Preparation of a radiobiology beam-line at the 18 MeV proton cyclotron facility at the CNA

A. Baratto-Roldán¹,²,* , M. C. Jiménez-Ramos¹, J. García-López¹,², M. I. Gallardo², M. A. Cortés-Giraldo², J. M. Espino¹,²

(1) Centro Nacional de Aceleradores (Seville, Spain)
(2) Universidad de Sevilla (Seville, Spain)
(*) abaratto@us.es

International Conference on Medical Accelerators and Particle Therapy

CNA, Seville, Spain
September 4th – 6th, 2019
CNA PROTON FACILITIES

Pelletron 9SDH-2 Tandem Accelerator

• Maximum terminal voltage of 3MV, corresponding to a maximum proton energy of 6 MeV;
• 6 experimental beam lines for different applications;
• Radiobiology beam line available for mono-layer cell culture irradiations with approximately 4 MeV protons.

Cyclone 18/9 Cyclotron Accelerator

• Maximum proton energy of 18 MeV;
• Extracted maximum beam intensity of 80 μA ± 10%;
• Used for production of PET radioisotopes;
• One external experimental beam line for different purposes.
LOW ENERGY PROTON BEAMS FOR RADIOBIOLOGY: WHY?

In current clinical practice, protons are considered to be 10% more efficient for cell killing with respect to conventional photon radiotherapy beams → **RBE = 1.1**

However, the RBE is a complex variable, which depends on many factors:
- Tissue type
- Biological endpoint
- Radiation Quality
- ...  

Mainly described by Linear Energy Transfer (LET)

**RBE increases with LET!**

Radiobiology experiments with protons at energies typically found at the Bragg peak region of clinical beams are of interest to reach a consensus on the RBE variation with LET.
Radiobiological experiments at proton and heavy-ion accelerators pose stringent conditions:

<table>
<thead>
<tr>
<th>PHYSICAL</th>
<th>BIOLOGICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogeneous dose distribution. Meaningful dose rates, comparable to those used in the clinics. Broad irradiation field to cover the whole sample area.</td>
<td>Strict control of the environmental parameters (temperature, pressure). Cell cultures exposed to air are vulnerable to bacterial contamination, meaning that the irradiation time must be kept under control.</td>
</tr>
</tbody>
</table>
1. Beam current:
   a. Ion source current set to the minimum $\sim 5$ mA;
   b. Completely **defocused** beam (detuned quadrupoles).

2. Beam broadening and homogeneity: scattering on heavy targets and air.
   a. Adjustments on steering magnets;
   b. Scattering on heavy targets and air.
EXPERIMENTAL BEAM LINE

Achieving dose homogeneity over the target area (≈ 35 mm diameter):

- Temporary impossibility to insert a scattering foil inside the beam line;
- Available exit window:
  - maximum diameter of 15 mm;
  - 125 µm PET

A

- Smaller beam size.
- Tungsten scattering foils of at least 150 µm placed in air.
- Longer exit window to sample distance.
- Lower energy range available.

- 500 µm thick aluminum foil inserted in the beam line (1.5 m upstream the exit window);
- New exit window:
  - 40 mm diameter;
  - 100 µm PET

B

- Bigger beam size.
- No need for scattering foils in air.
- Shorter exit window to sample distance.
- Higher energy range available.
SETUP FOR THE IRRADIATION OF BIOLOGICAL SAMPLES

PROTON BEAM DOSIMETRY:

• Parallel plates ionization chamber:
  - 3 kapton electrodes of 7.5 µm thickness
  - 2 air gaps of 6.75 mm
  - 44 mm of diameter

• EBT3 radiochromic films

SETUP

• PMMA sample holder specially designed to insert Petri culture plates.
• The cyclotron external beam line counts only on two Faraday cups (one with a scintillator foil) for beam diagnostics.

• Limited space available in the experimental room makes the insertion of new elements for beam diagnostics not easy.

Information about beam characteristics must derived from measurements in air and comparisons with Monte Carlo simulations with Geant4.
What about the energy spread? Nominal $\sigma$ of the energy distribution: 1% of the mean energy (0.18 MeV).

But:

Simulations done with an initial $\sigma = 0.13$ MeV better reproduce experimental data.

$\sigma_{\text{initial beam}} = 0.18$ MeV

$\sigma_{\text{initial beam}} = 0.13$ MeV
Homogeneity dependence of steering magnet parameters

- Beam homogeneity strongly depends on the current parameters chosen for the steering magnets in both transverse directions.
- Beam homogeneity might vary with irradiation time due to coils overheating

Adjustments on steering magnets necessary before every biological irradiation
Maximum deviations from mean optical density of the order of 2-6% at the sample position over the whole sample area

$\text{netOD}_{\mu} \approx 0.4$
EBT3 FILM PROTON DOSIMETRY

- Exit window thickness: 125 µm;
- 150 µm thick tungsten scattering foil placed in air, immediately after the exit window;
- Exit window to sample distance: 50 cm

Proton energy at sample position: 10.6 MeV

- Exit window thickness: 100 µm;
- 500 µm thick aluminum scattering foil inserted in vacuum, upstream first collimator;
- Exit window to sample distance: 25 cm

Proton energy at sample position: 12.6 MeV
EBT3 FILM PROTON DOSIMETRY

\[ D = f \frac{N^IC_p}{A} \cdot \frac{\Delta E}{\rho_{Lu}\Delta z} \]

\[ N^IC_p = \frac{Q^IC}{e} \cdot \frac{W}{\Delta E^IC} \]

\[ f = \frac{N_p(b)}{N^IC_p(a)} \]

Anna Baratto-Roldán
International Conference on Medical Accelerators and Particle Therapy
MC initial beam parameters:

- Gaussian energy distribution;
- \( E = 18 \text{ MeV}, \sigma_E = 0.13 \text{ MeV} \);
- Plane spatial distribution (spot size determined by first collimator \( \approx 8 \text{ mm} \) radius);
- Parallel momentum distribution along the beam axis

Beam 2-D dose profile after 0.5 cm of air (film attached to the flange).

No scattering foil inserted.
BEAM CHARACTERISTICS: SPATIAL DISTRIBUTION

EXPERIMENTAL

GEANT4

Geant4
Measured
Geant4 simulation tested and compared with dose profiles taken under different experimental conditions: **overall good agreement with experimental measurements.**

Beam dose profiles after 65.9 cm of air.
No scattering foil inserted.

Beam dose profiles after 25.3 cm of air.
500 µm foil inserted in vacuum.
FIRST IRRADIATION OF CELL CULTURES

Measurements carried out in collaboration with biologists of Cabimer.

- human bone osteosarcoma epithelial cells grown on mono-layers;
- 3 dose points (controls, 6 Gy and 10 Gy)
- Photon irradiation carried in parallel at Cabimer.

- Total irradiation time approx. 30 minutes
- Maximum duration of culture exposure to air approx 8 minutes
- Room temperature of 22 °C

At first glance, no evidence of stress response or damage due to environmental conditions.
CONCLUSIONS

✓ A system for the irradiation of biological samples (mono layer-cell cultures) has been developed at the 18 MeV proton cyclotron facility at the CNA.

✓ Two different setups have been proposed to achieve the necessary level of homogeneity over the whole sample area.

✓ A Geant4 simulation has been developed for the characterization of the beam line. Simulation results have been extensively compared with measurements under different experimental conditions, showing an excellent agreement.

✗ Workflow still too slow, the implementation of an automated system for sample positioning is foreseen.

✗ Petri dishes as those used do not allow for irradiation with medium, limiting the spectrum of biological experiments and applications. New systems and solutions are currently under study.

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 675265, OMA – Optimization of Medical Accelerators, and from the Spanish Ministry of Economy and Competitiveness under grant No FPA2016-77689-C2-1-R. The Monte Carlo simulations were carried out at the FIS-ATOM cluster hosted at CICA (Seville, Spain).