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

R. Delorme, Mathieu Agelou, H el ene Elleaume, Florence Taupin, M elanie
Flaender, Christophe Champion

► To cite this version:

R. Delorme, Mathieu Agelou, H el ene Elleaume, Florence Taupin, M elanie Flaender, et al.. Modeling and experimental validation of radiation-cellular media interactions in radiotherapy by photon activation of heavy elements. 7th International Symposium on Physical, Molecular, Cellular and Medical Aspects of Auger Processes, Aug 2011, J ulich, Germany. cea-02562503

HAL Id: cea-02562503

<https://cea.hal.science/cea-02562503v1>

Submitted on 5 May 2020

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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].

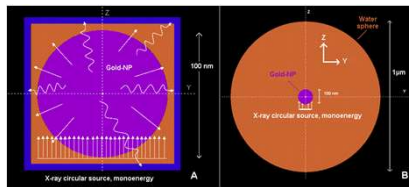
Objectives

- 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.

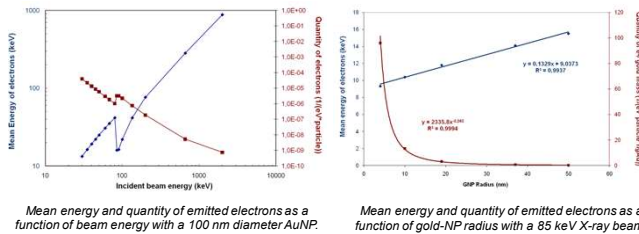
Simulation results

- 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  m water sphere.



- Study of electrons spectra:

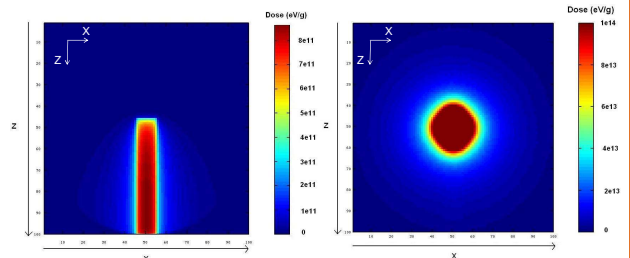


Mean energy and quantity of emitted electrons as a function of beam energy with a 100 nm diameter AuNP.

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

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

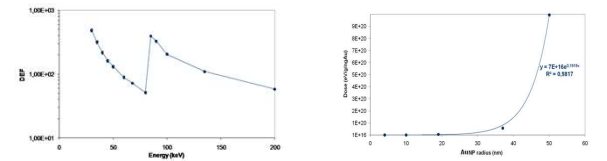
- Study of the dose one micrometer around the AuNP :



Deposited dose in the XZ plan without AuNP

Deposited dose in the XZ plan with 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 deposited dose in the water sphere with AuNP and without (DEF) as a function of energy

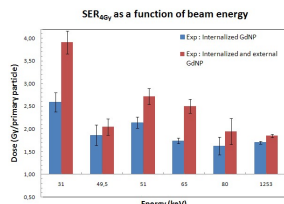
Mean deposited dose in the water sphere as a function of AuNP radius

Experimental results and modelling correlation

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

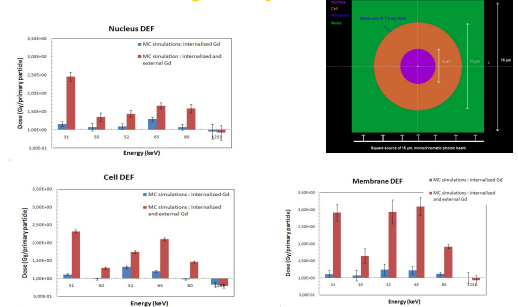
Study on rats gliomas cell line F98 according to the energy of irradiation, the dose and the internalization of NP in cells. First campaign of experiments with 2 nm diameter AuNP was done in December 2010.

- 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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