Internalization of Iron Nanoparticles by Macrophages for the Improvement of Glioma Treatment

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Keywords: macrophages, nanoparticles, synchrotron, radiotherapy, blood-brain barrier, cell-carriers

Rationale: An alternative approach for the improvement of radiotherapy consists in increasing differentially the radiation dose between tumors and normal tissues using nanoparticles (NPs) that have been beforehand internalized into the tumor. These high-Z NPs can be photo-activated by monochromatic synchrotron X-rays, leading to a local dose enhancement delivered to the neighboring tumor cells. In order to carry the NPs into the tumor center, macrophages are currently under study for their phagocytosis and diapedesis abilities. In this study, we characterized J774A.1 macrophages’ internalization kinetics and subcellular distribution of two types of iron NPs.

Materials and Methods: Three aspects of internalization were examined: first, the location of internalized NPs in J774A.1 macrophages following a 24h incubation with iron NPs was determined by optical microscopy after cell slicing. Subsequently, the iron intake after a 24h incubation with NPs was characterized using ICP-MS. The resulting cell viability was measured by Trypan Blue staining. Finally, the internalization dynamics were studied by absorbance measurements for 24 hours using a plate reader.

Results: J774A.1 macrophages are able to endocytose NPs: we measured ~61±10 pg of internalized iron per macrophage (initial iron concentration: 0.3 mg/mL in culture medium. The cell survival was higher than 80% for all tested conditions (initial iron concentrations in culture medium between 0 and 2.4 mg/mL). Finally, we determined that the internalization kinetics for J774A.1 had a typical saturation time of one hour. These results are currently used in Monte Carlo simulations to model photoactivation processes.

Conclusion: Macrophages seem to be promising vectors for NPs, being able to endocytose and retain them in their cytoplasm. Our following studies will attempt to shed light on their other potential abilities as “Trojan Horses”.