Photo-activation therapy with high-Z nanoparticles: modelling at a micrometer level and experimental comparison

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International Conference on Translational Research in Radio-Oncology and Physics for Health in Europe (ICTR-PHE 2012, Genève)

Présentation orale:

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Purpose: An innovative approach using X-rays interactions with heavy elements seems to open a promising way of treatment for resistant cancers, such as high-grade gliomas. Such a technique is developed at the medical beam line of ESRF using monochromatic X-rays in the 50-100 keV range for the treatment of brain tumors [1,2]. The use of gold nanoparticles to treat mice bearing subcutaneous tumors led to encouraging results [3]. However, the physical processes and biological impact of the photon activation of nanoparticles are not well understood. The experimental results cannot be explained from macroscopic dose calculations [4,5].

The aim of this study was to evaluate, at the cellular level, the dose enhancement in presence of nanoparticles and the properties of the secondary electrons production using the Monte Carlo transport code PENELOPE.

Material and Method: At first, upstream studies were done around the behavior of gadolinium and gold nanoparticles (GdNP and AuNP) under irradiation. The mean range, yields and spectra of electrons produced from the interactions of X-rays with a AuNP and a GdNP were calculated for diameters of 2 to 100 nm when irradiated with monochromatic photons from 25 keV to 2 MeV. The dose enhancement was calculated in water at one micrometer around the AuNP.

On another hand, dose calculations were done in a cellular geometry containing gadolinium-water mixture in order to compare with experimentations realized on the ID17 beamline of ESRF. Clonogenic assays have been performed on F98 cells to measure the "Sensitizer Enhancement Ratio" for 4 Gy of irradiation (SER_{4Gy}) with the presence of GdNP, for several irradiation energies (25 to 80 keV).

Results: An increase of electron production up to a factor 1000 is observed in presence of a AuNP. More electrons are produced from an AuNP than a GdNP because the gold is denser. The mean energy of the produced electrons increases with the beam energy, except after the K-edge of each element because of an enhancement of interactions with deeper atomic shells. The mean energy is lower after the gadolinium K-edge and provides a more local dose deposition compared to gold.

An auto-absorption of low energy electrons for NP with larger diameters is also observed.

From the comparison of the calculated dose enhancement factor (DEF) in the cellular geometry with the measured SER_{4Gy}, encouraging results are obtained (see the figure) but in-depth studies are still required. The electron spectra incoming on nucleus were also studied and provide interesting correlations.

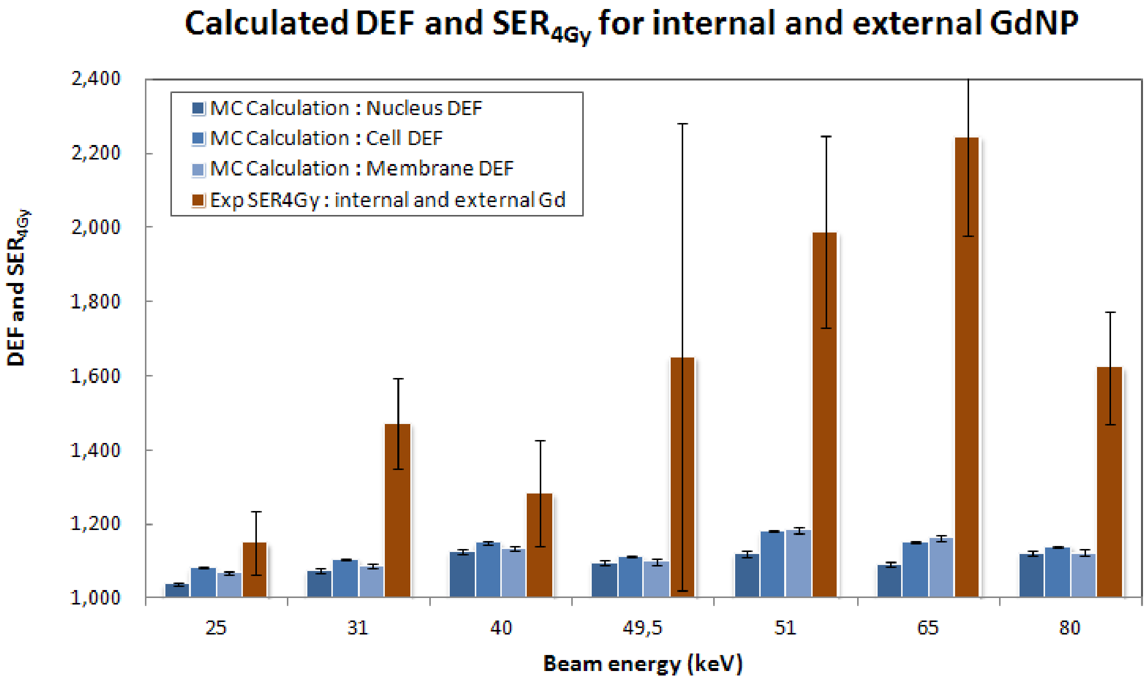

Figure : Comparison of the calculated Dose Enhancement Factor into a cell and the measured SER for six differents energies and two differents localisation of GdNP

Conclusions: In the near future, we plan to calculate the dose in a cellular geometry considering multiple nanoparticles instead of gadolinium-water mixture, and then considering many cells. With these results we aim to take into account the influence of multiple structures for a more realistic model and try to understand the current differences observed between the SER_{4Gy} and the DEF. Better physical observables are also required to explain the tendency of the biological response as a function of beam energy.

1. Adam, J. F., H. Elleaume, et al. (2003).Int J Radiat Oncol Biol Phys **57**(5): 1413-26.
2. Adam, J. F., A. Joubert, et al. (2006). Int J Radiat Oncol Biol Phys **64**(2): 603-11.
3. Hainfeld, J. F., D. N. Slatkin, et al. (2004) Phys Med Biol 49(18): N309-15.
4. Cho, S. H., et al. (2005). Phys. Med. Biol. 50 N163–73
5. Zhang, S.X., et al. (2009). Biomed Microdevices 11:925–933