Upgrade of the CNA Cyclotron External Beamline Towards High-Intensity and Pulsed Proton Beams for FLASH Radiobiology and Therapy Research

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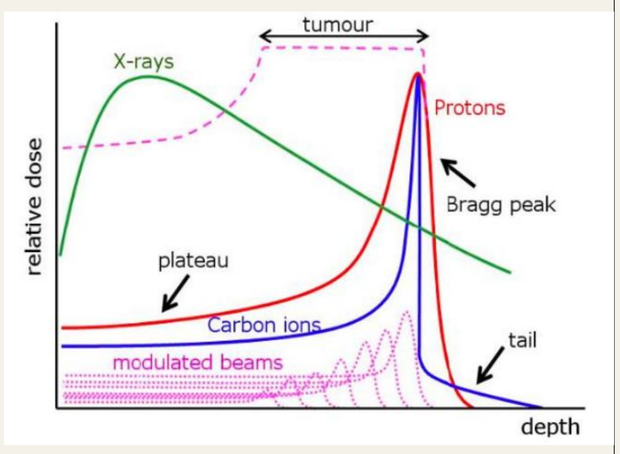
Introduction

Proton radiobiology plays a key role in understanding radiation-induced biological effects and developing innovative treatment strategies. In particular, FLASH radiotherapy has emerged as a promising approach capable of reducing normal tissue toxicity while maintaining tumour control through ultra-high dose rate irradiation (>40 Gy/s). To support both current radiobiology programmes and future FLASH studies, the CNA Cyclone 18/9 external beamline is being upgraded with new beam control, diagnostics, and beam manipulation systems, including an electrostatic chopper, movable slits, and dedicated simulation and dosimetry tools.

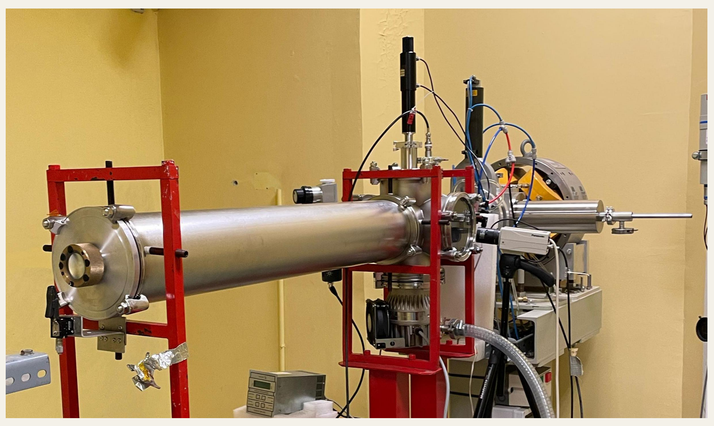
Proton Therapy and Radiosensitizer

Proton therapy offers significant advantages over conventional X-ray radiotherapy due to the localized energy deposition at the Bragg peak, reducing the dose delivered to surrounding healthy tissues. In recent years, gold nanoparticles (AuNPs) have emerged as promising radiosensitizers, showing enhanced biological effects in both in-vitro and in-vivo proton irradiation studies. However, the mechanisms responsible for this enhancement remain poorly understood, motivating further radiobiological investigations.



CNA Facilities

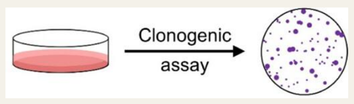
The CNA Cyclone 18/9 accelerator provides 18 MeV proton beams for research and radioisotope production. Its external beamline, originally developed for radiobiology and microdosimetry studies [2], delivers homogeneous 12–13 MeV proton irradiation fields (3 cm diameter) and is equipped with an ionization chamber for accurate dose measurements and biological sample irradiation.



Radiobiology Results

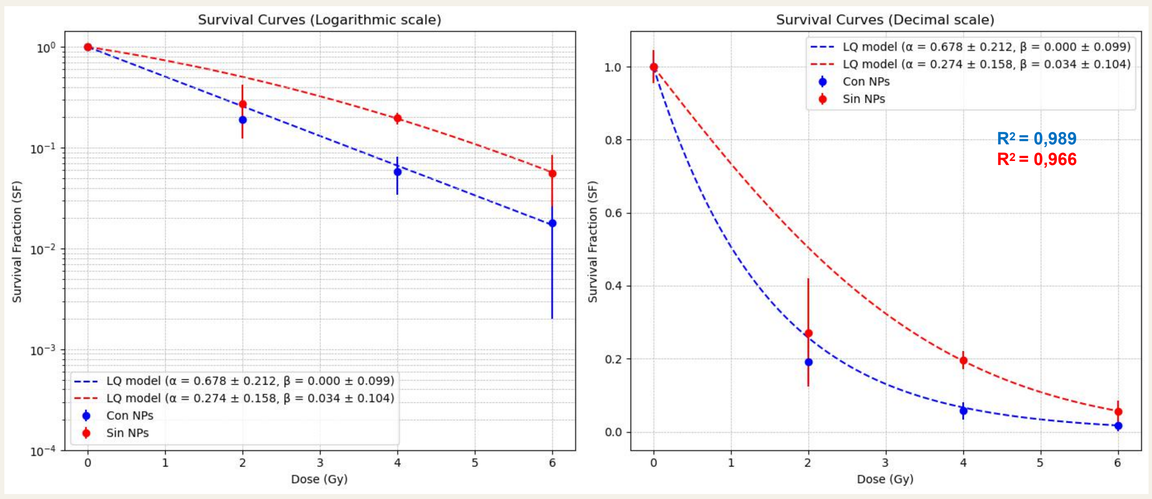
A one-way ANOVA was performed to assess statistical differences between control and AuNP-treated samples. Significant differences were observed for the 4 Gy irradiation group ($p < 0.05$).

$$\mathrm{PE} = \frac{Count_{control}}{Cell} \qquad SF = \frac{Count_{irradiated}}{Cell} \cdot \frac{1}{PE}$$



Survival curves were fitted using the linear-quadratic (LQ) model:

$$SF = e^{-\alpha D - \beta D^2}$$



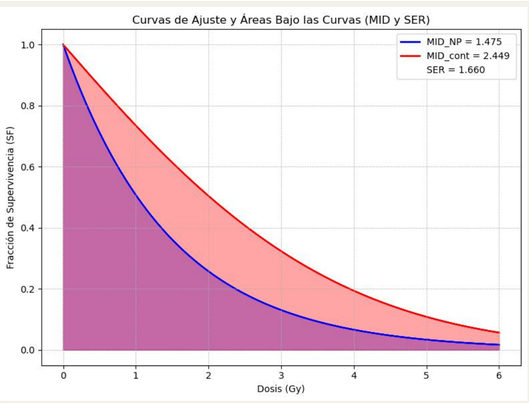
Radiosensitization Metrics:

MID (Mean Inactivation Dose)

$$MID = \int_0^\infty SF(D)dD = \int_0^\infty e^{-\alpha D - \beta D^2}$$

SER (Sensitizer Enhancement Ratio)

$$SER = \frac{MID_{cont}}{MID_{NP}}$$



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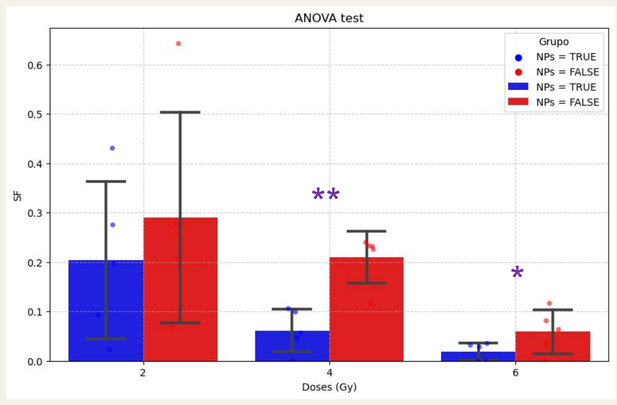
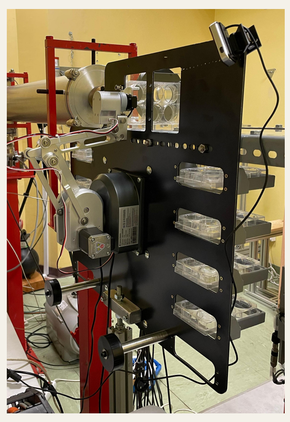
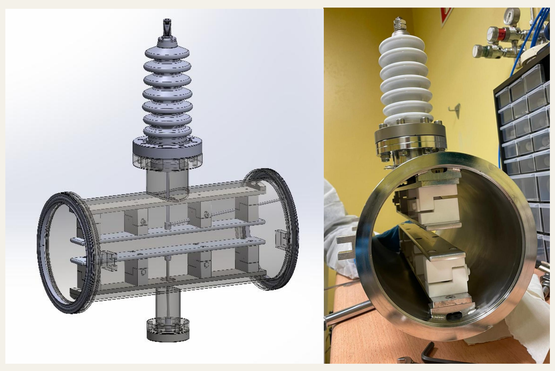
Dose (Gy)	f_stat	p_value
2	0,52	0,49
4	23,71	0,001
6	3,53	0,09



Beamline Upgrade

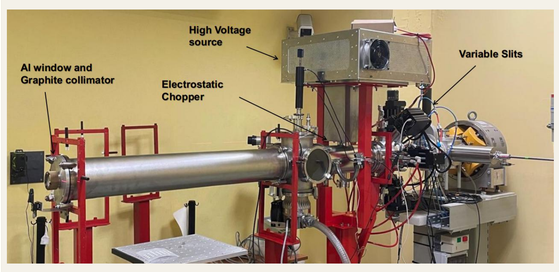




Robotic Sample Exchange
- Automated sample exchange
- Reduced handling time
- Improved biological conditions
- Remote operation

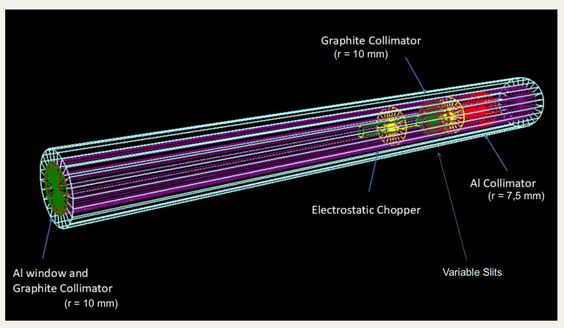
Electrostatic Chopper
- Pulsed proton beam generation
- FLASH-oriented operation
- Electrostatic beam deflection
- CST-optimized design

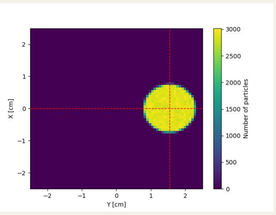
New Beamline and Optimization



Upgraded CNA beamline including the electrostatic chopper and others new elements.

A detailed TOPAS [3] model of the upgraded CNA beamline was developed to study beam transport and irradiation conditions. Simulations were used to optimize slit apertures and evaluate beam transmission and the centroid position of the beam after chopper deflection , supporting future FLASH beam delivery and experimental commissioning.





L/2 [mm]	Beam Transmission [%]
5	0.0034
6	1.25
7	4.72
8	5.64
Open	5.65

Summary

- Significant AuNP-mediated radiosensitization was observed in proton-irradiated HeLa cells (SER > 1).
- Improved biological irradiation conditions were achieved through the implementation of an automated sample exchange system.
- A fast electrostatic chopper was developed and installed to enable pulsed proton beams for FLASH studies.
- TOPAS simulations are being used to optimize beam transport, transmission, and irradiation conditions.
- The upgraded CNA beamline provides a versatile platform for future FLASH proton radiobiology research.

References

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