Instrumentation for hadrontherapy

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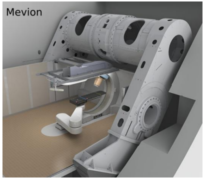
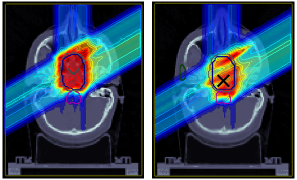
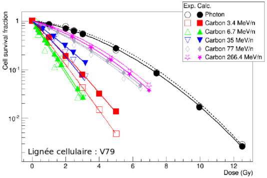
GANIL community meeting – October 19, 2022







Development of compact accelerators

- Cost reduction
- Easier implementation in hospitals
- (Not addressed in this talk)

Ion-range verification

- Strong impact of range uncertainties on dose distributions
- Illustration: proton irradiations with a 1 cm patient shift

$\Rightarrow$ Systems of ion-range verification highly desirable

Precise modeling of the biological dose

- Strong impact of ion type and energy on cell survival for a given dose
- Need for biophysical models (with a limited number of parameters)

$\Rightarrow$ Need for experimental data $\Rightarrow$ beams lines for cell irradiations

Outline

1. Ion-range verification

2. Beam lines for cell irradiations

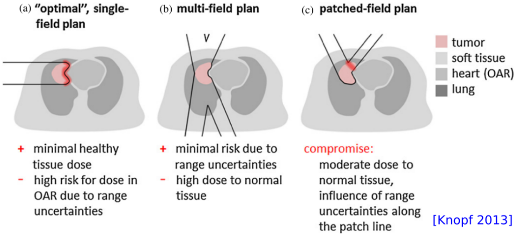
Introduction to ion-range uncertainties and verifications

Limitations of current treatment plans

- Large margins around the PTV: $\sim$ 1 cm for ranges of 20 cm
- "Non-optimal" field plans

$\Rightarrow$ Ballistic properties of ions not fully exploited

$\Rightarrow$ Ion-range verification highly desirable

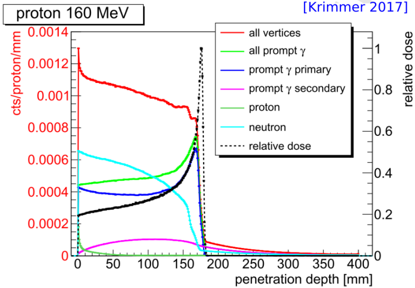


[Knopf 2013]

Ion-range verification with nuclear imaging

- Correlation between dose and nuclear reaction distributions (e.g. β^+ emitters and prompt gammas)

[Krimmer 2017]



PET

- Pioneering investigation (LBNL, [Maccabee 1969]) $\Rightarrow$ clinical studies in 1990's
- Modality still under development (INSIDE project in Italy, OpenPET in Japan) ([Bisogni 2017, Tashima 2016])

Range verification in PT: Prompt Gammas (PG)

Current modalities

- Main: PET and Prompt Gammas (PG)
- But also: Bremsstrahlung, ionoacoustic waves and post-treatment MR images
- Combination of several modalities considered (e.g. PET and PG [Parodi 2016])

PET vs PG

- Production rates: very similar

	PET	PG
Pros	- Mature technology - "Natural electronic collimation"	- Direct Emission ($\Rightarrow$ Real-time)
Cons	- Washout - Delayed emission	- Neutron background - High energy gammas

- Possibily to retrieve information on ion range from all PG features: position, energy and TOF

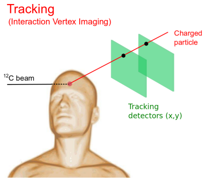
PG detection modalities + Interaction Vertex Imaging (IVI)

PG modalities [$\checkmark$: mandatory, ($\checkmark$): optional]

PG feat.	Imaging systems			Non-imaging systems			
	Phys. collim.	Elec. collim.	PG Time Imag. (PGTI)	PG Timing (PGT)	PG Peak Integ. (PGPI)	PG Energy Integ. (PGEI)	PG Spectro. (PGS)
Position	$\checkmark$	$\checkmark$					
Energy	($\checkmark$)	($\checkmark$)	($\checkmark$)	($\checkmark$)	($\checkmark$)		$\checkmark$
TOF	($\checkmark$)	($\checkmark$)	$\checkmark$	$\checkmark$	($\checkmark$)		($\checkmark$)
Statistical meas.					$\checkmark$	$\checkmark$	
Advantages	Direct measurement						
			Light devices				

CLaRyS collaboration

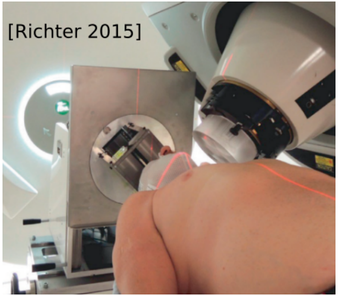
- IP2I Lyon, LPSC Grenoble, CPPM Marseille, CREATIS Lyon
- PG : Investigations/developments of 5 modalities out of 7
- Interaction Vertex Imaging (IVI): Detection of secondary protons (carbon ion beams)
  - Main advantage: tracking (need for collimation with PG)

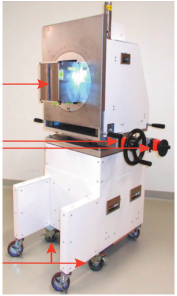


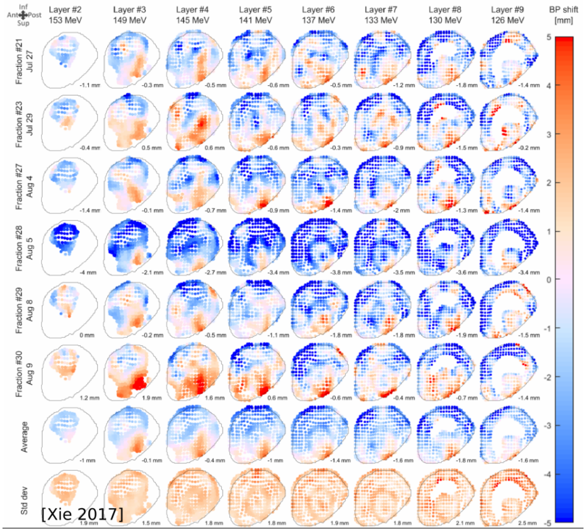
PG detection: the IBA prototype (the reference)

- Knife-edge slit camera (KES)
- Tested during treatments with passive and active beam delivery (2016, 2017)

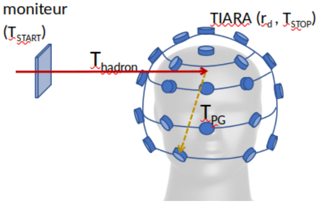
⇒ Millimetric precision achieved with large spots or “spot grouping”







Examples of French developments: Prompt Gamma Time Imaging (LPSC-CPPM-CAL)



Principles and developments

- Principle: Reconstruction of PG emission points from precise TOF measurement (a few 100 ps FWHM)
- Development: Prototype with
  - $\sim$ 30 detectors (PbF_2 + SiPM)
  - Time resolution: $\sim$ 245 ps (FWHM)
  - Dedicated reconstruction algorithm

Status

- In-beam tests of the detectors under progress + Simulation of a prototype with 30 detectors

$\Rightarrow$ Promising results [Jacquet 2020]

<table>
<tr><th></th><th>TOF resolution (FWHM)</th><th>#PG</th><th># Incident protons</th><th>Sensibility (2σ)</th><th>Intensity</th></tr>
<tr><td rowspan="2">Longitudinal shift</td><td>235 ps</td><td>3×10^4</td><td>10^8</td><td>1 mm</td><td>Single proton</td></tr>
<tr><td>2.35 ns</td><td>3×10^5</td><td>10^9</td><td>2 mm</td><td rowspan="2">Nominal intensity</td></tr>
<tr><td>Lateral shift</td><td>-</td><td>3×10^5</td><td>10^9</td><td>2 mm</td></tr>
</table>

Perspectives in GANIL (ion-range verification)

Investigation of the PG modalities with carbon ion beams

- At the moment, most studies and developments have been performed with proton beams

Complementary studies on IVI (Interaction Vertex Imaging)

- Few studies have been performed on this modality [Henriquet 2012, Muraro 2016, Finck 2017. . .]

PG cross sections measurements

- Clinical applications require precision of the order of a few percents

Outline

Need for cell irradiation beam lines

Radiobiogical studies (⇒ Talk of Gersende Alphonse)

- To quantify the cell damage as a function of radiation quality, doses, dose rates. . .
- To understand the cell response to irradiations

Contraints for biophysical models

- Need for biophysical models to predict biological dose
- Current models in TPS: mMKM (Japan) and LEM I (Europe)
- Use of cell survival curves (relevant outcome for tumor control + complications) to constrain and test the models:
  - Contraints: Mono-energetic beams
  - Tests: Spread-out Bragg Peak (SOBP):
    - Mixed field: several incident ion energies + secondary particles due to nuclear reactions
    - Biological dose $\neq$ Linear combination of the contribution of each particle of a given energy

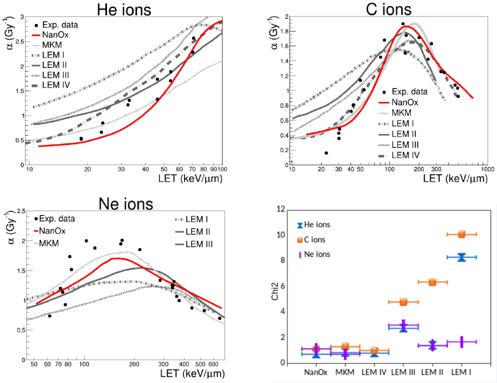
    ⇒ Use of an approximation (introduced by Kanai et al. in TPS) that has to be tested

NanOx model (IP2I): Benchmark with exp. data and 5 other biophysical models

Parameters

Param.	Cell nucleus diameter	Effective lethal function of nanometric targets
Input data	Cell microscopy	$\gtrsim$ 3 cell survival curves 1 RX + 2 ions (interm. and high LET ions)

α coefficients for HSG cell [Monini 2019]



Methods

- Three cell lines irradiated by monoenergetic ions
- 5 other biophysical models: MKM and LEM I–IV

Results

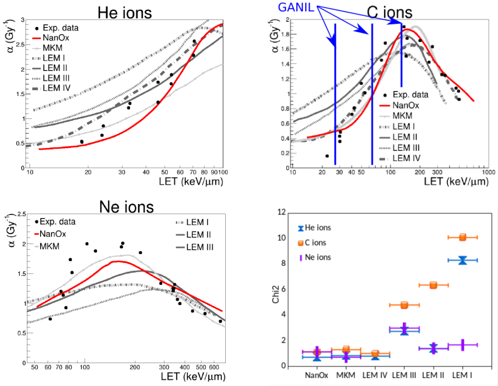
- "NanOx predictions are more often more accurate than the ones issued from the other biophysical models" [Monini 2019]
- Striking ability of the biophysical models to predict all relevant cell survival curves from a small set of experimental data

Importance of GANIL for cell irradiations and positioning in Europe/France

Room	Ion	Energy (MeV/u)	LET $\left(\frac{keV}{\mu m}\right)$	Range in H_2O (mm)
GANIL	$^{12}\mathrm{C}$	95 (D1)	28	$\gg 1$
		35 (D1)	63	
	$^{13}\mathrm{C}$	13.6 (SME)	134	0.8
ALTO	p	$\rightarrow$ 15	3	2.5
	α	$\rightarrow$ 10.75	17	1.5
	$^{7}\mathrm{Li}$	$\rightarrow$ 12.5	55	0.5
ARRONAX	p	$\rightarrow$ 65	1	$\gg 1$
	α	$\rightarrow$ 16	10	

- GANIL's carbon ion energies $\Rightarrow$ Sampling of the energy range of interest (with the increase of biological efficiency)
- Unique facility in France and few similar facilities in Europe for cell irradiations with carbon ion beams

α coefficients for HSG cell [Monini 2019]



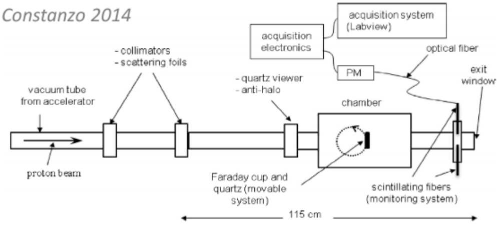
Brief history

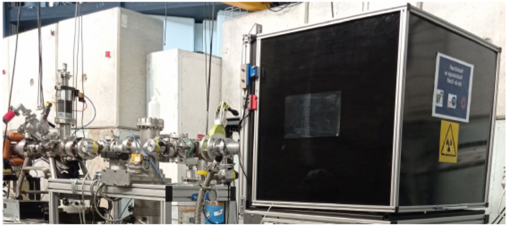
- 2012-2020: 3 MeV proton beams @ 4 MV VdG accelerator in Lyon ⇒ Now in the ALTO platform (IJClab)

Design

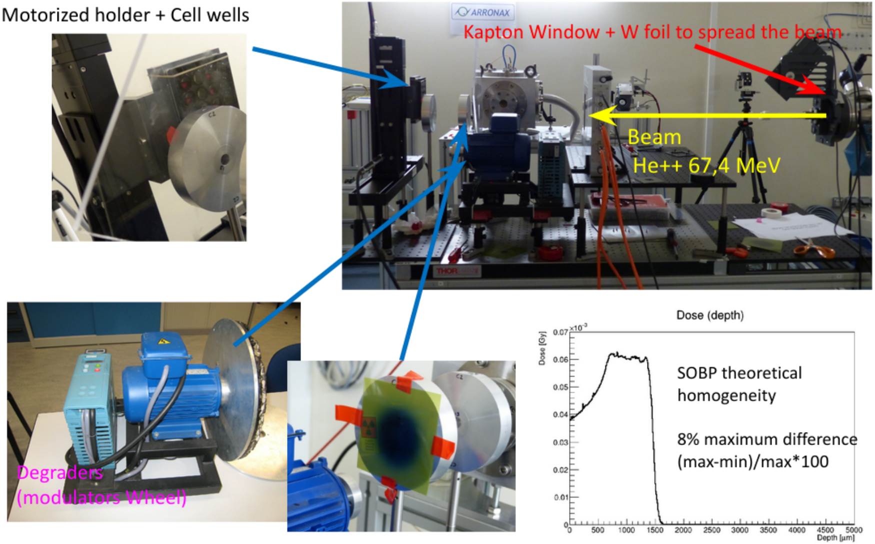
- Double scattering foils and collimation system (broad beam ~ 2 cm^2, $\pm 3\%$ homogeneity)
- Dose monitoring systems (Faraday cup, quartz, scintillating fibers) + Thermostatic sample-support
- Development of an analytical model of the line to quickly provide for instance the parameters of the line (e.g. foil thicknesses) as a function of ion type and energy

Constanzo 2014

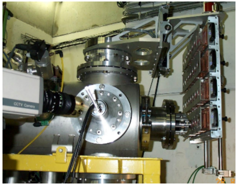




Example of beam lines: The ARRONAX beamline (ARRONAX-IP2I)



Current status and perspectives in GANIL (cell irradiation beam lines)



Current status

- Cell irradiation with IRRABAT (mono-energetic carbon ion beams in D1)
- Energy: $\sim$ 35 MeV/u (with degrader) $\rightarrow$ 95 MeV/u

Possible additional facilities and measurements

- Mono-energetic "low-energy" carbon ion beams @ SME (13.6 MeV/u)
- SOBP @ D1: SOBP of $\sim$ 1 cm with a distal position at 25 mm

Outcomes

- Cell response + cell survival
- Physico-chemical measurements such as radiolytic yields (model constraints + dosimetry)

Methodology

- 1^{st} meeting in September 2022: directions of GANIL, LARIA, CIMAP, GDR MI2B + M. Beuve (IP2I)
- Consultation of the community

$\Rightarrow$ Estimate of the beam time request (Go/No-go for a premilinary project)

Thank you for your attention!