Magnetic nanoparticles for theranostics applications

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Introduction
In the field of radiation therapy, high-Z nanoparticles (NPs) have been studied for their ability to increase tumor cell death upon irradiation. The mechanism(s) responsible for the radiosensitization effect remains poorly understood and mainly focused on the physical phenomenon. Recent studies suggest the role of some biochemical mechanisms on the observed radiosensitization effect. A correlation has been made between the inhibition of the detoxification enzyme in GNP-treated cells and the magnitude of the radiosensitization effect. Given these elements, we were interested to study if such inhibition behavior could be demonstrated for other kinds of NPs. Because of their biocompatibility and superparamagnetic properties, iron oxide nanoparticles (IONPs) were selected.

In vitro test
- No major cytotoxicity was observed at 10 to 200 μg of Fe/mL of 7nm IONPs PEG5000 (MTT test)
- Cellular iron content quantification (Table 1)

<table>
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<tr>
<th>Incubation time (hours)</th>
<th>Internalization (pg of Fe/cell)</th>
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<tr>
<td>6h</td>
<td>0.8 ± 0.1</td>
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<tr>
<td>24h</td>
<td>1.6 ± 0.4</td>
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<tr>
<td>48h</td>
<td>0.25 ± 0.03</td>
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Results

Cell viability was determined by MTT assay. A549 cells treated with an increasing concentration of IONPs.

Iron content in A549 was determined by Perl’s Prussian blue colorimetric assay at 6h, 24h; 48h for A549 cell line.

Table 1. Cellular iron content quantified by Perl’s Prussian blue stain method.

Evaluation of the activity of the detoxification enzyme for cells incubated with IONPs:
- Inhibition of 26% of detoxification enzyme in the presence of IONPs

Discussion
Iron oxide nanoparticles are well known in MRI applications but less in irradiation fields. This study aims to demonstrate the possible use of IONPs as a theragnostic agent. First, the evaluation of the activity of the detoxification enzyme of cells incubated with IONPs was determined and an inhibition 26% was shown after 24h of preincubation with IONPs. To attest that such inhibition can give rise to a radiosensitization effect, A549 cells were irradiated with X-ray. IONPs showed a radiosensitizing effect at 2 Gy to induce a 12% increase in cell death in IONPs treated cells compared to untreated cells. Superparamagnetic properties of PEGylated iron oxide nanoparticles were evaluated by recording relaxometric parameters and phantom MR images. In vivo Magnetic resonance imaging (MRI) experiments demonstrated circulation times exceeding 7 hours by observing the signal of the cardiac left ventricle.

Methods

X-ray irradiation
- The activity of the detoxification enzyme for A459 cell line incubated with and without 50 μg of Fe/mL of IONPs for 24h was evaluated.

Biodistribution
- MRI probe evidenced by: The monitoring of signal of the cardiac left ventricle.
- Persistent signal after 7h highlighting the long-time circulation.

Conclusion
Even though these nanoparticles are not defined as high-Z nano-objects, radiosensitizing properties were demonstrated by the decrease in the survival fraction and an AF < 0.12. Radiosensitisation seems to be related to the inhibition of detoxification enzyme in presence of IONPs. The evaluation of the biodistribution was then studied in mouse model. These elements make them good candidates as theragnostic agents.

References