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

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Summary

• Context and objectives
• Simulation results
• Experimental comparison
• Conclusions and Prospects
• **Photo-activation therapy**: combines low energy X-ray beams with high-Z elements (iodine, gold, gadolinium, platinum...).

**Ratio of X-ray mass energy-absorption coefficients Gd or Au / water (NIST)**

![Graph showing the ratio of X-ray mass energy-absorption coefficients between Gd or Au and water across different X-ray energies (MeV).]
• Technique started with iodinated contrast agents (Norman et al, Radiology (1978)).


• Cho et al. (Phys. Med. Biol. (2005)): Monte Carlo calculation of tumour dose enhancement with homogeneous gold up to a factor of 2.1 with Hainfeld’s conditions.

• Such radiobiological enhancement not explained by macroscopic physical model. Modelling at the lower scale.
Objectives, Monte Carlo simulations:

- **Gold and gadolinium nanoparticles** (AuNP & GdNP): dose and electron spectra emitted from NP.
- **Unicellular geometry with gadolinium**: comparison with experiments made at ESRF (*European Synchrotron Radiation Facility*).
- **Challenge**: find an appropriate physical observable to correlate with biological data.
Electron range in water (Penelope tables)

- $\approx 2.5 \mu m \rightarrow$ nucleus scale
- $\approx 40 \mu m \rightarrow$ cellular scale
- $\approx 140 \mu m \rightarrow$ tissue
- $\approx 50 \text{ nm} \rightarrow$ macromolecules
• **Penelope**: Monte Carlo code adapted for low energy electron and photon transport (lower limit of electron transport: 100 eV).

• First study: Dose deposition and spectra of secondary particles emitted from a single AuNP and GdNP.
Simulation results

Spectra from GdNP

- X-ray beam energy: 52 keV. Diameter of GdNP: 10 nm.
- Gd K-edge: 50.2 keV.
- Au K-edge: 80.7 keV.

- Relaxation cascade and X-ray interaction with shell and sub-shell well described in Penelope.
Electron spectra emitted from a 10 nm diameter AuNP and GdNP as a function of beam energy.

- **Quantity**
  
- More electrons produced in Gold except after the sharp Gadolinium K-edge.

- **Mean energy**
  
- Mean energy lower after the Gd K-edge, provides a more “local” dose deposition.
Dose deposition at 500nm around a AuNP of 100nm with a 85 keV X-ray beam.

- In water
- With a centred AuNP

AuNP: Increase of the dose up to a factor 100 with quasi-isotropic diffusion.
  
  ▪ Beam energies: 31, 49.5, 51, 65, 80 (synchrotron) and 1253 keV (Co60).
  
  ▪ 5 experimental conditions:
    
    - Control
    - Internal GdNP
    - External GdNP
    - Magnevist (cf. F. Taupin presentation on Friday)
    - Internal & external GdNP

▪ Concentrations:
  
  » Internal Gd: 0.6 mg/mL
  » External Gd: 1.6 mg/mL (cf. F. Taupin presentation on Friday)
Simulation: Unicellular geometry. Nanoparticles substituted with homogeneous water-gadolinium mixture localized into or outside the cell with the right Gd concentration.
• Maximum DEF obtained of ~1.17 for internal and external Gd.

Experimental comparison

Dose Enhancement Factor

DEF = \frac{\text{Dose (Gd)}}{\text{Dose (water)}}

- Experimental SER much higher (up to 2.25 for 65 keV).

\( \text{SER}_{4\text{Gy}} = \frac{\text{Survival at 4Gy (Gd)}}{\text{Survival at 4Gy (control)}} \)
• Normalization at 65 keV to compare the tendency between the Nucleus DEF and SER$_{4 Gy}$.

• Model and observable not well adapted for comparison with SER.

• Remarks:
  - Limited size of external volume.
  - Biological effects not limited to physical dose.
Experimental comparison
Electron spectra incoming on nucleus

- Comparison of electron spectra incoming on the nucleus for all energies and conditions.

- Normalized at 65 keV: Good correlation obtained.
Conclusions and Prospect

• Conclusions :
  - Nanoparticle model : Study of secondary particles emitted under irradiation for different beam energies and comparison Gd/Au.
  - Unicellular model : calculation of DEF and electron spectra incoming on the nucleus for different conditions.
  - Comparison with experimental data : encouraging results but the model needs to be improved.
  - Separate intrinsic biological effects and physical effects.

• Prospects :
  - Model nanostructures in cell and multicellular geometries with Geant4.
  - Access to more detailed track information's with Geant4 : provide other observables for experimental comparison.
• Supervisors:
  - Mathieu AGELOU
  - Christophe CHAMPION
  - Hélène ELLEAUME

• Coworkers:
  - Florence TAUPIN
  - Mélanie FLAENDERS
  - Jean-Luc RAVANAT

Thank You for your attention
Study of the size of external volume

- Study of the increase of the size of external volume for internal and external Gd condition. The X-ray beam size is equal to the external volume.
Electron spectra incoming on nucleus

**Quantity of excedant electrons incoming on nucleus (/control)**

- **Beam energy (keV)**
  - 25
  - 31
  - 35
  - 40
  - 50
  - 52
  - 58
  - 65
  - 80
  - 120
  - 1250

- **Quantity of excedant electrons (meV/keV)**
  - 1.0E+02
  - 1.0E+03
  - 1.0E+04
  - 1.0E+05

**Mean energy of excedant electrons (/control) incoming on nucleus**

- **Beam energy (keV)**
  - 25
  - 31
  - 35
  - 40
  - 50
  - 52
  - 58
  - 65
  - 80
  - 120
  - 1250

- **Mean energy of excedant electrons (keV)**
  - 10.000
  - 100.00
DEF 1µm around 1 NP

- **Gd properties:**
  - K-edge: 50.2 keV, Z: 64, density: 7.9 g/cm³
- **Au properties:**
  - K-edge: 80.7 keV, Z: 79, density: 19.3 g/cm³

- 1µm dose deposition of particles emitted from a AuNP as a function of energy and diameter: