Metallated nanoparticles as dual-imaging theranostic system in a glioblastoma mouse model

Nanosystem as theranostic

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Abstract

Introduction: Glioblastoma multiforme (GBM) is considered the most lethal of the malignant primary brain tumors [1]. In fact, even after aggressive treatment, survival rates are approximately 12-15 months after diagnosis [2]. Recently, nanosystems have become promising candidates for GBM diagnosis and treatment, due to their exceptional magnetic properties, biocompatibility and blood brain barrier (BBB) penetrability [3]. In our previous investigations, metallated doped conjugated polymer nanoparticles (CPNs) (conjugated with fluorescent polymer F8BT) were visualized in tumors by T2 weighted (T2W) MRI [4]. In this sense, this project aims to evaluate the biodistribution of two CPNs with different types of cores, Fe_3O_4 or $NiFe_2O_4$, in mice bearing GBM flank-tumors and control mice.

Methods: *In vitro* validation of both CPNs was performed in a phantom study with different CPNs dilutions (Fig. 1A). Afterwards, NOD-SCID mice were injected intravenously with CPNs with a Fe_3O_4 or $NiFe_2O_4$ core. CPN's biodistribution was studied by T2W magnetic resonance imaging (MRI) pharmacodynamics (Fig. 1C & D) and T2 maps (Fig. 1B) were obtained before and after the CPNs injection in a 7T system. An hour after injection, mice were sacrificed, organs were resected and studied by fluorescent imaging. Additionally, mice bearing C6-GBM flank tumors were studied by T2W MRI before and 15 minutes after intertumoral injection Fe_3O_4 or $NiFe_2O_4$ CPNs. Then, mice were sacrificed and flanks removed for fluorescence studies using a IVIS Lumina II system.

Results: We observed a higher CPNs uptake in the liver and a moderate accumulation in the renal cortex and the renal medulla as seen in T2W pharmacodynamics (Fig. 1C & D). The CNPs liver accumulation seem to be higher with Fe_3O_4 than $NiFe_2O_4$ core nanoparticles (Fig. 1C). Intratumor injection studies revealed that both CPNs can be visualized in flank tumors by T2W images, showing signal decreasing in the location where the CPNs were injected (Fig. 2A). Both CPNs were also detected in the xenograft tumors by fluorescence imaging and not observed in not injected (control) tumors (Fig. 2B).

Discussion: Overall, results suggest that both CPNs are good candidates to study whether they reach and accumulate in the tumor of an orthotopic and xenograft GBM model

Figure 1

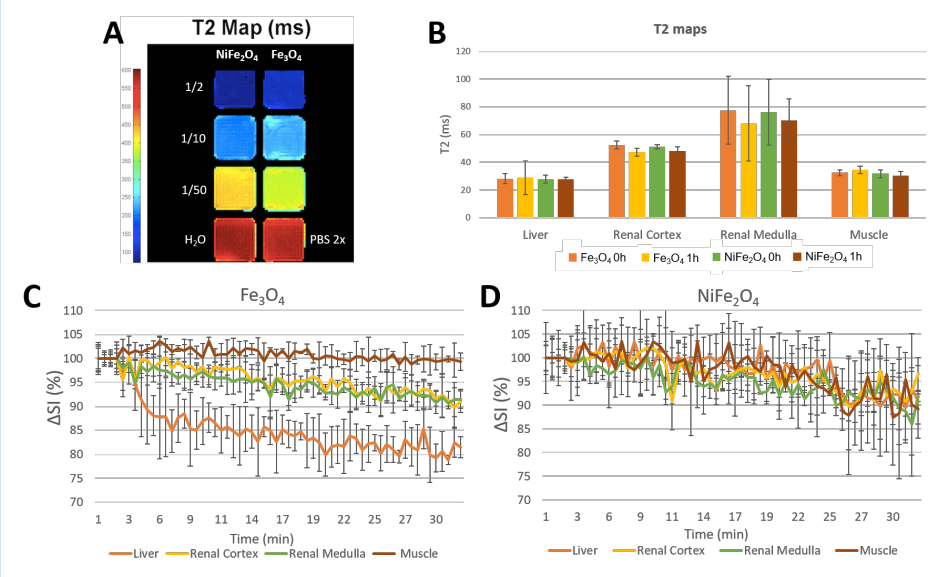

Figure 1: A) T2 map *in vitro* study of the CPNs with $NiFe_2O_4$ or Fe_3O_4 core in different dilutions and using water and PBS2x as controls. B) T2 (ms) values in different organs, obtained from T2 maps before and one hour after CPNs injection. C, D) Examples of T2W pharmacodynamic study of a mouse treated with Fe_3O_4 CPNs (C) and a mouse treated with $NiFe_2O_4$ CPNs (D).

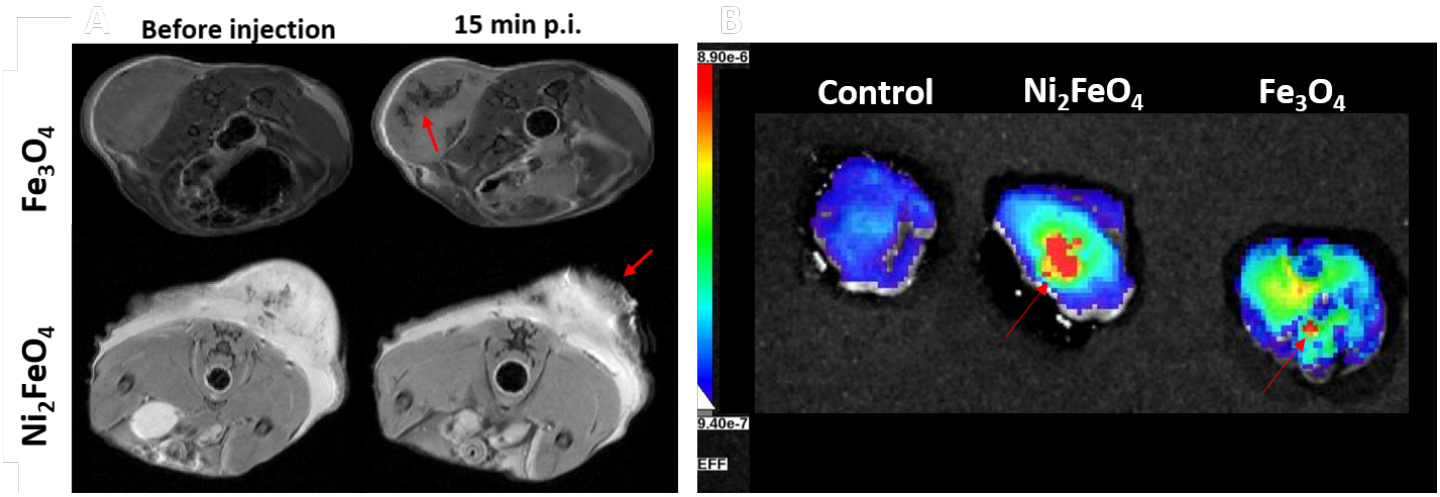

Figure 1: A) T2W images of mice bearing GBM tumor flanks before and after 15 minutes of the intratumoral injection of CPNs, Ni_2FeO_4 (first row) and Fe_3O_4 (second row). B) Fluorescence image (efficiency units) of a control tumor flank (without CPNs injection), a tumor injected with Ni_2FeO_4 and a tumor injected with Fe_3O_4. Red arrows point to CPNs accumulation.

References

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