PORTU-1: Neutron autoradiography with Nuclear Track Detectors in Boron Neutron Capture Therapy

Agustina M. Portu[1,2] and Gisela Saint Martin[1]

[1]*National Atomic Energy Commission (CNEA), Argentina*
[2]*National Scientific and Technical Research Council (CONICET), Argentina*

The success of Boron Neutron Capture Therapy (BNCT) strongly depends on the intratumor delivery of ^{10}B. The knowledge of ^{10}B atoms localization at the tissue and even the cellular level is essential to evaluate the probability of a successful therapy and to understand the observed post-irradiation effects. Only a small number of techniques allow precise studies of boron microdistribution, being the Neutron Autoradiography with Nuclear Track Detectors (NTD) an attractive option due to its high resolution and relative low-cost. It is based on the ability of NTDs to register the damage produced along the ion trajectories, where the material remains altered in a permanent way. In the case of BNCT, the latent damaged zones on the NTD surface are yielded by exposing a boron-loaded biological matrix, in contact with the NTD, to a thermal neutron flux: the alpha and lithium particles emitted in the BNC reaction that can reach the detector create latent tracks. Latent tracks can then be revealed by a chemical attack (etching) with an appropriate solution. The etching velocity close to the ion trajectory is higher than the etching velocity in the bulk unirradiated material (V_b). This preferential attack velocity makes it possible the development of the etch pits (or tracks) in order to be observed by electron or optical microscopy, depending on the etching conditions. When analyzing biological samples (e.g. tissue sections), boron microdistribution can be assessed by mapping the nuclear tracks and correlating their positions with the histological image.

Polymers such as pollyallildiglycol carbonate and polycarbonate have been extensively used as NTD for boron imaging of samples coming from BNCT protocols. Several approaches have been described by different BNCT groups, allowing both qualitative and quantitative analyses. Depending on the neutron fluence and the etching conditions, tracks in the autoradiographies can be overlapped. Thus, the optical collective effect on the detector surface can be analyzed to describe boron distribution in terms of shades of gray. Conversely, if nuclear tracks are separated enough to allow individual counting, track density can be translated to ^{10}B concentration using a calibration system. The material used as a reference standard must behave similarly as the biological samples, especially in terms of energy deposition and particle ranges.

Different methods have been explored in order to increase spatial resolution of neutron autoradiography. In particular, it can be enhanced by using the same sample for the histological analysis and neutron autoradiography generation. With this purpose, the biological sample has to be carefully processed in order to obtain accurate results. In fact, as the sample is removed from the detector before the chemical etching, the use of reference marks to correlate the regions of interest in both the histological and autoradiographic images is necessary, and has been extensively reported. Different filtering and segmentation procedures on the digital images have been proposed.

Moreover, if tissue structures and nuclear tracks were simultaneously observed, a more precise knowledge of the localization of boron atoms could be achieved. High resolution quantitative radiography seeks to preserve the biological sample during the etching process, by means of the use of thin detector films. Another technique consists of interposing a UV-C exposure step between the irradiation with thermal neutrons and the staining and histological analysis. V_b in the NTD can increase considerably because of photodegradation. When a biological sample is put in contact with the detector, it partially protects the NTD from the UV-C action. Thus the etching solution will attack the detector surface at different velocities depending on the sample topography and an imprint of the biological material will be formed. Both imprint and tracks are revealed in the same process.

The neutron autoradiography is a powerful and versatile methodology. The different approaches vary in complexity and resolution and should be selected depending on the objective of the study. They have been used to determine boron microdistribution in different *in vitro* and *in vivo* biological models. Moreover, the methodology was applied to samples coming from patients subjected to biodistribution studies. The information obtained from the autoradiographic analyses provided essential information to numerous research works: evaluation of boron compounds, comparison among different cell lines response, correlation with BNCT efficacy in radiobiological studies, dosimetric evaluation in non-uniform boron distribution scenarios and microdosimetry analysis.