Experimental report

08/02/2023

Proposal: LTP-3-2 **Council:** 10/2018

Title: Determination of neutron relative biological effectiveness factors for Boron Neutron Capture Therapy andtest of different boron compounds b

Research area:

This proposal is a new proposal

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Samples: Cell irradiation samples

Instrument	Requested days	Allocated days	From	To
FIPPS	6	0		
PF1B	48	14	13/06/2019	18/06/2019
			18/06/2019	20/06/2019
			01/06/2021	05/06/2021

Abstract:

Boron neutron capture therapy (BNCT) is an experimental form of radiotherapy based on the combined effect of the uptake of a 10B-containing compound and the irradiation with low energy neutrons.
The measurements proposed in this project pursue the advance in two key research lines for improving BNCT: one is the accurate calculation of the photon equivalent dose in BNCT which is essential for the treatment planning and the second is the search of better boron compounds for the therapy. Both lines require radiobiological experimentation.
In the first problem we want to improve the data on the relative biological effectiveness factors for the main dose contributions: thermal, gamma from H capture and boron dose. The PF1b line at ILL is unique for these measurements due to the high flux and the lack of gamma contamination in the beam.
The second one is the study of compounds that can potentially deliver much more boron atoms to the tumor cells, which would represent a major advance for the therapeutic capability. For this purpose boron-loaded nanostructures are specially promising because they can carry a lot of boron atoms to the tumors via the enhanced permeation and retention eff

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INSTITUTE LAUE-LANGEVIN EXPERIMENTAL REPORT

Experiment LTP-3-2: Determination of neutron relative biological effectiveness factors for Boron Neutron Capture Therapy and test of different boron compounds (2021)

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Objective

Neutron radiobiology data are critical for an accurate treatment planning in Boron Neutron Capture Therapy. The determination of the relative biological effectiveness (RBE) of the boron compound used in clinical trials of BNCT, called Compound Biological Effectiveness factor (CBE) determines the boron dose, which is the main dose component at the tumor.

The cold neutron line PF1b of ILL is a perfect instrument to measure this value, as it is a pure thermal-equivalent beam equivalent to which produces the therapeutic effect in BNCT.

Therefore it is a suitable place to test new boron compounds for their potential use in BNCT. The aim of this experiment was to compare the effect of BPA administration and two new boron compounds: (1) a fluorescent BODIPY-anionic boron cluster conjugate, and (2) polymeric nanoparticles functionalized with iodinated COSAN.

Experimental setup

The irradiation of the culture cells were performed at the very pure cold neutron line PF1b, thanks to its bent guide which prevents contamination from fast neutrons or photons from the reactor core. The cells were grown in quartz cuvettes, very thin to avoid as much as possible secondary photons from the culture medium. This medium has just a thickness of 2 mm (inner space of the cuvettes). Quarts is very transparent to neutrons, which avoids activation and secondary radiation.

The cuvettes were place at the beam exit as illustrated in Fig. 1.

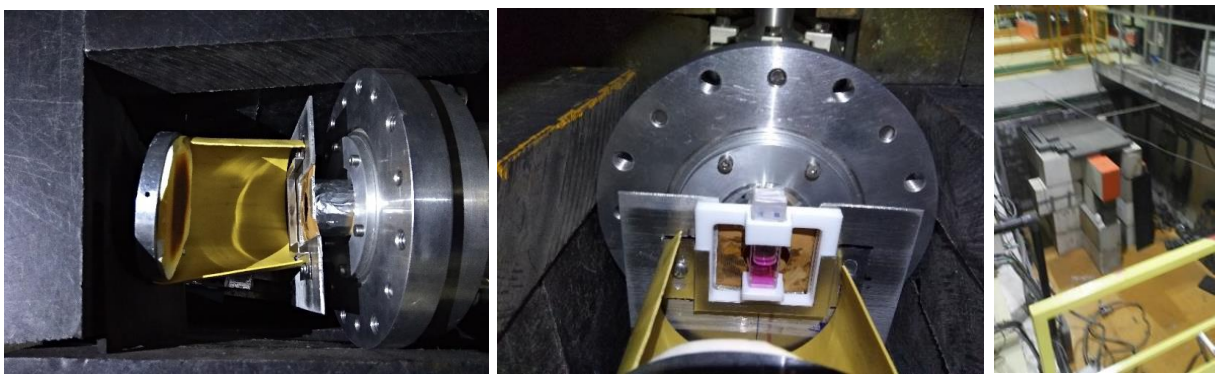

Fig. 1. *Set up of the experiments. Left: top view of the beam exit (on the right in the picture), the beam stop (on the left). Center: view of the set-up with the sample holder and the quartz cuvettes containing the cell culture (culture medium is pink). Right: casemate shielding of concrete and lead.*

Cells

The tumor cell lines used were: Cal33 (tongue squamous cell carcinoma) and CCD10 as a sample of normal cells. Cells were incubated 24 hours before irradiation inside quartz cuvettes (2 mm large). They were incubated with the boron compound for 4h. For the irradiation, the cuvettes are placed in the teflon holder. After irradiation the cells are recovered from the cuvettes with trypsin, counted and prepared for survival assays.

Measurements

The neutron flux was measured from with a Gold foil and a Ge detector. The dose rate for the beam at the cells (both neutron and photon) was estimated from Monte Carlo simulations with MCNP v.6.2 with the geometry of the cell-containing cuvettes boxes, resulting in a mean neutron dose rate at the cells of 0,260 Gy/min (quartz 1) and 0,127 Gy/min (quartz 2) for 10 ppm of Boron, gamma dose rate of 0.018 Gy/min and 0,014 Gy/min, respectively.

Results

Cal33 + BPA						
% Survival						
C	1	2	3	4	5	6
100	0,64412238	1,28824477	1,93236715	2,31884058	5,95813205	23,9130435
100	1,48148148	1,04018913	1,371158392	3,68794326	11,9779354	68,321513
100	1,03916867	0,70343725	1,151079137	3,06954436	23,0215827	30,6954436

Cal33 + comp.1 (S174)					
% Survival					
C	1	2	3	4	
100	12,9157345	32,1252796	48,9187174		40,2684564
100	20,8333333	30	66,6666667		137,5
100	20	140	116,666667		200

CCD10 + BPA						
% Survival						
C	1	2	3	4	5	6
100	4,27225131	3,92670157	4,083769634	3,76963351	2,35602094	5,10471204
100	3,2284264	3,88324873	3,654822335	1,82741117	1,71319797	3,8071066
100	1,61797753	2,10674157	2,02247191	3,03370787	4,21348315	8,84831461

CCD10 + comp1 (S174)					
% Survival					
C	1	2	3	4	
100	9,49450549	16,4835165	47,47252747	66,2637363	
100	9,12941176	15,2941176	53,17647059	63,0588235	

Cal33 + comp.2 (Cos-Fl-2)					
Porcentaje de supervivencia					
C	1	2	3	4	
100	51,2682379	107,833895	113,5802469	143,434343	

CCD10 + comp2 (Cos-Fl-2)					
% Survival					
C	1	2	3	4	
100	2,57142857	2,85714286	107,142857		
100	129	152	348	210	