Development of Boron-Loaded Silica Nanoparticles as Theranostic Agents for ^{19}F MRI and BNCT in Melanoma

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Melanoma is one of the most aggressive cancers, notorious for its resistance to conventional therapies and poor prognosis in advanced stages [1]. **B**oron **N**eutron **C**apture **T**herapy (BNCT) represents a promising approach for this radioresistant cancer. This therapy involves the administration of molecules containing the ^{10}B isotope. This isotope captures irradiated neutrons and releases short-range ionizing radiation, selectively damaging cancer cells that have previously accumulated the boron compound. However, the clinical implementation of BNCT faces major challenges, particularly the development of efficient boron delivery systems that can reach sufficient intratumoral concentrations, as well as the need for reliable imaging methods to monitor boron biodistribution in real time [2].

To address these challenges, we designed a nanoplatform based on mesoporous silica nanoparticles (NPs) engineered with a core–shell structure encapsulating perfluoro-15-crown-5-ether (PFCE), which provides a strong and quantifiable ^{19}F MRI signal. NPs were also designed for BNCT through their functionalization with a novel borocaptate (BSH) modified organosilane synthesized in our laboratory. Surface functionalization was further optimized with silane-polyethylene glycol (PEG) derivatives, which improved the NPs aqueous colloidal stability.

Comprehensive physicochemical characterization confirmed the successful synthesis of the multifunctional nanoparticles. Transmission electron microscopy (TEM), dynamic light scattering (DLS), thermogravimetric analysis (TGA), and nitrogen sorption measurements established their structural integrity, size homogeneity, and surface area. ^{1}H NMR spectroscopy and Attenuated Total Reflectance Fourier-transform infrared spectroscopy (ATR-FTIR) confirmed the presence of PEG and BSH functionalities. ^{19}F NMR spectroscopy alongside inductively coupled plasma optical emission spectroscopy (ICP-OES) enabled quantification of fluorine and boron contents, with reproducible B/F ratios obtained across independent syntheses. ^{19}F MRI phantom studies also validated the strong imaging signal. *In vitro* cytotoxicity was evaluated on A375 melanoma cells and normal human dermal fibroblasts (NHDF) using MTT assays. The nanoparticles exhibited low toxicity, underscoring their suitability as theranostic agents.

To enhance their specificity, the nanoparticles will later be functionalized with RGD peptide by photochemistry. This vectorization will target integrins frequently overexpressed on cancer cells [3]. Ongoing studies aim to investigate cellular uptake pathways, nanoparticle accumulation in 2D and 3D melanoma spheroids, and subsequent *in vitro* neutron irradiation assays to validate BNCT efficacy. *In vivo* biodistribution experiments in murine models are planned to confirm the quantitative imaging-guided therapeutic potential of this platform.

In summary, this work reports the design of the first silica-based theranostic nanosystem designed for BNCT and ^{19}F MRI, offering a promising strategy for cancer treatment by enabling quantifiable intratumoral boron accumulation while minimizing side effects.

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[3] : Gu, Y.; Dong, B.; He, X.; Qiu, Z.; Zhang, J.; Zhang, M.; Liu, M.; Pang, X.; Cui, Y. The Challenges and Opportunities of αvβ3-Based Therapeutics in Cancer: From Bench to Clinical Trials. *Pharmacol. Res.* 2023, *189*.