Tehran Research Reactor as a Neutron Source for Boron Neutron Capture Therapy in Iran: A Cancer Treatment Plan for Future

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Abstract**—**In cancer treatment it is required that most of the cancer cells to be destroyed, either by the treatment itself or with the help from the body's immune system. Although today's standard treatments - surgery, radiation therapy and chemotherapy - have successfully cured many kinds of cancers, there are still many treatment failures. A new experimental cancer therapy called boron neutron capture therapy (BNCT) now has been fascinated many scientists to study and apply this technique in the field of cancer treatment particularly brain and skin tumors. BNCT is a binary radiation therapy modality that brings together two components that when kept separate have only minor effects on cells. The first component is a stable isotope of boron (boron-10) that can be concentrated in tumor cells by attaching it to tumor seeking compounds. The second is a beam of low-energy neutrons. Boron-10 in or adjacent to the tumor cells disintegrates after capturing a neutron and the high energy heavy charged particles produced destroy only the cells in close proximity to it, primarily cancer cells, leaving adjacent normal cells largely unaffected. In this technical review, we discuss BNCT and its use for cancer treatment in Iran and planning for future application of BNCT in clinical approach.

Keywords— BNCT, Iran, Future.

I. Introduction

NEUTRON capture therapy (NCT) is a noninvasive therapeutic modality for treating locally invasive malignant tumors such as primary brain tumors and recurrent head and neck cancer. All of the clinical experience to date with NCT is with the non-radioactive isotope boron-10, and this is known as boron neutron capture therapy (BNCT). The potential efficacy of BNCT has led many scientists to work on an this area[1],[2] .

BNCT is a binary radiation therapy modality that brings together two components that when kept separate have only minor effects on cells. The first component is a stable isotope of boron (boron-10) that can be concentrated in tumor cells by attaching it to tumor seeking compounds. The second is a beam of low-energy neutrons. Boron-10 in or adjacent to the tumor cells disintegrates after capturing a neutron and the high energy heavy charged particles produced destroy only the cells in close proximity to it, primarily cancer cells, leaving adjacent normal cells largely unaffected.

BNCT can be performed at a facility with a nuclear reactor or at hospitals that have developed alternative neutron sources. A beam of epithermal neutrons penetrates the brain tissue or other tissues, reaching the malignancy. Once there the epithermal neutrons slow down and these low-energy neutrons combine with boron-10 (delivered beforehand to the cancer cells by drugs or antibodies) to form boron-11, releasing lethal radiation (alpha particles and lithium ions) that can kill the tumor [1] (Fig. I).

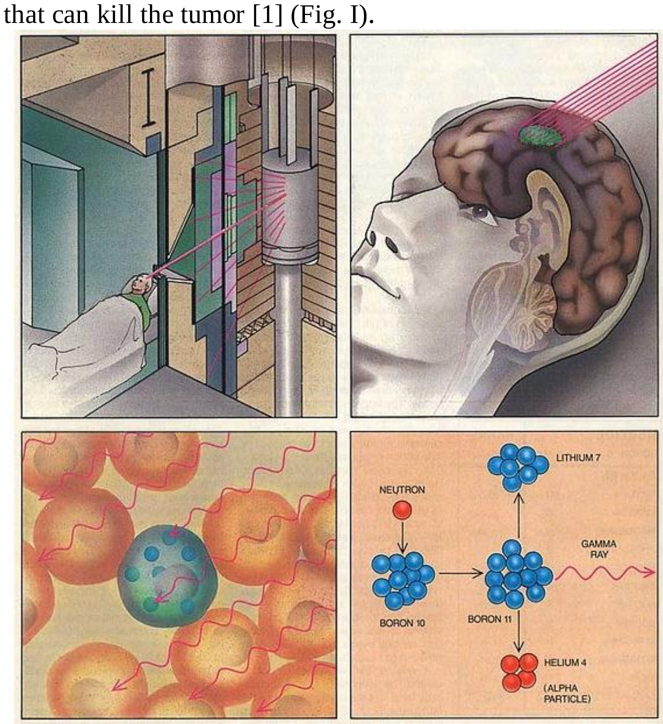

Fig. 1.

Clinical interest in BNCT has focused primarily on the treatment of high-grade gliomas and either cutaneous primaries or cerebral metastases of melanoma, most recently, head and neck and liver cancer. Neutron sources for BNCT currently have been limited to specially modified nuclear reactors, which are or until the recent Japanese natural disaster, were available in Japan, United States, Finland and several other European countries, Argentina and Taiwan. Accelerators also can be used to produce epithermal neutrons and these are being developed in several countries, but none

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are currently being used for BNCT [3], [4]. Over the past 25 years research on boron neutron capture therapy (BNCT) has progressed relatively slowly but steadily with the greatest progress in the field of clinical studies. These specifically have included the use of BNCT to treat a variety of malignancies other than high grade gliomas and melanomas. However, there are a number of key areas where little, if any, significant progress has been made [5].

Boron neutron capture therapy (BNCT) theoretically allows the preferential destruction of tumor cells while sparing the normal tissue, even if the cells have microscopically spread to the surrounding normal brain. The tumor cell-selective irradiation used in this method is dependent on the nuclear reaction between the stable isotope of boron ((10)B) and thermal neutrons, which release alpha and (7)Li particles within a limited path length (-9 microm) through the boron neutron capture reaction, (10)B(n,alpha)(7)Li. Recent clinical studies of BNCT have focused on high-grade glioma and cutaneous melanoma; however, cerebral metastasis of melanoma, anaplastic meningioma, head and neck tumor, and lung and liver metastasis have been investigated as potential candidates for BNCT. To date, more than 350 high-grade gliomas have been treated in BNCT facilities worldwide. Current clinical BNCT trials for glioblastoma (GBM) have used the epithermal beam at a medically optimized research reactor, and p-dihydroxyboryl-phenylalanine (BPA) and/or sulfhydryl borane Na(2)B(12)H(11)SH (BSH) as the boron delivery agent(s) [6].

However, the first BNCT trials took place in the USA in the early 1960's, BNCT is still far from mainstream medicine. Nonetheless, in recent years, reported results in the treatment of head and neck cancer and recurrent glioma, coupled with the progress in developing linear accelerators specifically for BNCT applications, have given some optimism to the future of BNCT [7]

II. BNCT In Iran

The first studies in Iran to establish BNCT Center occurred according to studies carried out in Atomic Energy Organization of Iran. In the first step a filter composed of tandemly aluminum and iron plates were embedded in the reactor canal in which neutron A particles were released. Figure I represents neutron channel in Tehran Research Reactor system [8].

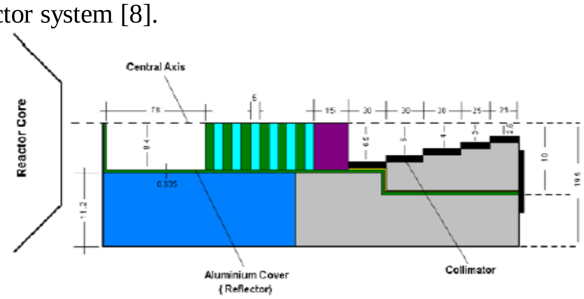

Fig. 1. Neutron Channel In Tehran Research Reactor System

However, in recent research plans, use of uranium plates have been studied to establish BNCT according to other studies carried out in drug research reactors [9].

Performing successful BNCT experiments needs a suitable neutron source. Important factors of the neutron beam are flux and energy that are very important in the selection of neutron source. In most centers that use this method for treatment, reactor is a neutron source, which according to characteristics of the reactor appropriated neutrons are very high. High cost of constructing a BNCT center with using of reactor caused seeking other sources such as accelerator indirectly and radioisotope source directly that each has their own advantage and disadvantages. There is a study in Iran in which an analysis Am-Be neutron source, using neutron filter technique and suitable moderators have been investigated. The advantages of Am-Be neutron source are being inexpensive, easy portability, small size and well-designed shields. Figure II represents the proposed model for filters are to be used in Am-Be neutron source [10].

Fig. 2. The Materials Position To Am-Be Neutron Source.
1= Am-Be Neutron Source, 2= Alumin Oxide, 3= Graphite, 4= Titanium And 5= Cadmium.

Recently a neutron system for BNCT was also proposed. The system includes ^{252}Cf neutron source, neutron moderator/reflector arrangement, filter and concrete. To capture fast neutrons, different neutron filters Fe, Pb, Ni and PbF2 with various thicknesses were simulated and studied. Li (with 1 mm thick) was used for filtering of thermal neutrons. Bi with thickness of 1 cm was used to minimize the intensity of gamma rays. Monte Carlo simulation code MCNPX 2.4.0 was used for design of the neutron system and calculation of the neutron components at the output port of the system [11].

In other study investigation on the use of the Tehran Research Reactor (TRR) as a neutron source for Boron Neutron Capture Therapy (BNCT) has been performed by calculating and measuring energy spectrum and the spatial distribution of neutrons in all external irradiation facilities, including six beam tubes, thermal column, and the medical room. Activation methods with multiple foils and a copper wire have been used for the mentioned measurements [12].

In contrast to rapid development of BNCT in the area of cancer treatment in several countries, in Iran, the application of BNCT in cancer treatment is in its infancy. We are also planning to investigate feasibility of Tehran Research Reactor as a neutron source for BNCT in Iran in the following areas:

1. Using BNCT for patients with brain, head or neck cancers

2. Using BNCT for cellular research by exposing cancer cell cultures to boron neutron source and follow up the cellular toxicity or gene expression

III. Conclusion

Since clinicians and physicists at several Research Centers have treated a large number of patients with malignant gliomas and head and neck cancer, and since BNCT is a promise for eradicating tumors in patients with cancer, it is of importance to develop such system in Iran as a country facing a considerable cancerous cases who need promising treatment.

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