Compton imaging for dosimetry and real time monitoring in boron neutron capture therapy

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***Abstract*—Boron Neutron Capture Therapy (BNCT) is an emerging radiotherapy technique that exploits the high neutron capture cross-section of ^{10}B to deliver targeted high-LET radiation to tumor cells while sparing surrounding healthy tissue. Effective clinical implementation requires accurate in vivo determination of boron concentration during treatment to enable precise dose monitoring. The i-TED Compton Camera Array, originally developed for high count-rate neutron-induced reaction measurements at CERN, offers promising capabilities for BNCT dose monitoring due to its low neutron sensitivity, high efficiency, and large field-of-view. We report on a series of experiments at the FIPPS beamline (ILL, France) to evaluate i-TED performance under progressively challenging background and count rate conditions, including borated water and hydrogen-rich environments mimicking clinical scenarios. Results show that while the system can identify the 478 keV gamma-rays from boron under realistic boron-to-hydrogen ratios, high count rates induce gain shifts that degrade low-energy gamma detection. Strategies to mitigate these effects, including optimized scintillator thicknesses and angular event selection, are proposed. These findings provide a clear path toward adapting i-TED for real-time BNCT dose monitoring in clinical environments.**

***Keywords* — Boron Neutron Capture Therapy, Compton Imaging, Dosimetry, Gamma-ray Imaging**

I. INTRODUCTION

Boron Neutron Capture Therapy (BNCT) is an experimental form of radiotherapy of growing interest in the last decade. It is based on the administration of a non-toxic, non-radioactive drug labelled with ^{10}B, which is selectively uptaken by cancerous cells. ^{10}B has a very large neutron capture cross-section, releasing an alpha particle and a ^{7}Li nucleus with high LET [1]. Therefore, a neutron irradiation of the patient after they have been injected with the boron compound is expected to damage or kill cancerous cells while sparing healthy tissues nearby. For this reason, BNCT has been proposed for amorphous and infiltrating tumors in critical organs, such as glioblastomas or head and neck cancers [2].

BNCT has experienced an expansion in recent years due to the development of accelerator-based neutron sources of enough intensity to provide treatment in clinical settings, which are now available in Japan as part of the National Health System, with other facilities under clinical trials in China, Korea and Finland. This has come together with the discovery of boron carriers of easy manufacturing and administration, low levels of toxicity and sufficient tumor-to-normal cell selectivity, such as BPA.

One of the major challenges still to be addressed in BNCT is the boron concentration determination during a treatment [3], which would enable an accurate dose monitorization and report, providing a strong support to the efficacy and safety of the treatments by allowing to reduce current margins applied to avoid damaging healthy tissues. Current methodologies are prone to inaccuracies and are based on several assumptions that propagate to large uncertainty levels. Several proposals have been suggested so far, particularly taking profit from the 478 keV gamma ray emitted in 94% of the boron neutron capture reactions. Those proposals are based on the SPECT [4, 5, 6] and the Compton imaging techniques [7, 8, 9]. In general, SPECT proposes devices with higher intrinsic resolution. However, the bulky designs with large collimators near the patient irradiation area generate secondary dose to the patient and increase significantly the background rate in the detectors, thereby reducing the sensitivity to 478 keV gamma rays and thus to boron concentrations much higher than those applied in clinical use [10]. Compton cameras, on the other hand, offer the advantage of a reduced volume, allowing to close the patient-to-detector distance, which in turn improves spatial resolution. This comes with the drawback of very large count rates, which could easily overwhelm the acquisition systems of the detectors when operating under nominal clinical conditions.

The i-TED Compton Camera Array, developed under the

HYMNS ERC project for neutron-induced reaction cross-section measurements of astrophysical interest at n_TOF (CERN) [11], is an excellent starting point for the development of a dose monitoring device for BNCT. This has also been proven by its application towards other medical applications such as in range verification in proton- and heavy-ion therapy [12, 13]. Due to its original design devoted to operating in high-count rate conditions in a very intense neutron radiation environment, which resembles that of a BNCT treatment, its low neutron sensitivity, high efficiency, and large field-of-view provide an outstanding candidate for this application [14].

In a recent campaign, we performed the first pilot tests of the use of i-TED for BNCT, by measuring small amounts of boron and generating images of the location of the boron neutron capture reaction in the FIPPS beamline at ILL (Grenoble, France). Those tests were performed in vacuum conditions and under a very low background environment, and were also used to measure the boron uptake of several cell lines of interest. [15]

The successful results from that pilot campaign have then been followed by a subsequent campaign which we have devoted to the identification of major challenges and elements for the improvement of this device towards its clinical application in BNCT, under the AMA ERC project.

II. Materials and Methods

The second experiment at ILL was focused on progressively exposing the i-TED to increasingly higher background and count rate conditions, in order to test its robustness and extract valuable input on key aspects to develop the next version of the camera, fully oriented and optimized for its use in BNCT.

The experiment was performed at the FIPPS beamline, in this case under free-air conditions, a neutron flux of 10^8 n/cm^{2}s in a pencil beam of 1.5 cm in diameter. The full array of four i-TED modules in cross-configuration was used to maximize detection efficiency, thus enabling 3D imaging reconstruction.

A varied set of different configurations was used, including, from teflon bags with a boron deposit (lowest background), and successively, petri dishes with a boron deposit, petri dishes filled with borated water, a polyethylene block with a petri dish inside; and finally, a water container, filled with clean and borated water, with the petri dish inside (highest background). Fig. 1. Shows some of those configurations.

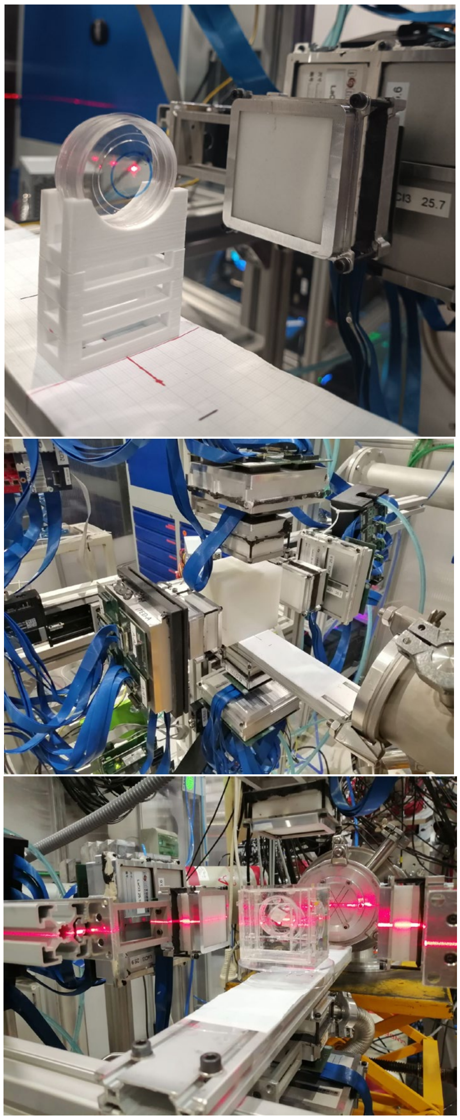

Fig. 1. Pictures from different setups used during the experiment at ILL used to analyze the performance of i-TED under progressively more challenging conditions in terms of background radiation. The *top* picture uses a 8 ml borated water dish, the *center* picture shows a polyethylene block, with one borated water dish inside, and the *bottom* picture shows a water container, also with a borated water dish inside.

Apart from that experimental campaign, another recent development is the implementation of a rotatory gantry, which enables the use of a single i-TED module for 3D image reconstruction with tomographic capabilities, and therefore minimizing the impact of the device in the treatment, both as a volume located near the patient that could reduce the positioning options, and also reducing the secondary neutron radiation redirected to the patient through scattering from the detector. This rotatory gantry, together with the List-Mode Maximum Likelihood Expectation Maximization (LM-MLEM) image reconstruction algorithm, developed by our group [14] have been recently validated by means of point-like gamma radiation sources, as shown in Fig. 2. An additional effort has been taken to optimize the performance of such algorithms by the use of parallelized algorithms, capable of being executed both in CPU and GPU architectures [16], leading to close to real-time data processing in the steps from data filtering to 3D image generation in the case of GPU.

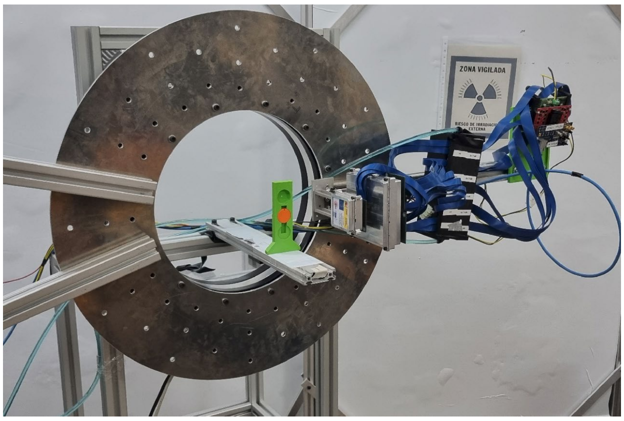

Fig. 2. Rotatory system used to validate the 3D imaging system with tomographic capabilities. One i-TED module and its electronic data acquisition system is coupled to the rotary gantry, and a counter-weight is added in the opposite side of the setup. A radioactive sample is located at the center of the field of view, along the rotation axis.

III. RESULTS AND DISCUSSION

The campaign at ILL provided a set of measurements with very valuable information regarding the challenges that a BCNT treatment poses to dose monitoring devices.

Those measurements were performed both with and without boron to test the sensitivity and background levels, and also check the impact of boron-related events in the overall count rate. Fig. 3. shows the add-back coincidence energy deposited spectra for those sets of measurements of increasing complexity. For the simplest cases (teflon bag and dry dish with extra shielding around the detectors, magenta and violet), count rates are low enough (<70 kHz) that pileup and dead time effects do not affect the acquisition. In general, the spectra are dominated by the events produced by boron (478 keV), present both in the environment (due to boron-based neutron absorbers in the walls of the experimental hall and the beam dump), and particularly the 2.224 keV gamma-rays generated by neutron captures in hydrogen. This contribution dominates the spectra once any hydrogen-rich material is introduced to the beam, namely water or polyethylene present inside or around the dishes. In the experiment, the amounts of hydrogen relative to boron were kept as similar as possible as in an actual treatment, in order to keep a reliable signal to background ratio. For that reason, boron concentrations of 65 and 100 ppm of ^{10}B were used, which are typical low and high boron concentrations inside the tumors.

Once the additional shielding was removed (cyan), the overall count rates go over 100 kHz and pileup starts to be noticeable as a soft increase in the high energy tail of the spectrum.

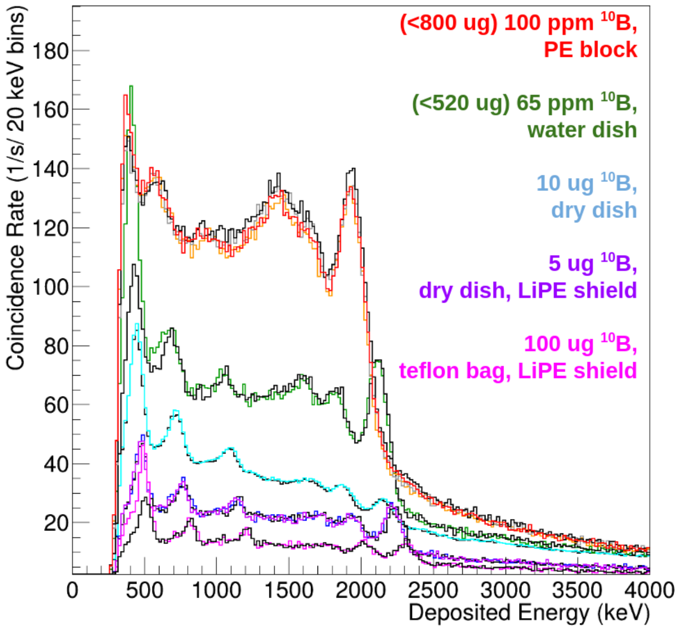

Fig. 3. Add-back coincidence deposited energy spectra obtained under increasingly higher background and count rate conditions, from a small teflon bag holding 100 μg of ^{10}B, to a dry dishes with small amounts of 10B deposited on it, with and without an extra neutron shielding; with a borated water dish and with an additional polyethylene block around it. Black lines corresponding to each of the colour ones, refer to the equivalent measurement without boron in the sample, thus acting as dummy or reference measurement for each configuration.

Moreover, a shift in the estimated energy deposited starts to appear evident, which further worsens as the conditions become harsher. A linear relation between the observed count rate and the energy shift of the peaks is clearly observed, with a similar trend for all deposited energies, as can be noticed both for the 478 and 2224 keV lines.

That fact requires special attention for boron imaging, since that gain shift hinders the detection of low energy gamma rays, in particular if they fall below the detection threshold. This is crucial in the case of the signal detected in the scatterer crystal, where typically the energy deposited is lower. In our case, once we reach 250 kHz, that gain shift is so large that the boron peak is not observed anymore. This occurred, with our detection settings, still far from the maximum expected acquisition count rate achievable by the PETsys electronics, around 500-600 kHz.

On the plus side, at the highest count rate for which 478 keV gamma-rays are still observed, our detection system is clearly capable of identifying the 478 keV gamma rays coming from the boron sample over the background (green line). Those conditions, though not to the level of beam intensity and count-rates, do more or less match the expected boron to hydrogen concentration ratios in the tumor and nearby tissues, which ensures an adequate sensitivity level for our detector, once the count rate and related issues are removed.

These observations summarize a strong influence of high count rates on the performance of the detectors, and therefore a series of strategies need to be applied to upgrade i-TED towards BNCT use in clinical environments.

The use of thinner scintillator crystals is a key aspect to reduce the count rates and their related effects. In particular, by changing the nominal 15 mm and 25 mm thicknesses of scatterer and absorber crystals to 6 mm and 10 mm, respectively, the total count rate can be reduced by a factor of 3, while maintaining or even improving the coincidence to overall count rate ratio. This means that the detector is more efficient at identifying coincidence events, even if the total count rate reduces. A second aspect of this thickness reduction is particularly relevant to the scatterer. The total energy deposited in the scatterer is usually smaller than to the absorber, and often, for small scattering angles, this deposited energy falls below the detection threshold. Thinner crystals allow to reduce the value of that detection threshold, as our previous studies with scintillators of various thicknesses have shown. Additionally, this reduction of the scatterer detection angle enables yet another signal enhancement technique, related to back-scattering events (those in which the original gamma ray scatters in the absorber detector and then is absorbed at the scatterer, which cannot be distinguished by timing due to the short distance between the two events). For 478 keV gamma rays, the back-scattering events usually are mixed with events coinciding with forward scatterings of 60-70º. Therefore, if low energy deposited events can be detected, and therefore many low angle scattering coincidences can be used for imaging, then by rejecting all events above 60º and only keeping those with lower reconstructed angles, the signal-to-background ratio greatly improves, by removing artifacts usually observed in tangential sides of the reconstructed images generated from misidentified back-scattering events.

IV. Conclusions

The experimental campaigns at ILL have tested the feasibility of using the i-TED Compton Camera for detecting the 478 keV gamma rays from ^{10}B neutron capture under conditions approaching those of a clinical BNCT treatment. The device exhibits adequate sensitivity to clinically relevant boron concentrations even in hydrogen-rich environments, provided that count rate–induced gain shifts are mitigated. Our observations highlight the critical impact of high count rates on spectral stability and low-energy gamma detection, which must be addressed to ensure robust imaging performance. Reducing scintillator crystal thicknesses offers a practical means to lower total count rates, improve coincidence efficiency, and enable enhanced signal-to-background discrimination through optimized angular filtering. Together with the integration of a rotatory gantry and real-time image reconstruction algorithms, these upgrades position i-TED as a strong candidate for BNCT dose monitoring systems. Future work will focus on implementing these design changes and validating their performance under full-intensity, clinically relevant neutron irradiation conditions.

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