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Vincent Fiegel, Giovanna Rosa Fois, Guillaume Blain, Manon Evin, Quentin Mouchard, Charbel Koumeir, Noël Servagent, Craff Emeline, Mohammad Ghalei, Vincent Métivier, et al.

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# RADIOLYTIC ROS PRODUCTION MECHANISM UNDER PROTON FLASH CONDITIONS : COMBINATION OF EXPERIMENTAL AND SIMULATION INVESTIGATION

V.Fiegel and G.R.Fois, G.Blain\*, M.Evin, Q.Mouchard, C.Koumeir, N.Servagent, E.Craff, M.Ghalei, V.Métivier, F.Poirier, V.Potiron, S.Supiot, F.Haddad, G.Delpon, J.Vandenborre, L.Maigne, S.Chiavassa

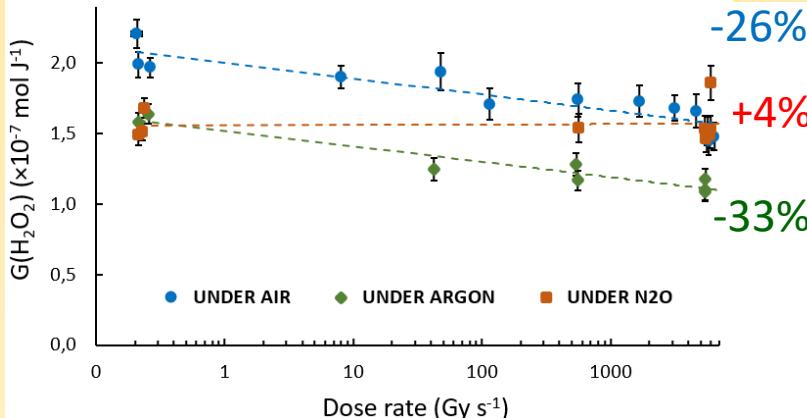
## Previous results

Using pulsed 68MeV H<sup>+</sup> beam of the radiobiological platform at ARRONAX, a strong decrease of G(H<sub>2</sub>O<sub>2</sub>) with increasing UHDR in the plateau region was shown [1]. By now, a new irradiation cell was designed to control the atmosphere. Elucidate oxygen and radical recombination roles during the radiochemistry step of pure water UHDR irradiations is now possible.

## Materials and Methods

- 68MeV H<sup>+</sup> plateau
- Doses : 10 to 80Gy, 3x replicates
- Conv 0,25Gy/s
- Single pulse UHDR 40 to 7kGy/s
- Ghormley's UV-vis H<sub>2</sub>O<sub>2</sub> titration protocol
- Pure milliQ Water 18,2MΩ.cm
- Synthetic air ( 80%N<sub>2</sub> / 20% O<sub>2</sub> )
- Saturated with pure argon (No O<sub>2</sub>)
- Saturated with pure N<sub>2</sub>O (No O<sub>2</sub>, e<sup>-</sup><sub>hyd</sub> scavenger)

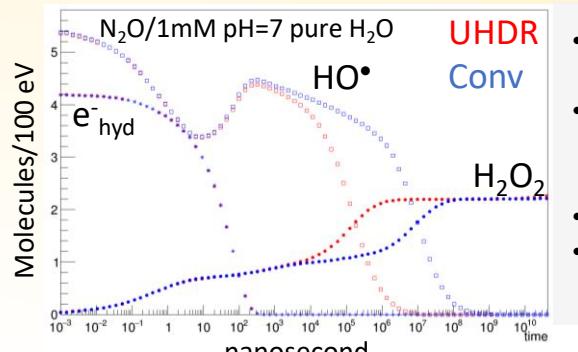
## G(H<sub>2</sub>O<sub>2</sub>) production Yield vs dose rate under 3 atmospheres : O<sub>2</sub>, No O<sub>2</sub>, e<sup>-</sup><sub>hyd</sub> scavenger



## Mechanism proposal

- UHDR boosts  $\text{HO}^{\cdot} + \text{e}_{\text{aq}}^- \rightarrow \text{HO}^-$  due to better k and diffusion
- e<sup>-</sup><sub>hyd</sub> acts like as HO<sup>·</sup> scavenger, leading to less H<sub>2</sub>O<sub>2</sub>
- In line with reduced G(HO<sup>·</sup>) under UHDR observed in Litt. [2]
- O<sub>2</sub> doesn't affect ROS reduction under UHDR

## G4-DNA simulation of UHDR radiolysis with N<sub>2</sub>O scavenger

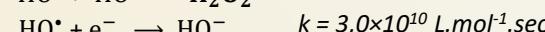


- As a first trial, H<sub>2</sub>O<sub>2</sub>, HO<sup>·</sup> and hydrated electron G-values along time are obtained until 1 minute
- Experimental H<sub>2</sub>O<sub>2</sub> trend is described by the model, with the same production yield for both UHDR and CONV.
- The good order of magnitude is calculated.
- Kinetic evolution of radicals for all conditions need to be investigated

[1] Blain et al, Radiation Research 198 (3), 318-324

[2] Kusumoto et al, RSC Advances 10:38709-14, 2020

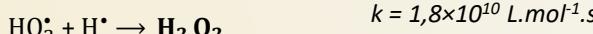
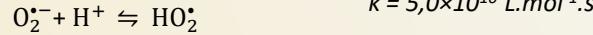
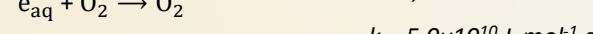
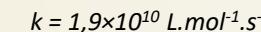
## Under Argon condition, no O<sub>2</sub> : competition



Other quick reactions with e<sup>-</sup><sub>hyd</sub> leading to H<sub>2</sub>

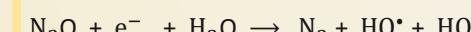
**UHDR effect**

## Under Air condition, O<sub>2</sub> adds this :



**UHDR effect**

## Under N<sub>2</sub>O condition, no O<sub>2</sub>, e<sup>-</sup><sub>hyd</sub> is scavenged



$$k = (9,1 \pm 0,2) \times 10^9 \text{ L.mol}^{-1}.\text{s}^{-1}$$

**NO UHDR effect**

## Conclusions / Outlook

- ✓ Key-role of hydrated electron in the decrease of G(H<sub>2</sub>O<sub>2</sub>) production yield observed under UHDR condition up to 7kGy/s
- ✓ No influence of dissolved O<sub>2</sub> on the specific radical recombination process under UHDR
  - ROS production mechanism under UHDR seems to be driven by radicals diffusion and recombination
- ☐ Direct hydrated electron detection using time resolved UV-Vis absorption is in progress, allowing access to kinetic information to be used as input for modeling and mechanism studies
- ☐ G4-DNA modeling improvement started to reach a better experiment-model fit