Boron Determination in Blood and Tissue Samples using Prompt Gamma Activation Analysis

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Introduction: Boron Neutron Capture Therapy (BNCT) of liver metastases is investigated at the University of Mainz, Germany. Before BNCT can become a real alternative to established treatments of the liver many parameters have to be determined. Consequently a preclinical trial has been started to investigate boron distributions in different types of tissue and blood. In the present work, Prompt Gamma Activation Analysis (PGAA) has been used to determine the boron concentrations in blood and tumour-free tissue. The results presented show a strong correlation of the amount of boron to the surgical procedure.

Experimental: The preclinical trial is focussed on patients with liver metastases in one liver lobe. The standard surgical procedure for these patients is the resection of the cancerous liver lobe, called hemi-hepatectomy. In the trial, an additional infusion of a boronophenylalanine-fructose (BPA-F) is administered to the patients during a period of 2 hours until the moment of resection. During that time, blood samples are taken. After the resection, tissue samples are taken from the resected part of the liver. The weight of the blood samples is around 1 g, the weight of the tissue around 0.1 g.
For this work, measurements have been performed at the PGAA facilities at the HFR in Petten, The Netherlands [1] and at the FRM II in Munich, Germany [2]. For the measurements, the samples have been filled into Polyethylene (PE) or Teflon Vials. To determine the boron concentrations a series of standards containing different concentrations, of boron in water has been measured with each series of samples. Because of variations in the beam intensity or geometry effects, every boron signal has been weighted with the hydrogen signal as an internal standard using the k_0-method. Due to the large amount of hydrogen in the PE Vials they create a certain background. Because of the small mass of the tissue specimens, this background leads to a relevant uncertainty. To avoid this, all tissue samples have been measured in Teflon vials, which contain no hydrogen. The mass of the blood samples is high enough to use the PE Vials.

Results: Figure 1 shows the average results of the blood samples for the first four patients in the preclinical trial for both facilities. Patient 3 shows the typical run of the curve. The other curves vary because of the course of the surgery. Due to a blocked filter, less BPA was administered to patient 1 until minute 116. Then the filter was changed and the infusion speed had to be increased to finish in the given time. With patient 2, a blood vessel broke in minute 30 and the patient lost 3 L of blood. By dilution through a blood transfusion, the BPA concentration was growing slower. Additionally, surgery was faster so that the infusion speed had to be increased again. Patient 4 had a light bleeding throughout the whole surgery, so that the blood was continuously diluted by transfusions. All these meanderings are apparent in the figure. The difference between the two facilities is below 5%.

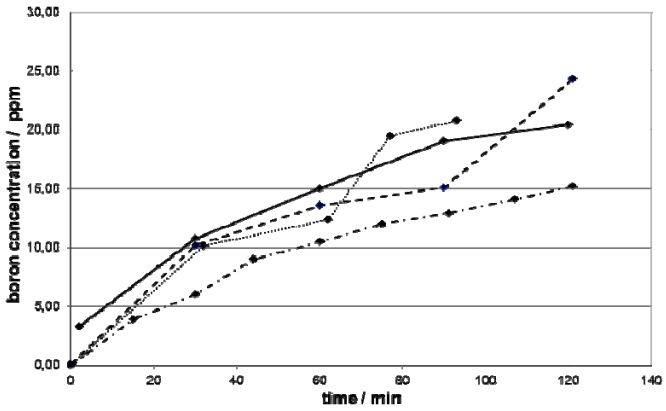

Figure 1. Pharmacokinetic curves for the first four patients from (Patient 1 – dashed; Patient 2 – dotted; Patient 3 – solid; Patient 4 – dotted)

Table 1 shows the results of the average boron concentrations in tissue for both facilities and a blood to tissue ratio made of the maximum blood boron concentration and the average tissue boron concentration of both facilities. The determined ratio seems to be constant around 1.9 except for Patient 1, which is rooted in the sudden increase of the blood boron concentration in the end. When the maximum concentration is calculated without this increase the ratio decreases to 1.9, as shown by the values in brackets (Table 1).

Table 1. Boron tissue concentrations and blood to tissue ratios for the first four patients

P#	^{10}B tissue conc.		Max. ^{10}B blood conc.	blood : tissue ratio
	Petten	Munich		
1	9.3 ± 0.3	9.0 ± 0.1	23.4 ± 1.0 (17.5 ± 0.7)	2.6 ± 0.1 (1.9 ± 0.1)
2	12.0 ± 2.0	12.0 ± 2.4	20.8 ± 0.6	1.7 ± 0.2
3	10.1 ± 1.1	9.8 ± 2.5	20.1 ± 1.1	2.0 ± 0.3
4	8.3 ± 0.3	8.4 ± 0.4	15.1 ± 0.5	1.8 ± 0.1

References

[1] C.P.J. Raaijmakers et al., Acta Onco 34, 1995, 517-523.
[2] P. Kudejova et al., J Radio Nuc Chem 278, 2008, 691-695.

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