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Phantom studies of neutron capture of boron containing magnetic nanoparticles

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Abstract: *The main burden that hinders the translation of neutron capture therapy drafts to human trials is the difficulty to deposit a sufficient amount of boron in the targeted tumour areas. Magnetic nanoparticles containing B-10 isotopes attempt to be enriched in tumour tissues selectively by the means of external magnetic fields to overcome these restrictions. First pilot measurements of the neutron depth penetration investigated the neutron flux density in dependence of depth, presence of boron and additional presence of iron oxide nanoparticles. These irradiation experiments on different phantoms evidenced no disturbing attenuation effects of the applied boron and the co-present nanoparticles in the samples.*

Keywords: *BNCT, Nanoparticles, Magnetic Drug Targeting*

Introduction

Boron Neutron Capture Therapy (BNCT) is since a long time under study in different research areas and even a series of clinical studies have been performed.[1]
The most common boron compounds used in BNCT research are the boron rich closomer sodium borocaptate (BSH) and the L-4-boronophenylalanine (BPA) both mostly labeled with enriched in ^{10}B. After the introduction in the body, via i.p. or i.v. or in a more direct way the target region is irradiated with neutrons in order to induce the nuclear reaction on the ^{10}B (Fig. 1).

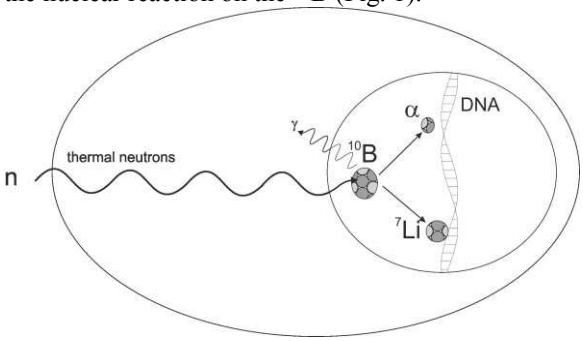

Fig. 1: Nuclear reaction of B-10 with thermal neutrons.

The success of BNCT is strongly dependent on the improvement of the selectivity of B-labelled compounds for cancer tissues in order to establish a sufficient dose ratio between tumour cells and healthy tissues as blood vessels and normal brain during a sufficient time span. This ratio may be obtained by a concentration of B of 20 ppm in the tumour. One strategy is to enrich B in tumour tissues by the means of magnetically directed nanoparticles. The successful deposition of classical active agents by Magnetic Drug Targeting (MDT) using respective magnetic fields has already been proven.[2-4] For the fusion of both BNCT and MDT the behaviour of the neutron inside the tissues has to be investigated. Therefore the neutron flux density has to be sufficient to target deposited boron underneath. Moreover as the boron substrate is connected to magnetic nanoparticles these particles should not have any shielding effects on neutrons. In this study we investigated the neutron flux density on agarose gel phantoms in dependence on depth and in presence of boron containing layers and additional co-presence of magnetic nanoparticles.

Methods

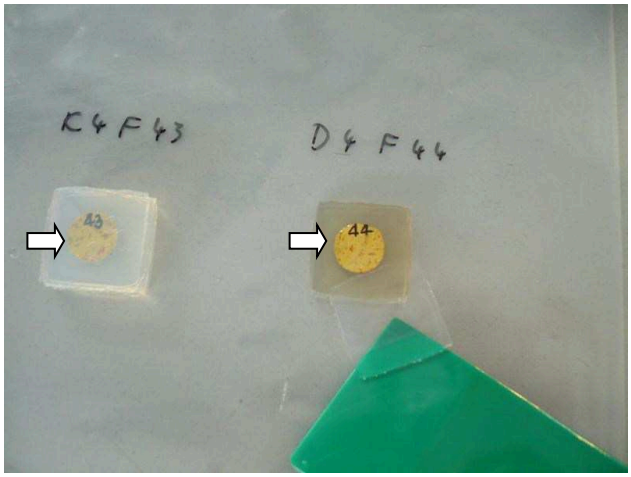

Fig. 2: Agarose gel phantoms consisting of 10 slices each. A gold foil (highlighted by arrows) for the activation analysis was positioned beyond the investigated layer.

Gel phantoms: Experimental gel phantoms consisting of agarose (1.5%) and the neutron "captureable" isotope B (natural Boron, ca. 20%wt ^{10}B) in a selected concentration as boronic acid were developed to investigate the behavior of the neutrons in dependence of the depth. For these experiments a cold neutron beam (25 K) at the Forschungs-Neutronequelle Heinz Maier-Leibnitz was used.[5] In detail, a gel phantom is made of 10 slices, each 2 cm x 2 cm x 1mm (Fig. 2). A series of irradiations were performed using pure agarose gel. In a second experimental set up one slice was substituted with the agarose gel containing B in a concentration of 100 ppm. The

depth of this B-loaded slice was changed, namely it was positioned in the 1st, 2nd, 3rd, 5th, 7th and 9th slice of the phantom. ICP-AES analysis evidenced the homogenous distribution of B within the slices. Moreover, another set of phantoms was built using boron slices additionally doped with iron oxide nanoparticles (300 ng/g).

Analysis: The respective neutron fluxes in the investigated cube layers have been determined by gold foil activation: $^{197}Au(n,\gamma)^{198}Au$. Half-life $T_{1/2}$= 2.695 d.

Results

The results obtained from the irradiation experiments show that the neutron flux is strongly dependent on the depth of the slices (Fig. 3) and the presence of B is not affecting the neutrons going through the slices. The neutron flux density cannot be distinguished whether a boron containing layer was in the cube or not.

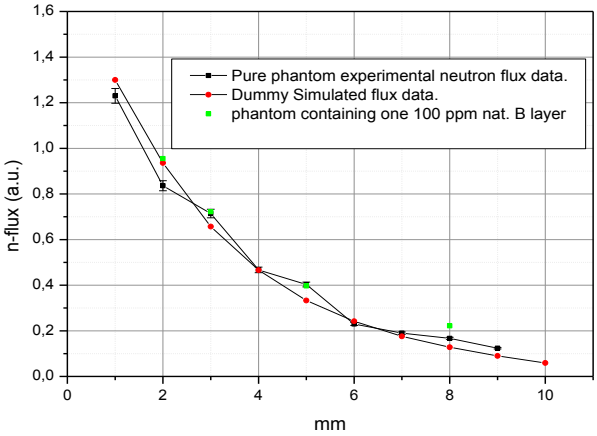

Fig. 3: Neutron flux density in pure agarose phantoms (data derived from experimentals and from simulations) and in a phantom containing 100 ppm B in one layer in different depths.

Furthermore no additional attenuation could be recorded when measuring the slices containing iron oxide nanoparticles (300 ng/g) in co-presence to boron (100 ppm) in the same layer (Fig. 4).

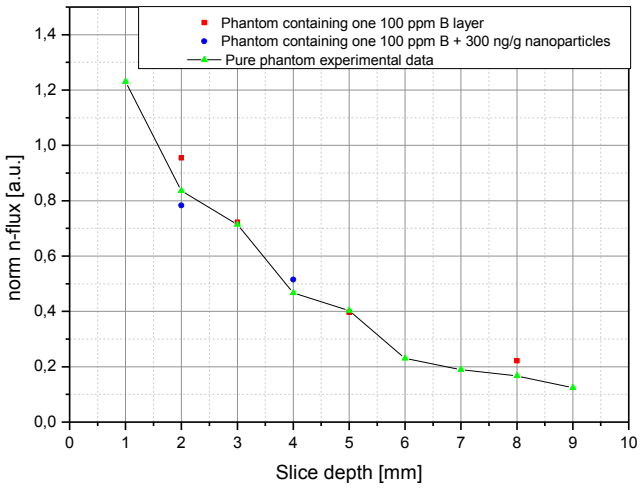

Fig. 4: Neutron flux depth profile for Agarose gel loaded with 100 ppm of B and a selected iron oxide nano-particles concentration of 300 ng/g.

Discussion

The important result that boron as well as iron oxide nanoparticles do not attenuate the neutron flux in the phantoms could clearly be demonstrated within these experiments. This is an essential precondition that a sufficient neutron flux density would reach a boron deposition underneath. All these measurements were carried out in a cold neutron beam using thin vials. A former simulation shows that even much better results could be reached using hot neutrons that are soon available at the FRM II.[6] Further experiments are necessary to evaluate the BNCT reactions in phantoms that are closer to the reality of living organisms.

Acknowledgement

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