## Time-Of-Flight based Prompt Gamma detection with TIARA



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## Range monitoring in proton therapy

Ballistic advantage

=> higher sensitivity to irradiation errors



Example: anatomical modifications between treatment and treatment planning

#### Treatment planning



**Treatment delivery** 



Courtesy of CAL

Range uncertainties are especially critical in Intensity Modulated Proton Therapy (IMPT)



Courtesy of CAL

## Range monitoring with Prompt Gamma (PG) rays

The PG vertex distribution is **spatially** and **temporally correlated** to the absorbed dose



- $1 \text{ MeV} < E_{PG} < 10 \text{ MeV}$
- PG emission ~ ps
- PG yields ~ 1%/proton/cm

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- PG emission ~ ps
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#### Constraints and expected performances



- Ideally, one PG profile per spot, or spot grouping to increase statistics
- Millimetric proton range accuracy with limited statistics

Development of dedicated detectors with high sensitivity

## **Prompt Gamma Timing (PGT)**



Indirect measurement of proton range from the distribution characteristics of:

TOF = Tstop – Tstart

Tstart from:

- Beam RF signal (original approach)
- Beam monitor



**Figure 9.** Comparison of experimental (histograms) and modeled time profiles (solid lines) of a PMMA target varied in thickness. All experimental curves are normalized to one incident gigaproton (10<sup>9</sup> protons). The experimental PGT spectra energy ROI is *All*4440 (3.2 MeV–4.6 MeV). The modeled PGT spectra are based on the *simG*4 profile for  $g_x$ . The absolute time offset of the modeled data was set to fit the mean for 5 cm PMMA thickness. The experimental detector setup (figure 7) was taken into account to incorporate the influence of the prompt  $\gamma$ -ray time of flight on the spectral shape. The modeled system time resolution is  $\sigma_{\Sigma} = 450$  ps (9).

Golnik et al. Phys. Med. Biol. 59 (2014) 5300

#### Outline

Advantages and challenges in Prompt Gamma Timing (PGT)

Towards a new approach: Prompt Gamma Time Imaging (PGTI) with TIARA Detector development Experimental validation of TIARA Future perspectives

## Advantages : no need for collimation



#### Compton camera



# Electronic collimation

#### **Prompt Gamma Timing**



$$\epsilon = \epsilon_{\gamma} \times \frac{S}{4\pi r^2}$$

e.g.  $\epsilon_{\gamma} \simeq 0.2$ ; S = 4 cm<sup>2</sup>; r = 20 cm  $\epsilon \simeq 10^{-4}$  per detector module

#### No collimation means:

- Relatively high detection efficiency (easy to upgrade)
- Compact and light detection system
- Reduced amount of material to avoid secondary neutrons and PGs

=> Impact on Signal To Noise ratio

\*Pictures from CLaRyS collaboration

Detector development

## **Advantages: TOF neutron rejection**



- 148 MeV protons impinging on a ٠ human head phantom (ICRP110)
- 30 perfect detectors surrounding the phantom (d=15 cm)

Vertex distribution

Ecut = 3 MeV



#### **Experimental proof** (CLaRyS<sup>\*</sup> collaboration)

- 95 MeV/u <sup>12</sup>C beam on PMMA
- BaF<sub>2</sub> at d>50cm from target



Testa et al. Radiat Environ Biophys 49, 337–343 (2010)

#### A TOF resolution of ~ 1 ns is enough to reject most neutrons

y detectors

\* IP2I, LPSC, CPPM, CREATIS

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**Challenges in PGT** 

Detector development

## **Challenges in PGT optimisation**

#### At single-event scale : improve time resolution

- Time resolution on reference time (Tstart)
  => Development of a dedicated beam monitor
- 2) Time resolution of PG detector (Tstop)
  => Development of a dedicated γ detector (TIARA)
- 3) Beam temporal structures

At pencil beam scale : improve detector sensitivity

- 1) SNR and background
- 2) Detector arrangement





Cyclotron

# Temporal structures of main accelerators

(CNAO) (IBA, Varian) (S2C2	IBA) *
<sup>12</sup> C protons	
Typical intensity (ions/s) $10^7$ $10^9$ $10^{10}$ $10^7$	11
Period (s) 4–5 Ø 10 <sup>-</sup>	-3
Macro-structureSpill duration (s) $\sim 2$ $\varnothing$ $8 \times 10^{-10}$	0 <sup>-6</sup>
Ions/spill $10^7$ $10^9$ $\varnothing$ $10$	8
Period (ns) ~500 10 16	5
Micro-structureBunch width (ns) $\sim 100$ $0.5-2$ 8	
Ions/bunch 1–10 n.a. 200 10	5

Synchrotron

\* values at extraction

Synchro-cyclotron

#### At the time-scale of $\gamma$ detectors (ns)



# Temporal structures of main accelerators

nain accelerators		Synchrotron		Cyclotron	Synchro-cyclotron
		(CNAO)		(IBA, Varian)	(S2C2 IBA) *
		<sup>12</sup> C	C protons		
Typical inte	107	109	10 <sup>10</sup>	10 <sup>11</sup>	
	Period (s)	4-5		Ø	10 <sup>-3</sup>
Macro-structure	Spill duration (s)	~2		Ø	8×10 <sup>-6</sup>
	Ions/spill	$10^7$ $10^9$		Ø	108
	Period (ns)	~500		10	16
Micro-structure	Bunch width (ns)	~100		0.5-2	8
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\* values at extraction

#### At the time-scale of $\gamma$ detectors (ns)



S2C2 synchro-cyclotron: 8 ns bunch width, 7 p/bunch, thin target



Jacquet et al. Scientific report (2023) 13:3609

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Jacquet et al. Scientific report (2023) 13:3609

Perspectives

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#### **Reduce bunch-width related time uncertainty**

**TIARA Validation** 

Lower the beam intensity to Single Proton Regime (SPR)



## **Challenges in PGT optimisation**

At single-event scale : improve time resolution

- Time resolution on reference time (Tstart)
  => Development of a dedicated beam monitor
- 2) Time resolution of PG detector (Tstop)
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#### At pencil beam scale : improve detector sensitivity

- 1) SNR and background
- 2) Detector arrangement





Detector development

## Improve detector sensitivity: SNR and background

#### In order to maximise the SNR

- Increase detection efficiency
- Avoid detector pile-up
- Reject background

#### **Electrons**

Few, mostly rejected with acquisition threshold

#### **Protons**

Few, cut on the E vs TOF distribution

#### **Neutrons**

TOF rejection does not work at PG profile fall-off  $\Rightarrow$  Affect proton range measurement

#### **Secondary PGs**

Same energy and timing of primary PGs. => Affect proton range measurement



#### A practical example

- 148 MeV protons
- 30 perfect detectors
- Energy threshold = 3 MeV





Challenges in PGT

Detector development

## **Improve detector sensitivity: detector arrangement**



determination of the fall-off.





TOF distributions from detectors placed at different angles **cannot be summed up in the time domain**.

But, we need to increase the number of detectors in order to:

- Increase the detection efficiency
- Have a uniform response all over the proton range (for dosimetry)
- Build a system compatible with IMPT

Detector development

## Towards a new approach: Prompt Gamma Time Imaging (PGTI) with TIARA

## The TIARA (Tof Imaging ARrAy) detector



• Light and cheap

#### **Cherenkov-based gamma detector**



#### Targeted time resolution = 100 ps rms

**Cherenkov detectors instead of conventional scintillators** 

- Faster
- Shorter pulses and low LY (pile-up)
- Higher density => higher det. efficiency
- Very low sensitivity to background (threshold process)!

## From PGT to Prompt Gamma Time Imaging



**Issue:** TOF distributions from detectors placed at different angles **cannot be summed up in the time domain**.



#### A dedicated image reconstruction: PGTI

 $TOF = t_{stop} - t_{start} =$ 

$$T_{proton}(\mathbf{r}_{v},\mathbf{v}_{p}) + T_{PG}(\mathbf{r}_{v},\mathbf{r}_{d})$$

2 unknowns:  $\Gamma_{\rm v}$  = PG vertex

V<sub>p</sub> =proton speed

Allows combining the response of multiple detectors:

- Increase the detection efficiency
- to reach uniform sensitivity all over the ion range
- for IMPT compatibility
- From range monitoring to PG imaging

Detector development

## First approach: biased PGTI reconstruction



DOES NOT provide actual PG distribution in case of anatomical variation but sensitive enough to detect a variation from TPS

Detector development

## **Biased PGTI reconstruction: MC validation**

SPR scenario: 10<sup>8</sup> protons, 100 ps rms

#### **MC** validation

- 100 MeV protons •
- Air cavity of variable thickness . (1 mm steps)
- 30 detection modules (1 cm<sup>3</sup>) ٠
- 0.6% overall detection efficiency •
- **SNR = 1** (very conservative!)



Reference profile = 1 cm thick air cavity

PGTI with TIARA

Jacquet et al. Phys. Med. Biol. 66 (2021) 135003;

**Challenges in PGT** 



## **Biased PGTI reconstruction: MC validation**

#### **MC** validation

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proton statistics





Measured parameter	CTR (RMS)	# protons	# PG	Accuracy at 1 $\sigma$	Accuracy at 2 $\sigma$	Beam Intensity	Goal
Range shift	100 ps	107	3 x 10 <sup>3</sup>	2	3	CDD	Pre-treatment
	100 ps	10 <sup>8</sup>	3 x 10 <sup>4</sup>	1	1	SPK	probing
	1 ns	10 <sup>9</sup>	3 x 10 <sup>5</sup>	1	2	Nominal	On-line monitoring

Jacquet et al. Phys. Med. Biol. 66 (2021) 135003;

## Measurement of lateral beam displacement with TIARA and COG



N = total number of PG detected  $n_i$  = number of PG detected in module  $_i$  $Y_i$  = x coordinated of gamma detector



Jacquet et al. Phys. Med. Biol. 66 (2021) 135003

M. Jacquet

PhD thesis

# Possible to distinguish a lateral beam displacement of 2 mm ( $2\sigma$ ) at PB scale

With a position sensitive beam monitor, possible to determine the beam direction => 1D PGTI reconstruction is relevant

Challenges in PGT

Detector development

## **Detector development**

Beam monitor

The TIARA block detector

## **TIARA beam monitor**



25 x 25 x 1 mm<sup>3</sup> plastic scintillator (EJ-204) readout by SiPMs



#### **Performances for single protons**

- DTR = 51 ps  $\sigma$  at 63 MeV
- Detection efficiency = 100%
  - Spatial resolution = **~1.8 mm σ for single protons** <<1 mm for the beam barycentre





**Spatial resolution** 

#### **Time resolution**



 Beam energy measured by TOF at Medicyc (63 MeV) with 0.3% accuracy.





#### Proteus One at 148 MeV



Challenges in PGT

PGTI with TIARA

Detector development: beam

## **TIARA block detector**



#### Cherenkov detectors (PbF<sub>2</sub>) coupled to SiPMs HPK 6075

- short pulses and low LY (pile-up)
- high density => high det. efficiency, very compact
- very low sensitivity to background (threshold process)!
- NO energy measurement



CTR = Coincidence Time Resolution; DTR = Detector Time Resolution

Detector development:  $\gamma$  module

## **TIARA block detector: improvement of CTR and detection efficiency**

Jacquet/André PhD theses

3 vears of R80				
Prototype v1	v2			v5
Crystal Crystal	$\mathbf{pF}_2$ 2 cm <sup>3</sup> PbF <sub>2</sub>	(1.5 000 Port	<b>1</b> .5×1.5×	$2 \text{ cm}^3 \text{ PbF}_2$
SiPM HPK30	50	HPK S	750	
Nb. of SiPMs			<b>A</b> 4 <b>A</b>	
Objective	Simple design	Improve detection	efficiency .	Compact layout
		Improved or equa	timeresolution	
Front-end Commen	ciâl LPSC, single channel	Hybrid read-out	Parallel read-out	Hybrid read-out
Beam monitor FE	Cividec C2	LP	SC	LPSC
Beam test June 20	21 🛛 🔍 April 2022	December 2022	June 2023	December 2023
CTR (ps FWHM) 317	256	222	208	251**
beam monitor DTR (ps FWHM) 157	157	68	68	120
PG DTR (ps FWHM) 275	202	211	197	220

All data are for 63 MeV protons and 3V OV. \*\* coincidence with plastic monitor

**Challenges in PGT** 

## **TIARA block detector: SNR (version v3)**



NICE

A. André PhD thesis

#### Medicyc (cyclotron, 63 MeV)





## **TIARA block detector: SNR (version v3)**

Medicyc (cyclotron, 63 MeV)

# <complex-block>



#### IBA S2C2 (synchro-cyclotron, 148 MeV)

Two sources of background

- protons from beam monitor
- protons from target

#### Thin target





Time difference [ns]

3

2



Perspectives

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target

5

**TIARA Validation** 

Counts

## **TIARA block detector: SNR (version v3)**



A. André

## **TIARA block detector: detection efficiency**



 $\epsilon_{opt}$ 

#### Very low light yield of Cherenkov detectors:

The optical efficiency gives the probability that an event occurring in the crystal is actually detected by the SiPMs.





Challenges in PGT

## **TIARA block detector: detection efficiency**



A. André PhD thesis

Comparison experiment-simulation with detection efficiency taken into account: detector at 13 cm from the beam axis



Interactions in the crystals do not justify the observed background

## **TIARA block detector: detection efficiency**



A. André PhD thesis

#### Comparison experiment-simulation with detection efficiency taken into account: detector at 13 cm from the beam axis



Interactions in the crystals do not justify the observed background

The background is mainly due to protons detected by the SiPM

Antoine Lacassagne CENTRE DE LUTE CONTRE LE CANCER DIGIGANCET NICE

#### Comparison experiment-simulation with detection efficiency taken into account: detector at 13 cm from the beam axis

Simulation: detector at 25 cm from the beam axis



#### **Experimental validation of TIARA**

Measurement of proton range accuracy at MEDICYC cyclotron

Final test of 8-channel TIARA prototype at P1 synchro-cyclotron

TIARA characterisation with protons and carbons at CNAO synchrotron

## 2021. Range accuracy with version v1 (63 MeV, SPR, cyclo)

Antoine Lacassagne CENTRE DE LUTTE CONTRE LE CANCER UNICANCER NICE

![](_page_35_Figure_2.jpeg)

#### Challenges in PGT \_\_\_\_\_

PGTI with TIARA

Detector development

## 2023. Range accuracy with version v5 (63 MeV, SPR, cyclo)

![](_page_36_Picture_1.jpeg)

#### The thin target is translated from 0 to 10 mm in steps of 1 mm

![](_page_36_Picture_3.jpeg)

 $10.41 \times + 14.6$ 

2

1e2

1.2

TOF difference [ps] 0.6 0.4

0.2

Ω

![](_page_36_Figure_4.jpeg)

PGTI with TIARA

## 2023. Range accuracy with version v5 (63 MeV, SPR, cyclo)

![](_page_37_Picture_1.jpeg)

2. TOF integral distributions

#### The thin target is translated from 0 to 10 mm in steps of 1 mm

![](_page_37_Picture_3.jpeg)

1e2

1.2

TOF difference [ps] 0.6 0.4

0.2

0

2

![](_page_37_Figure_4.jpeg)

PGTI with TIARA

A. André PhD thesis M. Pinson postdoc

#### 8 channels TIARA prototype

![](_page_38_Picture_3.jpeg)

Irradiation of RANDO anthropomorphic phantom with sinus empty...

![](_page_38_Picture_5.jpeg)

Antoine Lacassagne

unicancer

... and **sinus filled** with ultrasound gel.

Detector development

## 2024. Validation with version v5

On-going analysis

Antoine Lacassagne CENTRE DE LUTTE CONTRE LE CANCER Unicancer NICE A. André PhD thesis

![](_page_39_Figure_3.jpeg)

Challenges in PGT

PGTI with TIARA

Time difference [ns]

Detector development

Time difference [ns]

TIARA Validation: synchro-cyclotron

Time difference [ns]

Perspectives

Time difference [ns]

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## Protons from synchrotron (100 MeV, $I = 6 \times 10^6 \text{ p/s}$ )

![](_page_40_Figure_1.jpeg)

![](_page_40_Figure_2.jpeg)

![](_page_40_Picture_3.jpeg)

A. André

PhD thesis

#### Challenges in PGT

#### PGTI with TIARA

#### Detector development

#### **TIARA Validation: synchrotron**

## Protons from synchrotron (100 MeV, $I = 6 \times 10^6 \text{ p/s}$ )

![](_page_41_Figure_1.jpeg)

![](_page_41_Figure_2.jpeg)

CNAC/ The National Center for Oncological Hadrontherapy

![](_page_41_Figure_4.jpeg)

• Evaluation of proton range measurement accuracy on-going

> Protons from monitor stopped in the target

> > Thick target

2

Without target

Box 16 (downstream)

A. André

PhD thesis

![](_page_41_Figure_7.jpeg)

#### Challenges in PGT

Detector development

Time difference [ns]

1

Ó

З

## Carbon ions from synchrotron (200 MeV/u, $I = 7.5 \times 10^6$ ions/s) Preliminary

![](_page_42_Figure_1.jpeg)

PGTI with TIARA

Detector development

29/35

M. Pinson

postdoc

## Carbon ions from synchrotron (200 MeV/u, $I = 7.5 \times 10^6$ ions/s) Preliminary

![](_page_43_Figure_1.jpeg)

PGTI with TIARA

29/35

M. Pinson

postdoc

#### **PGTI** as a range monitoring technique

- Works with all common accelerators: cyclotron, synchro-cyclotron, synchrotron
- ✓ Proton range accuracy < 2 mm ( $2\sigma$ ) for 3000 PGs, SPR and a simple target geometry
- 8-channels prototype developed and tested with complex anatomies (analysis on-going)
- ✓ Encouraging preliminary results for carbon ions

#### Performance evolution in SPR

Year	Experiment	#PGs	# protons	Energy (MeV)	Accuracy at 2 <i>o</i>
2020	TIARA, MC	3000	~107	100	3
2021	TIARA, experimental	600	<<10 <sup>7</sup>	63	4
2023	TIARA, experimental	3000	~107	63	1.65

#### **PGTI** as a range monitoring technique

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Encouraging preliminary results for carbon ions

Patient positioning	Treatment monitorin	g>	
SPR PGTI reconstruction Limited statistics CTR ~100 ps RMS	Average Clinical Intensity PGTI reconstruction High statistics available (spot grouping possib CTR ~ ns RMS	High Clinical Intensity COG reconstruction High statistics available (spot grouping)	ASH ?
		Beam intensity	
PGTI with TIARA	Detector development	TIARA Validation	Perspective

## **Acknowledgements and credits**

![](_page_46_Picture_1.jpeg)

## Funding agencies

IRS – Initiative de Recherche Stratégiques (project ANR-15-IDEX-02)

## 🌵 Inserm

PCSI TIARA (Convention n°20CP118-00)

![](_page_46_Picture_6.jpeg)

UNIVERSITÉ Grenoble Alpes

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![](_page_46_Picture_9.jpeg)

#### CAL/IN2P3 COMEX for the allocated beam time

**Petter Hofverberg** (CAL), **Marco Pullia** (CNAO) and their teams for the nice reception Some of the results have been obtained at CNAO experimental facility built in collaboration with INFN

![](_page_46_Picture_12.jpeg)

![](_page_46_Picture_13.jpeg)

![](_page_47_Picture_0.jpeg)

## Positions available in the TIARA collaboration

2 years Post-doc position starting as soon as possible

Learning methods for dosimetry in hadrontherapy with Prompt-Gamma Time Imaging

https://www.cppm.in2p3.fr/web/en/jobs/jobs/index.html Contact: Y. Boursier, CPPM, Marseille (boursier@cppm.in2p3.fr)

![](_page_47_Picture_5.jpeg)

#### PhD position starting October 2025

**TOF-based proton imaging with TIARA** 

Contact: S. Marcatili, LPSC, Grenoble (sara.marcatili@lpsc.in2p3.fr)