

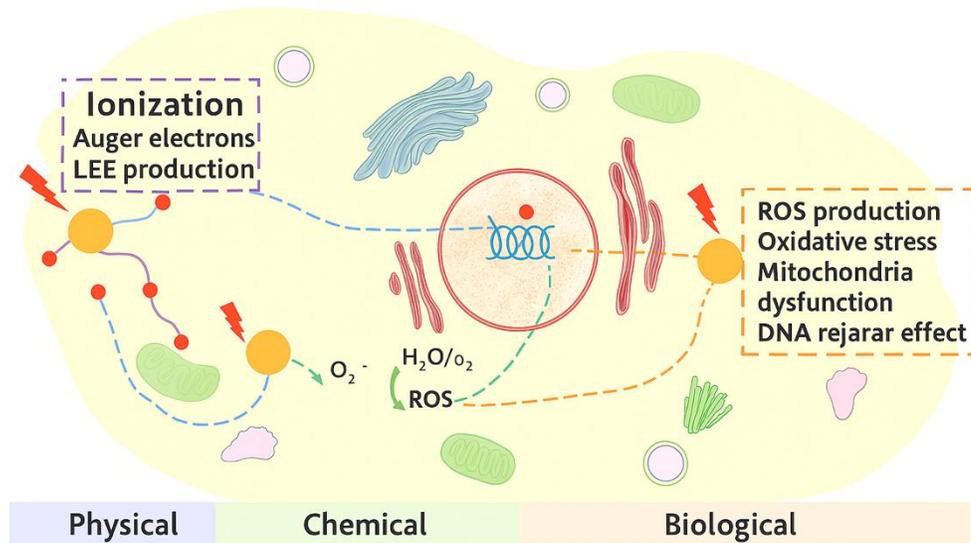
Technological Developments and Radiobiological Studies on Novel Hadron Therapy Techniques

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C. Blanch, M. Boronat, D. Esperante, J. M. Espino, J. Fuster, F. J. García-López, B. Gimeno, L. González, D.
Hermenegildo-Saucedo, P. Huertas, I. Mingarro, D. Pascual

Física Médica S8A
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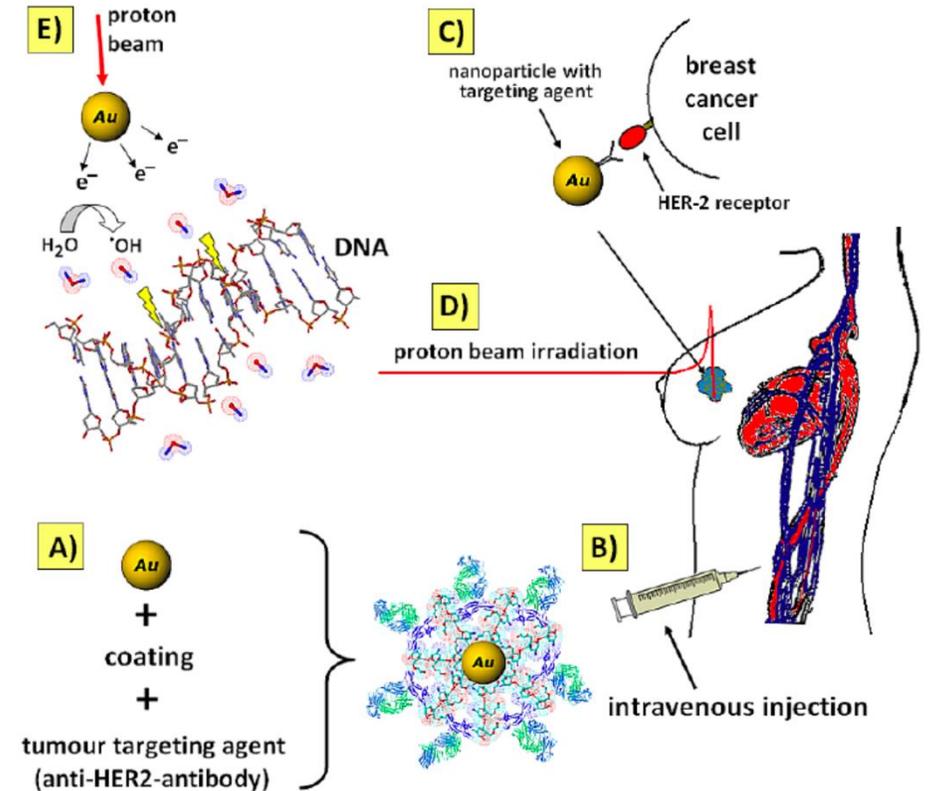
Metallic nanoparticles as radiosensitizers

- Several experiments *in-vitro* and *in-vivo* demonstrated the potential of high-Z NPs to enhance the efficacy of proton therapy



□ Main challenges :

- **Insert** the NPs **only** into the tumour cells
- **Control** the concentration and biodistribution within the treatment duration and after
- **Modelling** of the phenomenon for **treatment planning**
 - ✓ Subsequent mechanisms behind the effect are still controversial



Goals

□ Multidisciplinary collaboration

(Biochemist, Physicist, Biologist, Chemist)



Institut Universitari de Biotecnologia i Biomedicina BIOTECMED



□ Radiobiology experiments to study the radiosensitization effect of **gold NPs with protons**

- Evaluate, quantify the effect and modelling studies

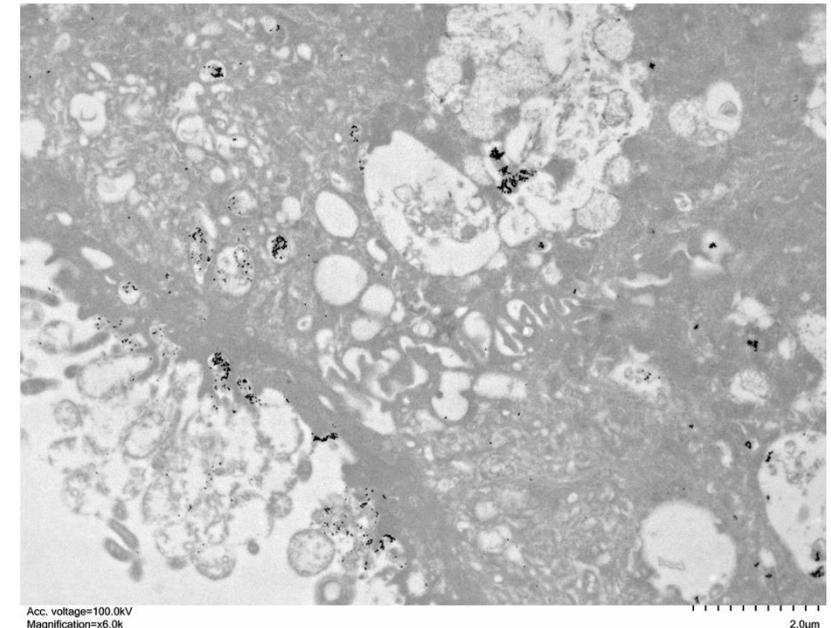
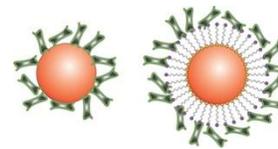
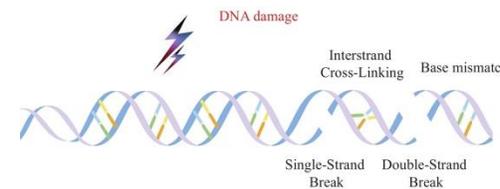
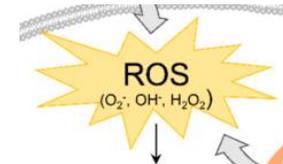
- ✓ Clonogenic assays

- Investigate the underlying mechanisms

- ✓ ROS

- ✓ DNA damage assays

- ✓ Proteomic studies



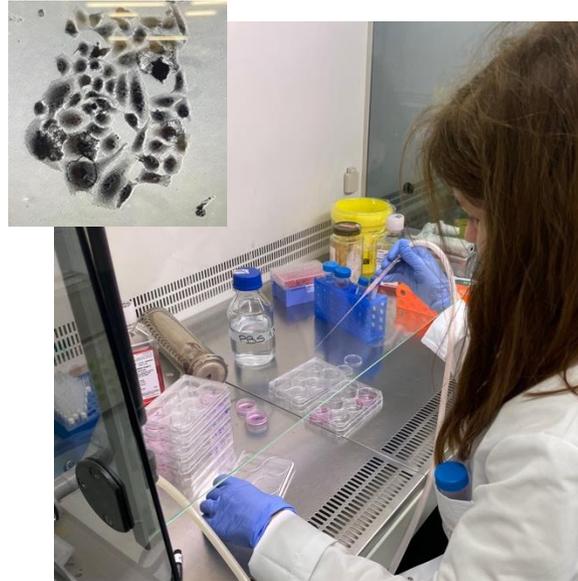
- Develop and test selective nanoparticles

- ✓ First prototype for prostate cancer under test

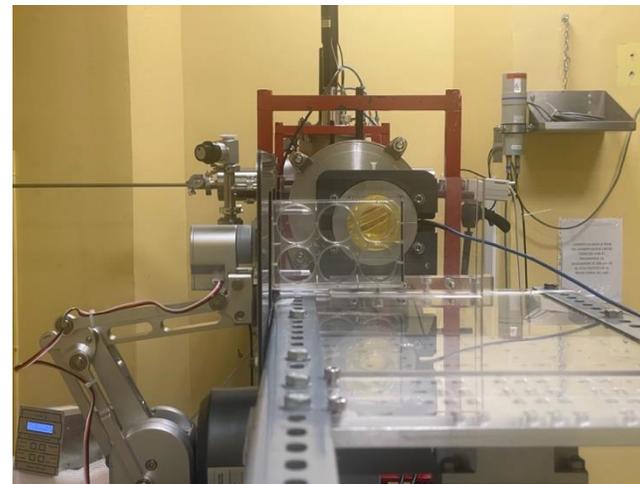


Radiobiology experiments

- ❑ Nanoparticles characterized at UV
- ❑ Biological samples for irradiation prepared at **CABIMER** (*Centro Andalúz de Biología Molecular y Medicina Regenerativa*)
- ❑ Irradiations performed at the Cyclotron External Beam Line at **CNA** (*Centro Nacional de Aceleradores*)
 - ✓ Optimized for 3 cm \varnothing homogeneous irradiation fields
 - ✓ In-line dose measurements



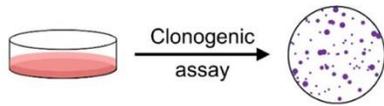
Operational since 2025
In collaboration with V. Girbés, J. L. Sanchez
Founded by : **Desarrollos para la terapia con protones (IP: Carmen Jiménez Ramos)**



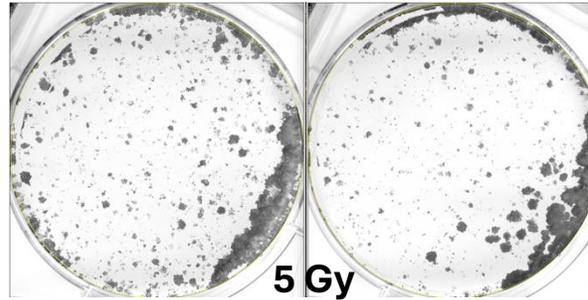
ETSE-UV 10 ANYS
Escola Tècnica Superior d'Enginyeria

Radiobiology experiments

- Experimental campaigns in 2022, 2023, 2024, with conventional 20 and 50 nm AuNPs from cytodiagnosics



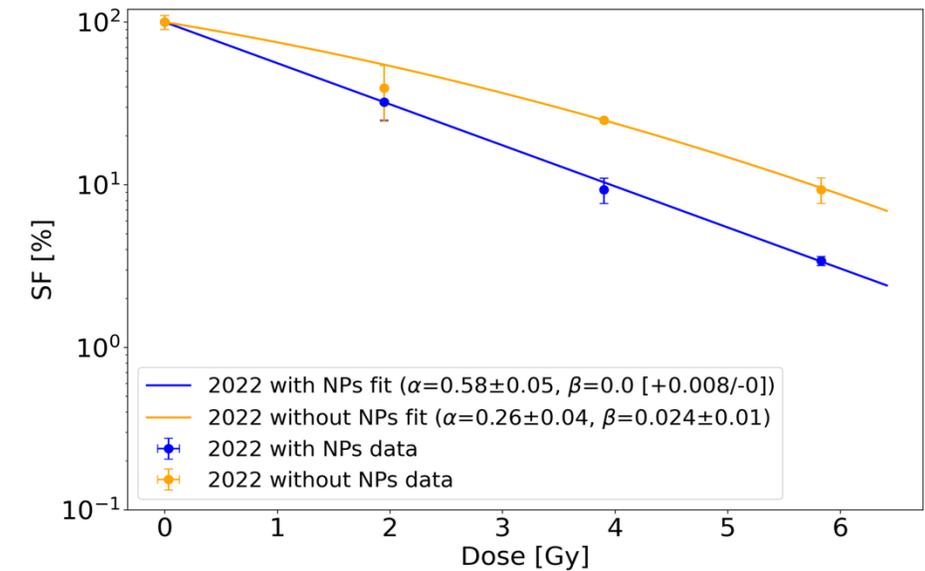
Without NP With NP



5 Gy

$$SF = \frac{\text{colonies after irradiation at } X \text{ Gy}}{\text{Seeded cells} \times PE} \times 100$$

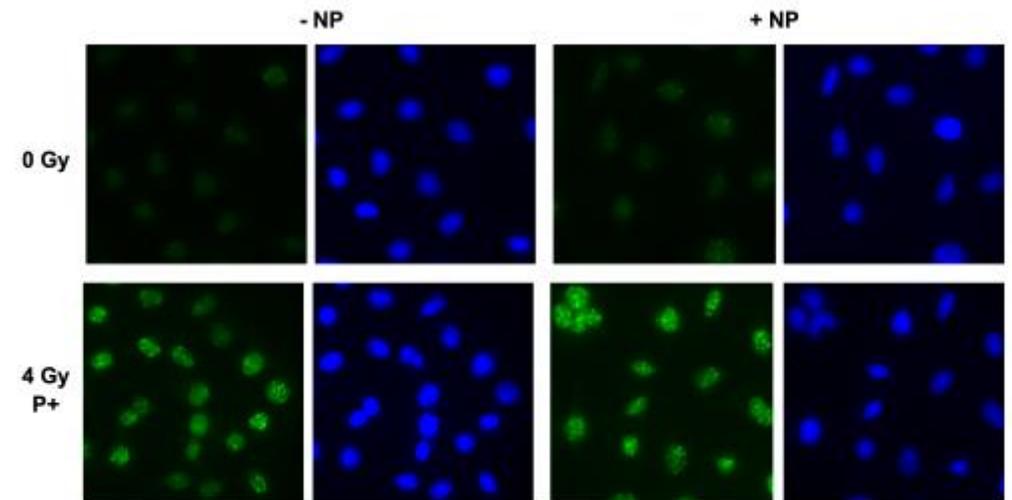
$$PE = \frac{\text{colonies without irradiation}}{\text{Seeded cells}} \times 100$$



- DNA-damage assays reveal an increase of different markers when AuNPs are used

*V Jornadas RSEF/IFIMED de Física Médica. N. Fuster-Martínez et al.,
Technological developments and evaluation of the radiosensitizing potential
of gold nanoparticles (AuNPs) for hadron therapy*

Article submitted under revision in Medical Physics Journal



FLASH proton therapy

Plan Complementario AstroHEP: Tecnologías avanzadas para la exploración del universo y sus componentes.

L. A.1: Desarrollo de instrumentación de vanguardia para futuros experimentos de Física de Partículas y Nuclear

Título de la actuación 1.4: Desarrollos para la terapia con protones (IP: Carmen Jiménez Ramos)



CNA Ciclotrón 18/9 MeV



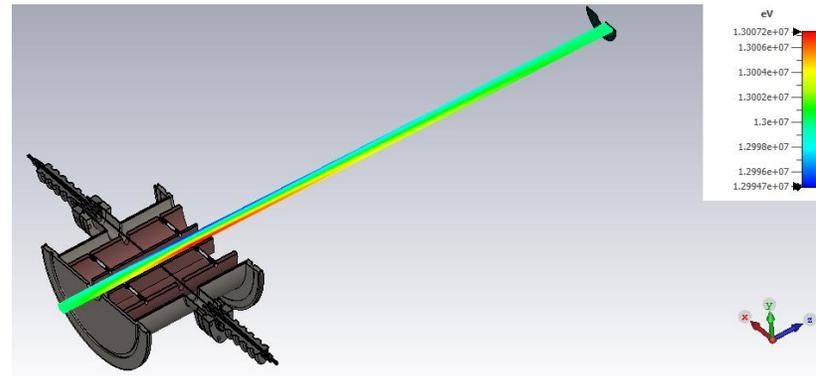
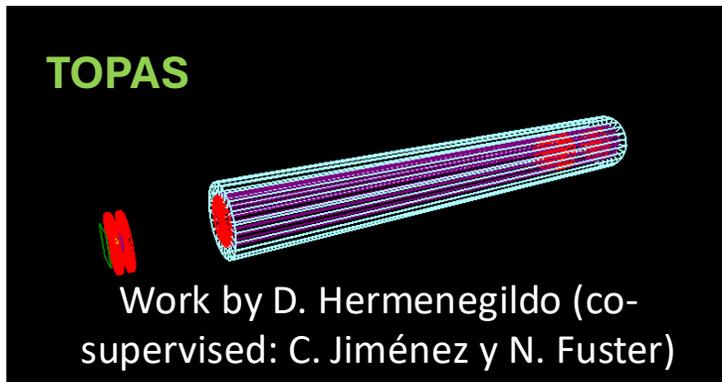
Objetivo

Design and fabrication of a new beam pulsing system for the external beamline of the CNA cyclotron (University of Seville, CSIC, Regional Government of Andalusia) for radiobiology studies in FLASH regime

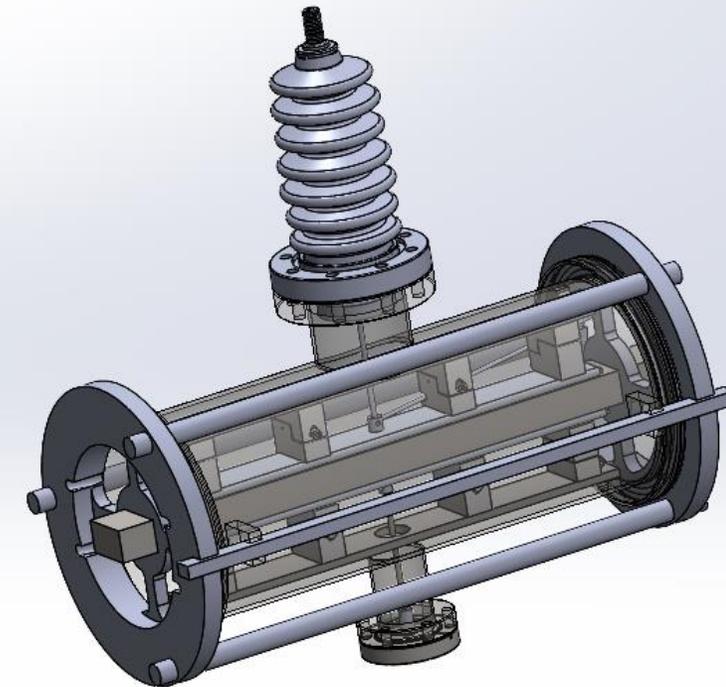
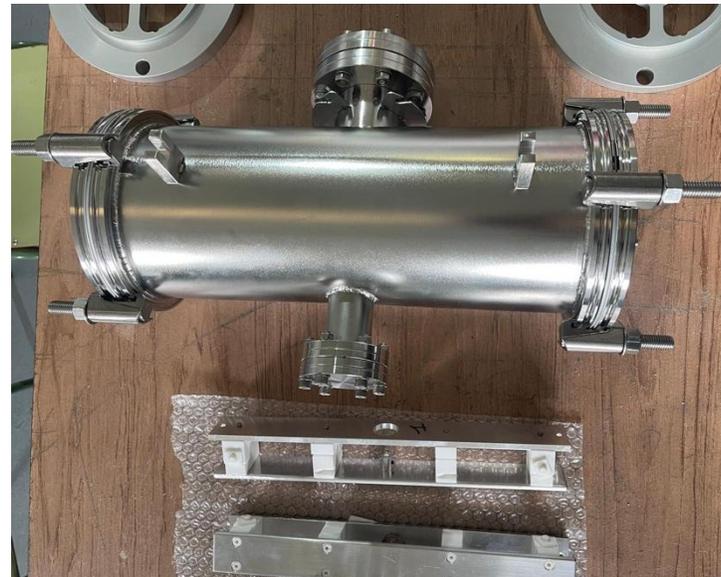


FLASH proton therapy

- ❑ Pulsing system designed and fabricated to be commissioned in early 2026
- ❑ Beam line and beam parameters optimization for radiobiology experiments on-going (TOPAS, Xsuite)



Pulse	30 kV
Rise/fall time	1 μ s
Pulse Rep. Rate	1 kHz
Chopping pulse width	10 - 50 μ s



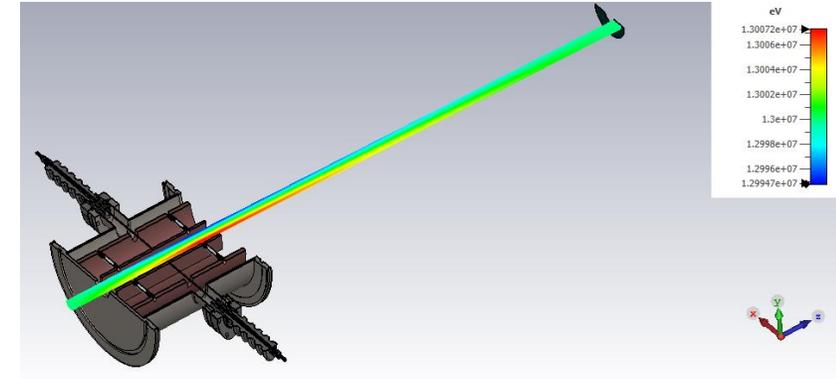
- ❑ Radiobiology experiments under FLASH conditions

EM and mechanical design by C. Blanch, D. Esperante, N. Fuster and *Neptury Technologies*

Ideas for financial support

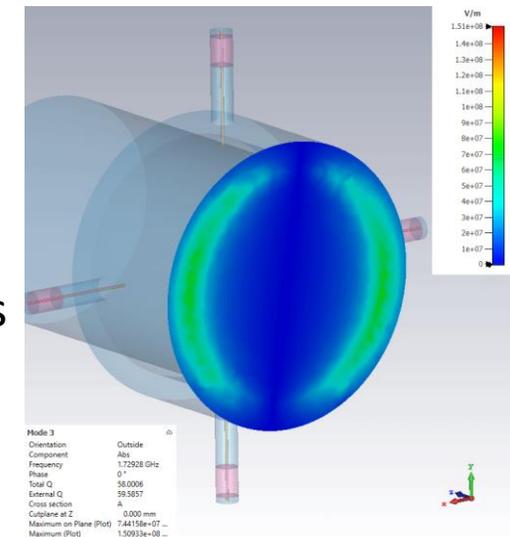
☐ Software

- Two years of **CST-PS license update** (~1200 euros per year)
 - ✓ 3D EM simulations
 - ✓ Eigenmode solver, PIC solver, Wakefield solver...
 - ✓ EM design, beam dynamics studies...



☐ Equipment:

- **High-performance oscilloscope** (> 40 GSa/s, High Resolution, High Band width)
 - ✓ Performance characterization of instrumentation, diagnostics for ALMA
 - ✓ Radiation measurements in future RF laboratory tests in view of the cavities for the ALMA energy upgrade
- **High performance Vector Network Analyzer**
 - ✓ RF and microwave components characterization
 - ✓ Useful for ALMA RF components characterization and future energy upgrade studies



☐ ALMA accelerator users first **workshop** to be organized in 2026.