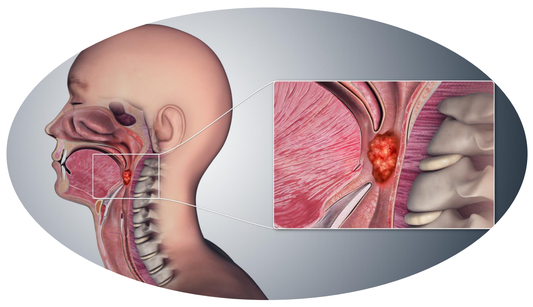
Development of a Novel Theranostic Boron-Containing Nanovector to Enhance Boron Neutron Capture Therapy Effectiveness in Head and Neck Cancers.

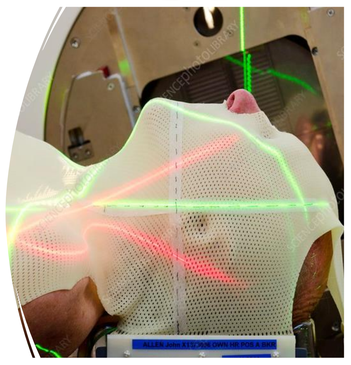
Géraldine Descamps, PhD[1]; Valentin Lecomte, PhD student[1]; Amandine Maes, PhD student[1]; Sven Saussez, MD., PhD[2]; Dimitri Stanicki, PhD[1]; Sophie Laurent, PhD[1]

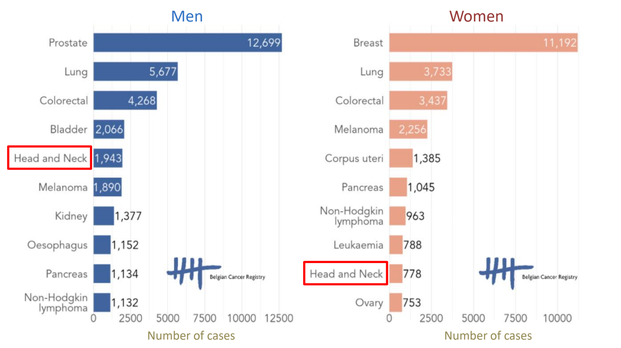
Department of General, Organic and Biomedical Chemistry, University of Mons, Belgium[1]; Department of Human Anatomy and Experimental Oncology, University of Mons, Belgium[2]

Head and Neck Cancers: urgent need to propose new therapeutic options

Head and neck cancers (HNCs) represent a significant global health burden, with high morbidity and mortality rates, particularly in advanced stages. Despite the availability of conventional treatments such as surgery, radiotherapy, and chemotherapy, their efficacy is often limited by severe side effects, treatment resistance, and high recurrence rates, leading to poor outcomes.



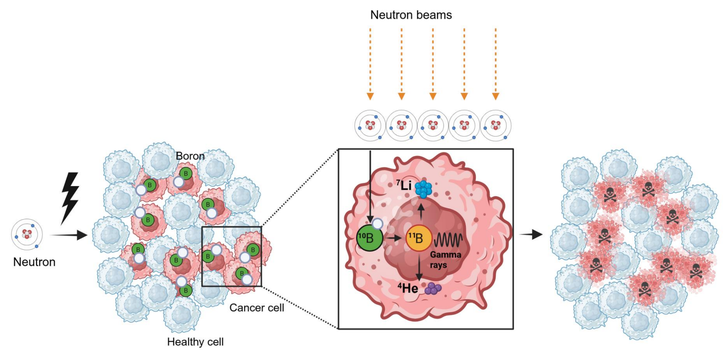




Belgian Cancer Registry

Resurgence of Boron Neutron Capture Therapy (BNCT) for advanced and recurrent cancers

BNCT limitations: optimization through the development of nanocarriers

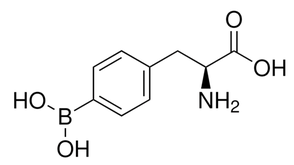


Biorender, based on Chen et al., 2022, J. Nanobiotechnology

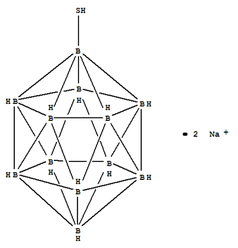
Boron Neutron Capture Therapy involves the administration of a non-toxic compound with stable ^{10}B atoms selectively incorporated into tumor cells.

Under neutron irradiation, ^{10}B converts to an unstable isotope ($^{11}B^{*}$), releasing alpha particle and lithium nucleus, specifically killing tumor cells.

4-borono-L-phenylalanine (BPA)



Sodium borocaptate (BSH)



Rapid clearance
Low tumor retention

Development of improved boron-based compounds with innovative properties

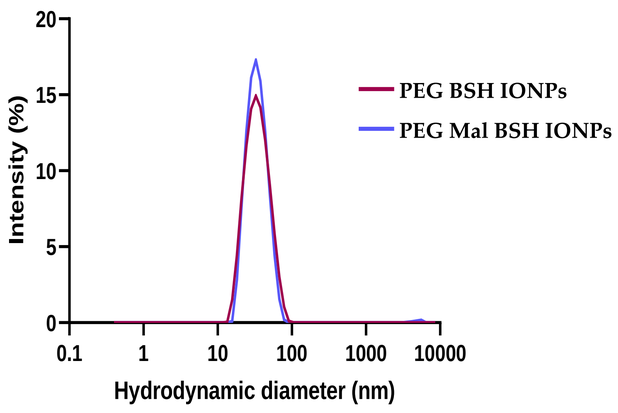
IMAGING CAPABILITIES

BIODISTRIBUTION

BORON ACCUMULATION

VECTORIZATION / SPECIFICITY

Synthesis of ^{10}B IONPs Demonstrates a Stable Formulation of Nanoparticles by Dynamic Light Scattering



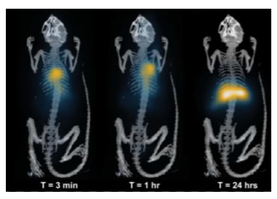
Two formulations of PEGylated iron oxide nanoparticles (IONPs) have been synthesized; the first was grafted with maleimide ligands before boron derivative addition, unlike the second, which only contains BSH adsorbed to PEG.

Both formulations show a stable hydrodynamic diameter of 32 nm, without aggregates, as determined by Dynamic Light Scattering.

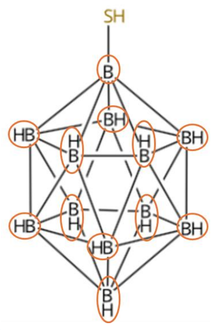
Superparamagnetic properties

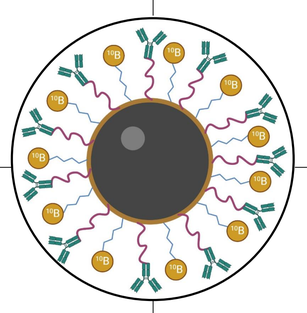
Real-time monitoring of NPs Biodistribution using **Magnetic Particle Imaging (MPI)**

➡ Provide **quantitative** data

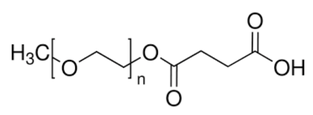


High boron payload





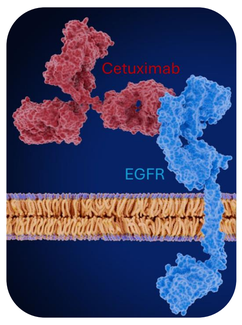
Favorable biodistribution profile



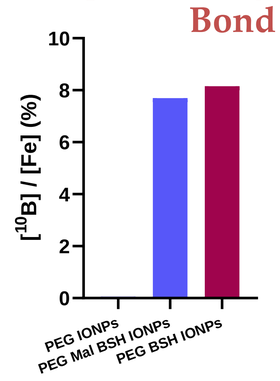
Higher circulation time ensured by the **polyethylene glycol (PEG)**

➡ Avoid NPs aggregation

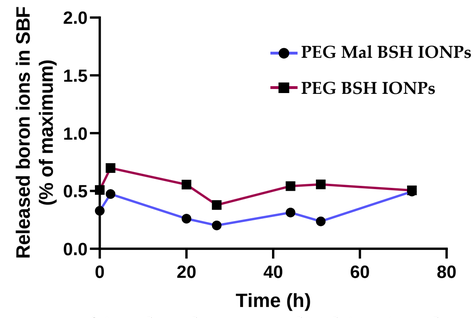
Cetuximab grafting for an active targeting



ICP Analysis Reveals a Significant Boron Grafting Efficiency Along With a Stable Bond in SBF

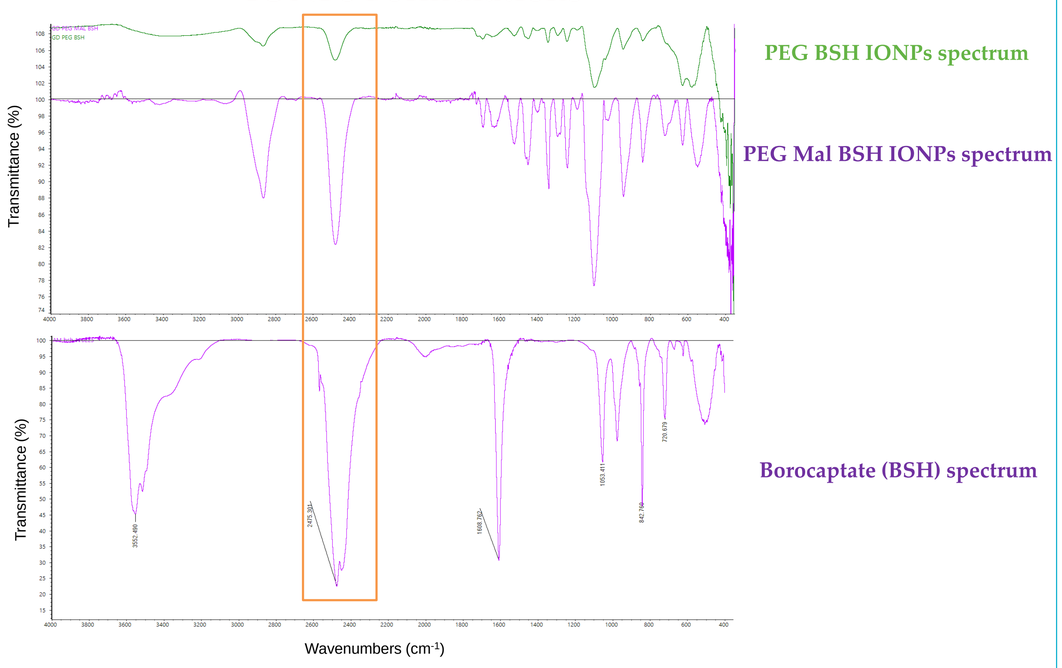


Boron quantification assessed by inductively coupled plasma (ICP) reveals boron-to-iron ratio of 0%, 7.7%, and 8.1% in PEG, PEG Mal BSH, and PEG BSH IONPs respectively.



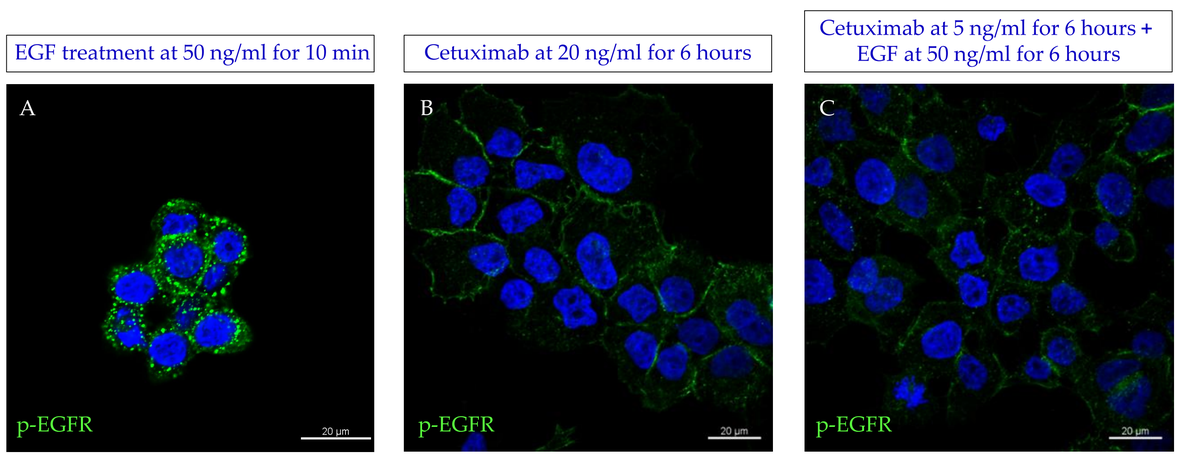
The stability of boron grafting has been studied in simulated body fluid (SBF) and demonstrated a minimal release of boron ions over time, ranging from 0.2 to 0.7%.

Infrared Spectroscopy Analysis Validates the Presence of Boron in IONPs Formulations



FT-IR spectrum analysis confirms that PEG BSH and PEG Mal BSH IONPs are successfully surface-modified with BSH. It is observed that, as compared with the BSH spectrum, both formulations also absorbed B-H bond at 2475 cm^{-1}.

Cetuximab Inhibits the Epidermal Growth Factor Receptor in Head and Neck Cancer Cells



Evaluation of the expression of the active/phosphorylated form of EGFR on FaDu HNC cells with and without EGF treatment at 50 ng/ml.

Following EGF stimulation, staining of phospho-EGFR shows a punctate distribution localized at the plasma membrane, suggesting the formation of activated receptor microdomains undergoing endocytosis (**A**). Following Cetuximab treatment, only a weak EGFR signal remains, indicating effective inhibition of receptor activation and potential receptor downregulation (**B**). The inhibition of EGFR by Cetuximab is confirmed even in the presence of EGF at a higher concentration (**C**).
These preliminary results are promising for further grafting of Cetuximab onto our nanoplatforms, and for the delivery of boron particles to head and neck cancer cells.

Conclusion and Acknowledgments

Preliminary results confirm the successful synthesis of boron-containing IONPs, highlighting stability and high boron content. Regarding its inhibitory effect on EGFR, Cetuximab will be grafted onto IONPs to favor active targeting and to enhance internalization in HNC cells. In the next steps, the biodistribution will be studied on murine models.

Géraldine Descamps benefits from funding from the Foundation against Cancer.

Contact: geraldine.descamps@umons.ac.be