardware combination ➡ Evolution / Revolution

Imaging Modality	Spatial Resolution (mm)	Acquisition time per frame(s)	Molecular probe mass required (ng)	Molecular sensitivity (mol/L)	Tissue penetration depth (mm)	Signal quantification capabilities
PET	1-2 (animal) **6-10 (clinical)**	1-300	1-100	10^{-11}-10^{-12}	>300	High
SPECT	0.5-2 (animal) **7-15 (clinical)**	60-2000	1-100	10^{-10}-10^{-11}	>300	Medium-High
Optical	2-5 (visible to IR)	10-2000	10^{3}-10^{6}	10^{-9}-10^{-11}	1-20	Low
MRI	0.025-0.1 (animal) **0.2 (clinical)**	0.1-100	10^{3}-10^{6}	10^{-3}-10^{-5}	>300	High
US	0.05-0.5 (animal) 0.1-1 (clinical)	0.1-100	10^{3}-10^{6}	Not well characterized	1-300	Low
CT	0.03-0.4 (animal) **0.5-1 (clinical)**	1-300	NA	Not well characterized	>300	Medium-High

From Craig S Levin. Eur J Nucl Med & Mol Imag. 2005, 32(14), S-325-45

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EVOLUTION in MEDICAL IMAGING (combination of existing equipment)

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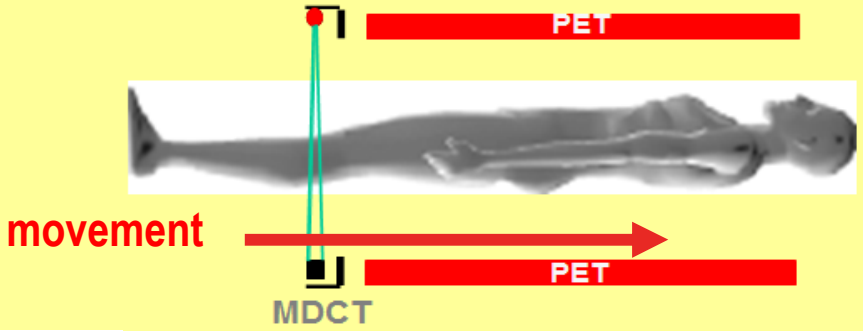
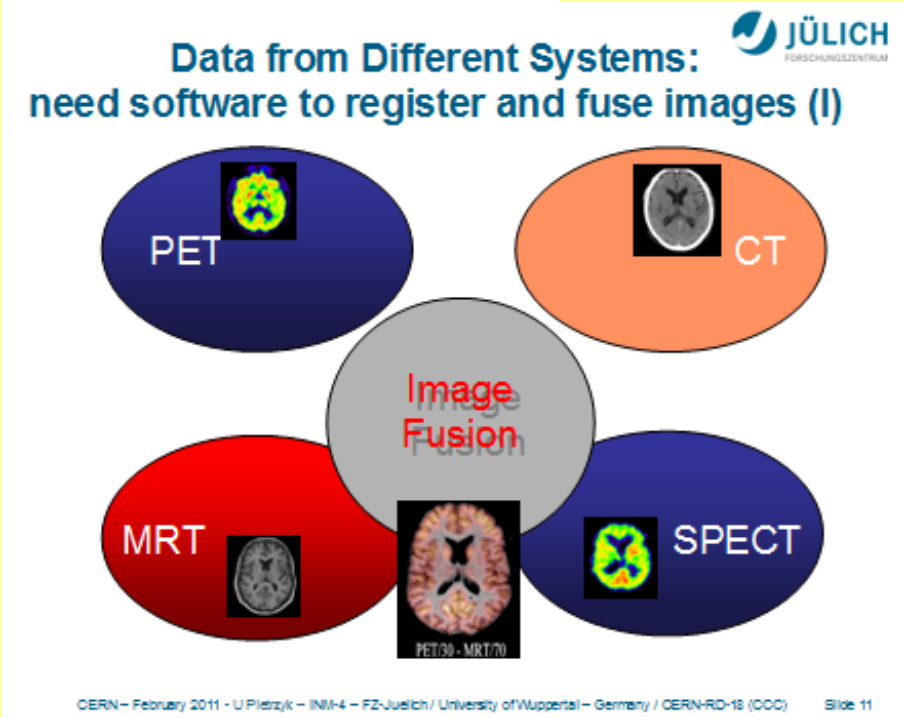
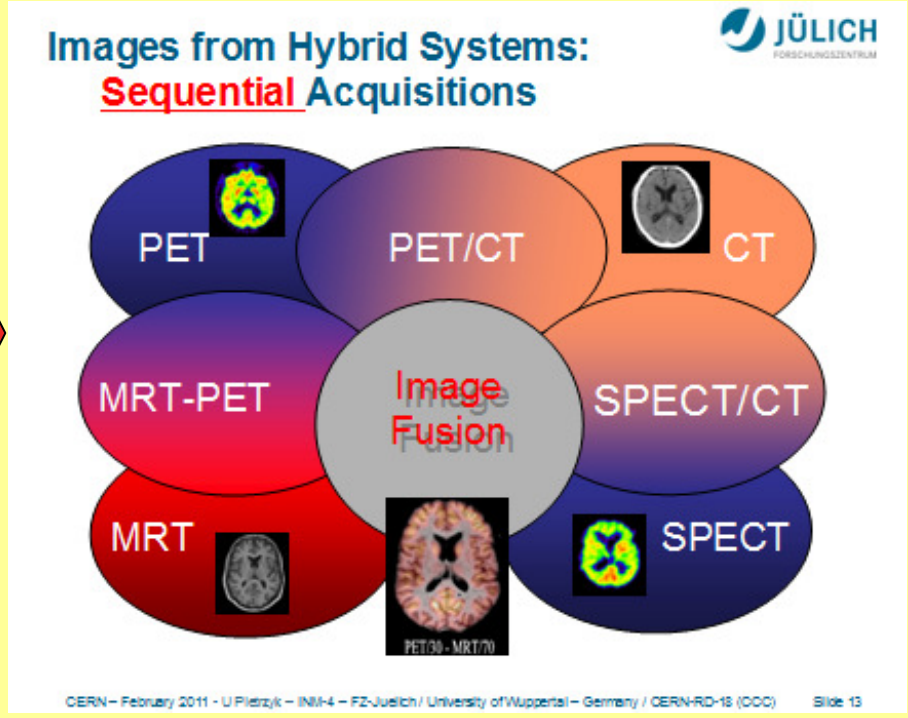
Example: **CT** **PET**







Data taken at different time / in different configuration / in different places…

Fusion only by software

Data taken at sequential time / with minimal movement of patient

Fusion by software

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Fusion imaging: from software to hardware

(from D. Townsend 2014)

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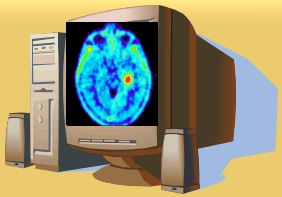
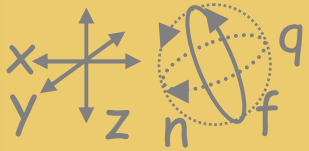
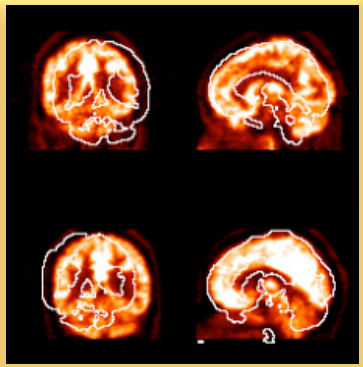
1990







Software-based fusion (semi-automated)

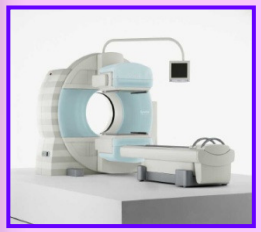
1993 - 1998

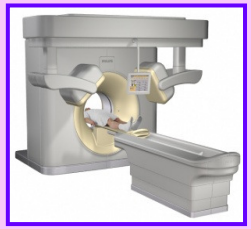
Hardware-adjunction: Prototype designs

2001

Hardware-adjunction: Commercial PET/CT

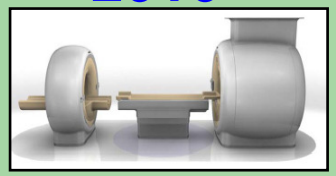
2004

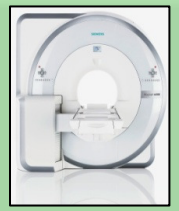


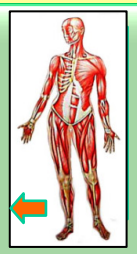


Hardware-adjunction: Commercial SPECT/CT

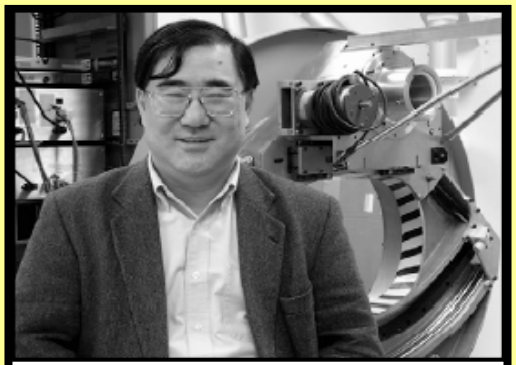
2010







Hardware-based fusion: Commercial PET/MR



Bruce H Hasegawa, PhD, 1951-2008
Participant ESI, Archamps In 1997

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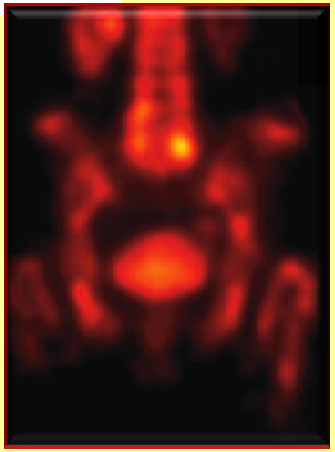
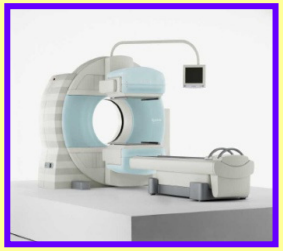
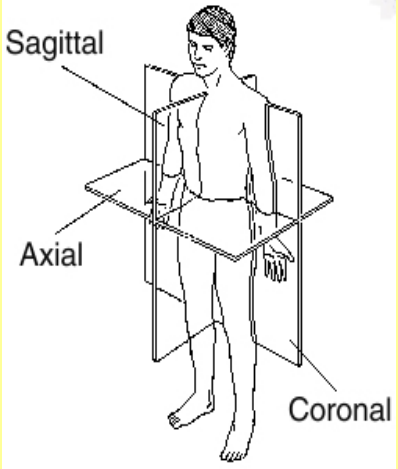
SPECT/CT in the clinic

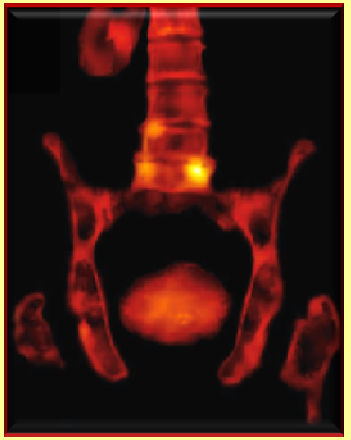
(From D. Townsend 2014)



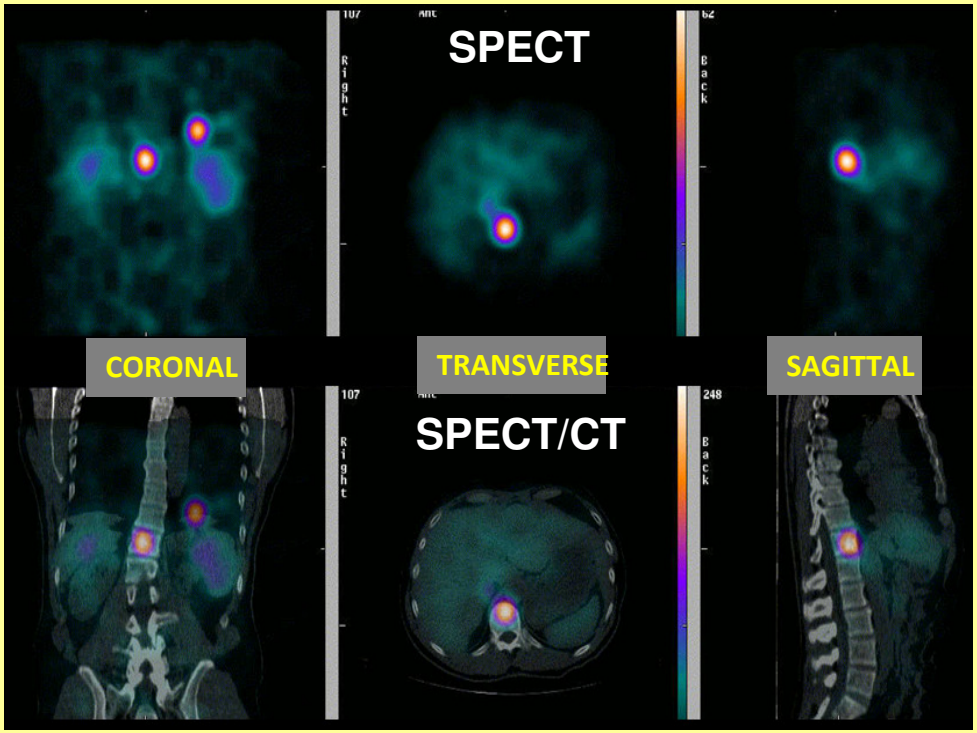
Conventional SPECT







SIEMENS xSPECT



Symbia TX

Discovery NM/CT 670

"CT is potentially more valuable for SPECT than for PET"

Bailey DL. Eur J Nuc Med & Mol Imag 2003; 30(7):1045-1046

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REVOLUTION in MEDICAL IMAGING

(Integrated devices from technical developments)

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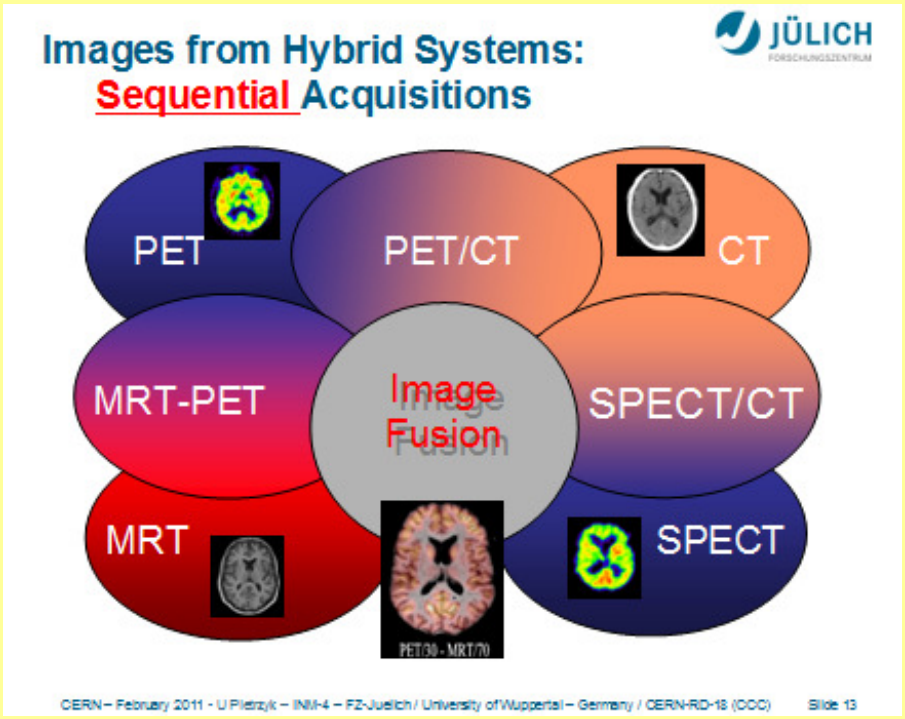
Integrated better than separated !

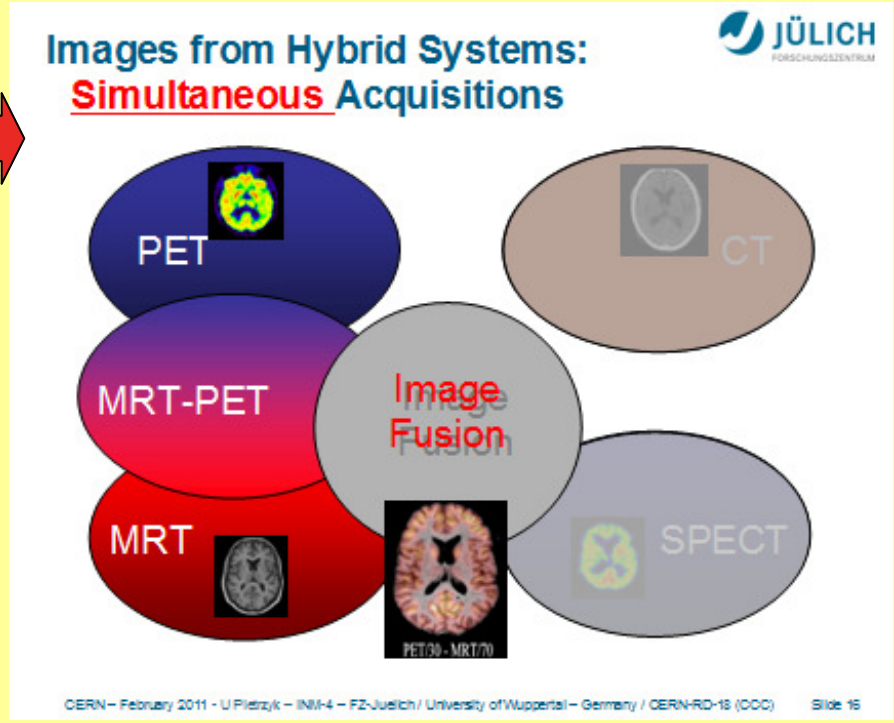
Example: **MRT**

PET

No movement !

(same hardware)





REVOLUTION is simultaneous Acquisitions without patient deplacement !!

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Integrated device versus Sequential one PET-MR

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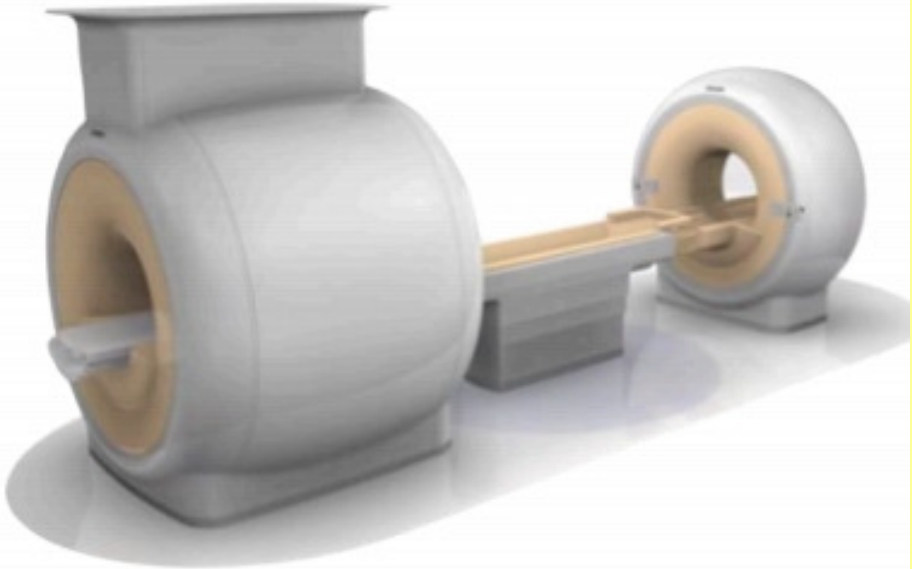

Integrated

- Short acquisition time ←
- More accurate fusion ←
- Dynamic data simultaneosly
- MR-based motion correction.
- Technically complex
- Higher cost ←

Sequential

- Technically easy ←
- Less expensive ←
- No simultaneous imaging ←
- Longer acquisition time ←
- Less accurate fusion
- Needs more space

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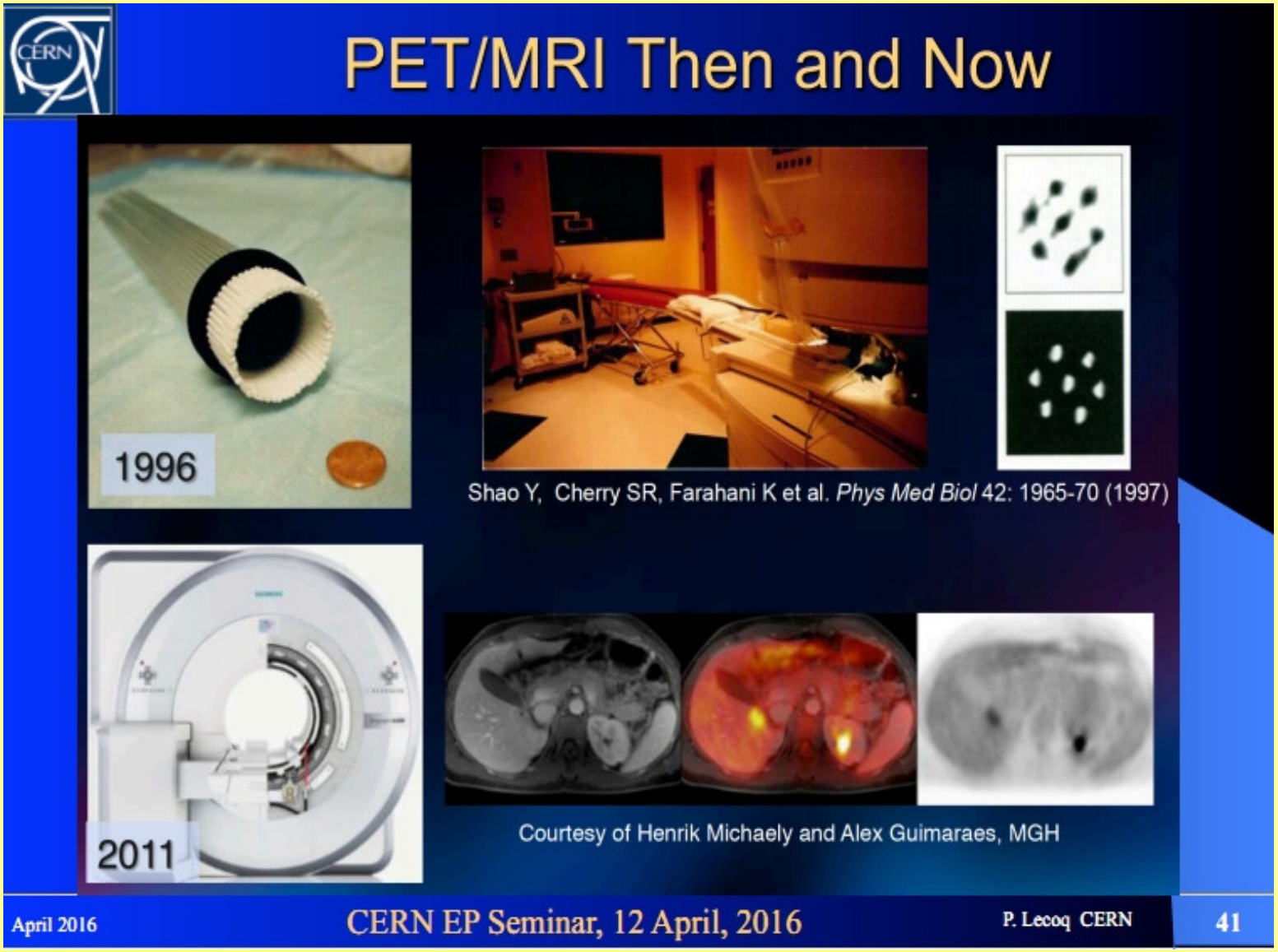
History

1996
Laboratory development

2011
Tests in Hospital (MGH Boston)



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Two Complementary devices

Why PET/MRI

MRI

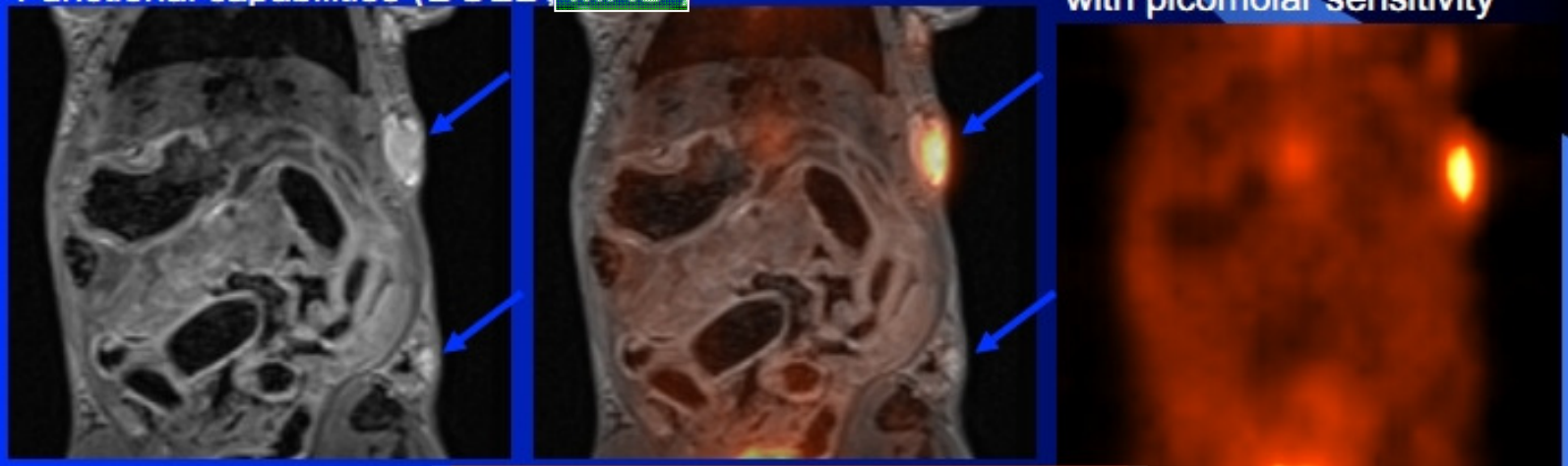
- high resolution
- high soft tissue contrast (≠ CT)
- No radiation exposure (≠ CT)
- Functional capabilities (BOLD, MRS)

+

PET

- high sensitivity
- target specific tracer
- molecular imaging

with picomolar sensitivity



1 + 1 = >3?

April 2016 CERN EP Seminar 12 April, 2016 P. Lecoq CERN 40

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Challenges for PET/MR

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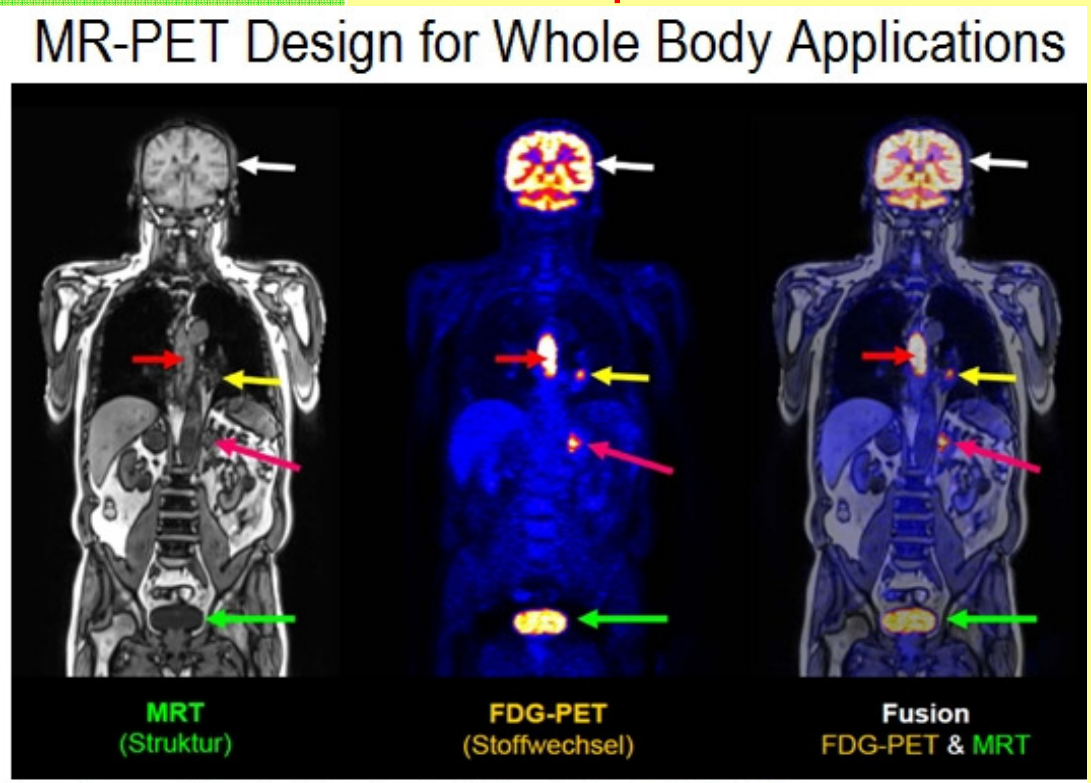
- MR-compatible PET detectors from technics (APD,Si-PM..) **OK**
- PET attenuation correction factors from MR images ??
- role for simultaneous MR and PET acquisition? **OK**
- financial cost (eventually) of the PET/MR system ??
- Used routinely for Small Animal PET then for patient **OK**

But already exceptionnal images …



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Why Imaging (SPECT, PET..)

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is useful in Oncology in:

- Help in **Diagnosis**
- Help in **Treatment plannings**
- Help **Post-treatment survey**

SPECT-CT & PET-CT are better than SPECT & PET alone….

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disease progression SURVEY (ex: Breast cancer)

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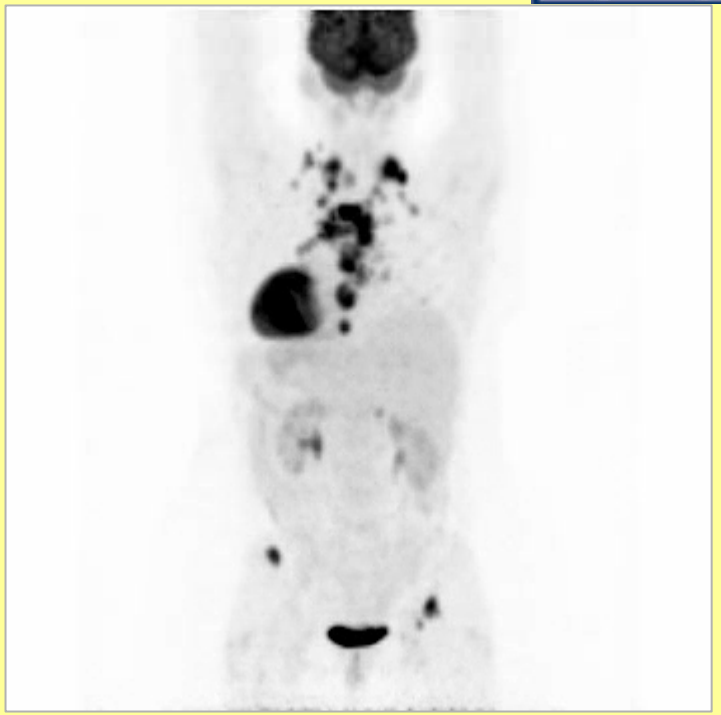
*

Two imagings at a 9 months interval :



28 min (8/05)

10.6 mCi, 115 min pi
4 min/bed, 7 beds
3i / 8s; 6f

15 min 9 months later (5/06)

10.5 mCi, 104 min pi
3 min/bed, 5 beds
3i / 8s; 6f

Scan duration: 15 min

Biograph

48 year-old female (200 lbs) with history of breast cancer. First PET showed intense uptake in bilateral supraclavicular, mediastinal and right parasternal nodes and the thyroid. 9 months later PET showed significant disease progression including sternum and pelvic region

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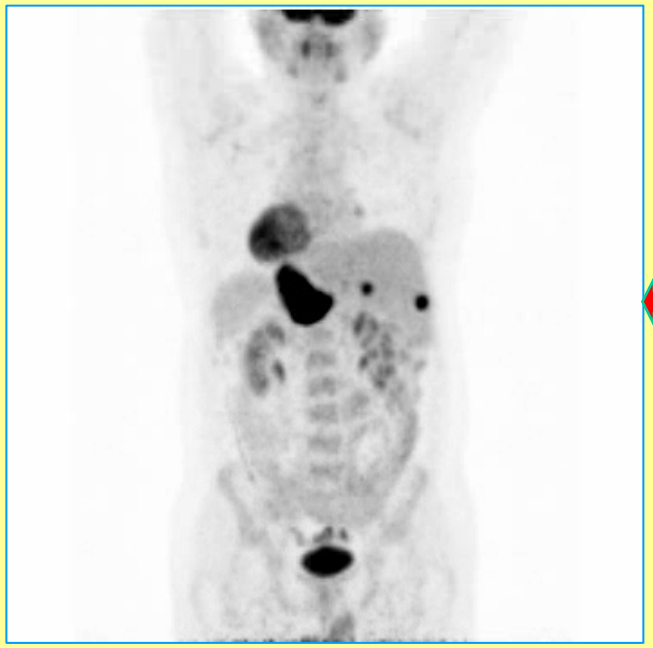
½ year Post / Pre treatment Survey

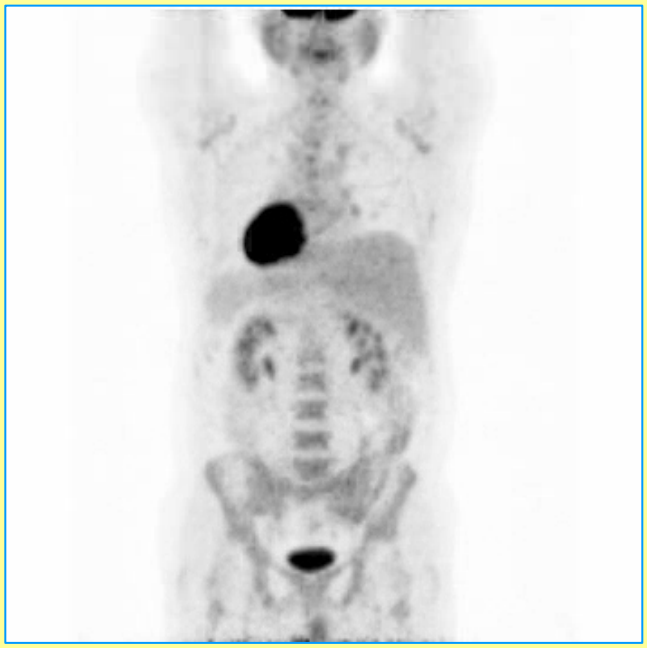
Restaging gastric cancer



Pre-therapy (4/06)

With Biograph

6 months later



Post-therapy (10/06)

Scan duration: 15 min
5 beds; 3 min/bed; 8s/3i/6F
10.6 mCi; 90 min post-injection

Scan duration: 15 min
5 beds; 3 min/bed; 8s/3i/6F
9.8 mCi; 90 min post-injection

Pre-therapy

Post-therapy

A 52 year-old male patient with history of gastric cancer imaged pre- and post-therapy (after ½ year)

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TREATMENT PLANNINGS

(Will be explained later by Alex Rijnders for Brachytherapy)

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Treatment plannings are compulsory for correct treatment

The Software start from Images

CT-SCAN ⟷ MRI or / and PET

- external contours
- densities
- anatomical structures
- beam data library

- anatomical structures

BEAM DEFINITION

Most Popular systems:

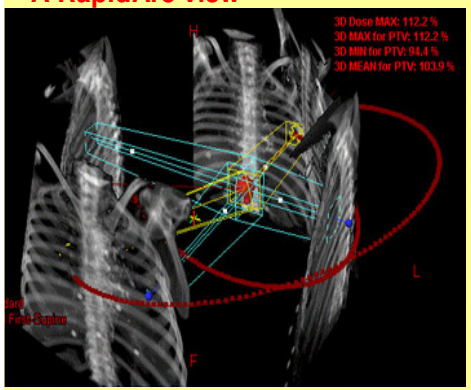
Pinnacle (Philips Medical systems)
ADAC -> Pinnacle3(Philips)
Monaco (CMS/Elekta)
Eclipse (Varian Medical Systems)
RapidArc: see(varian.com/us/oncology/treatments/treatment_techniques/rapidarc/resources.html
.....

TREATMENT PLANNING SYSTEM

OPTIMISATION

- Dose distribution
- Dose-Volume Histograms
- Biological indices

A RapidArc view



- Reconstructed radiographs (DRR)

SIMULATOR and/or ELECTRONIC PORTAL IMAGING

- Field shape or
- Position of leaves

BLOCK CUTTING DEVICE or MLC

- Treatment parameters
- Treatment time (monitor units)

ACCELERATOR

VERIFIY AND RECORD SYSTEM

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7. QUANTIFICATION

(SPECT & PET)

Elbasan Workshop July 2016 Yves LEMOIGNE / IFMP – Ambilly – France & CERN-Geneva-Switzerland

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Definition of SUV (Standardized Uptake Value):

Coeficient used in Oncology for semiquantitative analysis

The percent injected dose per gram of tissue:

$$SUV = CT.Ws / d_T.Dinj$$

Where: C_T (in mCi/cc) is obtained from counts/pixel/time from PET ROI.

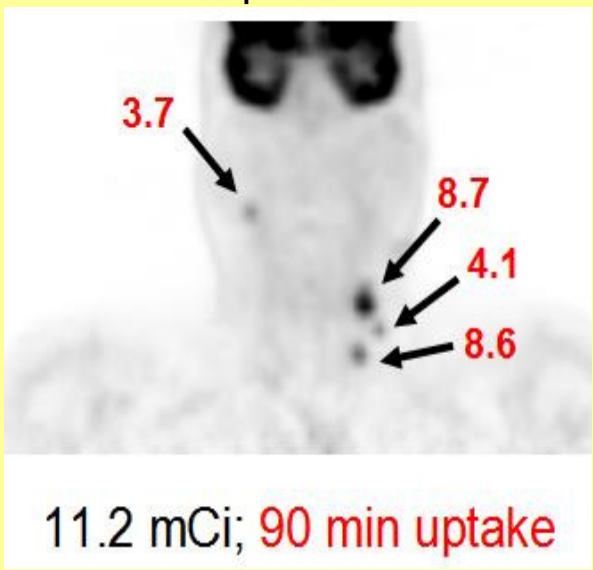
$d_T=W_T/V_T$ (weigth to volume of studied tissue) is the density in the region (often 1 g/cc)

D_{inj} being the injected dose

Ws is the total weight of the patient)

SUV=unitless parameter (from 1 to about 10)

Example of SUV



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8. EXAMPLES OF USES @ HOSPITAL

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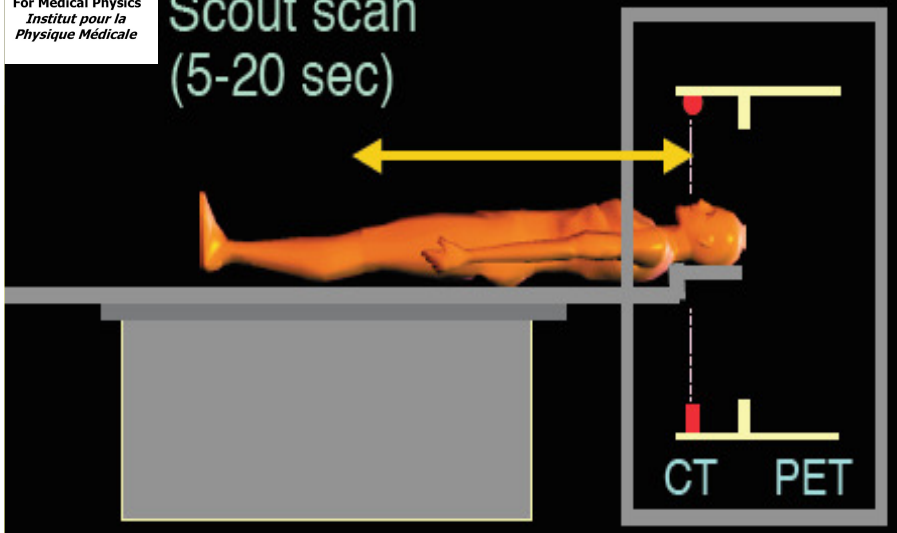
PET/CT (SPECT/CT) Scan protocol

Scout scan
(5-20 sec)

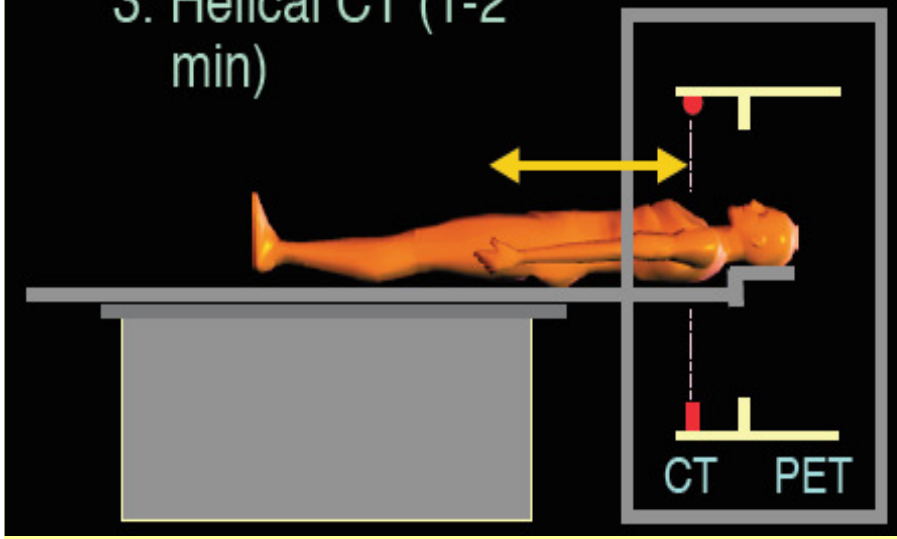


2. Selection of scan region (1-2 min)

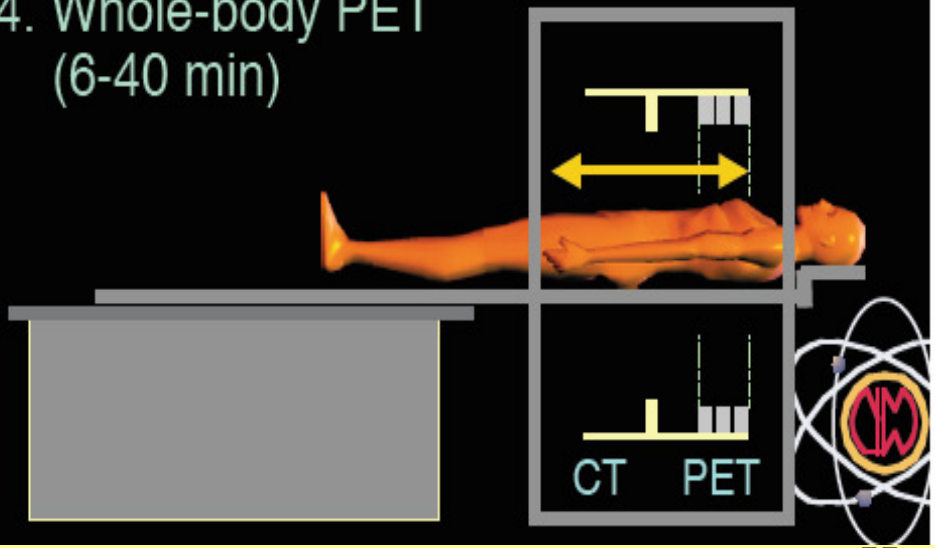
Scout scan image

4000 PET/CT scanners operational worldwide

3. Helical CT (1-2 min)



4. Whole-body PET (6-40 min)

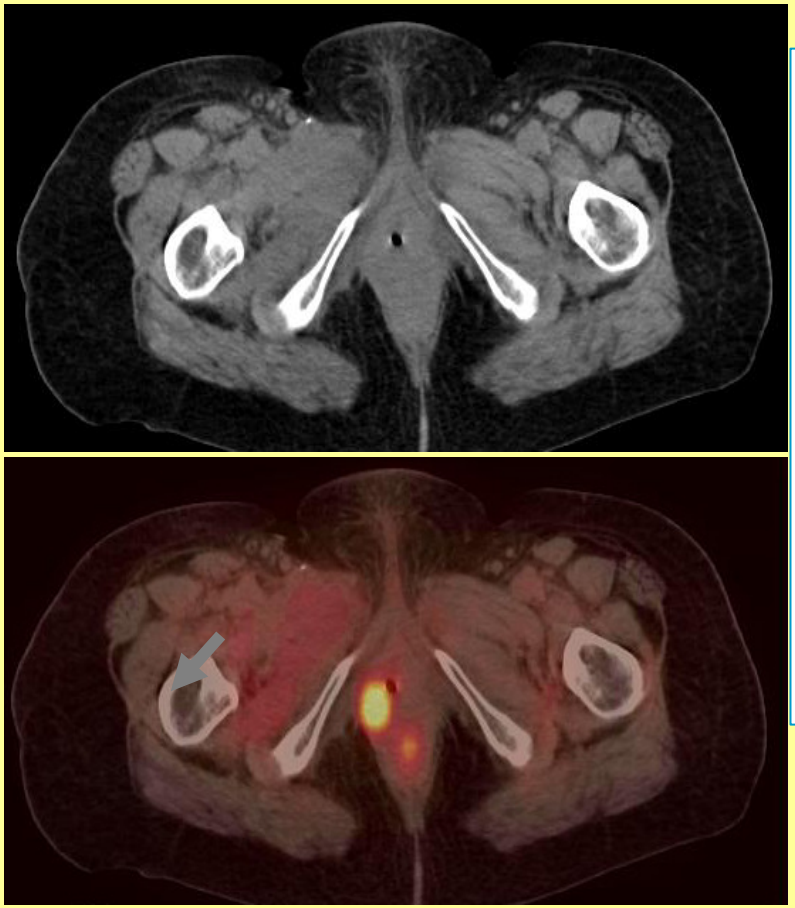


SURVEY : Vaginal cancer

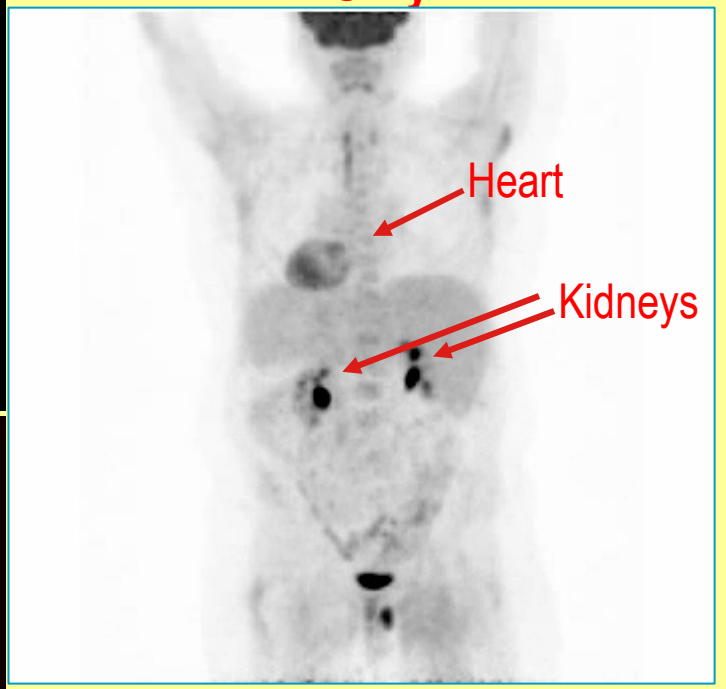
PET-CT is more powerful than PET alone….

CT only

PET+CT



* PET only



Biograph Scan duration: 15 min

5 beds; 3 min/bed; 8s/3i/6F

10.6 mCi; 90 min post-injection

A 50 year-old female patient restaged for vulvar cancer with history of NHL (Non-Hodgkin lymphoma),. The PET/CT scan shows focal uptake in right aspect of the vulva (SUV: 10.3). Adjacent focal anorectal uptake (SUV: 5.5). CT is negative with no abnormality seen. Only combination of CT and PET can show that!

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9. SPECIFIC DEVELOPEMENTS

(With come back to Ultrasound)

Time-of-Flight (TOF)

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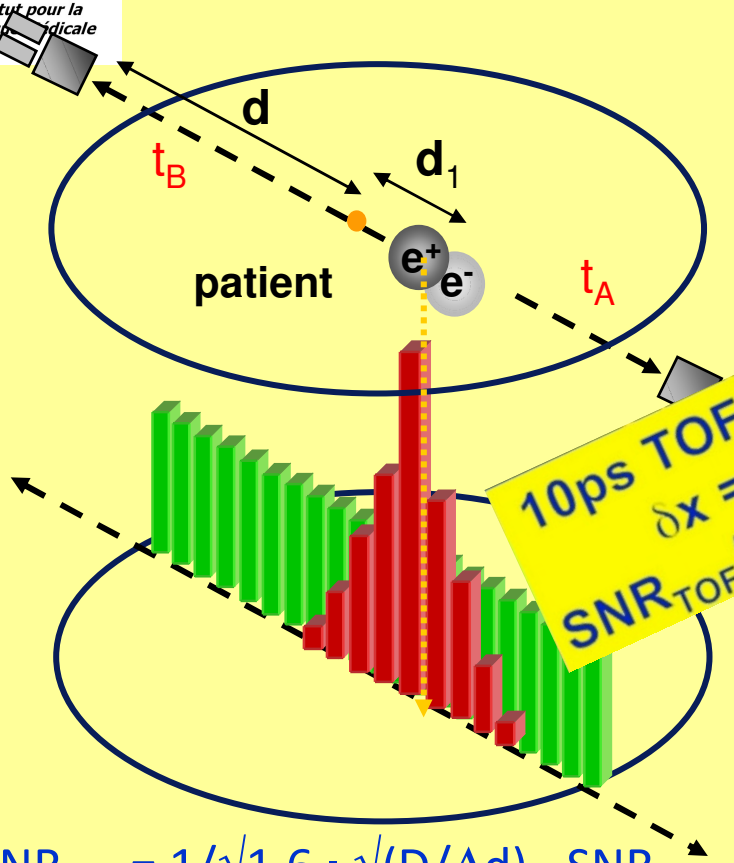
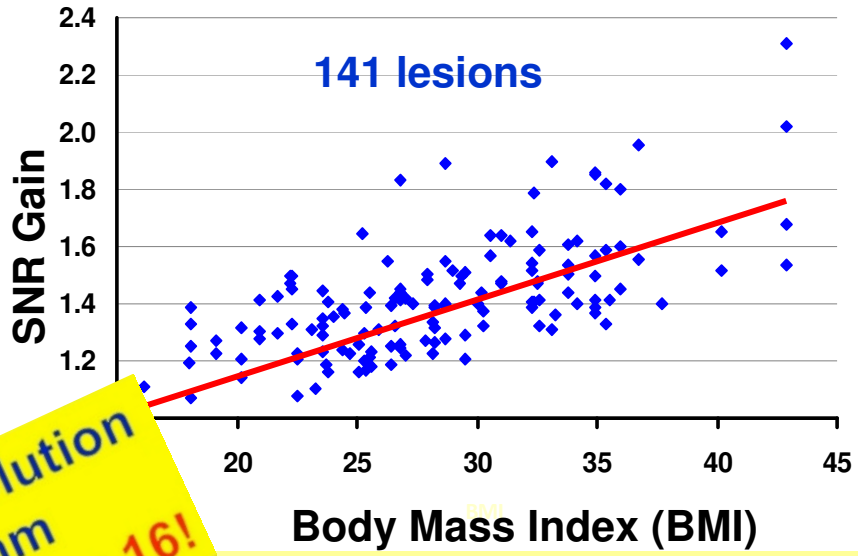
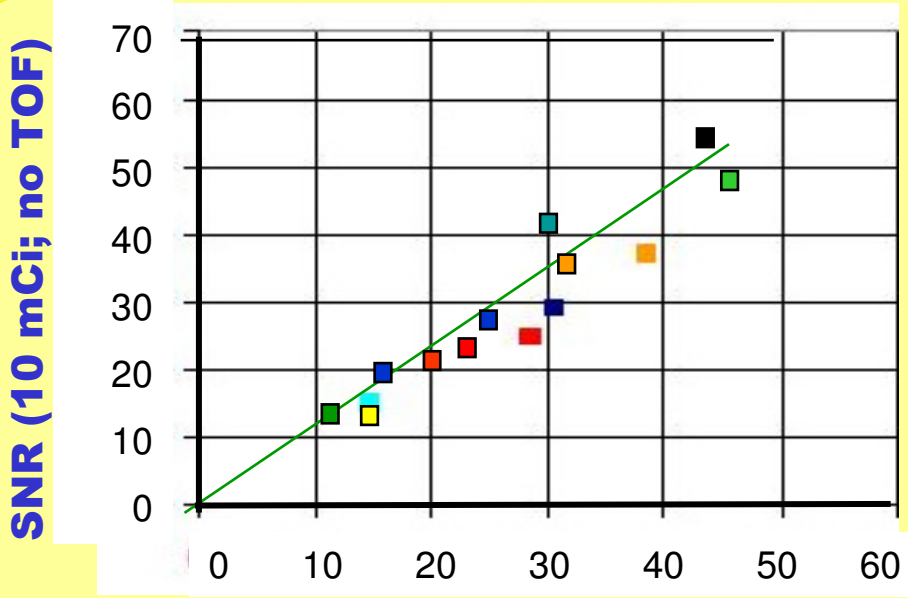


10ps TOF resolution
δx = 1.5mm
SNR_{TOF}/SNR_{CONV} = 16!



✓ Improved signal-to-noise



✓ Reduced radiation dose

$SNR_{TOF} = 1/\sqrt{1.6} \cdot \sqrt{(D/\Delta d)} \cdot SNR_{conv}$

Ds (ps)	Dx (cm)	SNR gain
100	1.5	5.2
300	4.5	3.0
500	7.5	2.3
1200	18.0	1.5

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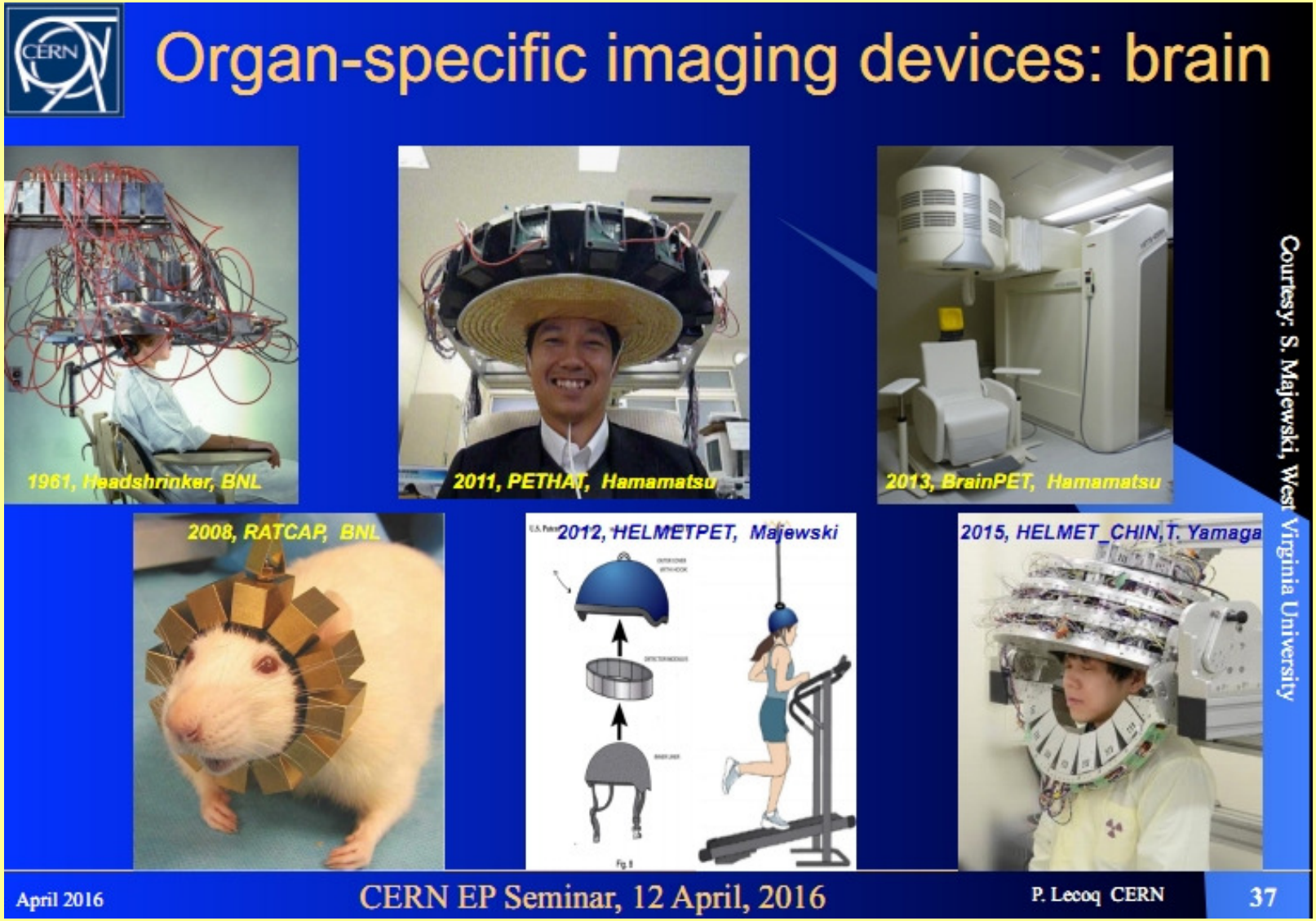
Already many specific devices



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Clear PEM is PET for Mammography

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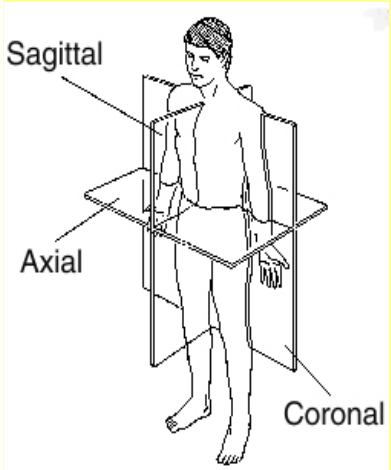

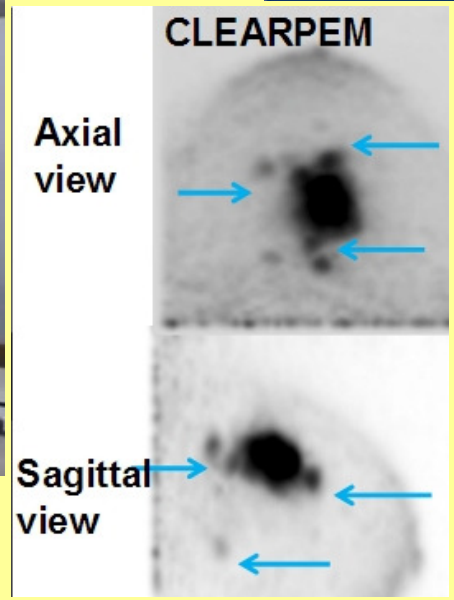

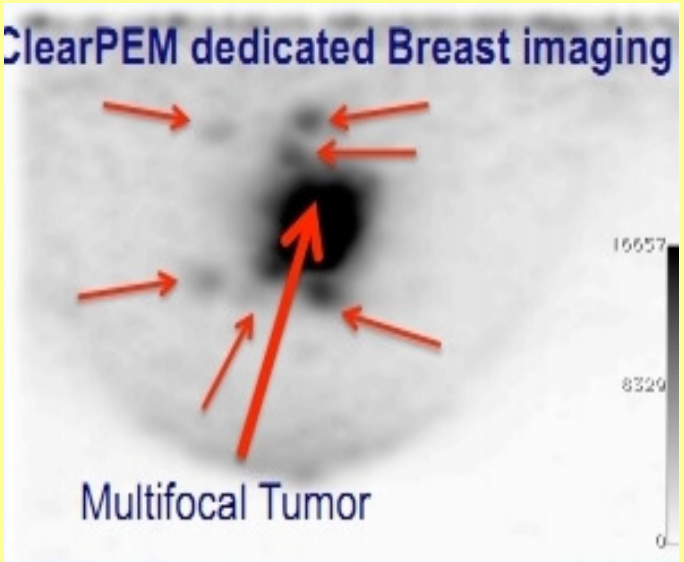

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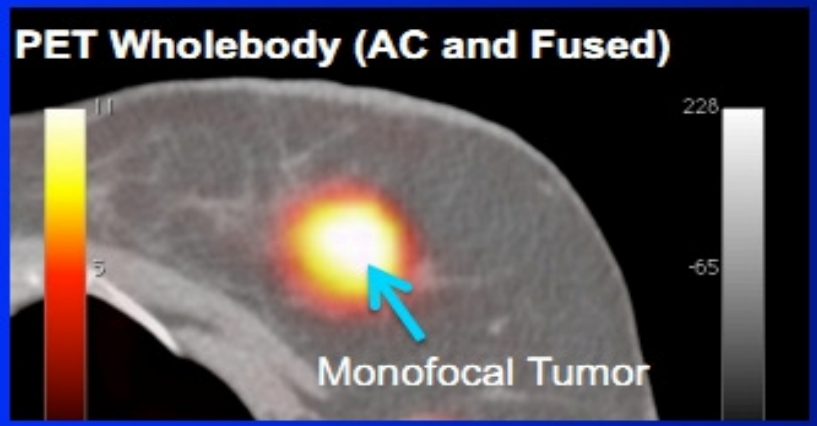
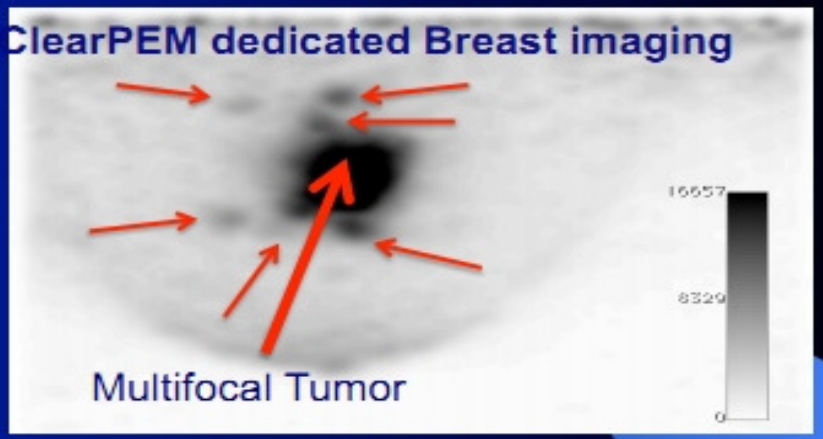
Why ClearPEM Specific device is needed

(PEM = Positron Emission Mammography)

ClearPEM breast cancer images

Same lesion seen by two medical imaging systems





➔Organ specific imaging devices can demonstrate superior performance as compared to commercialy available wholebody clinical scanners.

Not a priority investment area for large imaging companies they are a good target for our medical imaging community and open up commercial niches.

Studies show that **breast Multifocal tumors** have a **different biology**, with an increased potential to **metastize** to the axillary **lymph nodes**

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Hybrid Device PEM – US (with Elastography)

(now in clinical tests in Marseille-Nord Hospital)

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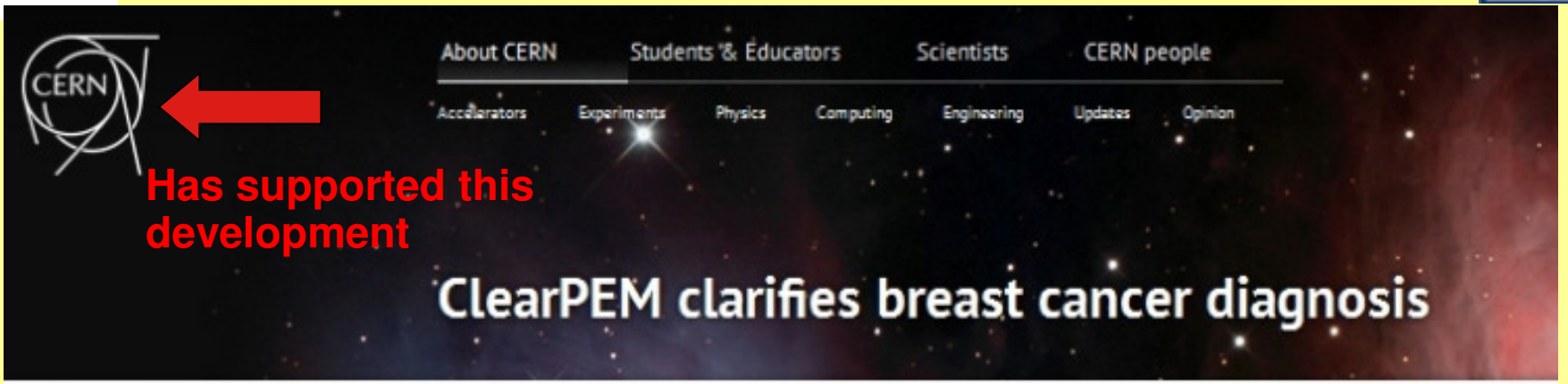

ClearPEM Sonic

A PET - US Hybrid Device for Mammography

A multimodal scanner to improve the diagnosis of breast diseases.


ClearPEM-Sonic installed at Hôpital Nord, in Marseilles. (Image: Benjamin Frisch/CERN)

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What is ClearPEM-Sonic

a multimodal scanner to improve the diagnosis of breast diseases.

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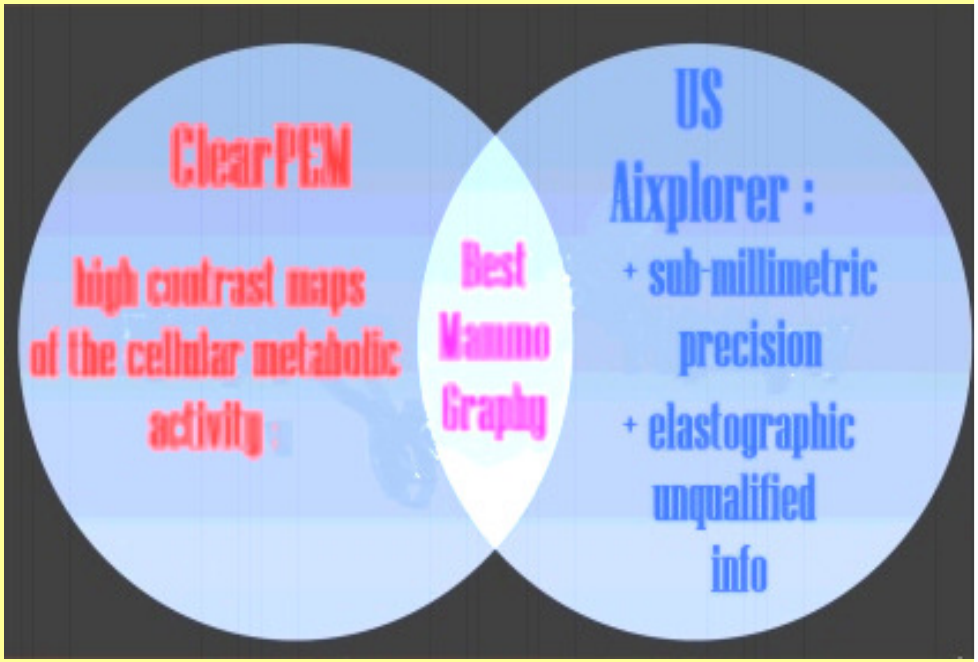
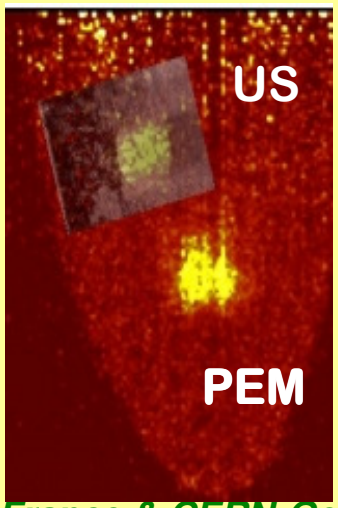
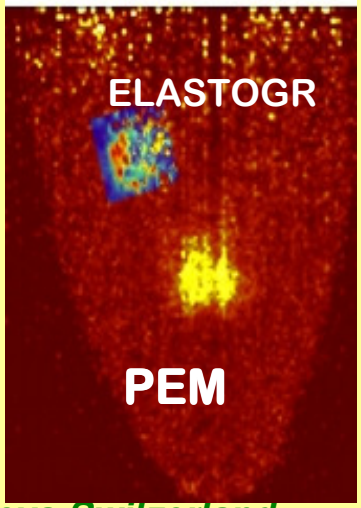
- Combines 3 info: METABOLIC, MORPHOLOGIC and STRUCTURAL in multimodal PEM + US imaging technology
- The ultrasound scanner provides a map of tissues density variation in the region of interest
- New generation ultrasound scanner (Aixplorer) capable of quantitatively mapping the elastic properties of tissues (ELASTOGRAPHY)



- It complements the functional information provided by the ClearPEM with morphologic and structural information about lesions provided by US
- Metabolic information can be rapidly compared with morphological ones, all fused in single 3D-images easily accessible by hospital staff.





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ENDO TOF PET US
Going further in specificity, sensitivity device
(only in development at CERN)

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Imaging tool for pancreas and prostate cancer biomarker development

4 Tools

- Endo = endoscope
  - 1 for pancreas
  - 1 for prostate

Spatial resolution Biopsy

- TOF = Time-of-Flight

Other organs background rejection

- PET
  - Endoscopic head close to organ
  - External plate for coin[illegible]

Anatomic + Molecular imaging

- US = Ultrasound

April 2016 CERN EP Seminar, 12 April, 2016 Courtesy P. Lecoq CERN 23

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In some Kind of Conclusion:
The Future Healthcare Mission

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* **Personalized Medicine** is an emerging approach for disease treatment and prevention that takes into account **individual variability in genes, environment, and lifestyle** for each person

* To get there, we need to incoporate **many different types of data**, from:

1. Data about the patient collected by health care providers and patients themselves
2. Metabolomics (the chimicals in the body at a certain point in time)
3. Microbiome (the collection of microorganism in or on the body)

→ IMAGING

THE RIGHT TREATMENT → TO THE RIGHT PERSON → AT THE RIGHT TIME

This requires targetting the cellular activity with the **highest possible sensitivity and specificity**

This requires **efforts on imaging instrumentation** : **Sensitivity, Spatial & Temporal resolution**

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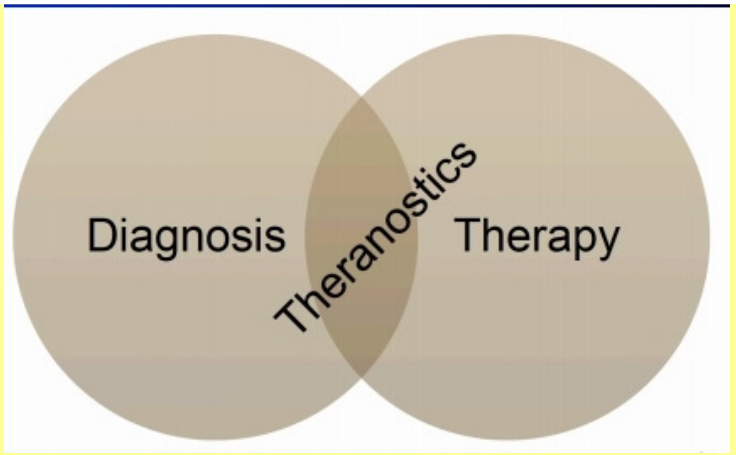
Theranostics



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Facing the chalenge of personalized medicine…

What is Theranostic?

- i.e. molecular diagnostic agent + targeted therapeutic.
- The basic architecture is:

- a **targeting agent** which directs the theranostic to a molecular target on the surface of a cell or tumor
- a chelate in the form of an **imaging agent** (which enables visualization of the target) or a **therapeutic drug** (for delivery of treatment to the target site)
- a **linker** to connect the two entities *(from Ronald Van Heertum, BioClinica)*

Exemple : Lutathera *, [177Lutetium-DOTA0 –Tyr3]-Octreotate, for* ***patients with Endocrine Gastroenteropancreatic tumors*** **, is a radiolabeled somatostatin analog that selectively targets somatostatin receptors over-expressed in these tumors.** (Lutathera is produced by our neighbour AAA ltd near CERN)

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10. CONCLUSION

During last decade: **Impressive progress** in Medical Imaging

Due to **enormous** work on the technical front:

- New detectors
- Software
- Training
- Radiation Protection

About 4000 PET/CT scanners operational worldwide (start in 2000')

PET/MR scanners are beginning now

All that is for the main benefit of patients….

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Thanks a lot for the gentle attention!