Infrared study of the biochemical effects in glioma cells induced by x-rays and Gd nanoparticles: first studies at SESAME synchrotron (Jordan)

I. Yousef 1,2, O. Seksek 3, J. Sulé-Suso 4, S. Gil 5, Y. Prezado 3 and I. Martínez-Rovira 3,6

1 (SESAME Synchrotron, Jordan); 2 (ALBA Synchrotron, Spain); 3 (Laboratoire d’Imagerie et Modélisation en Neurobiologie et Cancérologie, CNRS, France); 4 (Keele University, UK); 5 (Hospital Parc Taulí, Spain); 6 (Universitat Autònoma de Barcelona, Spain)

E-mail: immamartinez@gmail.com

One strategy to improve the clinical outcome of radiotherapy is to use nanoparticles (NP) as radiosensitizers. Along this line, numerous studies have shown the enhanced effectiveness of tumor cell killing when NP are associated to irradiation. However, the (physical and biochemical) mechanisms of action are not clear yet. Within this framework, vibrational spectroscopy (FTIR) was used to investigate the biochemical changes in F98 glioma cells induced by x-ray irradiations combined with Gd nanoparticles.

Introduction: Radiotherapy and nanoparticles

Radiotherapy (RT)
Main modality for cancer treatment. Limitation: high morbidity of surrounding healthy tissue, specially in the case of radiosensitive tumours (gliomas). New approaches are being explored to overcome its limitations.

Nanoparticles (NP)
The use with high-Z NP as potential tumour selective radiosensitizers is a recent breakthrough in RT [1]. Many biological studies have shown a significant gain in tumour control when NP are used in combination with RT [1-3].

The mechanisms of action are not clear yet. The radiosensitization effect of NP has not been only attributed to physical effects (local dose enhancement), but also to some biochemical processes induced by the NP.

Objective of this work:
Use infrared microspectroscopy to get deeper insights into the mechanisms underlying the amplification of radiation effects.

Materials & Methods

Experimental setup
F98 glioma rat cell line
AguIX nanoparticles 1 mM concentration
X-ray irradiator Doses: 0 to 20 Gy

Fourier Transform Infrared Microspectroscopy (FTIR)

- Vibrational molecular technique that has the potential to provide biochemical information of the cell on a microscopic scale, as well as functional information on the cell cycle, cell proliferation and cell death modes [6-7].
- Global infrared source at SESAME synchrotron (Jordan).
- Transmission mode (CaF2).
- Aperture size: 20 μm x 20 μm.
- At 0 and 24 hours post-irradiation.
- Data analysis performed by Principal Component Analysis (PCA): unsupervised statistical method for finding patterns in data of high dimensions.

Results & Discussion

Effect of NP (without RT)

PCA

- Main changes in phosphodiester vibrations of DNA and protein secondary structures.
- Possible correlation with changes in the cell cycle (cell arrest at radiosensitive phases) in the presence of NP [8].

Effect of NP (with RT)

PCA

- Decrease in intensity and changes in the position of phosphodiester peaks, which has been reported to indicate chromatin fragmentation as a result of radiation damage [9,10]. This damage is increased in the presence of NP (and dose).
- The conformational transition from α-helix to β-sheet results in the shift of Amide I vibration to lower frequency as a possible consequence of the processes leading to cell death [7,9].

Lipids region, 5 Gy

- Changes in relative intensity of the CH2/CH3 bands, indicating phospholipid membrane changes following oxidation or increased lipid metabolism due to cell death [12,13].

This results provide the basis to understand the biochemical effects induced by the Gd NP in the main biomolecules [14].

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