Monitoring of innovative radiotherapies

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[1]I2PI, [2]LPSC, [3]Subatech, [4]IJCLab-CNRS, [5]Arronax, [6]LLR, [7]CPPM

Journées Prospectives Santé IN2P3, Strasbourg, 5 février 2020

Innovative radiotherapies

Types of radiotherapies

- Photons irradiations (Linac, Gammaknife, IMRT...)
- Hadrontherapy (p and ^{12}C) $\Rightarrow$ need for ion-range
- Targeted therapies (radiopharmaceuticals, radiosensitizing agents, neutron capture therapies...)
  $\Rightarrow$ Need for targeting control

"New" parameters of the irradiation: fractionation...

- spatial: microbeams (synchrotron radiation) and minibeams (hadrontherapy)
- temporal: microbeams (synchrotron) et FLASH therapies (photons, electrons and ions) $\Rightarrow$ doses of the order of kGy/s – MGy/s
- Online monitoring of utmost interest

Control methods

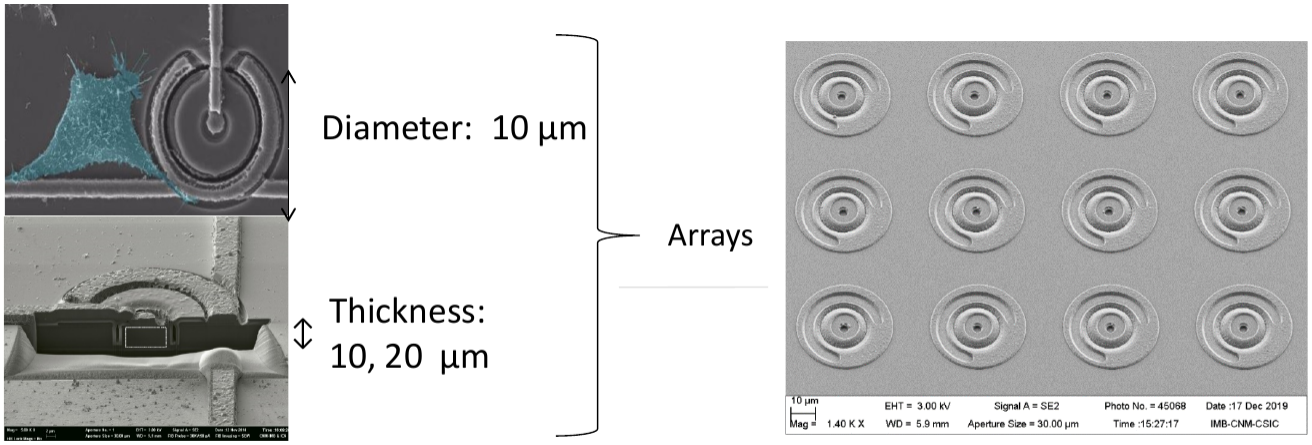
Methods	Projects	Radioth.	IN2P3 labs
Microdosimetry	CNRS-Momentum	Ions	IJCLab
Upstream flux control	IDORA	FLASH γ	LPSC
	PEPITES	Ions	LLR–ARRONAX
	DosiTrHaD	Ions	LPC Caen–CPO[a]
	Diamond detectors	Ions+γ+FLASH	LPSC + CLaRyS collab.
Online control	THIDOS	Targeted th.	IJCLab
	Bremsstrahlung	Ions	Subatech–ARRONAX
	CLaRyS	Ions	IP2I–CPPM–LPSC [b]
	TIARA	Ions	LPSC–CPPM–IP2I

[a] see R. Delorme's presentation
[b] CLaRyS collaboration

Outline

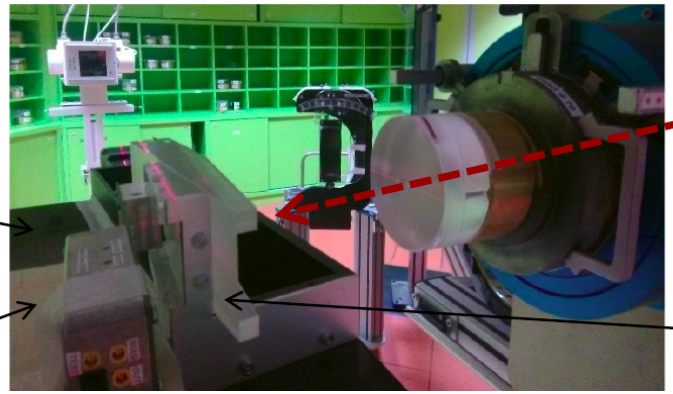
1. Microdosimetry (“off treatment”)
2. Upstream flux control
3. Online control

Detecteur: 3D-silicon microdetectors



C. Guardiola, Applied Physics Letters 107, 023505 (2015)

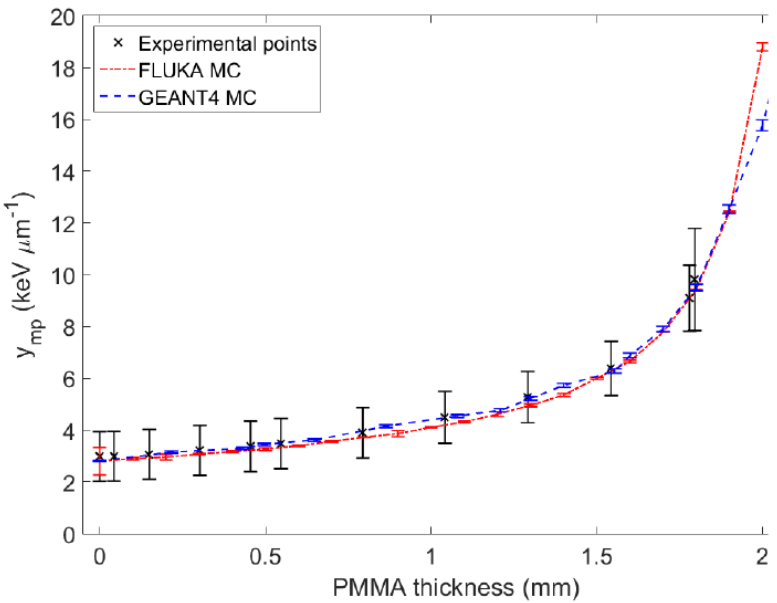
Tests in progress in a hadrontherapy center with a detector array



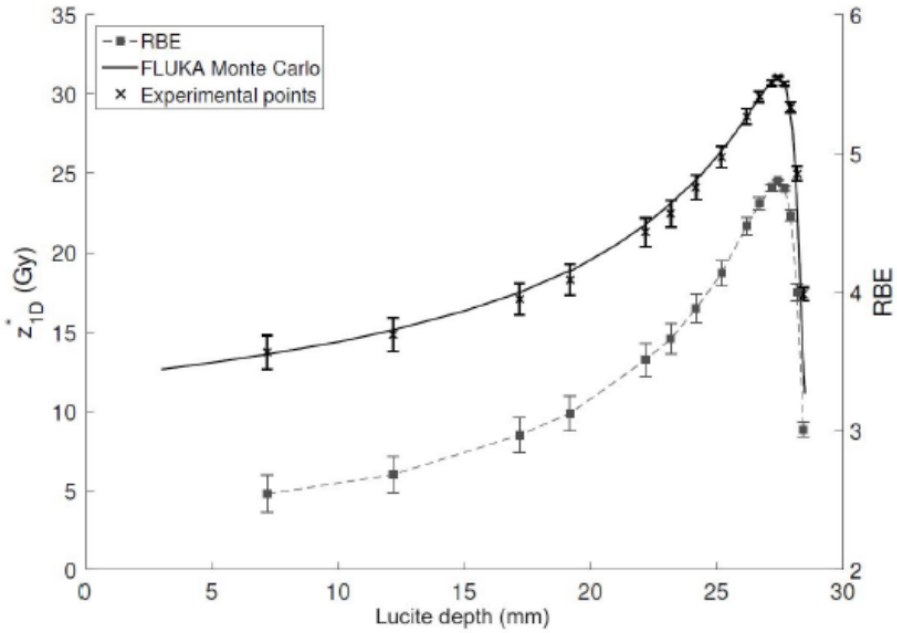
Results

- Tests in CNAO (National Centre of Oncological Hadrontherapy, Italy) with clinical beam intensities
- Good agreement between experimental and simulated (Monte Carlo) data

most probable lineal energy



RBE evaluation



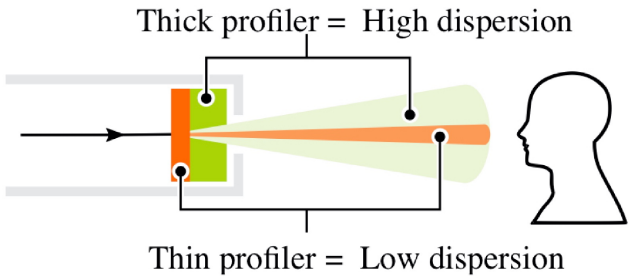
Prieto Pena et al., IEEE Transactions on Nuclear Science, Vol. 66, No. 7, July 2019

Outline

1. Microdosimetry (“off treatment”)
2. Upstream flux control
3. Online control

Origins

- R&D LLR after meeting with IBA
- ANR (2018-2021) LLR-ARRONAX-CEA
- P2IO (2018-2019)



Objectives

Perturbation minimum du faisceau
→ Budget Matière : 10 µm WET

Dose déposée minimum de 10^8 Gy
→ Radioresistance

Strategy

- PEPITES (Profileur à Electrons secondaires Pour Ions ThérapeutiquES)
- Prototype development (2021) for implementation in ARRONAX (objective of the ANR project)

⇒ First experience to move then on hadrontherapy facilities

Signal

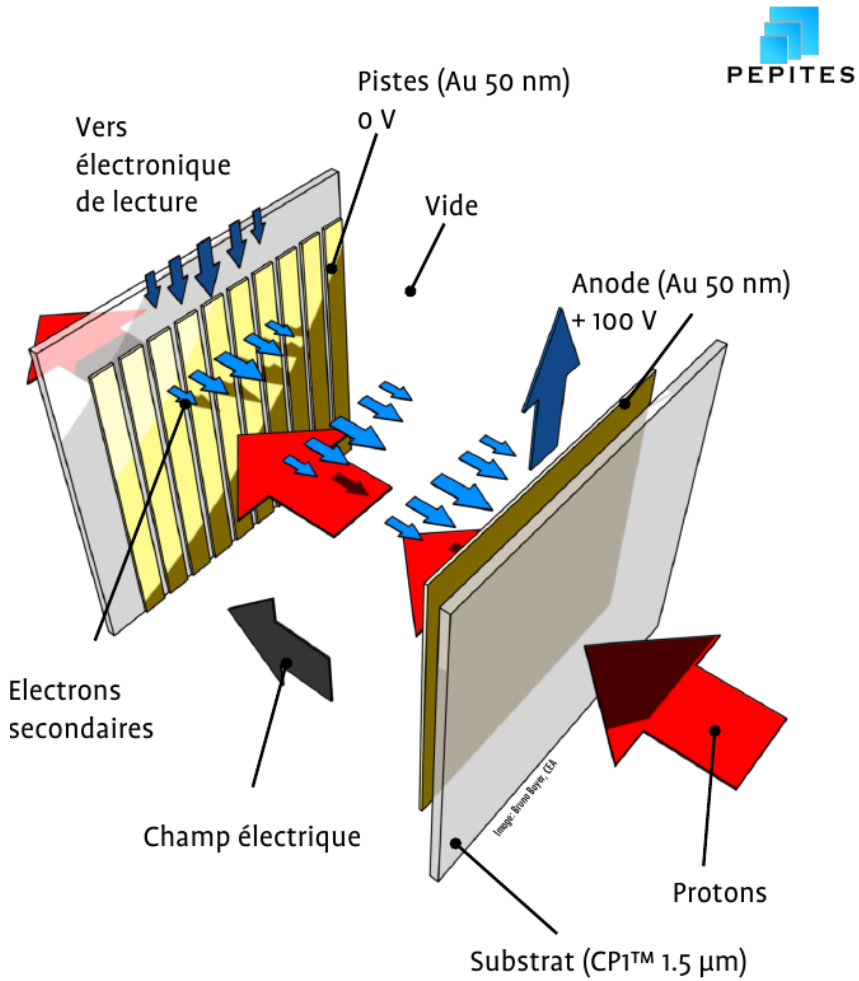
Seconday electrons emission

- Surface processes
- Low energy (quelques eV)
  - ⇒ nécessité de travailler dans le vide
- Taux proportionnel au dE/dx
  - ⇒ Utilisation d'un grand Z (Au)
  - ⇒ Linéarité

Substrate

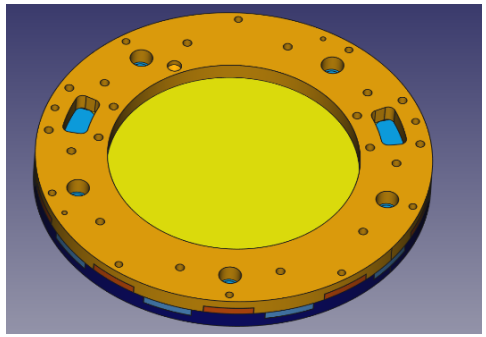
CP1™ (Colorless Polyimide) :

- Thermostable
- Radiorésistance
- Used for sun sails!



Manufacturing

- Common thin fil deposition: Chemical vapor deposition (CVD)



Context

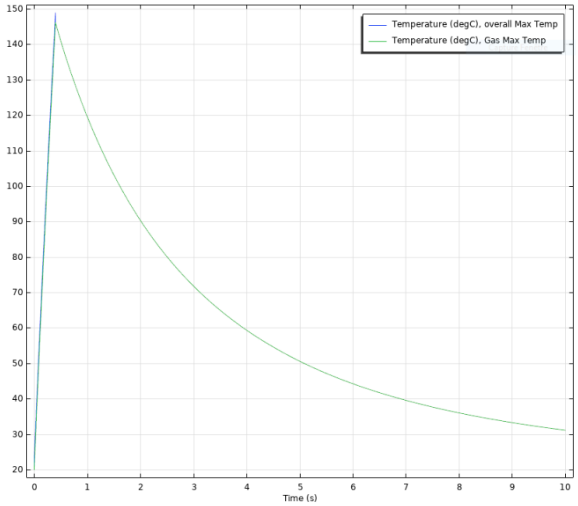
- Power of pulsed beam: $\times 1000$ (power peak of 1 MW !!)
- Treatment delivery: 0.3 s
- Saturation of current beam monitors: charge recombination

Objective: new beam monitors for linacs operated in FLASH therapy

- New monitor chamber design without saturation
- Development of a specific electronic readout with large dynamic: (1–1 000 000)
- Real-time measurements (< 800 µs) for each linac pulse
- Global precision better than 0.1%

Development

- Valorization with SATT funding (15 month engineer)
- Detector design done ⇒ Manufacturing in progress
- Temperature resistance validated
- Second version 2 en cours de tests



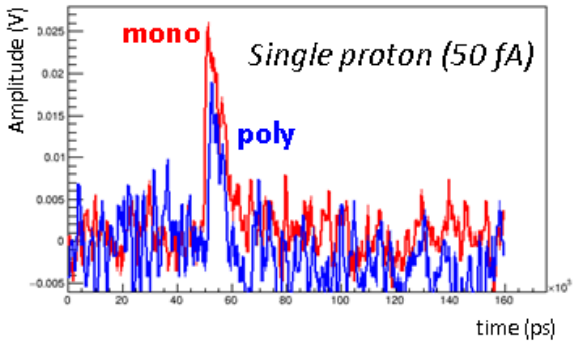
Tests

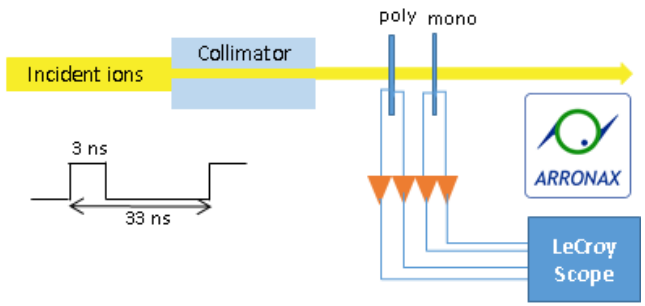
- High power beam provided by a compagny (February 2020) to measure:
  - Detector temperature resistance
  - Detector linearity
  - No transient state from the first pulse

Declaration of invention (CNRS)

- Patent submission if proof of concept in real irradiation conditions
- Co-development wih the compagny

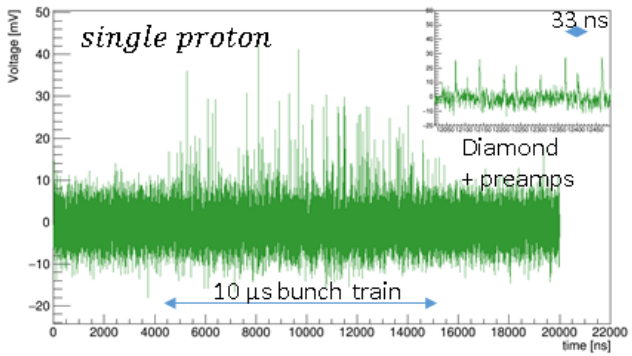
Polycristalline *vs* monocristalline

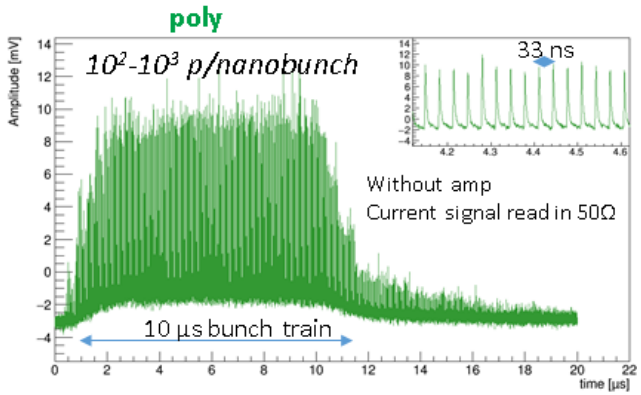




- "Poly": Shorter pulses and detection efficiency $> 95\%$

Detection mode: "Single proton unique" *vs* Proton bunches



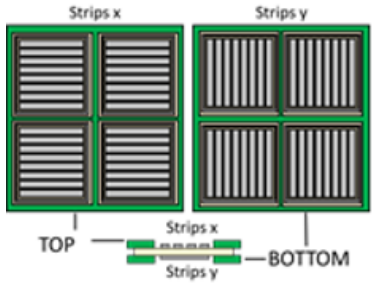


- Single proton: tagging with 100 ps (rms) resolution $\Rightarrow$ TOF (prompt gammas)
- Proton bunches: Proton counting in nano bunches and bunch tagging

Hodoscope in hadrontherapy

• Prompt-Gamma Timing

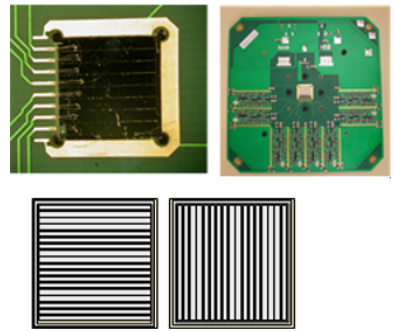
- "Single proton" mode
- Monocristalline demonstrator
- Custom fast discrete preamp



4 sCVD (4,5x4,5 mm^2 chacun)

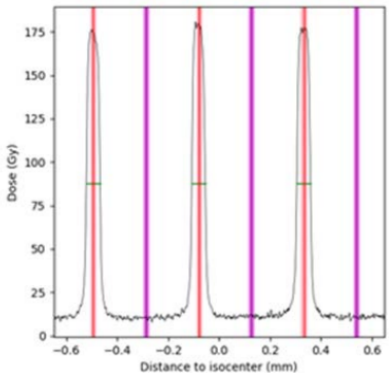
• TOF Prompt-Gamma Imaging

- "Proton bunches" mode
- Polycristalline demonstrator
- Custom ASIC

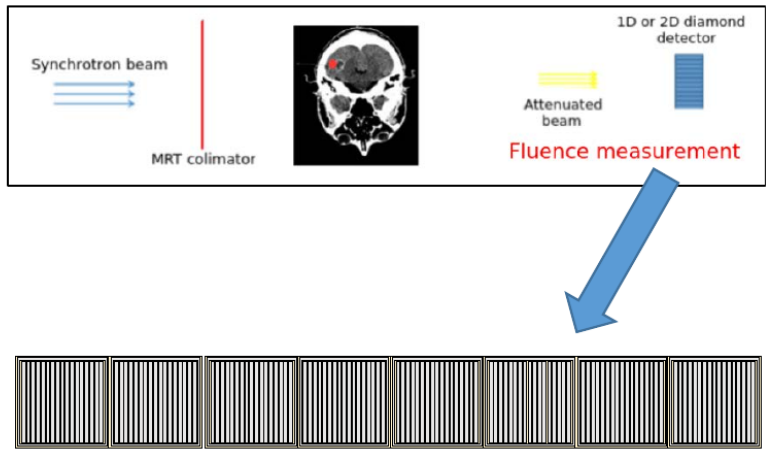


1 pCVD (20 × 20 mm^2)

Microbeam radiation therapy (portal control device)



MRT: 50 µm beamlets with high peak-dose rate (> 10 kGy/s)



8 sCVD (4.5 × 4.5 mm^2 each), 200µm pitch vertical strips
Multichannel QDC ASIC

Outline

1 Microdosimetry (“off treatment”)

2 Upstream flux control

3 Online control

THIDOS: Control of targeted therapy for thyroid disease (IJCLab)

Context et objectives

- Targeted therapy booming
- Need for precise and personalized dosimetry to optimize treatments
- Collaborations: IRSN and Institut du Cancer de Toulouse

$\Rightarrow$ THIDOS: New instrumental strategies (ambulatory camera) and methods to improve dose control (iodine 131)

Material

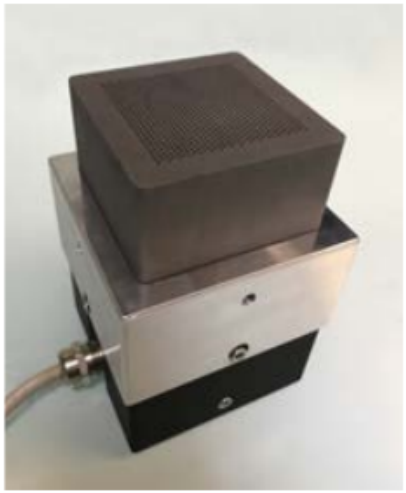
- Design of ambulatory camera (10×10 cm^2) with high spatial resolution
- Biokinetic measurement of iodine 131 before and after the treatment (thyroid and organ at risk). Iodine 131 : β^- 600 keV max + γ 364 keV

Methods: Camera optimization

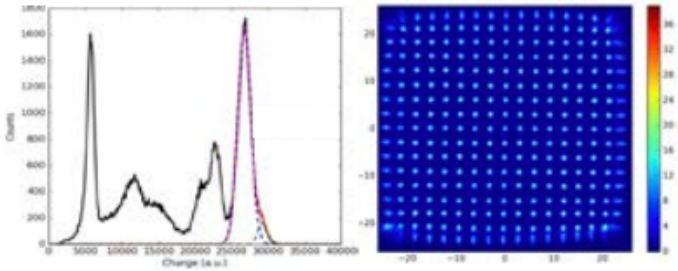
- Scintillators: project GAMINS (CSNSM, IPNO) + SiPM + readout boards: project SIPMED (LAL, pôle OMEGA)
- High energy gamma collimator: MC simulation (Gate)

THIDOS: Control of targeted therapy for thyroid disease (IJCLab)

Premier prototype
5x5 cm^2 de la caméra



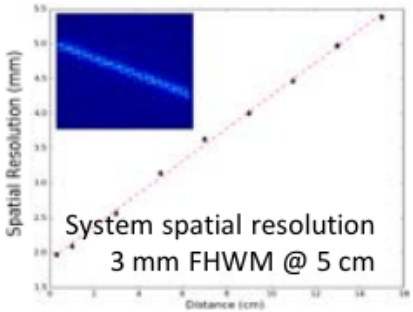
$CeBr_3$ + Collimateur en tungstène (impression 3D)

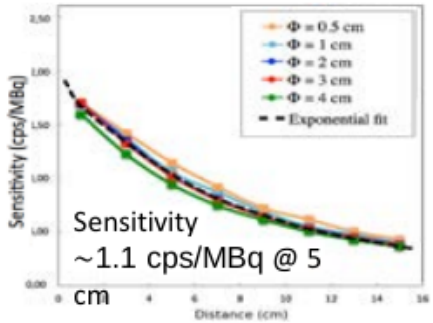


Résolution spatiale et distorsion sub-millimétriques

Résolution énergétique < 8% (@356 keV)

Réponses intrinsèque et globale de la caméra

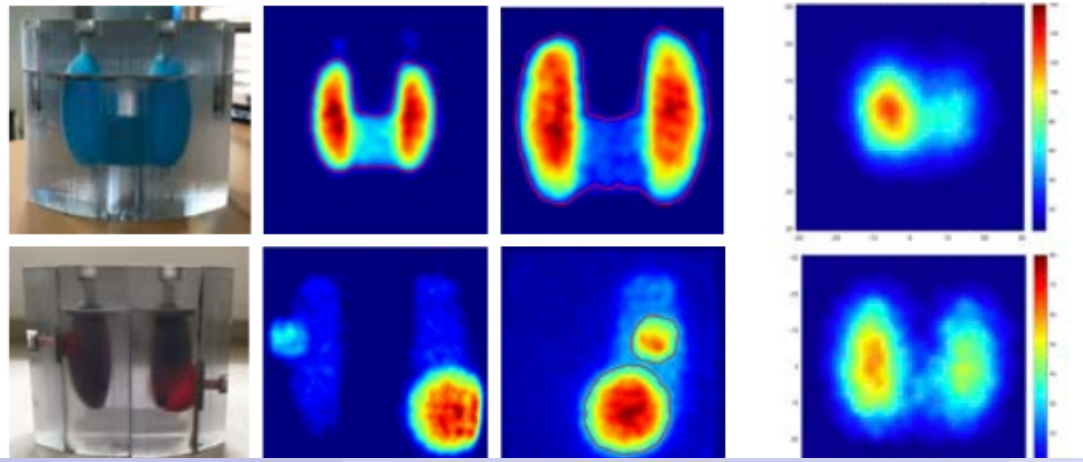




Fantômes thyroïde (IRSN)

Caméra MoTi
Anterior and lateral views

Siemens Symbia T2
(SR of 13.4 mm @ 10 cm)



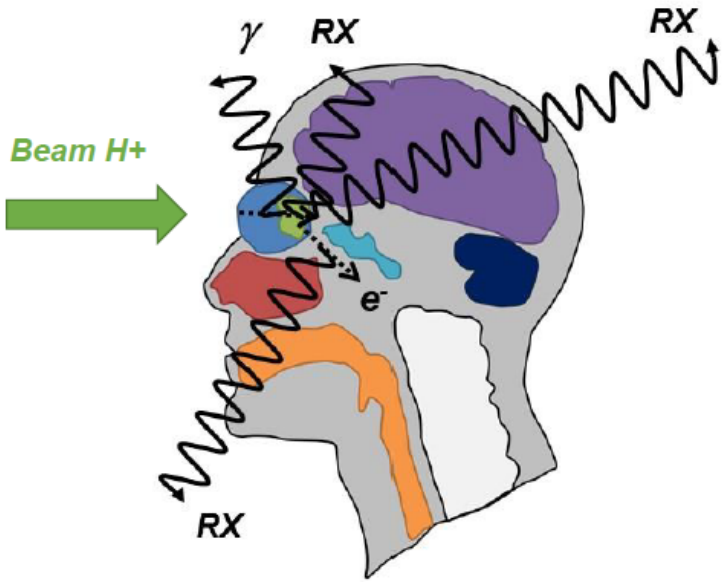
Coefficient de recouvrement de l'activité > 96 % dans la thyroïde et les nodules

Principle

- X-rays detection between 15 and 100 keV

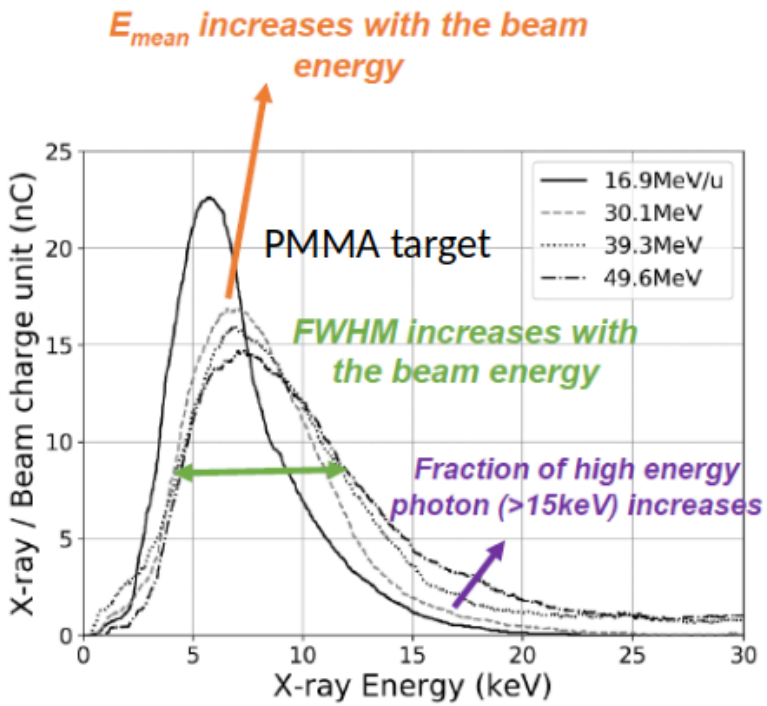
$\Rightarrow$ information on beam energy

$\Rightarrow$ information on target heterogeneities



First results

- Measurements with a silicon detector having a low efficiency beyond 10 keV

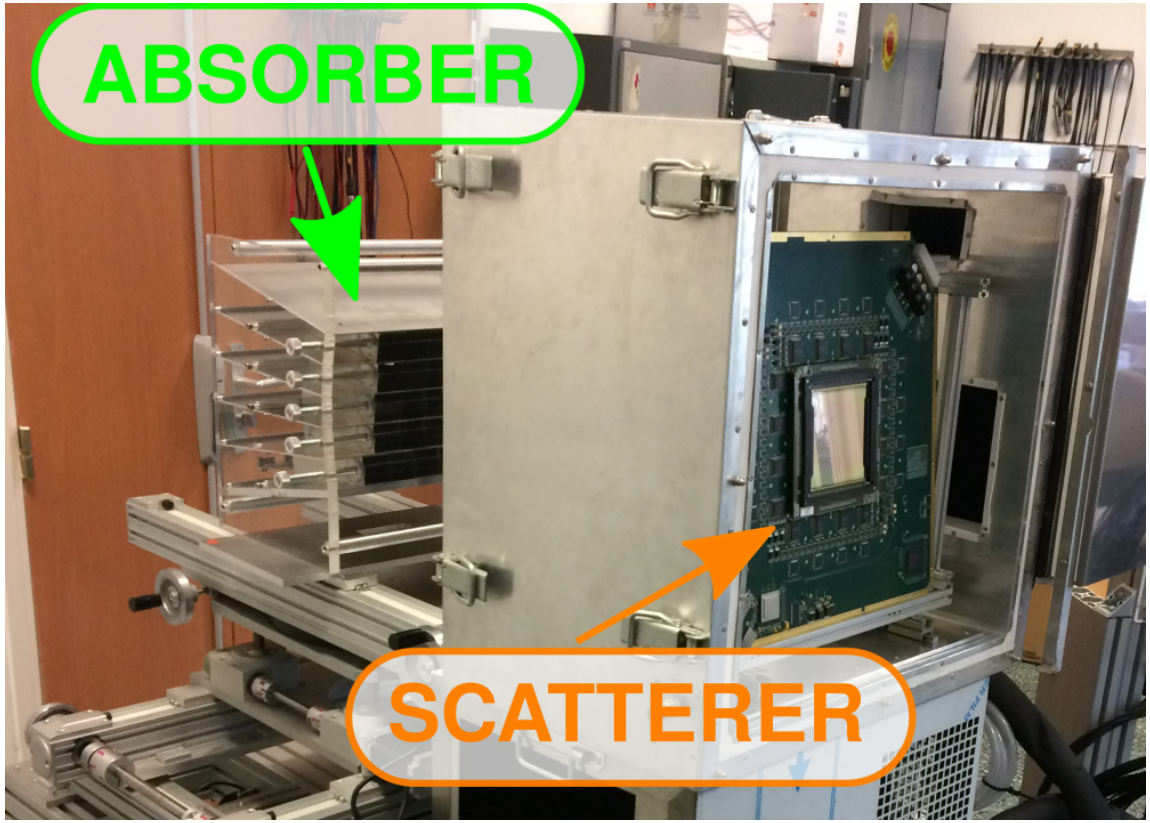


Objective

- Development of "TOF" gamma cameras for hadrontherapy verification

2 modalities

- Compton camera
- Collimated camera (Multi-Parallel Slit camera)



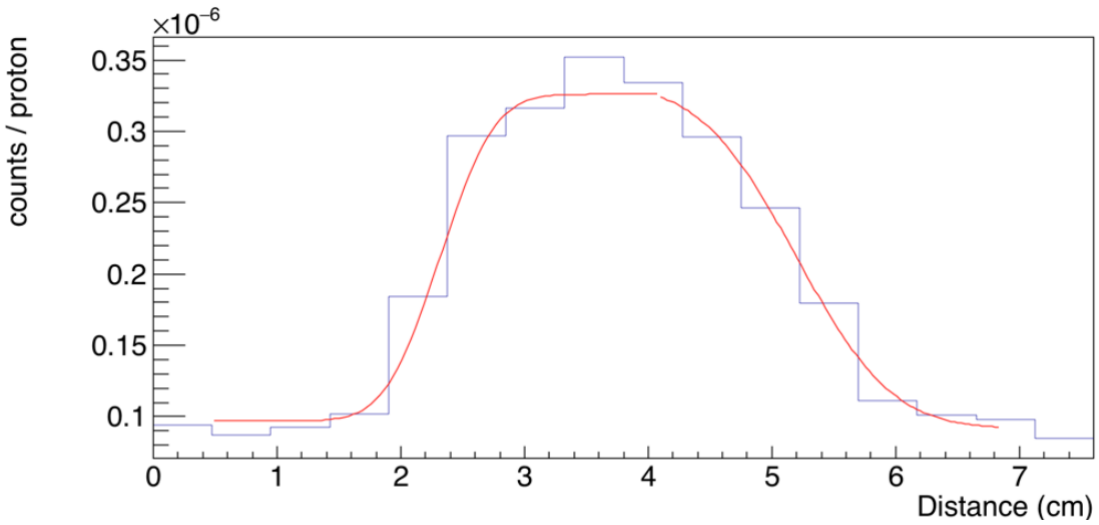
Detectors

- Absorber (for both cameras): BGO scintillators
- Scatterer of the Compton camera: 7 silicon detectors (DSSD)
- Beam hodoscope: Diamond detectors

First measurements

- Low energy research beamline in CAL-Nice
- 65 MeV protons irradiating a PMMA target (31 mm range) with clinical intensities

⇒ PG profile in agreement with expectations



Current status

- Collimated camera: test of the electronics and first measurements
- Compton camera: firmware of the scatterer planned in 2020.

End of the development

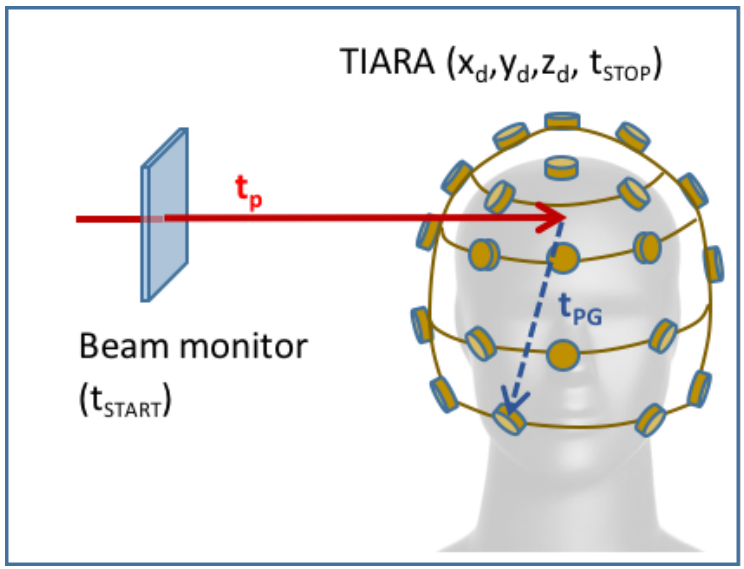
- Mid 2021

Set-up

- TIARA: a Time-of-flight Imaging ARrAy for hadrontherapy
- $\sim$ 30 small detectors (spatial information)
- **pure Cherenkov detectors + SiPM**

$\Rightarrow$ Fast (coinc. time resolution with hodoscope)

- High detection efficiency (per detector)



Goal: 3D reconstruction of PG vertices

- only measuring proton plus PG TOF
- within first irradiation spot (10^8)

$$t_{STOP} - t_{START} = t_p(\vec{x_v}) + t_{PG}(\vec{x_v})$$

100 ps (rms) time resolution

Achievable

- fast beam monitor
- single proton regime

Results (MC simulations)

- **a 2 mm proton range shift detectable at 2σ within one spot**

Conclusion and perspectives

Instrumentation challenges

- Current modalities of treatment (e.g. ion-range in hadrontherapy)
- New modalities: spatial (mini and micro beams) and temporal fractionation (photon and ion FLASH therapies)

Current R&D

- Development/characterization of new detectors (upstream flux measurement)
- New detection systems (online control) designed by means of MC simulations
- Structuring developments with complementary know-how

Opportunities

- International: continuation of European projects with networks like Medinet, Biophysics@FAIR collaboration, ENLIGHT network
- National: Future research facilities in CAL-Nice and ARCHADE $\Rightarrow$ Ambitious and federative projects