Development of theranostic nanoplatform suitable for quantitative ^{19}F MRI and tailored for Boron Neutron Capture Therapy (BNCT)

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Introduction

Radiotherapy (RT) is used in 30% to 50% of cancer treatments, often alongside chemotherapy or surgery. However, RT is not suitable for all types of cancer and can lead to short- or long-term side effects due to tissue toxicity in the irradiated area. This damage affects both cancerous and healthy tissues. **[1]** To address these limitations, alternative treatments like Boron Neutron Capture Therapy (BNCT) are emerging. In BNCT, a molecule containing the stable isotope boron-10 (^{10}B) is injected into the patient, where it selectively accumulates in cancer cells. The patient is then exposed to an epithermal neutron beam, which ^{10}B readily absorbs due to its high affinity for slow neutrons. After capturing a neutron, ^{10}B briefly becomes boron-11 (^{11}B), then decays into a lithium-7 (^{7}Li) nucleus, an alpha particle, and gamma rays (in 90% of cases). These particles generate ionizing radiation with a high linear energy transfer, which is confined to the cancer cells that have absorbed the boron isotope. **[2,3]**
This targeted approach holds potential for treating cancers that are located near sensitive tissues or are resistant to conventional radiotherapy, such as melanoma.

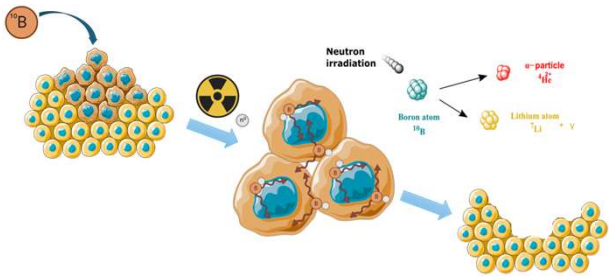


Fig. 1 : Principle of BNCT. Created with Biorender, Smart Servier Medical Art, Laird M. *& al.*, Nanoscale Adv., 5, 2537, 2023

Strategies

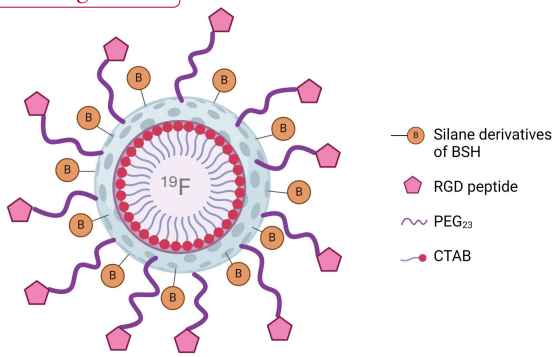


Fig. 2 : Schematic representation of the nanoplatform. Created with Biorender

The efficacy of BNCT treatment is strictly dependent on the concentration of the isotope within the tumour. Several critical aspects of current boron drugs require improvements. Areas in which our nanoplatform could make a significant contribution are: **[4]**

Compatibility with quantitative Imaging Techniques:

Use of a core-shell structure that encapsulates Perfluoro-15-Crown-5-Ether (PFCE) emulsion suitable for quantitative ^{19}F MRI. [5]

Biocompatibility:

The shell is made of mesoporous silica which is well-known for its biocompatibility.

High Tumor Selectivity:

The silica shell offers considerable chemical versatility for surface functionalization, allowing for the grafting of BSH (Sodium mercaptododecaborate ^{10}B-$Na_2B_{12}H_{11}SH$) or peptides such as RGD to target integrins that are over-expressed in certain type of cancerous cells.

Results

The initial experiments focused on the preparation of nanoparticles with a core-shell structure, consisting of a PFCE nanoemulsion stabilized by the cetyltrimethylammonium bromide (CTAB), and surrounded by a mesoporous silica shell. mPEG$_{23}$ silane was also grafted on the shell to improve the colloidal stability (NP-PEG$_{23}$).

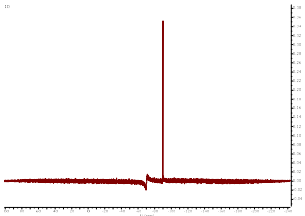


Fig. 3 : 60 MHz ^{19}F NMR confirmed the fluorinated content of the NP-PEG$_{23}$

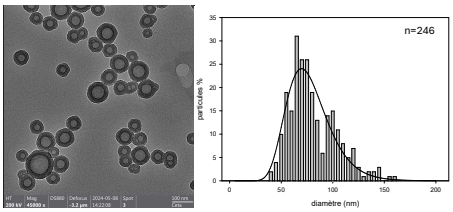


Fig. 4 : Transmission electron microscopy confirmed **core-shell** structure of NP-PEG$_{23}$, with an average diameter of 85 ± 28 nm (PDI: 1.52)

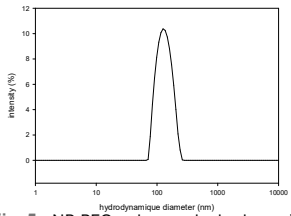
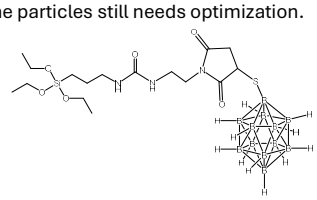


Fig. 5 : NP-PEG$_{23}$ shown a hydrodynamic diameter of 139 nm (PDI : 13 %) determined by Dynamic Light Scattering

Perspectives

To obtain a nanoplatform suitable for BNCT, our nanoparticles still require some improvements:

- BSH-modified silane derivative has already been prepared, but the grafting onto the particles still needs optimization.



- ^{19}F MRI phantoms will be performed to ensure that the concentration of encapsulated fluorine is sufficient for imaging.
- Next steps will also include *in vitro* cytotoxicity and internalization assays on A375 melanoma cell line, as well as *in vivo* biodistribution study on murine models.

Conclusion

Although BNCT shows great promises, several key challenges remain. Through its core-shell structure, these nanoparticles incorporate a PFCE emulsion for quantitative ^{19}F MRI, and a mesoporous silica shell that enhances biocompatibility and chemical versatility. Preliminary experiments have confirmed the successful synthesis of these nanoparticles, demonstrating fluorine content and good colloidal stability. Further optimization and testing are underway to improve their potential in BNCT applications.

Acknowledgments

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