# Development of Theranostic Silica Nanoparticles Combining Quantitative $^{19}$F MRI and Boron Neutron Capture Therapy. (BNCT)

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Melanoma is an aggressive cancer, known for its resistance to conventional therapies. Indeed, most melanoma cells exhibit radio- and chemoresistance and rapidly adapt to targeted therapies.**[1]** Boron Neutron Capture Therapy (BNCT) is a promising alternative, as it selectively destroys cancer cells through neutron irradiation of $^{10}$B accumulated in the tumor. However, due to the low intra-tumor concentration of the currently approved compounds, there is a need to develop trackable boron-based drugs that can reach higher tumoral concentrations.**[2]**

To meet these objectives, we propose a nanoplatform (NP) based on mesoporous silica nanoparticles (MSN) with a core-shell structure encapsulating a PFCE emulsion (Perfluoro crown-ether), which provides the $^{19}$F MRI quantitative signal. The NP is tailored to BNCT through its functionalization with borocaptate (BSH) modified organosilane synthesized in our laboratory. The currently optimized nanoparticles are stabilized by polyethylene glycol (PEG) coating which stabilizes the NP in physiological fluids and culture media.

Their physicochemical properties were evaluated using various characterization techniques, including dynamic light scattering (DLS), transmission electron microscopy (TEM), $^{1}$H and $^{19}$F NMR/MRI, inductively coupled plasma (ICP) analysis, and Fourier-transform infrared (FT-IR) spectroscopy. The cytotoxicity of the NP was also evaluated using MTT assays on the A375 melanoma cell line. To improve their specificity, the nanoparticles will be functionalized with a RGD peptide targeting integrins, known to be frequently overexpressed on cancer cells.**[3]** The next steps of the project also include *in vitro* studies of nanoparticle internalization pathways and accumulation in 2D and 3D melanoma (A375) and fibroblasts (HDF) cell models, followed by *in vitro* neutron irradiation tests, and *in vivo* biodistribution analysis on murine models.

In summary, this project aims to demonstrate the feasibility of using our nanoparticles for BNCT, offering a promising approach to cancer treatment with quantifiable boron intra-tumour accumulation and fewer side effects.

[1] PDQ Adult Treatment Editorial Board. PDQ Cancer Information Summaries; National Cancer Institute (US): Bethesda, MD, USA, 2002.

[2] IAEA. Advances in Boron Neutron Capture Therapy; Vienna, 2023.

[3] Gu, Y. *& al*., Pharmacol. Res. 2023, 189, 106733.