Translational Research in Applications in Medicine of the Nuclear Physics Group of IPARCOS

JM Udías for IPARCOS

People

- 9 PhD: 2 PTU (JLH, DSP), 2 CU (LMF, JMU), 1 RyC (MPL), 1 PAD (PI), 1 Margarita Salas Postdoc (PG). Several Other postdocs (2). (3 Female and 6 male)
- 1 Electronic engineer (JAJ) and an Electronics Technician (LMG) both funded by TAU-CM.

- About 20 PhD. Students and some other MSc. Students. Strong Involvement in Nuclear Physics Master (National and European version, with Erasmus+ mention), and Biomedical Physics Master.

- 2 PhD defended every year

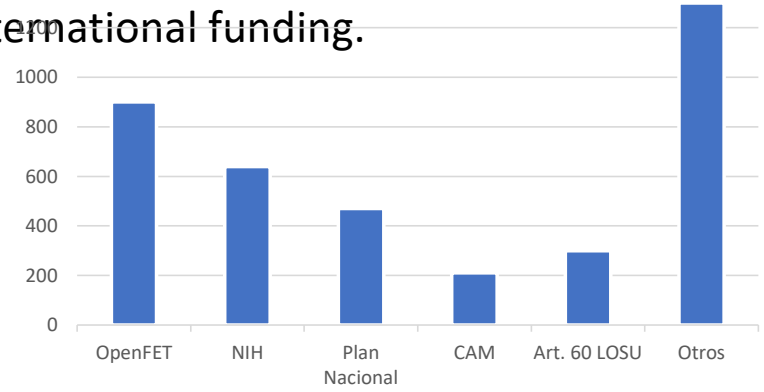
- 3 Patent applications submitted in 2024

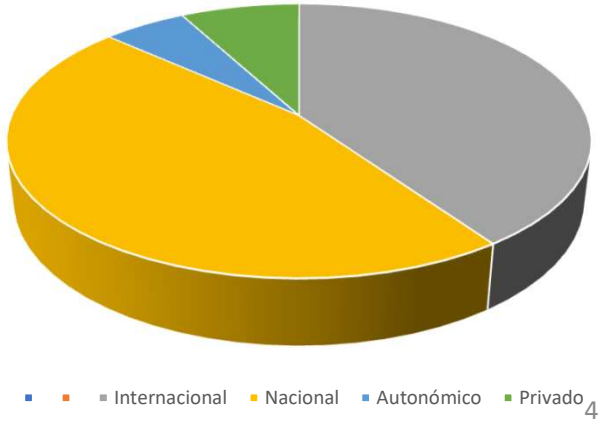
Areas of work:

- Intra-operatory radiotherapy
- Range verification in protontherapy, FLASH, radiobiology
- Nuclear Imaging, mainly PET
- Other image modalities

Some Funding (after 2022)

- 900 keuros. Two OpenFET Pathfinder European Projects: RETIMAGER and GAMMA-MRI, (JMU, LMF), H2020, EU, 2022-2027.
- 640 keuros. NIH (USA): Multicolor-PET y HRST-BrainPET (JLH, JMU), 2022-2027.
- 470 keuros. National plan: radFLAP (DSP), FASCINA (LMF and JLH), INVENTOR (MPL and PIG), 2022-2026.
- 210 keuros. Local (Madrid) gov. funding: ASAP (LMF) 2023-2025.
- **1,300** keuros. Other national funding (PRTR): CPP NewMBI (JMU), PDC-3PET (JLH), PLEC-FLASHonCHIP (DSP), TED- PROTOTWIN (JLH, LMF), TED-NINPHA (SEP), MISIONES-I+D in AI-TARTAGLIA (JLH), **2023-2025.**
- 500 keuros. Private funding, transfer and collaboration agreements with companies: GMV; SEDECAL/SMI, Siemens, ITHERA. (JLH y JMU), 2023-2025.
- 4 Meuros total secure funding (2022-2025), 46% National, 5% local gov., 12.5% private funding, 40% international funding.





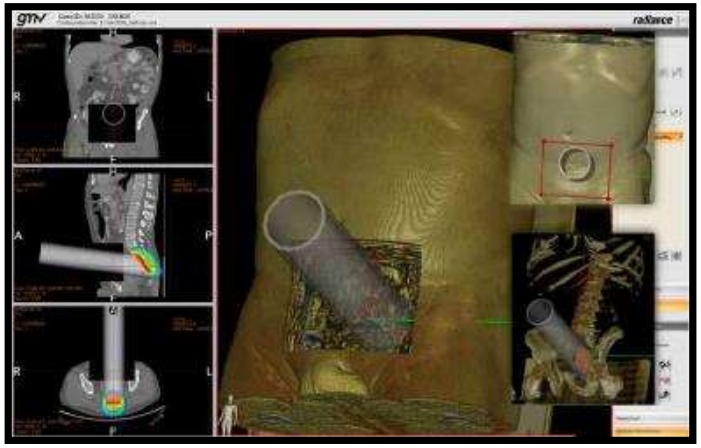
Radiotherapy

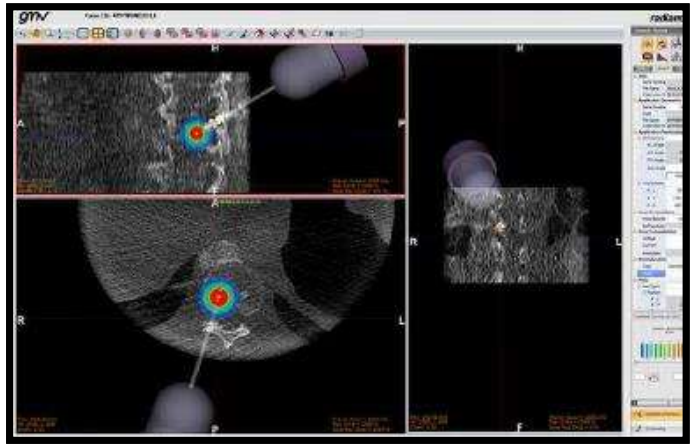
Intraoperatory Radiotherapy (Paula IG)

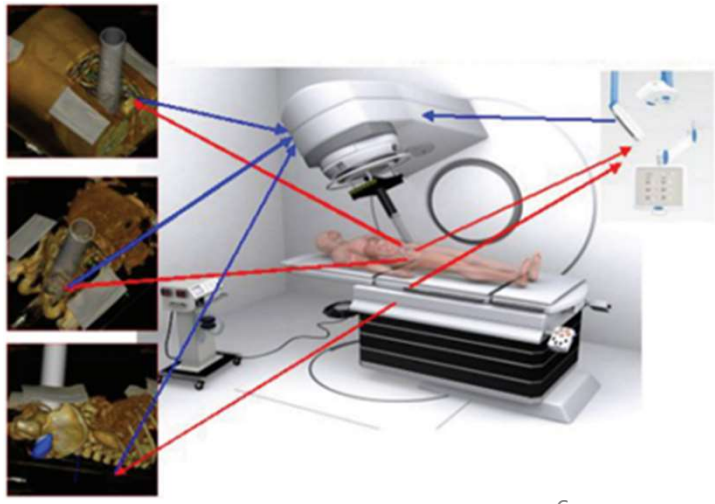
Radiance, by GMV

•First comercial TPS for IORT. First prototype for electrons in 1997. Realistic dose calculation for electrons in 2010. Extended to Intrabeam in 2012. FDA and UE approved in 2016.

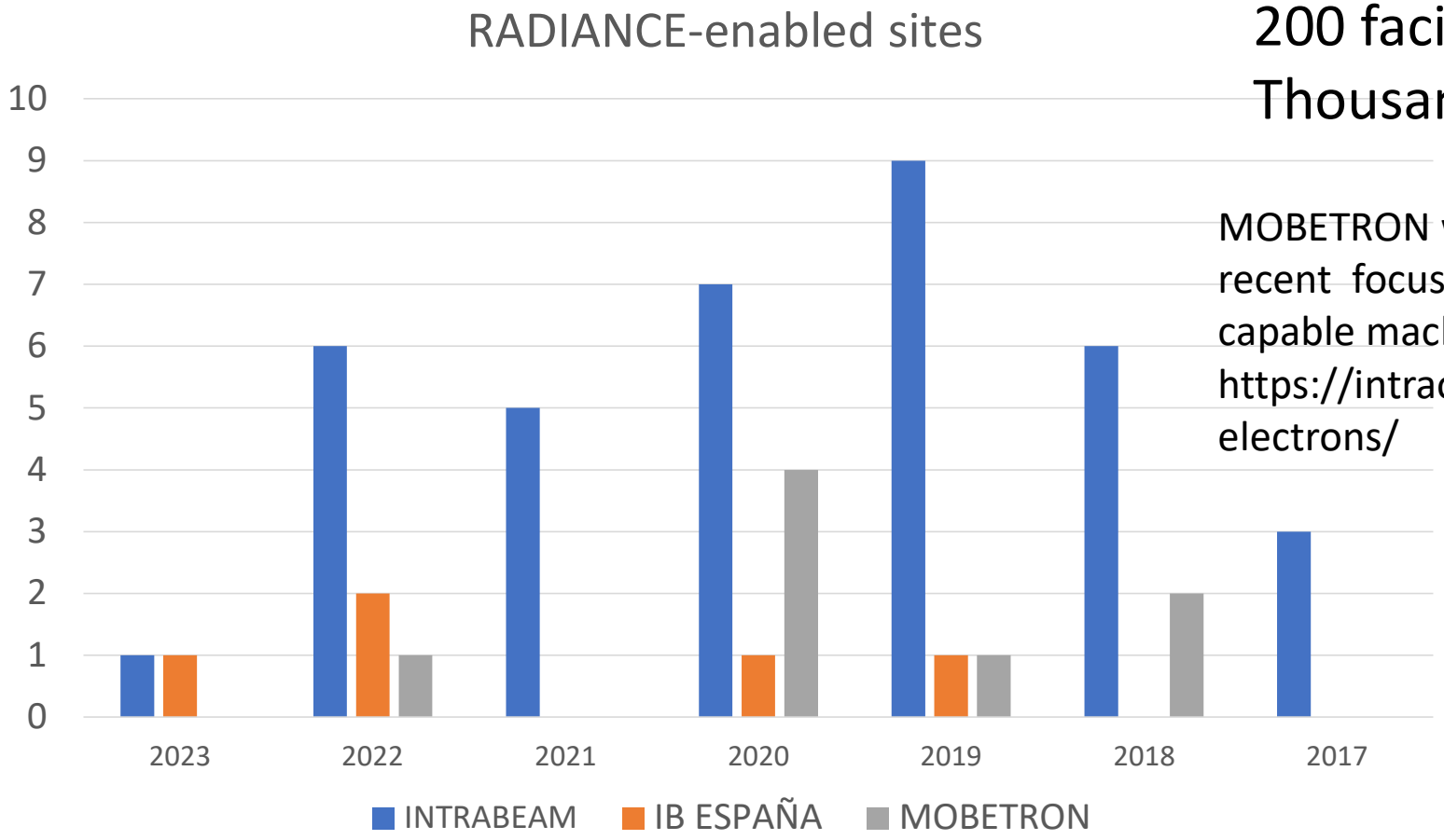
• Ultra fast Monte Carlo dose computation. Requires Accelerator (LINAC or X-ray source) modelization and easy commissioning tool. This is what we do at GFN-IPARCOS.







Radiance became the standard TSP distributed alongside MOBETRON (Intraop) and Intrabeam (Zeiss) devices



200 facility-years

Thousands of patients treated

MOBETRON was not a such sale, as intraOP recent focus was in developing a FLASH-capable machine https://intraop.com/flash-radiotherapy-electrons/

Protontherapy

ASAP-CM: Advanced Strategies and new Approaches for Protontherapy

PROGRAMAS ACTIVIDADES I+D BIOMEDICINA 2022, local gouvernement Coordinated from IPARCOS (LM Fraile). 820 keuros total funding (2023-2025)

12 years in a row that GFN@IPARCOS coordinates networks from the local gov. of Madrid

Comunidad de Madrid

S2022/BMD-7434

D. Sánchez Parcerisa

L.M. Fraile

Grupo de Física Nuclear & IPARCOS
Universidad Complutense
Madrid, Spain

Instituto de Investigación Sanitaria
del Hospital Clínico San Carlos (IdISSC)
Madrid, Spain

ASAP-CM - Partners

2018 – 2022

Ciemat

RADIOBIOMED

IEM CSIC

Pronto Protontherapy and nuclear techniques for oncology

2023 – 2026

SEÑALIZACIÓN

CMAM

NANO-BIO

IEM CSIC

Ciemat

RADIOBIOMED

UIN

IdISSC Instituto de Investigación Sanitaria

GBM

quirónsalud

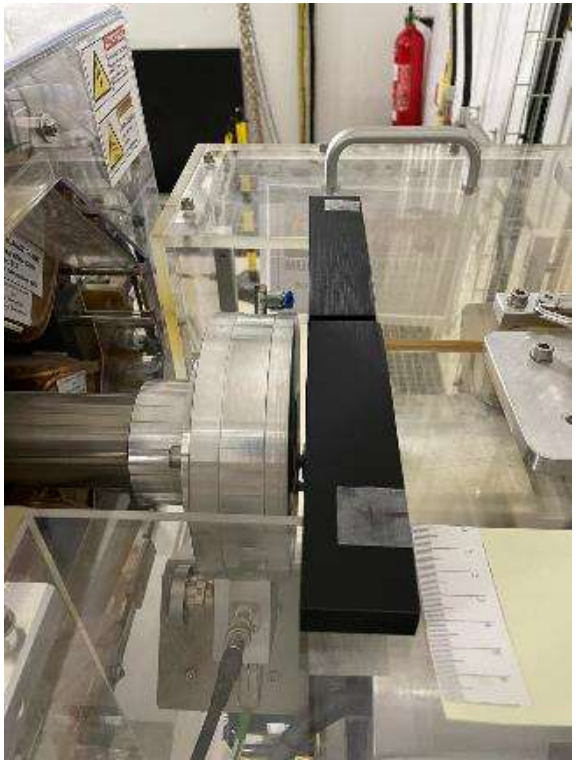
Clínica Universidad de Navarra

Hospital Universitario de Fuenlabrada

Hospital Universitario La Paz

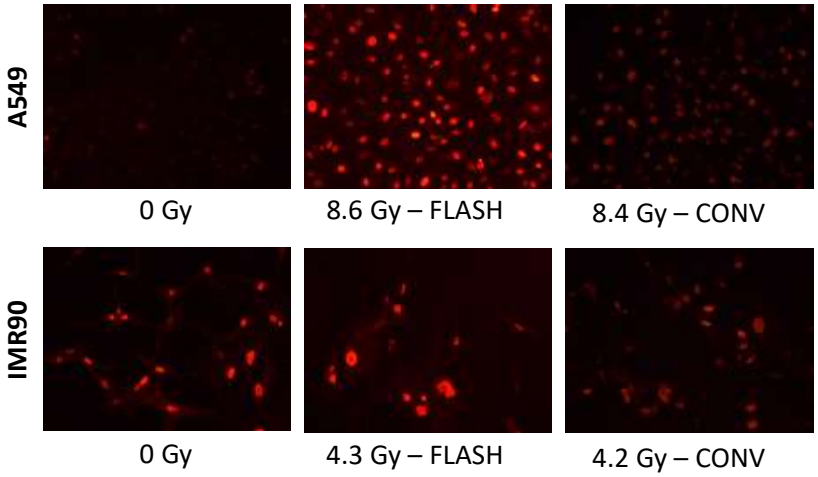
ASAP-CM

Characterized a FLASH irradiation area at Quiron protontherapy center and performed cell irradiations (Daniel SP)

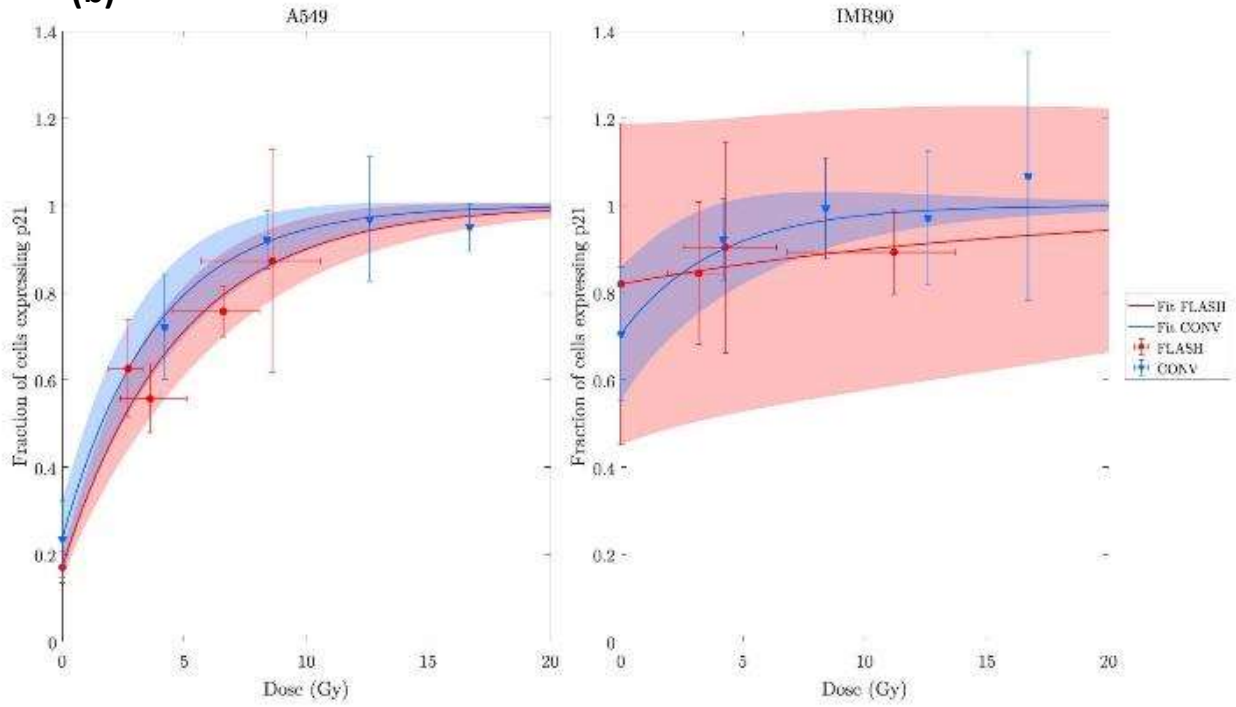


FLASH at Quiron (800 Gy/s) p21 cell arrest marker

(a)



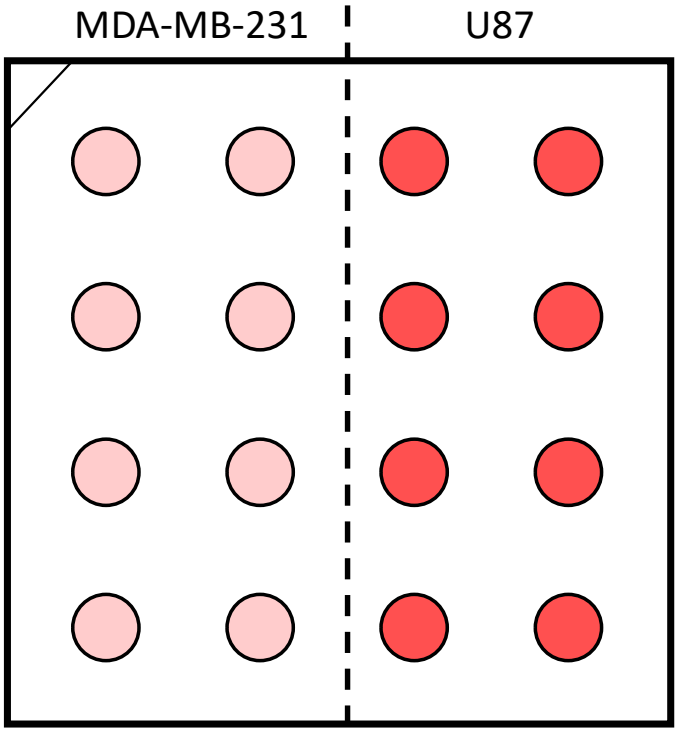
(b)

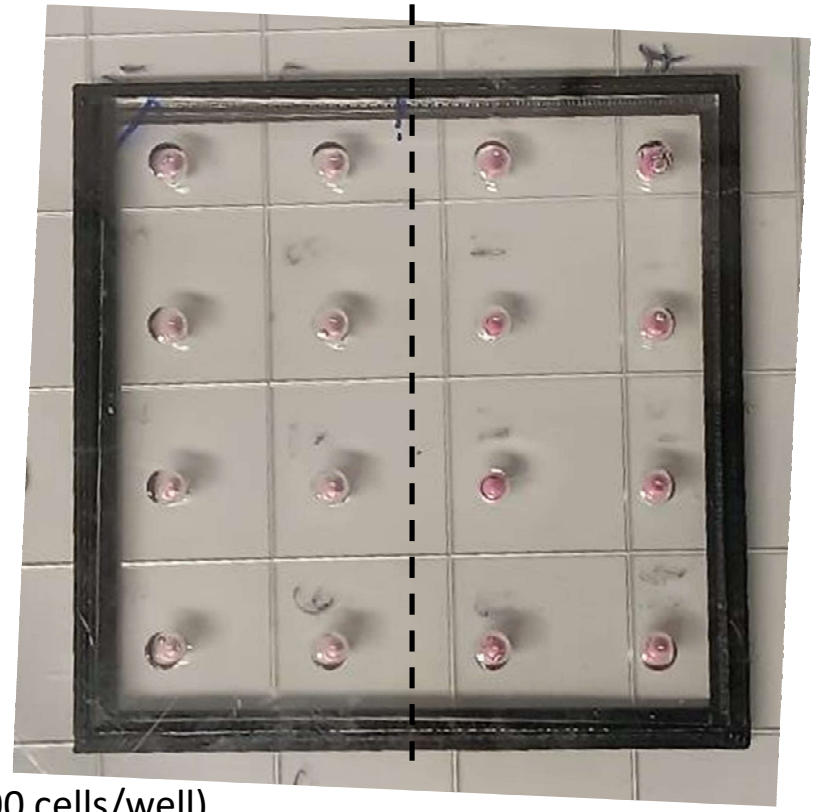


Images from the p21 – immunofluorescence, representative doses of the two irradiations for both cell lines. **(b)** Fraction of cells expressing p21 for the A549 cells (left) and for IMR90 cells (right) for FLASH/CONV rates + fit to model. The shaded areas correspond to the uncertainty of the fittings at 1 standard deviation.

Chip design (FLASHonCHIP, DSP)

The wells were previously treated with FBS (during 5') and EtOH (during 30´)



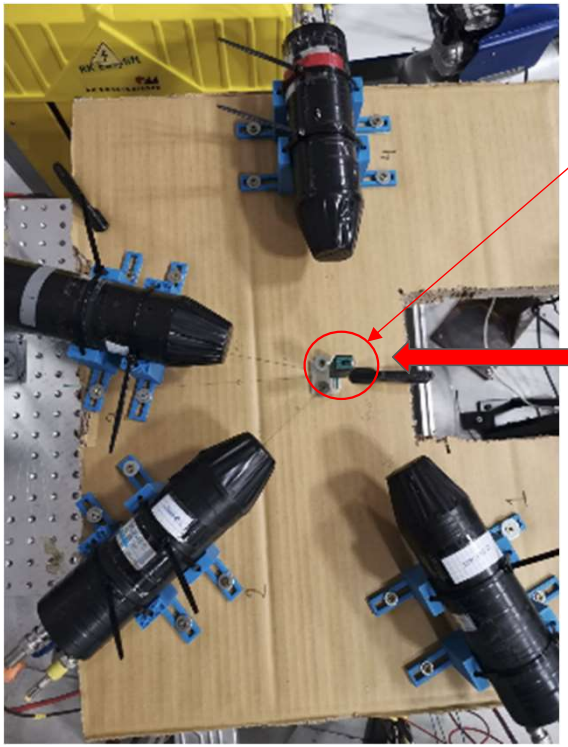


MDA-MB-231 – Breast Cancer (5.000 cells/well)

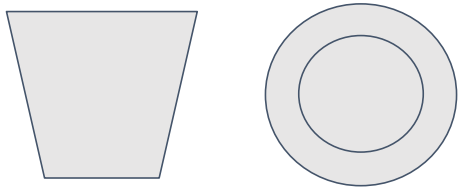
U87 – Glioblastoma (10.000 cells/well)

Prompt-gamma analysis in $H_2{}^{18}O$ proton irradiation experiment (LMF)

- $H_2{}^{18}O$ irradiation with protons from 2MeV up to 10MeV
- On-beam measurements -> high count rates



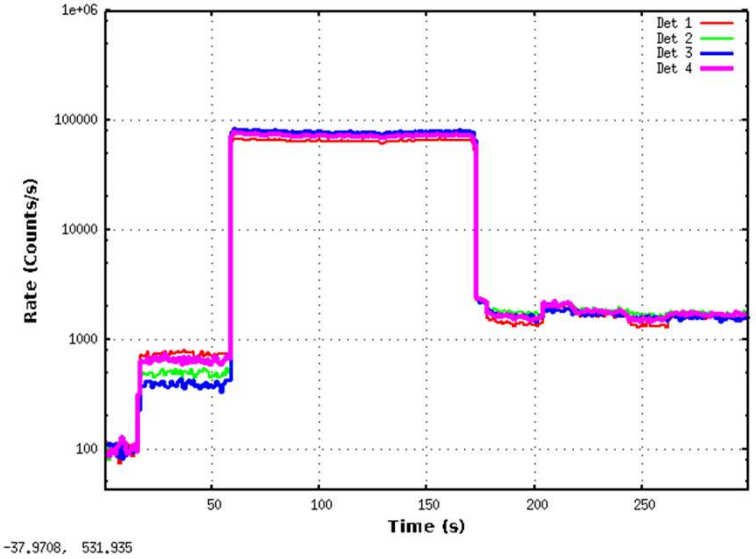
LaBr3 truncated cone scintillators



PMT HAMAMATSU H10570Q

DAQ → CAEN 5751 (GSample/s)

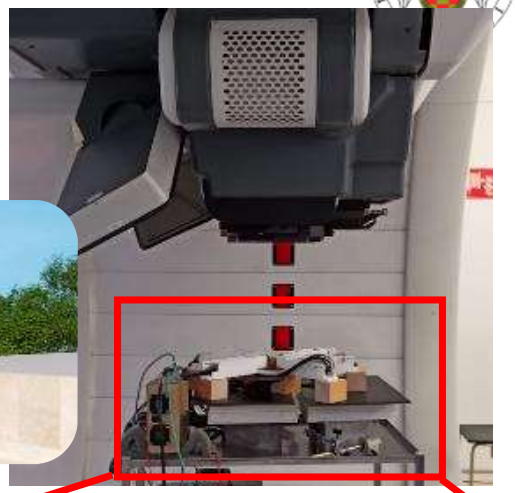
Target → H2O18
Energy Beam → 6 MeV
Rates ~ 80k counts/s

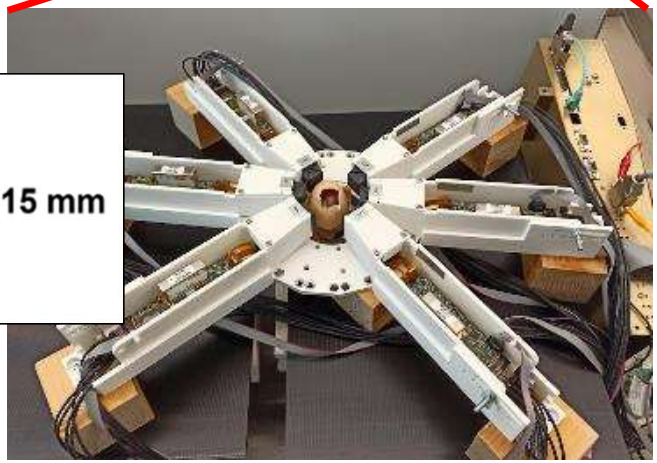


On-the-fly proton range verification

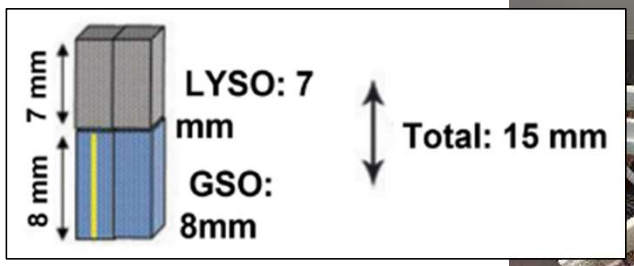
2020 **On-line** PET In-vivo → 2022 **On-the-fly activation** → 2023 **On-the-fly dose reconstruction**

2020. In-beam PET system MINIPET: on-line measurements in a chicken embryo model





- **6 detectors** consisting of a **338 crystal array** with 1.55 mm pixel pitch DOI correction with phoswich LYSO (7mm)+GSO(8mm).
- Good spatial resolution (0.5 mm) and a scanner field of view (FOV) of **4 cm(axial) × 2 cm (transaxial).**
- World record processing capabilities:
  - **+100 millions** of single events per second
  - **+10 million** coincidences per second sorted out to disk



SEDECAL

España, S.,*et al.* (2022). In vivo production of fluorine-18 in a chicken egg tumor model of breast cancer for proton therapy range verification. Scientific Reports, 12(1), 1-12.

2. Experiment

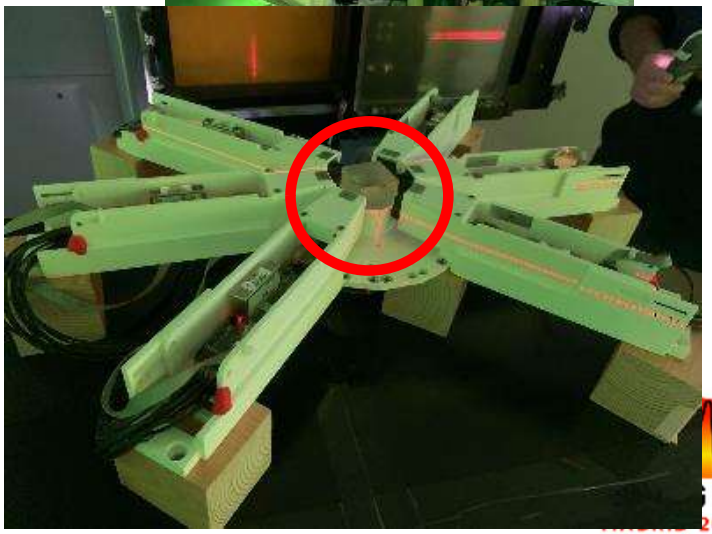
Set-up

Proton beam
70-230 MeV

The experiment was performed at the **Quironsalud protontherapy center** (Pozuelo de Alarcón, Madrid)

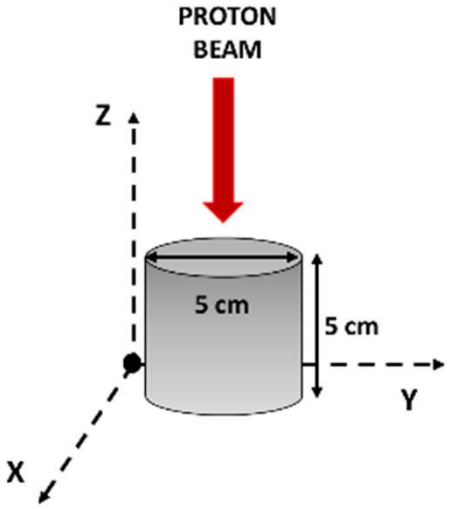
IBA, Proteus®ONE

PMMA phantoms

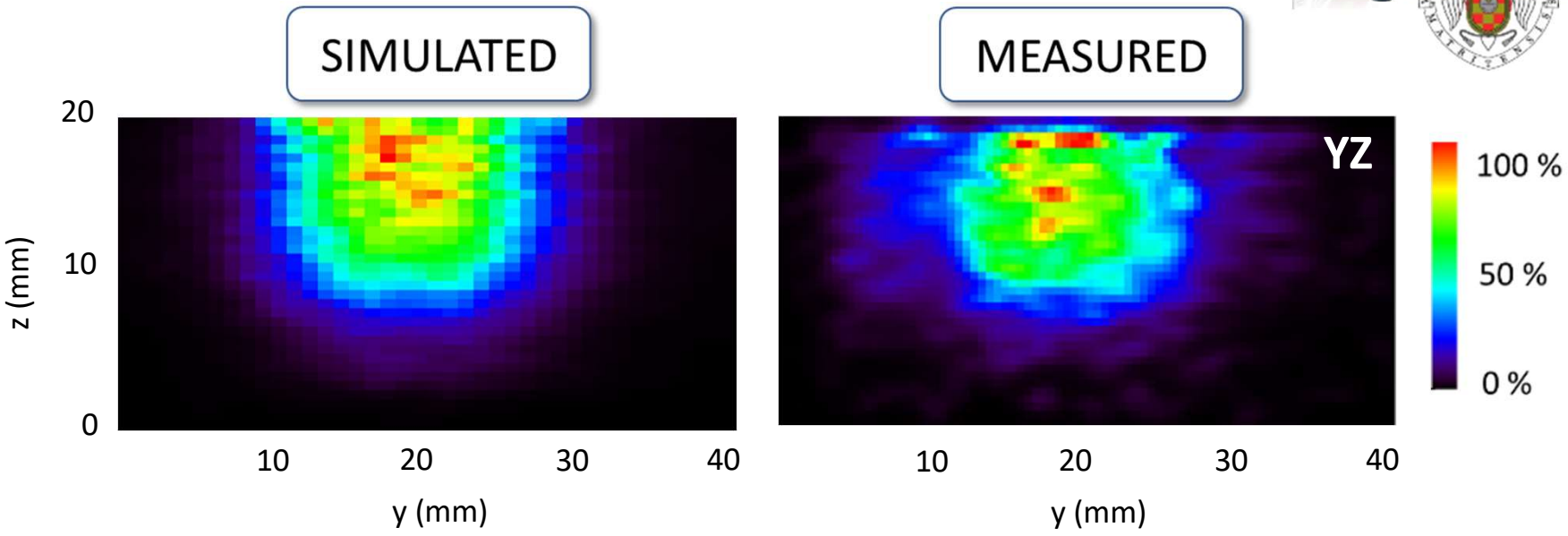


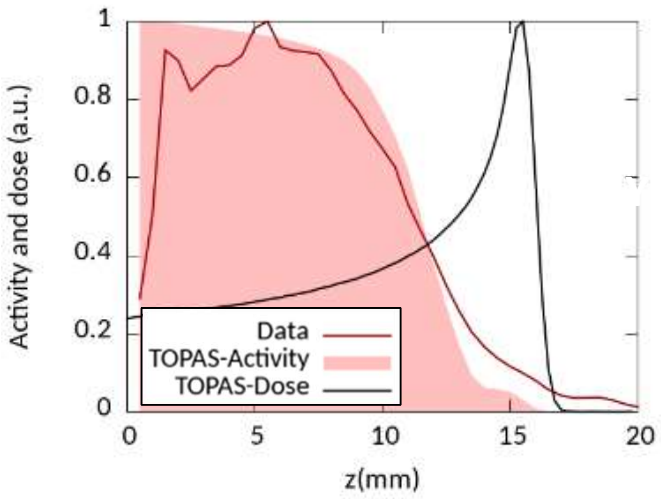
3c. Results-coincidences

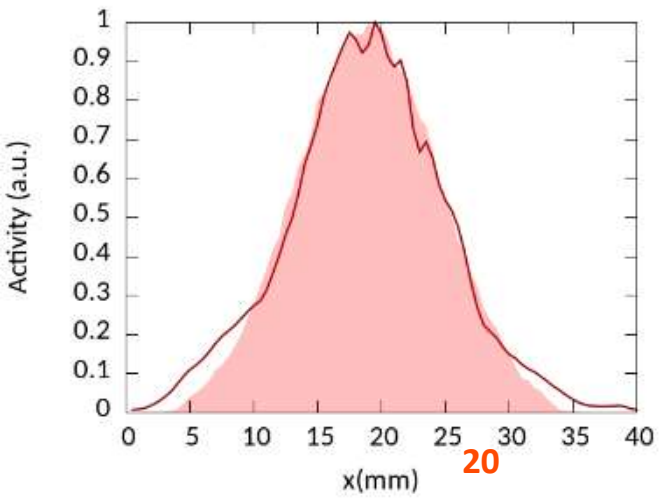
- MLEM with variable PSF



Normalized 1D profiles







3d. Towards dose reconstruction

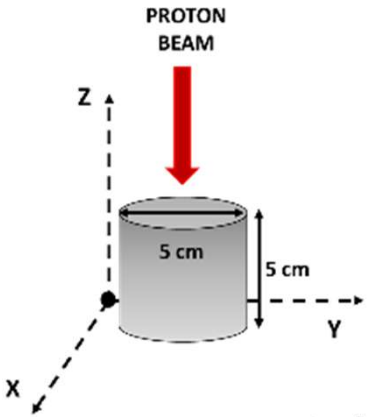
IPAH

2020
On-line PET
In-vivo

2022
On-the-fly PET activation

2023 ??
On-the-fly dose reconstruction

- Dose and activity of a theoretical 70 MeV proton beam after irradiation. The assumed delivered dose was 10 Gy.



In-beam Dose Estimation tool from PET measurements (IDE-PET) for range verification

V.V. Onecha et al.

PTCOG 61
MADRID 2023

Nuclear Imaging: mPET (JLH)

nature biomedical engineering

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Article | Published: 03 July 2023

Simultaneous quantitative imaging of two PET radiotracers via the detection of positron–electron annihilation and prompt gamma emissions

Edwin C. Pratt, Alejandro Lopez-Montes, Alessia Volpe, Michael J. Crowley, Lukas M. Carter, Vivek Mittal, Nagavarakishore Pillarsetty, Vladimir Ponomarev, Jose M. Udías, Jan Grimm & Joaquin L. Herraiz

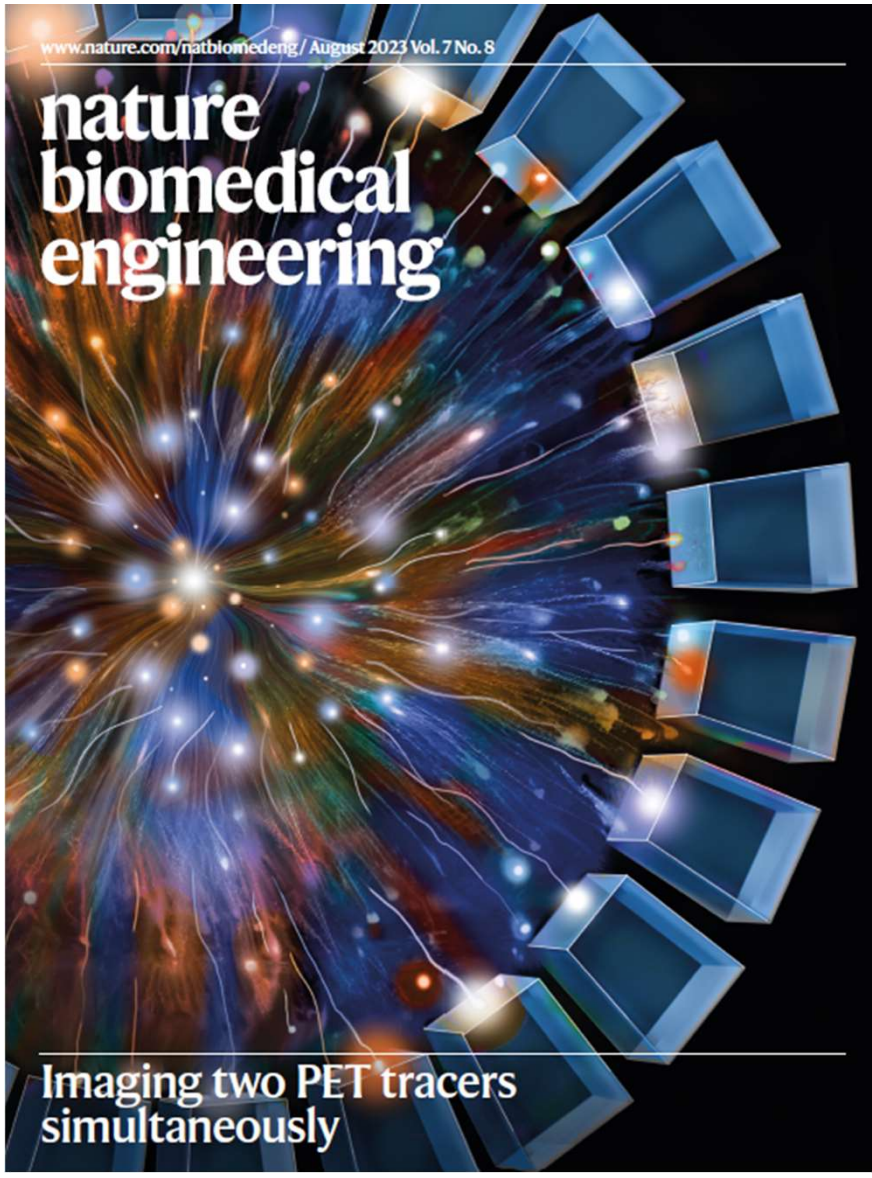
Nature Biomedical Engineering **7**, 1028–1039 (2023) | Cite this article

2478 Accesses | **2** Citations | **55** Altmetric | Metrics

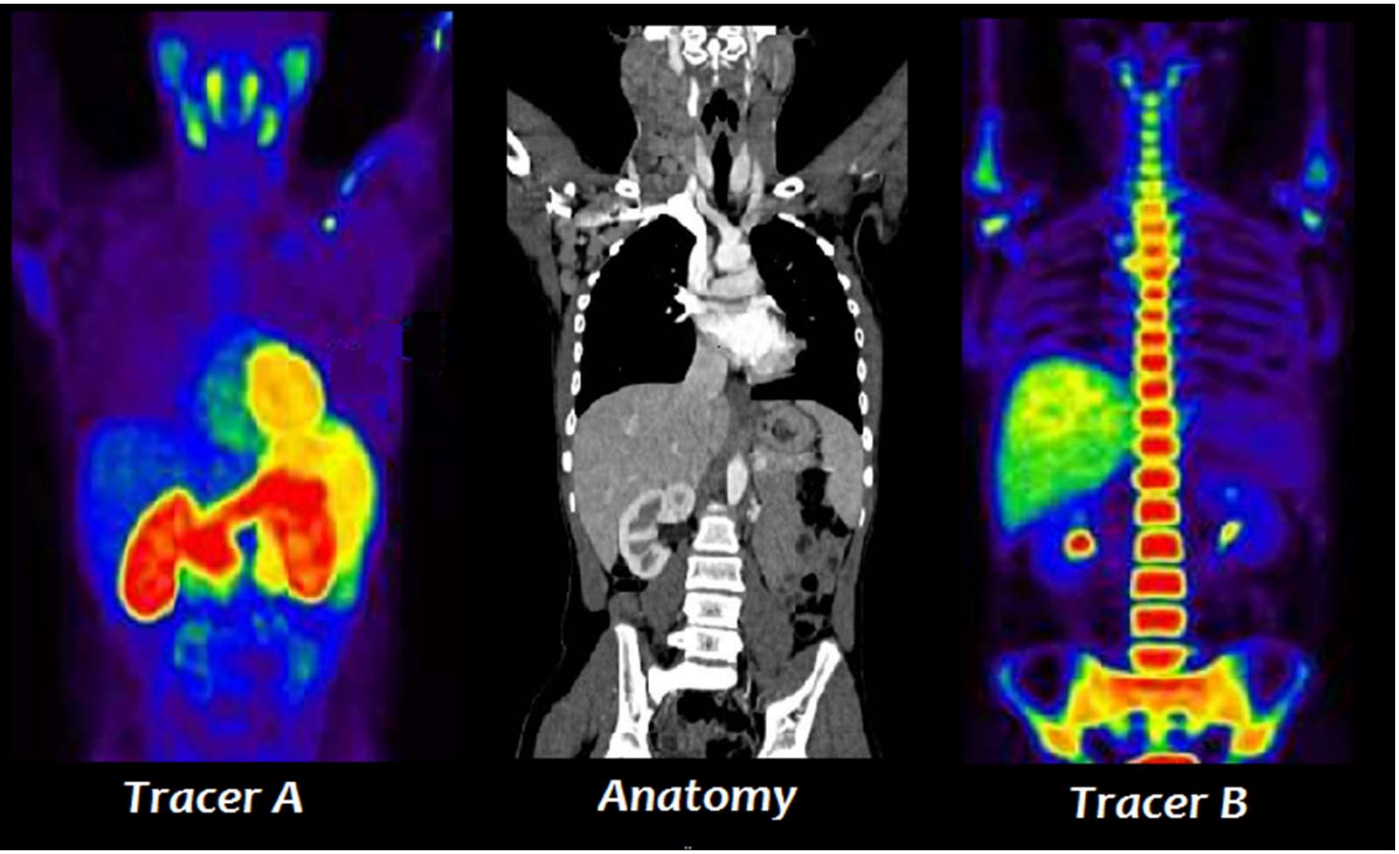
PMID: 37400715

https://doi.org/10.1038/s41551-023-01060-y

https://bioengineeringcommunity.nature.com/posts/doubling-pet-imaging-capacity-with-a-new-reconstruction-algorithm



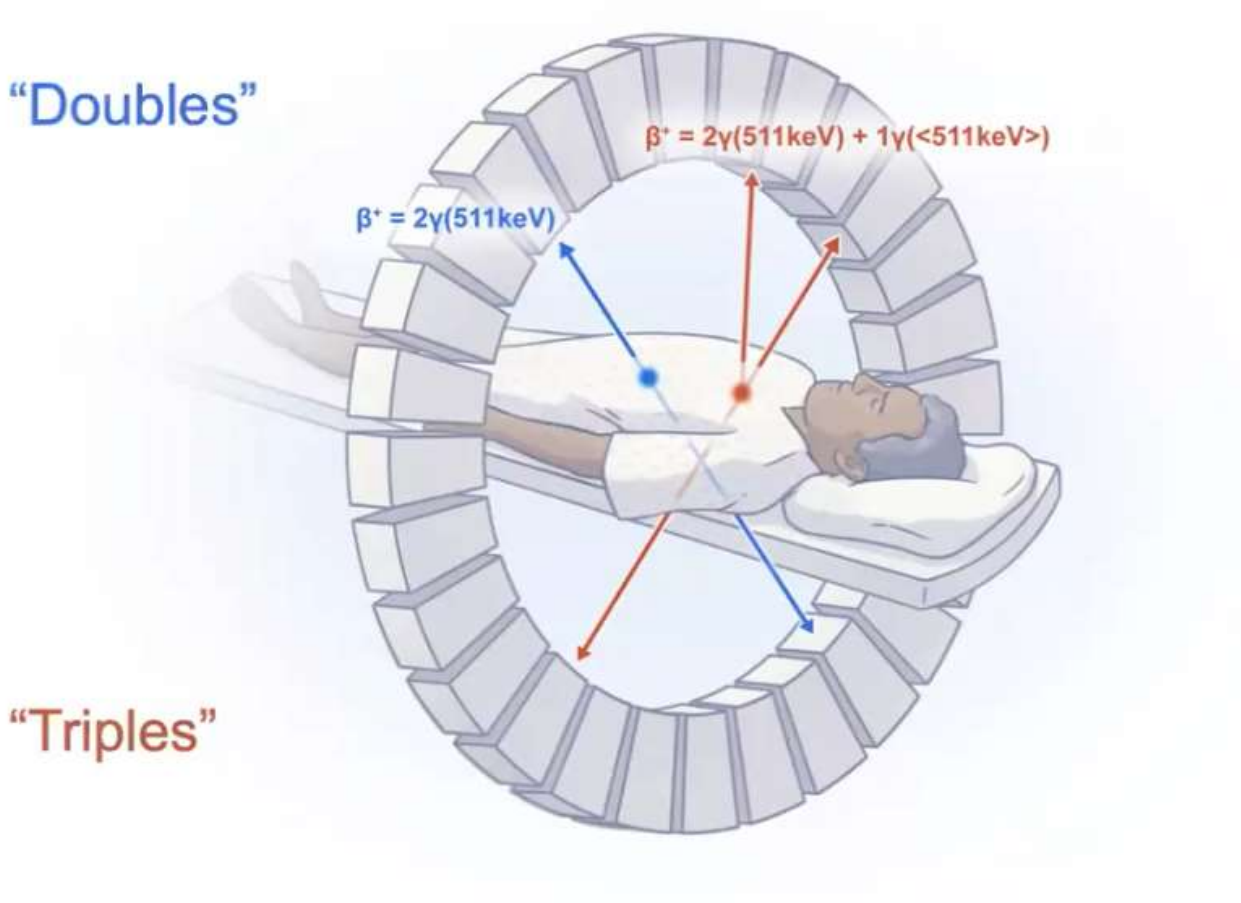
Simultaneous imaging of ≥2 radionuclides



ADVANTAGES:

- Improved diagnosis accuracy
- Personalized treatment planning
- Therapy selection and monitoring
- Research applications
- Save time and money
- Patient comfort
- Perfect spatial and temporal coregistration

PET vs. Multiplexed PET (mPET)



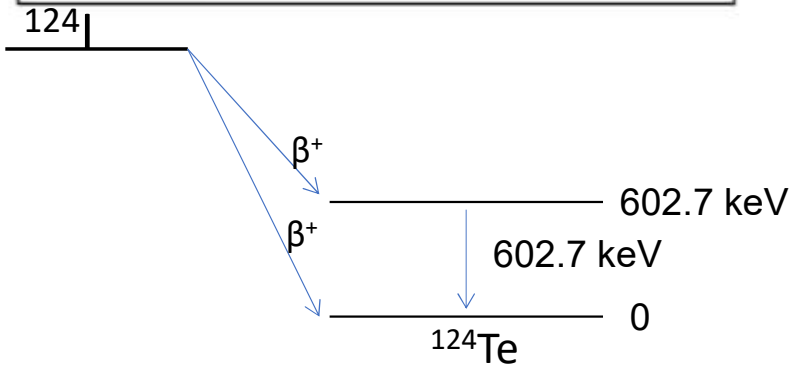
1) Use Standard (β^+) & **Non-Standard ($\beta^+\gamma$)** Radionuclides

2) Detection of Doubles and **Triple Coincidences**

3) Image Reconstruction & Separation

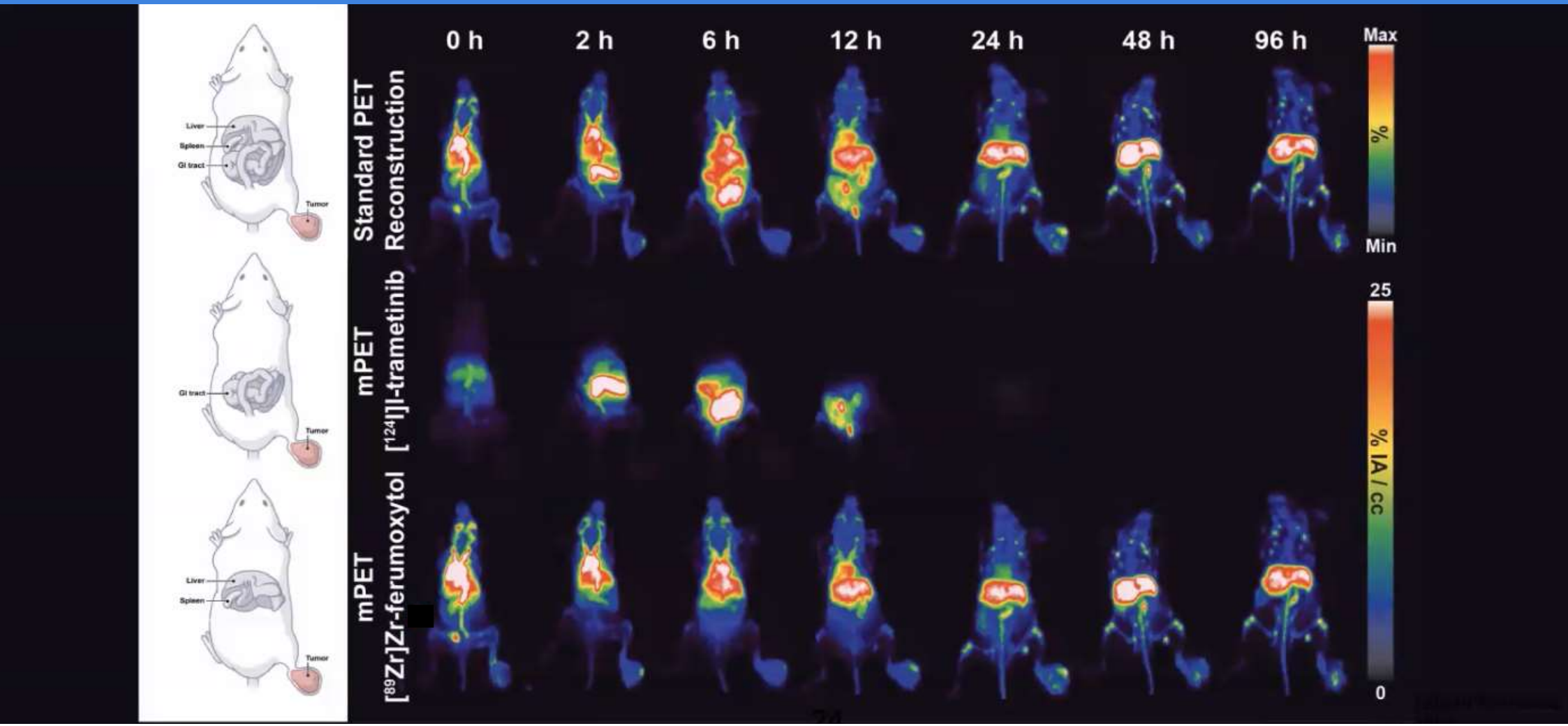
Standard (β^+) and Non-Standard Radionuclides

Doubles	Half-life	β^+ yield (%)
^{15}O	2.04 m	100
^{13}N	9.96 m	100
^{11}C	20.36 m	100
^{68}Ga	68 m	89
^{18}F	109.7 m	97
^{64}Cu	12.7 h	17.6
^{89}Zr	3.3 d	23



Triples	Half-life	β^+ yield (%)	Main Prompt γ [keV] & (β^+ γ / β^+ yield)
^{82}Rb	1.27 m	95	777 (13%)
^{52m}Mn	21.1 m	97	1434 (96%)
^{60}Cu	23.7 m	93	1333 (88%)
^{94m}Tc	52.0 m	70	871 (96%)
^{110m}In	1.15 h	62	658 (99%)
^{120}I	1.35 h	46	560 (72%)
^{44}Sc	3.97 h	94	1157 (100%)
^{86}Y	14.7 h	33	1080 (83%), 627 (33%)
^{76}Br	16.2 h	26	559 (58%)
^{72}As	1.08 d	88	834 (79%)
^{124}I	4.18 d	23	602 (51%)
^{52}Mn	5.59 d	29	744 (90%), 1434 (100%)

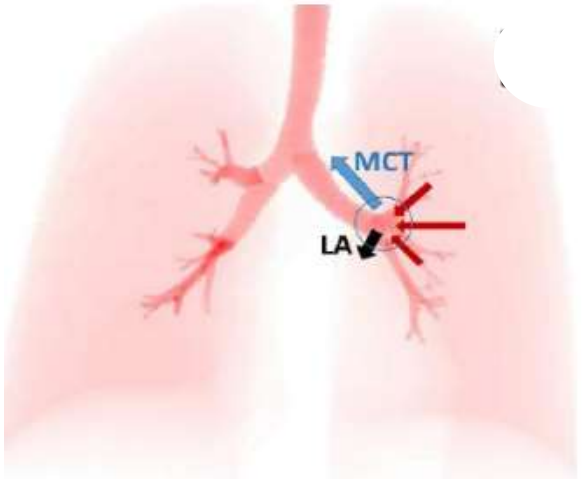
EXAMPLE 4: Nanoparticles – Drug Tracking with mPET



EXAMPLE 5: Liquid Absorption Imaging with mPET

- **^{13}N-NH_3 (Small-molecule)** – Muco-ciliary Transport + Liquid Absorption
- **^{76}Br-Albumin (Macromolecule)** – Muco-ciliary Transport

Differences in the transport of both molecules provides a 3D measurement of the liquid absorption in the lungs.



Biograph TP

NIH R21 Grant EB020849-01
P.I. Jose Venegas (Massachusetts General Hospital)

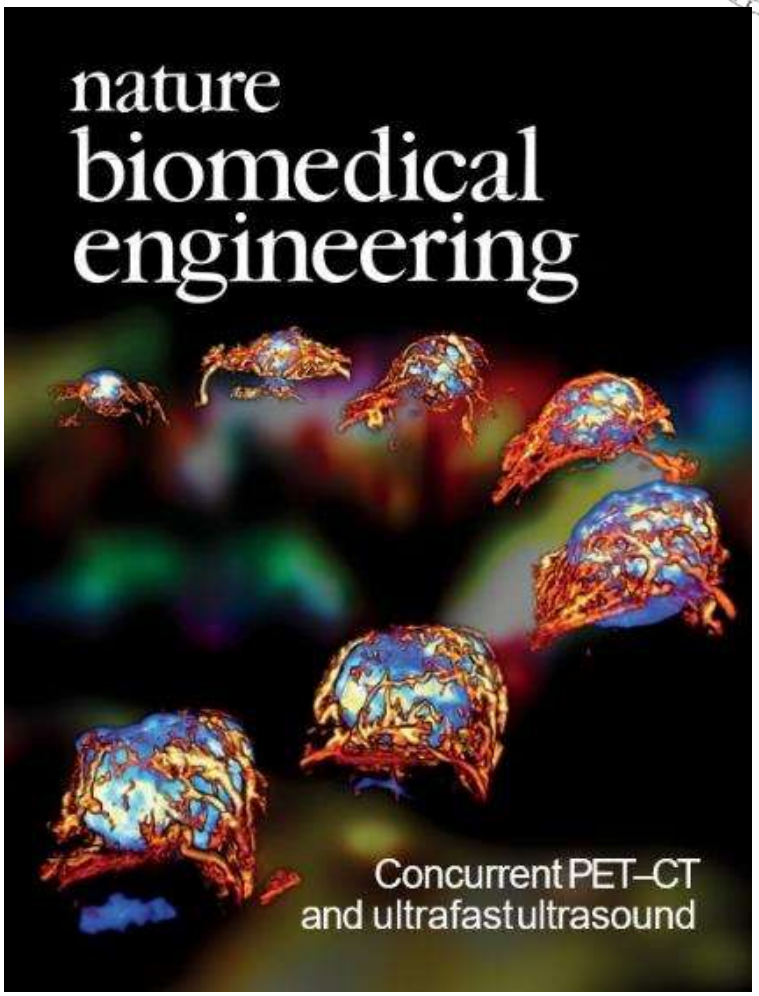
Multicolor PET research at UCM has been funded by NIH with 450 kUSD to assess its potential in preclinical and clinical settings, incorporating additional high energy resolution spectroscopic detectors, and test in clinical settings at SKCC (New York).

An application for an OpenFet grant (H2020) with partners groups from Germany, France and the Netherlands, is being submitted as we speak, for the first in-human clinical trials of the MultiPET principle

Advanced Multi-modality Imaging (MPL)

PETRUS : PET Registered Ultra-fast UltraSound imaging

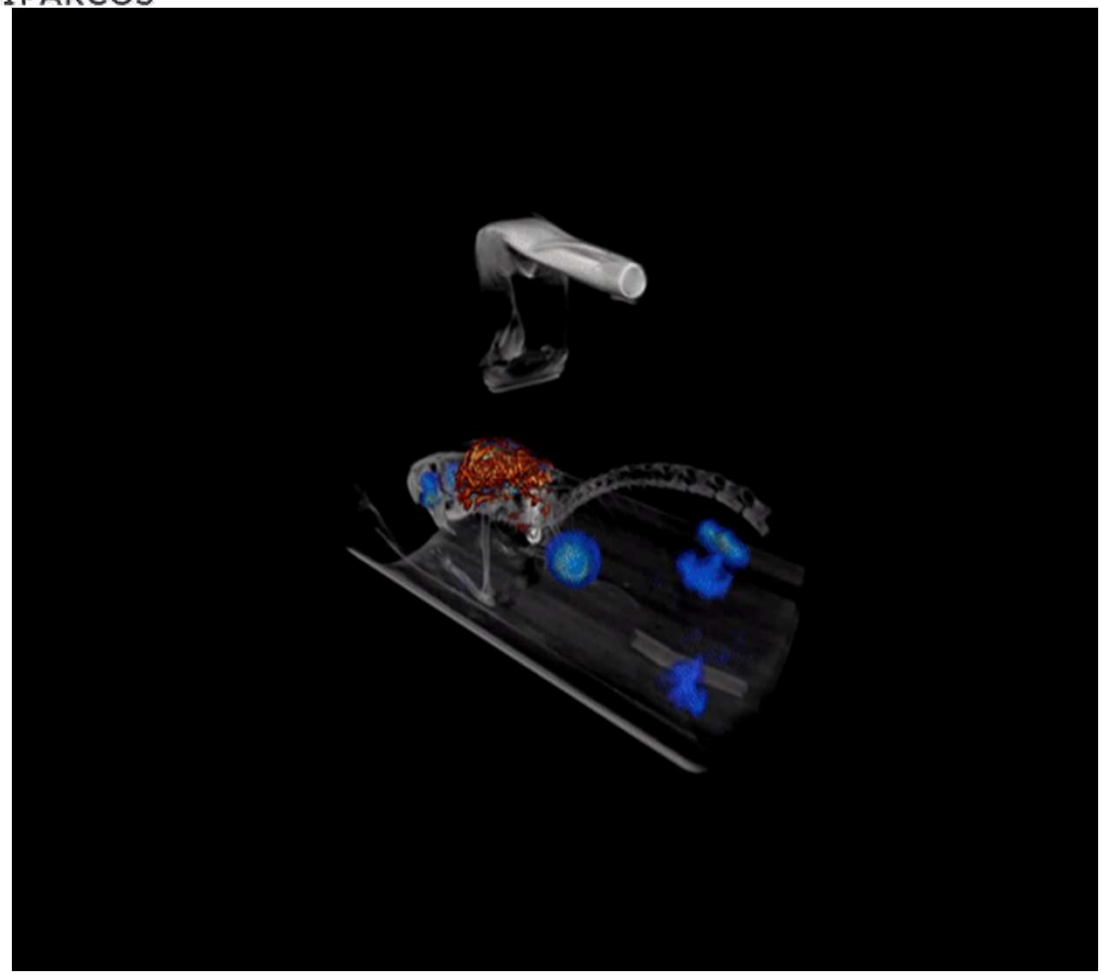
PETRUS : Device combining PET, CT,
Ultrafast Ultrasound imaging [1]

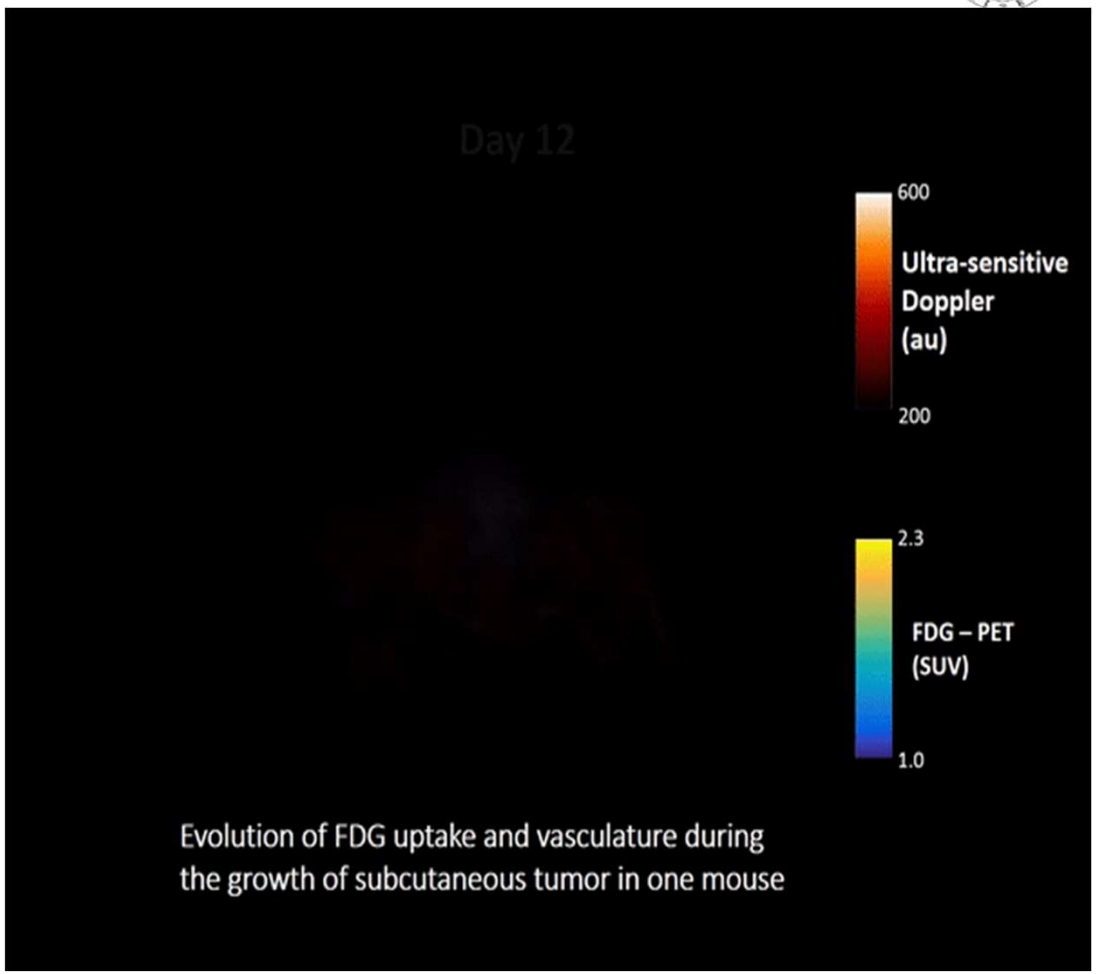


Provost, J.,et al. (2018). Simultaneous positron emission tomography and ultrafast ultrasound for hybrid molecular, anatomical and functional imaging. *Nature biomedical engineering*, *2*(2), 85-94.

PETRUS: PET/CT/Ultrafast Doppler imaging

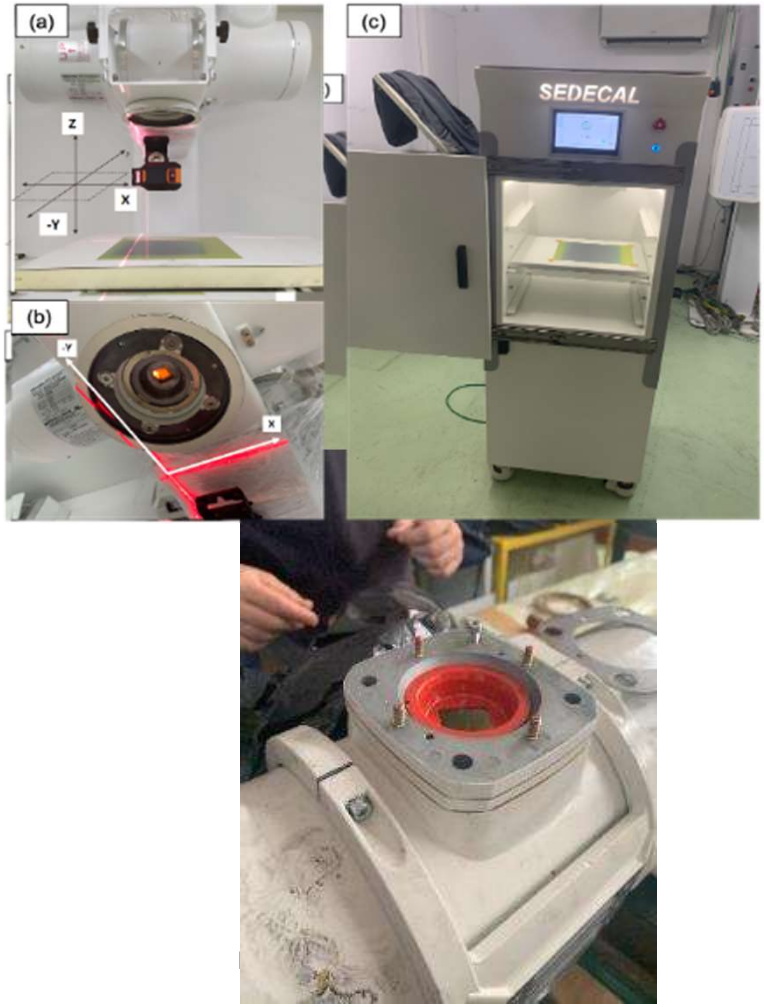
Xenografted tumor in a mouse (in vivo, reproducible, simultaneous acq.)

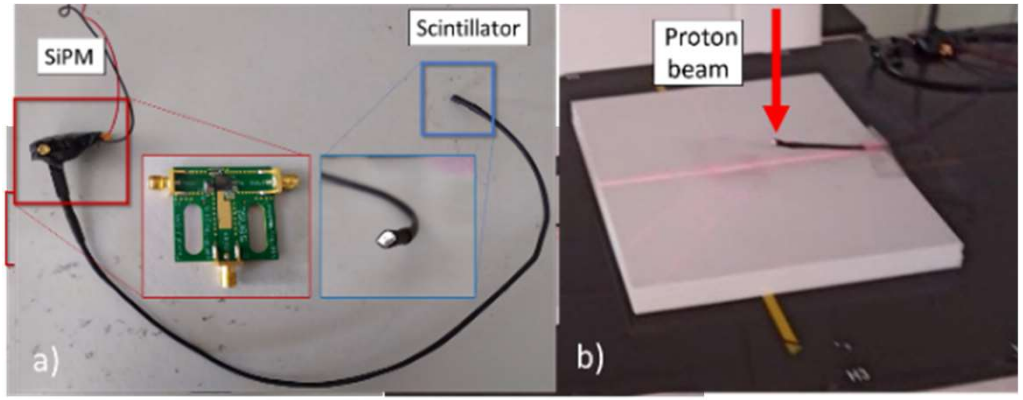


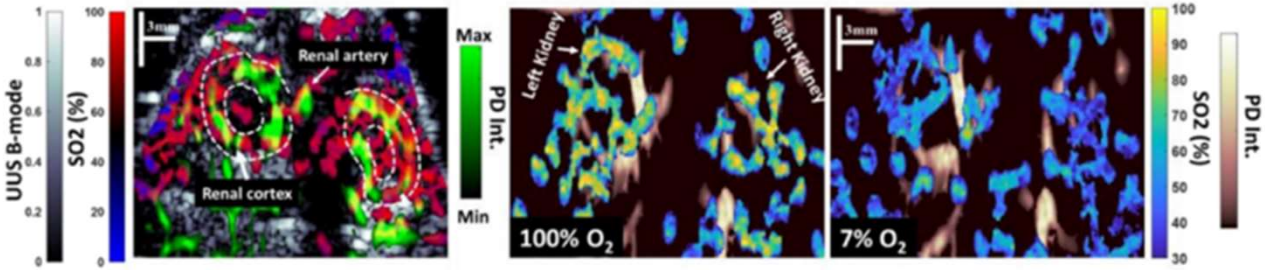


Provost et al., Nature in Biom. Eng. 2018; Pérez Liva et al., PMB 2018; Pérez Liva et al., MIB 2021, Fachin, et al., Therasn. 2020

IN Vivo ExploratioN of Tissue respOnse to Radiation (INVENTOR) PID2022-137114OA-I00, Mailyn PL, Paula IG







(Left) Overlay of the pulse echo (anatomical imaging), SO_2 (tissue oxygenation) and power doppler (PD) images of the two kidneys of a heathy mouse. (Right) Power Doppler (PD) and SO_2 images during O_2 challenge. (Sarkar,Pérez-Liva 2022)

Nuclear Imaging: Other

Several other projects:

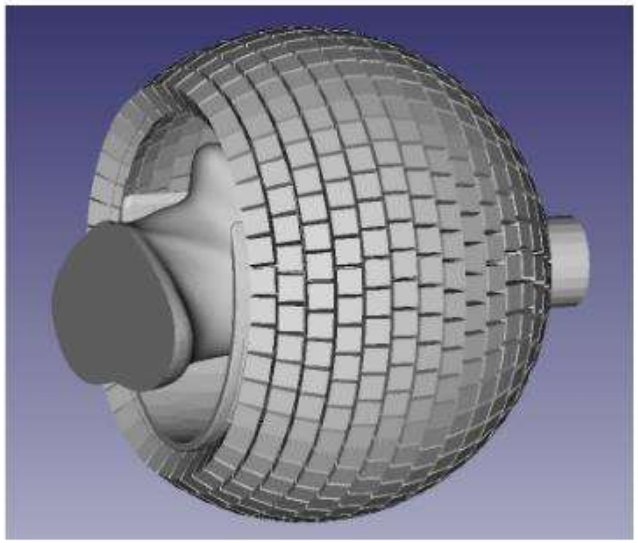
newMBI: low cost, high sensitivity, high IQ molecular breast imaging system (MBI)

non-invasive sampling of radiotracer activity (SEP)

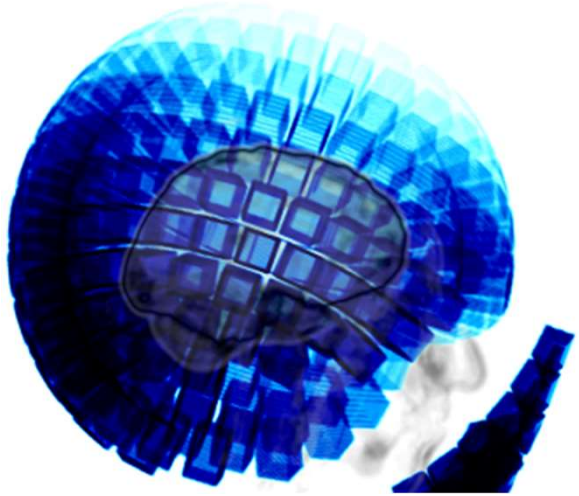
Brain PET dedicated scanners, with MGH (USA) on one side (HRST-BRAINPET) and with SEDECAL on the other hand (HELMET-PET)

Dedicated PET BRAIN SCANNERS

HRST-BRAINPET-2 (Martino's Center, MGH) Ciprian Catana *et al*, jnumed118.217901. 8 MUSD total funding, up to may 2025. 180 keuros for GFN@IPARCOS



HELMET-PET By SEDECAL, SMI and UCM/IPARCOS. JM Ortega, JM Arco and JM Udías. Funded by CDTI (490 keuros up to june 2024, 4.5 Meuros up to december 2025 after demonstrator passes tests. 200 keuros for GFN@IPARCOS



Thank you!