WS101-13: Cells response under high dose rate and multi-bunch irradiation

E. Bayart[1], A. Flacco[1], O. Delmas[1], L. Pommarel[1], D. Levy[1,2], M. Cavallone[1], F. Megnin-Chanet[3], E. Deutsch[4], V. Malka[1,2]

[1]Laboratoire d'Optique Appliquée, ENSTA-CNRS-Ecole Polytechnique, UMR7639, 91761 Institut Polytechnique de Paris, Palaiseau, France
[2]Department of Physics of Complex Systems, Weizmann Institute of Science, Rehovot 7610001, Israel
[3]Unité de Biophysique Moléculaire (INSERM Unité 350), 91405 Orsay Cedex, France
[4]Radiotherapy Department, Gustave Roussy, 94800 Villejuif, France

Radiation therapy is a cornerstone of cancer management in which ionizing radiation is used to deposit energy in the cancer tumor. The improvement of spatial dose distribution in the target volume by minimizing the dose deposited in the healthy tissues and organs have been a major concern during the last decades that is reached when using proton beams. The possibility to produce energetic protons of relevance for therapy has triggered strong interest in laser community that questions on the feasibility of laser plasma accelerators approach. In parallel of the research on the quest of high protons, the study of radiation biology is very interesting due to the unique irradiation conditions they can produce, in terms of peak current and duration of the irradiation.

We will present the implementation of a beam transport system optimized for in vitro irradiation of biological samples [1]. A set of four permanent magnet quadrupoles is used to transport and focus the beam, efficiently shaping the spectrum and providing a large and relatively uniform irradiation surface. Real time, absolutely calibrated, dosimetry is installed on the beam line, to enable shot-to-shot control of dose deposition in the irradiated volume. Results of cell sample irradiation are presented to validate the robustness of the full system. Laser-plasma-based particle accelerators are able to emit pulsed proton beams at extremely high peak dose rates (~10^9 Gy/s) during several nanoseconds with a high repetition rate in the range of (0.1 to 10 Hz).

The effect of such extremely high proton dose rates on highly resistant human glioblastoma cell lines, SF763 and U87-MG, was compared to conventionally accelerated protons and X-rays [2]. No significant difference was observed in DNA double strand breaks generation (γH2AX foci detection) and cells killing. The variation of the repetition rate of the proton bunches produced behavior of the radio-induced cell susceptibility in HCT116 cells only. This feature appeared to be related to the presence of the PARP1 protein and an efficient parylation process.

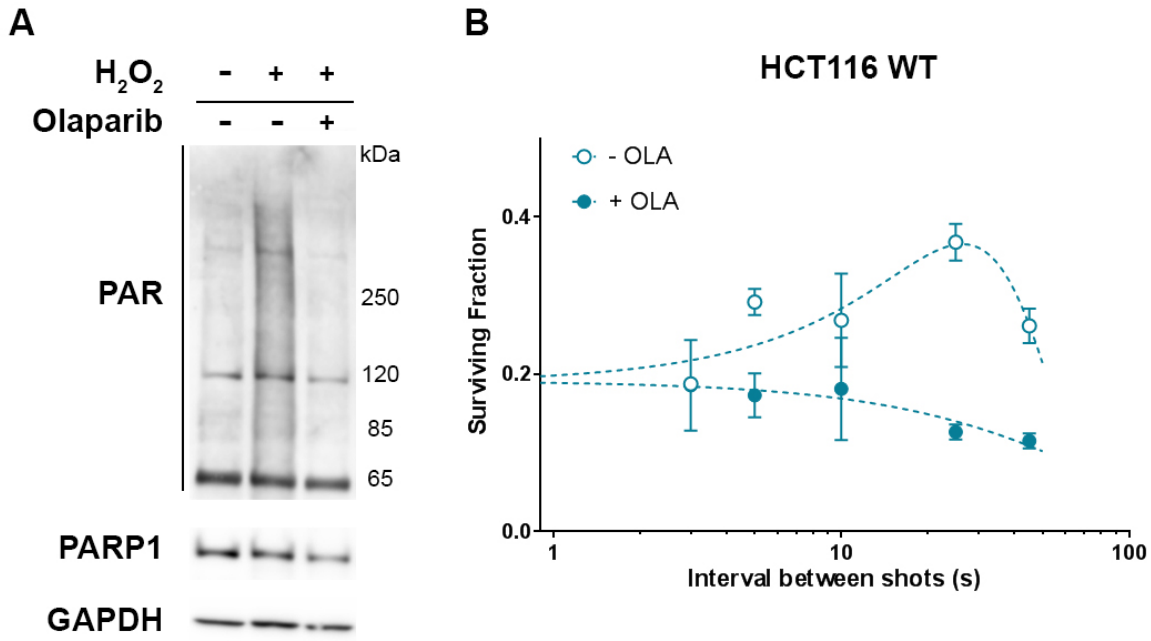

Figure 1: Effect of PARP1 inhibition on cell survival oscillation in response to the variation of the delay between LDP bunches. (A) Western Blot detection of the PARP1 protein and parylation in total protein extracts from HCT116 WT cells left untreated, treated 10 min with 1 mM hydrogen peroxide (H_2O_2) or treated one hour with 200 nM Olaparib before H_2O_2 treatment. (B) HCT116 WT cells were left untreated (black circles) or treated one hour with 200 nM Olaparib (white circles) and were then exposed to five bunches of LDP (3.5±0.77 Gy). Each data point represents the mean of three replicates obtained in two independent experiments. Comparisons of the cell survival were performed using by two way ANOVA multiple comparisons test (Tukey's multiple comparisons test).

[1] L. Pommarel, B. Vauzour, F. Mégnin-Chanet, E. Bayart, O. Delmas, F. Goudjil, C. Nauraye, V. Letellier, F. Pouzoulet, F. Schillaci, F. Romano, V. Scuderi, G. A. P. Cirrone, E. Deutsch, A. Flacco, and V. Malka, Spectral and spatial shaping of a laser-produced ion beam for radiation-biology experiments, PRAB, **20**, (2017), 032801

[2] Bayart E., Flacco A., Delmas O., Pommarel L., Levy D., Cavallone M., Megnin-Chanet F., Deutsch E., Malka V., Fast dose fractionation using ultra-short laser accelerated proton pulses can increase cancer cell mortality, which relies on functional PARP1 protein, *in preparation*