

Determination of Boronophenylalanin (BPA) in healthy liver and tumour tissue of patients with liver metastases of colorectal carcinoma

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Patients suffering of colorectal carcinoma develop distant metastases in 50 to 80 % with the metastases being confined to the liver in almost half of those cases.

BNCT for patients with multiple, bilobar liver metastases was established at the University of Pavia with the first case being treated by Pinelli et al in Dec. 2001 [1]. Here, BPA was administered intravenously before explanting the liver and irradiation in the thermal column of the TRIGA-Reactor in Pavia. An accumulation of BPA in tumour vs. healthy liver tissue of 6:1 was determined here. Noteworthy is that the tissue samples were collected before explanting the liver.

The surgical process requires extensive experience in the field of liver transplantation and preservation of the liver during the extracorporeal treatment. This includes perfusion of the liver artery with preservation solution and reducing the liver temperature to 4°C. The question remains whether there are any wash-out effects during this procedure and if yes, will the accumulation remaining in tumour tissue still be enough for the irradiation therapy?

We plan to implement BNCT for colorectal liver metastases at the University of Mainz in cooperation with the University of Pavia.

Our project will be performed in two steps. The first step will be to determine the accumulation of BPA in tumour and healthy liver tissue in patients before and after partial liver resection and washing the liver specimen with preservation solution. Furthermore, additional pharmacokinetic data will be obtained from blood and urine samples taken in intervals during surgery. Satisfying results provided we would proceed with step 2 which is to treat a patient with multiple liver metastasis and extracorporeal irradiation of the whole liver.

We have started to examine the first samples of three patients. These patients suffer from colorectal liver metastases and they need a partial liver resection (fig.1). Our task is to determine the accumulation of BPA in tumour

and healthy liver tissue. BPA was administered in a concentration of 200 mg/kg intravenously, throughout the surgical procedure blood samples were taken every 30 minutes.

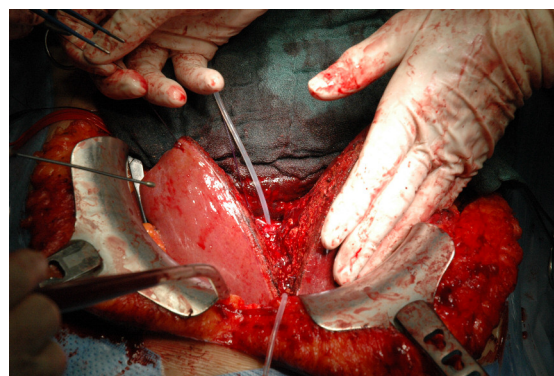


Fig.1: Resection of a liver lobe

After the resection of the liver, the specimen was perfused with preservation solution (250 ml through the artery and 1500 ml through the portal vein) and tissue samples were taken from the surface and depth of the organ to provide data for the spatial boron distribution. The samples were frozen in liquid nitrogen and prepared for analysis by the Department of Pathology by autoradiography and ICP-MS. In addition, the neutron and gamma dose was measured, using the liver specimen as matrix. Gold foils and thermo-luminescence detectors were fixed at different parts of the organ and irradiated in the thermal column. The analysis of the data is in progress. In case of an accumulation of BPA in tumour vs. healthy liver tissue of at least 3:1 in 3 patients we would proceed with the remaining 12 patients. The work on this project was kindly supported by the Boehringer Ingelheim Foundation

[1]: Pinelli et al. "TAORMINA: From the First Idea to the Application to the Human Liver". Research and Development in Neutron Capture Therapy. Proceedings of the 10th International Congress on Neutron Capture, Monduzzi editore, Bologna, 2002, 1065-1072