

accuracy derived from the experiment was: DD (5%) - 83.4% and 68% pixels passing, DTA (3mm) - 99.0% and 96.7%, gamma parameter (for DD (3%), DTA (3mm)) - 90% and 75.5% respectively for AAA and PBC algorithms. The comparison between studied parameters DD, DTA and γ for both algorithms implicated AAA as an appropriate approach in radiotherapy treatment planning.

Keywords: Radiotherapy planning algorithms, radiology, medical physics.

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Nuclear fragmentation in protontherapy

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The effect of nuclear fragmentation in the passage of 180MeV protons through the human body tissue is discussed. Prostate cancer protontherapy with these intermediate-energy protons is discussed in light of model calculation.

Keywords: Nuclear fragmentation, protontherapy, prostate cancer

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Internalization of iron nanoparticles by macrophages for the improvement of glioma treatment

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Rationale: An alternative approach for the improvement of radiotherapy consists in increasing differentially the radiation dose between tumors and healthy 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[1]. This

enhancement is due to secondary and Auger electrons expelled from the NPs by the radiations. In order to carry the NPs into the tumor center, macrophages are currently under study for their phagocytosis and diapedesis abilities[2] (*cf.* Figure adapted from [3] and [4]). In this study we characterized J774A.1 macrophages' internalization kinetics and subcellular distribution of iron NPs and compared them to the internalization abilities of the F98 glioblastoma cell line.

Materials and Methods: Three aspects of internalization were examined: first, the *location of internalized NPs* in J774A.1 macrophages and F98 glioblastoma cells following a 24h incubation with iron NPs (0.3 mg/mL in the cell culture medium) was determined by optical microscopy after cell slicing. Subsequently, the *iron intake* after a 24h incubation with NPs (0.3 mg/mL and 0.06 mg/mL in the cell culture medium) was characterized for the two types of cells using ICP-MS. Finally, the *internalization dynamics* were studied by live phase-contrast microscopy imaging for 11 hours and by absorbance measurements for 24 hours using a plate reader.

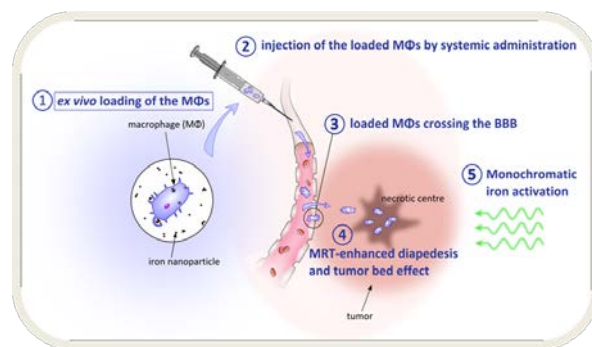
Results: F98 tumor cells and J774A.1 macrophages are both able to endocytose NPs: we measured $\sim 61 \pm 10$ pg of internalized iron per macrophage compared with $\sim 33 \pm 5$ pg per F98 cell (initial iron concentration: 0.3 mg/mL in culture medium). F98 internalizing NPs for 10 hours showed stress signs during the first minutes after the NPs injection, but behaved like F98 control cells during the rest of the experiment. Finally, we determined that the internalization kinetics for J774A.1 had a typical saturation time of one hour.

Conclusion: Macrophages seem to be promising vectors for NPs, being able to endocytose and retain in their cytoplasm larger quantities of NPs than tumor cells. Our following studies will attempt to shed light on their other potential abilities as "Trojan Horses".

Keywords: radiotherapy; nanoparticles; cell-carriers

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First clinical application of a prompt gamma based *in vivo* proton range verification using a knife-edge slit camera

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