

Neutron autoradiography to study ^{10}B microdistribution in lung

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Neutron autoradiography allows the study of ^{10}B local distribution in biological samples coming from BNCT protocols [1]. If a tissue section previously infused with a boron compound (e.g. boronophenylalanine, BPA) is put in contact with a nuclear track detector (NTD) and the sample-detector assembly is irradiated with thermal neutrons, the reaction $^{10}\text{B}(n, \alpha)^7\text{Li}$ takes place and the products impact on the detector, generating a latent damage. This damage can be magnified by an etching process, in order to visualize it with an optical microscope. The spatial distribution and original concentration of ^{10}B in the sample can be inferred through the mapping of these nuclear tracks. In the framework of the Argentine project that seeks to apply BNCT as a treatment for lung metastasis [2] [3], this work aims at extending the neutron autoradiography technique to the study of microdistribution of boron in lung. For this purpose, several aspects for the generation of autoradiographic images of both normal and metastatic BDIX rat lungs were studied.

BDIX rats were infused with BPA and euthanized after 3 h. Lung tissue was sectioned at different thicknesses in a cryostatic microtome and mounted on polycarbonate (Lexan) foils, used as NTD. The assemblies were irradiated at the thermal column of the RA-3 nuclear reactor (CNEA). In order to perform a qualitative analysis, samples were exposed to a neutron fluence of 10^{13} n cm⁻² and a 4 minutes etching with a KOH solution at 70°C. Grayscale images that showed boron distribution in the tissue were obtained. For quantitative analysis, autoradiographic images were generated with a neutron fluence of 10^{12} n cm⁻² and an etching time of 2 minutes. In this way, the measurement of individual tracks allowed the determination of the absolute boron concentration using a calibration curve.

Through normal lung sample studies, an optimum section thickness was determined in 30 μm , from which the track density remains constant and independent of the thickness. No differences in uptake of the different structures of normal lung tissue were observed. It was determined that boron distribution is homogeneous with a global ^{10}B concentration value of 8.1 ± 0.8 ppm. On the contrary, samples with metastasis showed a preferential boron uptake in the tumor areas with respect to the surrounding tissue, resulting in a ratio of 1.4 ± 0.1 . Finally, boron retention was studied in samples coming from lungs subjected to a perfusion process after boron infusion. This analysis is of special interest to understand the distribution and the amount of boron in BNCT protocols with *ex vivo* irradiation of organs that need preservation procedures. Although more studies to confirm these findings are planned, preliminary results revealed that there are not significant differences in the amount of boron measured in samples taken pre or post application of preservation techniques.

References

1. A. Portu, A.J. Molinari, S.I. Thorp, E.C.C. Pozzi, P. Curotto, A.E. Schwint, G. Saint Martin, Neutron autoradiography to study boron compound microdistribution in an oral cancer model., *Int J Radiat Biol.*, 91(4), 329–335, (2015).
2. R. Farías, M. Garabalino, S. Ferraris, J. Santa María, O. Rovati, F. Lange, V.A. Trivillin, A. Monti Hughes, E.C.C. Pozzi, S.I. Thorp, P. Curotto, M. Miller, G.A. Santa Cruz, S. Bortolussi, S. Altieri, A.M. Portu, G. Saint Martin, A.E. Schwint, S.J. González. Toward a clinical application of ex situ boron neutron capture therapy for lung tumors at the RA-3 reactor in Argentina. *Medical Physics* 42:4161 (2015).
3. V.A. Trivillin, A. Serrano, M.A. Garabalino, L.L. Colombo, E.C. Pozzi, A. Monti Hughes, P. Curotto, S.I. Thorp, R. Farías, S.J. González, S. Bortolussi, S. Altieri, M.E. Itoiz, R.F. Aromando, D.W. Nigg & A.E. Schwint. Translational boron neutron capture therapy (BNCT) studies for the treatment of tumors in lung. *International Journal of Radiation Biology*, 95(5), 646-654, (2019).