Public-private collaboration in the development of medical imaging applications

M. Seimetz

Instituto de Instrumentación para Imagen Molecular (I3M), CSIC-UPV, Valencia

OMA Careers Workshop
Seville, September 2-3, 2019

Outline

Who I am

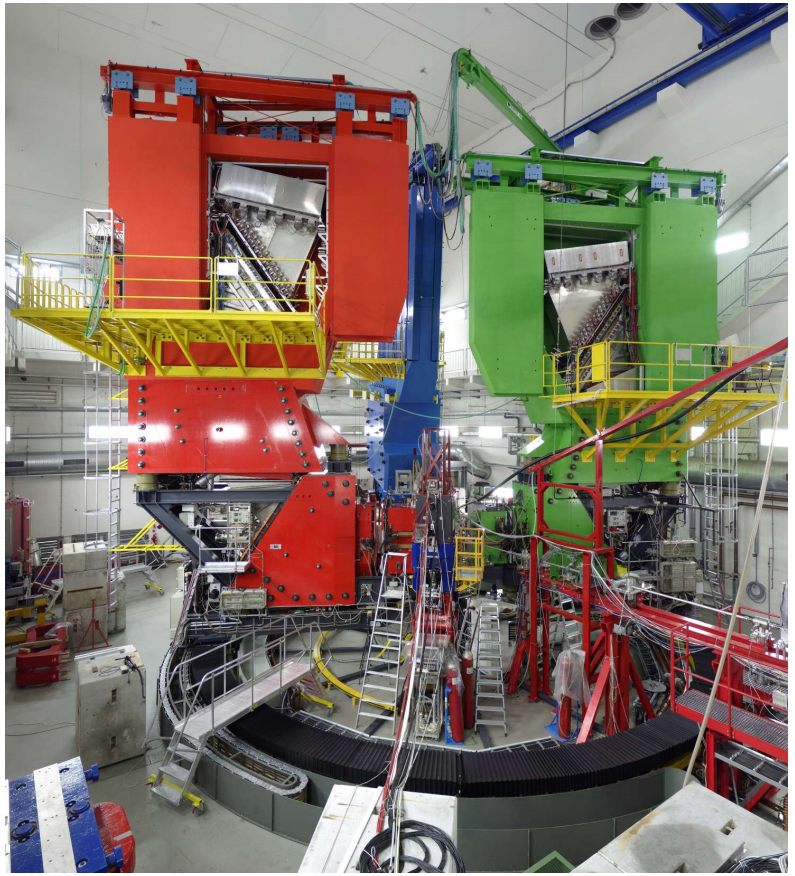
Hadronic Physics (1998-2006):

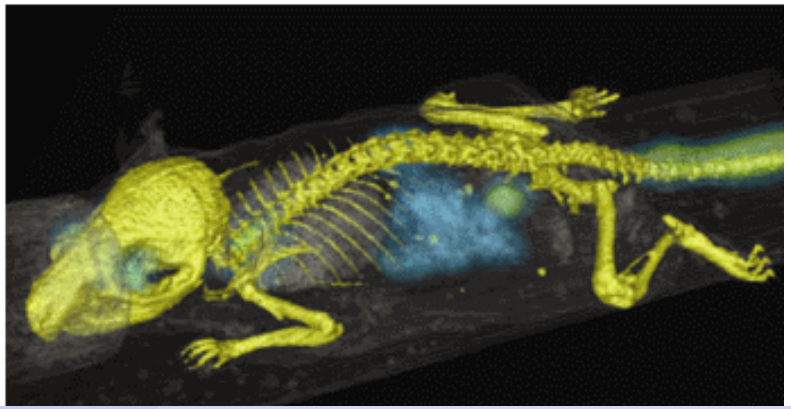
- Accelerator MAMI B (Mainz)
- COMPASS exp. (CEA Saclay/CERN)
- CB-ELSA (Bonn).

Reconcile career and family
(rather, make a choice).

Medical applications of nuclear physics:

- Medical imaging (Oncovision, Valencia, 2007-2012)
- Laser-ion acceleration (I3M, Valencia).





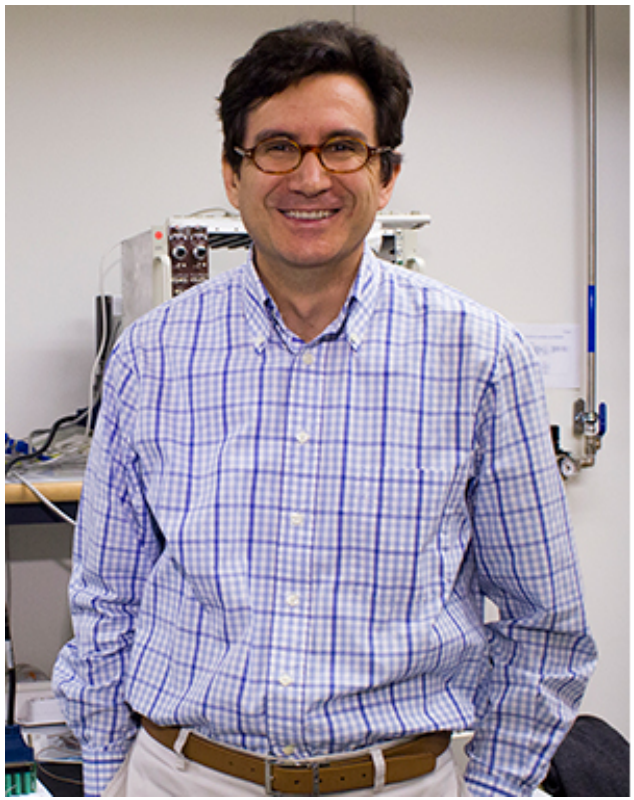
Who I am not

Worm's-eye view:

- Employee and group leader in spin-off company (not founder or executive manager)
- Senior Scientist at CSIC (not faculty leader).

Different perspective: José María Benlloch

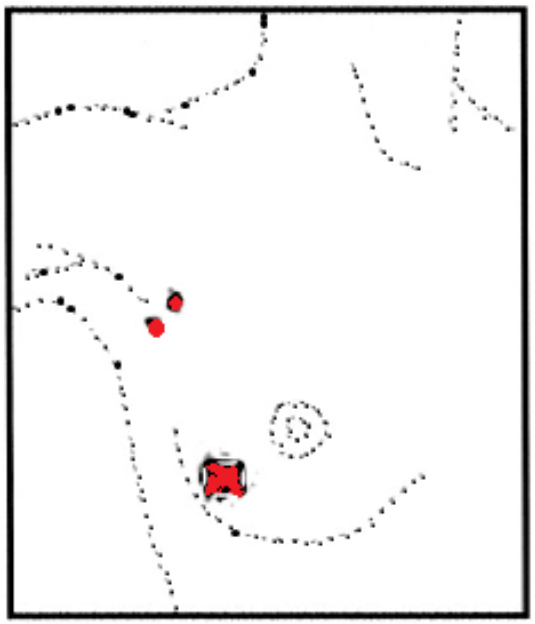
- Director of I3M
- Founder of Oncovision (and other spin-offs)
- Jaime I Prize for Novel Technologies 2008
- Spanish National Prize in Investigation 2014
- ERC Advanced Grant
- Member of European Academy of Sciences.

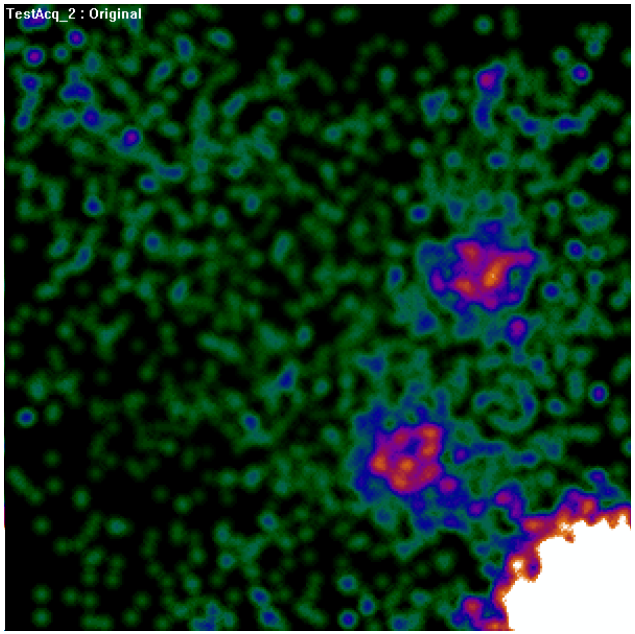


Oncovision: Scientific Mission

Tumour localization with radioisotopes:

- Administration of radiotracer (^{99m}Tc-Pertec, ^{18}F-FDG, ...)
- Concentration at spots of high metabolic activity
- Localization with external gamma detectors.





Oncovision: Scientific Mission

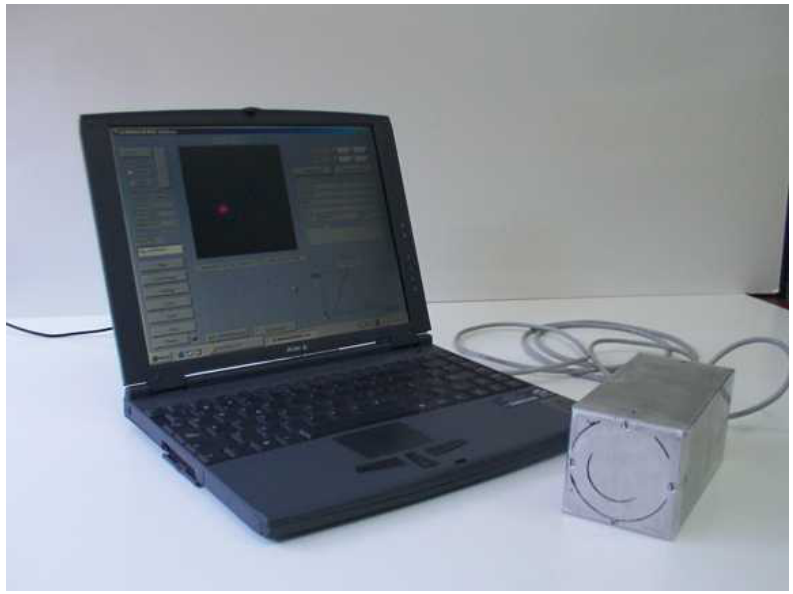
Medical gamma camera:

MiE Scintron

Surgical gamma probe:

Care Wise, C-Trak

Initial idea: Compact gamma camera for sentinel node detection.



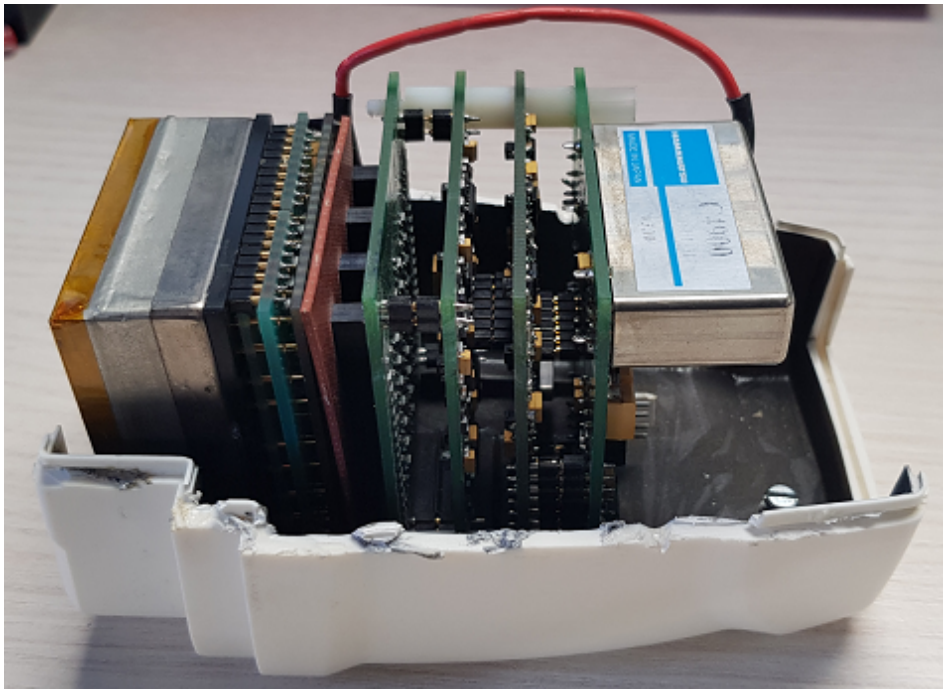
Lab model, 2003

- Image acquisition during cancer surgery
- Weight 1.4 kg, length 15 cm
- Higher sensitivity wrt gamma probe.

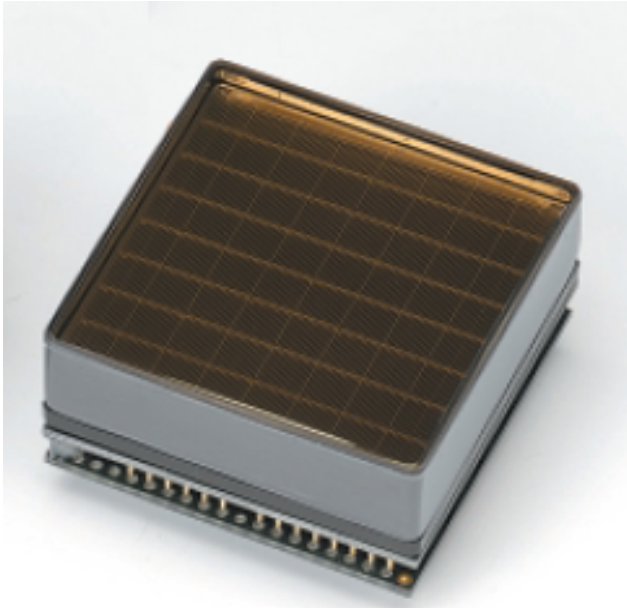
Gamma imaging module

Technology based on nuclear physics

Self-contained imaging system (80-200 keV)



- CsI(Na) crystal
- Position-sensitive PMT



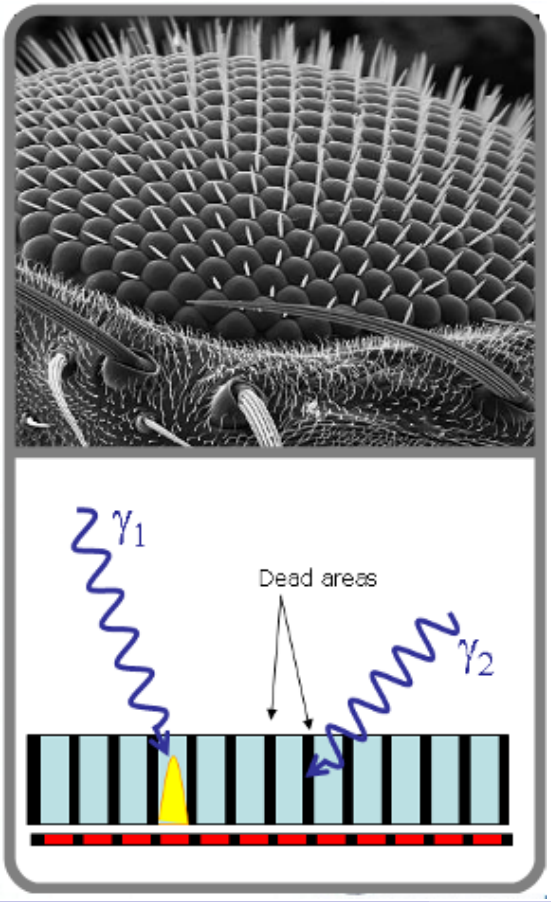
Hamamatsu H8500

- Anode resistor network
- Readout with Anger logic
- HV supply.

Scintillator crystal

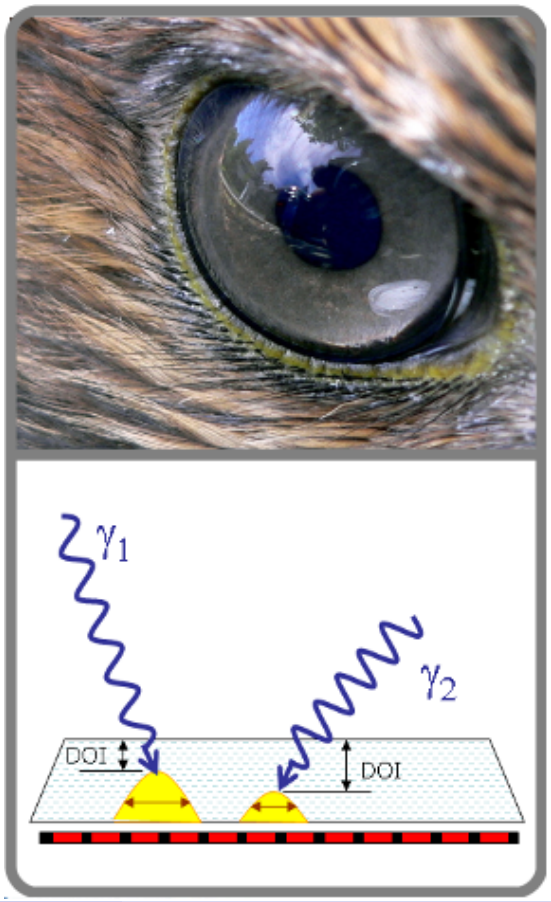
Pixelated crystals:

- One crystal per photon detector
- Resolution given by pitch
- No depth information.



Oncovision: Monolithic crystals

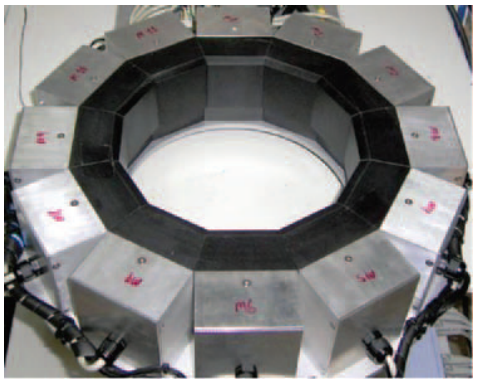
- Lower cost
- Measure photon distribution
- Depth of interaction (DOI).



Application to PET

Same detector matched to Positron Emission Tomography:

- Higher energy (511 keV)
  $\Rightarrow$ thicker crystal
- Modular structure



- Patient in prone position
- 170 mm FOV
- 15 min acquisition time
- Higher sensitivity than whole-body PET.

Mammi
MOLECULAR BREAST IMAGE

20+ units in clinical use

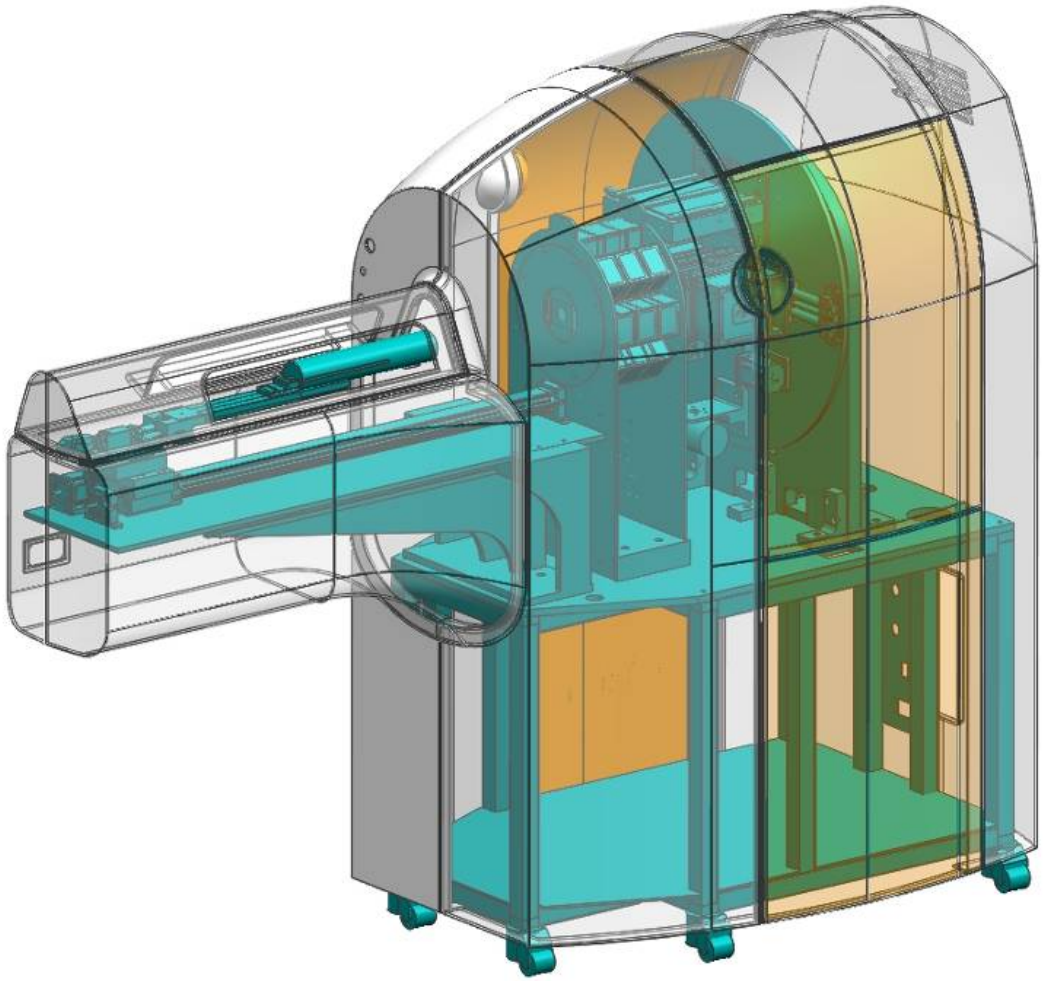
Preclinical imaging

Ibira animal PET
seeing beyond

40+ units sold

Small animal tomography:

- 1-3 PET rings (steady)
- 2 SPECT modules (rotating)
- CT scanner
- Preclinical research (mice, rats)
- Now licensed by Bruker Biospin
- MRI compatible with SiPM arrays.



Technology transfer

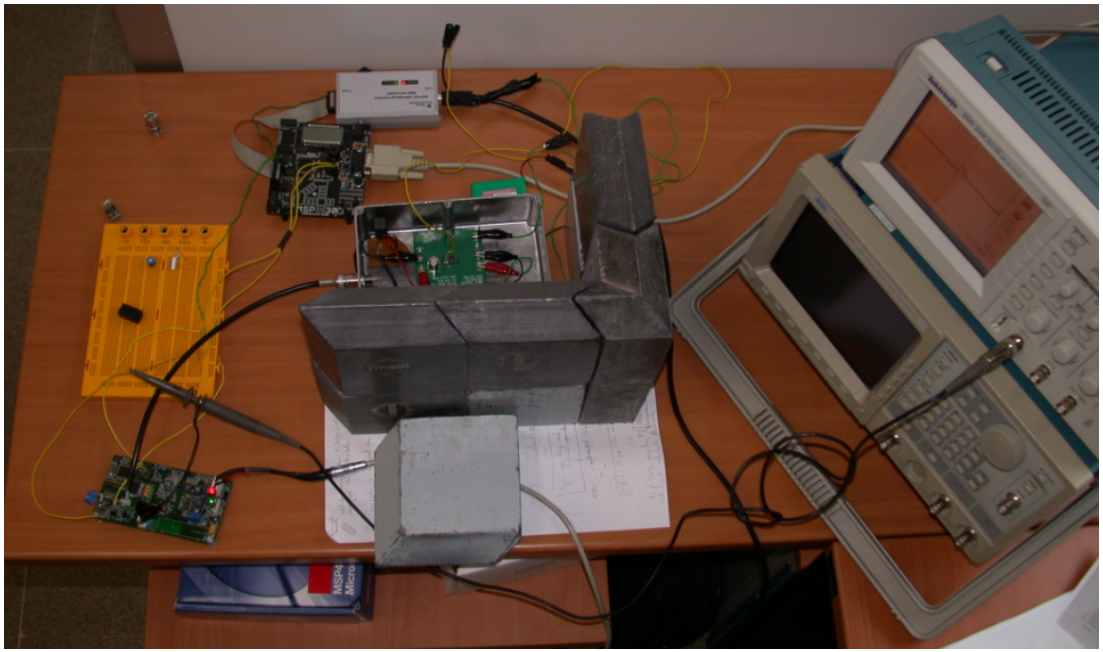
R+D/lab model	Prototype/ product dev.
IFIC/I3M	Oncovision

Don't underestimate product development!

- Practical needs
- Regulatory constraints
- Self-contained device
- Ergonomics and safety
- Cost-effectiveness.

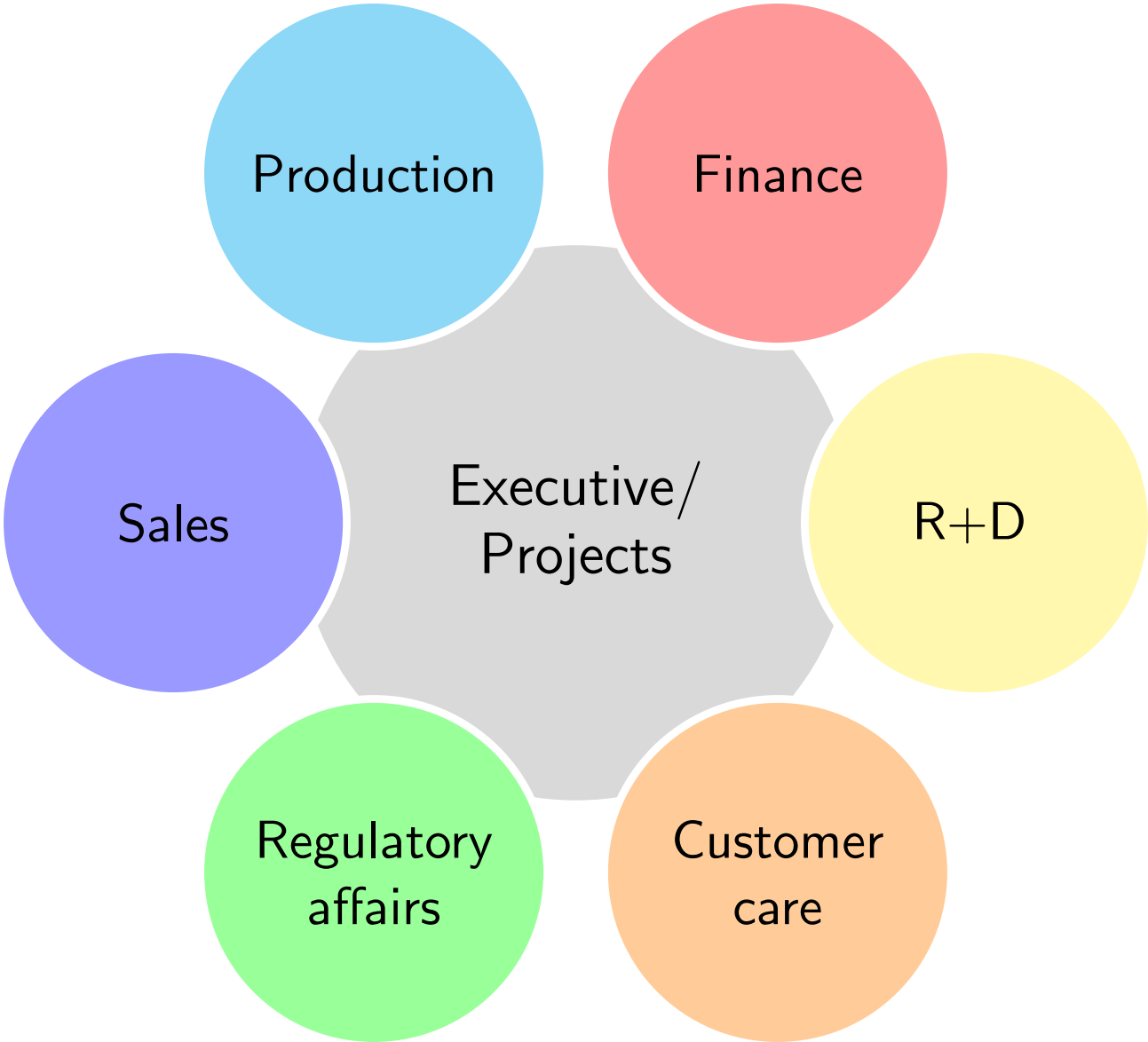
Technology transfer

From basic lab tests ("it's almost done")...

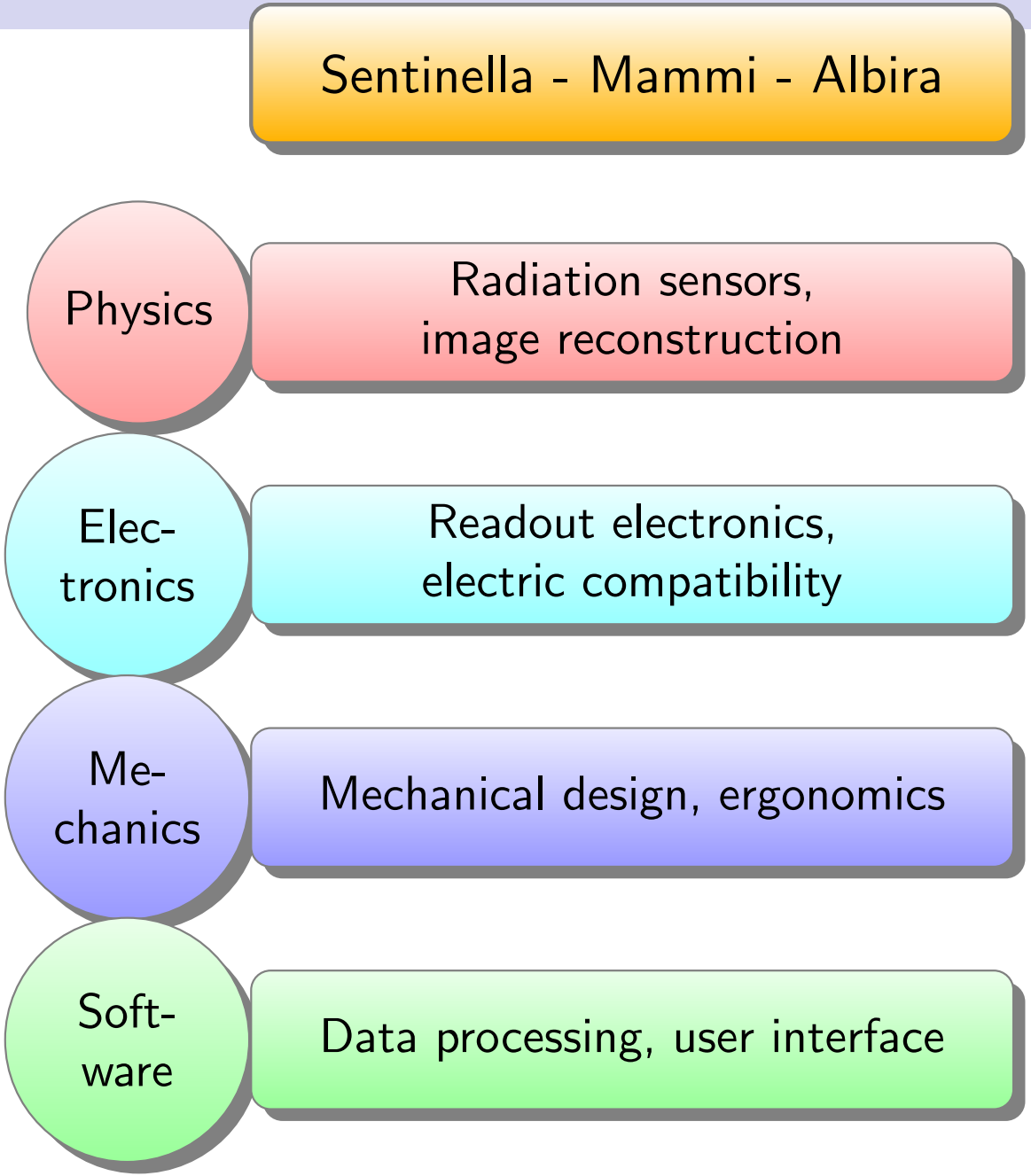


... to the final product (2 years).

Oncovision: The company



R+D department



Career in Oncovision

Company: founded in 2003; ∼60 employees in 2012, 20 in R+D.

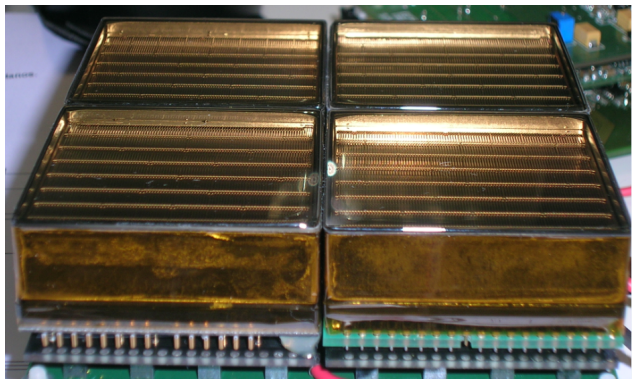
My activities:

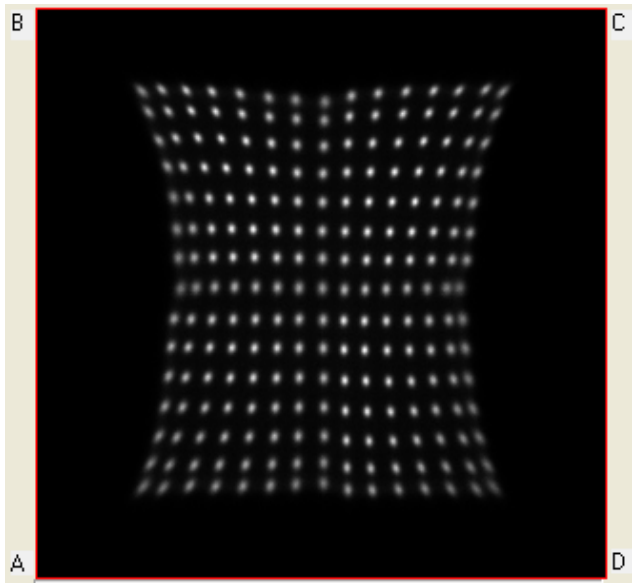
- April 2007: Senior Scientist in Physics (cofinanced by Torres Quevedo grant)
- Supervisor of Radioactive Installations
- January 2009: Head of Physics
  5 employees and collaborators from I3M (physics degrees or PhD, telecom. engineers)
- Training in project management.

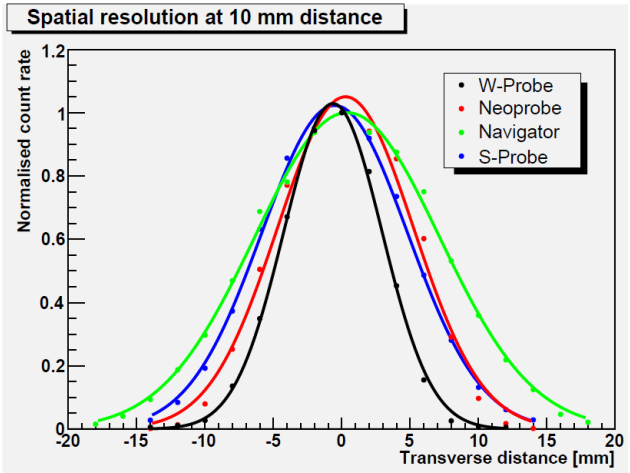
Hierarchy: "The boss is the one who controls the cash."
Not me - subordinated to Projects.

Physics contributions

- Design of radiation sensors
- Construction and testing of lab models
- Design of collimators and shielding
- Gamma event reconstruction (X, Y, Z, E)
- 3D reconstruction and correction algorithms
- Physical characterisation of imaging systems
- Collaboration with other R+D areas.



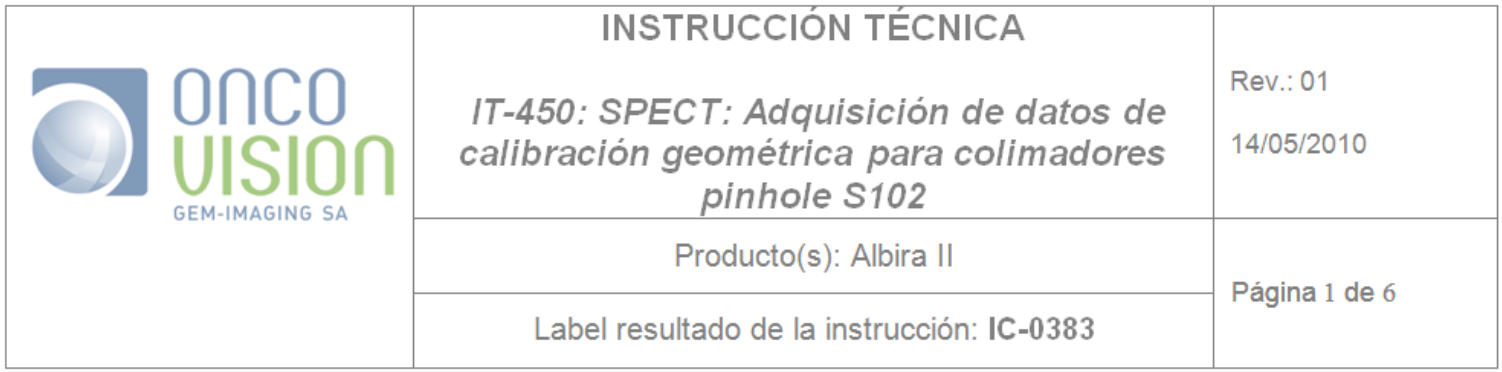




Physics contributions

ISO 9001 certified quality control system for traceability of components and reproducibility of manufacturing processes.

- Definition of acceptance criteria for critical components
- Technical instructions for manufacturing processes
- Implementation of international standards (e.g., NEMA)
- Assessment of long-term stability of imaging systems
- Documentation for certification (e.g., FDA classification of Albira CT as cabinet X-ray system).



ONCOVISION GEM-IMAGING SA	INSTRUCCIÓN TÉCNICA *IT-450: SPECT: Adquisición de datos de calibración geométrica para colimadores pinhole S102*	Rev.: 01 14/05/2010
	Producto(s): Albira II	Página 1 de 6
	Label resultado de la instrucción: **IC-0383**	

Oncovision by hindsight

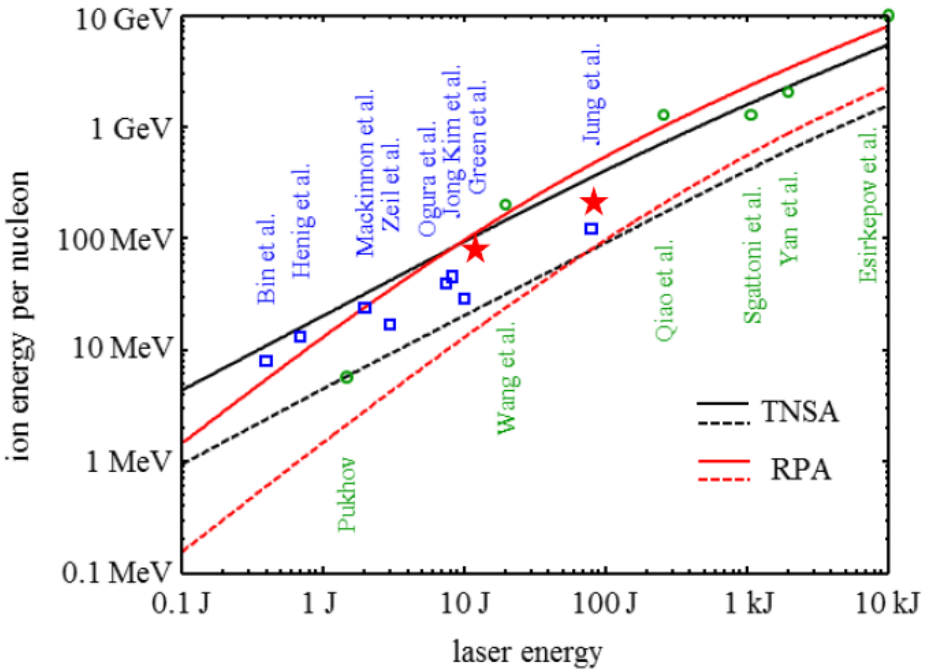
October 2012: Re-start as a postdoc at I3M

- Change permanent contract for temporary project
- Scientifically more challenging
- Little perspective of further promotion in the company
- However, life-enhancing experience with fantastic colleagues
- Many-sided activities
- Helpful insights for research career.

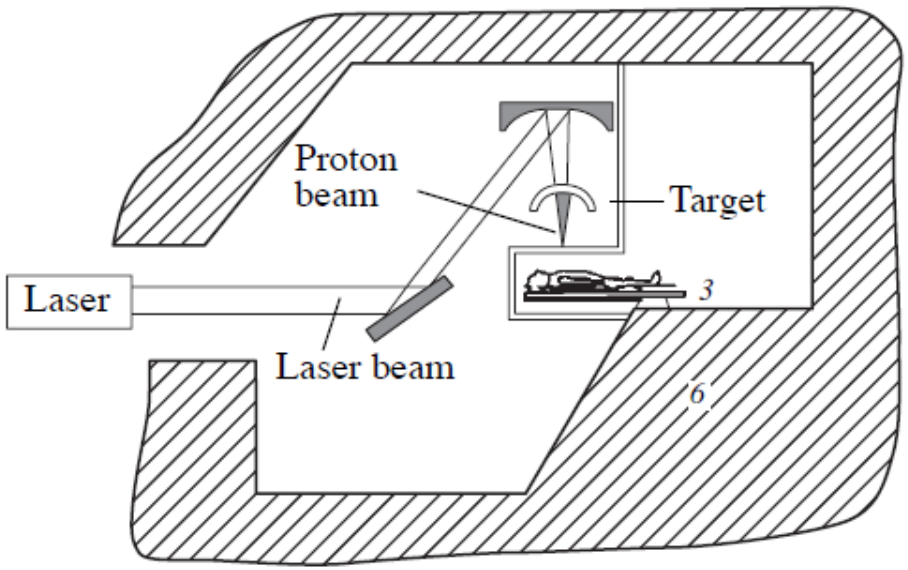
Laser-proton acceleration

Target Normal Sheath Acceleration:

- First observed in 1999
- TW and PW laser facilities
- Record chasing (highest energies, monoenergetic beams)
- Medical applications discussed from the beginning.



J. Schreiber, HP LSE 2 (2014)

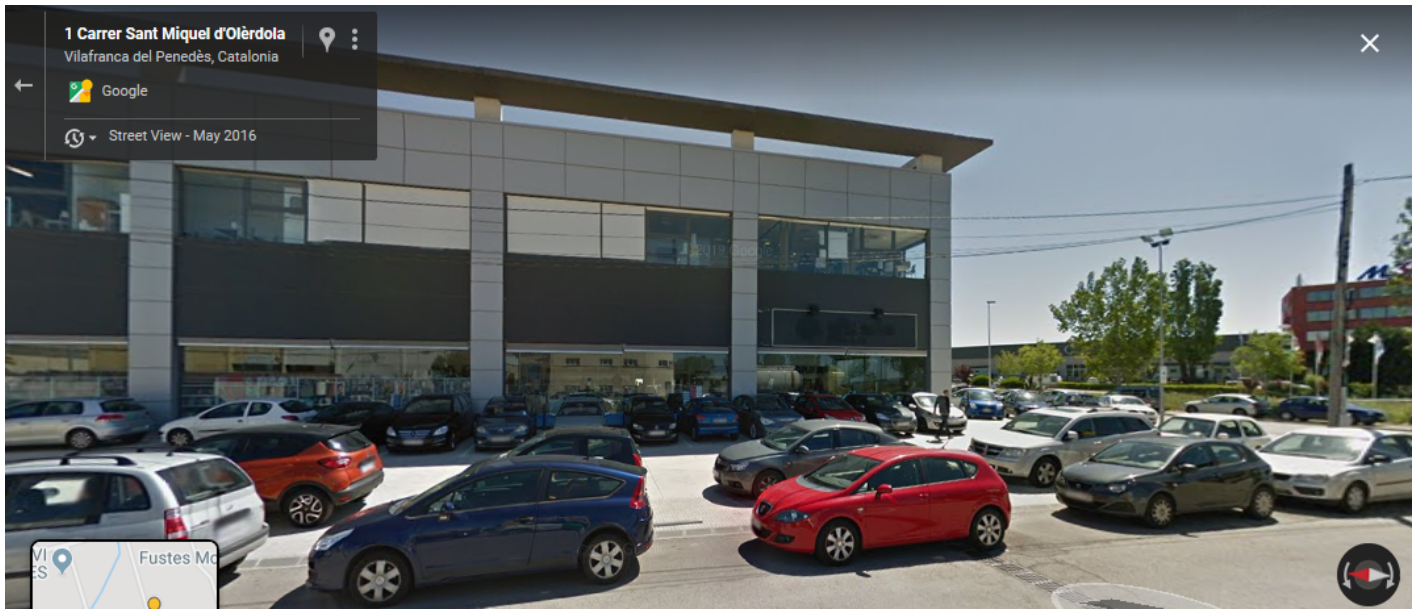


S.V. Bulanov, Plasma Phys. Rep. 28 (2002)

PLA: Laser-proton acceleration for everybody

Proton Laser Applications S.L. (PLA), Olèrdola (Barcelona), 2012:

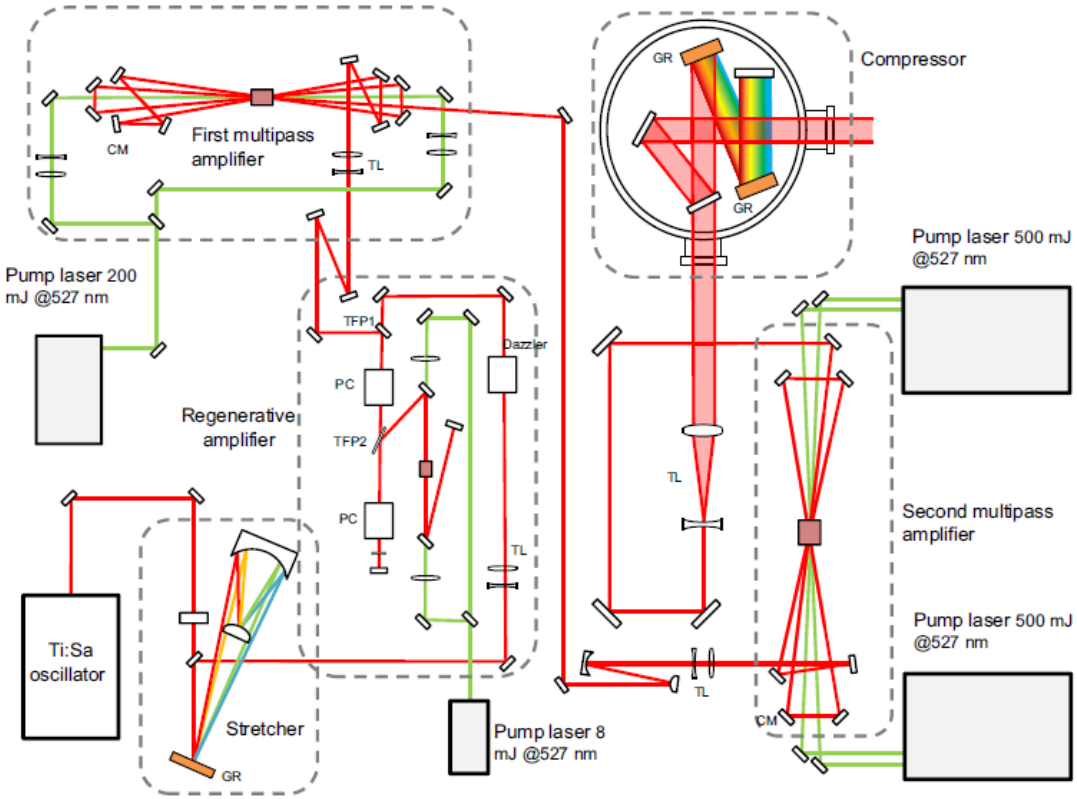
- Founded by 2 scientists, 1 laser engineer, 1 owner-manager
- Laser lab in industry complex close to national road
- Aim: develop TW-class Ti:Sapphire lasers
- Complete accelerator setup for radioisotope production
- 3 hours drive from Valencia.

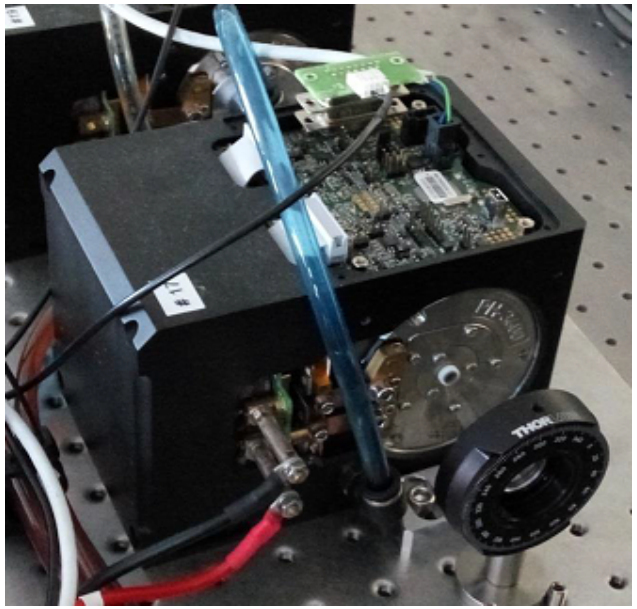


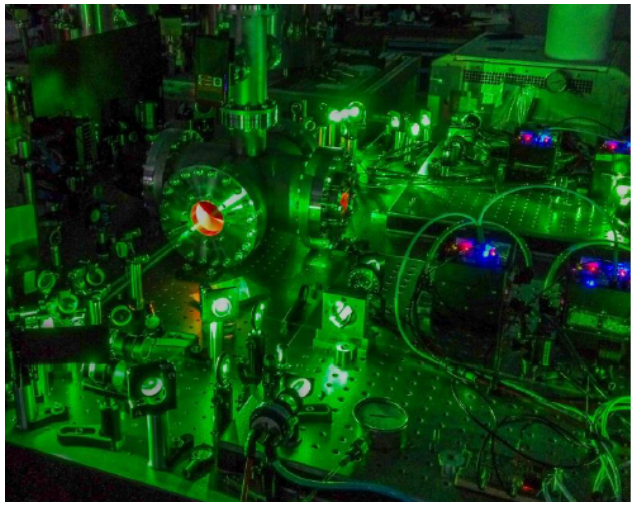
Google Street View

The PLA laser

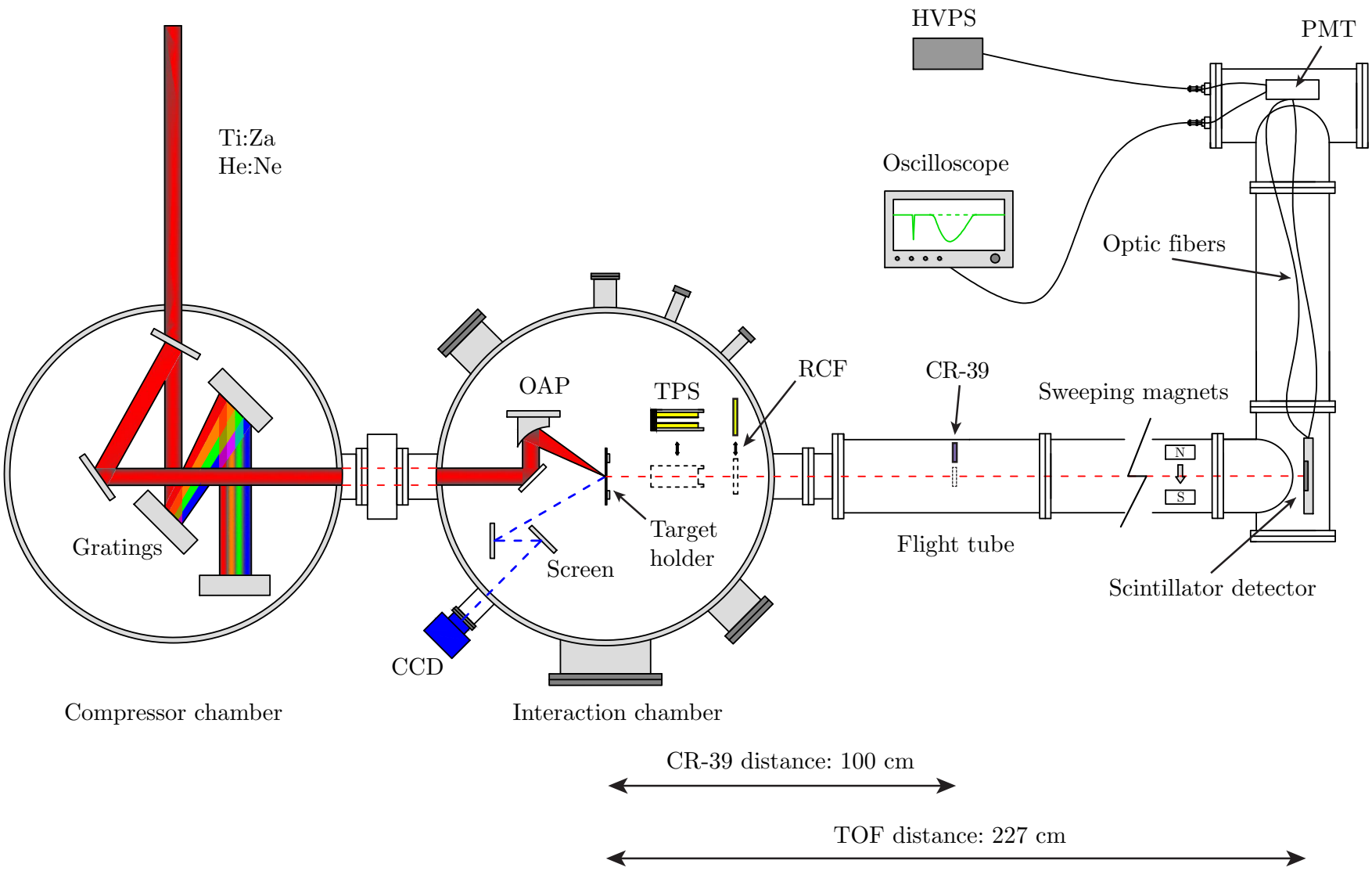
- Diode-pumped YAG/YLF modules
- 3 amplification stages
- 4 TW/55 fs, 10-100 Hz
- Contrast ratio 10^{-8} with saturable absorbers.





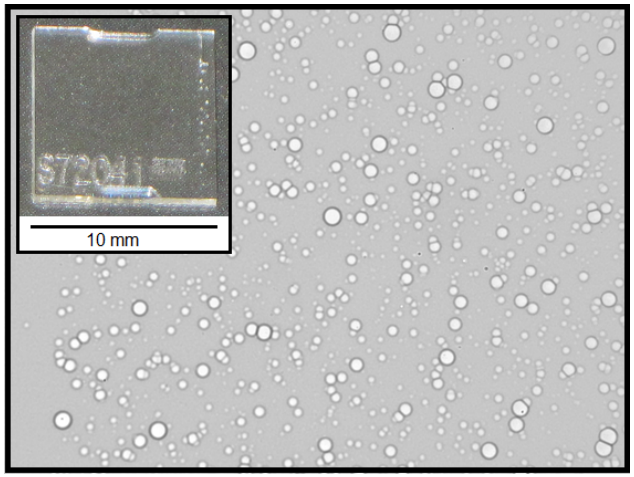


PLA: Experimental setup



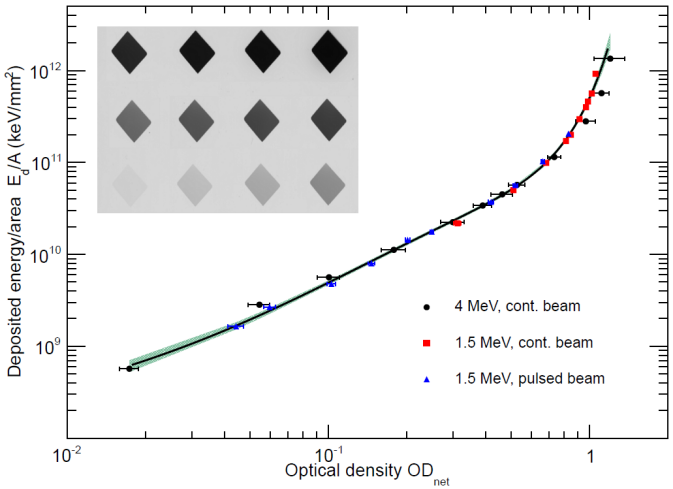
Proton detectors by I3M

PADC (CR-39)



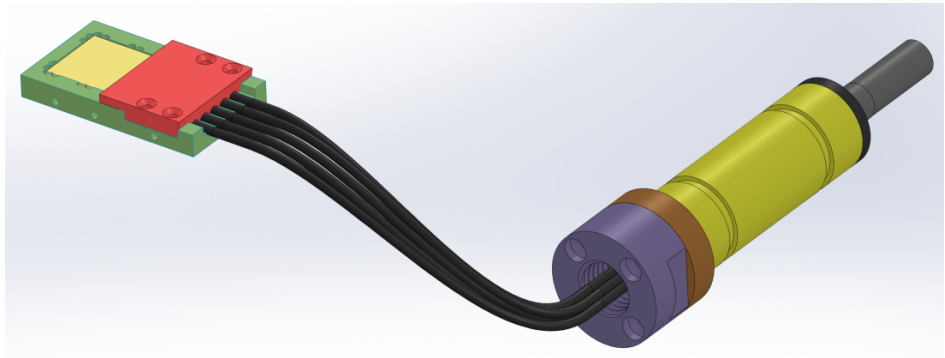
MS, RSI 89, 023302 (2018)

Radiochromic film (RCF)



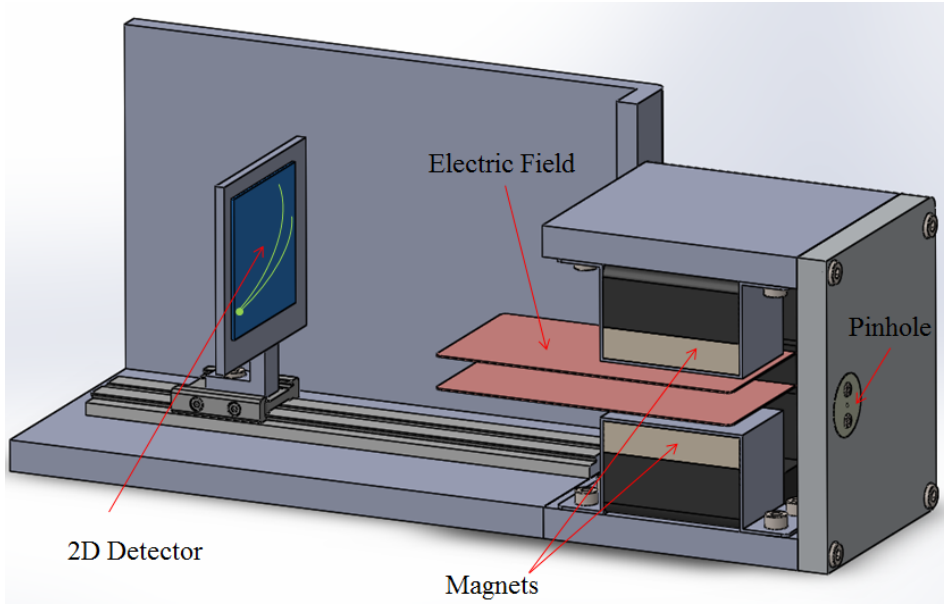
MS, TNS 62, 3216 (2015)

Time-of-flight (TOF)



MS, TNS 62, 3216 (2015)

Thomson parabola (TPS)



P. Bellido, IEEE NSS-MIC 2015

PLA: Staff and collaborators

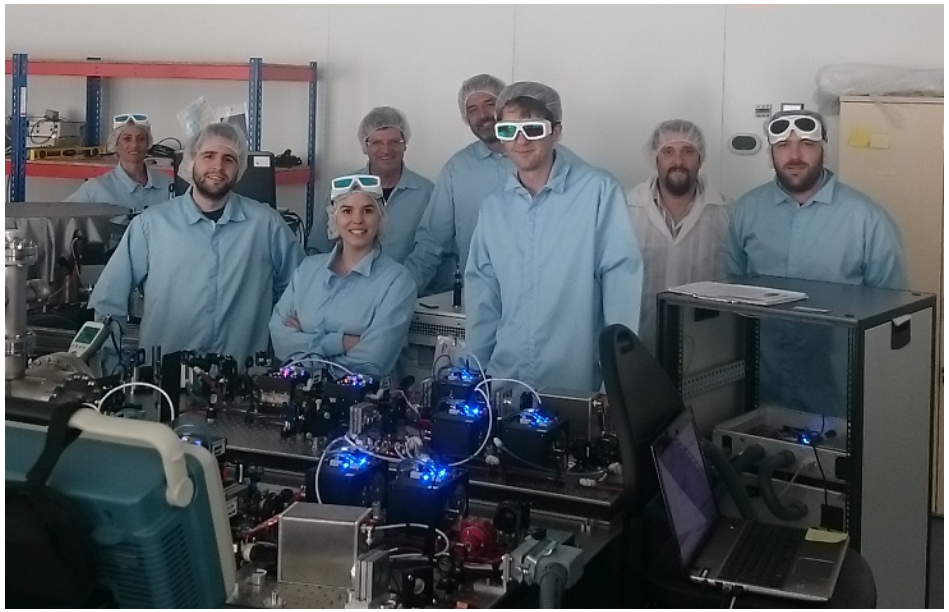
The guys who did the hard work:

- Alexandro Ruiz (PhD), Roberto Lera (PhD student), Salvador Torres: laser dev.
- Pablo Bellido (PhD student): exp. setup, detectors, target alignment.

Support from Barcelona and Valencia:

- Rossella Zaffino (postdoc): MEMS targets
- MS: detector dev., data analysis.

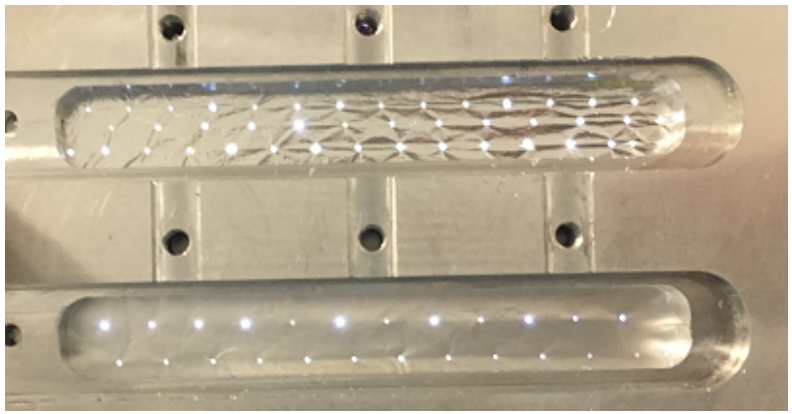
A very small team... but it worked!



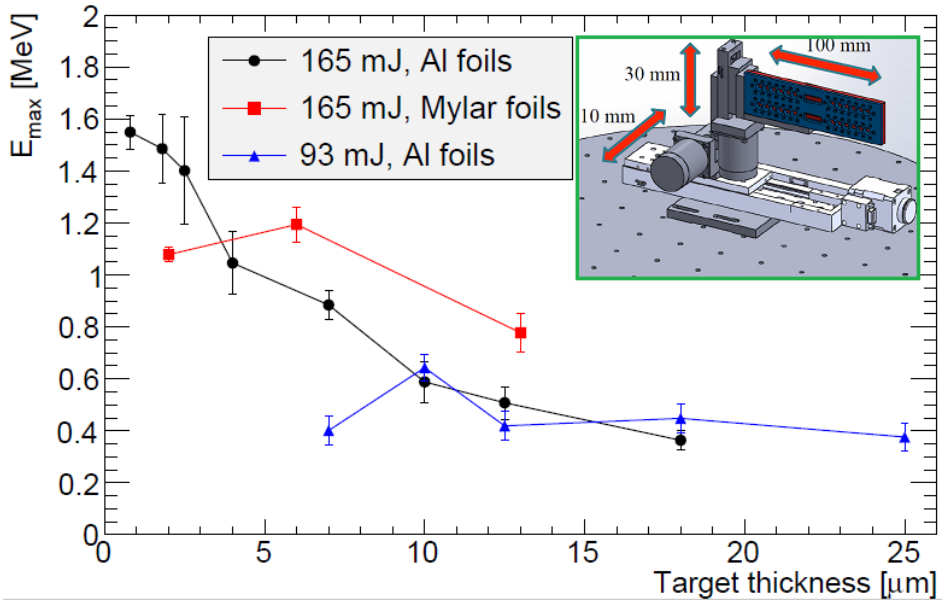
protonlaser

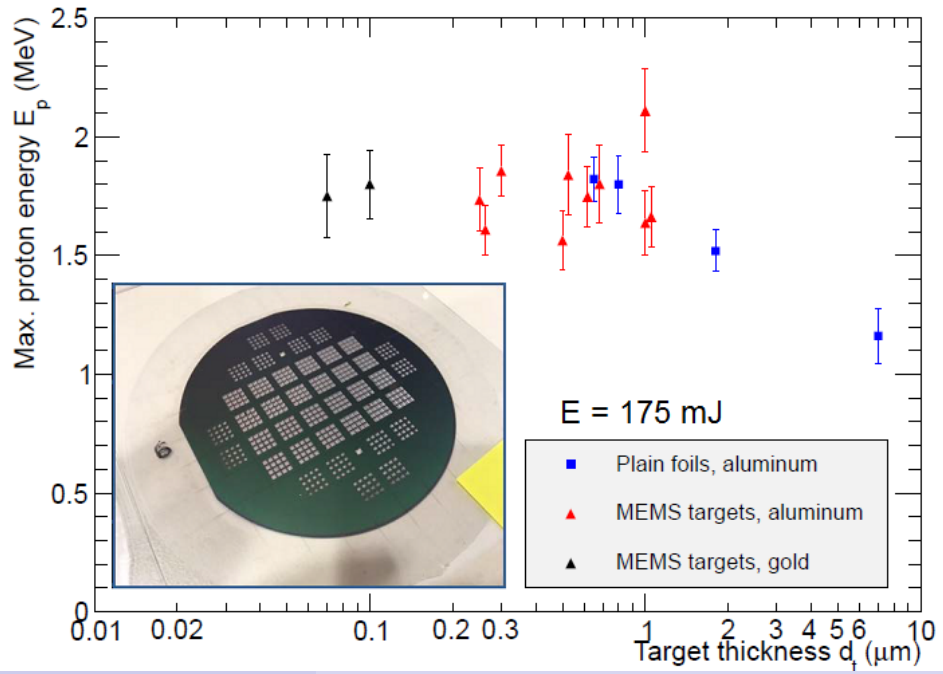
Results from PLA

- Single shot targets, ⌀5 mm:
  Al, pure/alum. mylar, 0.8-25 µm
- Multi-shot foils:
  Al, pure mylar, 0.65-7 µm



- MEMS membranes (1 mm^2)
  on Si wafers: Al (0.25-1 µm),
  Au (70-100 nm).





B. Bellido, J. Instrum. **12**, T05001 (2017)
R. Zaffino, Microelectron. Eng. **194**, 67 (2018)
R. Zaffino, J. Phys. Commun. **2**, 041001 (2018)
R. Zaffino, J. Phys. Conf. **1079**, 012007 (2018).

The end of PLA

Operation successful but the patient died:

- First realization of laser-proton acceleration in Spain
- Excellent opportunity for PhD students
- Major upgrade required to reach 5-10 MeV protons
- Constant operational costs
- Sales (laser systems) below expectations
- Technical achievements higher than commercial success
- However, not one “golden” invention
- Failure in September 2017. Not unusual for tech start-ups...

I3M at present: collaboration with L2A2, Santiago de Compostela
See poster by Juan Peñas.

Experiences and popular myths

Finance:

- Big budget (in comparison to university):
  Yes, as long as high priority (some projects stopped with 80% of work done).
- Infinite (private) funding:
  Tech start-ups need a lot of money. Several years w/o return. Try to find several independent investors. Public support required (not only credits).
- High salaries: Maybe outside Spain...
- Safe job: Not really. In case of doubt, the one with the highest salary has to leave first.

Experiences and popular myths

Seize the day (or Time is money):

- Deadtime constraints: Yes. Do the final testing by this afternoon but the other guy hasn't finished with the software yet.
- Very short timeline from lab model to customer: Sometimes maybe even too short...
- You get all the equipment you need: No Tiger for Albira...
- Life is faster: Now, former colleagues say I my life is calm and easy.

Experiences and popular myths

How much science in R+D?

- Much paperwork: Yes. Mostly, technical instructions and internal reports.
- Scientific output: Not many publications or conference contributions. "Don't tell our secrets!"

Bell labs are not everywhere (9 Nobel Prizes).

Possible conflicts of interest between researchers and managers:

- Build to sell: Results are not *per se* interesting. Only positive (competitive) results may be presented. Promises are taken literally.
- "Give me a figure": Concentration on relevant output or ignorance to the complexity of the real world?
- Egocentrism: The company rules.

I3M collaboration with private partners

Ongoing collaborations (research projects, R+D agreements, contracts):

- Bruker Biospin: Molecular imaging sensors (preclinical applications). Simultaneous PET/MRI thanks to SiPM arrays.

- Oncovision: Molecular imaging sensors (clinical applications)

- Bioemtech (Athens): Gamma cameras
- Tesoro Imaging: MRI scanners

- Radosys (Budapest): Proton/ion detection with CR-39 (see poster).

Acknowledgments

Colleagues from I3M which provided information for this presentation:

- José María Benlloch
- Antonio González
- Joseba Alonso.

Special thanks to the fellows from Oncovision and PLA!

Thank you for your attention!