Dosimetry for proton irradiation of 3D cell models at ultra-high dose rate

G. Milluzzo[1], P. Chaudhary[1,2], H. Ahmed[1], D. Doria[3], James Green[4], Sean McCallum[1], A. McIlvenny[1], A. McMurray[1], Boris Odlozilik[1], K. Prise[2], M. Borghesi[1]

1) Centre for Plasma Physics, Queen's University Belfast, Belfast, BT7 1NN, UK
2) Centre for Cancer Research & Cell Biology, Queen's University Belfast, BT9 7AE, UK.
3) National Institute for Physics and Nuclear Engineering, ELI-NP, Str. Reactorului, nr. 30, P.O.Box MG-6, Bucharest-Magurele, Romania
4) Central Laser Facility, STFC Rutherford Appleton Laboratory, Didcot OX11 0QX, U.K

Charged particle-based radiotherapy is currently one of the most accurate technique for the treatment of radioresistant tumours and it is employed in an increasing number of centres worldwide using conventional RF accelerators. Moreover, the acceleration of ions and protons by employing the alternative acceleration mechanism based on high-power laser-matter interaction is nowadays attracting significant interest showing the possibility to achieve unexplored radiobiological regimes with short-pulse durations and extremely high dose-rates [1]. In this framework, one of the main aims of the A-SAIL project involving many UK investigators, is the study of the biological effects, in cell and tissue models, of the short bursts of ions produced by laser-driven sources and many experiments with laser-driven protons around 10-15 MeV have been performed so far using the VULCAN laser system at Rutherford Appleton Laboratory as reported in [2]. So far proton energies used for cell irradiation were limited to 10-15 MeV level due to the insufficient flux at higher energies needed to irradiate the samples with 1 Gy dose-lavel. An experimental campaign was recently carried out with the PW VULCAN laser system and thanks to improvements in laser-matter interactions, proton bunches with an energy around 35 MeV were used to irradiate biological samples with a dose range between 1 Gy and 5 Gy. Protons were accelerated from the interaction of the PW VULCAN laser with a 15 um Au foil target and energetically dispersed using a 1 T magnet. Biological samples, plated as 2D monolayers on a dish, were placed inside an isolated vertical holder in air after a thin kapton window. The sufficient dose achieved with high-energy protons allowed to irradiate in-vitro 3D model cells, requiring high energy to assure a uniform dose deposited in the whole 3d cell thickness. 3D neurosphere cultures result very relevant and interesting for radiobiological studies since they allow miming the tumour architecture, providing a snapshot of the tumour microenvironment. In particular, 3D Glioblastoma (GBM) neurospheres, which are more radioresistant than cells grown in 2D monolayer due to some hypoxic regions in their interior, were irradiated in the experiment. Indeed, the extremely high-dose rate of laser-accelerated protons can also have a relevant role on the biological damage especially on hypoxic regions leading to an enhanced response if compared with the 2D cell models [3]. The 3D GBM neurospheres were immersed in the cell culture medium and placed at the bottom of a thin walled polypropylene tube with an internal diameter of 2-3 mm as it is shown in figure 1. The dose released on the cells was evaluated by placing EBT3 RCF in front and behind the tube. The depth-dose profile along the 2 mm thick tube where the 3D cells were deposited was also evaluated with an RCF stack phantom. Moreover, the dose as well as the energy distribution at the cell plane and in depth were predicted modelling the experimental setup with the Geant4 Monte Carlo toolkit. Details on the experimental setup, the dosimetry arrangement and the preliminary the outcomes of the experiment will be presented in this contribution.

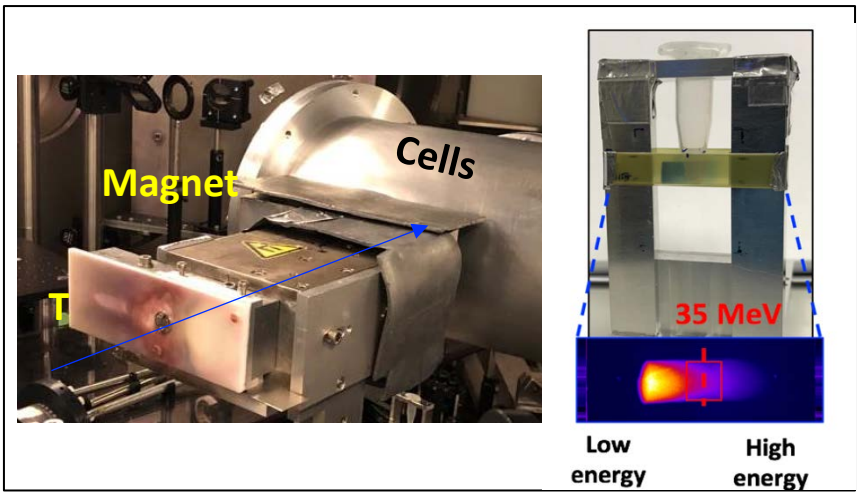

Figure 1. Left. Picture of the experimental setup showing the Target position (T), the magnet and the position of the cells in air. Right. 3D neurpsheres placed within the eppendorf tube and irradiated with 35 MeV protons and RCF dose measurement.

[1] P. Wilson, *et al.*, Revisiting the ultra-high dose rate effect: implications for charged particle radiotherapy using protons and light ions,The British Journal of Radiology, **85** (2012), e933–e939.
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[3] A. Mohyeldin *et al*, Cell Stem Cell. **7**, 150 (2010)