BORON NEUTRON CAPTURE THERAPY SETUP
FOR A LINEAR ACCELERATOR*

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Received October 10, 2008

An experimental facility at Bucharest Tandem accelerator (FN-15 Tandem Van de Graff from High Voltage Engineering Corporation) was developed to produce thermal neutrons. This facility was used to perform some exploratory experiments in order to understand and to define the requirements imposed on a real Boron Neutron Capture Therapy (BNCT) facility.

Key words: Tandem accelerator, lithium target, neutron production, BNCT, L-4-Boronophenylalanine.

1. INTRODUCTION

The idea suggested by Locher in 1936 [1] to use the $^{10}$B thermal neutron capture to treat the brain tumors was followed by numerous papers and experimental set-ups trying to exploit it. Based on some basic papers regarding the on-line neutron production by particle accelerators [2–4], the nuclear reaction chosen for neutron production was:

$$^7\text{Li}(p, n)^7\text{Be}$$

*Boron Neutron Capture Therapy* (BNCT) arises from the propensity of the $^{10}$B nucleus to capture thermal neutrons; the resultant unstable $^{11}$B nucleus produces a lithium ion and an $\alpha$ particle, as well as 0.48 MeV $\gamma$-radiation:

$$^{10}\text{B} + n \rightarrow ^7\text{Li} + ^4\text{He}$$

$^{10}$B is linked to an alanine ($\alpha$-amino acid) to form the L-4-Boronophenylalanine, which is injected in the biological material subjected to thermal neutron irradiation. In the case of BNCT, the cancerous cells, having a more dynamic metabolism, accumulate the alanine – and implicitly the $^{10}$B – much faster than the normal ones.


The main features included in our project regarding the neutron production and BNCT were related to:

- The use of the multipurpose Tandem accelerator which is already available in our institute;
- The use of lithium compounds instead of metallic form in order to prevent the difficulties in handling a highly reactive element;
- The long irradiation times necessary to induce decidable effects in biological cells prevented the use of living tissues; instead we used aqueous cells solutions which can be preserved for longer periods.

The same features, above described, brought the following experimental set-backs:

- Small intensities for the incoming protons beam - the maximum proton beam current provided by the Tandem accelerator is about a few $\mu$A;
- As a corollary of the previous set-back: low production rate for neutrons;
- Insufficient biochemical data regarding the tissue and living organs behavior under neutron irradiation and alanine injection.

2. EXPERIMENTAL SET-UP

The scientific literature emphasizes both the advantages and the disadvantages of the on-line neutron production [5, 6]; our approach preferred the on-line production due to its simplicity, cost effectiveness and mainly to the availability of the Tandem accelerator.

The Tandem accelerator is able to deliver beams of various ion species, including protons, but with currents limited to a few $\mu$A. Therefore, in order to use a beam with high intensity, we preferred to extract the proton beam on the $0^\circ$ pipeline, without steering it through an analyzing magnet.

The lithium targets described in the literature involve the extraction of the proton beam into air, followed by its injection in a chamber containing vaporous lithium. However, a lithium target is very difficult to handle, because it is highly chemical reactive and it has a very low melting point (180.50°C). Also, the placement of a chemical active metal in vacuum and heating it with the impinging proton beam raises great problems with the preservation of the vacuum and the corrosion of pipes, gaskets, pumps, gauges, etc.

As it was previously mentioned, at the Tandem accelerator we are dealing with low proton beam currents ($\sim \mu$A). Therefore it was concluded that it would be more convenient to transfer from vacuum into air neutron fluencies instead of proton fluencies.
In order to solve this problem, we decided to use in our experimental set-up lithium compounds, that are less reactive and that have higher melting points (e.g. lithium oxide with the melting point at 1570°C, lithium nitride at 813°C and lithium hydride at 689°C). The only disadvantage of using lithium compounds instead of metallic lithium is that the yield of the produced neutrons will be smaller.

The lithium compound target was placed in the vacuum pipe of the accelerator directly into the proton beam. The neutrons produced in this target pass through an aluminum flange, reaching a paraffin moderator and then the irradiation area.

The target consisted of aluminum rings (20 mm in diameter) in which the lithium compound powder was mechanical compressed at 150 atmospheres in order to form a compact and self-supported target with the thickness of about 8 mm. The aluminum flange has a triple purpose:

- To separate the vacuum of the accelerator pipe from the external atmosphere;
- To sustain the target and to electrically insulate it;
- To sustain – on the vacuum side – an electrically insulated device dedicated to proton beam positioning and monitoring.

The neutrons produced in the \(^7\text{Li}(p, n)^7\text{Be}\) nuclear reaction pass easily through the aluminum flange and they are available outside the vacuum pipe.

To moderate the neutrons we used a paraffin cylinder; the calculus made with numerical simulations established a 30 cm length for the paraffin cylinder for 3 MeV incoming protons. The cylinder has a plane shape at one end (at the aluminum flange) and a convex shape at the other end, in order to create an isotropic distribution for the thermal neutron field; there is no reflector surrounding the moderator. Behind the moderator the gamma ray field was monitored with a general purpose dosimeter device.

3. NEUTRON SPECTRA MEASUREMENT

The neutron spectra measurements have been performed with a Bonner Spectrometer [7] with 6 polyethylene spheres (3, 4, 5, 8, 10 and 12 inches in diameter), the detector being a \(^3\text{He} \) based proportional counter.

The electronic components – both the analogical (HV power supply, preamplifier, amplifier and SCA) and the digital ones – are encapsulated in a small portable crate which is battery operated. The digital part was designed to acquire the TTL signals from the SCA, to display the number of counts per unit of time on a LCD display and to support a simple protocol on a RS 232 serial
interface. The heart of the digital electronics is a microcontroller Atmel; the implemented software permits:

- To set up the acquisition time;
- To start and stop the acquisition;
- To read the acquired data by a remote computer.

The master computer is a notebook which implements the acquisition program and neutron spectra unfolding; it is placed outside the experimental area in a radiation-safe environment.

The unfolding program which reconstructs the neutron spectra from the 7 measurements with the $^3$He (6 polyethylene spheres and the necked detector) is based on BUNKI algorithm [8, 9].

Performing the neutron spectra measurements, we assumed some limitations:

- Using the $0^\circ$ beam pipe there is a fraction of neutrons which are not produced by the $^7$Li (p, n) $^7$Be threshold reaction; this fraction is coming from the hazardous collisions of the proton beams with the pipes and slits;
- The neutron field is not sufficient uniform along the diameter of the large Bonner spheres (10 and 12 inches).

4. RESULTS AND DISCUSSIONS

Our research activity was performed in two stages: the first one dedicated to the optimization of the thermal neutron production, while the second one was dedicated to the neutron irradiation of biological cells.

In the first stage we measured the neutron spectra after the moderator for various incoming proton energies and by using different lithium compounds targets. Our aim was to maximize the ratio between the thermal and the fast neutron fluencies. The neutron producing reaction is a threshold reaction, so we started our experiment by using 2.5 MeV incoming protons; in order to increase the neutron fluency, we increase the energy up to 4.5 MeV.

All fluency measurements have been performed for 20 s for each target, incoming proton energy and Bonner sphere detector. The incoming proton beam current was about 1 $\mu$A.

After these measurements, the following conclusions arise:

- Lithium hydrate is the best target candidate, having the highest neutron productivity;
- Due to the small neutron fluencies at low proton energies (2.5 MeV), we decided to increase the energy of the impinging protons beyond the initially assumed limit of 3 MeV.
A supplementary complication appeared: at low energies, the proton beam was quite spread, exceeding by far the target dimensions; by increasing the beam energy up to 4.5 MeV, the beam self-collimated and focused on the target. If for 3 MeV protons, the neutron fluency is about 10000 neutrons/cm², by using 4.5 MeV protons, the neutron fluency increased to four times higher value, for the same proton current. However, by using 4.5 MeV protons, a fast neutron component arises, whose contribution is about 10% from the thermal component.

The unfolded spectra of thermal and fast neutrons after the moderator, produced by the bombardment of a lithium hydrate target with 4.5 MeV protons are presented in Figs. 1 and 2.

The second stage of the research consisted in neutron irradiation of biological cells.

After the neutron spectra measurements have been performed, a calibration constant linking the neutron thermal fluency and the output (counts) of the detector surrounded by the 5 inches Bonner sphere was established. During the irradiation of the biological samples, only the detector inside the 5 inches Bonner sphere was used for neutron fluency measurements and monitoring.

The biological cells in an aqueous solution were irradiated for many hours (22 hours on average) in an isotropic thermal neutron field and at a constant temperature (37°C). As it was already mention, by using higher proton energies, the improvement of the neutron fluency is counterbalanced by the apparition of a high-energy neutrons component. In order to reduce the energy deposited by this
fast neutron component in the samples, we used thin targets for the biological samples. The cells samples are aqueous solutions in which the cells are floating; the samples are placed in thin glass cylinders with the generator normal to the proton beam direction. To prevent the cells deposition at the bottom of the cylinder, the sample holder were slowly rotated (one revolution per minute) around the proton beam axis.

The thermal neutron fluency was monitored and recorded during the irradiation with the 5 inches Bonner detector. The overall irradiation times had different values for each experiment, since some technical breaks and the variations of the proton beam intensities (from hundreds of nA to a few μA) had to be taken into account. The irradiations were performed trying to maximize the thermal neutron fluency and, at the same time, fitting the experiment into a strict time-table.

The γ-ray dose was measured with an ordinary integral dosimeter device which does not take into account the contribution of the 0.48 MeV γ-rays produced in $^{10}$B(n, α)$^7$Li reaction.

The obtained experimental results are summarized in Table 1.

The neutron doses are effective doses and were calculated according to the microdosimetric model presented in reference [11] and also coherent with the calculation from neutron thermal spectra. The supplementary dose coming from $^{10}$B was calculated for the recoil products, alpha particles and $^7$Li assumed to be stopped in one cell. When a biological sample in a BNCT experiment is irradiated with thermal neutrons, there are three nuclear reactions contributing to
Table 1
Experimental results

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>Neutron fluency (neutrons/cm²)</th>
<th>Irradiation time</th>
<th>Neutron dose without ^10^B (mGy)</th>
<th>Gamma dose (mGy)</th>
<th>Neutron dose exclusively from ^10^B (30 ppm L-4-Boronophenylalanine concentration) (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.97×10^9</td>
<td>19h 30min</td>
<td>12</td>
<td>0.6</td>
<td>67</td>
</tr>
<tr>
<td>2</td>
<td>0.80×10^9</td>
<td>16h 45min</td>
<td>10</td>
<td>0.5</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>1.15×10^9</td>
<td>16h</td>
<td>14</td>
<td>0.96</td>
<td>79</td>
</tr>
<tr>
<td>4</td>
<td>0.56×10^9</td>
<td>23h</td>
<td>7.2</td>
<td>0.4</td>
<td>38</td>
</tr>
<tr>
<td>5</td>
<td>2.60×10^9</td>
<td>36h</td>
<td>33</td>
<td>2.2</td>
<td>180</td>
</tr>
</tbody>
</table>

the total dose: ^10^B(n, α)^7^Li, ^14^N(n, p)^14^C and ^1^H(n, γ)^2^H. The maximum quantity of ^10^B which is added through the introduction of L-4-Boronophenylalanine in a biological sample is 30 ppm.

As it can be seen from the results presented in Table 1, fluencies of the order of 10^9 neutrons/cm² were obtained through the bombardment for 22 hours of a lithium hydrate target with 4.5 MeV protons.

However, as it is mentioned elsewhere [10, 11], the working fluency for BNCT on living organisms should be around 10^{11} neutrons/cm². This value was derived from radiological safety limitations (12 Gy for brain) and maximum boron concentration in living tissues (30 ppm); this value applies for human patients in brain irradiation.

The neutron fluency value obtained in our experiments is almost two orders of magnitude lower than the fluencies needed for human brain cancer treatment. However, taking into account the high quality factor for the α-particles and Li recoil nucleus (∼20), the above-mentioned fluency is enough to produce decidable biological effects, similar to the ones induced by the irradiation with an equivalent dose of 1 Sv.

5. CONCLUSIONS

The experiments reported in this paper showed that it is possible to use the newly developed experimental facility at the Bucharest HVEC FN-15 Tandem accelerator in order to produce thermal neutrons by bombarding lithium compounds targets with relatively low-energy proton beams. Irradiations on biological cells in aqueous solutions were performed as well; the produced neutrons had fluencies high enough to induce decidable effects on the irradiated cells.

These experiments showed that the HVEC FN-15 Tandem accelerator is not suitable for BNCT studies on tissues or living organisms, since a much more
intense proton beam at lower energies are required, in order to take advantage of the $^7\text{Li}(p, n)^7\text{Be}$ threshold reaction for neutron production. However, the set-up described in this paper can be used successfully used for thermal neutron irradiation studies on aqueous solutions of cells.

To experience gained in this project can be further exploited for BNCT studies, especially if a new accelerator with improved characteristics – i.e. capable of providing higher beam currents at relatively low energies – will be available.

REFERENCES

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