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ASSESMENT OF BORON NEUTRON CAPTURE THERAPY (BNCT): COMPACT NEUTRON GENERATORS

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Abstract Boron Neutron Capture Therapy (BNCT) is an effective and promising treatment of tumour types which are resistant to conventional therapies. The characteristics of boron neutron capture therapy (BNCT) for cancer treatment demand, in addition to sufficient fluxes of epithermal neutrons, proper conditions of the neutron sources—compact layout, flexible operation, compatibility with hospital setting, etc. The lack of proper neutron sources that can be applied to the infrastructure of hospital or clinical facilities is a major problem. Compact neutron generators (CNGs), which are the most compact and least expensive, were a potential, alternative, solution to existing BNCT treatment facilities based on nuclear reactors. This paper will provide information about the latest CNGs technology development that has contributed to the Boron Neutron Capture Therapy (BNCT) technology improvement.

Keywords BNCT, CNGs, Neutron Sources, Cancer Treatments

INTRODUCTION

Boron Neutron Capture Therapy (BNCT) is a very promising treatment for patients suffering from glioblastoma multiform, an aggressive type of brain cancer, where conventional radiation therapies fail (Fantidis, J.G., et.al. 2013). Boron neutron capture therapy (BNCT) which bases a cancer treatment on the neutron-capture reaction of $^{10}B(n,D)^{7}Li$ is by far the most researched modality among all the possible neutron-capture therapeutic processes.

BNCT is a binary treatment modality, first a ^{10}B compound is delivered to the patient and is accumulated differently in cancer cells than healthy tissue; then, when a high boron concentration ratio between tumor and healthy issue is reached, the patient is irradiated with neutrons inducing the $^{10}B(n,\alpha)^{7}Li$ reaction. The alpha particle emitted and the ^{7}Li nuclei created have high Linear Energy Transfer (LET), and an associated high Relative Biological Effectiveness (RBE) α particle, ≈150 keV/μm and ≈175 keV/μm for ^{7}Li ion (Moss, R.L., 2014). The mean free path is about 7 μm and 4 μm for α particle and for ^{7}Li, respectively (Fantidis, J.G., et al., 2013; Fantidis J.G., and Antoniadis A. 2015). Hence their energy deposition is limited to the diameter of a single cell. Therefore, it is possible to selectively irradiate cancer cells that have taken up a sufficient amount of 10B, while simultaneously sparing normal, healthy cells (Moss, R.L., 2014).

Clearly, BNCT is a complex, multidisciplinary enterprise, encompassing the fields of neutron sources, pharmaceuticals, medical imaging, radiobiology, and clinical planning and implementation. In spite of a long history of research first conceived in 1930s and of experimentation in early 1950s, progress of BNCT so far has fallen behind the photon- and ion-beam therapies in practical prevalence and treatment scope. For example, preclinical trials and treatments to date have taken place only at improvised neutron-delivery stations at fission-reactor sources that are not entirely devoted to medical purposes. Only two ^{10}B-carrying drugs have been approved for treating head and neck cancers. The lack of proper neutron sources that can be integrated to the infrastructure of hospital or clinical facilities is a major problem (Loong, C.-K., et.al. 2014).

A compact neutron source based on $^{2}H(d,n)^{3}He$ (D-D) or the $^{3}H(d,n)^{4}He$ (D-T) fusion reactions yielding 2.45 MeV and 14.1 MeV neutrons, respectively, has been suggested for BNCT use. These reactions have positive Q values and thus, low bombarding energy is required in comparison to the other neutron-producing reactions. The fusion neutron source is compact in size and also safe for hospital use. The fusion-based neutron sources are commercially available. Such neutron sources used to be very common in neutron research facilities and at universities, and thus, the technology required is well known. (Koivunoro, H. 2012). A CNG accommodates the ion source, electron shield, acceleration structure and a target in a single housing. Thus they are substantially smaller and less expensive than accelerators/reactors. (Loong, C.-K., et.al.). The drawback is the production of fast neutrons at considerably lower neutron fluxes. The modern target uses a deuterium (D^+) or tritium (T^+) absorbing material such as titanium backed by liquid cooled copper. The titanium readily absorbs the D^+ or T^+ ions forming a titanium hydride. Succeeding D^+ or T^+ ions strike these embedded ions and fuse, resulting in (d,d), (T,d) or (t,t) reactions and releasing fast neutrons. (Loong, C.-K., et.al. 2014)

2. MATERIALS AND METHODS

2.1 Compact Neutron Generators

Compact NGs are becoming an attractive alternative to nuclear reactors and radioactive neutron sources in a variety of fields of neutron science, medical research and various material analysis applications. Traditionally compact NGs have been used in oil well logging industry, using DT fusion reaction for high energy 14 MeV neutron production. These NGs generate DT neutron yield in the range of 10^8 to 10^{11} n/s. There are yet others, which are made by universities or national laboratories, like VNIIA made generators (sold in US by Del Mar Ventures) and Lawrence Berkeley National Laboratory's Plasma and Ion Source Technology Group (generators commercialized by Adelphi Technology Inc.) (Anonim A., 2012)

The Plasma and Ion Source Technology Group (P&IST) at the E.O. Lawrence Berkeley National Laboratory has been developing high power DD NGs for various applications. These NGs are differentiated from the commercial manufacturers mainly by the method by which the plasma is generated and by the use of DD, instead of DT, fusion reaction (Anonim A., 2012). Those two kinds of Compact Neutron Generators will be the main focus in this article.

The information gathered about the CNGs development progress were based on the last 5 years of research which were made possible and affordable through Universitas Gadjah Mada direct access.

3. RESULTS AND DISCUSSION

Both D-D and DT CNGs have advantages and disadvantages. These challenges triggered scientists and engineers to develop the technology. The latest are shown below.

3.1 D-D Compact Neutron Generators

An extensive set of calculations performed with MCNP4B Monte Carlo code in 2013 have shown that the combination of TiF_3 which integrates a conic part made of D_2O, then followed by a TiF_3 layer is the optimum moderator design. The use of BiF_3 as spectrum shifter and γ rays filter, Titanium as fast neutron filter and Lithium as thermal neutron filter is necessary in order to obtain an epithermal neutron beam with high quality. The materials considered for the design of the facility, were chosen according to the EU Directive 2002/95/EC, hence, the use of cadmium and lead was excluded. The simulations show that, even if the neutron flux is below the recommended value for clinical treatment, the proposed facility is a good alternative for clinics which cannot afford to build and maintain a small nuclear reactor. (Fantidis, J.G., et.al. 2013).

In the same year optimization of the Beam Shaping Assembly (BSA) has been performed using the MCNP4C Monte Carlo code in Iran to shape the 2.45 MeV neutrons that are produced in the D–D neutron generator. Optimal design of the Beam Shaping Assembly (BSA) has been chosen by considering in-air figures of merit (FOM) which consists of 70 cm Fluental as a moderator, 30 cm Pb as a reflector, 2 mm ^{6}Li as a thermal neutronfilter and 2 mm Pb as a gamma filter. The neutron beam can be evaluated by in-phantom parameters, from which therapeutic gain can be derived. Direct evaluation of both set of FOMs (in-air and in-phantom) is very time consuming. In this research a Response Matrix (RM) method has been suggested to reduce the computing time. This method is based on considering the neutron spectrum at the beam exit and calculating contribution of various dose components in phantom to calculate the Response Matrix. Results show good agreement between direct calculation and the RM method. (Kasesaz, Y., et.al. 2013)

3.2 D-T Compact Neutron Generators

A Boron Neutron Capture Therapy (BNCT) facility based on a DT neutron generator was optimized by designing the beam-shaping assembly. With the aim of the MCNP4B Monte Carlo code different beam-shaping assembly (BSA) configurations were considered. Lead was selected as reflector material while CF_2, D_2O, Fluental, PbF_4, PbF_2, BiF_3, BiF_5, MgF_2, Al_2O_3, AlF_3, TiF_3, BeD_2, CaF_2 and ^{7}LiF were examined as spectrum shifters. In order to improve the quality of the beam titanium, nickel-60, iron and titanium alloy ($Ti_6Al_{14}V$) were simulated as fast neutrons filters while lead and bismuth were considered as gamma filters. An extensive set of calculations performed with MCNP4B Monte Carlo code have shown that the combination of ^{7}LiF which accommodates a conic part made of

D_2O, then followed by a TiF_3 layer is the optimum moderator design. The use of three different materials for further reduction of fast neutrons, thermal neutrons and gamma rays is necessary. ^{60}Ni, Cd and Bi were chosen respectively for these purposes. The epithermal neutron flux obtained at the beam exit window turned out to be 3.94×10^{9} n cm^{-2} s^{-1} while fulfilling all the recommended IAEA in- air Figure of Merit (FOM) criteria. The assessment of the dose profiles in head phantom and the in- phantom FOM are also presented. The proposed assembly configuration may provide an attractive option for centers wishing to install a BNCT facility (Fantidis J.G., et.al. 2015).

Rasouli and Masoudi designed The BSA for optimization in 2011 and continued in 2014 to simulate many configuration material for BSA. The results show that considering these limits together with the widely accepted IAEA criteria makes it possible to have a more realistic assessment of sufficiency of the designed beam. Satisfying these criteria not only leads to reduction of delivered dose to skin, but also increases the advantage depth in tissue and delivered dose to tumor during the treatment time. Other research of evaluation of BSA design of DD CNGs that had been designed by Rasouli and Masoudi in 2012 were conducted in Thailand. Three BSA designs based on the D-T reaction for BNCT are discussed. It is found that the BSA configuration designed satisfies all of the International Atomic Energy Agency (IAEA) criteria. It consists of 14 cm uranium as multiplier, 23 cm TiF_3 and 36 cm Fluental as moderator, 4 cm Fe as fast neutron filter, 1 mm Li as thermal neutron filter, 2.6 cm Bi as gamma ray filter, and Pb as collimator and reflector. It is also found that use of specific filters is important for removing the fast and thermal neutrons and gamma contamination (Asnal M, et al. 2014).

The feasibility of boron neutron capture therapy (BNCT) for liver tumor with four sealed neutron generators as neutron source had been researched. Two generators are placed on each side of the liver. The high energy of these emitted neutrons should be reduced by designing a beam shaping assembly (BSA) to make them useable for BNCT. However, the neutron flux decreases as neutrons pass through different materials of BSA. Therefore, it is essential to find ways to increase the neutron flux. The feasibility of using low enrichment uranium as a neutron multiplier is investigated to increase the number of neutrons emitted from D-T neutron generators. The neutron spectrum related to our system has a proper epithermal flux, and the fast and thermal neutron fluxes comply with the IAEA recommended values. Four generators are used at the same time to form a yield of 4×10^{11} n/s and two generators are placed on each side of the liver. A beam shaping assembly for BNCT is designed based on the use of low enrichment uranium as multiplier system for D–T neutron source. According to our results, a 20 cm thickness of AlF3 as the first moderator and a 22 cm thickness of fluent is the best option for the moderator to achieve a proper epithermal neutron flux. The study of the beam quality shows that using a layer of thin ^{6}LiF filter to remove thermal neutrons and Bi to reduce gamma contamination is necessary to meet the free beam port parameters by IAEA (Zheng Liu, et.al. 2014).

4. CONCLUSION

Much of the research that has been conducted in the last 5 years major was to explore about increasing the configuration materials for BSA in order to meet the IAEA recommendation of neutron output which will be used for treatment and reducing unuseful output. The other studies related to BNCT are still in progress, such as dosimetry, detection and protection radiation, nuclear security, economic aspect, and affordability for hospital to install this facility. Comprehensive research is still required to make this technology feasible to install and sustain. In other words, Indonesia still has a wide opportunity to conduct more research in order to contribute and improve this advanced cancer therapy.

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