Modeling and experimental validation of radiation-cellular media interactions in radiotherapy by photon activation of heavy elements

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Context

- Context : some resistant tumors such as high-grade gliomas are still incurable with the current treatments and require a more specific targeting of cancer cells.
- Principle: Radiotherapy by photon activation of heavy elements is a combination of a high-Z elements (I, Au, Gd) injection into the tumour with an irradiation of low energy X-ray beam allowing to increase the localised deposited dose.
- Promising treatment: *in vivo* studies brought to light a very important survival enhancement factor in the presence of gold nanoparticles (AuNP) [1, 2].
- Limitation: physical processes and radiobiological damages caused by these heavy elements are not well understood and cannot be explained from macroscopic dose calculations [3, 4].

Objectives

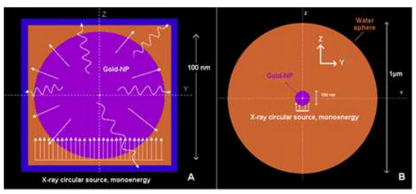
- Monte-Carlo modelling of X-ray interactions with media composed of gold or gadolinium nanoparticles (NP) in a micrometer scale.
  - Characterisation of electron spectra emitted from a NP.
  - Study of dose with a cellular geometry in order to compare with experiments.
- *In vitro* experiments with NP provided at ESRF to optimize the radiosensitivity according to different parameters.
- Comparison of the results in order to correlate some physical phenomena with a biological impact.

Simulation results

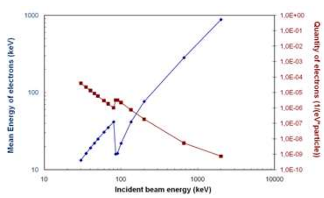
Characterisation of the effect of AuNP as a function of NP radius and beam energy :

A) Geometry used for the study of secondary electrons (orange virtual detector) and photons (blue virtual detector) emitted from the irradiated water or gold sphere.

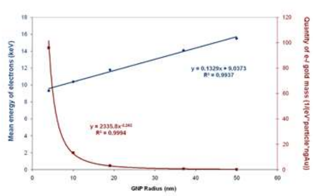
B) Geometry used for the study of dose. One AuNP in the centre of a 1 µm water sphere.



- Study of electrons spectra:



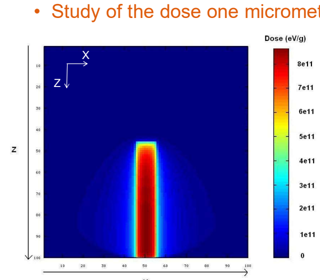
Mean energy and quantity of emitted electrons as a function of beam energy with a 100 nm diameter AuNP.



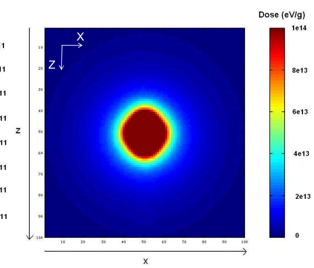
Mean energy and quantity of emitted electrons as a function of gold-NP radius with a 85 keV X-ray beam.

→ Following theses results, an optimization of beam energy and AuNP radius can be provided according to NP targeting.

- Study of the dose one micrometer around the AuNP :

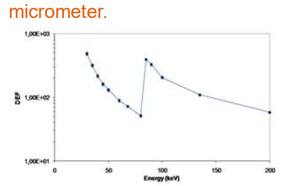


Deposed dose in the XZ plan without AuNP

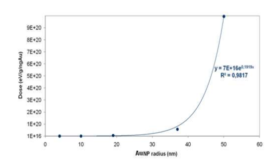


Deposed dose in the XZ plan with a AuNP (R=50nm)

→ The AuNP acts as a quasi-isotropic diffuser of the dose and increases it until a factor 1000 in a scale lower than the micrometer.



Ratio of the mean deposed dose in the water sphere with AuNP and without (DEF) as a function of energy



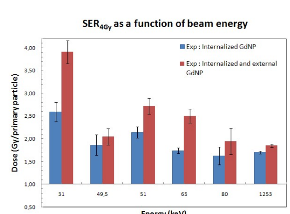
Mean deposed dose in the water sphere as a function of AuNP radius

Experimental results and modelling correlation

In vitro experiments released on the medical beam line of ESRF (ID17):

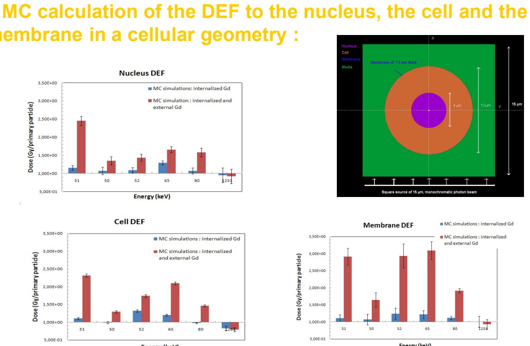
Study on rats gliomas cell line F98 according to the energy of irradiation, the dose and the internalization of NP in cells. First campaign of experiments with 2 nm diameter AuNP was done in December 2010.

- Second campaign of experiments with 1 nm GdNP (May 2011) :
- Beam energy studied : 31, 49.5, 51, 65, 80 and 1253 keV (Co60).
- 3 Conditions : - Control
- Internalized GdNP in cells ([Gd] = 0.3 mg/ml)
- Combination of internalized and external GdNP ([Gd] = 1.8 mg/ml).



Result of Survival Enhancement Ratio for a 4 Gy dose (SER_{4Gy}) in the presence of GdNP or not as a function of beam energy

MC calculation of the DEF to the nucleus, the cell and the membrane in a cellular geometry :



Dose Enhancement Factor calculated with MC code Penelope for conditions similar to the experiments

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