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Production of epithermal neutron beams for BNCT

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Abstract

The use of boron neutron capture therapy (BNCT) for the treatment of deep-seated tumors requires neutron beams of suitable energy and intensity. Simulations indicate the optimal energy to reside in the epithermal region, in particular between 1 and 10 keV. Therapeutic neutron beams with high spectral purity in this energy range could be produced with accelerator-based neutron sources through a suitable neutron-producing reaction. Herein, we report on different solutions that have been investigated as possible sources of epithermal neutron beams for BNCT. The potential use of such sources for a hospital-based therapeutic facility is discussed. © 2002 Elsevier Science B.V. All rights reserved.

1. Introduction

BNCT is a two-component therapeutic modality currently considered for the treatment of a number of malignant tumors resistant to other chemo- and radiotherapeutic methods. In particular, this kind of hadrontherapy could reveal useful in the treatment of Glioblastoma Multiforme (GBM), an aggressive type of brain cancer [1]. The method is based on the radiation damage produced by high LET particles emitted in the ^{10}B neutron capture reaction ^{10}B(n,α)^{7}Li. To obtain a high tumor control probability with minimal collateral effects on healthy tissues, an adequate concentration of ^{10}B has to selectively accumulate in the tumor cells by means of specific borated compounds. The patient is then irradiated with neutron beams of energy and intensity suitably chosen so that a maximum density of thermal neutrons is reached in the proximity of the tumor area.

Clinical BNCT trials are currently undergoing at nuclear reactors; however, the development of high intensity accelerators could lead to high-quality, safe, and cost-effective epithermal neutron sources for BNCT (see for example Ref. [2]). In fact, compared to nuclear reactors, accelerator-based sources may allow to produce epithermal neutron beams with higher spectral purity and lower contamination of γ-rays, and the use of low-energy accelerators may enable the operation of BNCT facilities in metropolitan areas.

We report on a study of different neutron producing reactions that could be used in conjunction with high-current accelerators, to produce epithermal neutron beams for BNCT. The main features of the reactions and the requirements of the primary particle beam are presented and discussed, in particular, regarding the potential use of such sources in hospital-based BNCT facilities.

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2. Optimal energy of therapeutic neutrons

The optimal energy of a neutron beam for the treatment of deep-seated tumors can be investigated by means of simulations of the dose deposition in tissues. To this end, we have used the GEANT/Micap package [3]. A realistic description of the geometry and of the head composition was used, with a tumor region located at 5 cm depth inside the brain. In the simulations, ^{10}B was specifically included in normal and tumor tissues, in concentrations of 10 and 43 parts-per-million respectively. These loading are typical of BPA, a ^{10}B-carrier currently used in clinical trials. RBE values of 1.6 and 2.3 were chosen for protons and α-particles, respectively.

The quality of the neutron beam was assessed by analyzing several figures of merit of the simulated dose distribution, as a function of the neutron energy. Fig. 1a shows the therapeutic gain (TG), defined as the ratio between the dose released to the tumor and the maximum dose to normal tissues, for a tumor depth of 5 (solid symbols) and 8 cm (open symbols). One observes that the optimal neutron energy for the considered tumor location and ^{10}B concentration is between 1 and 10 keV. Neutrons of lower energy thermalize at depths smaller than the tumor location, while for higher energies, recoiling protons lead to a sharp increase of the dose released to the normal tissues, in particular, to the skin and at the brain surface. The depth-dose profile in brain is shown in Fig. 1b for a 4 keV neutron beam.

Although monoenergetic neutron beams with energies of 1–10 keV cannot be readily produced, one should try to approach such a condition in order to optimize the therapeutic effect. In the case of reactor-based sources, the energy distribution of the neutron beam can be optimized by an appropriate choice of the material and geometry of the beam shaping assembly. A large improvement in the quality of the epithermal neutron beam could be achieved by using an accelerator and a suitable proton- or deuteron-induced reaction for neutron production. The choice of the beam energy and of the target is mainly dictated by the need of a high yield of low-energy neutrons ($E_n < 1$ MeV), and a small contamination of high-energy neutron and γ-rays. Furthermore, the size and cost of the accelerator could be minimized by choosing a low energy for the primary beam, while the target should present good mechanical and thermal properties. Finally, a stable residue should be produced in the reaction, to reduce safety problems associated with storage and disposal of the targets.

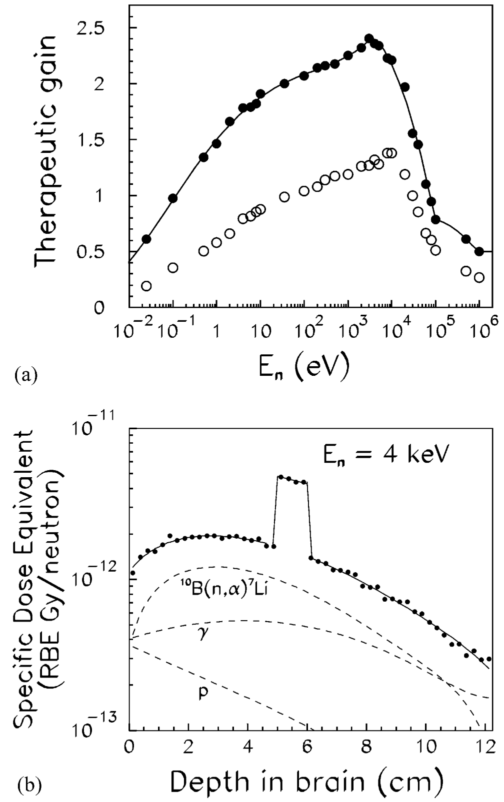

Fig. 1. (a) Ratio between the BNCT dose released to tumor and the maximum dose to normal tissues as a function of neutron energy. (b) Depth-dose distribution in the brain for a neutron beam of 4 keV energy. The symbols represent the total dose, while the dashed curves depict the partial doses produced by the various reactions occurring in biological tissues (n–p elastic scattering, the ^{1}H(n,γ)^{2}H, the ^{14}N(n,p)^{14}C and the ^{10}B(n,α)^{7}Li capture reactions).

Several approaches can be used in the choice of the primary beam energy and conversion target. Various proposed solutions rely on the use of the ^{7}Li(p,n)^{7}Be reaction at energy $E_p \sim 2.5$ MeV or on the ^{7}Be(p,n)^{7}B reaction at $E_p > 3$ MeV [4,5]). For these reactions, the proton beam current needed to produce neutron fluences adequate for the therapy ranges from 1–30 mA, depending on the required quality of the therapeutic neutron beam. The use of the Li(p,n) reaction, however, is complicated by the low melting point of the target (170°) and by the production of the radioactive ^{7}Be residue. On the other hand, the Be target is useful only at a relatively higher proton energy. For this reason, alternative approaches for the production of epithermal neutrons are being investigated.

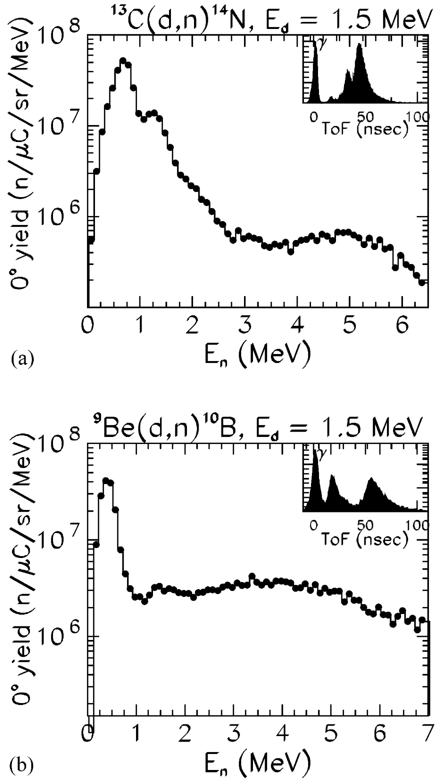

Fig. 2. Efficiency-corrected energy spectrum and time-of-flight distributions (inside panel) of neutron emitted in the ^{13}C(d,n)^{14}N (panel a) and ^{9}Be(d,n)^{10}B reactions (panel b), at an incident energy of 1.5 MeV. The threshold on the light output of the scintillator cells was kept to 10 keV electron-equivalent, corresponding to a neutron energy threshold of 100 keV.

3. Neutron-producing reactions at low energy

A promising approach is represented by (d, n) reactions at low energy. Most of these reactions present a positive Q-value, which in principle allows for the use of deuteron beams of energy as low as 1 MeV. To investigate the feasibility of this latter approach, we have performed a systematic study of the yield, energy and angular distribution of neutrons emitted in low-energy (d, n) reactions [6]. The measurements were performed at the 88″ Cyclotron of Lawrence Berkeley National Laboratory, USA, in collaboration with groups from the Nuclear Science and Life Science Divisions of LBNL. The setup used in the measurements consisted of five liquid scintillator cells, with n/γ discrimination properties and a minimum threshold of 100 keV on the neutron energy, reconstructed by time-of-flight relative to the cyclotron RF. Among the different targets investigated at deuteron energies $E_{\mathrm{d}} < 2$ MeV, only ^{9}Be and ^{13}C present a yield sufficiently high to be of interest for the production of epithermal neutrons for BNCT, with the Be target producing neutrons almost a factor of 2 greater than that produced by ^{13}C. Fig. 2 shows the energy distribution and TOF spectrum for both targets. Due to the large contamination of high energy neutrons, the ^{9}Be(d,n) reaction does not produce epithermal neutrons with the intensity and spectral characteristics adequate for BNCT. On the contrary, the relatively large-yield and low-contamination of high-energy neutrons make the ^{13}C(d,n)^{14}N reaction at $E_{\mathrm{d}} = 1.5$ MeV potentially interesting for a hospital-based facility, thanks also to the good thermal and mechanical properties of the C target and the low-energy of the primary beam, which would result in a relatively simple and inexpensive accelerator. The solid histogram in Fig. 3 represents the spectrum of epithermal neutrons that would be produced by the ^{13}C(d,n)^{14}N reaction with a moderator of LiF 25 cm thick, a reflector of Al_2O_3, a delimiter of lithiated polyethilene and an ^{6}Li layer for thermal neutron filtering. The current required for a treatment time of 15 min was estimated for this reaction to be around 100 mA, a value within reach of the high-intensity accelerator technology currently being developed.

Finally, a class of suitable neutron sources is represented by the near-threshold reactions. In this case, the low-yield of neutrons is compensated by

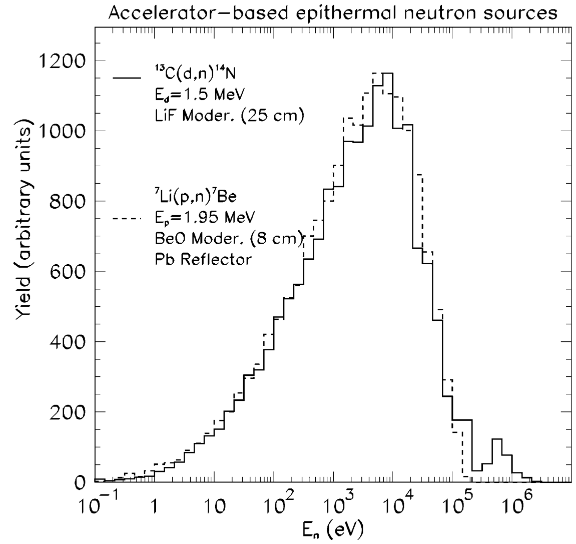

Fig. 3. Epithermal neutron energy spectra produced with the $^{13}C(d,n)^{14}N$ and the near-threshold $^7Li(p,n)^7Be$ reactions. The optimal beam shaping assembly used for each reaction is indicated.

their low-energy permitting moderation for clinical application. The dashed histogram in Fig. 3 shows the epithermal neutron spectrum that can be produced with the ^{7}Li(p,n) reaction at 1.95 MeV, and with a beam shaping assembly comprised of 8 cm thick BeO and a Pb reflector. The use of this reaction requires an estimated proton beam current of 5 mA. Such an intense beam could become feasible with commercial accelerators or with the high-current RFQs like the one presently being developed at the INFN Laboratori Nazionali Legnaro within the TRASCO project.

In conclusion, among the different reactions studied, the ^{13}C(d,n) and the near-threshold Li(p,n) reactions represent, in our opinion, the most interesting solutions for a hospital-based BNCT facility. This is due in part to the relatively low-cost and small-size of the accelerator. Before high-intensity accelerators become available, however, higher-energy reactions might more conveniently be used in conjunction with the presently available research accelerators, to produce neutron beams for in vitro or animal studies on BNCT.

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