Reial
Acadèmia
de Medicina
de la
Comunitat
Valenciana

Desarrollos Tecnológicos en Imagen

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Professor CSIC

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  - 1 de julio de 2011.

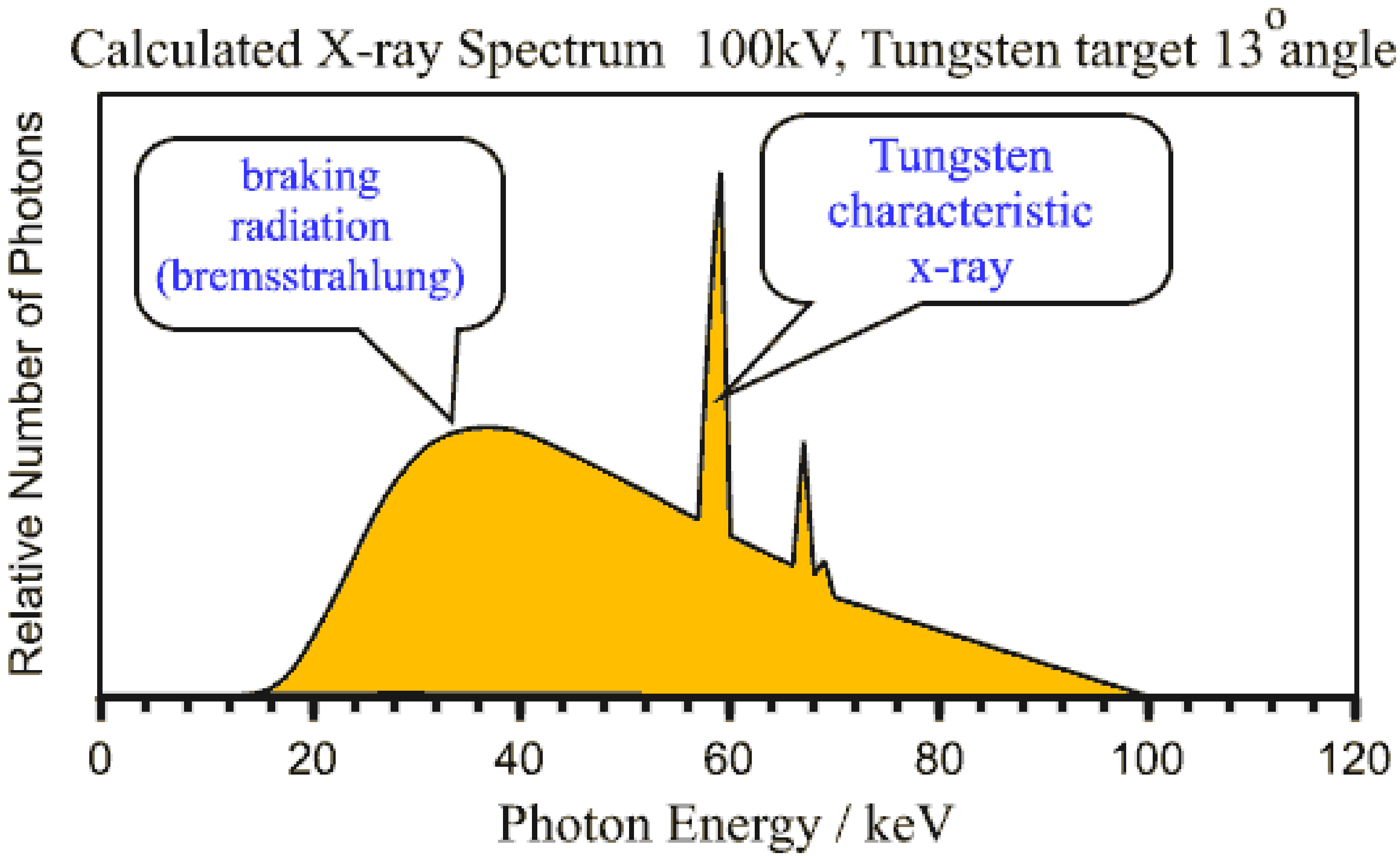
Desarrollos Tecnológicos en Imagen

- TAC
- RM
- PET
- PET/RM.
- Imagen Intraquirúrgica.

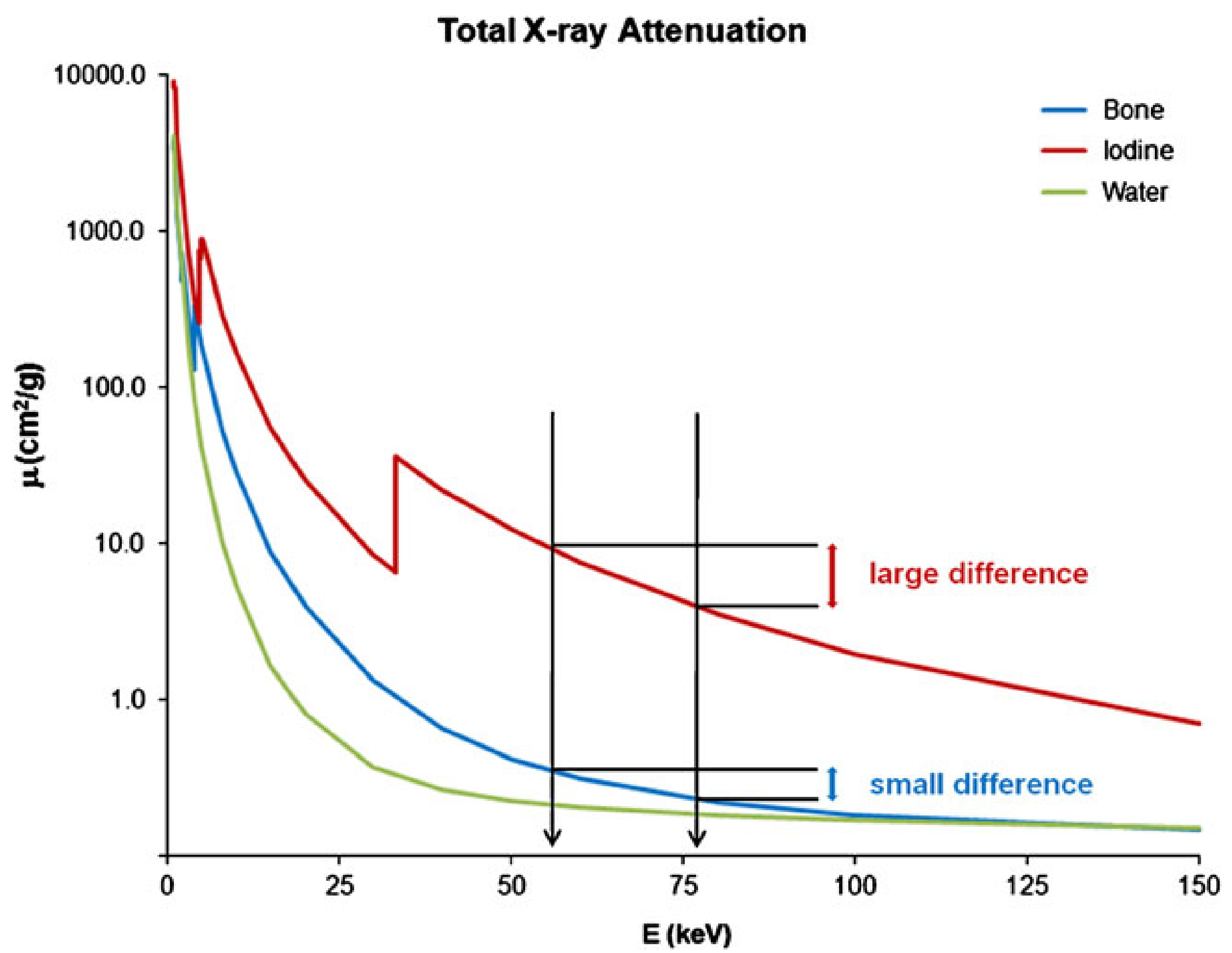
Desarrollos Tecnológicos en Imagen

- TAC:
  - Spectral CT.
  - Photon Counting.
  - Phase Contrast.

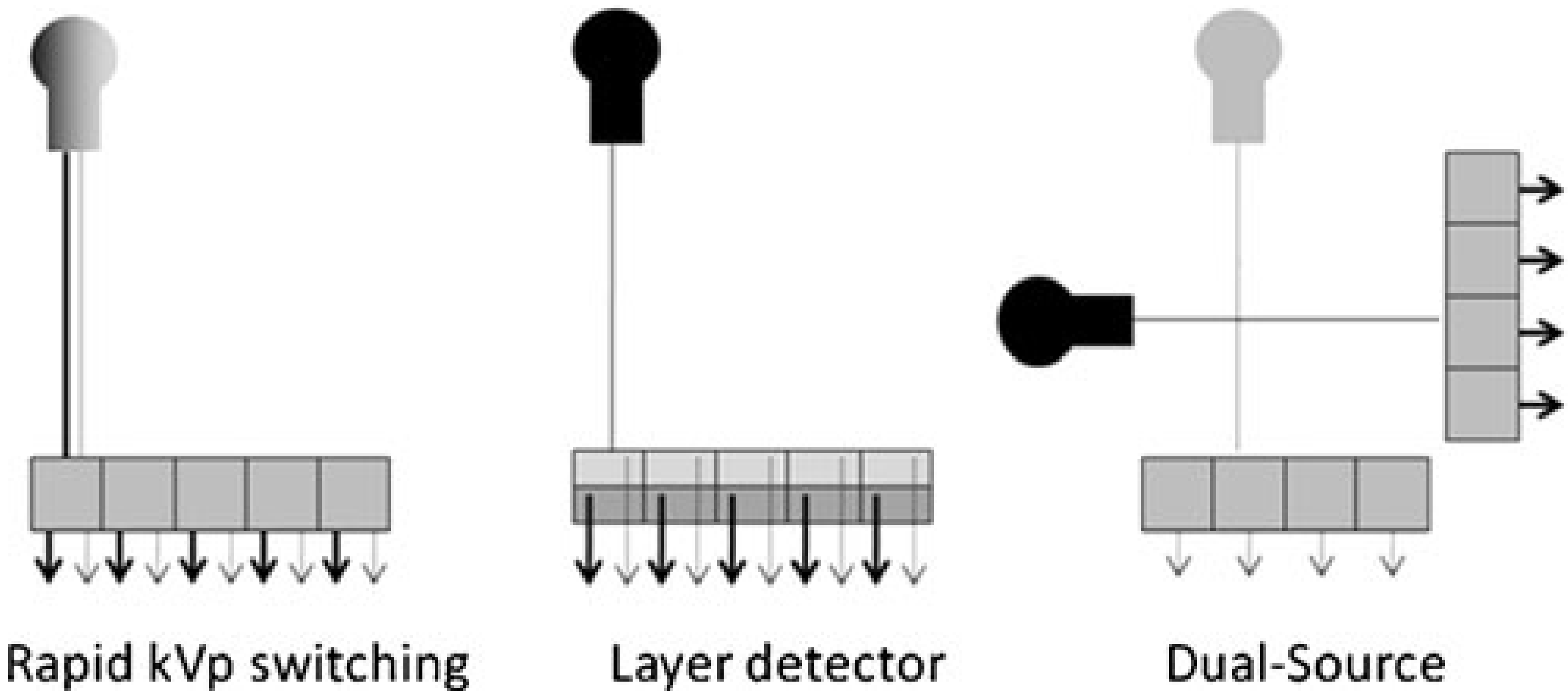
X-RAY EMISSION SPECTRUM



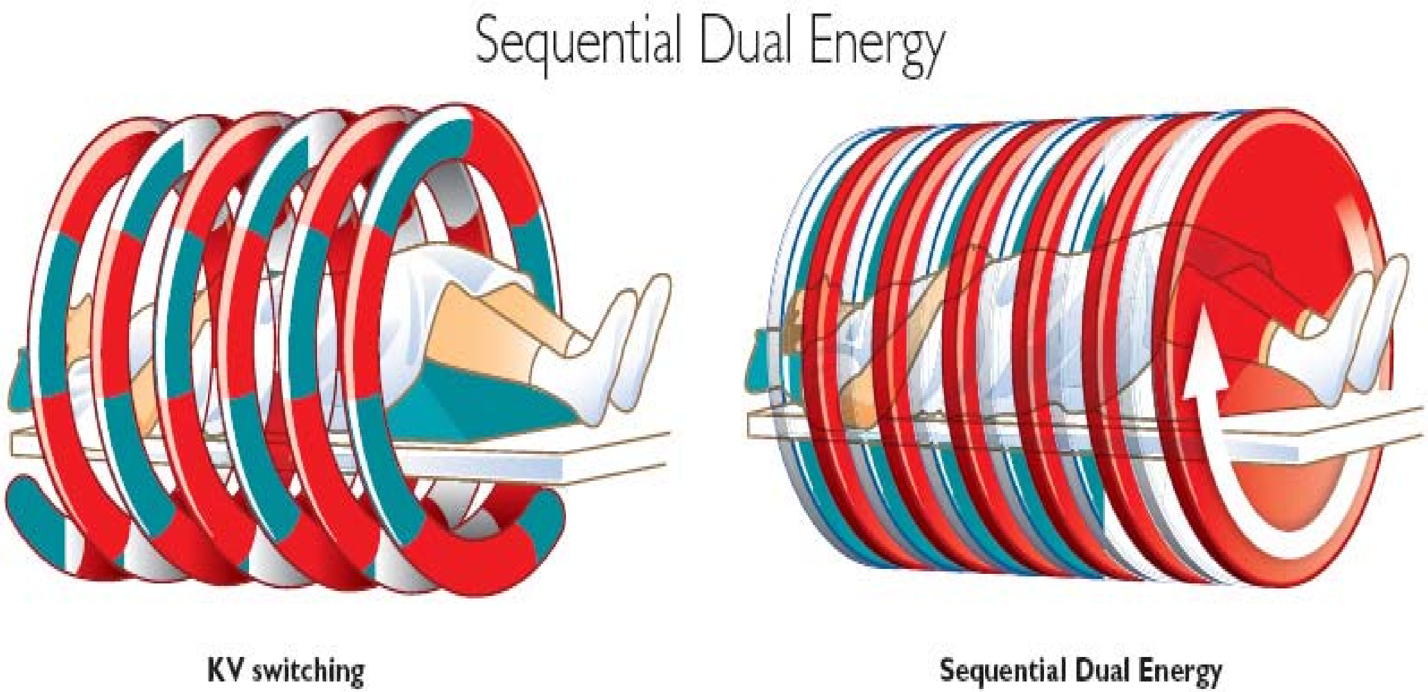
MATERIAL-SPECIFIC CURVES VS. PHOTON ENERGY



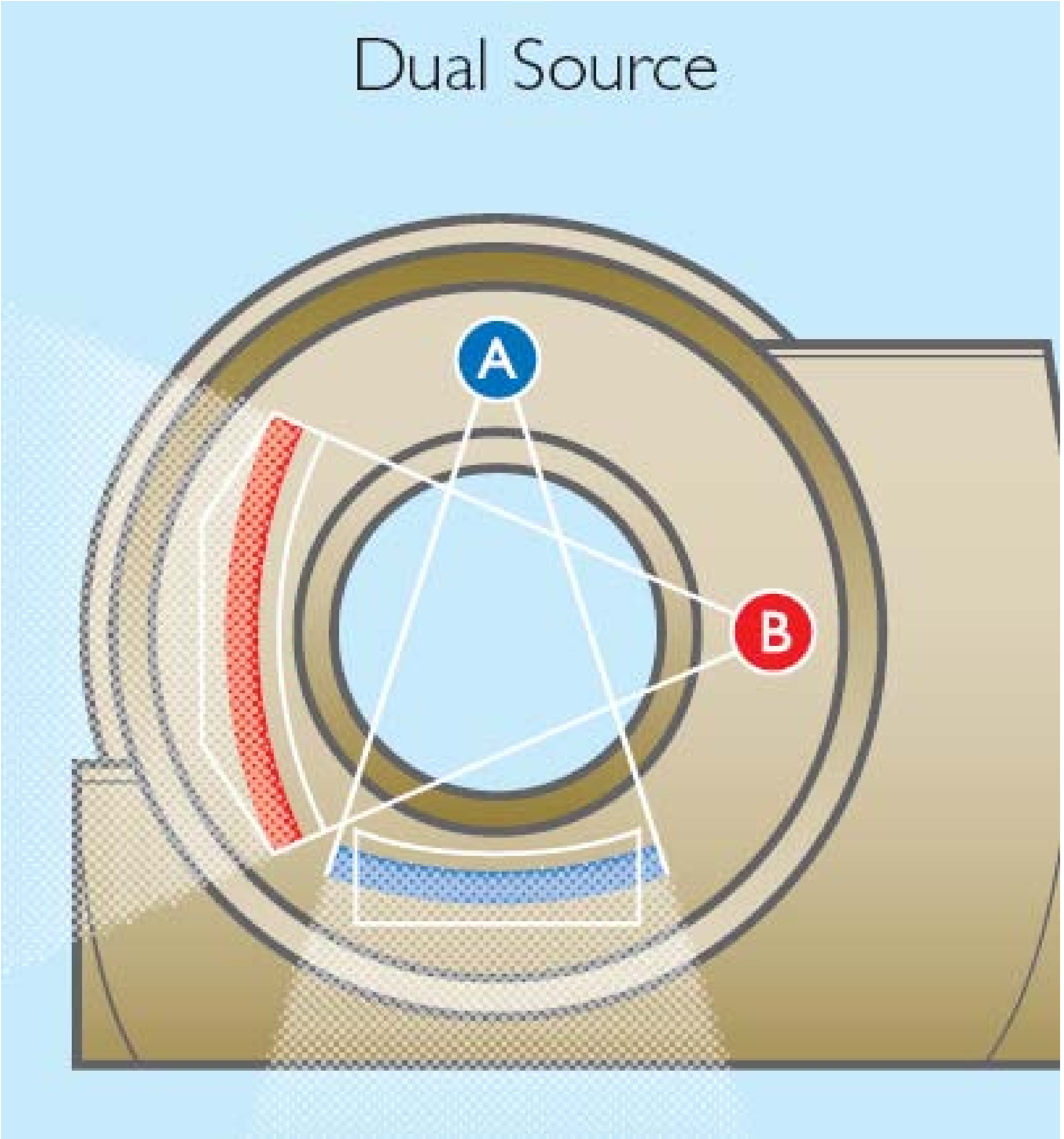
DIFFERENT HARDWARE APPROACHES TO DUAL-ENERGY CT IMAGING



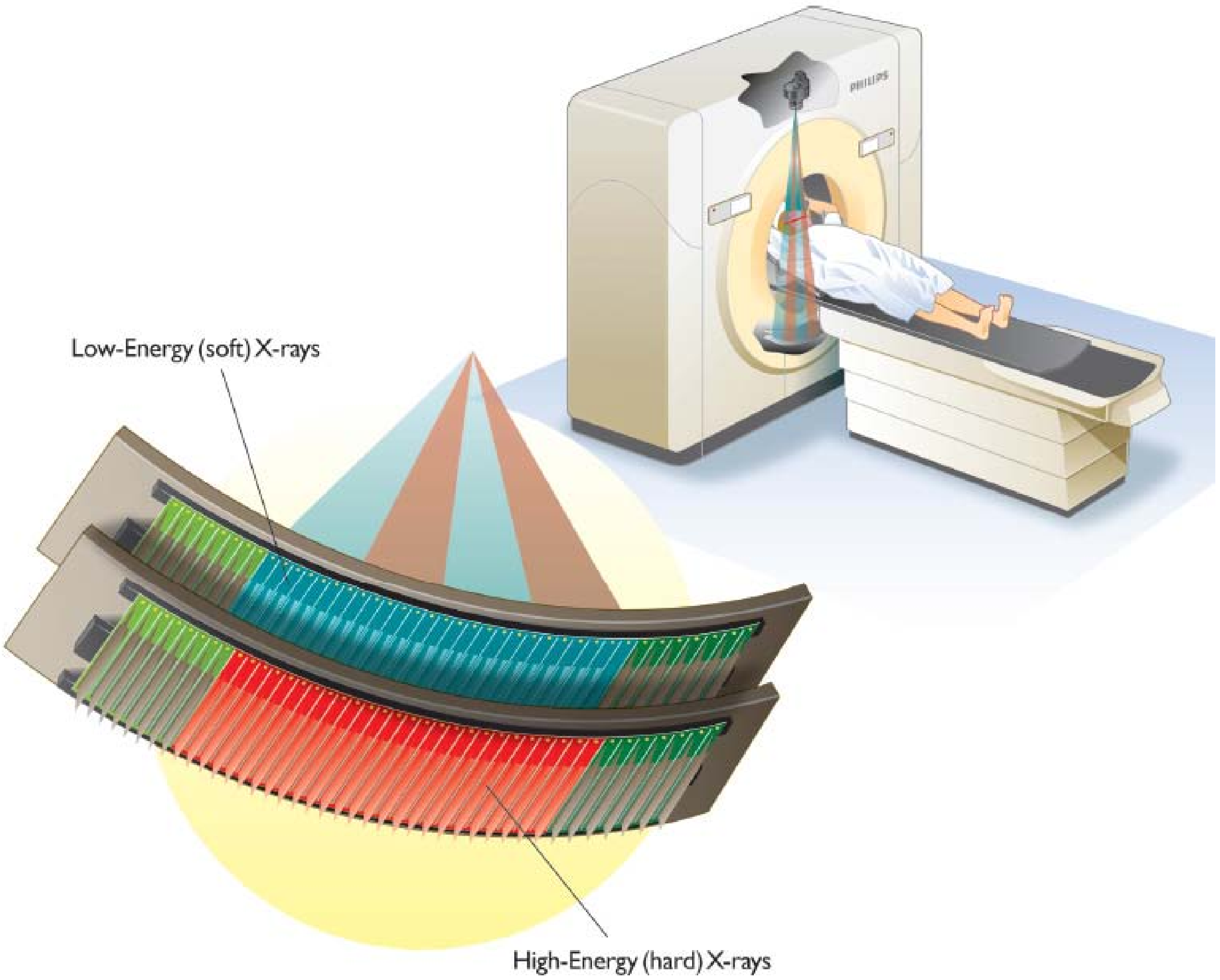
RAPID KV SWITCHING vs SEQUENTIAL



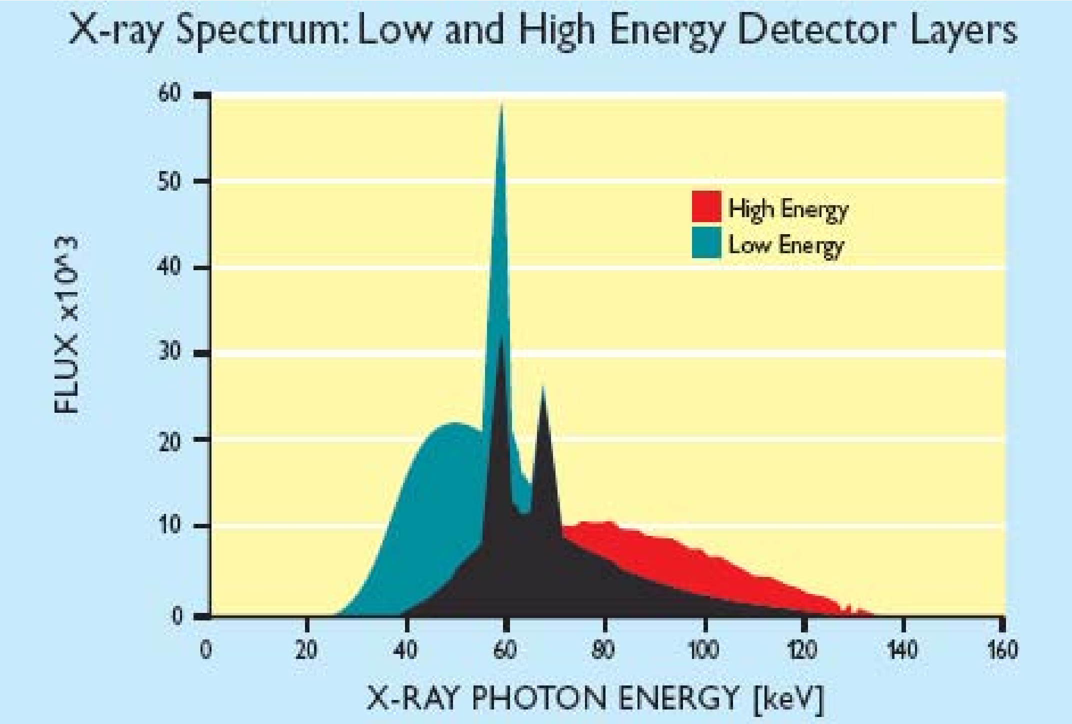
DUAL SOURCE



DUAL DETECTOR LAYER



DUAL-ENERGY CT

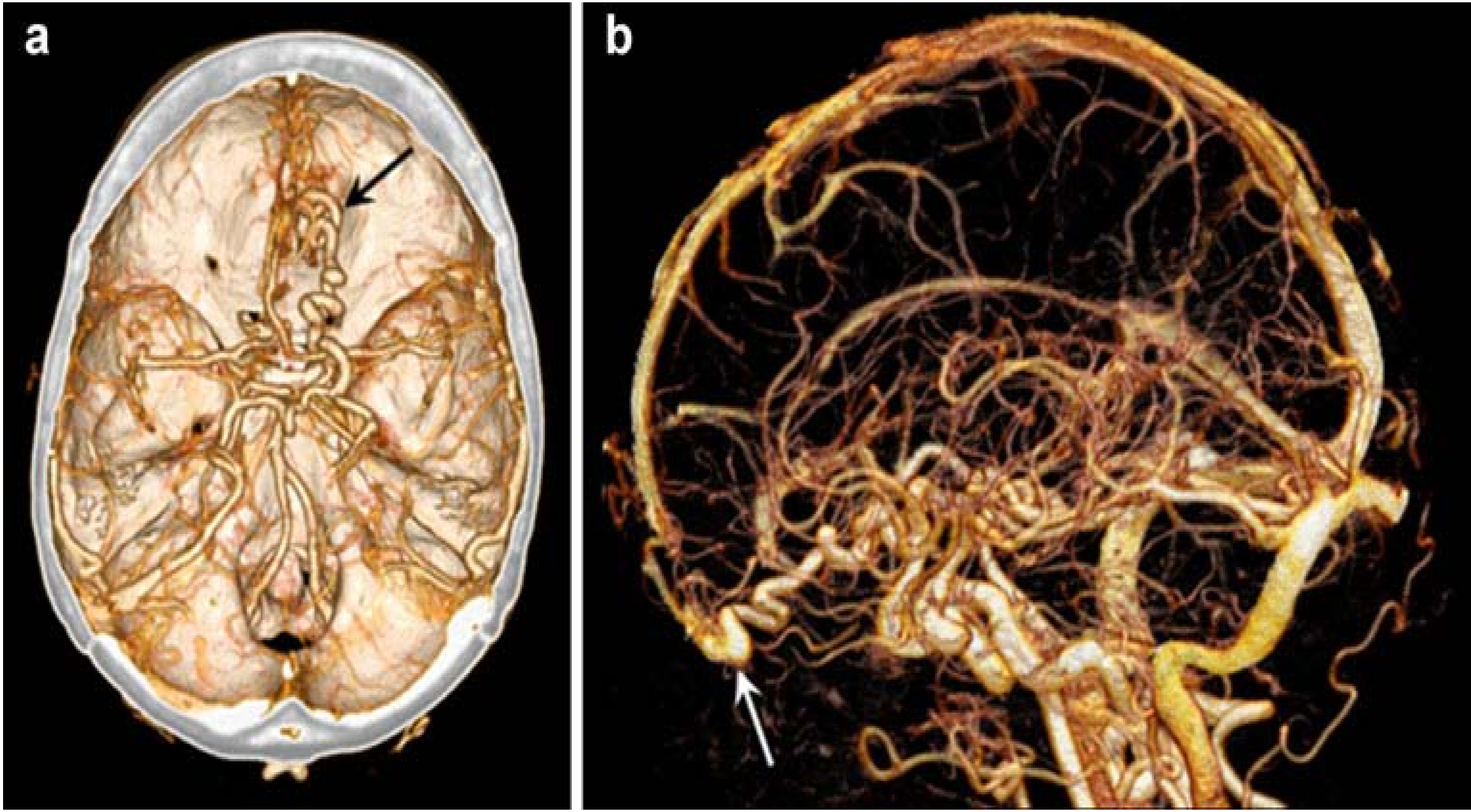


Simultaneous multi-energy detectors separate low-and high-energy X-rays into two distinct signals. The total signal equals the total image above

DUAL-ENERGY CT APPLICATIONS

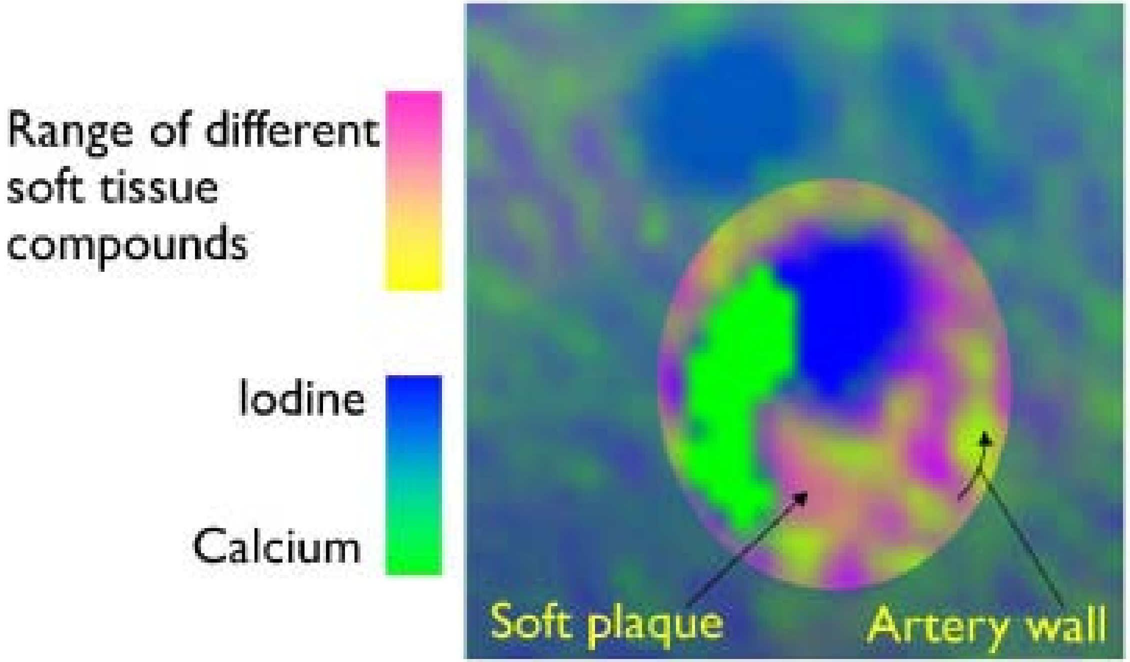
- Differentiation of materials.
- Identification and Quantification of contrast material.

DUAL ENERGY CRANIAL CT ANGIOGRAPHY



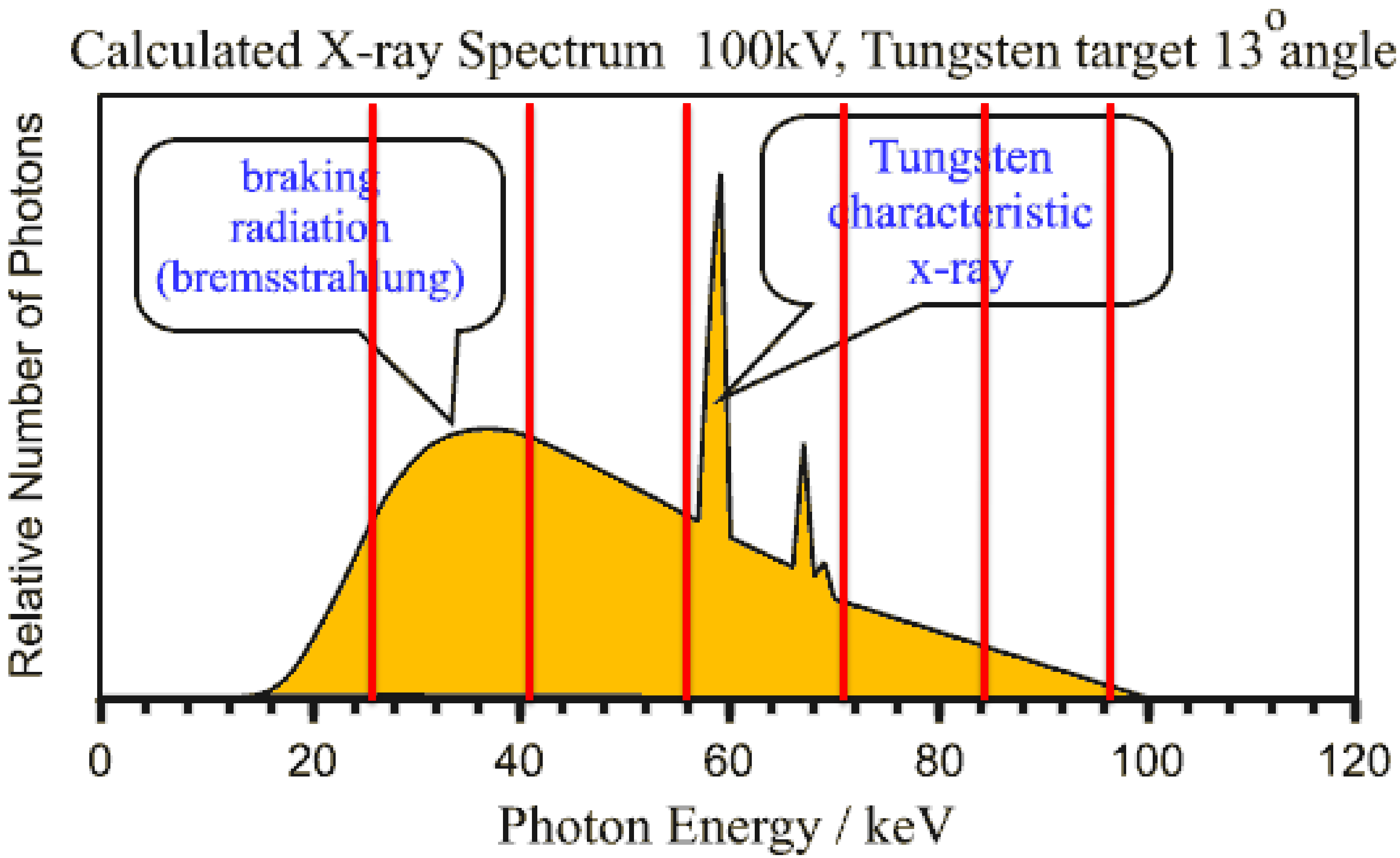
Arterio-venous malformation in the right frontal lobe.
Automated bone removal is precisely achieved, allowing improved delineation of the malformation with drainage into the superior sagital sinus.

SOFT & HARD PLAQUE DIFFERENTIATION



differentiate soft plaque from hard plaque in the heart, and make more informed decisions on the vulnerability of the plaque or the necessity of interventions? Shown here is separation of iodine from calcified lesion in a carotid vessel scanned at HUMC.

SIMULTANEOUS MULTI-ENERGY

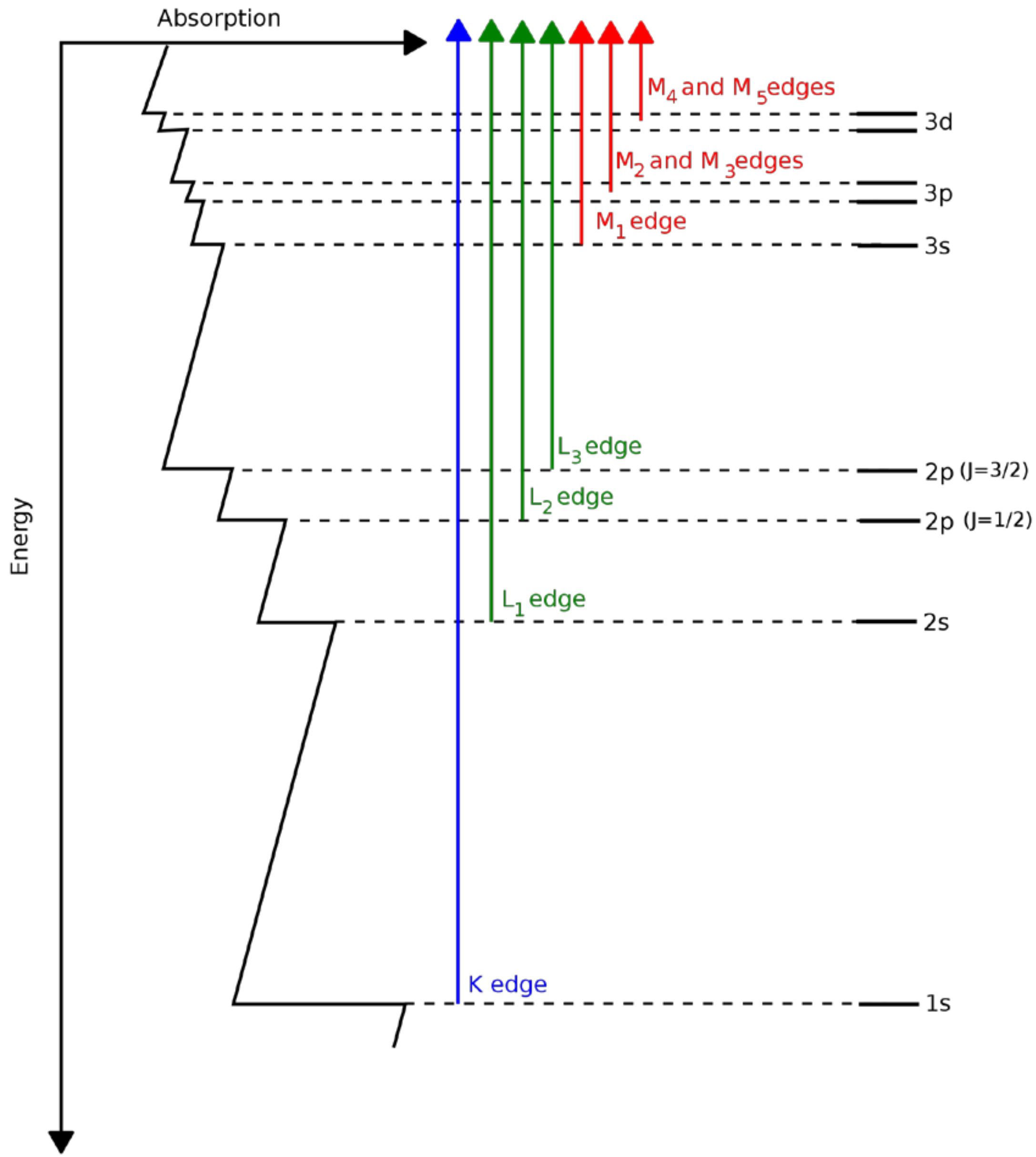


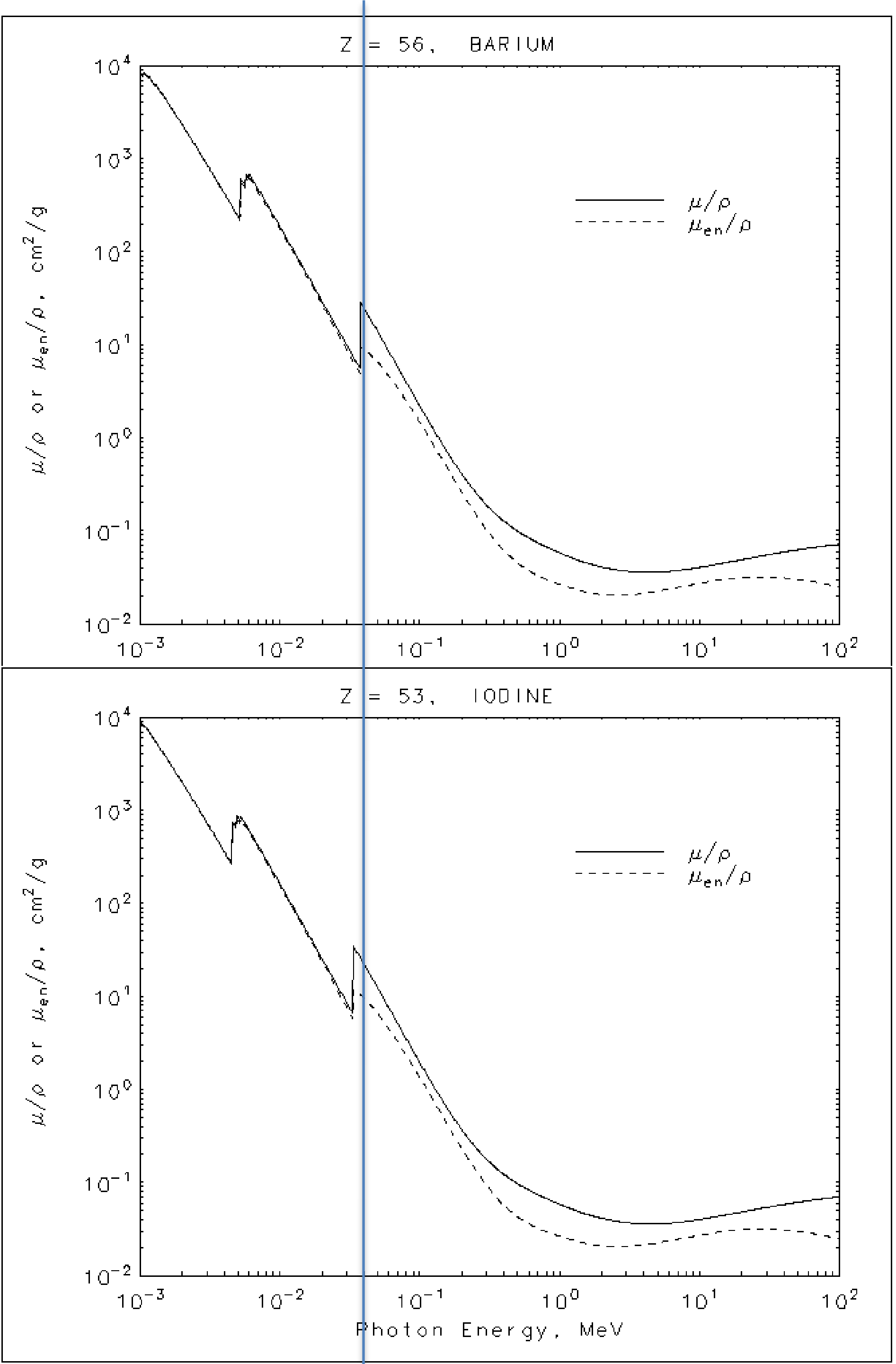
Photon-counting detectors image the spectrum of X-ray radiation in "energy bands" in order to form images based on the analysis of the spectral-signature of tissues.

MULTI-ENERGY CT

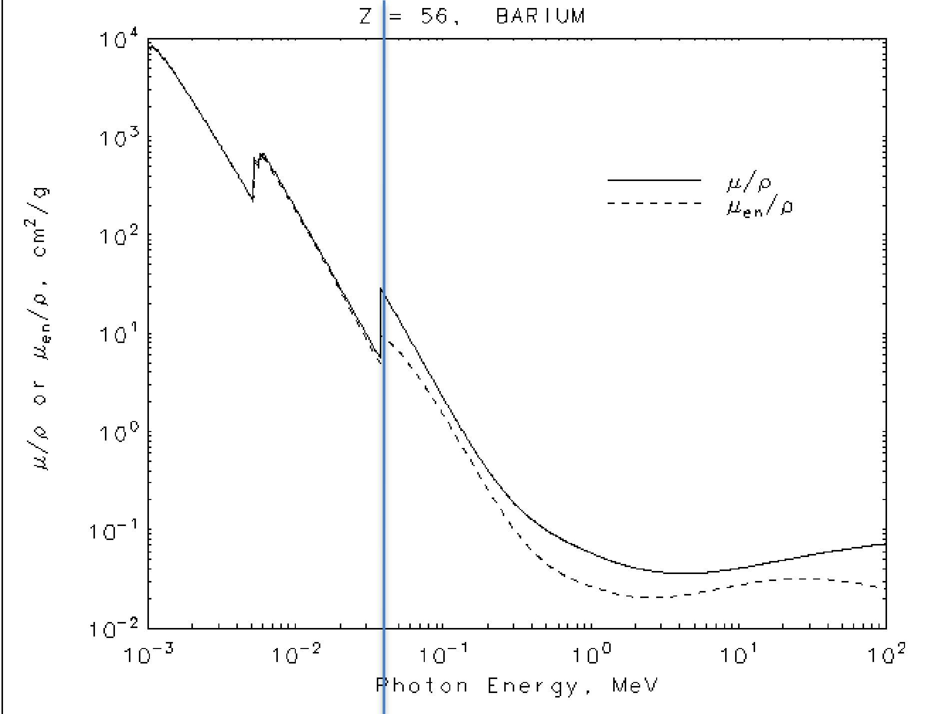
- K-edge multiple contrast agents.
- Heavy elements: iodine, barium, gadolinium, gold and platinum.
- Iodine, barium and background tissues identification and separation demonstrated in mice.
- Triple renal or liver study can be performed in a single examination. Dose reduction, patient movement elimination & patient throughput improvement.

K-SHELL ELECTRON IONIZATION

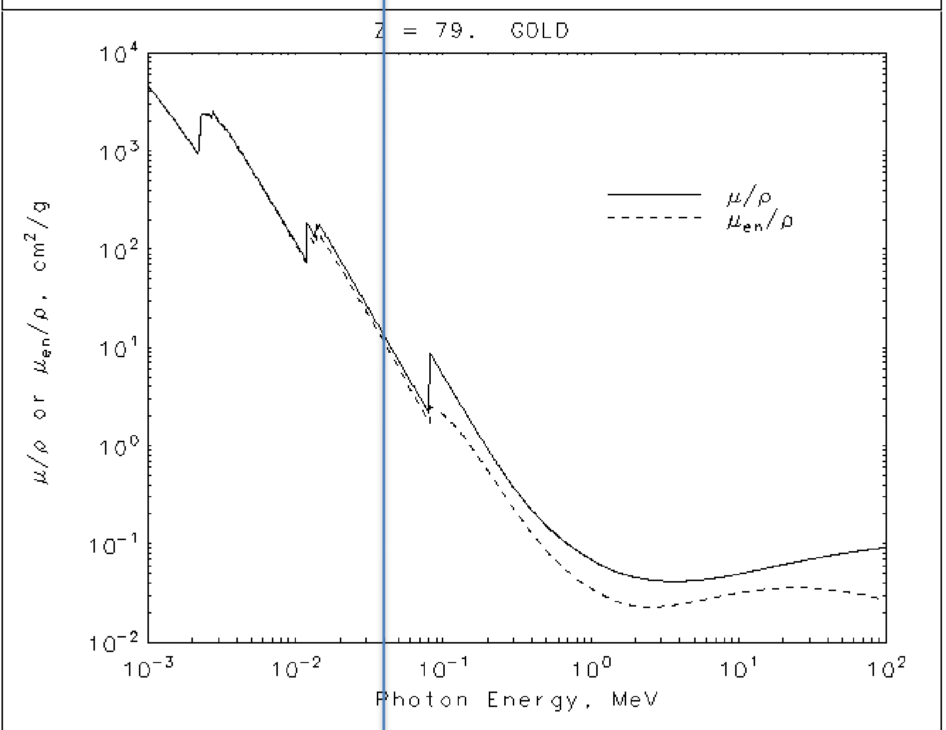




ideal K shell binding energies for absorption of X-rays,
33.2 keV and 37.4 keV



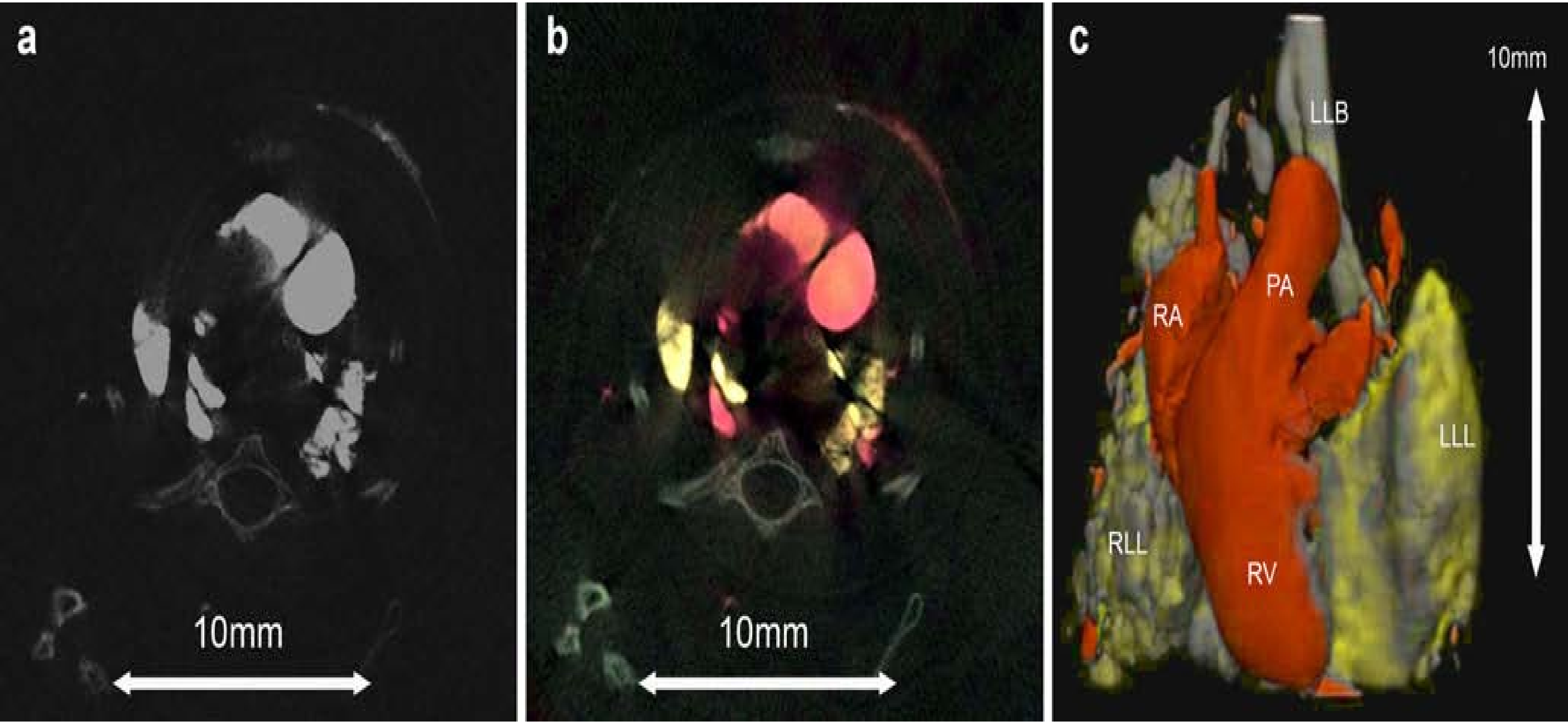
Z = 56, BARIUM
μ/ρ
μ_{en}/ρ
μ/ρ or μ_{en}/ρ, cm^2/g
Photon Energy, MeV
10^{-3}
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
10^{4}
10^{3}



Z = 79, GOLD
μ/ρ
μ_{en}/ρ
μ/ρ or μ_{en}/ρ, cm^2/g
Photon Energy, MeV
10^{-3}
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
10^{4}
10^{3}

MULTI-ENERGY CT

- New contrast agents.
- Gold labeled functional nano-particles targeted to specific enzymes or cells.
- Quantify the amount and locate the particles.
- Better intrinsic tissue contrast to characterize tissues. Example: characterization of atherosclerotic plaques by determining iron and calcium content to evaluate the risk of plaque rupture.

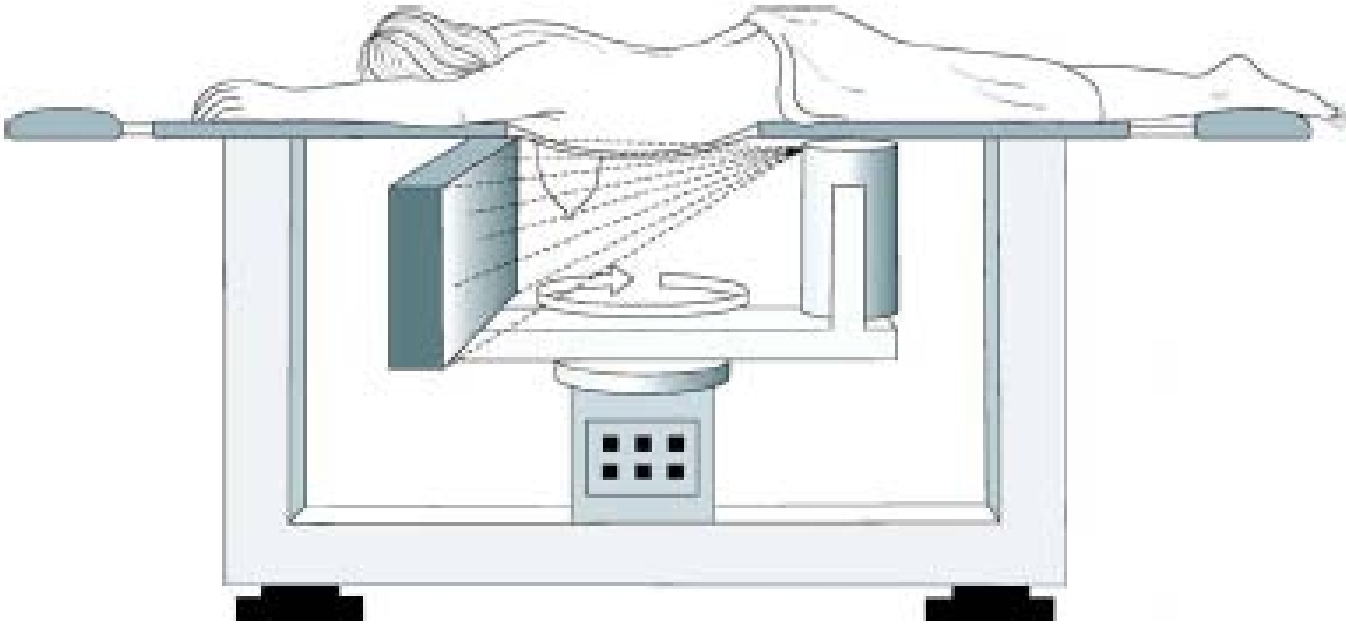


Multi-energy CT allows differentiation of iodine, barium and bone in mouse. Single-energy image demonstrates similar attenuation values of iodine, barium and bone, which cannot be distinguished on the basis of CT numbers at energies >23 keV (A). Multi-energy CT data enable differentiation of iodine in circulation (red colour coding), barium in lungs (yellow) and bone (white) on transverse (B) and volume-rendered CT images (C). Note iodine and barium both have high Z-numbers and are solely differentiated on the basis of k-edges being 4 keV apart. Left lower bronchus (LLB), left lower lobe (LLL), pulmonary trunk (PA), right atrium (RA), right lower lobe (RLL), right ventricle (RV)

THE IDEAL CT SCANNER

- Only One X-ray source.
- Highly pixellated detector.
- Detect One X-ray Photon at a time and measure its energy. Photon counting.

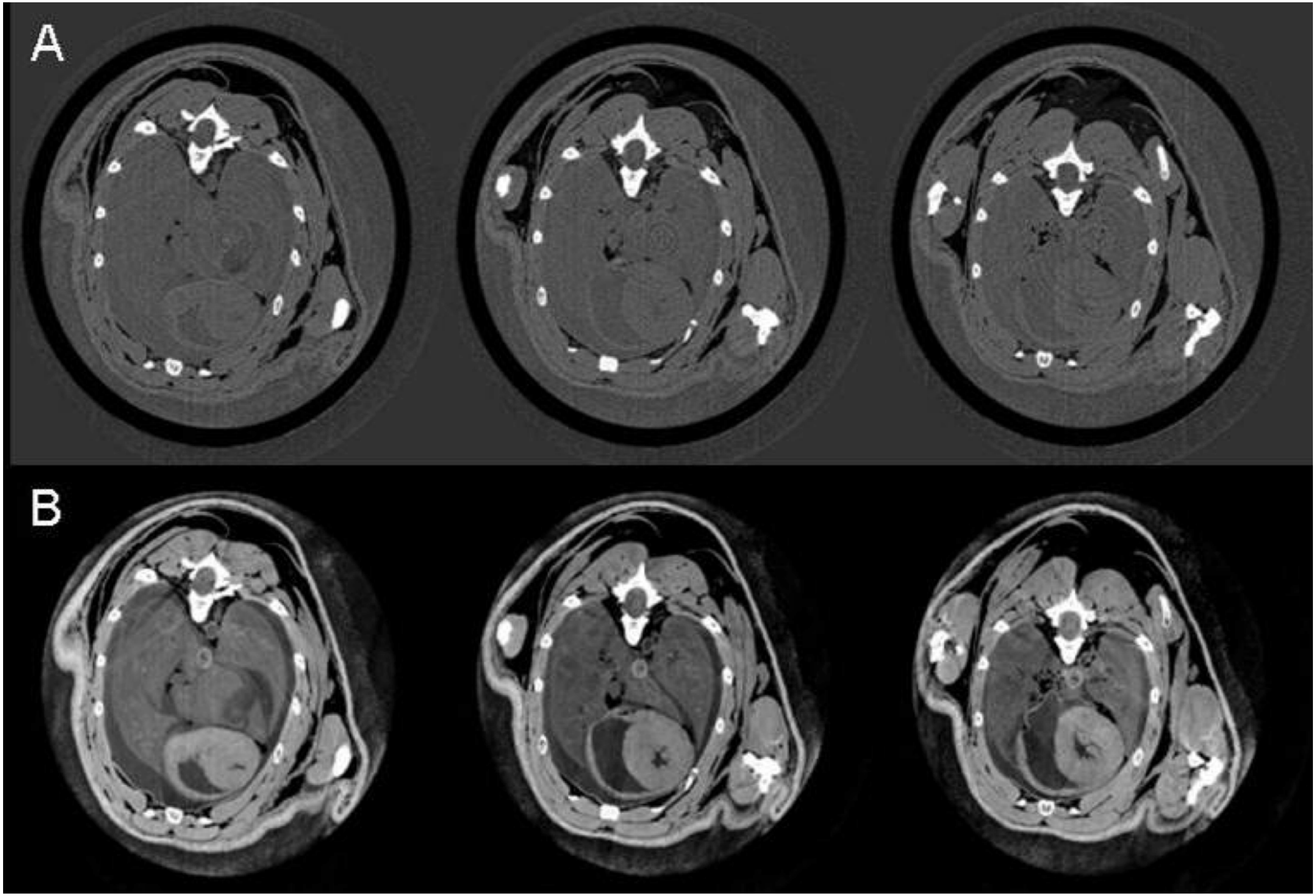
MULTI-SPECTRAL BREAST CT



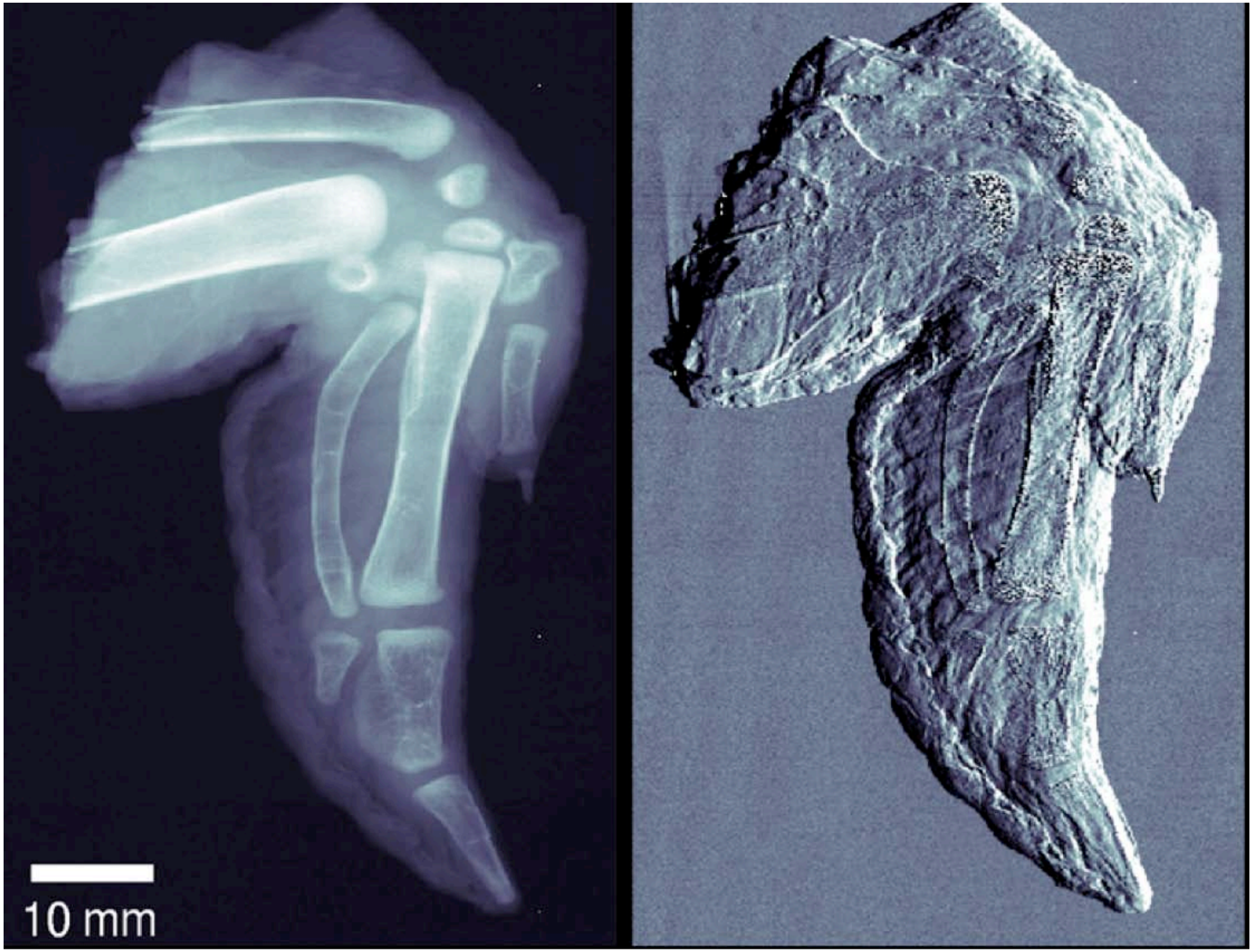
PHASE CONTRAST CT IMAGING

- For soft tissues with little absorption (e.g. breast tissue, vessels, muscle, cartilage) conventional X-ray techniques provide poor contrast, compared with visualization of osseous structures.
- Over the last years, several phase-contrast imaging techniques have been developed, which rely on the phase shift of X-rays due to refraction rather than absorption. There is emerging evidence that such an approach provides increased soft tissue contrast.
- Due to the potential of using higher energy levels, PCI may allow for image acquisition at considerably decreased radiation dose.

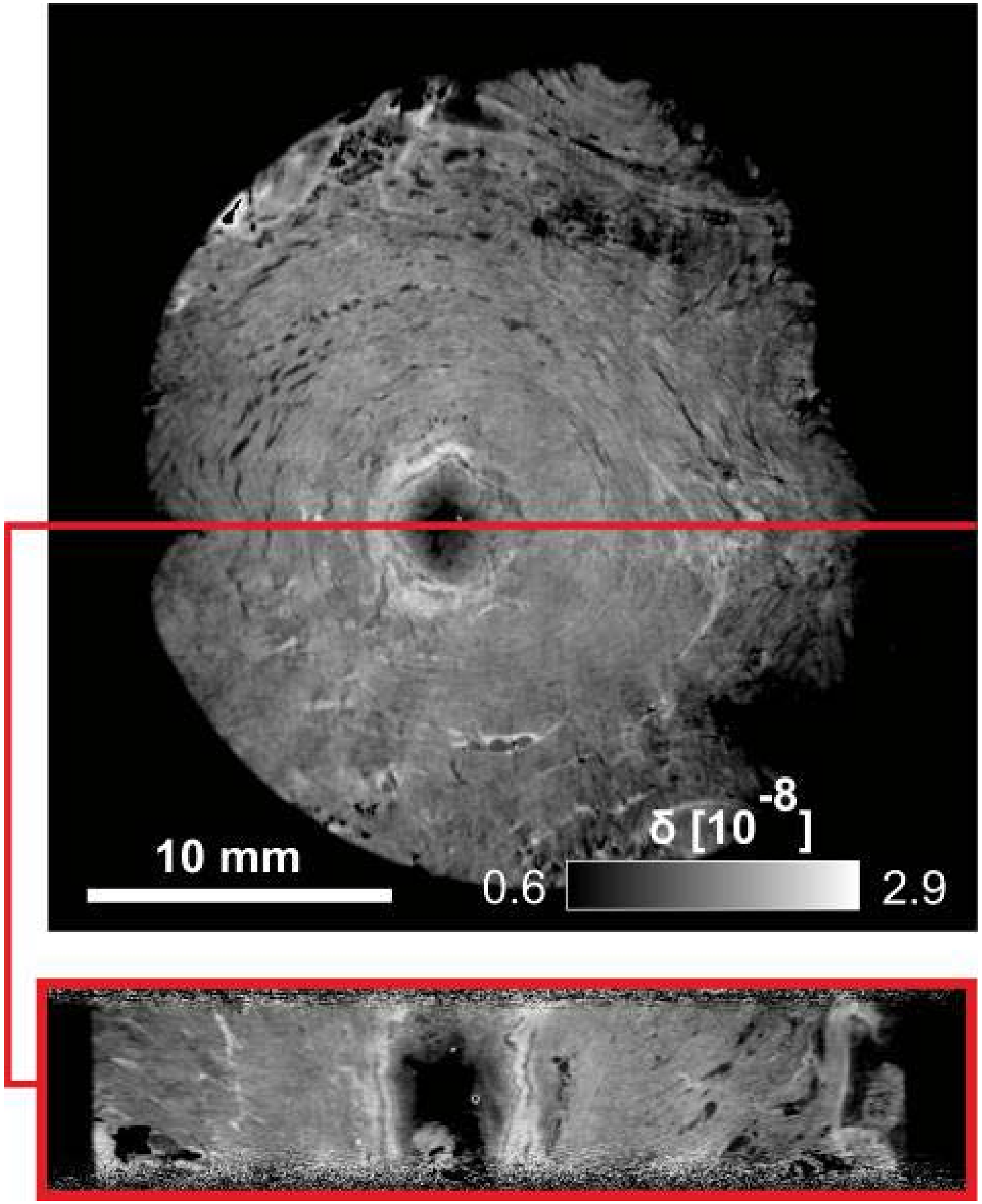
- technology required X-rays of spatial and temporal coherence that were not easily available.



Cross sections of a mouse scanned in absorption contrast tomography (A) and phase contrast tomography (B), demonstrating superior soft-tissue contrast in phase contrast at exactly the same dose level. The grey values of both conrasts were windowed to the best contrast in each case (A. Tapfer, M. Bech & F. Pfeiffer, unpublished).



2D X-ray image of chicken wing in absorption contrast (left) and phase contrast (right) demonstrating superior contrast in non-osseous tissue (from F. Pfeiffer et al. Nature Materials **7**:134 (2008)).

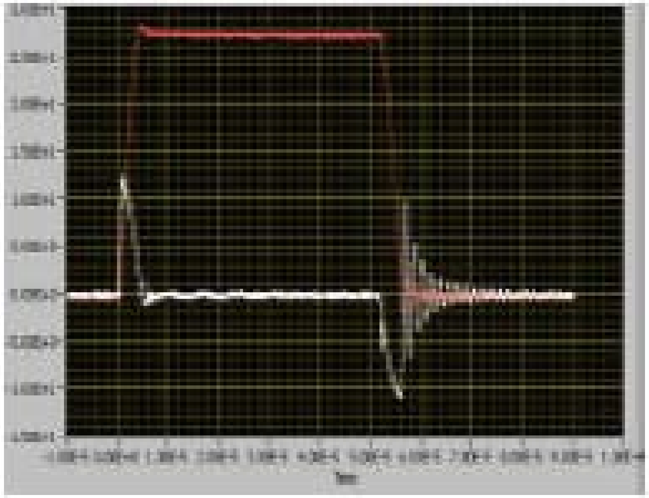


Cross section of human urethra scanned with phase-contrast tomography using monochromatic synchrotron radiation. Only poor contrast in absorption image (not shown) (from B. Müller, in SPIE Proceedings, 2010)

Desarrollos Tecnológicos en Imagen

- MR
  - Ultrafast gradients.
  - Driving Magnetic nanoparticles.

ULTRAFAST GRADIENTS



Ultra-fast Gradients without Peripheral Nerve Stimulation. Clinical study with 25 subjects demonstrated no PNS at high dB/dt (13,000 T/s) with short rise times.

The Economist

Dental X-rays

Little and not often, please

Confirmation that dental X-rays can be bad for you

Apr 14th 2012 | from the print edition

IF YOU are a suspicious type you may be disturbed by the fact that, despite reassurances of the safety of the procedure, dentists and their technicians, when administering X-rays, usually step out of the room while the deed is done. Not only that, they often drape a lead-lined apron over your body to protect your vital organs. Well, all but one: your brain.

Less is more

A study by Elizabeth Claus, of Yale University, just published in *Cancer*, suggests your suspicions might be justified. Dr Claus thinks she has identified, in those who have had dental X-rays often, a significant rise in the admittedly small risk of developing a brain tumour.

- No radiation: strong public health incentive
- Market: $50K x 10K dentists in USA alone

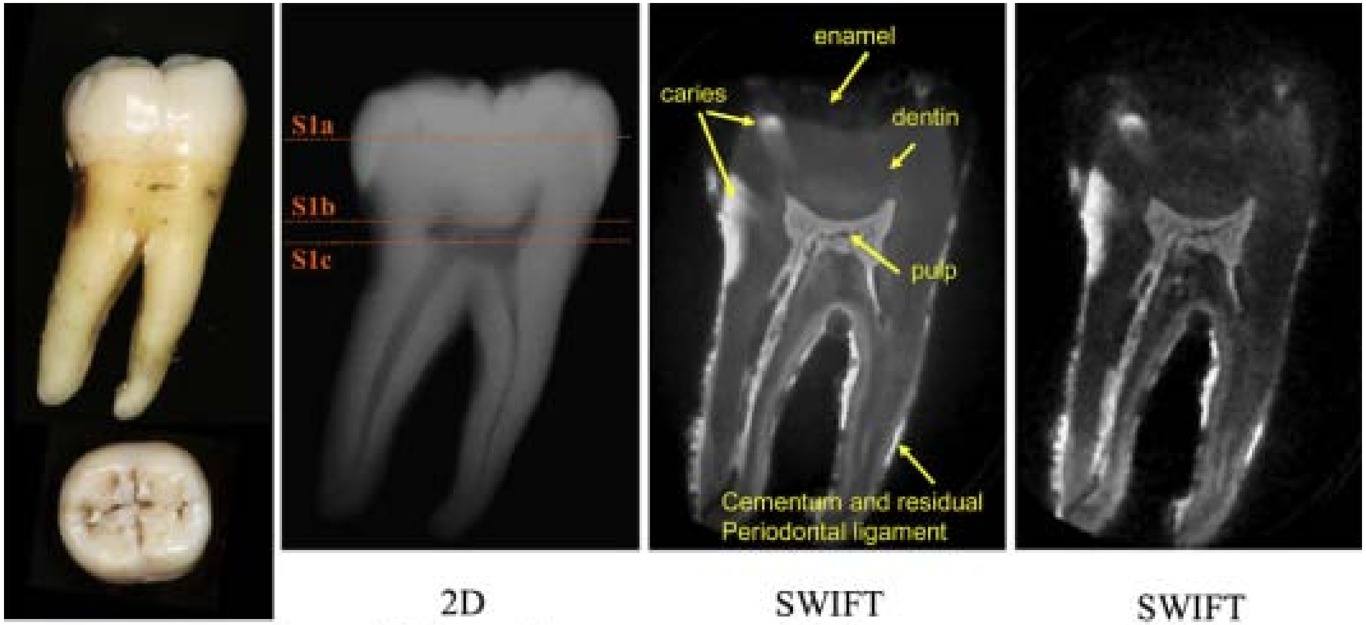
Original Article

Dental X-Rays and Risk of Meningioma

Elizabeth B. Claus, MD, PhD[1,2]; Lisa Calvocoressi, PhD[1]; Melissa L. Bondy, PhD[3]; Joellen M. Schildkraut, PhD[4]; Joseph L. Wiemels, PhD[5]; and Margaret Wrensch, PhD[5,6]

Dental MRI: Clinical

- Can see pulp, bone better than with x-rays
- Can be cheap, handheld



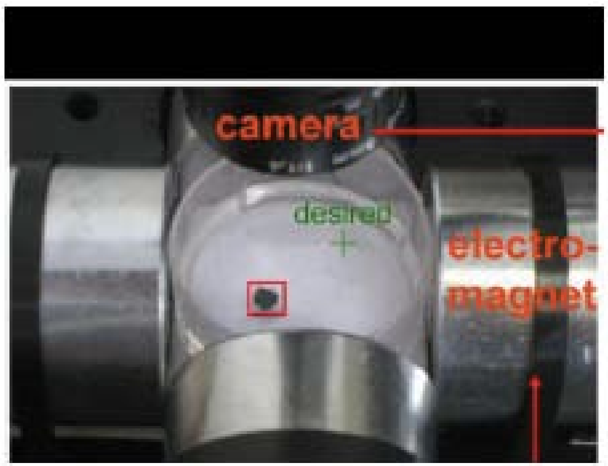
Photograph

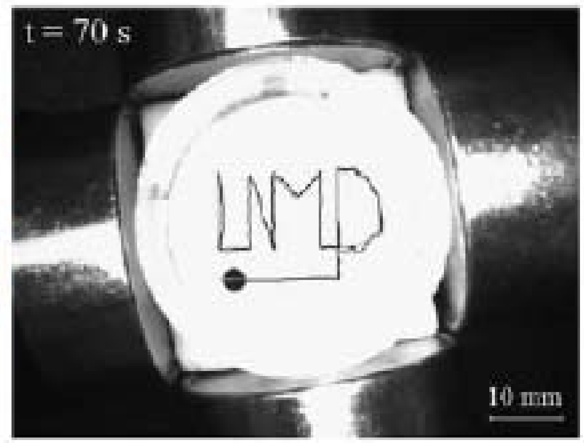
2D Radiograph

SWIFT 24 min

SWIFT 100 sec

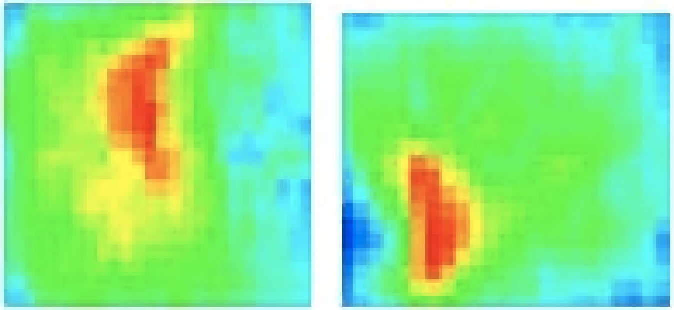
DRIVING MAGNETIC NANOPARTICLES





Built control circuitry for manipulating MNPs. Magnetic array (on left) draws logo with MNPs in one minute (on right)

Propulsion of MNPs in Tissues. 1-T magnets directionally smear MNPs from bolus injections (on left) in chicken muscle tissues (on right) within 1 minute.

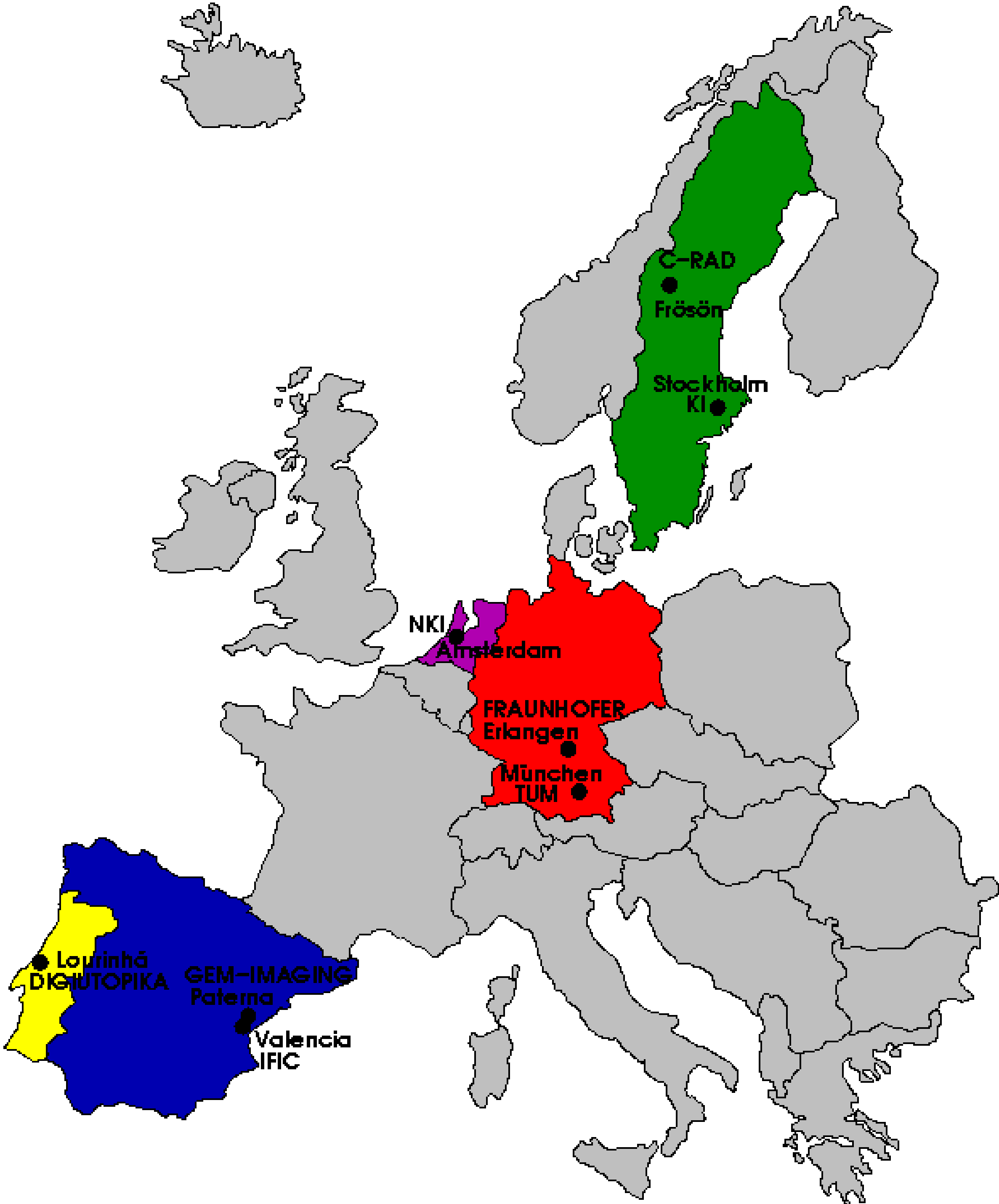


MRI of MNP Foci. Spin echo image sequence demonstrates 1-cm displacement of MNPs.

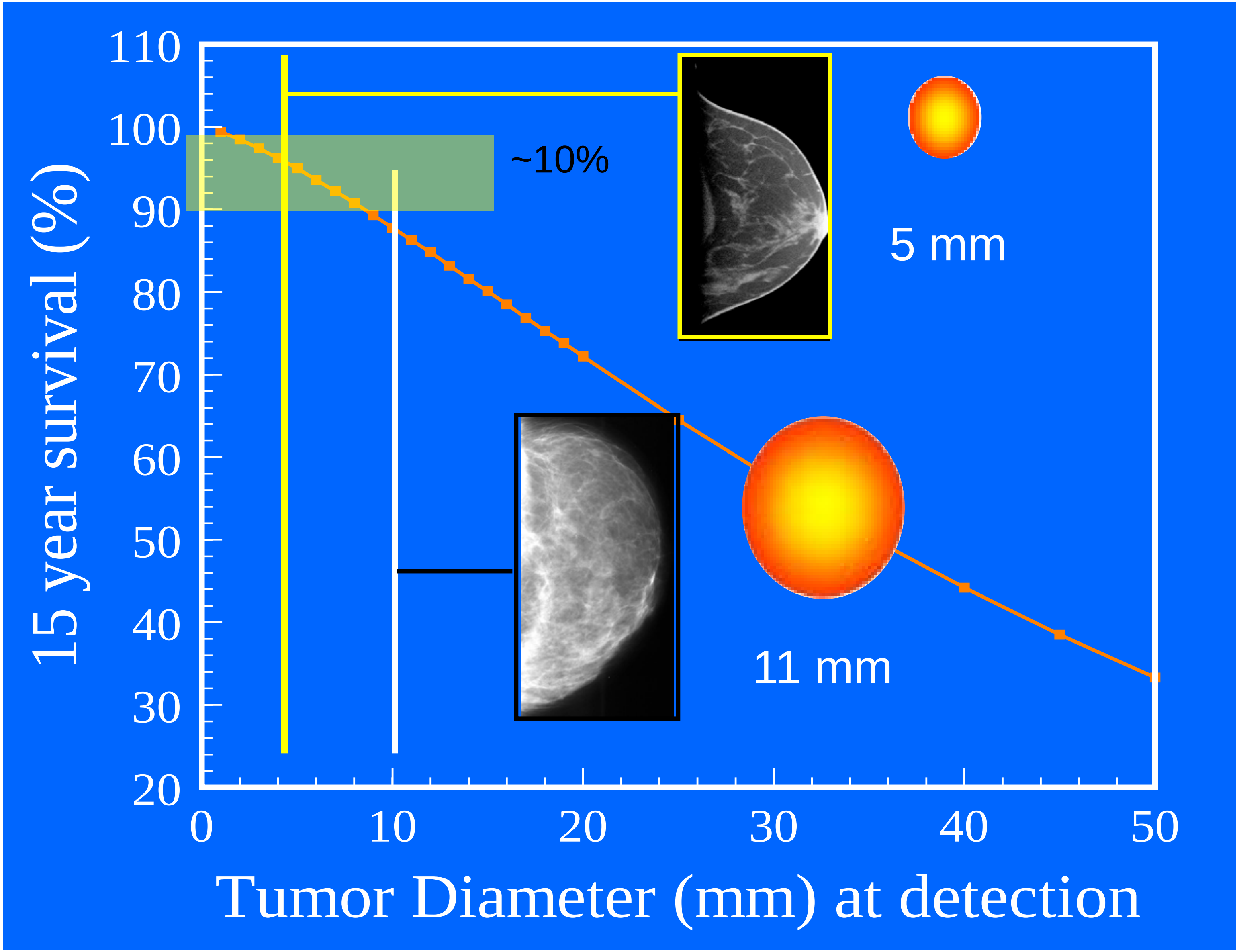
Desarrollos Tecnológicos en Imagen

- PET
  - Dedicated devices.

EUROPEAN PROJECT MAMMI: Mammography with Molecular Imaging 3,9 M€

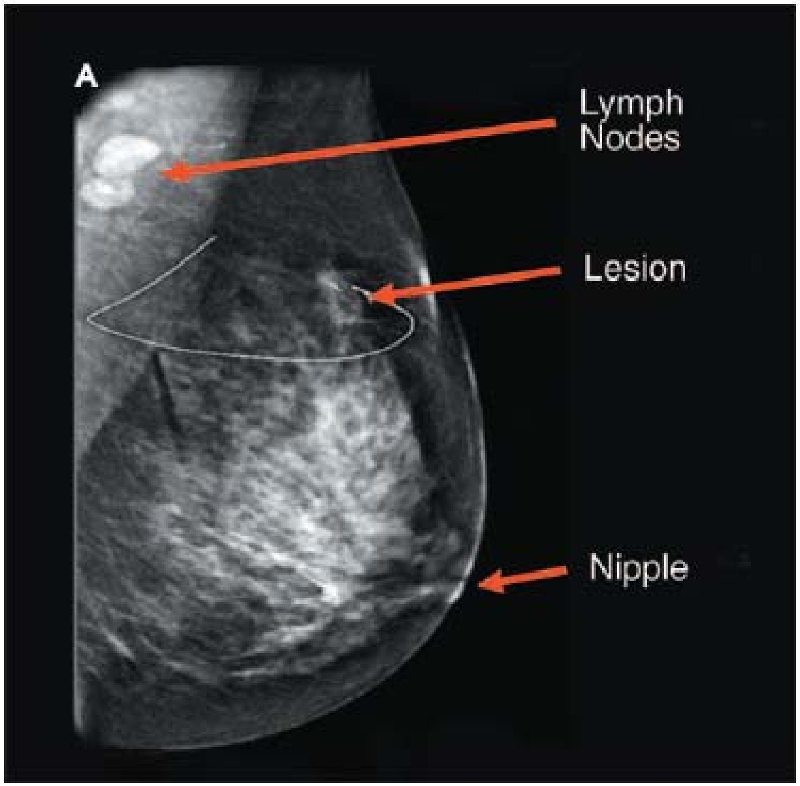


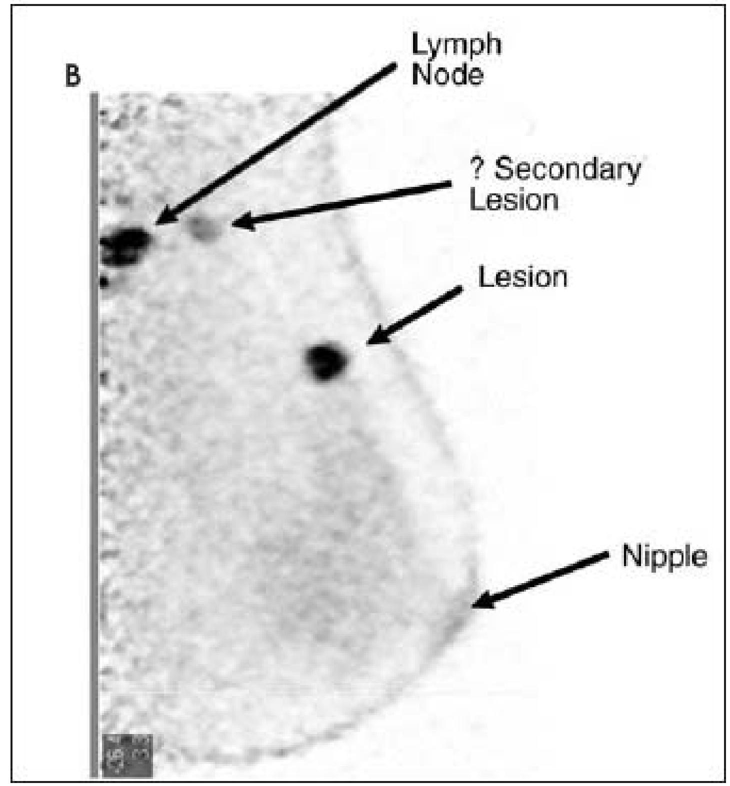
Predicting the survival of patients with breast carcinoma using tumor size, JS Michaelson, M Silverstein, J Wyatt, et. al. *Cancer* 2002; 95: 713-723



(slide provided by Dr Simon Cherry, UC Davis)

IMAGEN MORFOLÓGICA VS FUNCIONAL





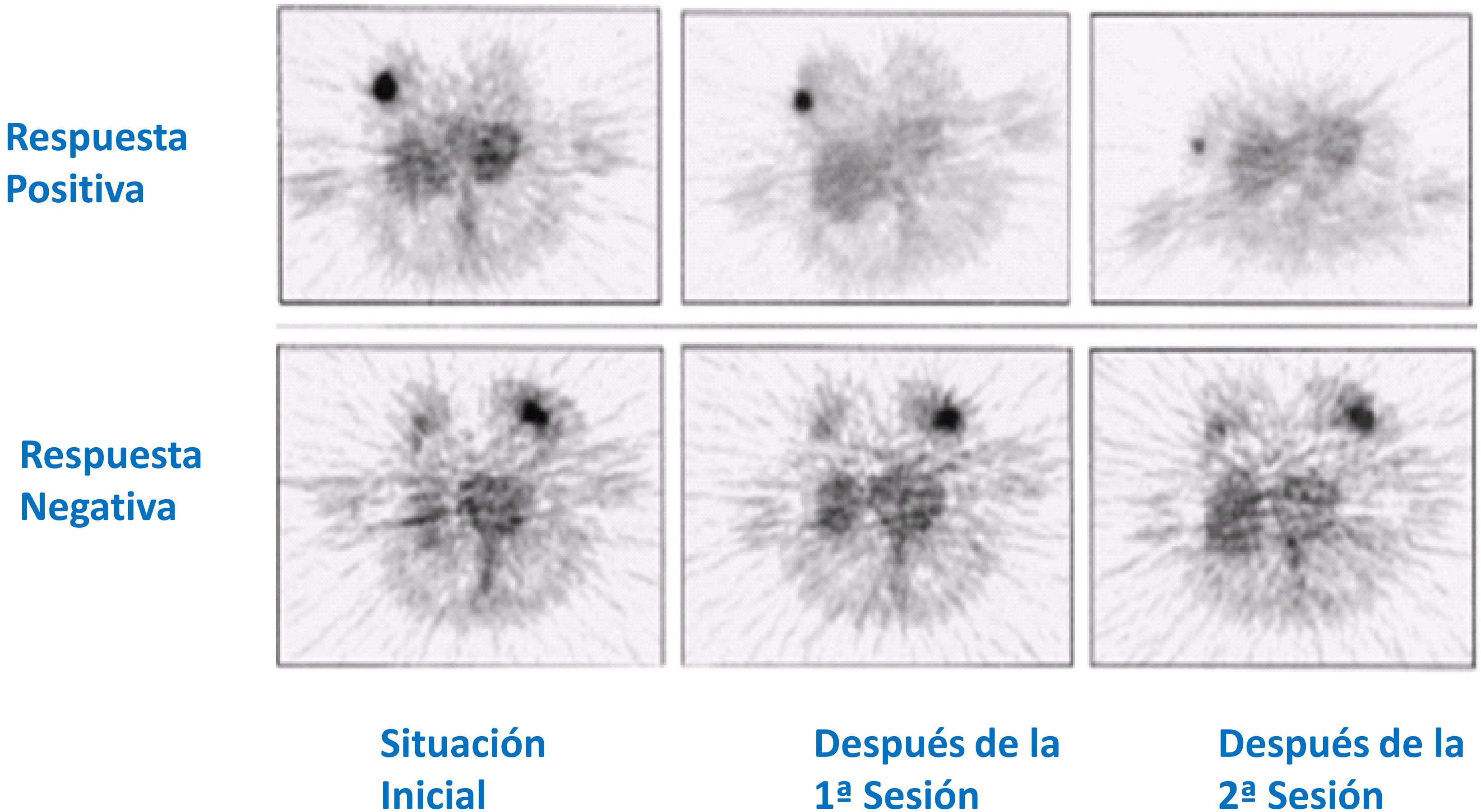
The role of positron emission mammography in breast cancer imaging and management

Kathy Schilling, MD, Peter Conti, MD, PhD, Lee Adler, MD, and Lorraine Tafra, MD

SONDAS MOLECULARES

- Actualmente, se utiliza la FDG (consumo de glucosa) en el 99% de los casos.
- FDG es únicamente un marcador de consumo energético.
- Se necesitan marcadores más específicos fundamentalmente para oncología y neurología.

CARCINOMA de MAMA: Predicción del PET/FDG sobre la Respuesta a la Quimioterapia



Schelling et al., J of Clin Oncol 2000; 18:1689

VALORACIÓN TEMPRANA con PET-FDG de la RESPUESTA al TRATAMIENTO

El Reto

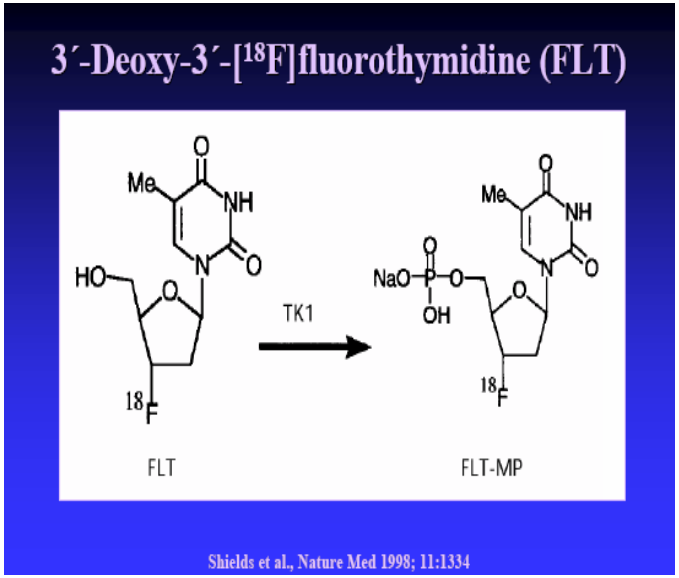
Se necesita definir como utilizar mejor el diagnóstico del PET para:

- **Mejorar el resultado de los que no responden. (diferente o terapia más intensiva).**
- **Mejorar el resultado de los que responden (terapia menos intensa).**

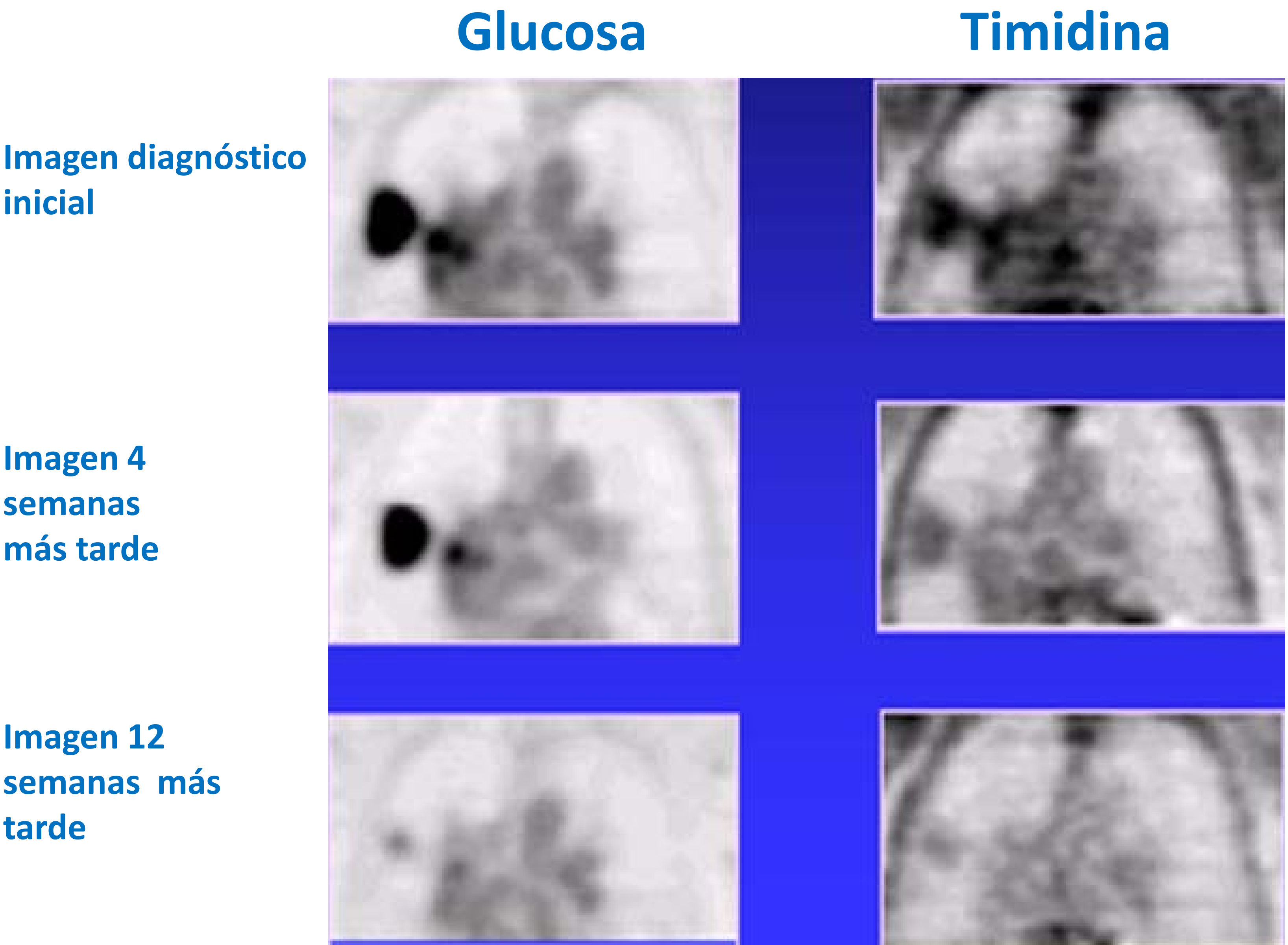
FLT: TIMIDINA

PRECURSOR DEL ADN, SE INCORPORA AL ADN.

EVALUACIÓN DIRECTA DE LA PROLIFERACIÓN TUMORAL.

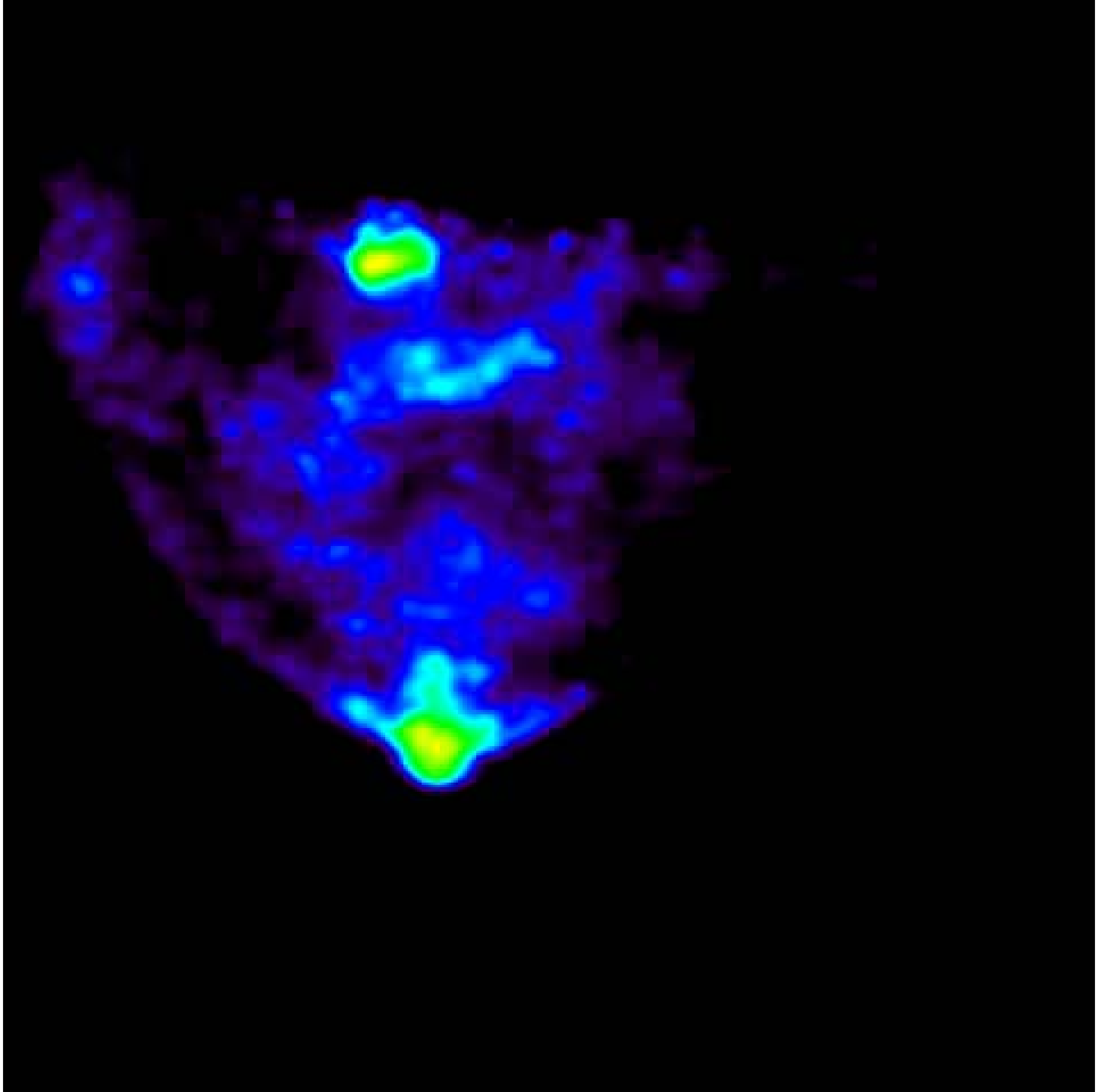


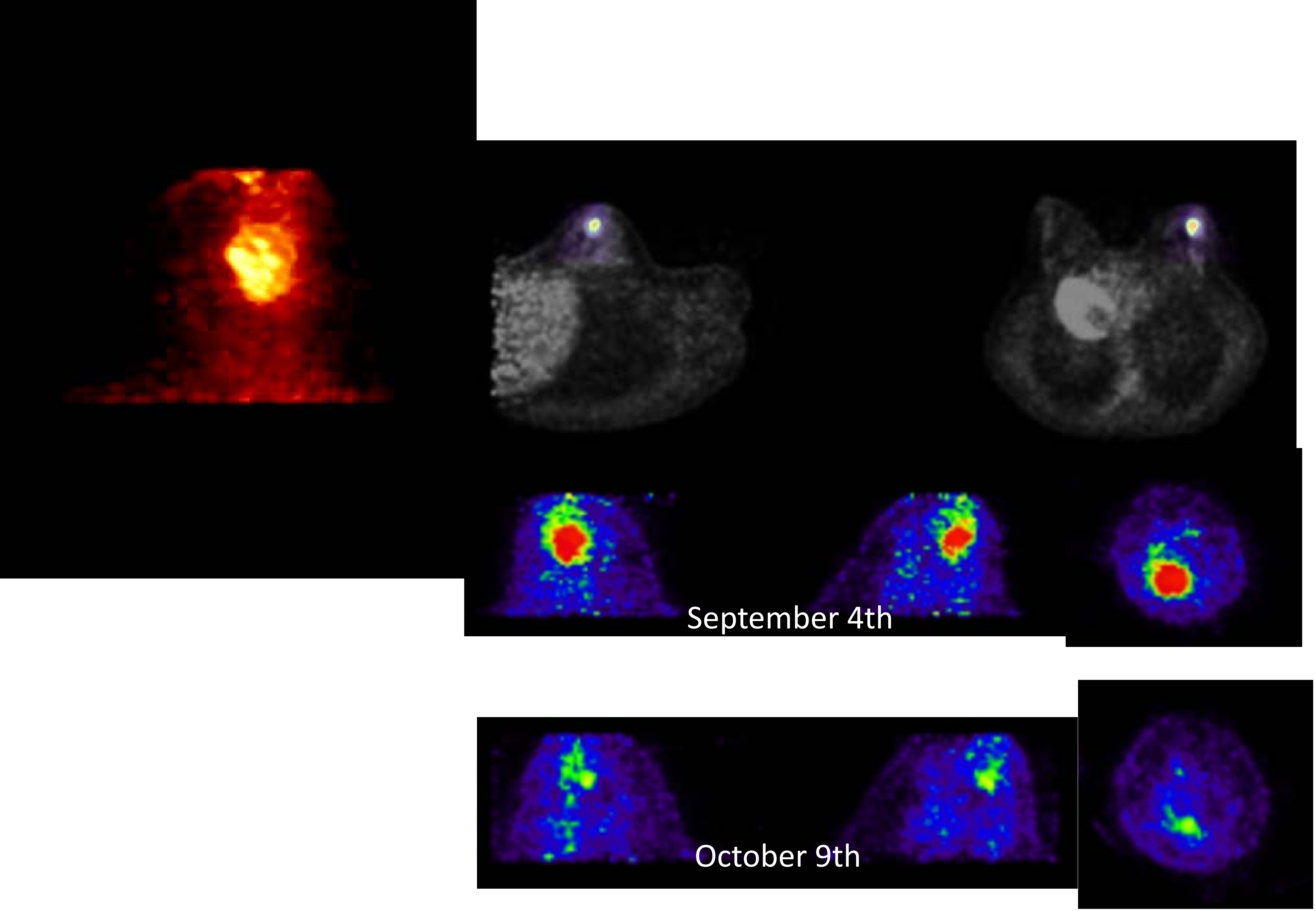
RESPUESTA a laTERAPIA:



FINAL PROTOTYPE

ONCO VISION
GEM-IMAGING SA



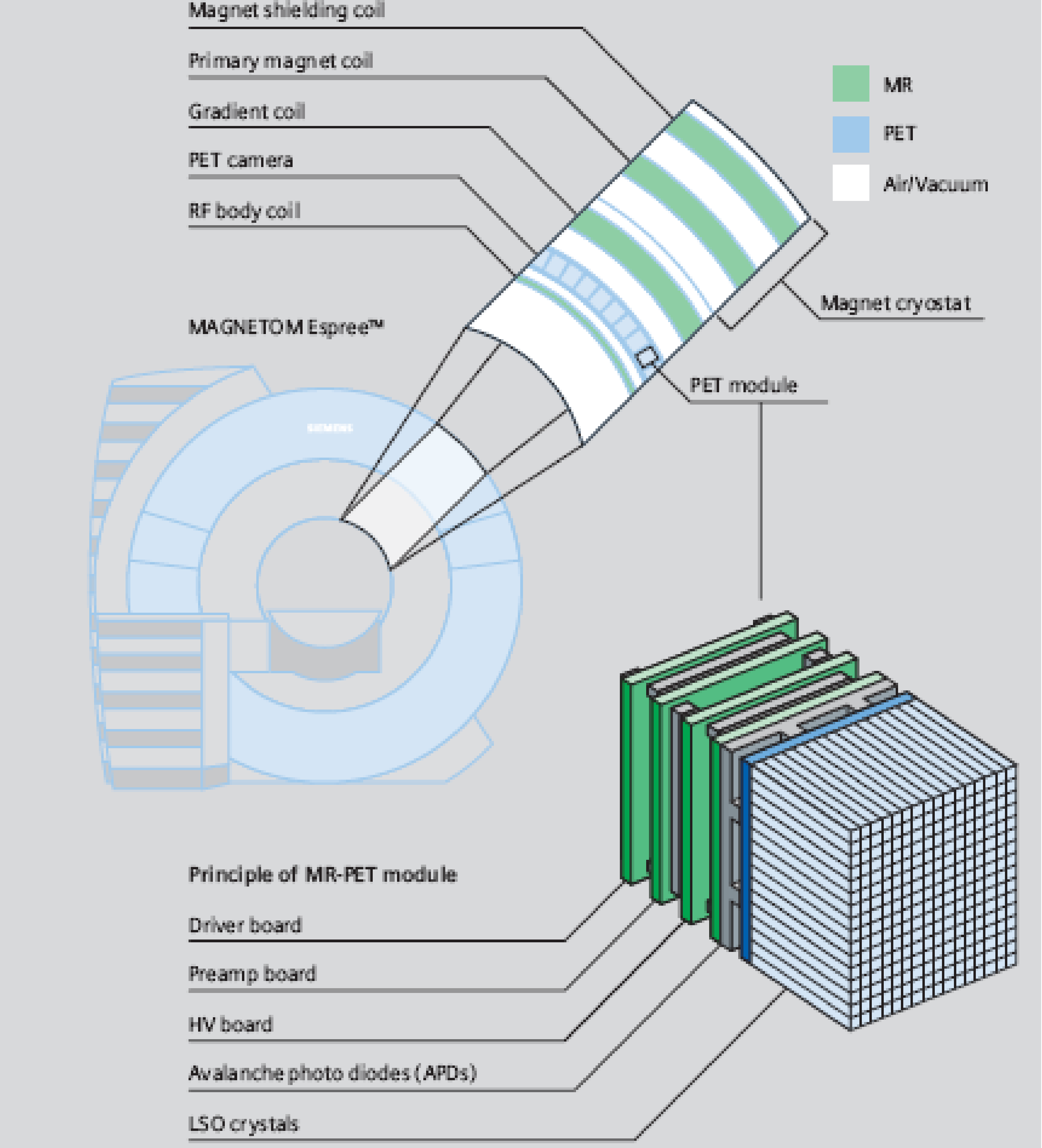

September 4th
October 9th

Desarrollos Tecnológicos en Imagen

- PET/RM

PET/RM SECUENCIAL

Philips Gemini TF (PET) and Achieva 3 T (MRI)



Magnet shielding coil
Primary magnet coil
Gradient coil
PET camera
RF body coil
MR
PET
Air/Vacuum
Magnet cryostat
MAGNETOM Espree™
PET module
Principle of MR-PET module
Driver board
Preamp board
HV board
Avalanche photo diodes (APDs)
LSO crystals

SIEMENS Biograph mMR

Munich MR-PET Consortium

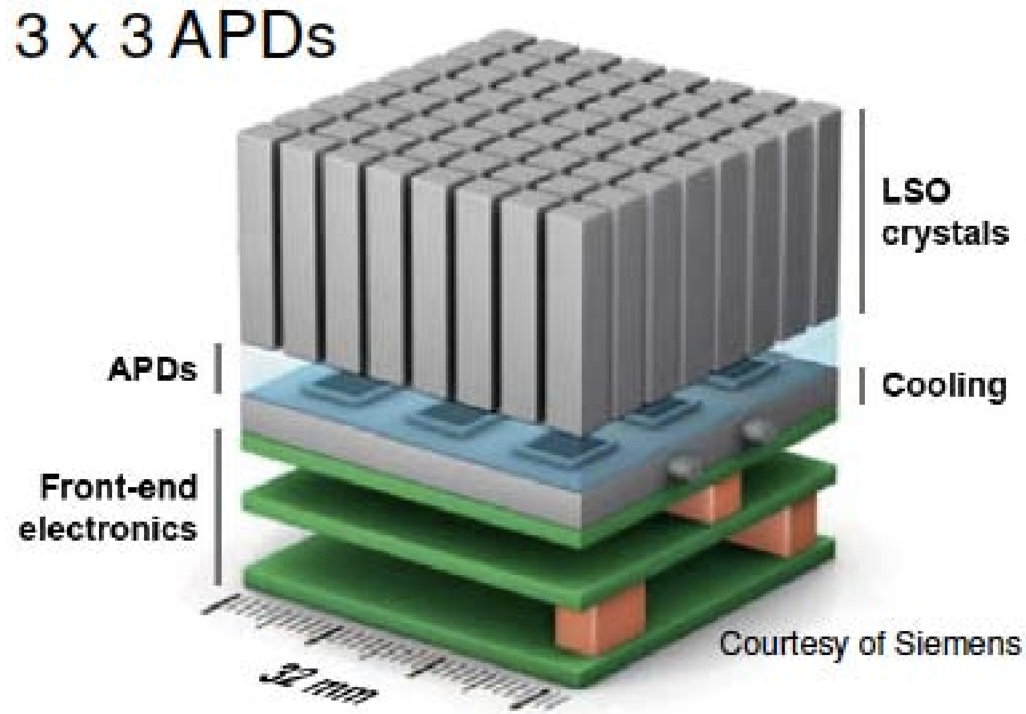
Departments of Nuclear Medicine and Departments of Radiology of

TUM LMU

SIEMENS Biograph mMR

8 anillos formados por 56 bloques detectores cada uno:

- Diámetro 65,6 cm
- FOV transaxial 59,4 cm
- FOV axial 25,8 cm



448 bloques de detectores
28,672 cristales
4,032 APDs

mCT vs mMR

	Biograph mMR	Biograph mCT[+]
Ring diameter	65.6 cm	84.2 cm
Axial FOV	25.8 cm	21.8 cm
Energy window	430 – 610 keV	435 – 650 keV
Sensitivity (0 cm)	1.50 % (1.50 %)	0.97 %
(10 cm)	1.38 % (1.38 %)	0.95 %
Scatter fraction[1]	36.7 %	33.2 %
Spatial resolution[2]	4.3 mm (4.3 mm)	4.4 mm

[+] B. W. Jakoby et al., Phys. Med. Biol. **56** (2011) 2375-2389

[1] at low activities
[2] near the centre of the FOV
( ) values with MR sequence running

NUEVAS TECNICAS de DETECCIÓN en PET/RM

SiPM: Fotomultiplicadores de Silicio.

CZT: Detectores de estado sólido.

Silicon Photomultipliers (SiPMs)

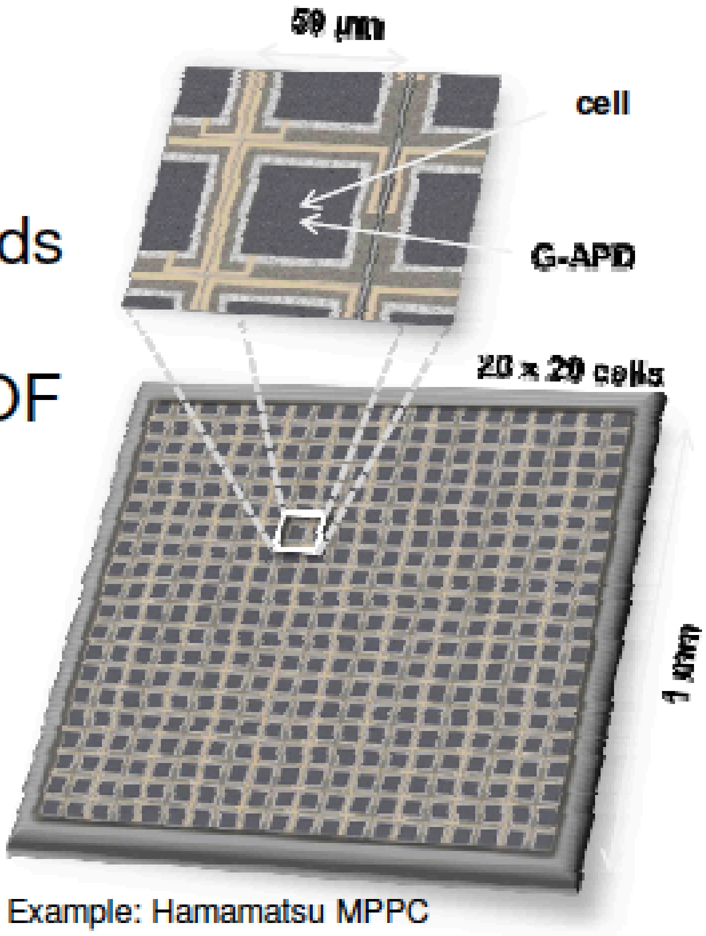
- Array of Geiger-mode APDs

Pros

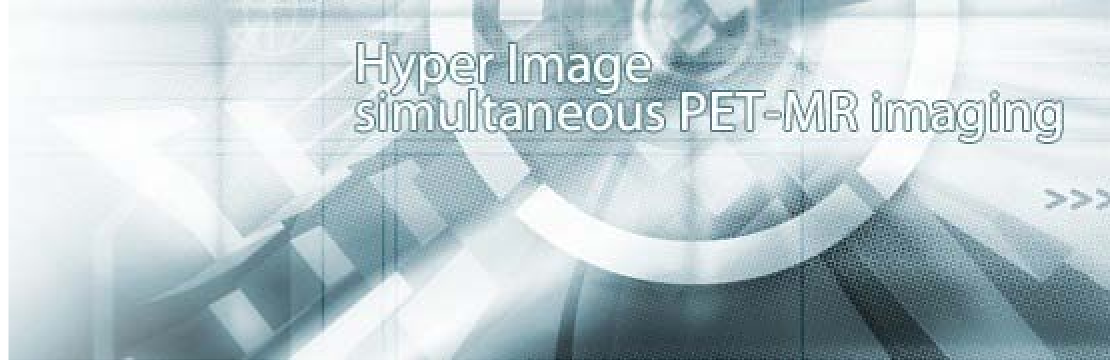
- Insensitivity to magnetic fields
- High gain (> 10^5)
- Fast (~ 1 ns rise time) → TOF

Cons

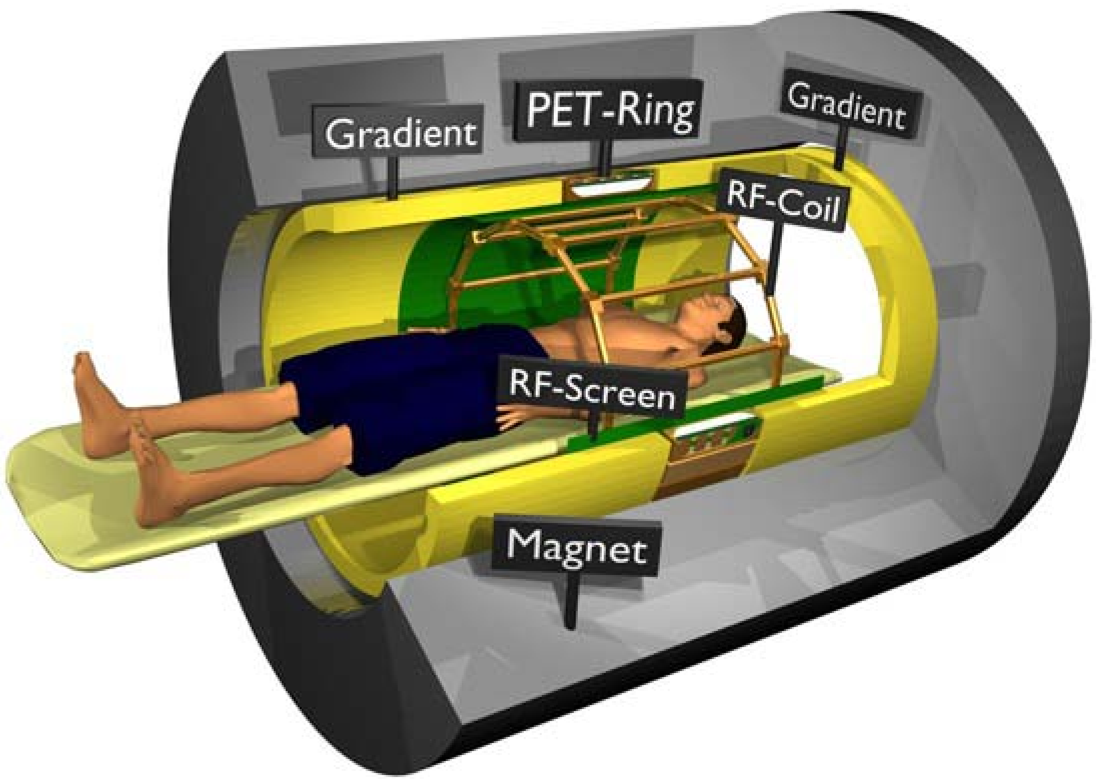
- Limited dynamic range
- Optical crosstalk
- Temperature dependence



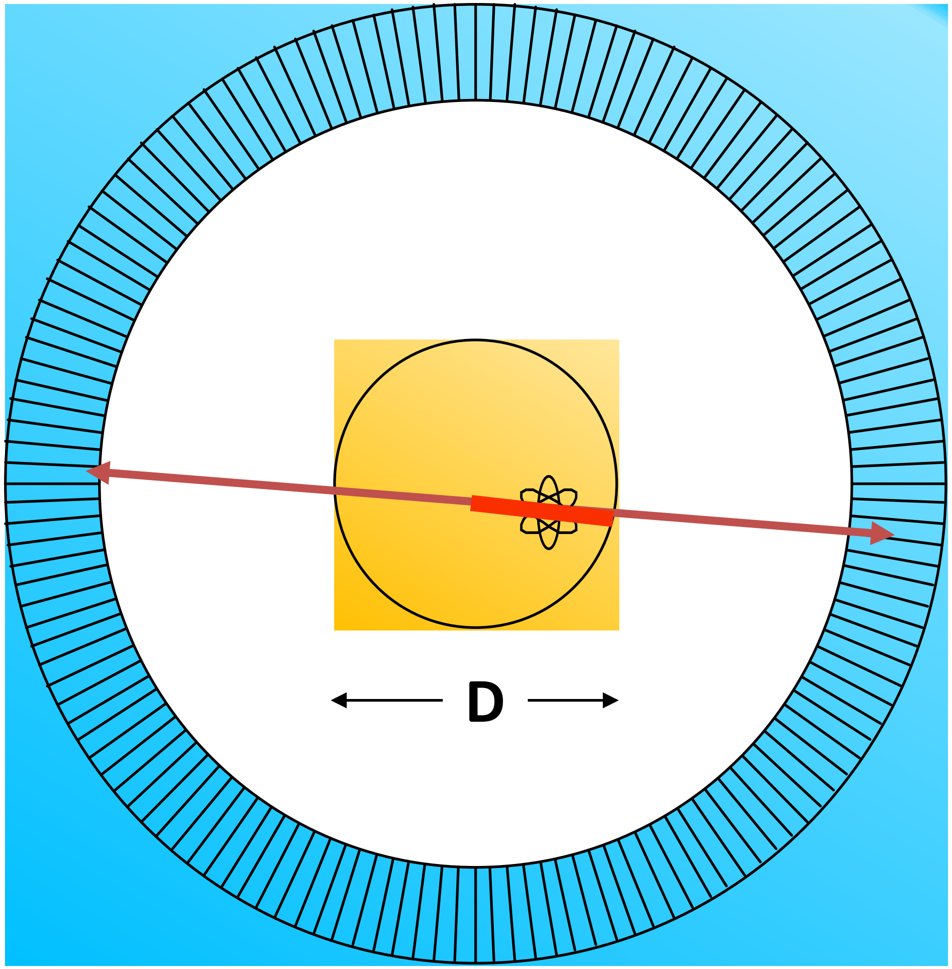
Example: Hamamatsu MPPC



http://www.hybrid-pet-mr.eu/



Time-of-Flight PET

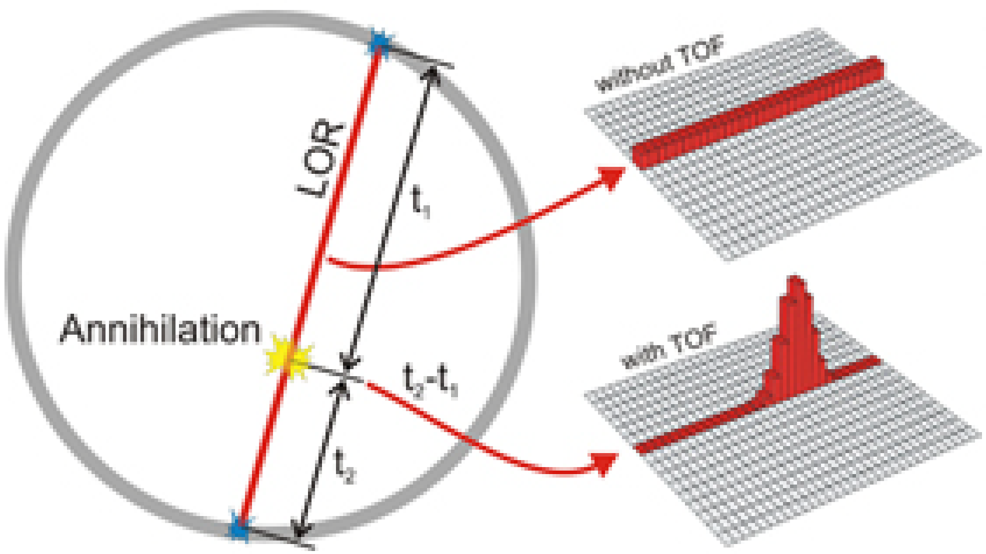


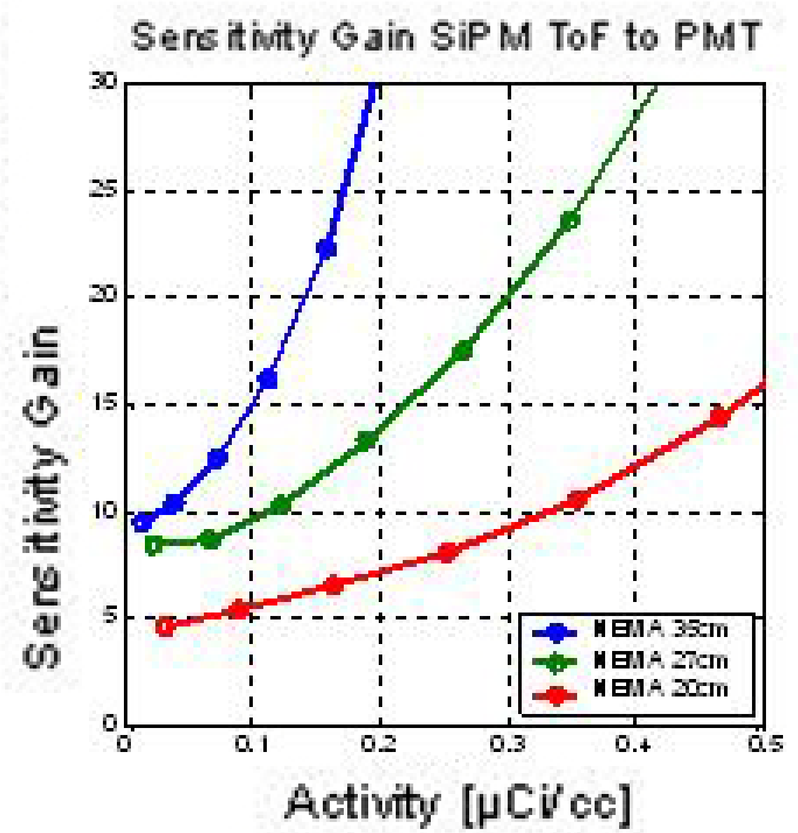
- Medida del tiempo de vuelo (TOF) para localizar fuente en el LOR.
- Información TOF reduce ruido de la imagen.
- PET TOF en 1980 con BaF2 y CsF
- 500 ps resolucion temporal

$\Rightarrow$ 8 cm resolucion espacial

- Reduce el error en un factor $2D/c\Delta t$
- 500 ps resolucion temporal $\Rightarrow$ reducción en el error en un factor de 5

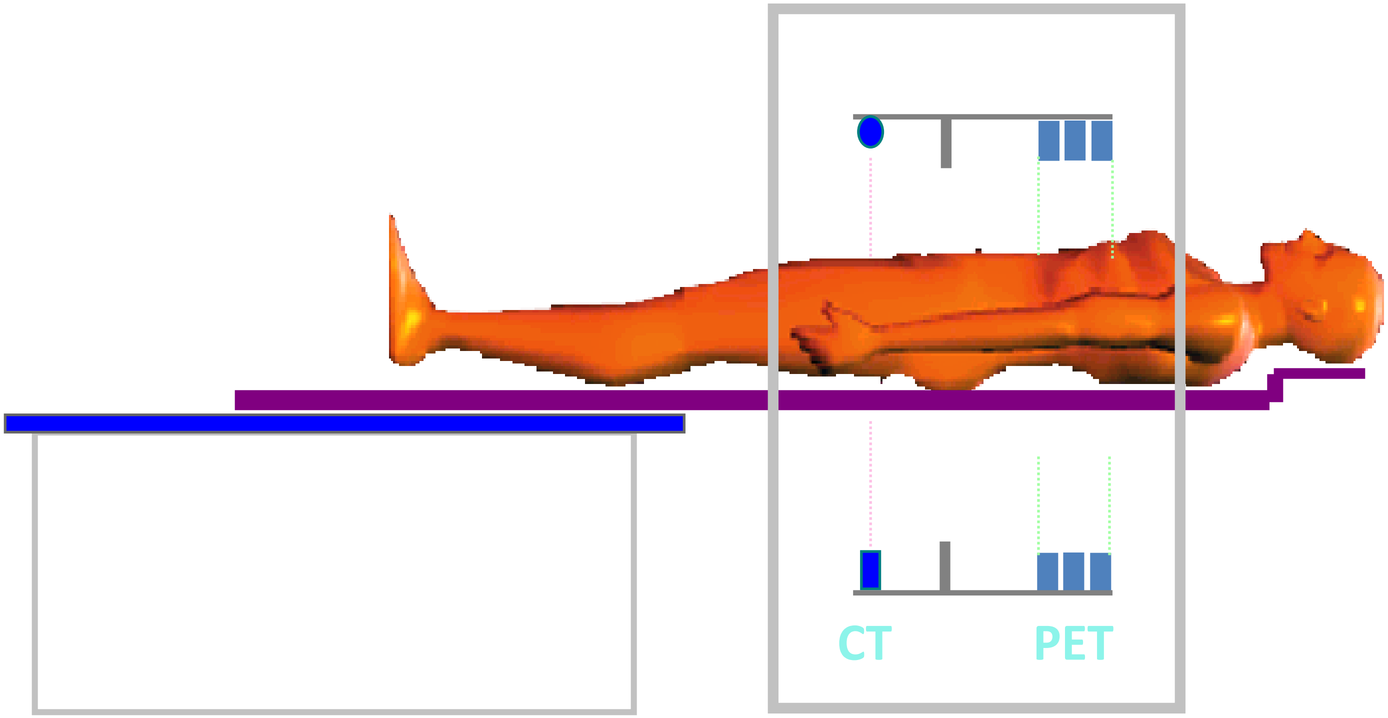
TOF-PET con detectores SiPM



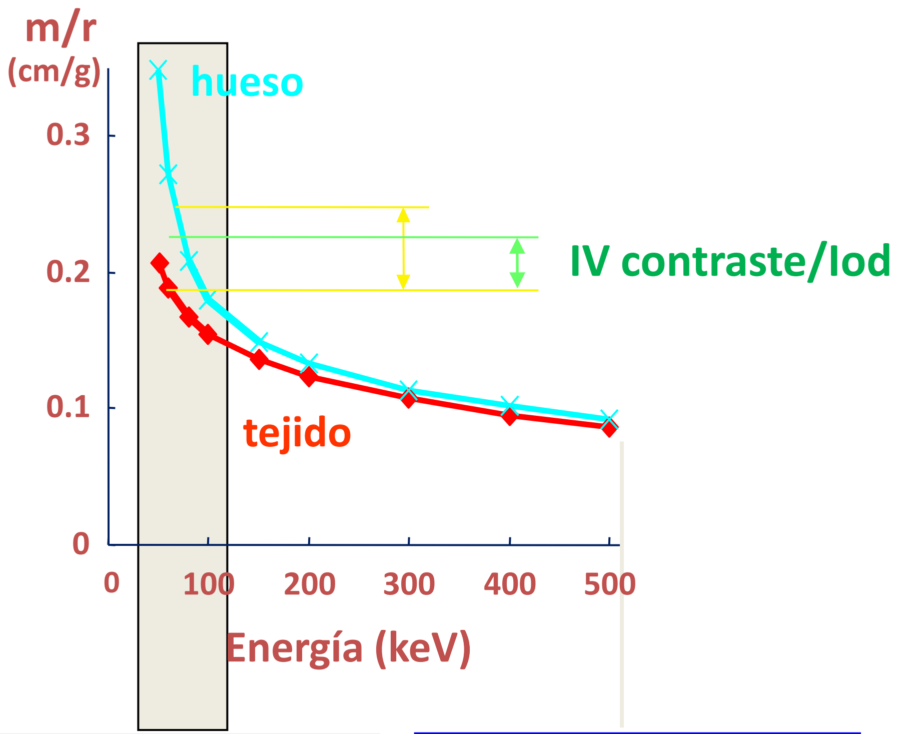


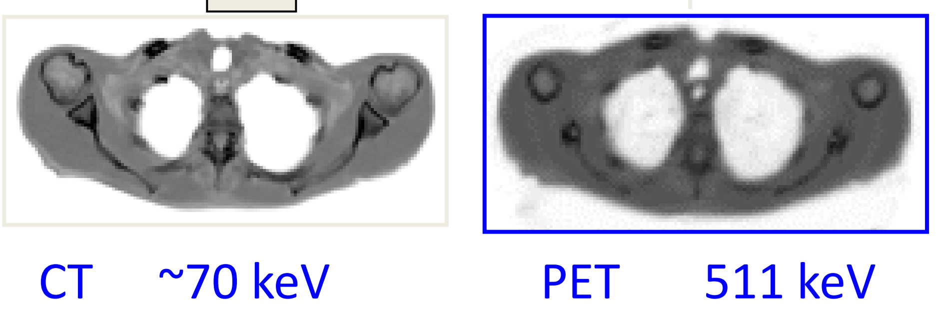
CORRECCIÓN de ATENUACIÓN

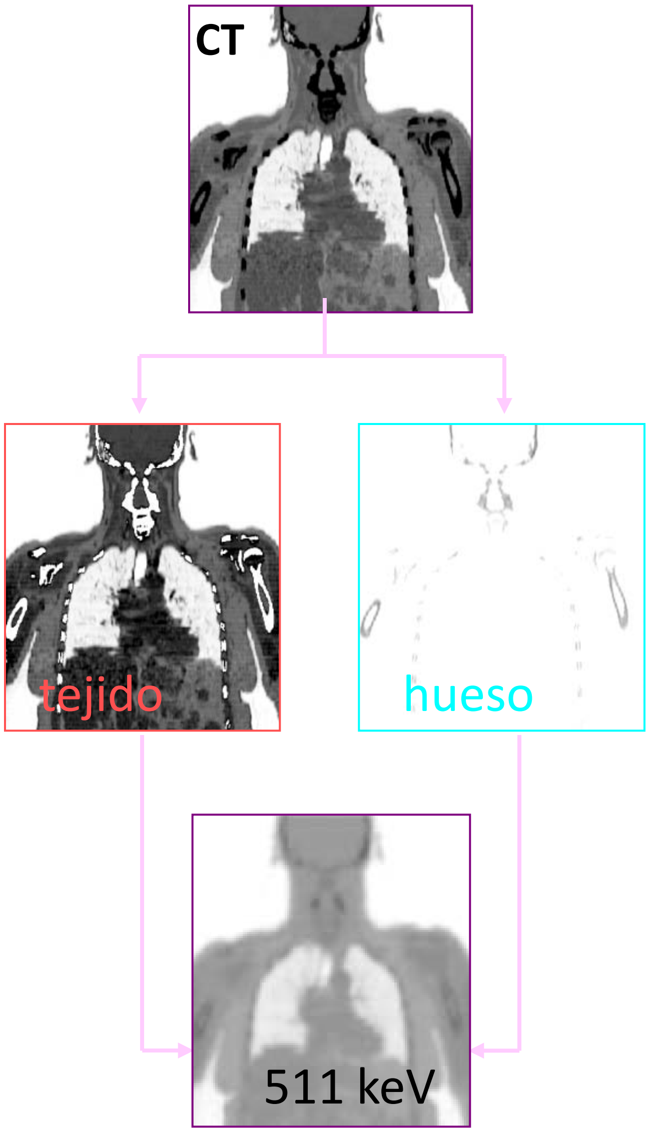
en PET/TAC



PET- Correccion por atenuación con datos del TAC *Kinahan 1998*







PET-Corrección de Atenuación con datos de TAC

Método Híbrido

$\mu_{PET}=0{,}096 \cdot \mu_{CT}$ para HU ≤ 300

$\mu_{PET}=0{,}079 \cdot \mu_{CT}$ para HU > 300

$\mu_{CT}=\mu_{w}\,(HU/1000) + 1$

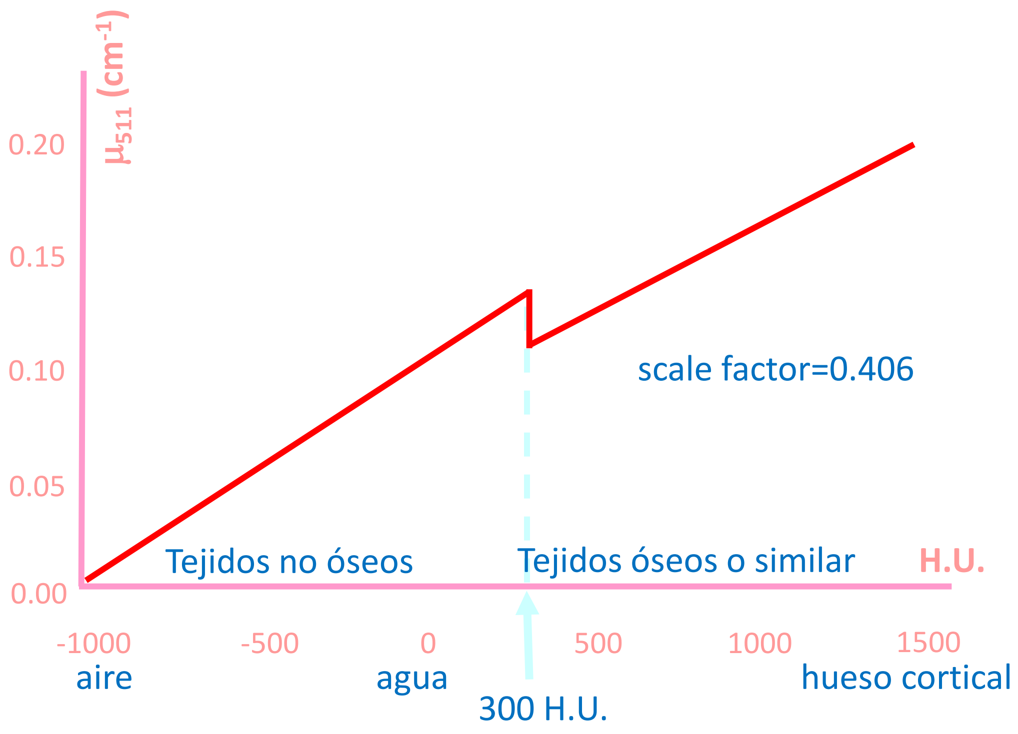


Imagen Escalada

Adaptación a resolución de PET

Forward projection

CORRECCIÓN de ATENUACIÓN con RM

La corrección de atenuación con imágenes de RM no es tan directa: las imágenes de RM no representan mapas de coeficientes de atenuación (*μ maps).*

Las imágenes anatómicas de RM representan mapas de la densidad de los protones mientras que los rayos X (fotones) son proporcionales a la densidad de los electrones.

El aire y los huesos corticales no proporcionan una señal medible con RM.
Diferencia en 2500 HU en sus propiedades de atenuación para los fotones.

Más fácil para el cerebro que para el resto del cuerpo.

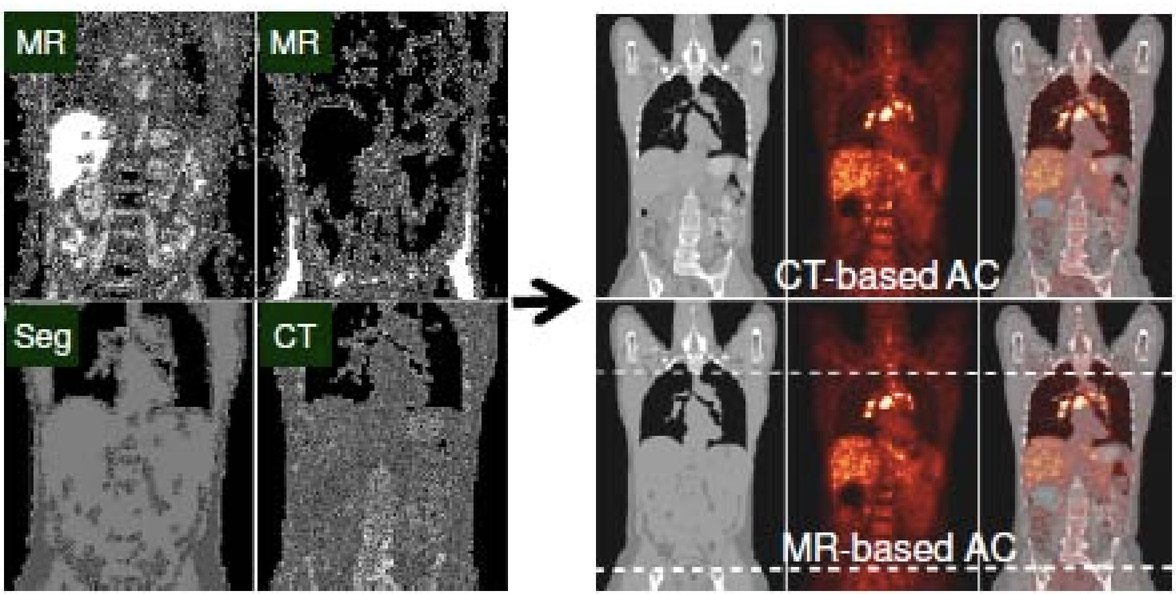
Para el cerebro, las aproximaciones son:
Segmentación de RM (Kops et al 2006, Zaidi et al 2003),
registro en un atlas de pares de imágenes de RM y TAC (Hofmann et al 2007).

El principio consiste en alinear la imagen adquirida con una imagen promedio de RM a partir de un atlas que contiene pares de exploraciones registradas de RM y TAC. La misma transformación determinada a partir del alineamiento de la RM del paciente con la RM del atlas se aplica al TAC a partir del atlas.

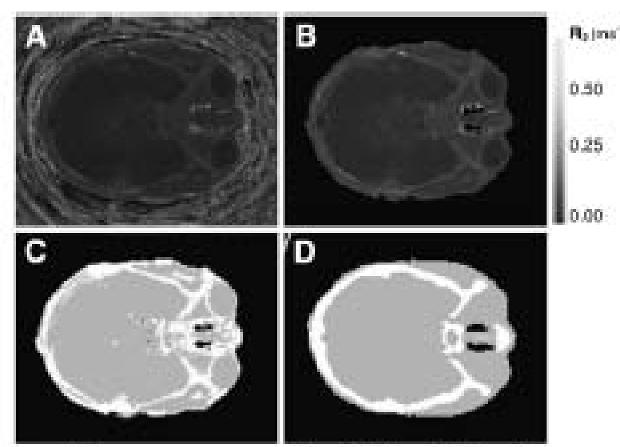
CORRECCIÓN DE ATENUACIÓN PET BASADA EN RM

CLASIFICACIÓN DE LOS TEJIDOS:
Segmentación pulmón, grasa y tejido blando.

+ Sencillo y rápido.
+ No hay hipótesis sobre la anatomía del paciente.
- Errores en lesiones dentro del hueso (hasta el 13% SUV).



Martinez-Möller et al. *J Nucl Med 2009*



Keereman et al. *J Nucl Med* 2010

CORRECCIÓN DE ATENUACIÓN PET BASADA EN RM

Secuencia Dixon de 2-puntos (18s/cama) para generar imágenes de agua y grasa

Utilizar umbrales apropiados para segmentar las imágenes de agua y grasa.

Fat image

Water image

Mapa de atenuación con 4 clases de tejido diferentes: fondo, pulmón, grasa y tejido blando.

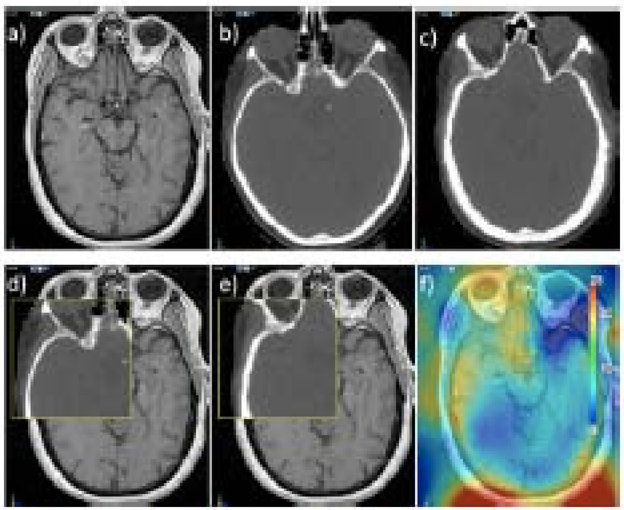
μmap

CORRECCIÓN DE ATENUACIÓN PET BASADA EN RM

Utilizar el ATLAS y aprendizaje de la máquina

Coregistro de RM con el atlas

+ Se detectan los huesos.
- Coregistro complicado y generación del atlas.
- Desviación de la geometría estándard?



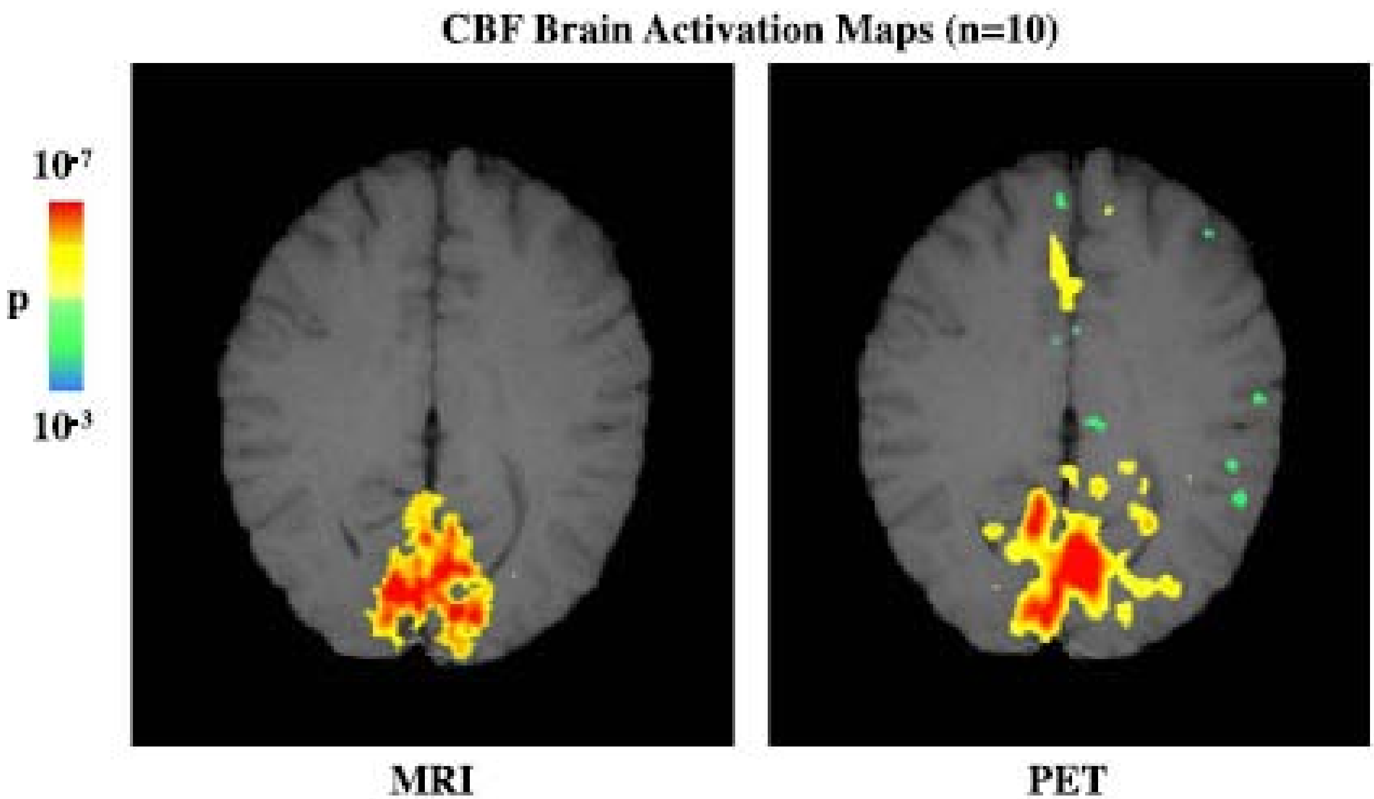
Schreibmann et al. *Med Phys 2010*

Hofmann et al. *Eur J Nucl Med 2009*

APLICACIONES del PET/RM

1. NEUROLOGÍA.
   - Enfermedades Neurodegenerativas.
   - Psiquiatría.
   - Epilepsía.
2. ONCOLOGÍA.
   - Cáncer de mama.

Cross-validation of MR perfusion measurements against the ^{15}O-PET gold standard.

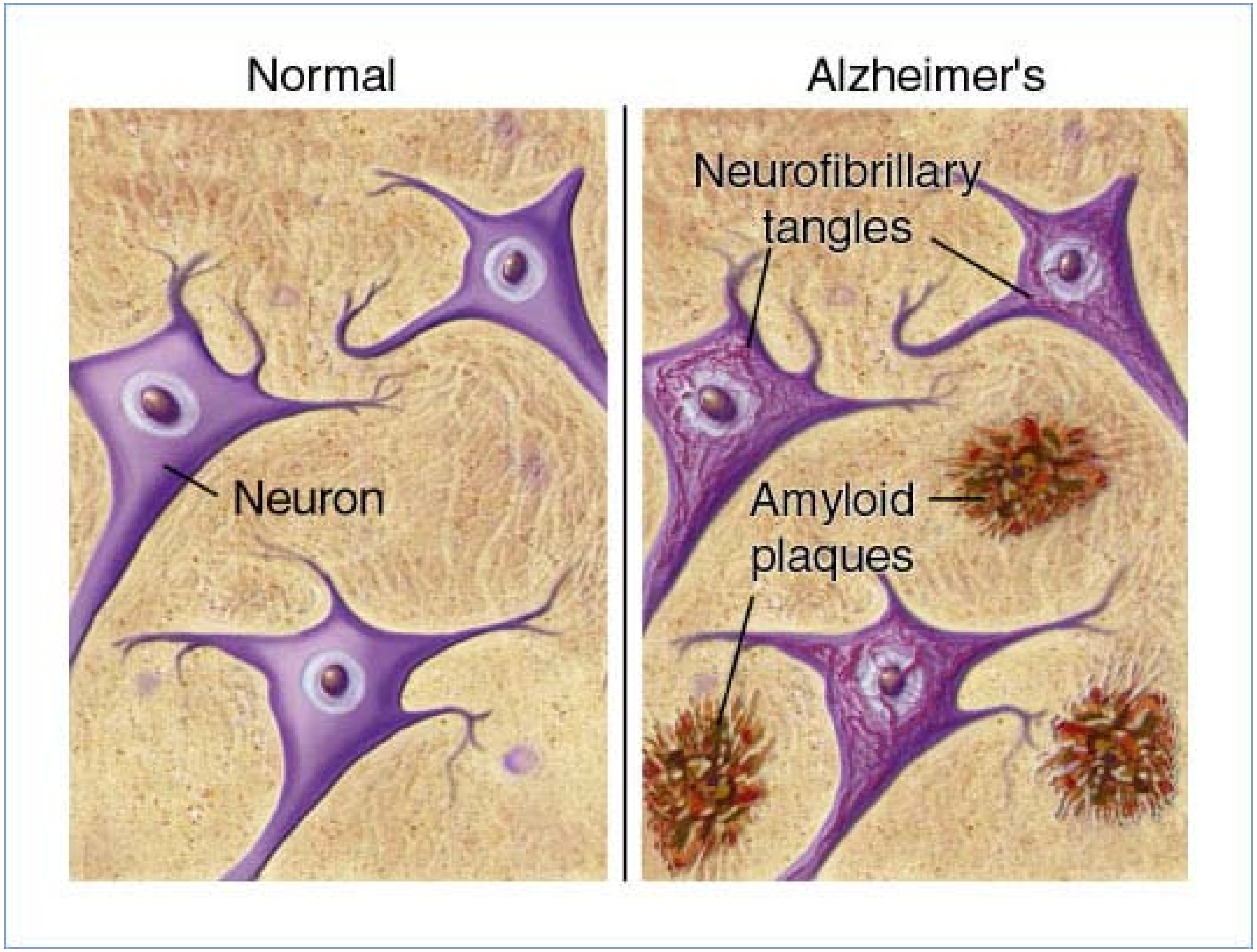


Functional maps of CBF averaged over 10 subjects during visual stimulation overlaid over the T1-weighted MRI image.

C.-M. Feng et al. / NeuroImage 22 (2004) 443–446

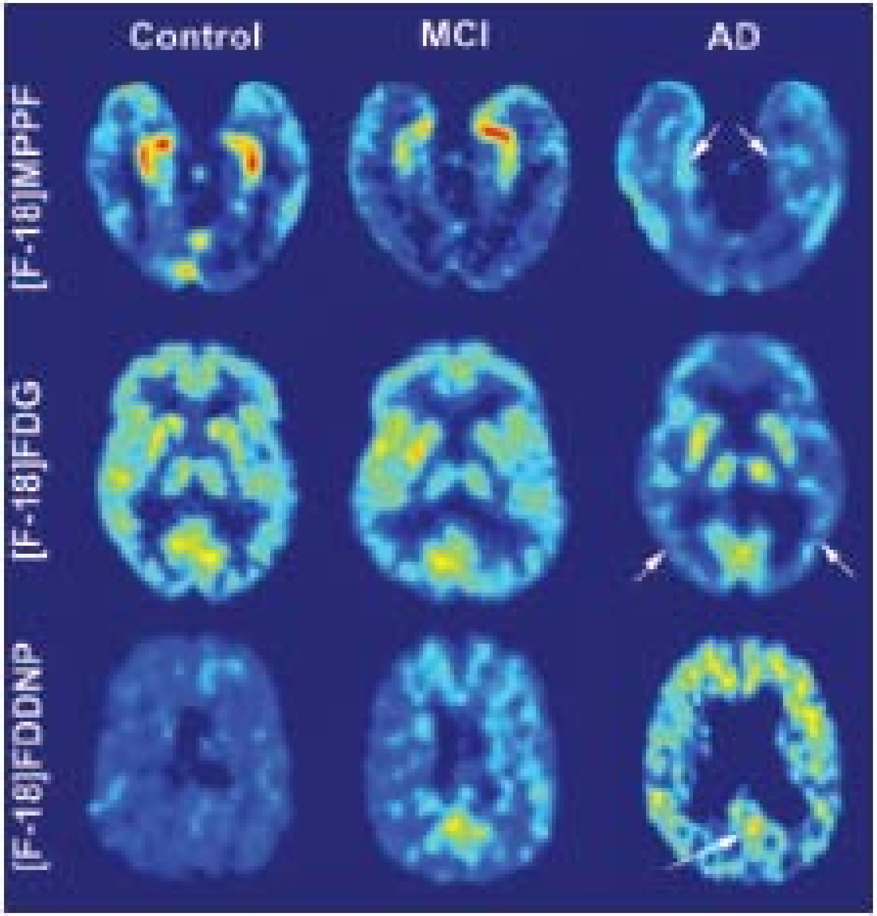
SONDAS MOLECULARES en NEUROLOGÍA.

ENFERMEDAD de ALZHEIMER

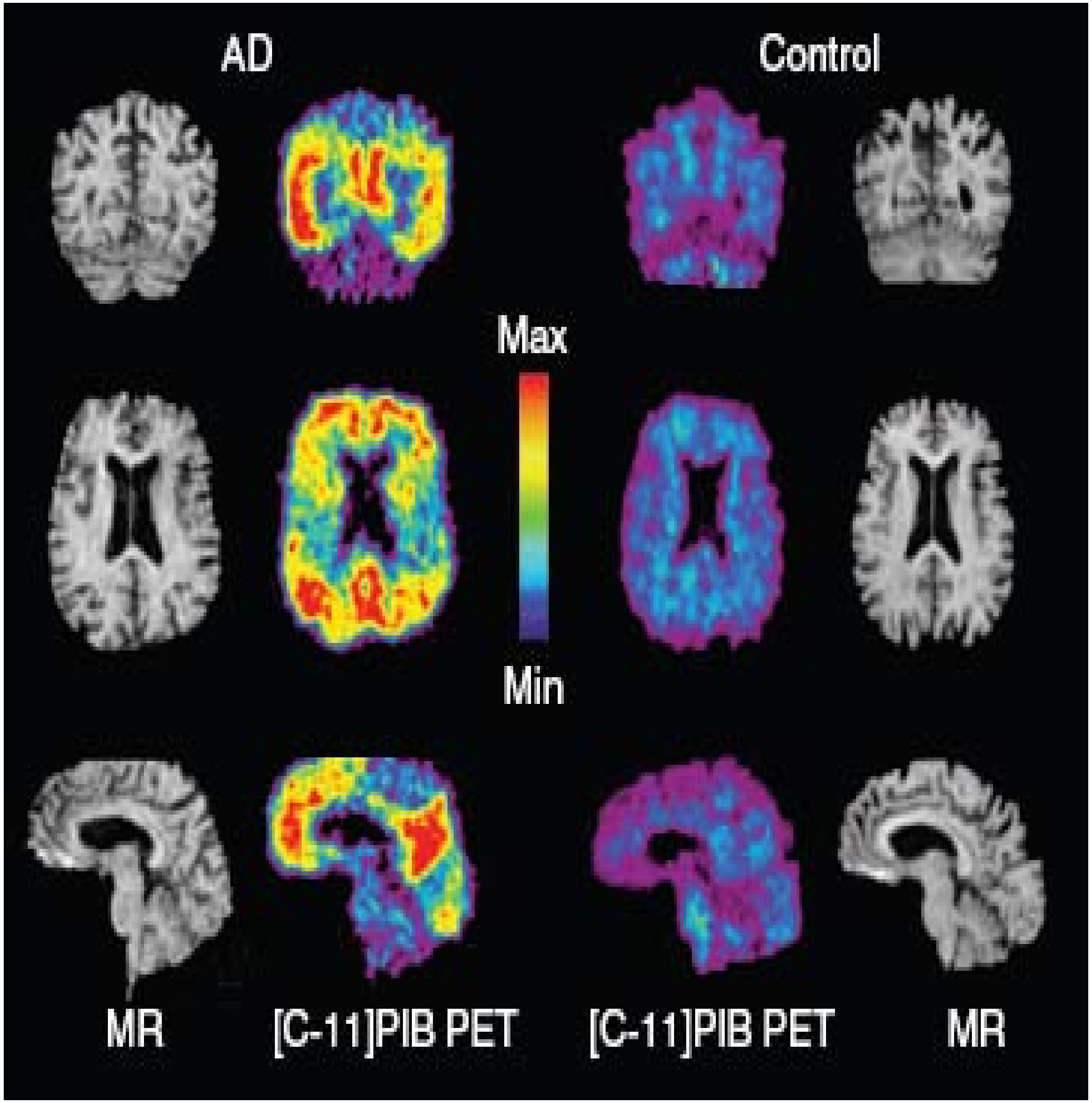


Serotonin 1A receptors in the living brain of Alzheimer's disease patients

Vladimir Kepe*, Jorge R. Barrio*†, Sung-Cheng Huang*, Linda Ercoli‡, Prabha Siddarth‡, Kooresh Shoghi-Jadid*, Gregory M. Cole§, Nagichettiar Satyamurthy*, Jeffrey L. Cummings¶, Gary W. Small‡, and Michael E. Phelps*†

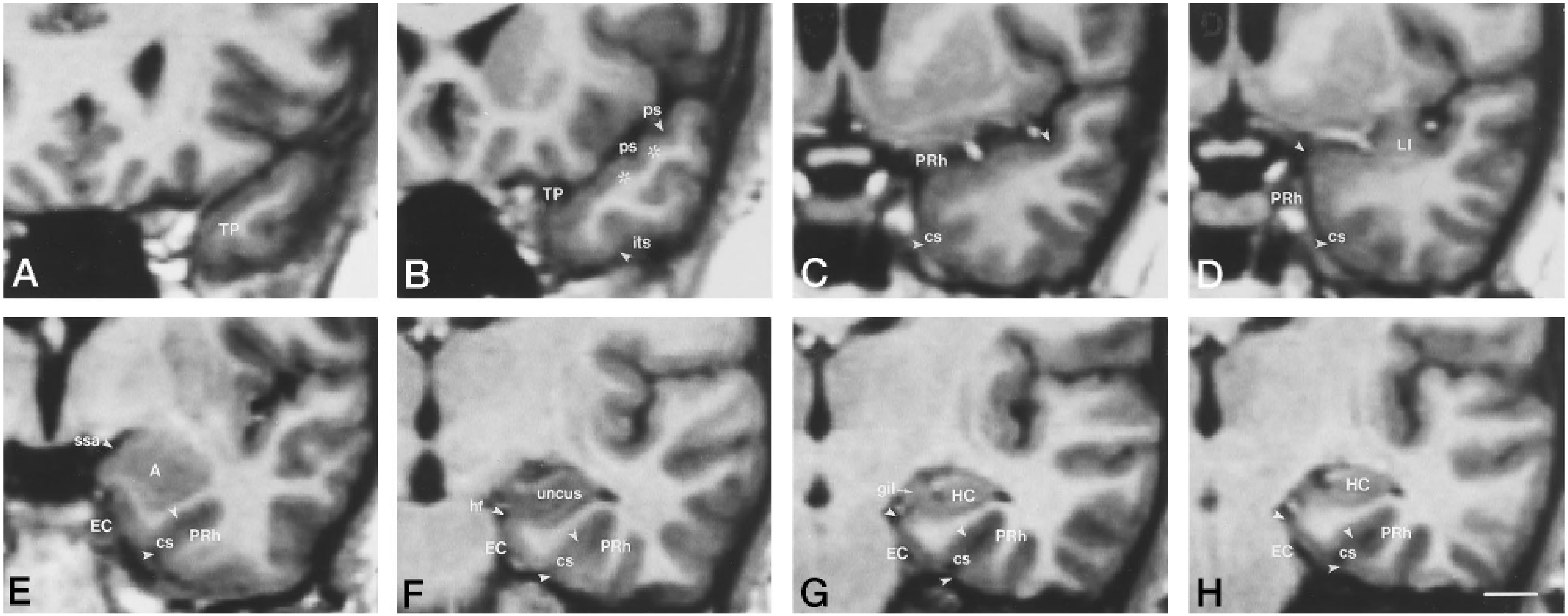


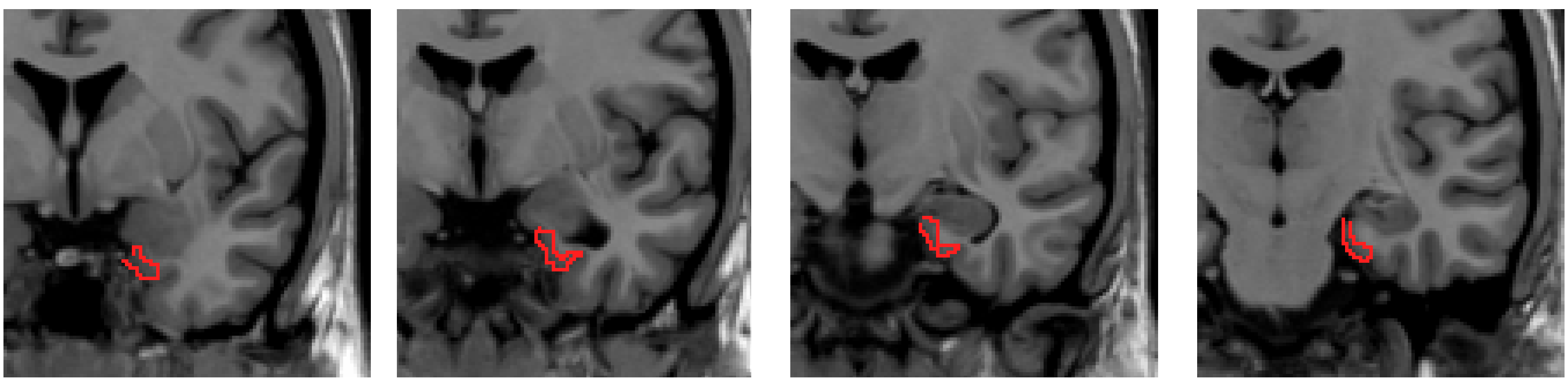
PNAS, 2006, 103 (3):702-7



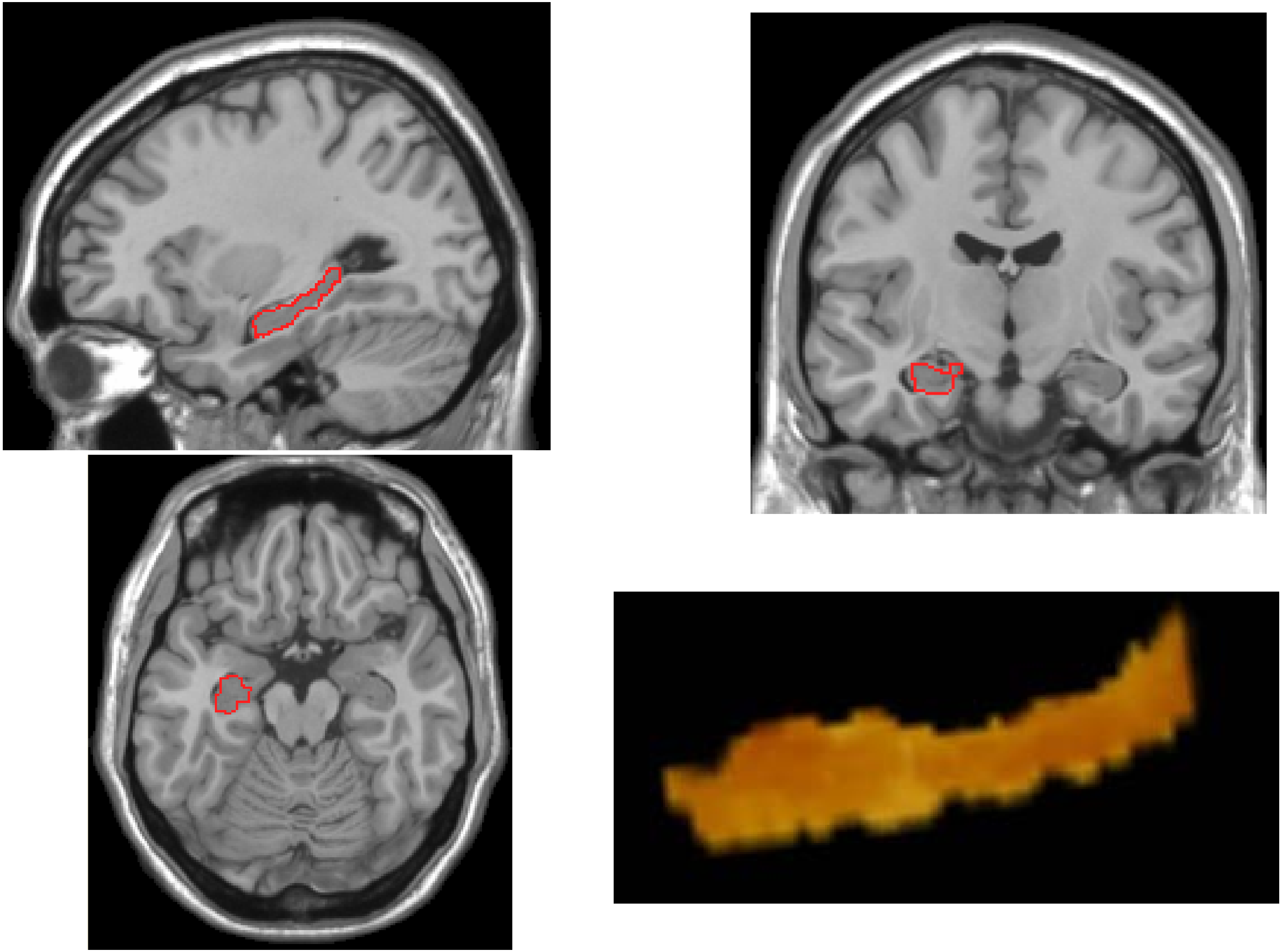
AD
Control
Max
Min
MR
[C-11]PIB PET
[C-11]PIB PET
MR

CÓRTEX ENTORRINAL

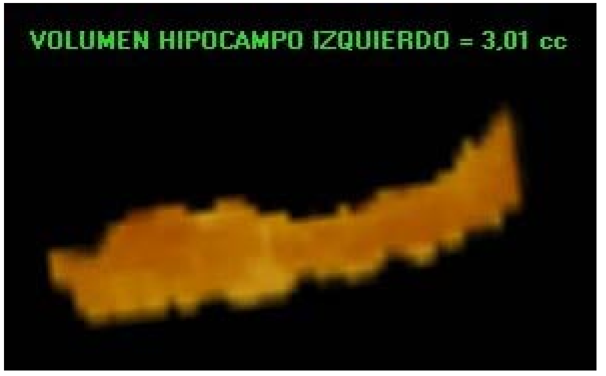


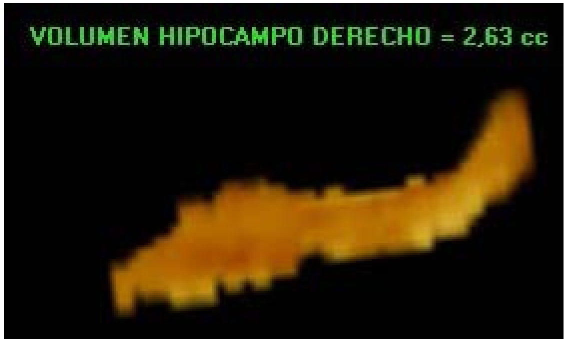


Insausti R, Juottonen K, Soininen H el al, *AJNR Am J Neuroradiol* 19 (1998):659 –671



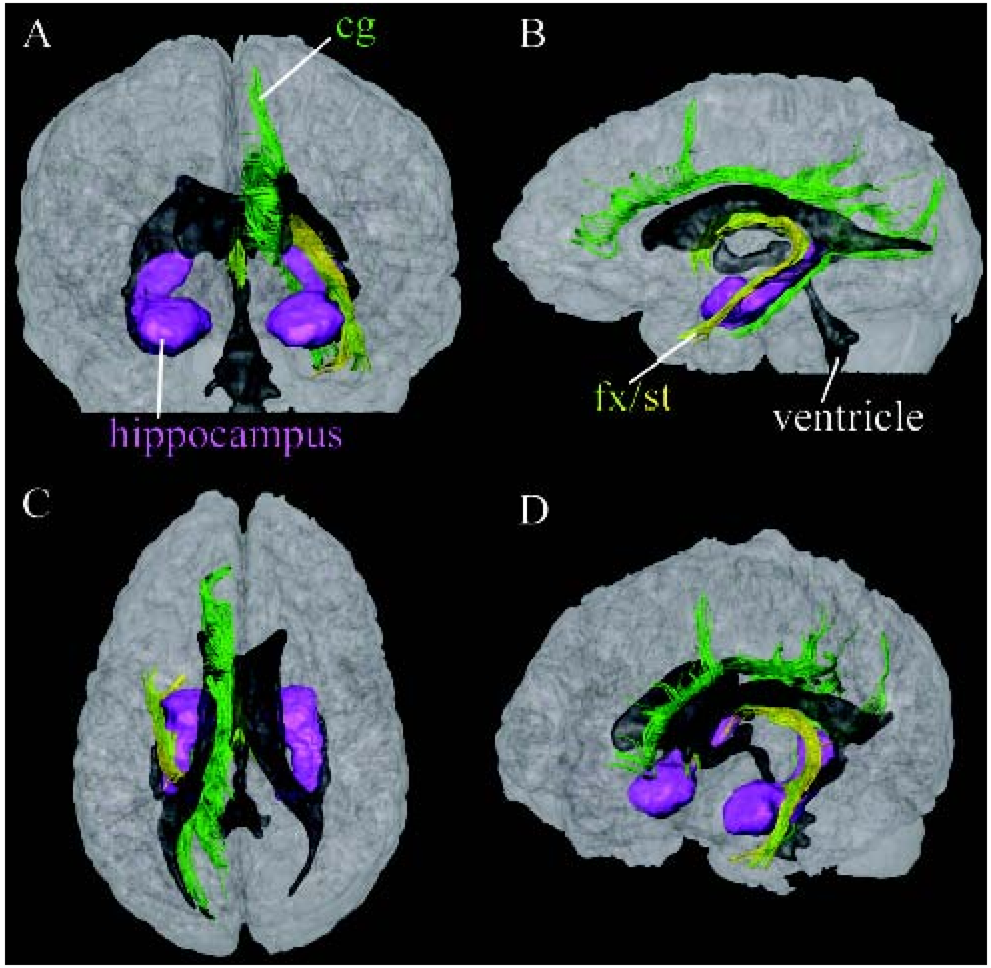
NORMAL





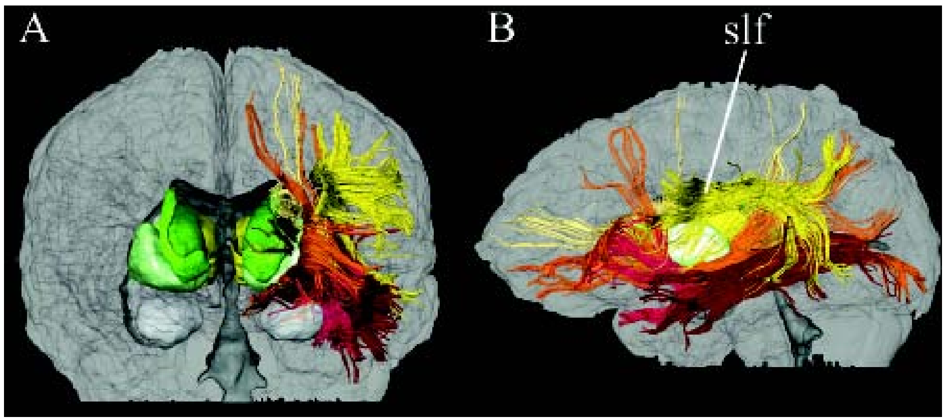
ALZHEIMER

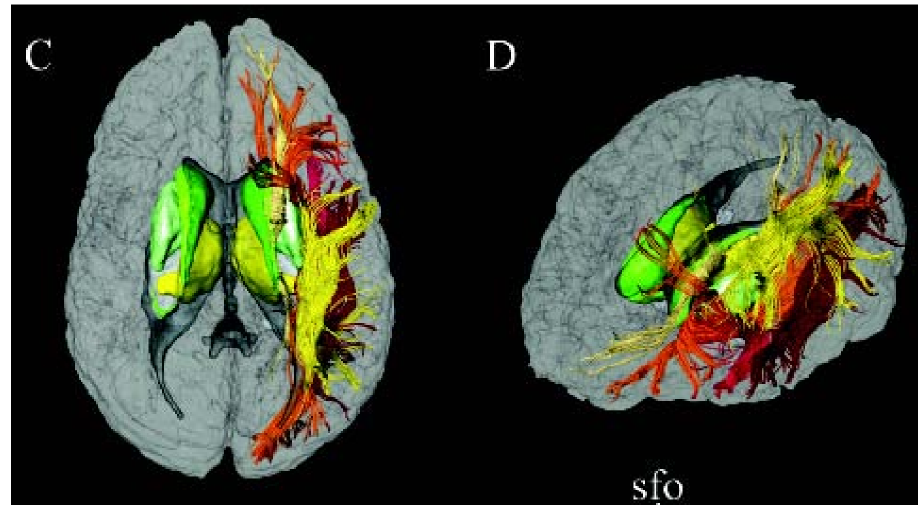
3D CIRCUITO LÍMBICO

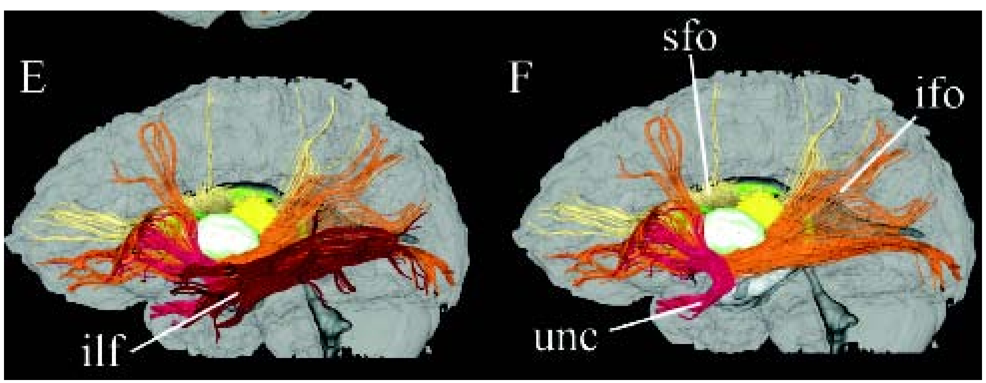


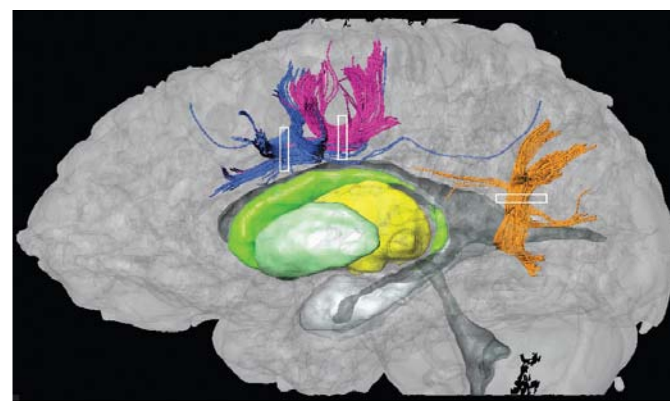
Wakana S, Jiang H, Nagae-Poetscher LM, et al. Radiology 2004; 230:77–87

3D VÍAS ASOCIACIÓN





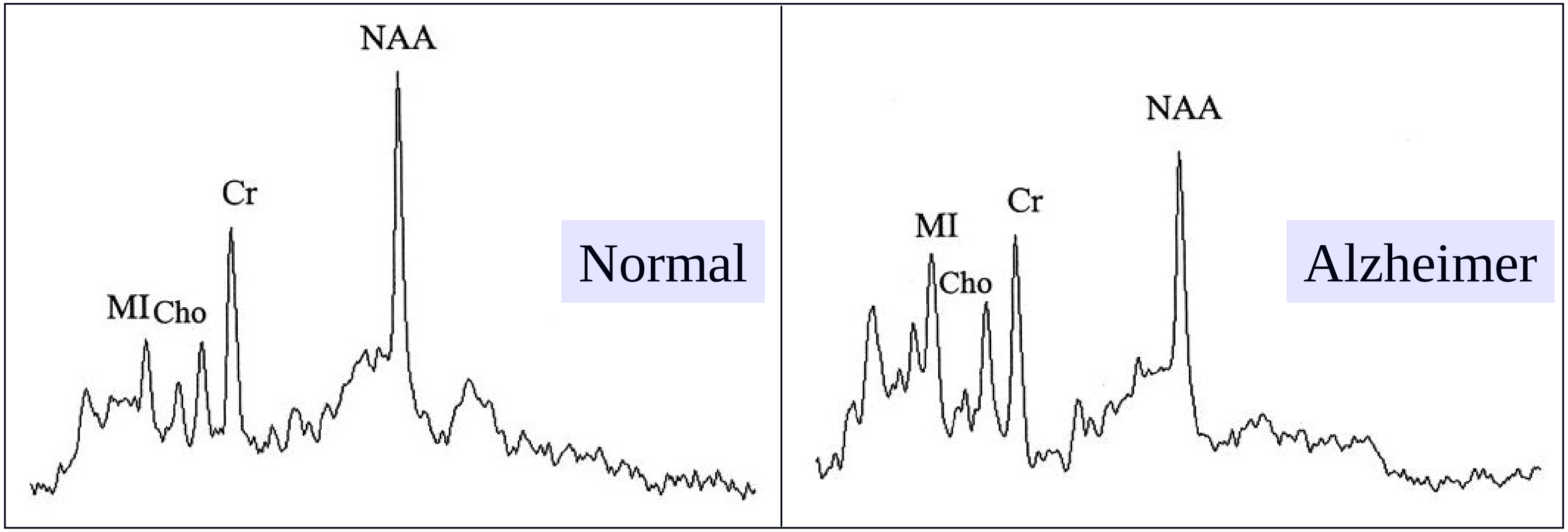




Wakana S, Jiang H, Nagae-Poetscher LM, et al. Radiology 2004; 230:77–87

ANÁLISIS MULTIVARIACIONAL

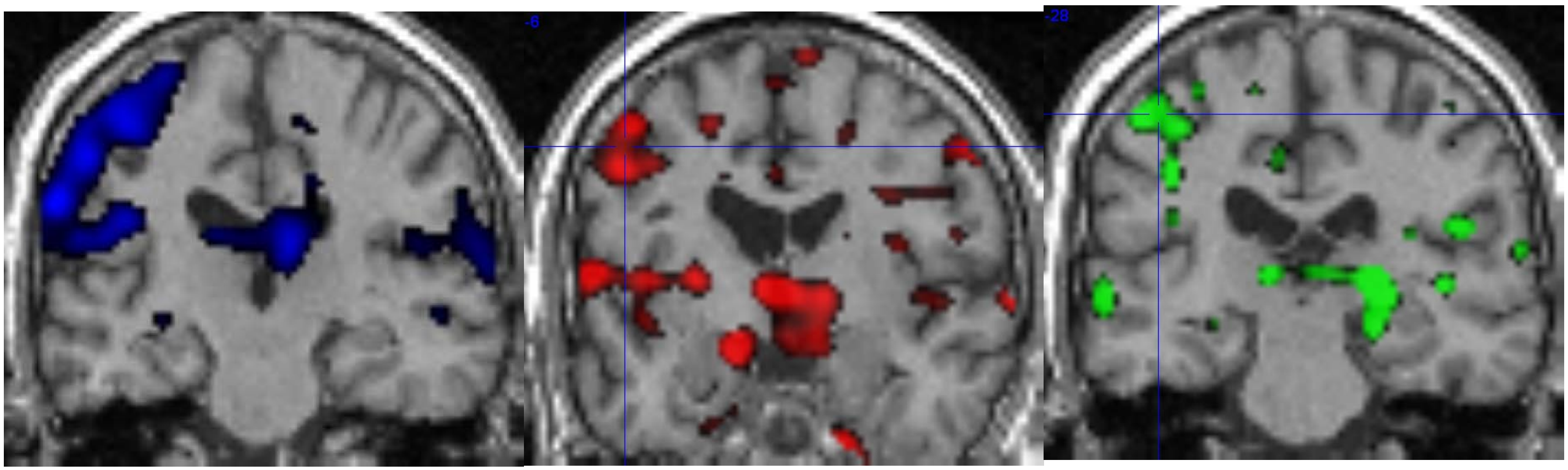
La correlación de información entre las diferentes técnicas de imagen proporcionará un diagnóstico más preciso



Multi-modality PET / MRI where to go?

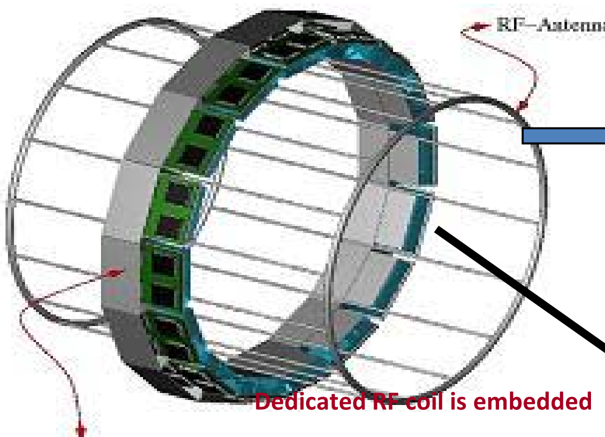
Combination of modality

Orthogona-lity



fMRI BOLD　　^{18}FDG PET　　^{11}C GR-205171 PET

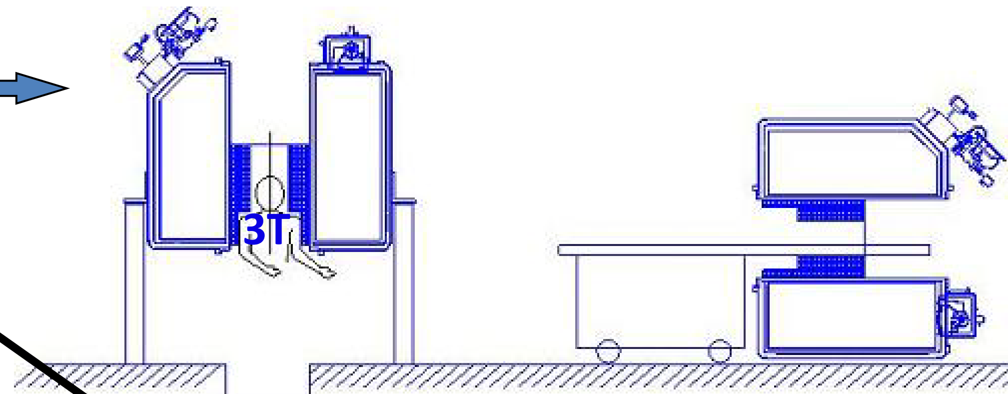
PET/MR project:



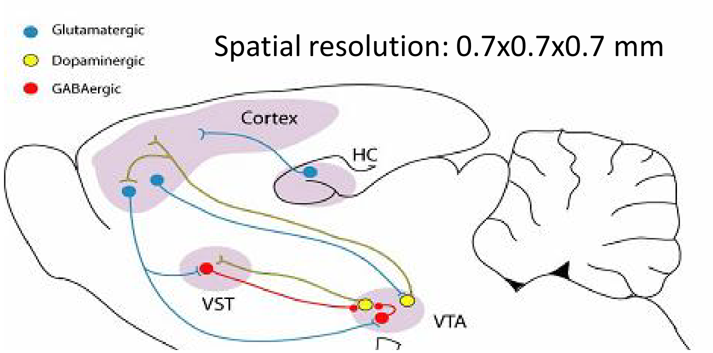
Dedicated RF-coil is embedded

in the dedicated PET-ring

New magnet design, GEMS-Oxford



Spatial resolution: 0.7x0.7x0.7 mm

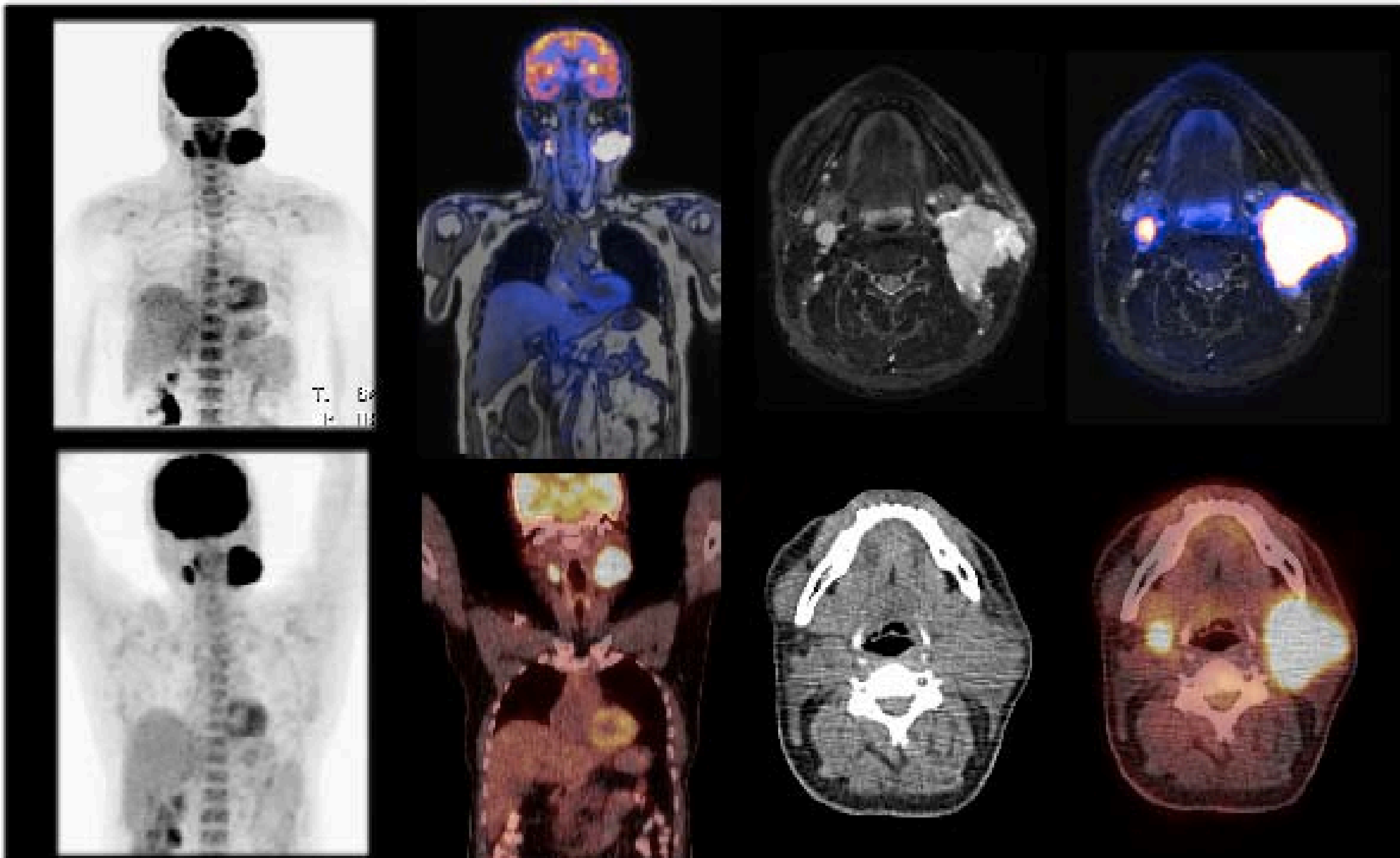


VTA= Ventral Tegmental Area

Academic Partners: Uppsala Univ., Karolinska, King's College, Univ. of Valencia

Courtesy, Jose´Benlloch & Bengt Nielsen et.al.

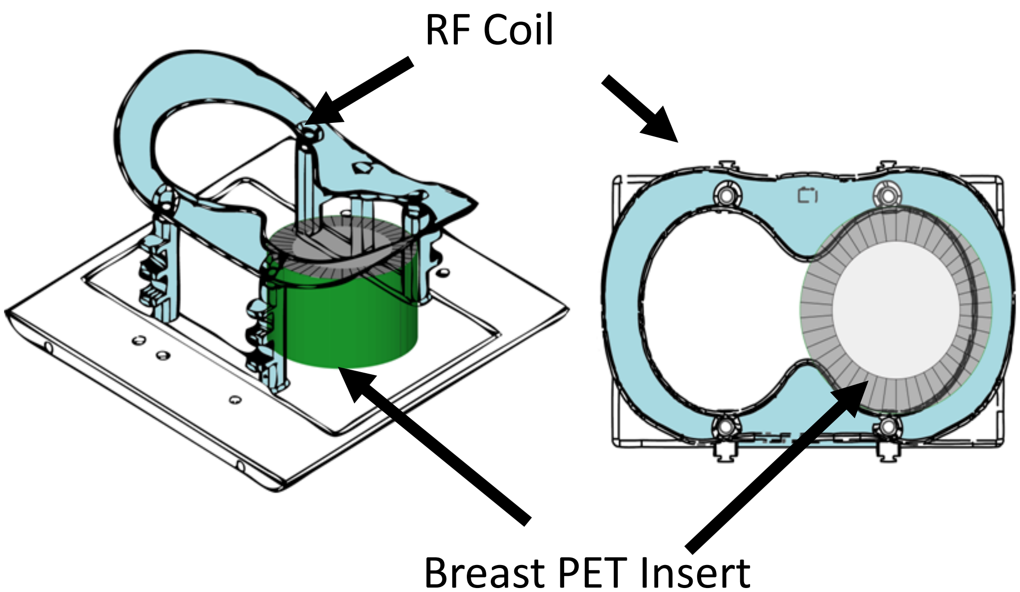
EJEMPLO CLÍNICO: LYMPHOMA CERVICAL

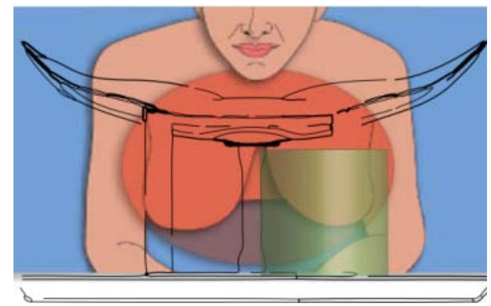


MR/PET Munich (TUM/LMU), funded by the DFG

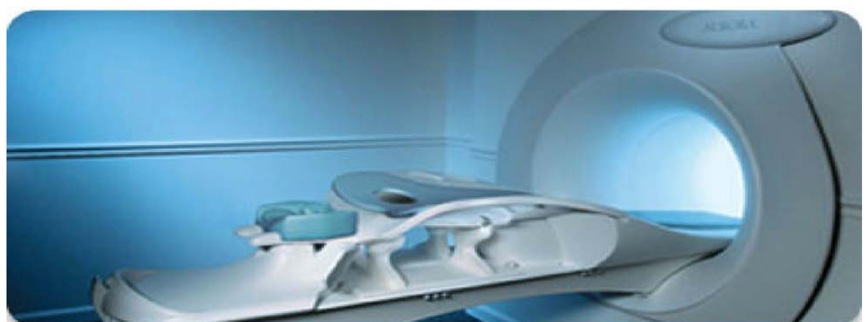
TUM LMU DFG

Simultaneous PET-MRI Breast Imaging



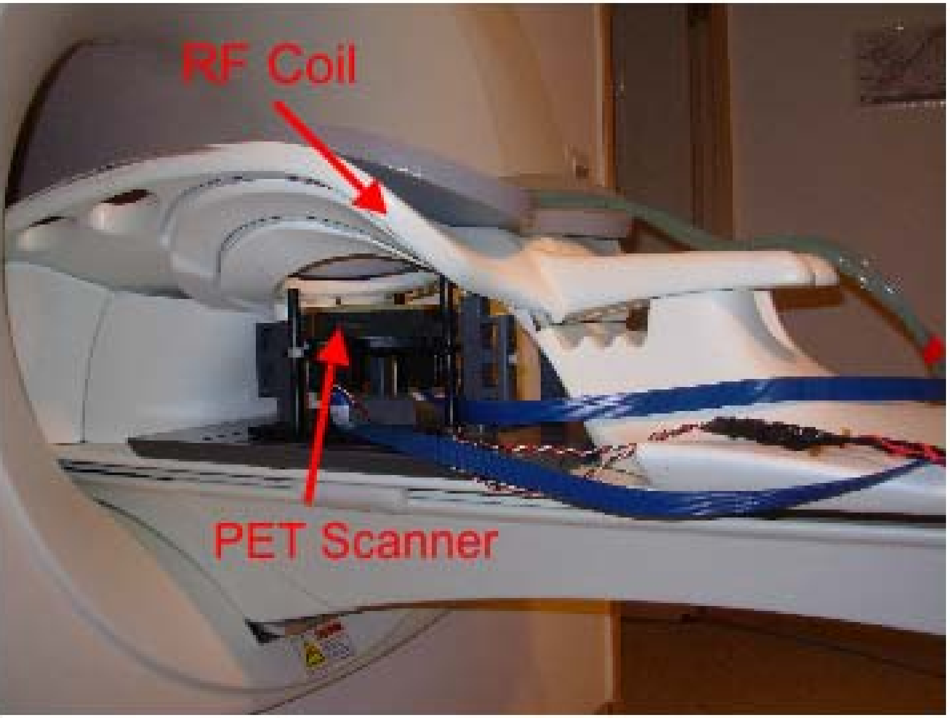


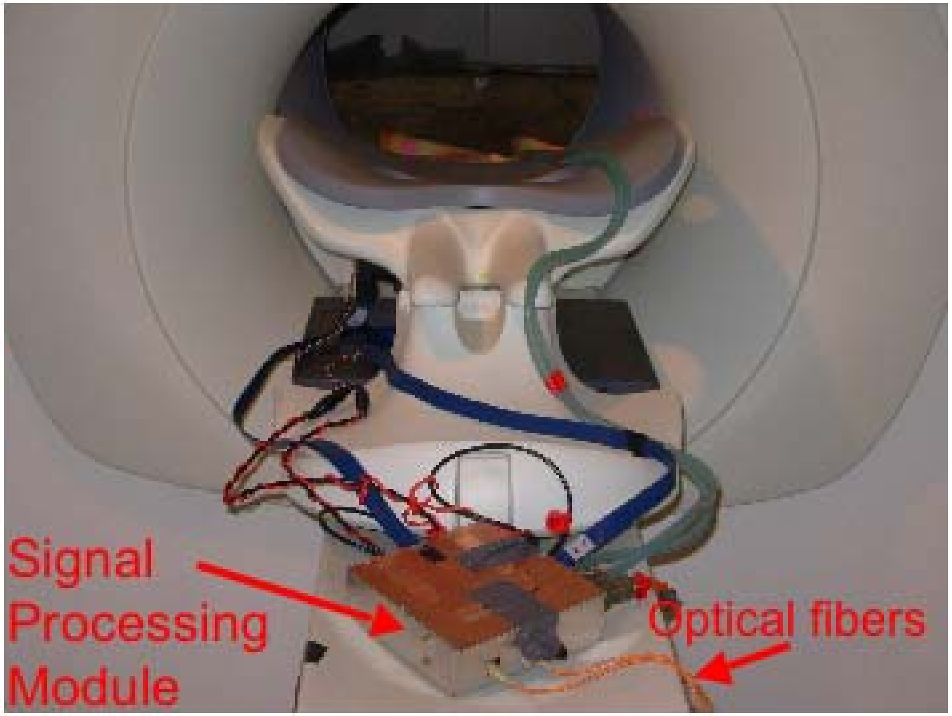
Patient positioned
with Breast PET insert
& Aurora Breast RF coil



Aurora Dedicated 1.5 T Breast MRI

Clinical Setup

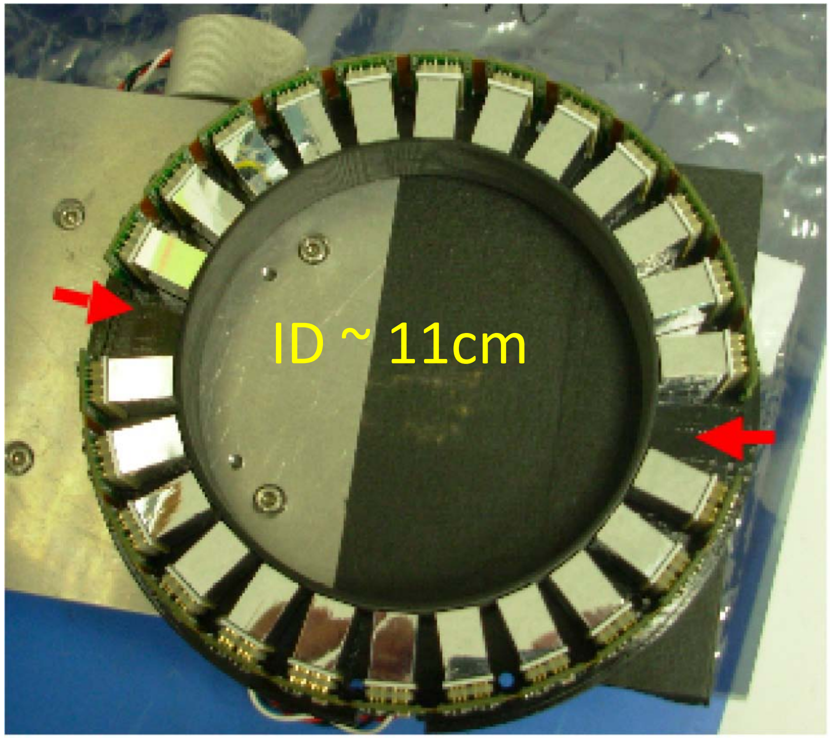




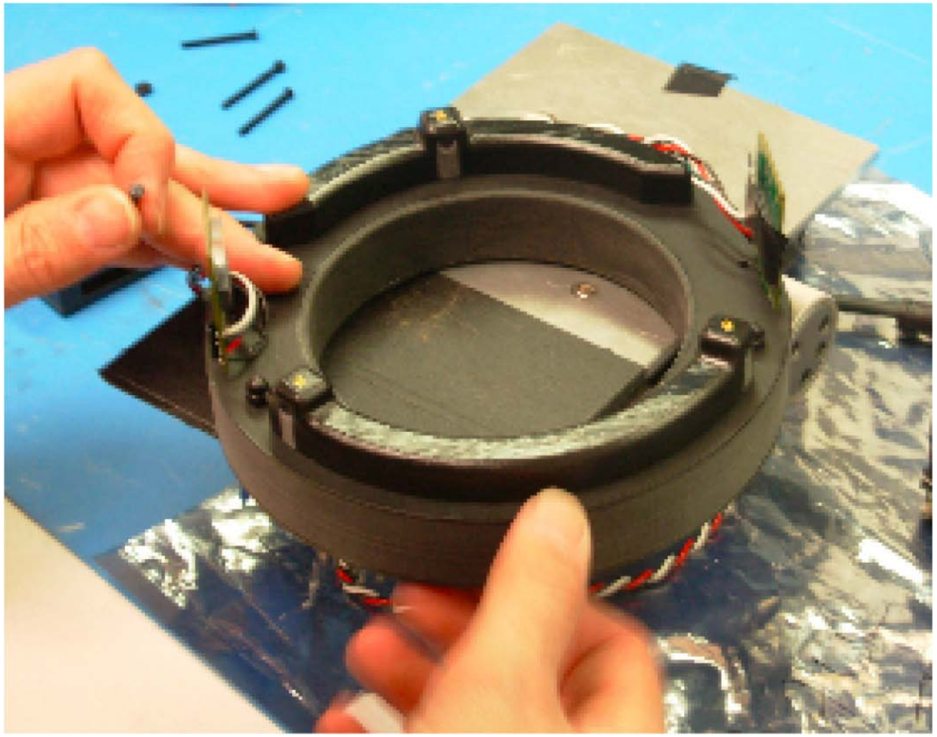
Clinical Setup - Phantom Scan

Clinical Prototype

Need larger ID and flexibility in axial coverage

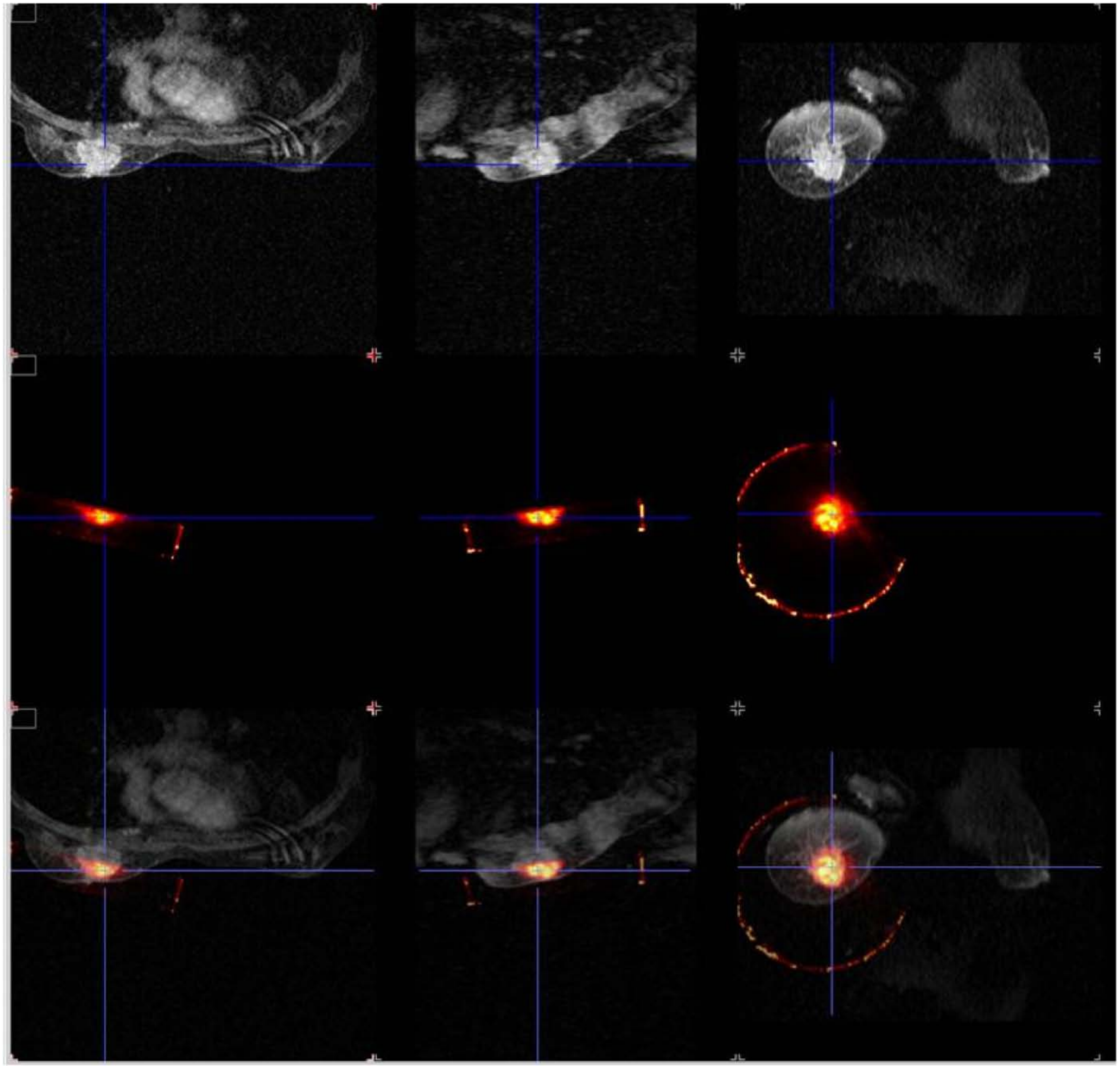


24 detector PET ring with a crystal wide gap on either side



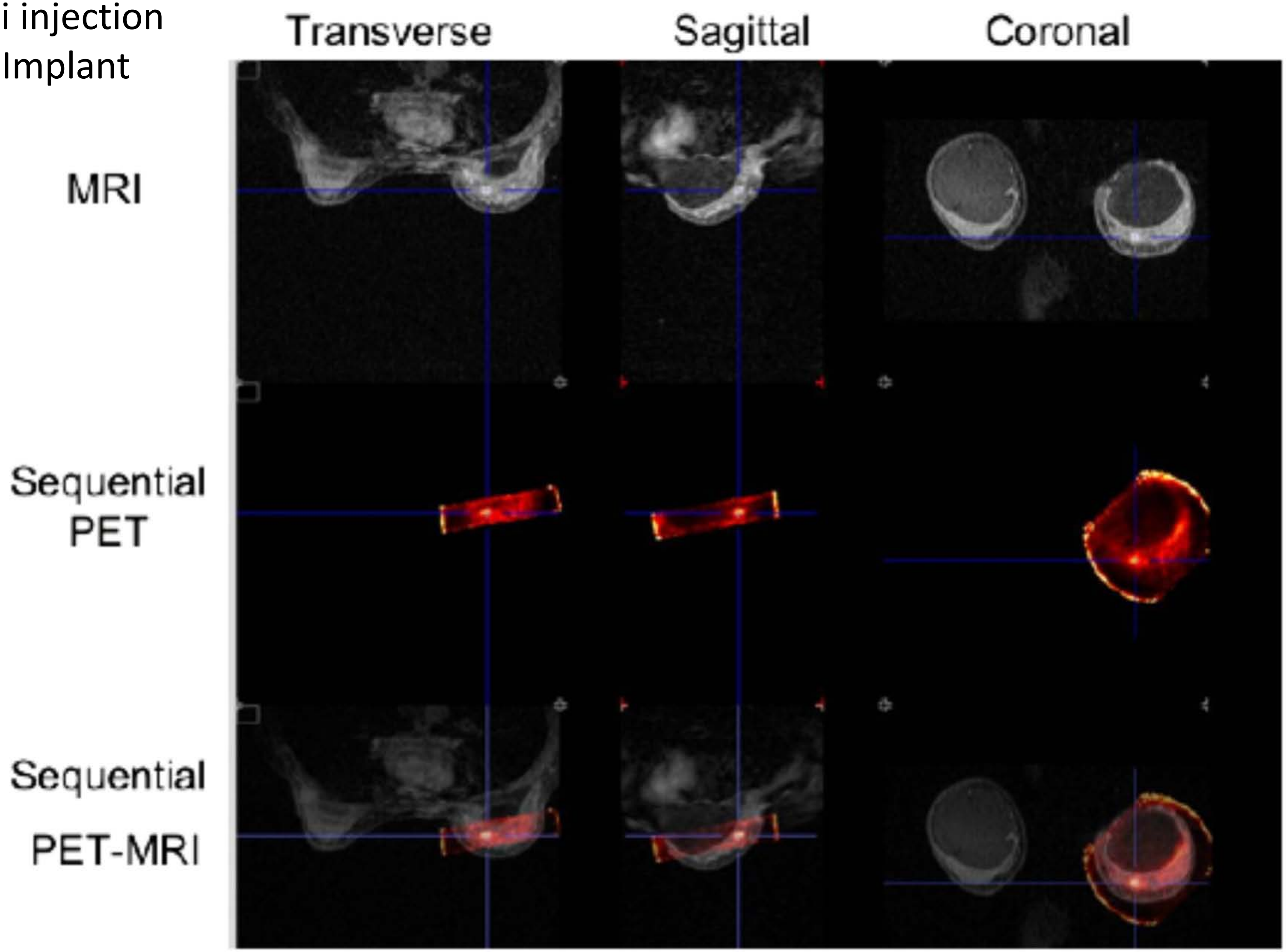
PET ring is assembled in a plastic housing

Patient 1 - Simultaneous PET-MRI

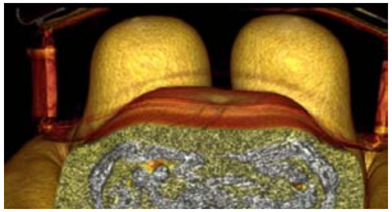


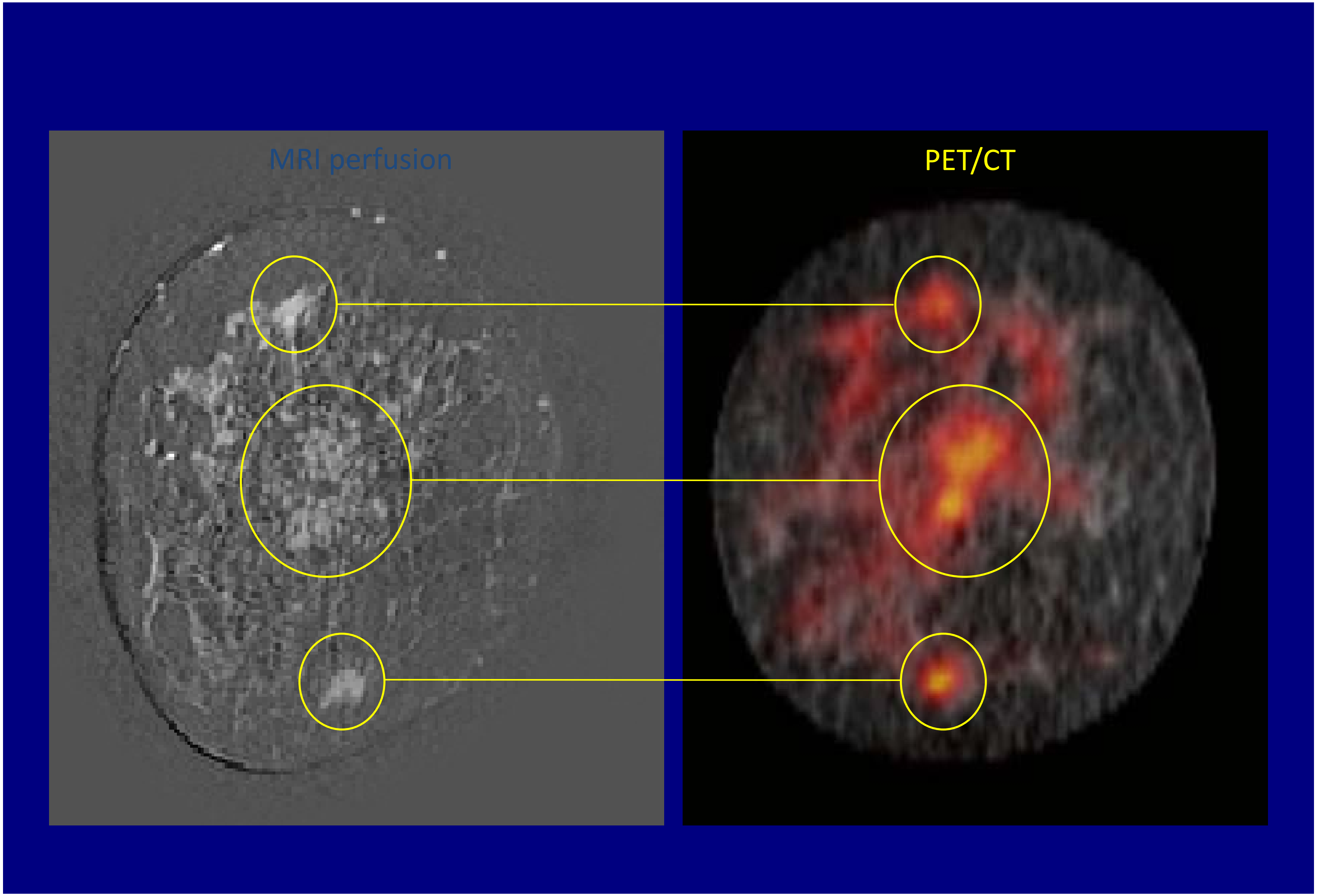
Patient 3 - Sequential PET-MRI

Subject 3 -
: 8.67 mCi injection
: Silicone Implant

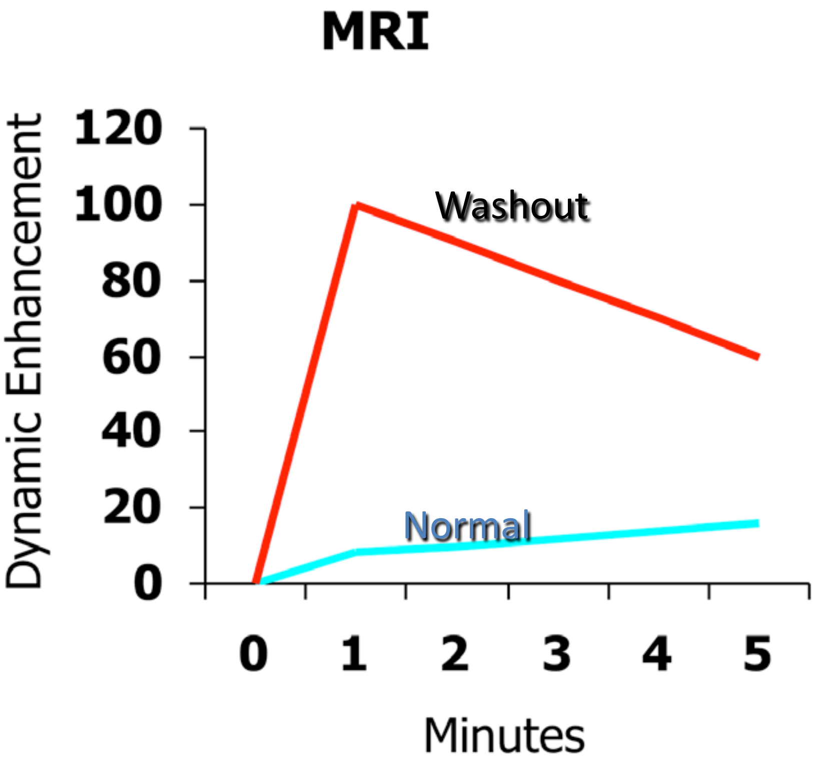


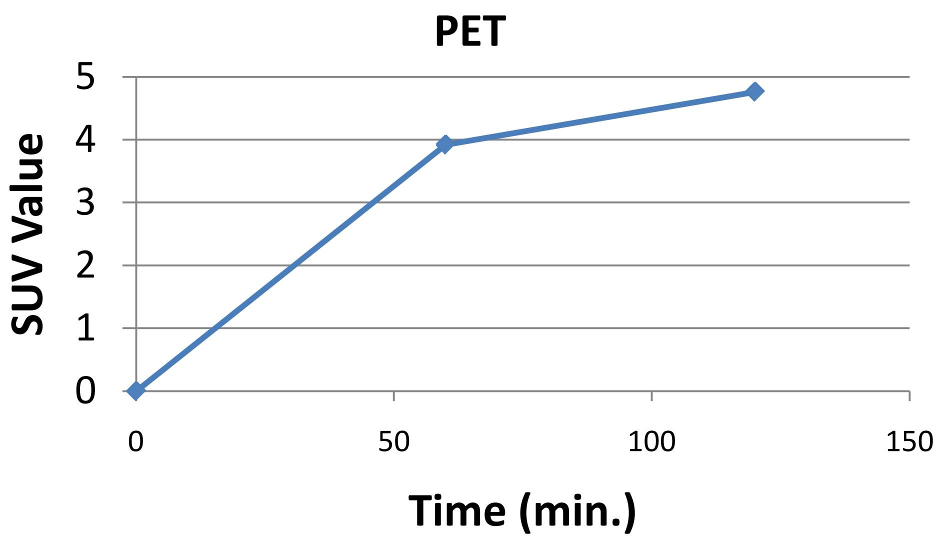
Análisis de Imagen Multimodal



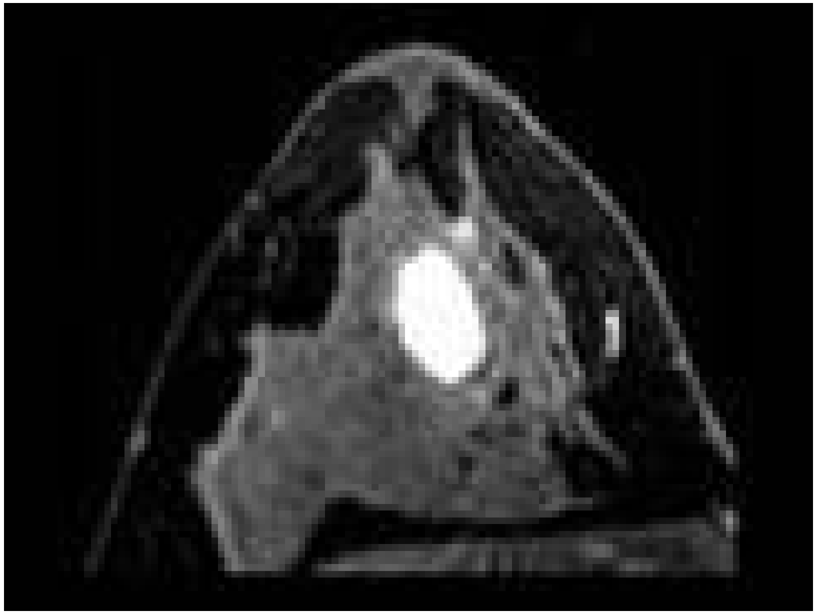


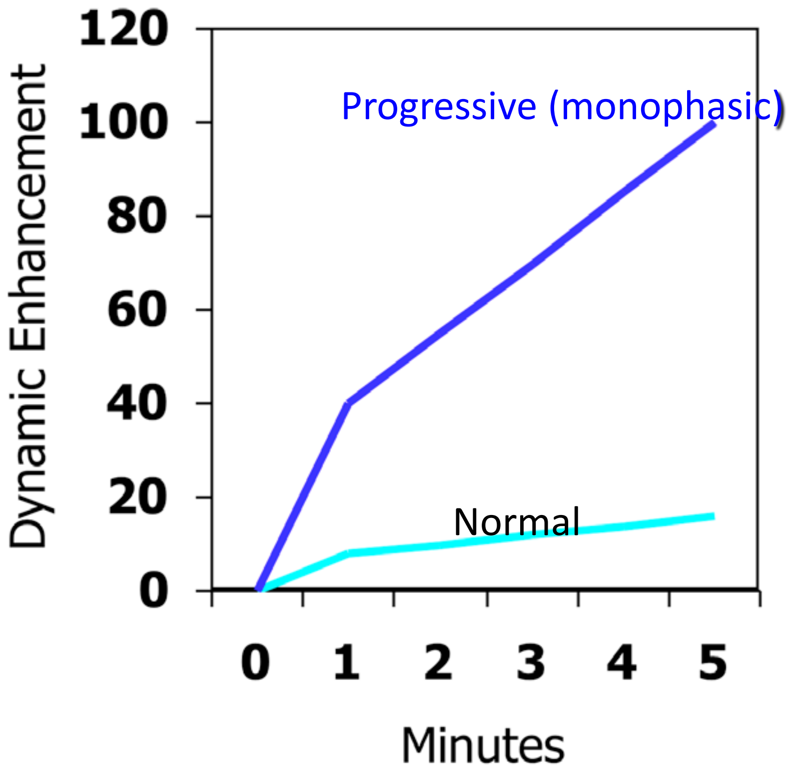
Malignant-like Enhancement

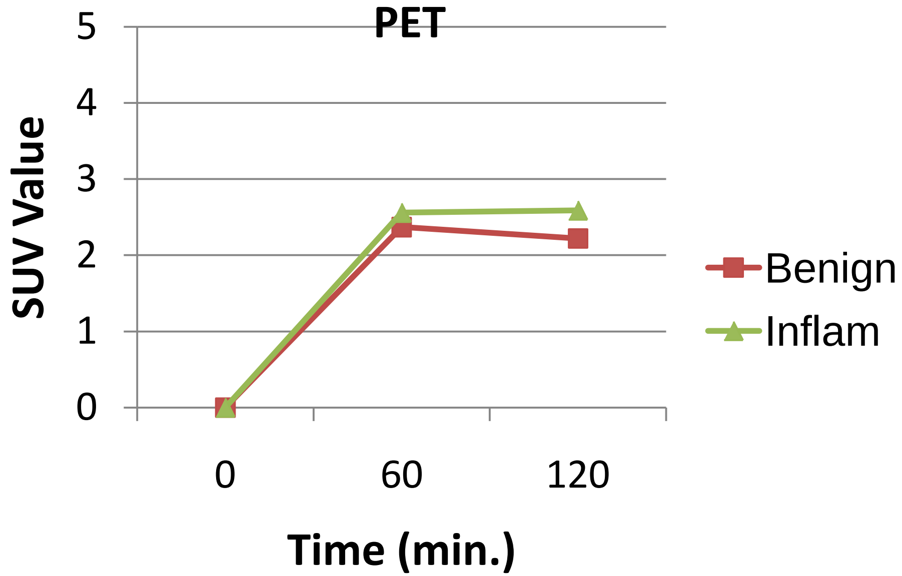




Benign Enhancement Pattern

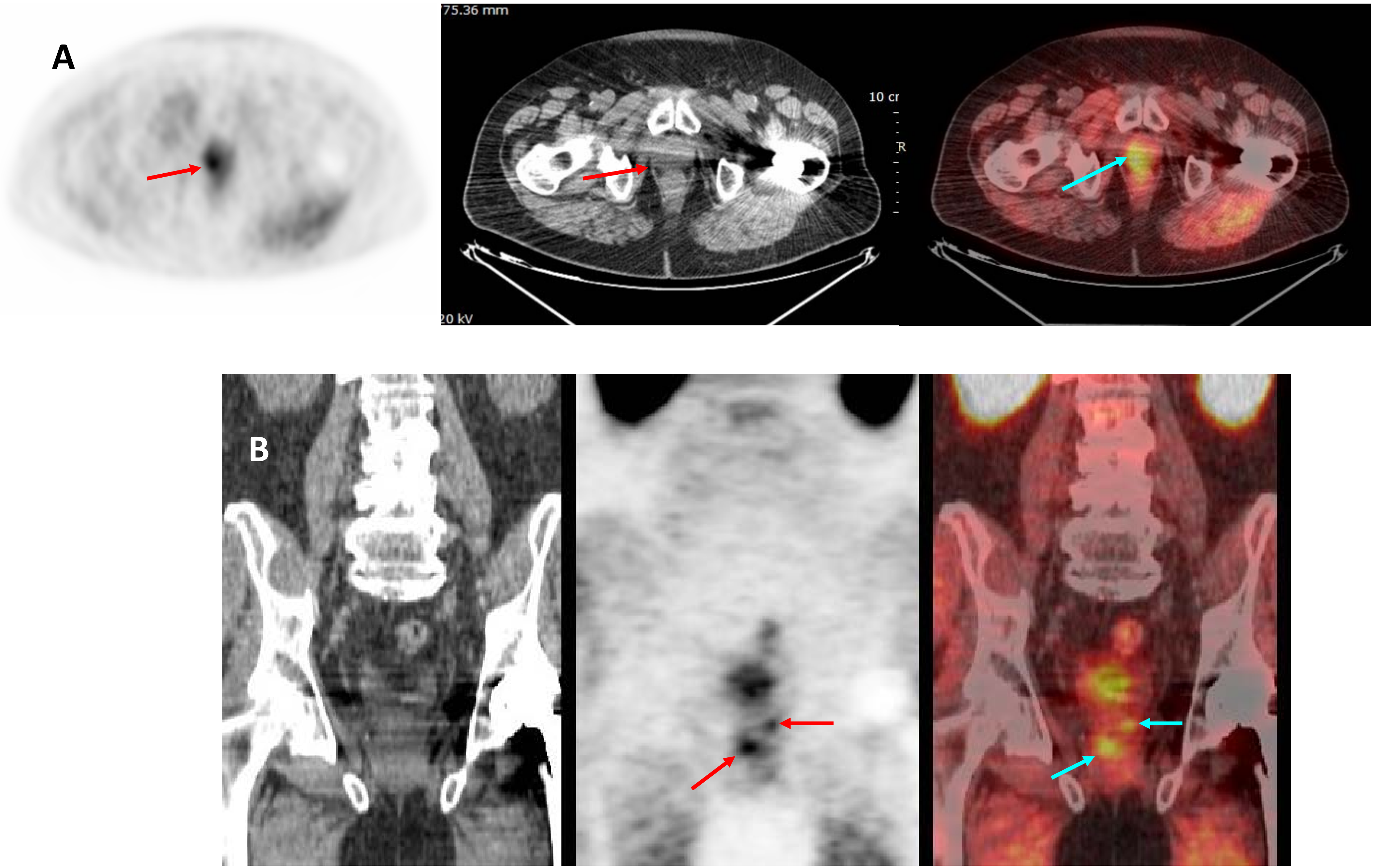




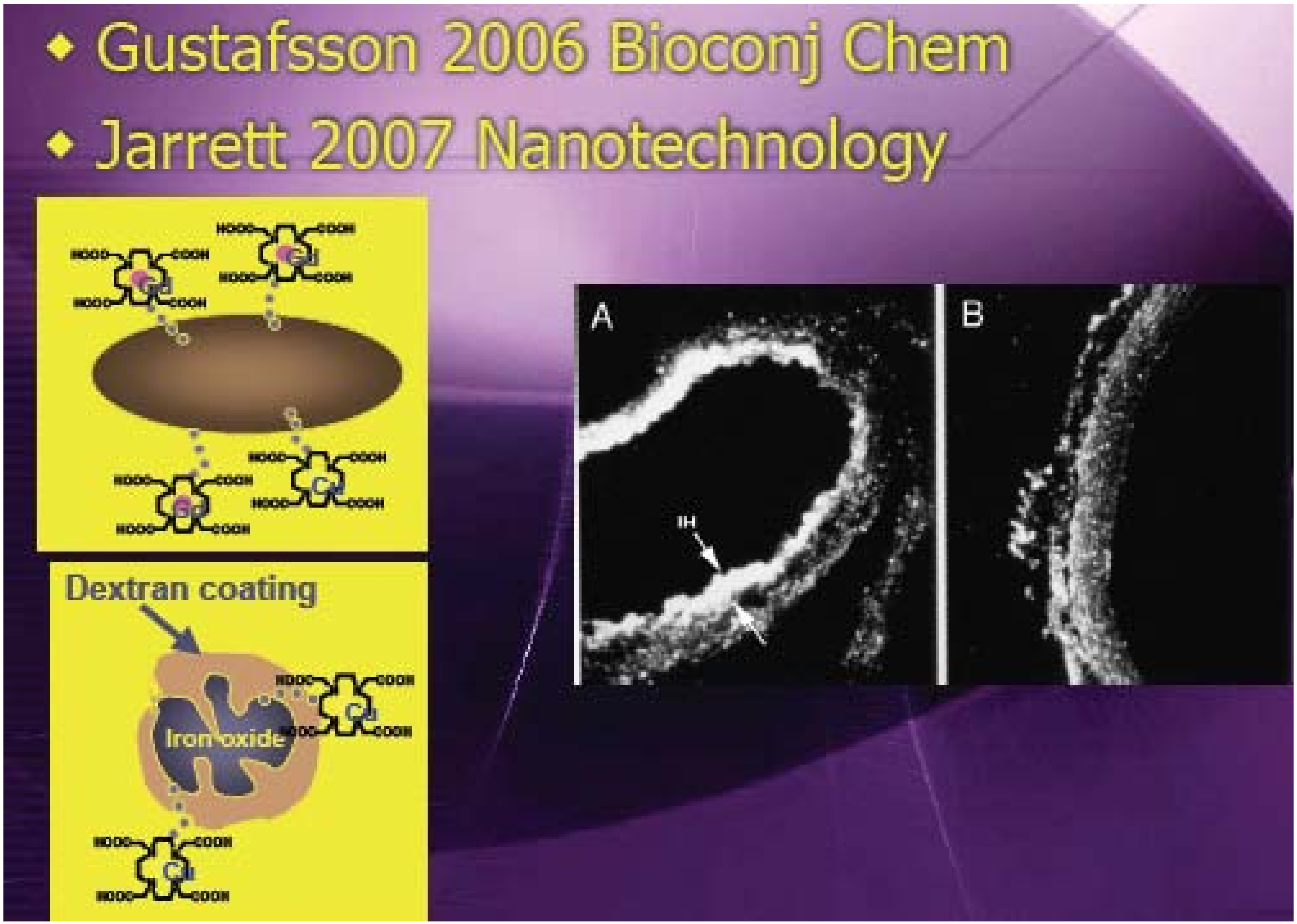


Things to Remember

- The power of PET and MRI lies in the ability to analyze the images, not in making nice pictures
- Think about kinetics as a way to better utilize PET and MRI data
- Think about ways to retrofit the 30,000 MR scanners in the world to make PET/MR available for the clinic


A
75.36 mm
10 cr
R
20 kV
B

SIMULTANEOUS PET & MR PROBES



MULTIMODALITY IMAGING IN THE OPERATING ROOM

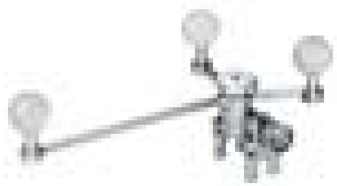
- Standard Navigators.
- Enhanced Navigators with Real Time Imaging:
    - Ultrasound.
    - MR.
    - Molecular Imaging.

STANDARD NAVIGATORS

- Standard Navigators were introduced in 1995 in the field of neurosurgery.
- Trackers are positioned on the surgical instruments to help the surgeon navigate with previously acquired images (CT, MRI).
- Two companies dominate the market: MEDTRONIC & BRAINLAB

STANDARD NAVIGATORS

Infrared reflectors
to mark 3D position



Infrared laser to map the
countour of a surface

STANDARD NAVIGATORS

- Companies start to introduce multimodality in the operating field by using multimodal images (PET/CT) in standard navigators.
- Useful only in rigid areas of the human body (skull, rakis) where the previously acquired image remains unaltered.
- Not useful in soft tissue.

UltraSound Real Time Navigation

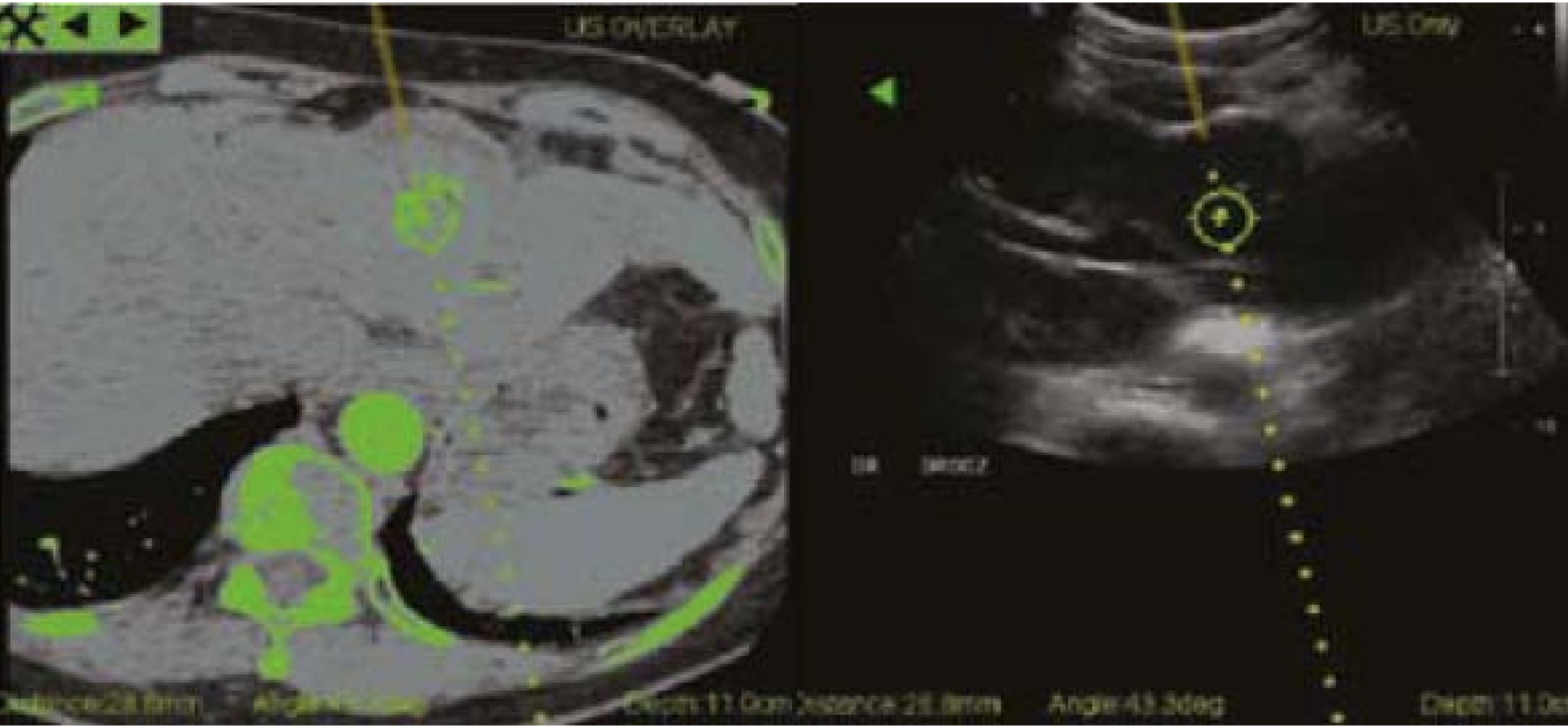
PHILIPS PercuNav Image fusion & Navigation System

Synchronizes real-time ultrasound with archived scans, to rapidly correlate anatomy and pathology.

Enables interventional radiologists to navigate tracked instruments when performing needle based procedures.

Biopsies, ablation and drainages.

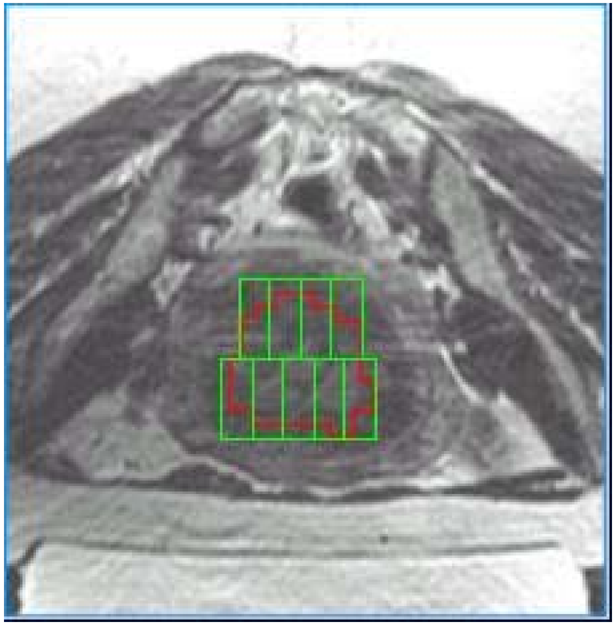
Fusion of ultrasound and other modality like MR, CT or PET. Upper right pane shows a real time ultrasound imaging of the liver and overlay on a CT image (upper left pane) with the target "T".

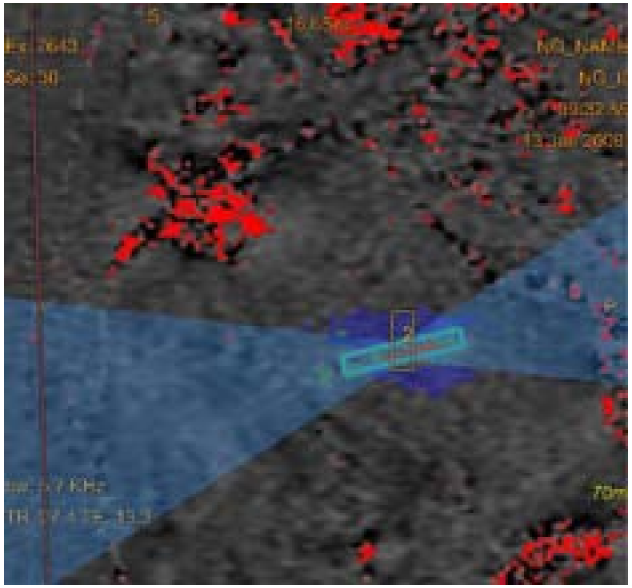


CT and ultrasound view of the lesion. The circle represents the crossing between the needle and the scan plane of the ultrasound. The solid yellow line is a projection of the out-of-plane needle onto the scan plane.

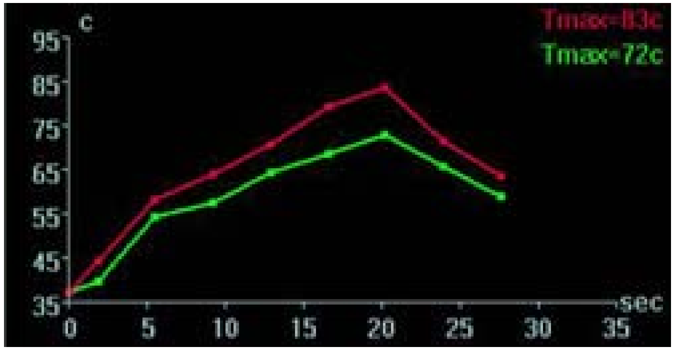
UltraSound Guided Biopsy

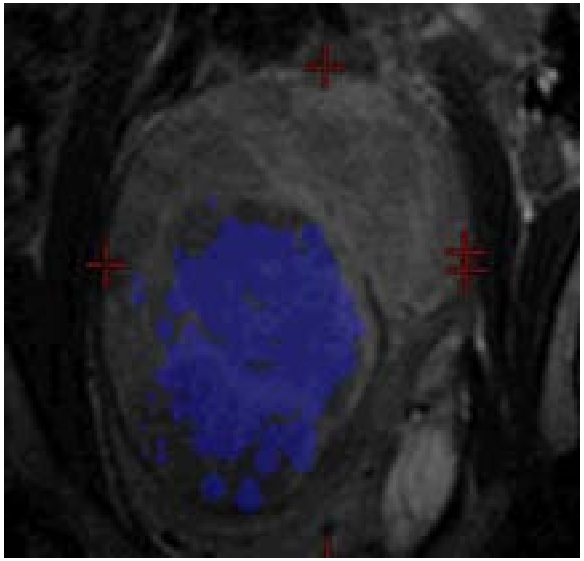
MRgFUS



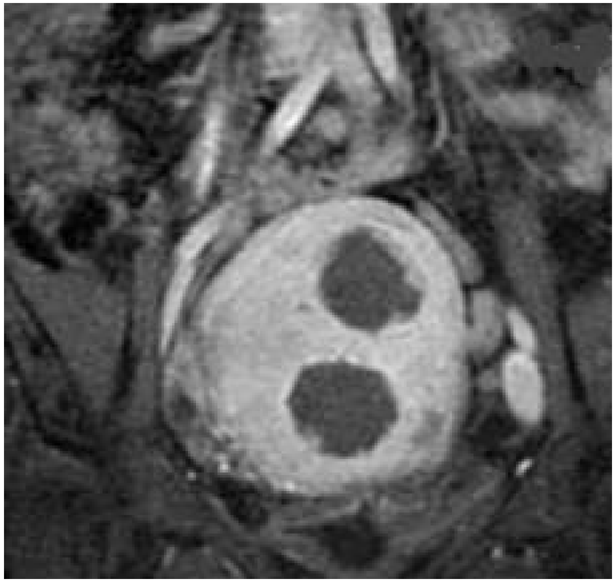


The focused ultrasound beam can be seen during the treatment





The system keeps track of which regions have reached thermal dose enabling the physician to determine if there has been sufficient heating.



two uterine fibroids that have been successfully ablated

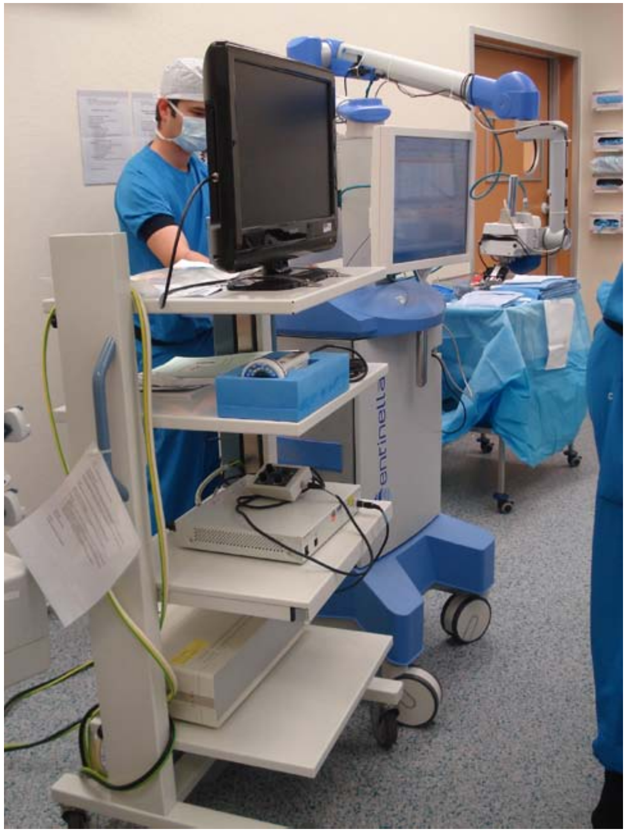
Molecular Imaging Real Time Navigation

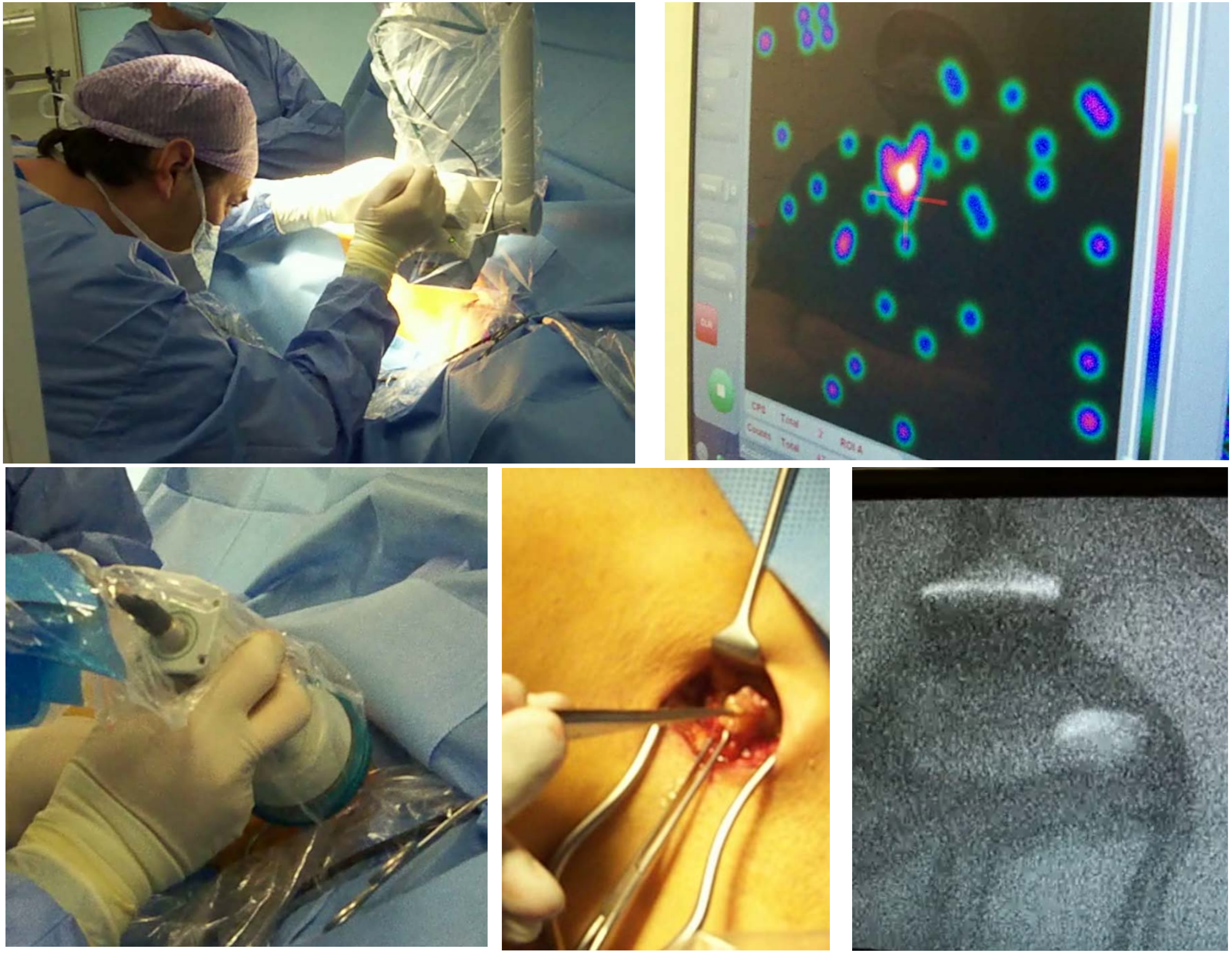
Why?

- Complementary Information.
- Localization.

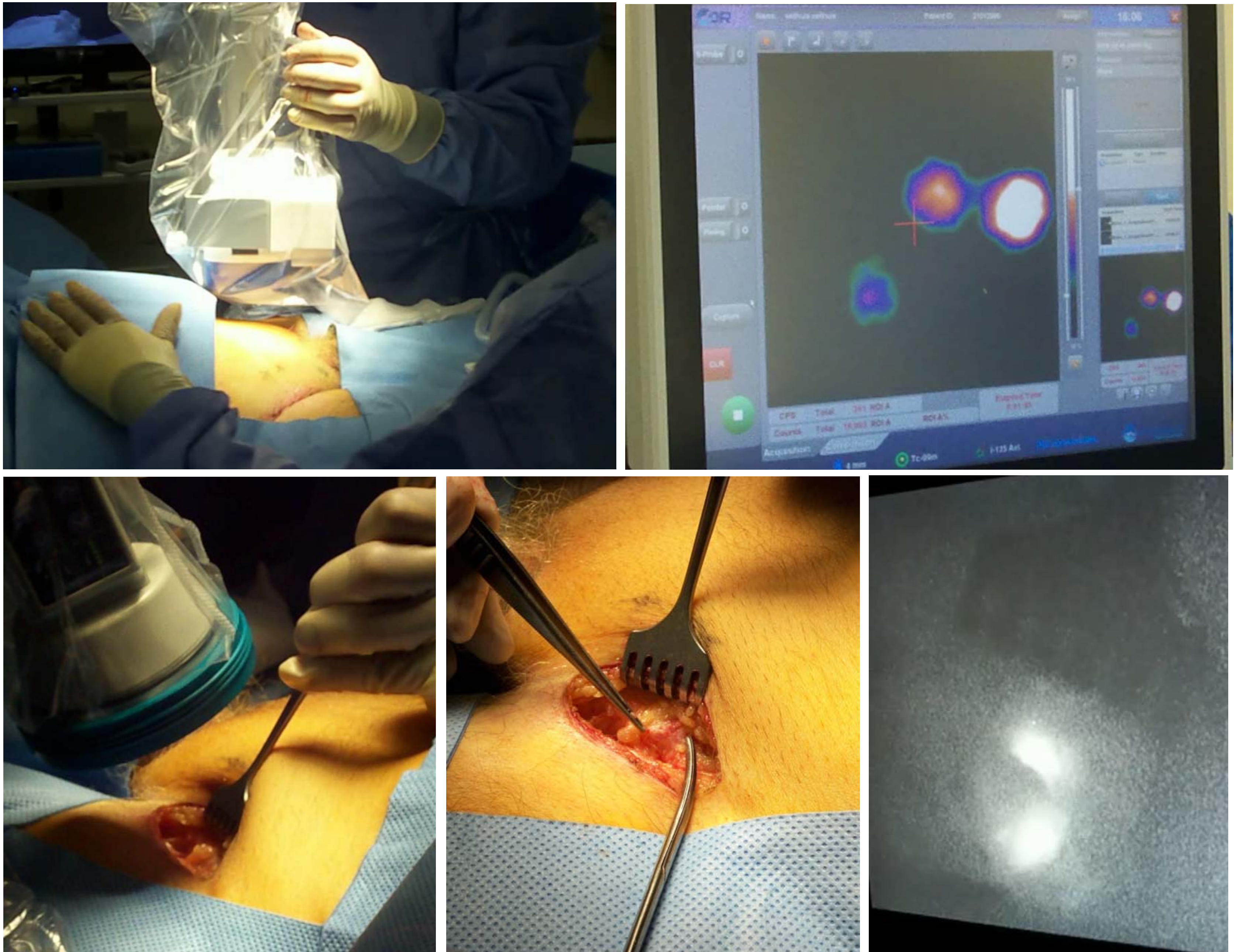
Our VISION:

- ◆ Functional (gamma ray) image guides the surgeon. A rough but very sensitive image is used to find the node or tumor.
- ◆ Once it is found, Morphological info (MR or US) will be used to optimize procedure.
- ◆ Fluorescence will provide higher resolution once the node or tumor is near the camera.





SENTINEL NODE AXILLA (SENTINELLA + HAMAMATSU)



SENTINEL NODE GROIN (SENTINELLA + HAMAMATSU)

Invención del Ciclotrón

NUEVO PARADIGMA de ACELERACIÓN de PARTÍCULAS

- **Ernest O. Lawrence, Berkeley 1932.**
- **Haces de partículas: Electrones.**

Proton Laser Applications, S.L.