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Manon Evin¹*, Vincent Fiegel², Grégory Delpon^{1,3}, Quentin Mouchard¹, Emeline Craff², Ferid Haddad^{1,2}, Charbel Koumeir^{1,2}, Lydia Maigne⁴, Vincent Métivier¹, Vincent Potiron^{3,5}, Noël Servagent¹, Stéphane Supiot^{3,5}, Johan Vandendorre¹, Guillaume Blain¹, Sophie Chiavassa^{1,3}

¹Nantes Université, IMT Atlantique, CNRS/IN2P3, SUBATECH, F-44000 Nantes, France, ²GIP ARRONAX, Saint-Herblain, France, ³Institut de Cancérologie de l'Ouest, Saint-Herblain, France, ⁴Université Clermont Auvergne, CNRS/IN2P3, LPC, 63000 Clermont-Ferrand, France, ⁵Nantes Université, CNRS, US2B, UMR 6286, F-44000 Nantes, France

*evin@subatech.in2p3.fr

Context

The investigation of the **FLASH effect's** underlying **mechanisms** requires pulsed radiolysis studies. To date, **irradiation parameters** that induce such biological effect are improperly defined. Decreases in the **radiolytic yield of H₂O₂** at ultra-high doses rate have been reported for electrons [1] and protons [2]. This final species of water radiolysis can be used as a probe to verify hypotheses such as species recombination of tracks or oxygen depletion. To that end, multi-beam studies are relevant. Furthermore, this aspect is primordial for **translational research**, as current treatments often require multiple beams to spare surrounding healthy tissues.

➔ Does multiple beams delivery preserve the effect of UHDR on the production of the reactive oxygen specie (ROS) H₂O₂?

Material and methods

- The **ARRONAX cyclotron** in Nantes delivers protons beam up to 70 MeV, at variable doses rates (0.2 Gy/s to 60 kGy/s) and time structures (millisecond macro-pulses).
- The experimental set-up for proton **radiolysis** [2] with a sample carrier holding designed PEEK radiolysis cells, allows the irradiation of the entire volume of Ultrapure water (Ø = 12 mm, depth = 15 mm) degassed under reconstituted air within the Bragg plateau.
- The **concentration of H₂O₂** is determined by UV-visible spectrophotometry (Ghormley method, [3]).
- Orthochromic OC-1 films** [4] were positioned at the cells entrance to ensure targeting and for *in vivo* dosimetry, as shown in Fig.1. Mean and maximum relative differences between film and online dosimetry are 0.5 % and 1.6 %, respectively.

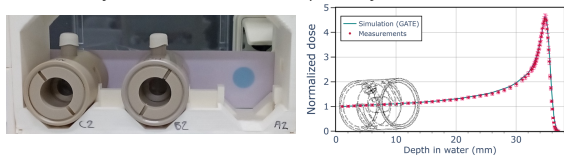


Figure 1. Left: a photograph of two radiolysis cells in front of the OC-1 films, Right: the depth of the radiolysis cell relative to the Bragg curve of 68 MeV protons, measured with a Markus Advanced (PTW) in water.

- 30 Gy** were delivered according to beam structures shown in Fig. 2. The impact of the number of the beams was evaluated in the UHDR mode at **8.6 kGy/s**, by delivering N times the same pulsed beam every 20 seconds but with a reduced duration of dt/N, with N equal to 1 (1x30 Gy), 2 (2x15 Gy), 3 (3x10 Gy), 5 (5x6 Gy) and 10 (10x3 Gy).

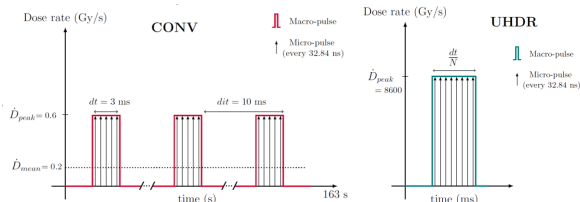


Figure 2. Beam structures used to deliver 30 Gy. For UHDR, dt=3.5 ms.

Results

Preliminary results (n=1) are presented in Fig. 3.

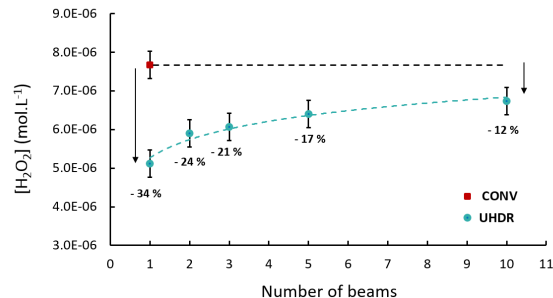


Figure 3. [H₂O₂] versus number of beams to deliver 30 Gy with protons under air.

Conclusion and perspectives

Our study investigated the impact of the number of beams on the concentration of Hydrogen Peroxide (H₂O₂) after UHDR proton irradiation:

- The decrease of the H₂O₂ concentration was **more significant with a single beam** than with multiple beams.
- The delivery of UHDR irradiations with multiple beams allows to obtain a differential effect compared to CONV irradiations but **with a lower amplitude**.
- In addition to the dose rate, the observed effect also depends on the **dose per beam** or the **total duration** of the irradiation.

Subsequent experiments will study the **time delay** between two beams to deepen this finding. Cross-experiments will be carried out with **biological models** (zebrafish embryos).

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