

BUSSER-1: In situ visualization of Boron element in biological tissues: latest advances with LIBS imaging

Benoît Busser ^{1,2*}, Ghadir Kalot ², Jean-Luc Coll ², Vincent Motto-Ros ³, and Lucie Sancey ^{2,4}

¹ Grenoble Alpes University Hospital 38043 Grenoble, France; bbusser@chu-grenoble.fr

**corresponding author*

² Institute for Advanced Biosciences, UGA INSERM U1209 CNRS UMR5309, 38700 La Tronche, France; Ghadir.kalot@univ-grenoble-alpes.fr; jean-luc.coll@univ-grenoble-alpes.fr; lucie.sancey@univ-grenoble-alpes.fr

³ Institut Lumière Matière UMR 5306, Université Lyon 1 - CNRS, Université de Lyon 69622 Villeurbanne, France; vincent.motto-ros@univ-lyon1.fr

⁴ RENOVA Consortium

Boron Neutron Capture Therapy (BNCT) is a radiotherapeutic modality based on the nuclear capture of slow neutrons on stable ^{10}B atoms followed by charged particle emission inducing extensive damage on a very localized level ($<10\text{ }\mu\text{m}$). To be efficient, a sufficient amount of ^{10}B should accumulate in the tumor area, while it should be almost cleared from the normal surroundings. There is a major need in developing ^{10}B -enriched compounds that selectively target tumors. Accordingly, the *in situ* visualization and quantification of B element in biological tissues is of major interest for studying the biodistribution, kinetics, tumor diffusion of select ^{10}B -rich molecules.

Elemental imaging of biological samples usually requires specific and highly complex equipment based on synchrotron radiation microanalysis (SXRF) or laser-ablation inductively coupled mass spectrometry (LA-ICP-MS). Alternatively, we developed an all-optical method for multi-elemental imaging of biological tissue, which has no counterpart due to its simple implementation, moderate cost and ease in use.

This instrument is based on Laser Induced Breakdown Spectroscopy (LIBS). It allows the *in situ* mapping and quantification of chemical elements within biological tissues in a label-free manner and with ppm-scale sensitivity and a pixel size of $10\times10\text{ }\mu\text{m}^2$. This technology is fully compatible with standard optical microscope systems [1]. The proof-of-concept was obtained by studying the bio-distribution of nanoparticles in tumors or organs (kidneys/liver) after i.v. administration in mice [2]. These experiments helped to describe and understand the kinetics of several metal-based (B, Gd, Au, Ag, Pt, TiO_2) nanoparticles *in vivo*. We recently upgraded our instrument to work faster and to image the elements contained in paraffin-embedded samples, which are the most frequent form of archived clinical specimens (surgical resections or biopsies). We imaged the presence of endogenous elements from human specimens of medical interest [3], such as skin or lung tissues with various diseases, including cancer. We also identified and quantified various exogenous agents, including carcinogens (e.g. Beryllium, Chromium, Cobalt...) in human tissues.

In the context of BNCT, we used LIBS to image B element in biological tissues and we demonstrated the tumor accumulation of ^{10}B -rich compounds *ex vivo*. The LIBS technology is highly versatile because almost any element, including Boron, can be imaged with high sensitivity in tissues.

References

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