AIFIRA

Applications Interdisciplinaires des Faisceaux d’Ions en Région Aquitaine

Philippe Barberet

Outline

1. Description of the facility
    1. Technical description
    2. Organisation & staff
    3. Running costs & funding

2. Scientific activity
    1. Ion beam analysis
    2. Micro-irradiation
    3. Detector characterization

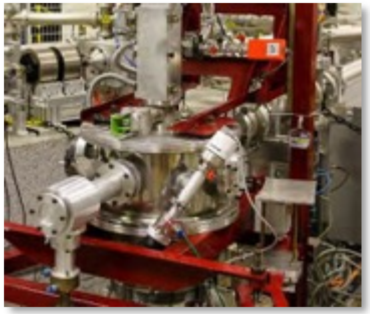
3. Evolution of the facility

The AIFIRA facility

AIFIRA : Applications Interdisciplinaires des Faisceaux d'Ions en Région Aquitaine

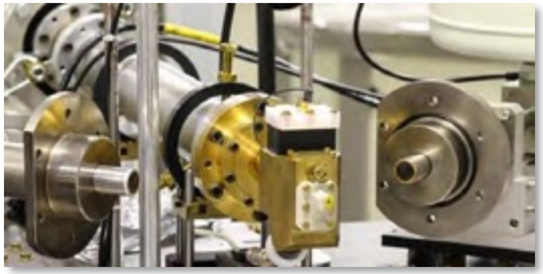
- Material analysis and irradiation using light ion beams (H^+, $^2H^+$, He^+)
- Single stage electrostatic accelerator (3.5 MV Singletron™, HVEE)
- 5 beamlines
- CENBG research facility opened to the scientific community & companies

Beamlines



- **Macrobeam**

  - Ion beam analysis at mm scale
  - RBS; NRA; PIXE; PIGE

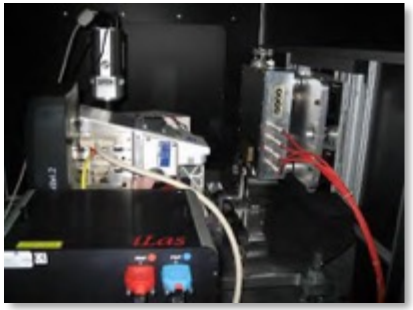


- **External beam**

  - Ion beam analysis for cultural heritage
  - PIXE; PIGE

- **Nuclear microprobe**

  - Ion beam analysis at the µm scale
  - RBS; NRA; PIXE; PIGE; ERDA
    IBIC; STIM; SED



- **Micro-irradiation**

  - Targeted irradiation of living cells with the µm precision

- **Physis beamline**

  - Production of secondary fields (n or γ) for nuclear physics and detector characterization

Organization & staff

CENBG head:

- F. Piquemal (Director)
- L. Serani (Technical director)

AIFIRA team : 3 people (1.5 FTE)

- Philippe Barberet, MCF UB, scientific coordinator (0.2 FTE)
- Stéphanie Sorieul, IR CNRS, operation coordinator (0.8 FTE)
- Philippe Alfaurt, IE CNRS, technical coordinator (0.5 FTE)

AIFIRA committee : beamtime reviewing and technological survey

- AIFIRA team
- Laurent Daudin, IE CNRS
- Guillaume Devès, IR CNRS
- Ludovic Mathieu, CR CNRS
- Stéphane Roudeau, IR CNRS
- Hervé Guégan, ARCANE

Operation & access

AIFIRA is a research platform (≈ 200 days of beamtime / year)

- Research projets of the CENBG teams
- Opened to external academic users
- Support to external teams using the facility

Services are provided by the ARCANE technology transfer unit (ADERA)

- Systematic measurements using well established techniques
- Contracts with industries
- Complete services
- 20 % of AIFIRA beamtime
- ~ 80 contracts / year

AIFIRA users

CNRS - IN2P3	CNRS - hors IN2P3	Autres
CENBG (UMR5797)	ICMCB (UPR9048/INC)	IRSN (LMDN)
LPC (UMR6533)	CRP2A (UMR5060/INSHS)	CEA (LIST/DSL)
IPHC (UMR7178)	CBM (UPR4301/INC)	IRSN (LE2M)
IPNL (UMR5822)	CELIA (UMR5106/INP)	
	PLACAMAT (UMS 3626/INC)	
	LCP (UMR8000/INC)	
	ECOLAB (UMR5245/INEE)	
	MFP (UMR5234/INSB)	
	INCIA (UMR5287/INSB)	
	CIRIMAT (UMR5085/INC)	
	PACEA (UMR5199/INEE)	
	Institut Fresnel (UMR7249/INSIS)	
	LAB (UMR5804/INSU)	

Running costs & funding

- Running costs = 90 k€ / year
  - 60 k€ : running costs and maintenance of the accelerator and the 5 beamlines
  - 20 k€ : electricity and fluids
  - 10 k€ : cover accidental breakdown of big equipment + regulatory controls

- Recurrent funding
  - 15 k€ IN2P3
  - ≈ 20 k€ University of Bordeaux (fluids)
  - 15 k€ ARCANE
  - Users fees : currently ≈ 10 k€ / year average

- Equipement on projects, e.g. in the last years :
  - iRiBio group CENBG (MITI, Physicancer INSERM …) : ≈ 60 k€ (last 5 years)
  - Région Nouvelle Aquitaine : “Plateforme Mutualisée” : ≈ 230 k€ (last 5 years)

Ion beam analysis (IBA)

Applications:

- Thin layers / materials
- Geology / geochemistry
- Achaeometry and cultural heritage
- Life science

Techniques : PIXE/PIGE, RBS, NRA, STIM, ERDA

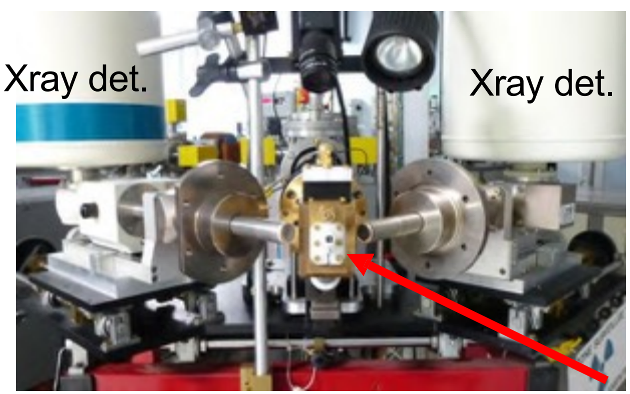
« Classical » IBA:

Quantification of light elements by RBS / NRA (e.g. Li)

Hydrogen mapping using ERDA

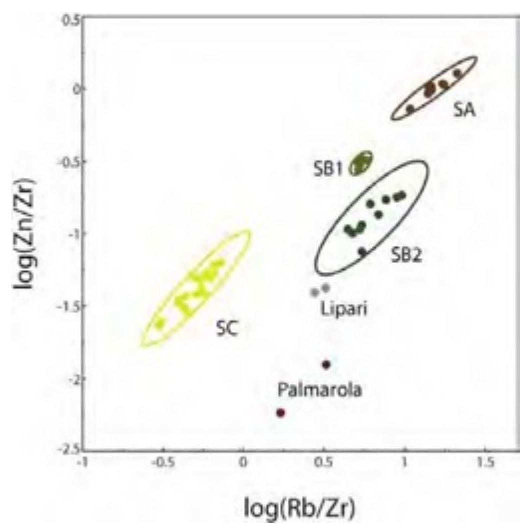
External beam: Non destructive measurements of the chemical composition of large and/or fragile samples

Collaboration CRP2A : Sourcing of obsidians from mediteranean basin



AIFIRA external beam

Beam extraction window



Orange, M. *et al.* *J. Archaeol. Sci. Reports* **12**, 834–844 (2017).
Le Bourdonnec, F. X. *et al.*, *NIMB* **358**, 271–275 (2015).

µ-IBA: Tissue & section analysis

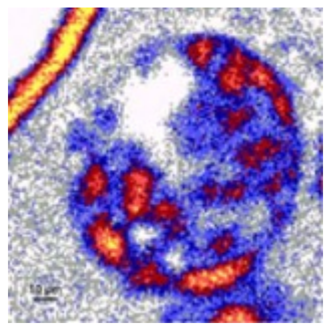
Analysis at the µm scale & elemental mapping

- Mainly used for life science application
- Main feature : quantitative measurement, µg/g sensitivity, imaging

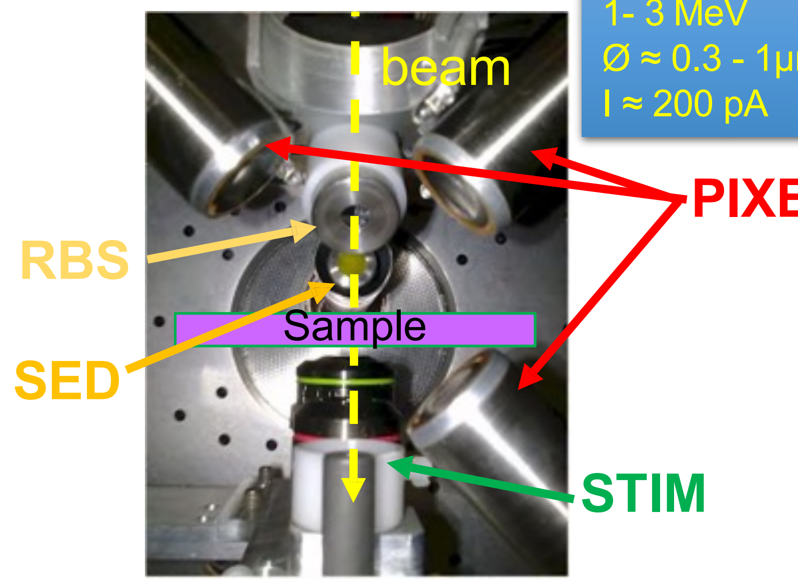
Development of bioactive materials used as bone substitutes (LPC Clermont)

Materials behaviour at the interface with living tissues

Release of trace elements in tissues



BEAM: H^+
1- 3 MeV
Ø ≈ 0.3 - 1µm
I ≈ 200 pA



J. Lao et al. Surface and Interface Analysis, 46 (10-11): 702-706 (2014).
J. Lao et al. Journal of Materials Chemistry B, 4 (14): 2486-2497 (2016).
J. Lao et al. Journal of Materials Science, 52(15): 9129-9139 (2017).

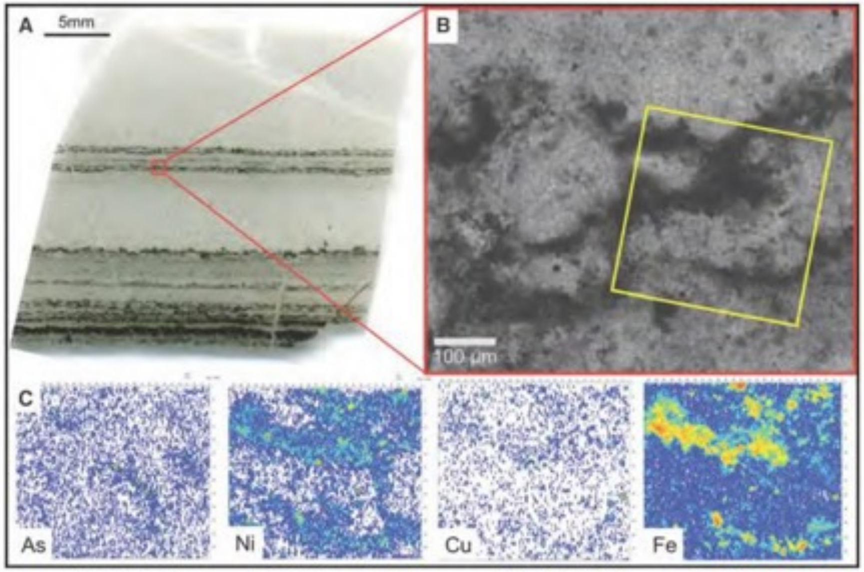
Patents
J. Lao, J. Lacroix, X. Dieudonné, E. Jallot. 'Implant with controlled porosity made of a hybrid material.'
J. Lao, J. Lacroix, X. Dieudonné, E. Jallot. 'Implant with controlled porosity comprising a matrix covered by a bioactive glass or by a hybrid material.'
J. Lao, X. Dieudonné, E. Jallot. 'Implant with variable porosity made of a hybrid material.'
J. Lao, C. Bossard, H. Granel, Y. Wittrant., E. Jallot, 'Implant with controlled porosity made of a hybrid material doped with osteoinductor nutriments.'

µ-IBA: Tissue & section analysis

Analysis at the µm scale & elemental mapping

Quantify the presence of hydrothermally transported inorganic elements in analogous sediments

- physical and chemical conditions for prebiotic reactions?

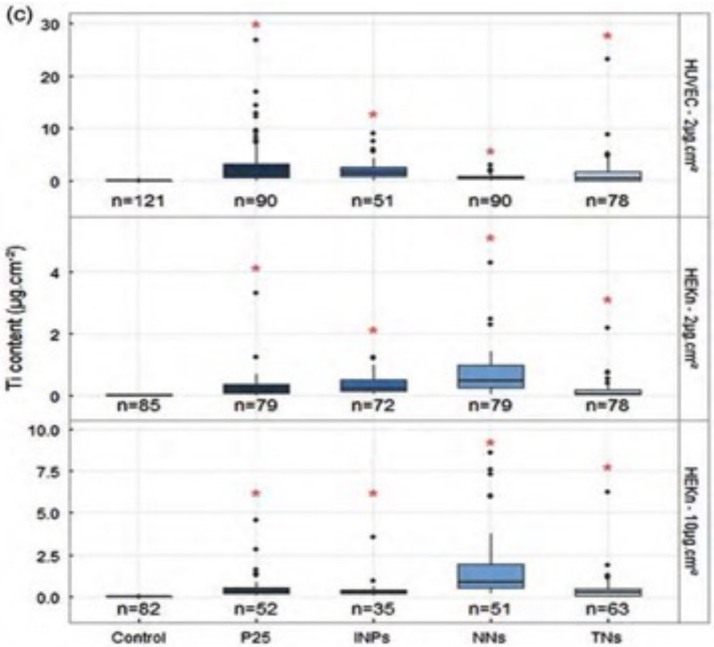


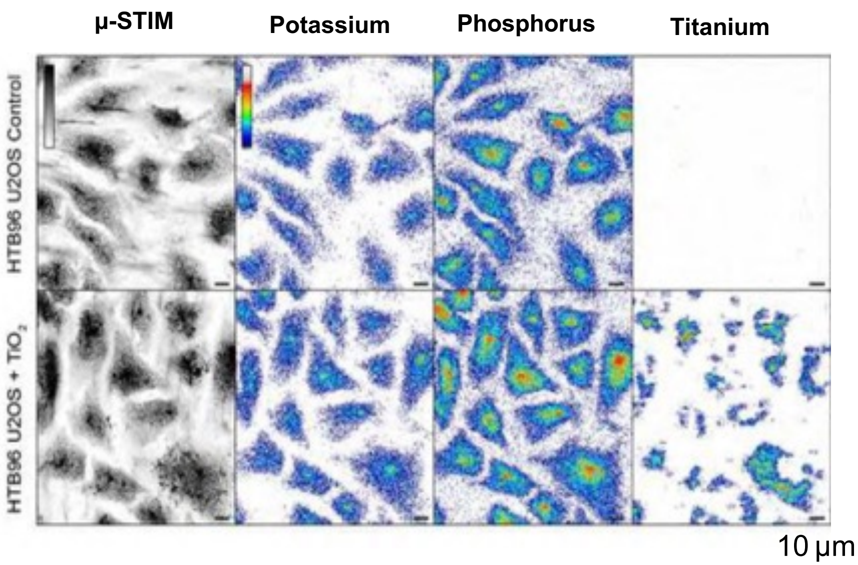
Westall, F. *et al. Geology* **43**, 615–618 (2015).
Westall, F. *et al. Astrobiology* **18**, 259–293 (2018).
Hickman-lewis et al. Geosciences 9, 359 (2019).

µ-IBA: single cells

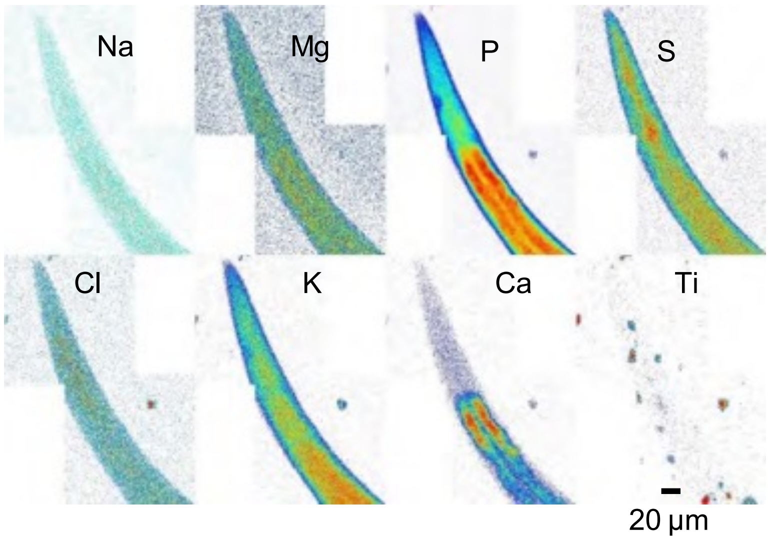
Analysis at the single cell scale

- Exposure to exogenous compounds, metals and nanoparticles (NPs)
- Up to now mainly toxicology studies





10 publications in the last 5 years

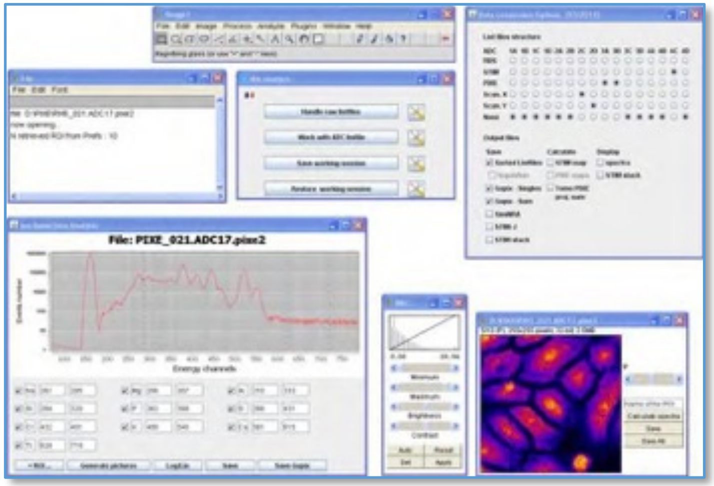


μ-IBA: starting projects

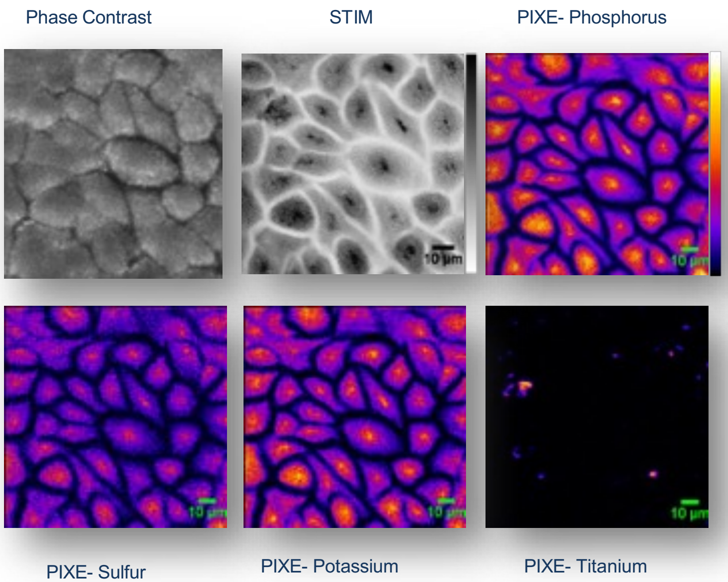
Internalization for treatment

- Metals, NPs or radio-isotopes designed to be internalized in cells

Ongoing work (iRiBio group @ CENBG):
- Standardizing the protocoles
- Increasing the analysis throughtput
- User-friendly data analysis



Devès, G. *et al.* NIMB **348**, 62–67 (2015).
Le Trequesser, Q. *et al.* *J. Chem. Biol.* **8**, 159–167 (2015).
Muggiolu, G. *et al.* *Journal of Vis. Exp.* e55041 (2018).

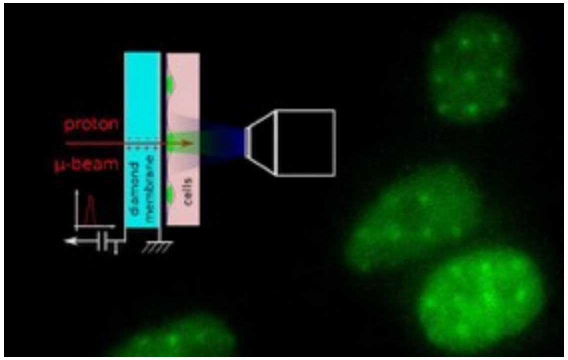


- **Automation ➔ 50-100 cells/day**
- **Correlative imaging**
- **Data processing …?**

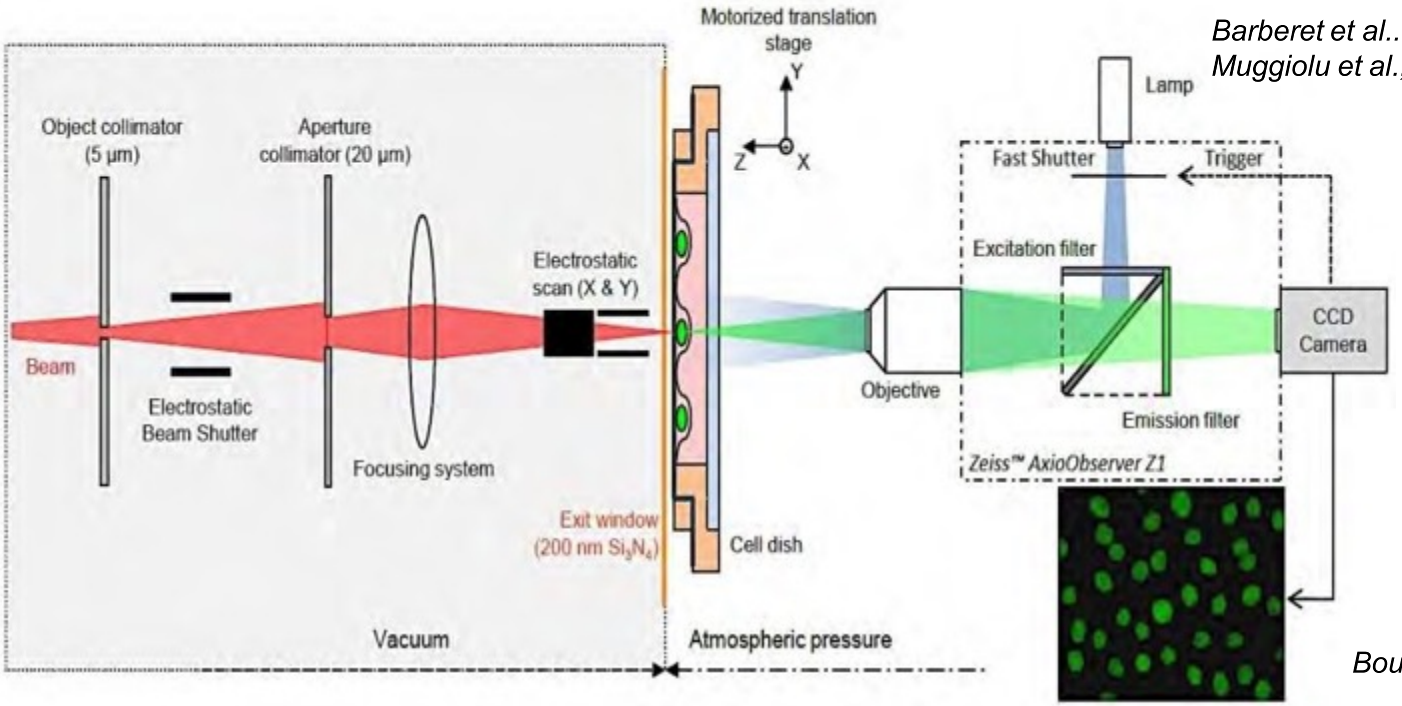
Targeted µ-irradiation

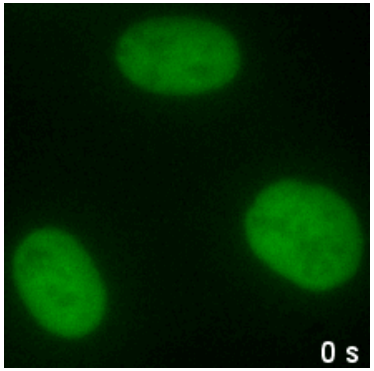
- 3 MeV protons / helium ions
- beam size ~ 1.5 µm (FWHM)
- Beam extracted in air to irradiate living cells
- Dose control down to a single particle
- Electrostatic beam scanning
- Online fluorescence time-lapse imaging

Latest developments:
Thin diamond detectors



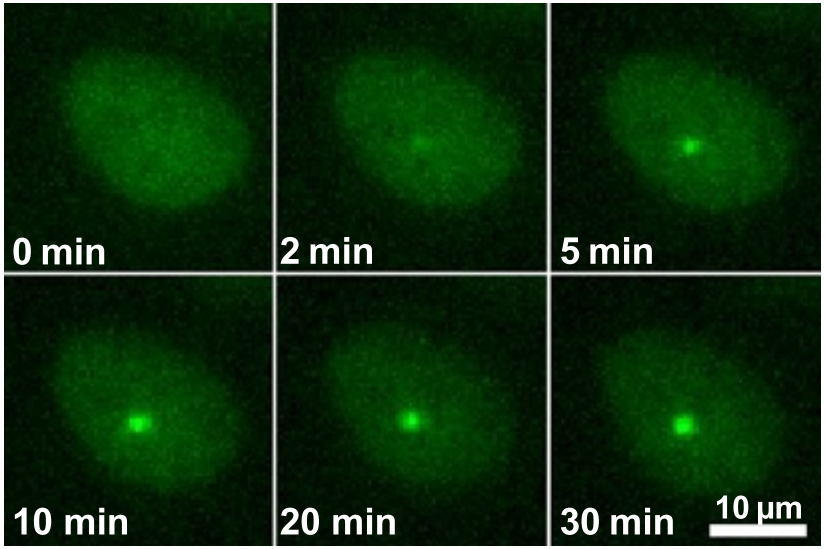
Barberet et al.. Appl. Phys. Lett. ***111****, 1–5 (2017)*
Muggiolu et al., Scientific Reports 7, 41764 (2017)

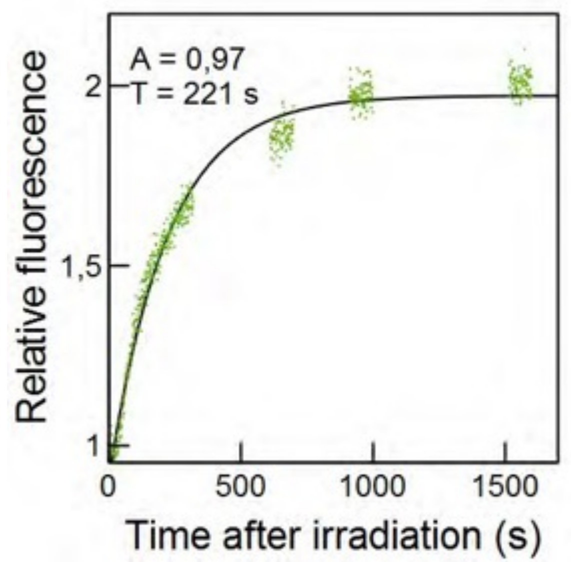




Bourret et al., NIMB 325 (2014)

Single cell targeting & protein kinetics





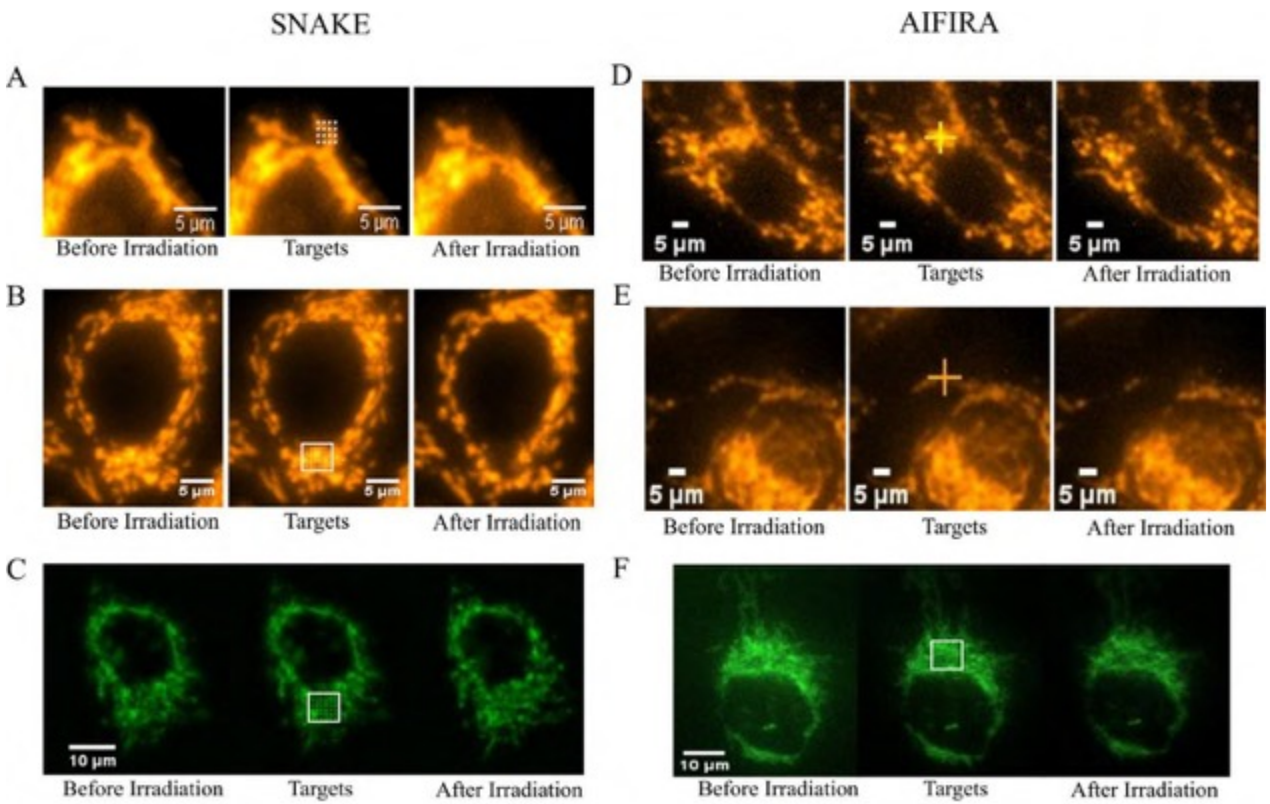
$$I_t = 1 + A\left(1 - e^{\frac{(t-t_0)}{T}}\right)$$

- Cell nucleus of a cell line with **GFP-**tagged protein involved in DNA damage repair
- Micro-irradiation with counted number of ions focused in a spot
- Fluorescence Spot: **Protein Accumulation** at the damage site

- Time-lapse acquisition after irradiation
- Real time measurement of **fluorescence intensity**
- ***T* = recrutement time (s)**
  ***A* = Max intensity value**

Marie Curie RTN : SPRITE (2013-2016)
Thesis of Giovanna Muggiolu, University of Bordeaux 2017
Muggiolu et al., Scientific Reports 7, 41764 (2017)

Single cell targeting & mitochondria



Universität der Bundeswehr München

TMRE
accumulates in polarized mitochondria

Matrix-roGFP
test for mitochondrial matrix integrity

55 MeV Carbons (SNAKE, Munich) and 3 MeV protons (AIFIRA, Bordeaux)

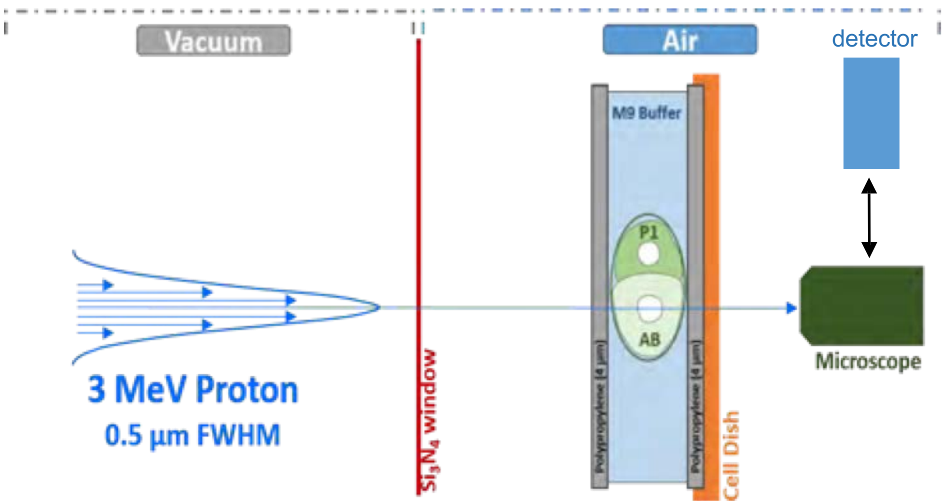
Radiation-induced change in mitochondrial membrane potential

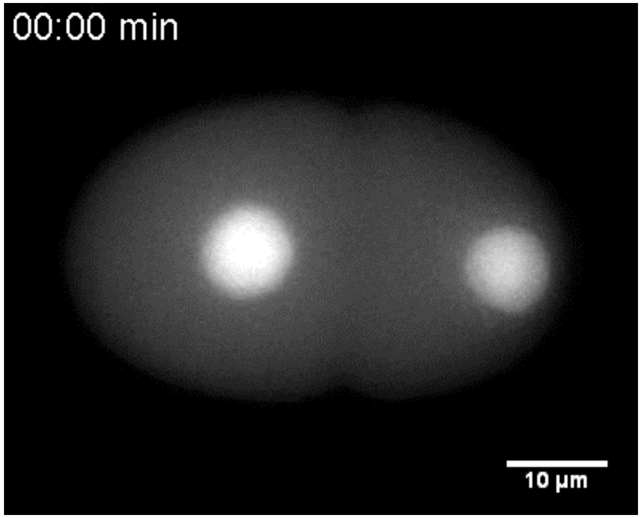
Walsh et al., Scientic Reports 7,46684 (2017)

Towards multicellular models

Challenge: targeting a single cell in an organism

Scheme of the irradiation setup





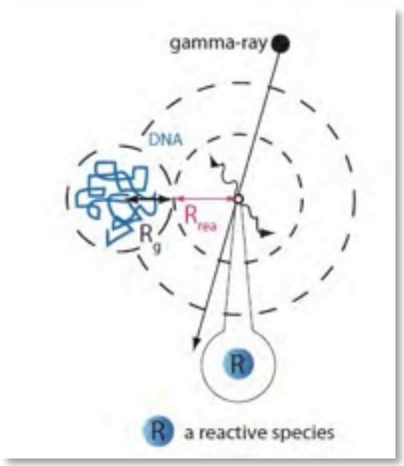
Torfeh et al., Scientific Reports 9:10568 (2019)

In progress & perspectives:
PRIME80: RADIANCe
"Etude des conséquences biologiques radio-induites sur le métabolismeARN chez Caenorhabditis elegans"

Biophysics – Study of DNA fragmentation

- INSIDE Project:

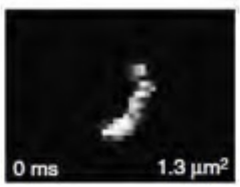
  IN SItu DEtection of DNA fragmentation induced by proton collision (MITI)



S.F.Shimobayashi et al., J.Chem.Phys. **138**, 174907 (2013)

Hyp:
If impact parameter < $R_{rea}+R_g$
□ probability p of DNA fragmentation

Towards DNA fragmentation *vs* impact parameter



Light intensity $I_{ADN}(t) = \int I(\vec{r},t)\,d\vec{r}$

« centre of mass »: $\vec{R}_{CM}(t) = \frac{1}{I_{ADN}(t)} \int \vec{r}\, I(\vec{r},t)\,d\vec{r}$

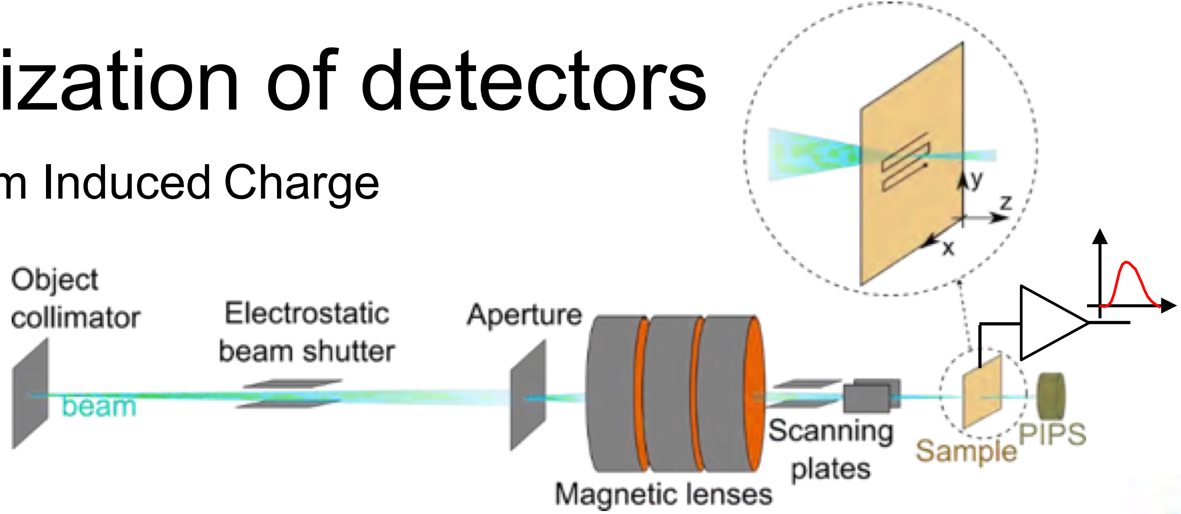
Giration radius: $R_g^2(t) = \frac{1}{I_{ADN}(t)} \int_R \left|\vec{r} - \vec{R}_{CM}\right|^2 I(\vec{r},t)\,d\vec{r}$

Tracking of phage T4 DNA at concentrations of 30 pg/µL
Mean inter-DNA distance ~ 20 µm

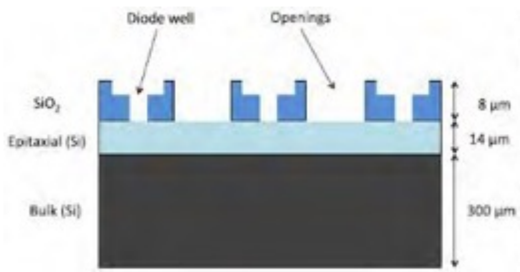
Observable providing hte DNA topology or the fragmentation dynamics ?

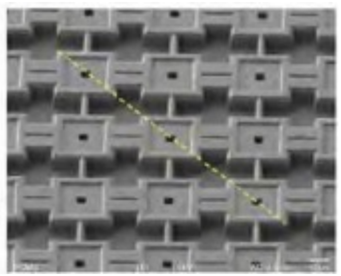
Characterization of detectors

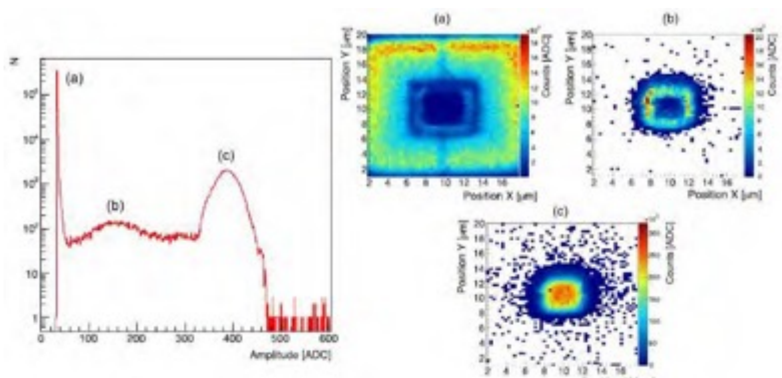
μ-IBIC : Ion Beam Induced Charge



Micro-scale characterization of a CMOS-based neutron detector







Context: Development of a neutron dosimeter in-phantom measurements in radiation therapy □ AlphaRad Sensor

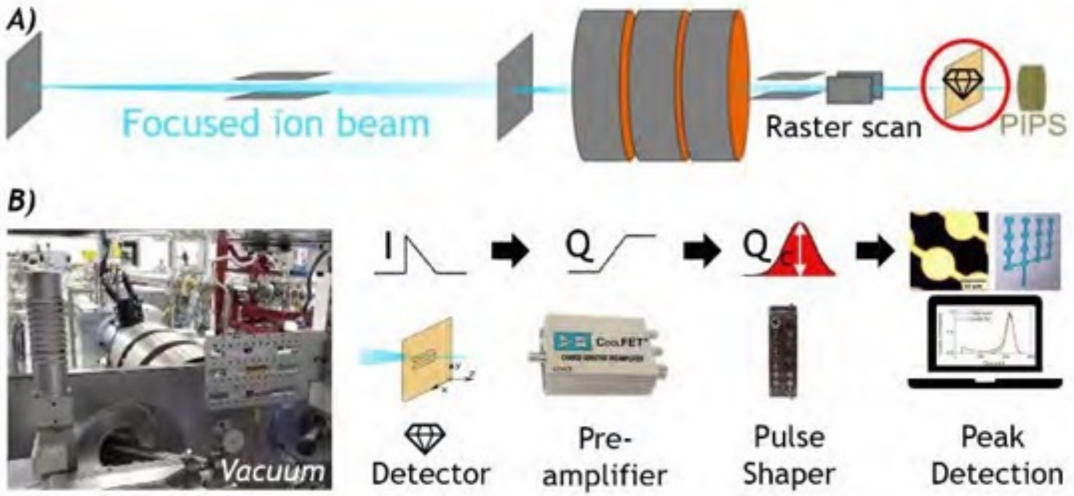
Aim:

- Precise calibration of the signal amplitude
- Charge collection in the different parts of the sensor ?

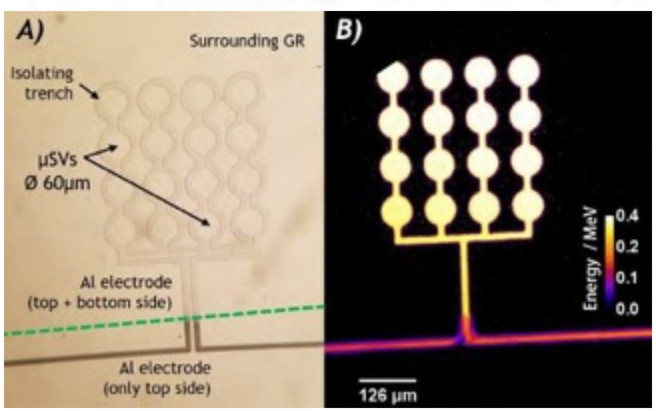
DeSIs group @ IPHC, Strasbourg : Arbor et al., NIM A 888 (2018) 103109

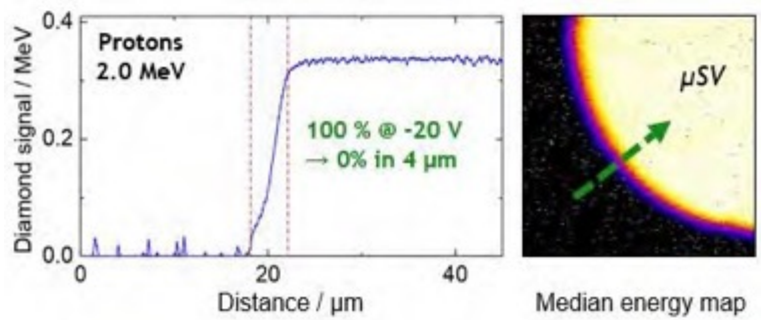
Characterization of detectors (2)

DIADEM Project:
Diamond membrane based microdosimetric system for radiation quality assurance in hadron therapy



Aim:
- Charge collection efficiency vs biasing
- Mapping edge effects & bounding
- Radiation damage





Zahradnik, et al. Physica Status Solidi (A), 1800383, 1–1 (2018)
Zahradnik et al. Submitted tor Review of Scientific Instruments (2020)

Characterization of detectors (3)

Use of mono-energetic ion beams to calibrate detectors:
- Nuclear physics
- Ion acceleration using high power lasers

Characterization of a gaseous proton-recoil detector for neutron flux measurements

ACEN group @ CENBG

Marini *et al. NIM A.* **841**, 56–64 (2017).

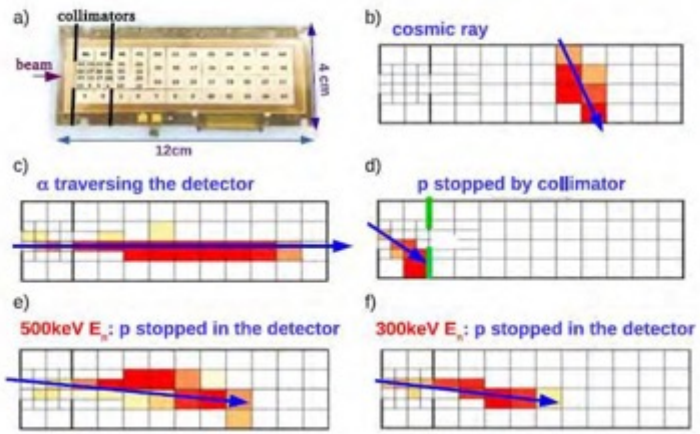
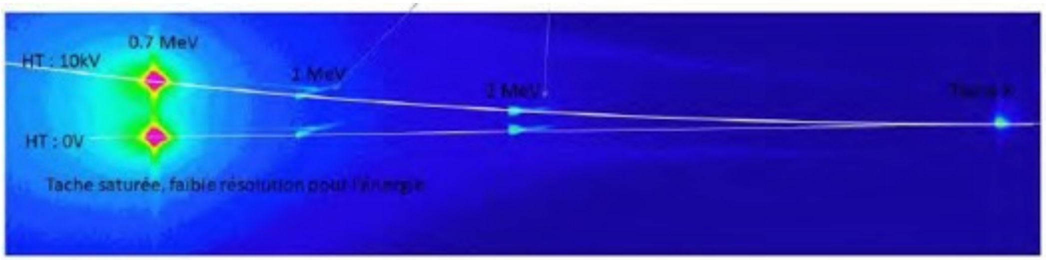


Figure 2. a) Detection plane segmentation b–f) examples of reconstructed trajectories.

Calibartion of Thomson parabola for experiments @ high power lasers

ENL group @ CENBG

Puyuelo-Valdes *et al. Phys. Plasmas* **26**, (2019).



Publications & users (2015-2020)

40 interdisciplinary publications

Journals :
Nanotoxicolgy, Radiation Protection Dosimetry, NIM A, NIM B, Advanced Energy Materials, Journal of Chemical Biology, Molecular Neurobiology, Electrophoresis, Geology, Thin Solid Films, J. Mater. Chem. B, Physics in Medicine and Biology, Analytical Biochemistry, ACS Appl. Mater. Interfaces, Scientific Reports, Journal of Archeological Science, ACS Chem. Neuroscience, Applied Physics Letters, Astrobiology, Journal of Anthropological Archaeology, Journal of Visualized experiments, Physica Status Solidi (A), Physics of plasma

≈ 20 laboratories :

- IRAMAT-CRP2A UMR5060
- CEA-DSM/LLAN
- ICMCB UPR9048
- IMS UMR5218
- IPNL UMR5822
- IRSN-LMDN
- ISTerre UMR5275
- ISTO UMR7327
- LPC UMR6533
- PACEA UMR5199
- CBM UPR4301
- CELIA UMR5106
- LCP UMR8000
- CEA-DSM/SRMA/LA25M
- Institut Fresnel UMR7249
- OASU-LAB
- INCIA UMR5287
- CEA-DST/LIST

Practical work for students

Projects for master students (nuclear physics specialization):

- Measurements of cross sections for nuclear and atomic reactions
- 2 days of beamtime / year

Projects for students in master of engineering: instrumentation

- Instrumentation & automation
- Design of detection systems for IBA normalization
- Up to now 1 day of beamtime / year

Internships for Bachelor and master students

Evolutions

Renewing the «Physics beamline» (funding Région Aquitaine 2016-2019 - 80 k€)

- Commissionning => end 2020

RÉGION Nouvelle-Aquitaine

Renewing the External beamline (funding Région Aquitaine 2019-2022 – 66 k€)

- Switching to SDD detectors

Upgrading microbeam line (DIADEM project – 30 k€)

PLAN CANCER 2014-2019

MERCI POUR VOTRE ATTENTION