A Deuterium-Deuterium Neutron Generator-Based Neutron Capture Therapy System for Brain Tumors

Mindy Hsieh Joo

Purdue University
A DEUTERIUM-DEUTERIUM NEUTRON GENERATOR-BASED BORON NEUTRON CAPTURE THERAPY SYSTEM FOR BRAIN TUMORS

by

Mindy Hsieh Joo

A Dissertation
Submitted to the Faculty of Purdue University

In Partial Fulfillment of the Requirements for the degree of

Doctor of Philosophy

School of Health Sciences
West Lafayette, Indiana
August 2018
THE PURDUE UNIVERSITY GRADUATE SCHOOL

STATEMENT OF COMMITTEE APPROVAL

Dr. Linda H. Nie, Chair

School of Health Sciences

Dr. Shuang Liu

School of Health Sciences

Dr. Jean M. Plantenga

Department of Veterinary Clinical Sciences

Dr. Keith Stantz

School of Health Sciences

Approved by:

Dr. Jason Harris

Head of the Graduate Program
To my husband

For being patient, supportive, and loving

Through all the ups and downs

To my son

For changing my life completely

And making me a stronger and better person
ACKNOWLEDGMENTS

First and foremost, I would like to express my deepest appreciation to my Major Professor, Dr. Linda Nie, for her endless support, guidance, and patience throughout my years at Purdue. Dr. Nie leads by example and sincerely cares about her students’ well-being. I have learnt a great deal from her just by observing her thinking process and actions. On the academic level, Dr. Nie taught me the fundamentals of conducting scientific research, problem solving, and innovative thinking. On a personal level, Dr. Nie inspired me by her integrity and passionate attitude. Dr. Nie is a role model that I hope to become in the future.

I am also grateful to my Advisory Committee members, Drs. Shuang Liu, Jean Plantenga, and Keith Stantz, for taking time from their busy schedule to help with this research. Their invaluable advice and critiques have made substantial impact on this work. I am thankful for the various insights and expertise they brought that improved my research greatly.

Last but not least, I would like to thank my past and current colleagues in the Nie laboratory. It has been my honor to have met and worked with all of them. Together they created such a pleasant and enjoyable atmosphere in and outside the lab and were always willing to help each other out. I could not have asked for a better learning environment than what I have experienced at Purdue.
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Boron neutron capture therapy (BNCT) is an attractive radiotherapy modality that utilizes high-LET particles to deliver the radiation dose. Different from conventional treatments, BNCT has the ability to target tumor cells by injecting patients with a boron-10 (B-10) compound that selectively accumulates inside the tumor and irradiating the target area with a neutron beam. The radiation dose produced is very localized due to the short travel range of the resulting particles and limited to the B-10 containing cells. The surrounding healthy tissues receive minimal dose. At present, the BNCT neutron sources are mainly nuclear reactors and large particle accelerators. These types of neutron sources have high capital expenses, are difficult to maintain and manipulate, require high voltage, and cannot be widely installed in clinical settings. A deuterium-deuterium (DD) neutron generator is a competitive alternative for neutron source due to its low cost, compact size, low acceleration voltage, and relatively simple installation. The objective of this dissertation research is to investigate and design a DD neutron generator-based BNCT system.

In the first study, the optimal neutron energy for BNCT of brain tumors at various depths was determined. When the neutron source had an energy in the epithermal range, between 0.5 eV and 10 keV, the dose ratio between the tumor and the brain was maximized. The alpha dose component accounted for approximately 80% of the total tumor dose. As
the neutron energy increased to 2.45 MeV, the alpha dose fraction was reduced to 5%. With an epithermal neutron source, 50% of the total brain dose originated from photons while neutrons and alphas contributed to the other 50%. Although higher energy neutrons delivered more dose per source neutron to the tumor, more than 80% of the dose was deposited by neutrons, and the brain received the same amount of dose as the tumor. The benefits of the high-LET particles were reduced because the high-energy neutrons were not thermalized when they reached the tumor site.

The second specific aim focused on designing a beam shaping assembly for a DD neutron generator source to moderate the fast DD neutrons and reduce radiation contaminations in the beam. The final optimized layout included a moderator combination of 45-cm Li$^7$F and 10-cm MgF$_2$, a 30-cm lead reflector, 10-cm lead collimator, and 0.02-cm cadmium filter. The neutron spectrum in air had 9.4 x 10$^4$ n$_{epi}$/cm$^2$-s, 0.03 for thermal-to-epitherml ratio, 5.9 x 10$^{-13}$ Gy-cm$^2$/n$_{epi}$, and 2.1 x 10$^{-13}$ Gy-cm$^2$/n$_{epi}$. For the in-phantom evaluation, the advantage depth (AD) was 12.5 cm, the advantage ratio was 4.4, and the dose rate at AD was 2.9 x 10$^{-3}$ cGy-Eq/min. The maximum skin dose was 0.6 Gy-Eq. The only deficiency of the system was the inadequate neutron flux that DD neutron generators currently produce.

Finally, the dose distributions of the designed BNCT system in a cadaver-based phantom were examined in MCNP. The brain obtained a maximum dose of 12.5 Gy-Eq, minimum dose of 1.2 Gy-Eq, and average dose of 5.3 Gy-Eq. Results from this dissertation demonstrated the feasibility of a DD neutron generator-based BNCT system for treatment of brain tumors.
CHAPTER 1. INTRODUCTION AND BACKGROUND

1.1 Glioblastoma Multiforme

1.1.1 Epidemiology

Glioblastoma multiforme (GBM) is the most common malignant tumor of the central nervous system and accounts for more than 60% of all brain tumors and half of all primary brain tumors in adults, occurring in 2-3 people per 100,000 population.\(^1\) Despite decades of research and advances in treatment techniques, GBM remains an incurable disease, and patient prognosis and outcomes are extremely poor, with a median survival of approximately 14-15 months. Less than 5% of patients survive five years after diagnosis.\(^2,3\)

GBM is classified as the most aggressive and lethal brain tumor and has been designated Grade IV by the World Health Organization.\(^4,5\) Distinct features of GBM from lower grade brain tumors are necrosis, heterogeneity, and infiltrating proliferation. The incidence rate of GBM is 1.6 times higher in men than women and 2 times higher in Caucasians than other races.\(^3\) The mean age is 64 years at diagnosis.\(^6\) Most GBM occurrences are primary, and these patients tend to be older and have poorer prognosis than those with secondary GBM. The only known risk factor for GBM is exposure to ionizing radiation.\(^7\)

Environmental and occupational exposures, such as to chemical carcinogens and smoking, have been loosely associated with the development of GBM.

About 61% of GBM occurs in the supratentorial regions of the brain, with the highest incidence in the frontal lobe, followed by temporal and parietal lobes.\(^8\) GBM rarely occurs in the cerebellum and the spinal cord. Clinical presentations of patients vary greatly with the size and location of the tumor.\(^9\) Common symptoms include increased cranial pressure, focal neurologic deficits, headache, and seizures.\(^10\) Initial diagnosis of the disease
includes imaging with CT or, most commonly, MRI, where GBM is presented in an irregularly shaped mass with a necrotic center and surrounded by edema and hemorrhage.

1.1.2 Standard of Care

The main challenges in GBM treatments are the location of the disease and its complexity and heterogeneity. The current standard of care for GBM patients has not changed significantly over the past decade and consists of maximally safe surgical resection of the tumor mass, followed by concurrent and adjuvant chemotherapy with radiation therapy (RT). Surgery is the main component in the management of GBM but, however, cannot cure the disease completely due to the high degree of invasiveness of GBM. GBM is known for its microscopic extension into the surrounding healthy brain tissues. Thus, the extent of surgical resection is dependent on tumor characteristics and the location of the involved brain, which is usually in the area that controls speech and motor functions. After surgery, infiltrating tumor cells will inevitably remain in the brain tissue, leading to disease progression or recurrence. A more extensive surgical resection is associated with better outcomes but needs to be balanced with the preservation of brain function. Chemotherapy treatment is usually initiated four weeks after surgery. When combined with other treatment modalities, chemotherapy drug, temozolomide (TMZ), has been shown to effectively prolong patient survival. Concurrently with RT, TMZ is first administered daily for six weeks. After the conclusion of RT, adjuvant TMZ is restarted for 12 to 18 months. Prior to 2005, RT alone had been the standard treatment. Later, a study found that patients who received RT with TMZ showed a significantly increase in the median survival compared to patients who had only RT (14.6 months versus 12.1 months). The current standard RT regimen is typically done with 3D conformal or IMRT beams,
delivering 1.8-2 Gy per fraction over six weeks for a total dose of 60 Gy to the target.\textsuperscript{11} The target volume is defined as the volume 2 to 3 cm beyond the tumor mass seen on MRI or CT scan. Dose escalation has been found to increase radiation toxicity without any benefits in overall survival.\textsuperscript{16}

1.1.3 Disease Recurrence

Regardless of aggressive multidisciplinary treatment, about 70\% of GBM patients will experience disease progression, and the rate of local recurrence is 80-90\%.\textsuperscript{17,18} Recurrence is very common in GBM due to the proliferation of residual cancerous cells. Approximately 80\% of recurrences occurred within the margins of the first surgery and RT.\textsuperscript{5,19,20} Figure 1.1 demonstrates an example of local GBM recurrence. Figure 1.1A shows the brain image of a GBM patient at diagnosis, and Figure 1.1B is after surgical removal of the tumor. The patient underwent the standard treatment regimen but experienced recurrence in the resection cavity 16 months after the first surgery (Figure 1.1C). Prognosis at recurrence is dismal for patients with recurrent GBM. The estimated medical survival is 9 months, and only 1\% live beyond 1 year.\textsuperscript{21} No standard of care is established for recurrent GBM patients.\textsuperscript{22} Treatment options include reoperation, supportive care, and systemic therapies. Patients with recurrent GBM may undergo a biopsy to rule out radiation necrosis and be considered for surgery again although the benefits remain unclear. Repeat surgery may help ease some clinical symptoms that are due to mass effect. Chemotherapy and other medications can be given to alleviate symptoms and improve quality of life. Re-irradiation of the disease area is usually not likely because the normal tissues have received the maximal tolerance dose from previous RT and the incidence of necrosis increases with dose.
Figure 1.1 MRI images of a GBM patient showing (A) the tumor in the left occipital lobe, (B) disease recurrence in close proximity to the surgical cavity and (C) local recurrence 16 months after the initial surgery.\textsuperscript{25}

1.2 Boron Neutron Capture Therapy

1.2.1 Principles

Boron neutron capture therapy (BNCT) is a binary treatment modality that is based on the nuclear reaction between thermal neutrons and boron-10 (B-10) nuclei (Figure 1.2). B-10 captures a thermal neutron and then undergoes a fission reaction, releasing an alpha particle and a lithium ion. The product particles have a very high linear energy transfer (LET) and short range as compared to conventional radiotherapy photons and electrons (Table 1.1). The mean travel range of these particles is approximately 10 \textmu m, similar to the size of a cell. As a result, the radiation dose deposited by these particles is confined to the cells that are in close proximity to the fission reaction and very localized. BNCT treatment requires two components: administration of a B-10 carrier compound and delivery of a neutron beam. Patient is first injected intravenously with a B-10 compound, which preferentially accumulates in the tumor cells. The target area with the tumor is then
irradiated with a neutron beam, initiating the fission reaction that generates the heavy particles. Due to the selective feature of the B-10 compound, a large fraction of the radiation dose is delivered to the tumor cells while the dose to the surrounding healthy tissues is minimized. The B-10 compound is nontoxic and nonradioactive until it is captured by a thermal neutron. While the healthy tissues receive low level of B-10 and non-specific background dose, the tumor-targeting B-10 compound presents a significantly greater concentration in the tumors and primarily governs the therapeutic ratio in BNCT.

![Figure 1.2 Schematic of boron neutron capture reaction.](image)

<table>
<thead>
<tr>
<th>LET (keV/µm)</th>
<th>Alpha</th>
<th>⁶⁰Co Photon</th>
<th>Electron (1 MeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range (µm)</td>
<td>150</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>4170</td>
<td>4120</td>
</tr>
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</table>

BNCT is a promising modality for treating malignant diseases that have poor prognosis and response to conventional treatments, such as GBM. As mentioned previously, GBM is characterized by a primary tumor mass with accompanying microscopic extensions into the normal brain tissues. Patients with GBM have poor
prognosis even with advance treatment modalities. Due to the selective accumulation of the B-10 compound and the characteristics of the high LET particles, BNCT has the ability to target microscopic tumor cells that current imaging techniques are unable to detect and conventional therapies fail to eradicate. Attempts to eliminate the invading GBM cells by extending the resection margins or administering high-dose radiation inevitably lead to adverse effects. BNCT provides not only a physical method of therapy but also has a biological component that the standard treatments lack.

1.2.2 Background and Early Clinical Studies

Shortly after the discovery of neutron by Chadwick in 1932, the neutron capture reaction became known to researchers, and it was proposed that such reaction could be applied to radiation therapy. Of all the nuclei that have a high tendency for absorbing thermal neutrons, the isotope B-10 was the ideal element for neutron capture therapy due to its large capture cross section (Table 1.2) compared to other elements. In addition, B-10 is stable and can be easily incorporated into a variety of chemical compounds. The earliest BNCT clinical studies were carried out at the Brookhaven Graphite Research Reactor (BGRR) in 1951. The first 24-month study enrolled ten patients with malignant cerebral gliomas. Patients were irradiated with thermal neutrons for 17 to 40 minutes, following administration of a B-10-enriched borax compound. Although the patients did not exhibit any serious radiation-induced effect, some experienced borax toxicity. The median survival of the ten patients was 96 days, similar to GBM patients treated with conventional therapies. The subsequent BNCT series was comprised of nine malignant glioma patients and used a less toxic B-10 compound, pentaborate. However, some patients exhibited radiation dermatitis of the scalp, sometimes deep ulceration. The median survival was
147 days for the second clinical trial. After the preliminary studies at BGRR, it was suggested that if a sufficient number of thermal neutrons could reach the tumor site, the complications from BNCT irradiation may be eliminated. As a result, a high-flux thermal beam was constructed and operational at the Brookhaven Medical Research Reactor in 1959. However, the clinical results were disappointing: the median survival of the 17 patients after BNCT was only 3 months. At around the same time, a separate study was carried out at the Massachusetts Institute of Technology (MIT) reactor, where 17 patients were irradiated. The median survival was 5.7 months, but brain edema and necrosis were observed within a few months. Due to a lack of evidence of substantial improvement in patient survival, all BNCT clinical trials were suspended in the United States in 1961. The renewal of BNCT investigations resumed in Japan in 1968 and presented promising results, where the 5 year survival rate was 58%. The common BNCT practice in Japan was to apply intraoperative radiotherapy, exposing the tumor bed directly to the radiation beam after tumor excision.

<table>
<thead>
<tr>
<th>Element</th>
<th>Cross section (barns)</th>
</tr>
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<tbody>
<tr>
<td>B-10</td>
<td>3850</td>
</tr>
<tr>
<td>Li-6</td>
<td>940</td>
</tr>
<tr>
<td>He-3</td>
<td>5333</td>
</tr>
<tr>
<td>N</td>
<td>1.84</td>
</tr>
<tr>
<td>H</td>
<td>0.33</td>
</tr>
<tr>
<td>C</td>
<td>0.0034</td>
</tr>
<tr>
<td>O</td>
<td>0.00018</td>
</tr>
</tbody>
</table>
The failure of the early BNCT clinical trials were attributed to two aspects: the inadequate tissue penetration of thermal neutron beams and the insufficient accumulation of B-10 in the tumors. The Brookhaven clinical trials used a variation of B-10 compounds, including borax, pentaborate, and boronic acid. These compounds were unable to yield a high tumor-to-brain ratio, and radiation-induced toxicities were frequently reported. Currently, there are two B-10 compounds that have shown to provide improved B-10 accumulation and are used in BNCT clinical trials: \( p \)-phenylalanine (BPA) and sulfhydryl borane (BSH). BSH could attain a tumor-to-blood ratio between 1.3:1 to 2:1, but it cannot cross the blood-brain barrier. As a result, BSH can only deliver boron to the main tumor mass but not to the infiltrating tumorous cells in the normal brain. In contrast, BPA is actively transported across the blood-brain barrier. The average BPA concentration in the tumor is 2-4 times greater than those in the blood and the brain. BPA was also found in the region several millimeters away from the main tumor mass, indicating that BPA was able to reach the infiltrating tumor cells.

The second reason for the poor clinical results was the use of thermal neutron beams. The superficial layers of tissues effectively attenuate thermal neutrons and absorb majority of the radiation dose. Thus, thermal neutron beams are more useful for irradiating melanoma and shallow tumors. After the initial BNCT clinical trials, much effort had focused on developing higher neutron energy beams to reduce the radiation dose to healthy tissues and to increase the penetrability of the beam. In the 1990s, reactor-based BNCT facilities at Brookhaven and MIT made modifications to the reactor to extract the epithermal neutrons and carried out clinical trials with epithermal neutron beams. In these clinical trials, many adverse effects were associated with a temporary increase in
intracranial pressure. The median survival for the patients was 13 months, comparable to with resection and standard treatments. These efforts were followed by other international developments, such as in Petten, Finland, Sweden, and Japan.\textsuperscript{49-52} The median survival overall ranged between 13 and 15 months. The study in Japan reported a median survival of 20.7 months. However, the Japan protocol consisted of intraoperative irradiation. Other groups have developed accelerator-based facilities and made considerable progress.\textsuperscript{53,54} The accelerator-based neutron sources are advantageous in certain aspects but still have yet to reach the same neutron intensity as the nuclear reactors. Further discussion on neutron sources is presented in Section 1.2.3.

The B-10 compound issue of BNCT is less pressing than the neutron source aspect. Studies have demonstrated the effectiveness of BPA and BSH in selectively delivering B-10 to the tumor cells. For the availability of BNCT neutron sources, however, there remains technical challenges that need to be overcome to establish a reliable clinical source.

1.2.3 BNCT Neutron Sources

1.2.3.1 Nuclear Reactors

From the first BNCT trials to the early 2000’s, nuclear reactors had been the only neutron source used for clinical studies. Initially thermal neutrons extracted from the reactor cores were utilized for clinical work. To improve the tissue penetrability of the neutron beam, institutions made modifications to their facilities to produce epithermal beams. There are two approaches to modify a reactor. The first approach is to add resonance scattering materials to scatter and moderate the fast neutrons in the reactor core along with filters to remove thermal neutrons and photons of the spectrum. The additional materials, however, also attenuate the useful neutron beam and reduce the neutron fluence.
The second approach is to place a fission converter plate adjacent to the moderator assembly. Reactor-based neutron sources (RBNS) can produce beam characteristics that approach the optimum for BNCT. The neutron spectrum of RBNS has an average energy of 2 MeV and can extend up to 10 MeV. Table 1.3 displays the neutron beam properties of some of the reactor-based BNCT facilities.

Table 1.3 Neutron beam properties of the earliest nuclear reactor-based BNCT facilities.

<table>
<thead>
<tr>
<th>Reactor</th>
<th>Reactor power (MW)</th>
<th>Epithermal flux ($10^9$ cm$^{-2}$s)</th>
<th>Fast neutron dose per epithermal fluence ($10^{-13}$ Gy-cm$^2$)</th>
<th>Photon dose per epithermal fluence ($10^{-13}$ Gy-cm$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FiR</td>
<td>0.25</td>
<td>1.1</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>BMRR</td>
<td>3</td>
<td>0.8</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>MITR</td>
<td>5</td>
<td>0.2</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>HFR</td>
<td>45</td>
<td>0.3</td>
<td>10</td>
<td>8.6</td>
</tr>
</tbody>
</table>

Despite that reactors can generate high quality neutron beams and are the only neutron source that can produce adequate fluence, they have several drawbacks, including the presence of radioactive materials, low public acceptability, high capital expenses, and difficulties in modifying the reactor configuration. If alternations to the neutron source are needed for clinical purposes, it can be complicated and time-consuming for a RBNS. Nuclear reactors are also dependent on political and economical factors, which have led to decommission and closure of most of such facilities. Reactors are not meant for clinical applications and thus, require complicated licensing procedure. These factors have prevented the installation of reactors in hospital settings. Since construction of new nuclear reactors is extremely unlikely, there will be a lack of BNCT facilities for treatment in the future.
1.2.3.2 Particle Accelerators

Accelerator-based neutron sources (ABNS) have several advantages over RBNS. First, ABNS can be turned off with no constant radioactivity being produced. ABNS also has lower capital expenses and are more familiar to clinicians in hospital settings. The most popular ABNS use proton beams with either a lithium or beryllium target. The characteristics of the two types of ABNS are shown in Table 1.4. The proton beam requires between 30 and 80 kW of power. The popular reaction is \(^{7}\text{Li}(p,n)^{7}\text{Be}\). With this type of ABNS, the threshold energy for the impinging protons is 1.88 MeV. Protons are accelerated up to 2.5 MeV, producing neutron beams with energy between 35 and 573 keV and an average energy of 233 keV.\(^{57}\) The advantage of this neutron source is that the neutron energy is very close the epithermal energy range and, thus, requires little moderation. However, in order to achieve an adequate neutron flux for BNCT of deep-seated tumors, it is necessary to increase the Li target thickness and the accelerator current to tens of mA, and the heat density deposited in the target becomes very high. Due to lithium’s low thermal conductivity and melting point, target integrity and the risk of target failure become an issue for p + Li BNCT neutron source. Another issue that arises is the accumulation of radioactive \(^{7}\text{Be}\) from target activation after extended use, which could cause implications associated to system contamination.\(^{58}\)
Table 1.4 Characteristics of accelerator-based BNCT neutron sources.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Proton energy (MeV)</th>
<th>Neutron production rate (n/min-mA)</th>
<th>Maximum neutron energy (MeV)</th>
<th>Target melting point (°C)</th>
<th>Target thermal conductivity (W/m-K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^7$Li(p,n)$^7$Be</td>
<td>1.89$^{59}$ 2.5$^{60}$</td>
<td>6.3 x 10$^9$ 9.3 x 10$^{11}$</td>
<td>0.067 0.573</td>
<td>180 85</td>
<td></td>
</tr>
<tr>
<td>$^9$Be(p,n)$^9$B</td>
<td>2.5$^{59}$ 4.0$^{59}$</td>
<td>3.9 x 10$^{10}$ 1.0 x 10$^{12}$</td>
<td>0.574 2.12</td>
<td>1287 201</td>
<td></td>
</tr>
</tbody>
</table>

An alternative to $^7$Li for the target material is $^9$Be. The $^9$Be(p,n)$^9$B ABNS is less common than the $^7$Li(p,n)$^7$Be type but doesn’t have the target manufacturing issue and radioactive products. The threshold energy for the reaction is 2.06 MeV. With a bombarding energy of 2.5 MeV, the maximum neutron energy was 0.57 MeV. However, to generate the same neutron production as the $^7$Li(p,n)$^7$Be reaction, the proton energy would need to increase to 4.0 MeV, which increases the neutron energy as well. As a result, additional moderator is required to moderate the high-energy neutrons.

While ABNS has the advantage of siting in a hospital and is less expensive than RBNS, they remain a tremendous financial investment for institutions. In addition, ABNS usually requires auxiliary equipment that may take up large spaces. Considerable improvements are still needed to reach the beam intensity and quality of RBNS. The identification of the effectiveness of BNCT in treatment of GBM is lacking due to the small patient size and the absence of a clinically appropriate neutron source. It is difficult to make substantial progress in BNCT without a reliable neutron source for widespread and accessible use. Compact neutron generators (e.g. deuterium-deuterium) is a competitive BNCT neutron source that can help with the challenges that BNCT encounters.
1.3 Deuterium-Deuterium Neutron Generator

A deuterium-deuterium (DD) neutron generator uses deuterium ions to induce fusion reaction ($^2\text{D} + ^2\text{D} \rightarrow \text{n} + ^3\text{He}$) and produce neutrons with an energy of 2.45 MeV. It has been operating in various settings around the world, such as universities, research institutions, and private industries. The main components of the generator include the plasma ion source, acceleration chamber, and target (Figure 1.3a). Deuterium is supplied to the plasma source from a bottle of compressed gas attached to the side of the generator rack. The gas flows into and is ionized by the plasma source that is powered by radiofrequency microwave. The deuterium ions are then accelerated toward a negatively biased titanium target in the acceleration chamber with a negative potential of -100 to -150 kV. As the ions impinge on the target, they implant and form titanium hydrate on the target surface. When the target surface is saturated with deuterium ions, subsequent ions that reach the target initiate the fusion reaction, releasing 2.45-MeV neutrons. When the generator is first started, neutron output will increase with time as the titanium hydrate begins to form. Once saturation is achieved, neutron output will stabilize. Unlike sealed sources, the production of neutrons is controlled by bombarding deuterium ions on the target and not limited by the age of the target. Therefore, the DD neutron generator has a considerably long life of operation. The most current model of the generator in our lab (Figure 1.3b) is capable of producing a neutron yield of $2 \times 10^9$ n/s.

DD neutron generators offer several advantages over nuclear reactors and large medical accelerators, including the compact size, competitive cost, ability to turn off completely, low acceleration voltage, and absence of radioactive materials. With sufficient effort and development, DD neutron generators may be able to compete with other neutron sources.
1.4 Monte Carlo N-Particle

Monte Carlo simulation, developed by Los Alamos National Laboratory, is a particle transport code that performs analytical calculations in 3-D geometry from particle interactions. It has the capability to simulate transport of photons, neutrons, and electrons and provides accurate dose calculations and distributions within a geometry. Users can input the source specifications and phantom configurations to model a radiological scenario. MCNP tracks the particles and determines the energy deposited by the particles based on the cross sections of each interaction. With a large number of particles, the MCNP results accurately predicts the experimental ones. This dissertation work used Monte Carlo
N-Particle (MCNP) simulations extensively to simulate irradiation design and determine radiation dose to various tissues.

1.5 Overall Goal and Specific Aims

The overall goal of this dissertation work is to design and optimize a DD neutron generator-based BNCT system and to examine the dosimetric properties of the neutron output. The following specific aims will assess the overall objective:

Specific Aim 1: Determine the optimal neutron energy for BNCT of the brain.

The objective of the first aim was to determine the dosimetric effects of monoenergetic neutrons on healthy tissues as well as brain tumor. This work was done using Monte Carlo simulations. A monoenergetic neutron source was placed behind a head phantom, and the doses to the brain, skin, and tumor were evaluated. Neutron energies between 0.5 eV and 2.45 MeV were investigated. Results from this specific aim will provide a baseline from which to design and compare our DD-based BNCT system.

Specific Aim 2: Design a beam shaping assembly for a DD neutron source.

We designed a beam shaping assembly for a DD neutron generator to moderate and adjust the neutron spectrum to the desired energy range found in Specific Aim 1. The results of our proposed BNCT system were compared to those of other BNCT neutron sources and international recommendations.

Specific Aim 3: Generate BNCT treatment plans in Monte Carlo with the optimized DD system.

BNCT treatment plans were generated using a whole-body phantom converted from a male cadaver and the optimized DD system from the previous aim. The beam angle and treatment setup were varied to examine the difference in dose distributions. Dose-volume histograms were generated for each treatment plan.
1.6 Innovation and Impact

Current BNCT clinical trials are performed at either a reactor-based or accelerator-based facility, which is not appropriate for general hospital settings due to the expenses, size, and architectural complexity. Development in BNCT has been limited by the lack of a suitable neutron source for clinical studies. The proposed DD-based BNCT system is compact, less expensive, and relatively easy to install. The advantages of the system include the reduction in cost of BNCT facilities and increase in access to BNCT for large patient populations. With an accessible neutron source, extensive BNCT data and experience can be collected. It is also expected that this research would stimulate interests in B-10 carrier development and future studies on improvements of present neutron generator technology. In addition, results from this dissertation research can be applied to BNCT treatment of other human diseases (e.g. head and neck cancers, hepatocellular carcinoma).

Few studies have investigated the efficacy of a DD neutron generator for BNCT and mainly focused on designing a beam shaping assembly and determining the in-air characteristics of the beam output. The proposed research is innovative in that dose distributions within tissues will be examined in detail and a dose-volume histogram will be generated.

1.7 Structure of Dissertation

The structure of the dissertation is organized by the specific aims. Chapter 1 consists of introduction to the research topic and background on relevant materials. Chapters 2 to 4 each present one specific aim. Chapter 5 summarizes the overall conclusion of the dissertation research and future directions.
CHAPTER 2.  OPTIMAL NEUTRON ENERGY FOR BORON
NEUTRON CAPTURE THERAPY OF THE BRAIN

2.1 Introduction

Early clinical work in BNCT had been performed using thermal neutron beams. However, thermal neutrons have poor tissue penetration and, as a result, deposit a substantial amount of dose to the skin and shallow soft tissues and are unable to reach deep-seated tumors. Patients from the early clinical trials often exhibited extensive brain necrosis and skin dermatitis after BNCT treatments. In the 1990’s, BNCT facilities began to transition from low-energy thermal neutron beam to higher-energy epithermal neutron beam to achieve better tissue penetration. Although the benefits of epithermal neutron beams were recognized in clinical trials, the fundamental characteristics of epithermal neutrons and of an optimal BNCT beam are still not well understood. The goal of this study was to examine the effects of neutron energy on BNCT of the brain and to determine the optimal neutron energy that is suitable for treatment of both shallow and deep-seated brain tumors. The dosimetric properties of monoenergetic neutron beams will be examined as a function of neutron energy, tumor position, and tissue depth. While other studies have performed similar work, our study would not only further confirm others’ results but also establish a set of baseline data for designing our own BNCT system and subsequent research works.
2.2 Materials and Methods

2.2.1 Monte Carlo N-Particle Simulation

Simulations were performed using MCNPX version 2.7.0. The simulation model consisted of a neutron source and a male head phantom. The neutron point source was placed at 3.5 cm from the posterior skin surface of the head phantom and aligned to the center of the brain. The source emitted monoenergetic neutrons isotropically, and the neutron energy was varied between 0.5 eV and 2.45 MeV. The head phantom design was based on the configuration described in the Medical Internal Radiation Dose (Figure 2.1). The normal tissues of the head phantom included the brain, skin, cranium, and soft tissues. Radiation dose was examined in the brain, skin, and tumor. The brain volume was 1402.15 cm$^3$, and the skin volume was 133.21 cm$^3$. Elemental compositions of the tissues were defined according to the International Commission on Radiation Units and Measurements (ICRU) Report 46 as shown in Table 2.1.

Two forms of tumor configuration were used. For average dose calculation, a spherical tumor with 2.5 cm in radius was placed in the brain along the central beam axis (Figure 2.2a). The location of the tumor was varied from 5 to 10 cm and defined as the distance between the posterior skin surface and the center of the tumor. Tumor location of 5 cm was the shallowest position, and the 10-cm location indicated that the tumor was in the center of the brain, as shown in Figure 2.2a. All doses calculated using this configuration were averaged over the tumor and normal tissue volumes.
Figure 2.1 Modified male head phantom based on MIRD.

Table 2.1 Elemental compositions of the male head phantom.

<table>
<thead>
<tr>
<th>Element (% weight)</th>
<th>Brain</th>
<th>Cranium</th>
<th>Skin</th>
<th>Soft Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>10.7</td>
<td>5.0</td>
<td>10.0</td>
<td>10.5</td>
</tr>
<tr>
<td>C</td>
<td>14.5</td>
<td>21.2</td>
<td>20.4</td>
<td>25.6</td>
</tr>
<tr>
<td>N</td>
<td>2.2</td>
<td>4.0</td>
<td>4.2</td>
<td>2.7</td>
</tr>
<tr>
<td>O</td>
<td>71.2</td>
<td>43.5</td>
<td>64.5</td>
<td>60.2</td>
</tr>
<tr>
<td>Na</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>P</td>
<td>0.4</td>
<td>8.1</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>S</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Cl</td>
<td>0.3</td>
<td>-</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>K</td>
<td>0.3</td>
<td>-</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Others</td>
<td>-</td>
<td>0.2 Mg, 17.6 Ca</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$\rho$ (g/cm$^3$)</td>
<td>1.04</td>
<td>1.61</td>
<td>1.09</td>
<td>1.03</td>
</tr>
</tbody>
</table>
For maximum doses, a series of tally cylinders were placed along the central beam axis within the brain starting at 1 cm depth and extending to 17 cm (Figure 2.2b). Each cylinder was 2 cm in diameter, 0.5 cm in height and had a volume of 1.57 cm$^3$. For skin dose, a 0.035-cm$^3$ cell was created and placed in the skin at the beam entrance. Due to the small volumes of the tally cells, the dose calculated in each cell was considered the maximum dose. Simulations were terminated when statistical uncertainty was within 5%.

![Figure 2.2](image)

Figure 2.2 (a) Male head phantom and a spherical tumor with 2.5 cm in radius. (b) Male head phantom and tally cylinders along the central beam axis.

2.2.2 BNCT Dose Calculations

The total BNCT dose is composed of several radiation components with differing LET characteristics. In addition to the boron dose deposited by alpha particles and lithium ions, other principal dose components include neutron and photon doses that are either inherent in the beam assembly or produced via interactions with normal tissues. Neutron dose is deposited via recoiled protons and originates from neutron scattering interaction with hydrogen, $^1$H(n,n')p, and capture interaction with nitrogen, $^{14}$N(n,p)$^{14}$C. Photons are
produced when neutrons interact with the assembly materials around the source as well as from neutron capture by hydrogens, \(^1\text{H}(n,\gamma)^2\text{H}\). Each dose component was assumed to act independently of one another and can be calculated individually. To determine the neutron and photon doses deposited in a given cell, the neutron and photon fluences were tallied and modified by their respective fluence-to-dose KERMA factors.\(^{71,72}\) For alpha dose, the neutron fluence was first modified by the alpha fluence-to-dose KERMA factors and then by the B-10 concentration in the specific tissue.\(^{73}\) The brain had 15 ppm of B-10 concentration. The skin and the tumor possessed 1.5 and 3.5 times the B-10 concentration in the brain, respectively. B-10 was assumed to be evenly distributed throughout the volume. The B-10 concentrations used in MCNP are listed in Table 2.2. The total dose in air was the sum of all dose components (neutron, photon, and boron) and expressed in unit of Gray (Gy) or Gy per source neutron.

<table>
<thead>
<tr>
<th></th>
<th>Tumor</th>
<th>Brain</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-10 concentration (ppm)</td>
<td>52.5(^{42})</td>
<td>15(^{43,66})</td>
<td>22.5(^{42,43,66})</td>
</tr>
<tr>
<td>CBE</td>
<td>3.8(^{74})</td>
<td>1.3(^{75,76})</td>
<td>2.5(^{77,78})</td>
</tr>
<tr>
<td>(\text{RBE}_\gamma/\text{RBE}_n)</td>
<td>1/3.3(^{74,79})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The biologically weighted total dose in a given tissue was calculated by summing the weighted dose components, as shown in Equation (1).

\[
D_{T,w} = CBE_w D_\alpha + \text{RBE}_n D_n + \text{RBE}_\gamma D_\gamma
\]  

(1)

where

- \(D_{T,w}\) = the weighted total dose to tissue \(w\)
- \(CBE_w\) = the compound biological effectiveness of boron dose for tissue \(w\)
\[ D_a = \text{boron dose} \]

\[ \text{RBE}_n = \text{the relative biological effectiveness of neutron dose} \]

\[ D_n = \text{neutron dose} \]

\[ \text{RBE}_\gamma = \text{the relative biological effectiveness of photon dose} \]

\[ D_\gamma = \text{photon dose} \]

The unit for the weighted dose is Gray-Equivalent (Gy-Eq) or Gy-Eq per source neutron to account for the different LET radiation types and relate to photon-equivalent units.

2.2.3 Evaluation Parameters

2.2.3.1 Average Dose Configuration

For average dose calculation using the head phantom with a spherical tumor (Figure 2.2a), the evaluation parameters consisted of the average dose for the brain, skin, and tumor as well as the dose ratio between the tumor and the brain as a function of neutron energy and tumor location. The average dose was the dose deposited to a given tissue averaged over the entire tissue volume.

2.2.3.2 Maximum Dose Configuration

While the average dose provides dose comparison among different tissues, it is not indicative of how the dose is distributed within a volume. For brain, because of the large volume of 1402.15 cm\(^3\), the dose could be concentrated in one region but still averaged over the entire volume. Therefore, assessment of maximum dose was considered as well.

For the head phantom with tally cylinders in Figure 2.2b, the evaluation parameters that were examined incorporate the maximum dose and are commonly used in the BNCT community: advantage depth and advantage ratio. Advantage depth (AD) is the depth in tissue where the tumor dose is equal to the maximum normal tissue dose. AD represents
the maximum depth for therapeutic benefits, beyond which the maximum tolerable normal tissue dose is exceeded. Advantage ratio (AR) is the ratio between the tumor dose and the normal tissue dose integrated from 1 cm depth to the AD. AR indicates the ability of the neutron beam to minimize dose to normal tissues. BNCT clinical studies have that brain was the dose-limiting tissue in BNCT irradiations. Thus, the maximum brain dose of 12.5 Gy-Eq was used to determine AD and AR in the study.\textsuperscript{81,82} AR and AD were evaluated as a function of neutron energy and depth.

2.3 Results

2.3.1 Average Dose

2.3.1.1 Tumor Dose

Figure 2.3 shows the total tumor dose per source neutron as a function of neutron energy for different tumor locations. All tumor locations had similar dose trends with neutron energy: the average tumor dose stayed relatively constant before 100 keV and increased substantially when the neutron energy increased from 100 keV to 2.45 MeV. The shallow tumors overall received more dose per source neutron, and the effect of neutron energy was less notable on the deep-seated tumors.
Figure 2.3 Total average dose to the tumor as a function of neutron source energy.

Figure 2.4 Neutron dose contribution to the total average tumor dose as a function of neutron source energy.
Figures 2.4 to 2.6 display the individual dose components in dose per source neutron of the total tumor dose in Figure 2.3. Figure 2.4 represents the neutron dose contribution as a function of neutron energy for all tumor locations. Neutron contribution was more prominent in shallow than deep tumors as well as when the neutron energy was above 10 keV. When the neutron energy was in the epithermal range or less, the dose contribution from neutrons didn’t vary greatly. At energy greater than the epithermal, neutron dose increased rapidly with energy. In addition, at those high neutron energies, the largest dose contribution out of all dose components was neutron. Figure 2.5 shows the dose contribution from alpha. Overall, shallow tumors received more alpha dose than deep tumors. For shallow tumors, the alpha dose contribution was at maximum when the neutron energy was at 5 eV for tumor locations of 5 and 6 cm, and at 1 keV for 7 cm. As the tumor location increased, the neutron energy that had the maximum alpha dose increased as well to 100 keV for tumor locations of 8 and 9 cm, and to 1 MeV for tumor location of 10 cm. When the neutron energy was below 100 keV, the alpha dose component was greater than the neutron component for all tumor locations. When the neutron energy was in the MeV range, the alpha dose contribution became less significant.
Figure 2.5 Alpha dose contribution to the total average tumor dose as a function of neutron source energy.

Figure 2.6 shows the photon dose component of the total dose as a function of neutron energy for all the tumor locations. In contrast to the alpha and neutron doses, the photon dose contribution stayed relatively constant with neutron energy and tumor depth. In general, the photon dose contribution decreased with increasing neutron energy, and shallow tumors received more photon dose than deep tumors. At high neutron energies, the tumor obtained the same dose relatively, regardless of the tumor location. When the tumor was situated in the middle of the brain, neutron energy had a modest effect on the dose.
The fraction of contribution from the individual dose components to the total tumor dose as a function of neutron energy is shown in Figure 2.7. For each dose component, the fraction was calculated by averaging the fractions at each neutron energy over all tumor locations. Alpha contribution was the largest of all dose components (between 0.7 and 0.8) when the neutron energy was less than 100 keV and dropped off rapidly when the energy increased to the MeV range. The neutron dose fraction was minimized at neutron energies below 100 keV and increased to greater than 0.9 at 2.45 MeV. The photon fraction stayed at less than 0.2 for most of the neutron energies and decreased further at 1 and 2.45 MeV.
Figure 2.7 The averaged dose fraction of the total tumor dose that originated from the individual dose components.

Figure 2.8 compares the average tumor dose and the dose components between neutron energy of (A) 10 keV and (B) 2.45 MeV. Although a 10-keV neutron beam delivered less dose per neutron source than a 2.45-MeV neutron beam, the total dose largely came from alpha particles, and the neutron dose contribution was the smallest. On the contrary, when the neutron energy was increased to 2.45 MeV, neutron accounted for almost all of the total dose, and alpha and photon dose fractions were substantially smaller.
Figure 2.8 The total tumor dose and the individual dose components as a function of depth for two neutron energies. (A) 10 keV and (B) 2.45 MeV.
2.3.1.2 Brain Dose

Figure 2.9 displays the total average dose to the brain as a function of neutron energy for all tumor locations. The total dose had subtle changes at low neutron energies. It increased and then decreased slightly with increasing energy. The lowest dose occurred at 1 keV, above which the total dose started to increase and then exponentially after 10 keV. The brain dose was not affected substantially by the tumor location. Figures 2.10 to 2.12 represent the neutron, photon, and alpha dose fractions of the total dose, respectively. The neutron contribution in Figure 2.10 exhibited similar trend as the total dose, where the dose showed gradual variations with energy when the neutron energy was less than 10 keV and increased exponentially at higher neutron energies.

![Figure 2.9 Total average dose to the brain as a function of neutron source energy.](image-url)
Figure 2.10 Neutron dose contribution to the total average brain dose as a function of neutron source energy.

The photon dose component is shown in Figure 2.11 as a function of neutron energy. The photon dose was greater with lower neutron energies and deeper tumor locations. Dose variation with neutron energy was less apparent than the neutron component. Figure 2.12 demonstrates the alpha dose component of the total brain dose. With higher neutron energies and shallow tumor locations, the brain obtained less alpha dose. When the neutron energy was in the eV range, the alpha dose in the brain was maximized.
Figure 2.11 Photon dose contribution to the total average brain dose as a function of neutron source energy.

Figure 2.12 Alpha dose contribution to the total average brain dose as a function of neutron source energy.
The fraction of the total brain dose that originated from the individual dose components is shown in Figure 2.13. The dose fraction at a given neutron energy was the average of all fractions at the same tumor location. For neutron energies below 10 keV, photon dose was the largest contributor to the total brain dose, followed by alpha then neutron. The photon fraction was around 0.5 before declining to 0 with increasing neutron energy. The alpha dose fraction was between 0.25 and 0.3 in the epithermal energy range and, like the photon fraction, decreased to 0 with increasing neutron energy. When the neutron energy was above 10 keV, the neutron dose component increased exponentially and was responsible for nearly the entire total dose at 1 and 2.45 MeV.

Figure 2.13 The averaged dose fraction of the total brain dose that originated from the individual dose components.
Figure 2.14 compares the average brain dose and the dose components between two distinct neutron energies: (A) 10 keV and (B) 2.45 MeV. Each figure represents the total dos deposited per source neutron as a function of tumor depth. When the neutron energy was in the epithermal range (10 keV), the brain received less dose per source neutron, and photon was the largest dose contributor while neutron was the lowest. When the neutron energy was at 2.45 MeV, the total brain dose was more than 30 times the dose with 10-keV neutrons, and the individual neutron dose was nearly the same as the total dose, indicating that the brain dose largely originated from the neutron beam.
Figure 2.14 The total brain dose and the individual dose components as a function of depth for two neutron energies. (A) 10 keV and (B) 2.45 MeV.
2.3.1.3 Dose Ratio

The dose ratio between the tumor and the brain as a function of neutron energy for all tumor locations is displayed in Figure 2.15. Deep-seated tumors overall had lower dose ratios than shallow tumors. The 5-cm tumor location had the largest dose ratio at all neutron energies, ranging between 13 and 17 in the epithermal range and between 4 and 13 in the fast energy range. For all tumor locations, the dose ratio initially increased with neutron energy and, after reaching a maximum value in the keV range, began to drop. The decrease was more noticeable when the neutron energy transitioned from epithermal to fast. As the tumor got deeper, the difference in dose ratio between epithermal and fast neutrons was less apparent. For the 10-cm tumor location, epithermal neutrons obtained dose ratios between 1 and 3 while fast neutrons’ were between 0 and 3. When the tumor was at 9 and 10 cm depth, the dose ratio with high energy neutrons was close to 1, illustrating that the tumor and the brain received comparable amount of dose.

Table 2.3 lists the neutron energy with the highest dose ratio and their values for all tumor depths. When the tumor was at a shallow location of 5 cm, 5-eV neutrons had the largest dose ratio between the tumor and the brain. As the tumor location continued to increase to the middle of the brain, neutron energies with the highest dose ratio values rose to 1 keV and 8 keV. Overall, the highest dose ratio occurred when the neutron energy was between 5 eV and 8 keV.
Figure 2.15 Dose ratio between the tumor and the brain as a function of neutron energy for all tumor locations.

Table 2.3 The dose ratio and the optimal neutron energy for BNCT of different tumor locations.

<table>
<thead>
<tr>
<th>Tumor location (cm)</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose ratio</td>
<td>16.8</td>
<td>11.5</td>
<td>7.9</td>
<td>5.4</td>
<td>3.7</td>
<td>2.5</td>
</tr>
<tr>
<td>Optimal neutron energy (MeV)</td>
<td>5E-6</td>
<td>1E-3</td>
<td>1E-3</td>
<td>1E-3</td>
<td>8E-3</td>
<td>8E-3</td>
</tr>
</tbody>
</table>

2.3.1.4 Skin Dose

The total average skin dose and its individual dose components as a function of neutron energy are displayed in Figure 2.16. Different from the tumor and the brain dose, the skin dose per source neutron was not affected by the tumor location if the neutron energy remained unchanged. The total skin dose first decreased when the neutron energy went from 0.5 eV to 1 keV, then increased quickly above the initial dose with increasing
neutron energy. Alpha dose was the largest dose component before 1 keV, followed by photon and neutron. Alpha and photon doses continued to decrease to increasing neutron energy while the trend for the neutron component was reversed. At 1 keV, the three dose components reached a crossover point and contributed similar amount of dose, and the neutron fraction increased exponentially. At above 100 keV of neutron energy, almost the entire skin dose came from neutrons.

![Graph showing total average skin dose and individual dose components as a function of neutron source energy.](image)

Figure 2.16 The total average skin dose and the individual dose components as a function of neutron source energy.

2.3.2 Maximum Dose

2.3.2.1 Advantage Depth and Advantage Ratio

Figure 2.17 shows the AD and AR data as a function of neutron energy. AD started at 5.24 at 0.1 eV, increased with neutron energy, and reached a maximum value of 9.26 at 2 keV. At neutron energies beyond 10 keV, AD started to decrease rapidly with increasing
energy and leveled out at 100 keV. The minimum value was 1.5. For AR, the value began at 5.48 at 0.1 eV and stayed relatively constant with energy until 8 keV. Similar to the trend in AD, AR declined with increasing energy beyond 8 keV and began to plateau at 100 keV. At neutron energies of 1 and 2.45 MeV, the AR had the minimum value of 1, or the brain and tumor tissues received the same dose.

![Figure 2.17](image.png)

Figure 2.17 The Advantage depth and advantage ratio as a function of neutron energy.

Figure 2.18 shows the maximum skin dose per source neutron and the normalized maximum skin dose as a function of neutron energy. The maximum dose per source neutron started low at 0.1 eV and decreased further with increasing neutron energy. The minimum occurred at 100 eV, however, beyond which the dose began to escalate. The increase was more rapid after 10 keV. The normalized dose curve was calculated based on and normalized to the maximum brain dose. Comparable to the curve for the dose per source neutron, the normalized dose first decreased with neutron energy until it reached
100 eV and began to increase after. At 25 keV, the normalized dose reached a maximum dose of 1.7 Gy-Eq and decreased again at higher neutron energies. The maximum skin dose was well within the reported tolerable dose, regardless of the neutron source energy.

![Figure 2.18 Maximum skin dose as a function of neutron energy.](image)

2.3.2.2 Dose Profile

The dose profiles for the tumor and the brain are shown in Figure 2.19 for neutron energy (A) 0.1 eV, (B) 2 keV, and (C) 2.45 MeV. The dose on the y-axis was normalized to the maximum tolerable brain dose of 12.5 Gy-Eq. When the neutron energy was 0.1 eV, the total dose to the tumor and the brain both decreased with increasing depth. The tumor received significantly more dose than the brain, and the alpha component made up the largest fraction of the total tumor dose while the neutron contribution was minimal. With 2-keV neutrons, the total tumor dose was less than that with 0.1-eV neutrons. The tumor exhibited a buildup region between 1 and 3 cm depths and acquired more dose than the
brain. The alpha component composed the largest fraction of the total tumor dose while neutrons remained the smallest dose contributor. The brain dose profile also did not decrease as fast as when the neutron energy was 0.1 eV. When the neutron energy was equivalent to those of a DD neutron generator (Figure 2.19c), the doses to the tumor and the brain were essentially the same. The total doses decreased with depth, and the buildup region seen in Figure 2.19b was eliminated. Alpha dose contribution was minimized, and neutrons made up the largest fraction of the total dose.

Figure 2.19 Dose profiles for the tumor, the brain, and the dose components as a function of depth for neutron energies of (A) 0.1 eV, (B) 2 keV, and (C) 2.45 MeV.
Figure 2.19 continued

(B)

(C)
2.4 Discussion and Conclusion

The purpose of the study was to examine the effect of neutron source energy on the dose deposited to different tissues and to determine the optimal neutron energy for BNCT for brain tumors. When the neutron energy was between 0.5 eV and 10 keV, the alpha dose component accounted for nearly 80% of the total tumor dose for all tumor locations. On the contrary, at 1 and 2.45 MeV, neutrons were the main contributor to the tumor dose. While the higher neutron energies were more efficient in delivering dose to the tumor in terms of dose deposited per source neutron, a large fraction of the delivered dose emerged from the inherent neutron beam. Epithermal neutrons deposited less dose per source neutron to the tumor; however, they produced the largest alpha dose fraction for all tumor locations. With an epithermal neutron beam, more neutrons were thermalized by the normal tissues when they reach the tumor site as compared to a thermal neutron beam, generating more alpha particles and lithium ions at the tumor site. The thickness of the brain tissue was insufficient to effectively moderate higher energy neutrons, or fast neutrons. As a result, the alpha contribution to the total tumor dose and the therapeutic advantage of BNCT were diminished.

The average brain dose stayed relatively constant with tumor location compared to the tumor dose. As the tumor moved deeper in the brain, more brain tissue was exposed to the neutron beam and thus, received more dose. In the epithermal energy range, photon was the largest dose contributor while neutron was the least. When the energy was increased further, the total dose increased exponentially, and the neutron dose exceeded the photon and alpha components. At 1 and 2.45 MeV, neutron was responsible for more than 90% of the total brain dose. In BNCT, in addition to maximizing the production of the high LET particles inside the tumor, it is also important to keep the risk of radiation
toxicities in the brain to as low as possible. Results demonstrated that epithermal neutrons reduced the dose deposited by neutrons to the brain while allowing the maximal nuclear interaction between thermal neutrons and B-10. Fast neutrons (> 10 keV) delivered significantly more dose to the tumor as well as to the brain, as evident in the dose ratio in Figure 2.15. The dose ratio was the highest in the epithermal range and was drastically reduced as the neutron energy increased, especially at 1 MeV and 2.45 MeV, indicating that the high-energy neutrons were depositing just as much dose in the brain as in the tumor.

The average and maximum skin dose per source neutron decreased when the neutron energy went from the thermal to the epithermal range and then increased substantially at the higher energies. Due to the lower neutron capture cross section for epithermal neutrons, the skin obtained less dose than when the neutron source energy was thermal. However, this benefit was offset at higher energy likely by the neutron scattering interaction with hydrogens, causing the dose to escalate again. The normalized maximum skin dose did not display the same trend as the average and maximum doses because it was calculated based on and fluctuated with the maximum brain dose and the amount of neutrons required to reach the brain tolerance. At high neutron energies, the maximum skin dose decreased because the brain tolerance was reached with fewer number of source neutrons. Therefore, the irradiation time was reduced and so was the skin dose. There has not been a consensus about the skin tolerance dose among literature. The dose ranges from 11 to 18 Gy-Eq. \(^{77,78}\) However, the maximum skin dose in the results was well below any of the reported tolerance dose and was not the dose-limiting factor in BNCT.

While the average dose provided comparison in doses in different tissues, it was not an accurate representation of the dose distribution within a tissue. For example, the
brain encompasses a large volume, and the dose may have concentrated in the region closest to the neutron source but was averaged over the whole brain volume. AD and AR are two figures of merit that are commonly used in the BNCT community and integrate the maximum brain dose into evaluation. Unlike conventional radiotherapy where the tumor is prescribed a therapeutic dose, BNCT treatment, and thus the tumor dose, is dependent on the brain tolerance dose, or 12.5 Gy-Eq. AD and AR examine the quality of the neutron source by incorporating the brain tolerance dose and determining the conditions in which the brain dose would be exceeded. The simulation results showed that epithermal neutrons would optimize both AD and AR, allowing treatment of deep-seated tumors and less dose delivery to the normal tissues. At high neutron energies, the AR was close to 1, indicating that the integrated doses to the tumor and the brain were essentially equal.

The dose evaluation in this study did not consider the cranium. However, clinical trials have not reported any adverse effect in the cranium in BNCT. If necessary, the cranium could be incorporated into the calculation by using the appropriate B-10 concentration and CBE value for the cranium. Studies have found that the B-10 concentration in bone is similar to that in soft tissues and have used a CBE value of 1.2 for bone dose calculation. In this study, only the posterior-anterior (PA) beam was examined. It would be beneficial to expand the study to include other beam orientations, such as lateral (LAL) and anterior-posterior (AP). The main distinction among the different beam angles is the radiation exposure to other normal tissues. The brain tends to receive more dose with a PA beam while more organs (e.g. lens) are exposed to the beam with a LAL or an AP beam.
In this MCNP simulation study, epithermal neutrons between 0.5 eV and 10 keV were found to be the optimal energy range for BNCT of the brain. Since tumor mass will extend several millimeters within the brain tissue, the range of neutrons will enable adequate dose coverage at different depths. The simulation results demonstrated that epithermal neutrons maximized the radiological advantages of using the high LET particles for the delivery of a therapeutic dose to the target. In terms of average dose, the alpha dose contribution to the tumor was the greatest when the neutron source was in the epithermal energy range and the lowest at high neutron energies. For the brain, the neutron dose had the minimal contribution at epithermal energies but accounted for a significant fraction of the total brain dose when the neutron energy was in the MeV range. With respect to the maximum brain dose, AD and AR were found to have the highest values when the source energy was between 0.5 eV and 10 keV. In addition, the skin dose was reduced with an epithermal neutron source. In conclusion, epithermal neutrons between 0.5 eV and 10 keV are optimal for BNCT of brain tumors.
CHAPTER 3. DESIGN OF BEAM SHAPING ASSEMBLY

3.1 Introduction

At present, the BNCT neutron sources are limited to nuclear reactors and large particle accelerators, which are costly to construct and maintain and cannot be widely incorporated into clinical settings. Due to the lack of a clinically appropriate neutron source, progress and involvement in BNCT research have been deficient. As an alternative, compact DD neutron generators possess the financial advantage and convenience over the conventional neutron sources. In the previous chapter, it was demonstrated that neutrons in the epithermal energy range between 0.5 eV and 10 keV were optimal for BNCT of brain tumors at depth between 5 and 10 cm. Epithermal neutrons are able to penetrate deeply into the brain tissues and are thermalized when they reach the tumor site. As the energy of DD neutrons is 2.45 MeV, a beam shaping assembly (BSA) is necessary to moderate the DD neutrons down to the desired epithermal range. In addition to moderation, the purpose of the BSA also entails removing any background radiation that adds dose to healthy tissues and doesn’t have any therapeutic benefits. The background radiation includes the fast and thermal neutrons inherent in the neutron beam as well as photons that are produced from neutron interactions with the BSA. An optimized BSA should maximize epithermal neutron output and reduce any unwanted radiation. The goal of this study was to design a BSA for a DD neutron source to moderate the fast DD neutrons and limit any contamination radiation in the neutron beam output.
3.2 Materials and Methods

3.2.1 Monte Carlo N-Particle Simulation

Simulations were performed using MCNPX version 2.7.0. The simulation model consisted of the MIRD head phantom, a neutron source, and a beam shaping assembly. The head phantom was the same as the one described in Section 2.2.1 with the tally cylinders along the central beam axis (Figure 2.2b). There were 32 tally cylinders in the brain and 1 in the scalp. The neutron source was configured based on the most current DD neutron generator in our lab, manufactured by Adelphi Technology Incorporated. The DD generator has a titanium target in size of 2 by 2 by 0.2 cm$^3$. When the fusion reaction occurs at the target, the resulting 2.45-MeV neutrons are evenly distributed over the target and emitted isotropically. Due to these features of the DD generator, the modeled neutron source in MCNP was characterized as a 2.45-MeV planar source, enclosed in an aluminum vacuum casing. It was positioned behind the head phantom, aligned with the center of the brain. The exact distance between the source and the phantom varied, depending on the design of the BSA. The BSA was placed between the head phantom and the neutron source and was comprised of several components: a moderator, reflector, collimator, and thermal filter. A schematic of a BSA layout is shown in Figure 3.1. In the simulations, 2.45-MeV neutrons started at the source and entered the BSA with monoenergetic neutron distribution until they reached the exit window where the head phantom was located. The BSA surrounded the neutron source to modulate the neutron energy and shape the spectrum to the desired energy range. Different materials, geometries, and combinations were examined for each BSA component to optimize the final neutron output. Some of the BSA components were determined separately, meaning that different materials were tested for the component while the other BSA elements stayed constant, but those elements were not
necessarily the same as the final optimized layout. Simulations were terminated when statistical uncertainty was within 5%.

![Figure 3.1 Schematic of the beam shaping assembly components and layout.](image)

3.2.2 Beam Evaluation

3.2.2.1 In-Air Figures of Merit

After the 2.45-MeV DD neutrons went through the BSA, the resulting neutron beam was evaluated in two ways: in air and in phantom. The in-air figures of merit (FOM) were determined at the beam exit window in air before the beam entered the head phantom. The parameters included the epithermal neutron flux ($\phi_{\text{epi}}$), the thermal-to-epithermal neutron ratio ($\phi_{\text{th}}/\phi_{\text{epi}}$), the fast neutron dose per epithermal ($D_f/n_{\text{epi}}$), and the photon dose per epithermal ($D_\gamma/n_{\text{epi}}$). Table 3.1 lists the FOMs and the recommended values proposed by the International Atomic Energy Agency (IAEA). The goal was to find the BSA layout
that would maximize the epithermal neutron flux while adhering to the recommended values for the other three FOMs or keeping them to as low as possible.

Table 3.1 The in-air figures of merit used for BSA optimization and the recommended values by the International Atomic Energy Agency.

<table>
<thead>
<tr>
<th>In-Air Parameters</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermal neutron energy</td>
<td>&lt; 0.1 eV</td>
</tr>
<tr>
<td>Epithermal neutron energy</td>
<td>0.5 eV to 10 keV</td>
</tr>
<tr>
<td>Fast neutron energy</td>
<td>&gt; 10 keV</td>
</tr>
<tr>
<td>$\phi_{\text{epi}}$ ($\text{n}_{\text{epi}}/\text{cm}^2\cdot\text{s}$)</td>
<td>&gt; 1E9</td>
</tr>
<tr>
<td>$\phi_{\text{th}}/\phi_{\text{epi}}$</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>$D_{\gamma}/\phi_{\text{epi}}$ (Gy-cm$^2$/n$_{\text{epi}}$)</td>
<td>&lt; 2E-13</td>
</tr>
<tr>
<td>$D_r/\phi_{\text{epi}}$ (Gy-cm$^2$/n$_{\text{epi}}$)</td>
<td>&lt; 2E-13</td>
</tr>
</tbody>
</table>

3.2.2.2 In-Phantom Figures of Merit

The in-phantom FOMs were assessed in the brain and skin tally cylinders. Additional to the AD and AR parameters mentioned in Section 2.2.3.2, the in-phantom FOMs also consisted of the Advantage Depth Dose Rate (ADDR), peak skin dose, and the required neutron flux. ADDR is the dose rate at the advantage depth and closely related to the treatment time. The BSA was optimized to maximize the AD, AR, and ADDR. The peak skin dose was also determined and compared to the maximum tolerable skin dose in literature. The required neutron flux is the flux that is needed to reach the brain tolerance dose within one hour and was calculated as a reference for future technology development. The ADDR and the required neutron flux were calculated based on the neutron flux of our most current DD neutron generator, $5 \times 10^9$ n/s.
3.3 Results

3.3.1 Thermal Filter

The thermal filter is the last component before the neutron beam exited the BSA completely and was placed immediately before the exit window. The purpose of the filter was to remove the thermal neutron component from the neutron spectrum since they have poor tissue penetration and cannot reach deep-seated tumors, depositing radiation dose to the skin and the normal tissues. The determination of the optimal material for the thermal filter was relatively straightforward. Figures 3.1 to 3.3 represent the capture cross sections for cadmium(Cd)-113, lithium-6, and gold(Au)-197, respectively. By examining the cross section for neutron capture interaction of different materials, Cd was found to be the ideal material for the thermal filter due to its substantially greater cross section at thermal energy. The cross section for Cd-113 is around $10^4$ barns whiles it is $10^2$ and $10^2$ for Au-197 and Li-6, respectively. Au-197 had a high thermal capture cross section. However, after undergoing neutron capture reaction, a high-energy prompt gamma is released, increasing the photon dose to normal tissues.
Figure 3.2 Radiative capture cross sections for cadmium-113 from data library END/B-VIII.0.

Figure 3.3 Radiative capture cross section for lithium-6 from data library END/B-VIII.0.
Cd was highly effective in removing thermal neutrons from the beam output. Thus, the smallest thickness of Cd that was just enough to reduce thermal neutrons without perturbing the epithermal neutron fluence was determined. Figure 3.5 displays the epithermal neutron fluence per source neutron and the thermal-to-epithermal neutron ratio as a function of Cd thickness. As the Cd thickness increased, the ratio decreased substantially because more thermal neutrons were removed from the beam. Thicker Cd filter diminished the epithermal fluence as well but not as significantly. A thickness of 0.02 cm of Cd was found to be the optimal thermal filter because it effectively reduced the thermal-to-epithermal neutron ratio to well below the IAEA recommendation without influencing the epithermal flux drastically.
3.3.2 Reflector

Due to the isotropic feature of the DD neutron source, a reflector is necessary to direct the neutrons toward the beam opening and to maximize the neutron flux in the forward direction. The reflector is the outermost component of the BSA and surrounds the neutron source as well as the other BSA components. Some of the materials that were considered for the reflector component of the BSA included bismuth, polyethylene, lead (Pb), and iron. With other BSA components remained constant, Pb was found to be the most effective material for the reflector. Figure 3.6 presents the epithermal neutron fluence per source neutron at the beam exist window as a function of reflector thickness for materials Pb and polyethylene. Both materials showed an increase in the epithermal fluence as the reflector thickness increased. However, Pb had a higher epithermal neutron flux than
polyethylene for all thickness and exhibited a larger increase in flux with thickness. The epithermal flux saturated at 8 cm of polyethylene but continued increasing at above 50 cm of Pb. The increase in flux with Pb reflector eventually began to slow down. While thicker reflector resulted in better epithermal flux, the amount of applicable Pb to the BSA system is limited by cost, exposure to the toxic metal, and the load limitation of the floor. As a result, a thickness of 30 cm was decided for the reflector.

![Graph showing epithermal neutron fluence as a function of reflector thickness for materials, lead, and polyethylene.]

Figure 3.6 Epithermal neutron fluence as a function of reflector thickness for materials, lead, and polyethylene.

3.3.3 Collimator

The collimator is located near the end of the BSA, right before the thermal filter. The purpose of the collimator was to limit the radiation field to the size of the target volume and to reduce radiation exposure to healthy tissues, without distorting the moderated
neutron beam. The collimator has similar functions as the reflector and, thus, similar materials were investigated for the collimator. The final collimator was 10-cm long of Pb and created a beam aperture of 12 by 12 cm$^2$.

3.3.4 Moderators

The moderator of the BSA component was responsible for moderating the DD neutrons from fast to epithermal energy and was placed immediately in front of the neutron source in the beam direction. Compared to other BSA components, the determination of the optimal moderator materials was more complicated and involved more trial-and-error. Table 3.2 lists some of the different materials and combinations that were examined for the moderator as well as the in-air parameters for each.

<table>
<thead>
<tr>
<th>Materials</th>
<th>$\varphi_{\text{epi}}$</th>
<th>$\varphi_{\text{th}}/\varphi_{\text{epi}}$</th>
<th>$D_r/\varphi_{\text{epi}}$</th>
<th>$D_f/\varphi_{\text{epi}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{AlF}_3$ (50)</td>
<td>1.8</td>
<td>0.01</td>
<td>14</td>
<td>1.8</td>
</tr>
<tr>
<td>$\text{Li}_7\text{F}$ (50)</td>
<td>1.5</td>
<td>0.04</td>
<td>6.6</td>
<td>1.8</td>
</tr>
<tr>
<td>$\text{Li}_7\text{F}$ (45) + $\text{MgF}_2$ (10)</td>
<td>1.0</td>
<td>0.05</td>
<td>5.5</td>
<td>2.4</td>
</tr>
<tr>
<td>$\text{Li}_7\text{F}$ (45) + $\text{AlF}_3$ (10)</td>
<td>1.2</td>
<td>0.04</td>
<td>5.6</td>
<td>3.4</td>
</tr>
<tr>
<td>$\text{AlF}_3$ (55) + $\text{MgF}_2$ (10)</td>
<td>83</td>
<td>0.03</td>
<td>5.4</td>
<td>2.3</td>
</tr>
<tr>
<td>$\text{MgF}_2$ (60)</td>
<td>80</td>
<td>0.05</td>
<td>6.4</td>
<td>2.7</td>
</tr>
<tr>
<td>$\text{CaF}_2$ (50)</td>
<td>1.5</td>
<td>0.01</td>
<td>39</td>
<td>2.2</td>
</tr>
</tbody>
</table>

3.3.5 Final Beam Shaping Assembly

Figure 3.7 displays the cross-sectional view of the final optimized BSA layout. The reflector was 30 cm of lead; the moderators included 45 cm of $\text{Li}_7\text{F}$ and 10 cm of $\text{MgF}_2$;
the thermal filter was 0.02 cm of cadmium, and the collimator was 10 cm of lead. The collimator confined the radiation field to 12 x 12 cm$^2$ to reduce radiation exposure to healthy tissues.

![Diagram of BSA layout](image)

Figure 3.7 Cross-sectional view of the optimized BSA layout.

3.3.5.1 In-Air Figures of Merit

The neutron spectrum at the beam exist window is shown in Figure 3.8 in epithermal neutron fluence per source neutron. The spectrum presented a peak in the epithermal energy range with limited thermal and fast neutrons. Table 3.3 shows the in-air FOMs of the neutron spectrum as well as the IAEA recommendations and data from existing BNCT facilities. The epithermal neutron flux of the optimized BSA system was 1.95 x 10$^{-5}$ n$_{epi}$/cm$^2$ per neutron source or 9.4 x 10$^4$ n$_{epi}$/cm$^2$-s. The flux was calculated based on 5 x 10$^9$ n/s, the neutron flux of our most current DD neutron generator. An
increase of four orders of magnitude was needed to meet the IAEA recommendation. The thermal-to-epithermal neutron ratio was 0.03 and in agreement with the recommended value. The fast neutron and photon doses per epithermal neutron were \(5.9 \times 10^{-13}\) and \(2.1 \times 10^{-13}\) Gy-cm\(^2\)/n\(_{\text{epi}}\), respectively. While they exceeded the IAEA criteria, they were within the range of existing BNCT facilities that are used for treating BNCT patients. In order to meet the IAEA epithermal neutron flux criterion, the DD neutron flux would need to increase to \(5.1 \times 10^{13}\) n/s.

![Figure 3.8 Neutron spectrum in air at the BSA exit window](image)

### Table 3.3

<table>
<thead>
<tr>
<th>Proposed System</th>
<th>IAEA(^{87})</th>
<th>Existing Facilities(^{87})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\phi_{\text{epi}}) (n(_{\text{epi}})/cm(^2)-s)</td>
<td>(9.4 \times 10^{9})</td>
<td>&gt; 1 \times 10^{9}</td>
</tr>
<tr>
<td>(\phi_{\text{th}}/\phi_{\text{epi}})</td>
<td>0.03</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>(D_{f}/\phi_{\text{epi}}) (Gy-cm(^2)/n(_{\text{epi}}))</td>
<td>(5.9 \times 10^{-13})</td>
<td>&lt; 2 \times 10^{-13}</td>
</tr>
<tr>
<td>(D_{\gamma}/\phi_{\text{epi}}) (Gy-cm(^2)/n(_{\text{epi}}))</td>
<td>(2.1 \times 10^{-13})</td>
<td>&lt; 2 \times 10^{-13}</td>
</tr>
</tbody>
</table>
3.3.5.2 In-Phantom Figures of Merit

Table 3.4 shows the in-phantom results and the desired DD neutron flux for the optimized layout. The AD was 12.5 cm, and the AR was 4.4. The ADDR was $2.9 \times 10^{-3}$ cGy-Eq/min. The DD neutron flux required to perform a BNCT treatment within one hour was $3.6 \times 10^{13}$ n/s. If the desired neutron flux was achieved, the ADDR would increase to 20.8 cGy-Eq/min. The peak skin dose was 0.59 Gy-Eq.

<table>
<thead>
<tr>
<th>AD (cm)</th>
<th>AR</th>
<th>ADDR (cGy-Eq/min)</th>
<th>DD neutron flux (n/s)</th>
<th>Peak skin dose (Gy-Eq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.5</td>
<td>4.4</td>
<td>$2.9 \times 10^{-3}$ (20.8)</td>
<td>$3.6 \times 10^{13}$</td>
<td>0.59</td>
</tr>
</tbody>
</table>

The dose profile for the neutron beam output of the optimized BSA is shown in Figure 3.9. The figure included the dose profiles for the tumor and the brain as well as the individual dose components. The dose was normalized to the tolerable brain dose of 12.5 Gy-Eq. The brain dose was the highest near the surface at 1.5 cm depth and continued to decrease with depth. Neutron was the main dose contributor to the brain, followed by alpha then photon. The tumor dose was about two to four times greater than the brain dose, depending on the depth. Contrary to the brain, the tumor exhibited a buildup region in the dose profile and reached a maximum dose of 47.9 Gy-Eq at 3 cm deep. Alpha dose accounted for majority of the total tumor dose.
3.4 Discussion and Conclusion

The objective of this study was to optimize the BSA layout for a DD neutron source to moderate the 2.45-MeV neutrons to the epithermal energy range. The final BSA configuration produced satisfactory in-air and in-phantom results. The epithermal neutron flux at the beam exist window was $9.4 \times 10^4 \text{n}_{\text{epi}}/\text{cm}^2\text{-s}$, about four orders of magnitude less than the IAEA recommendation. $\frac{\phi_{th}}{\phi_{epi}} = 0.03$, in agreement with the IAEA; $D_f/\text{n}_{\text{epi}}$ and $D_t/\text{n}_{\text{epi}}$ were greater than the IAEA criteria but comparable to those of existing BNCT facilities. For the in-phantom FOMs, the IAEA does not have any recommended values. Thus, our results were compared with those from literature. Table 3.5 shows the in-phantom parameters for the proposed DD system and other BNCT facilities with different neutron sources. MIT and THOR are reactor-based; Yanch et al and Birmingham are accelerator-based, and Han et al is DD-based. The ADDR and the irradiation time for our
system in the table were calculated as if the DD neutron flux was adequate for treatment. The AD and AR of our beam were comparable to other neutron sources. The ADDR and the irradiation time were lower than the reactor-based facilities but greater than the accelerator- and DD-based sources. Reactor-based BNCT systems had comparable AD and AR to other neutron sources but outperformed in ADDR and treatment time. This may largely be due to the greater neutron flux that reactors are able to produce. Accelerator-based facilities had varying results. Yanch et al. had lower AD but higher dose rate and could complete irradiation in 32 minutes. The Birmingham accelerator beam had better penetration (higher AD) but much longer treatment time. To our knowledge, Han et al. is the only study that included in-phantom FOMs for evaluation of a DD-based BNCT system. Despite their assumption of $1 \times 10^{11} \text{n/cm}^2\text{-s}$ for the neutron flux, the treatment time was unpractically long while our DD-based system had a more reasonable irradiation time. The variations among the facilities could be attributed to the types of neutron source. In addition, the dose calculation factors and simulation models (e.g. source position and beam aperture size) used could also contribute to the differences. For example, Yanch et al. applied a 10:1 boron ratio between the tumor and the brain and biological factors of 1, 1.6, and 2.3 for photon, neutron, and alpha, respectively. The THOR design used a 3.6:1 ratio, and the biological factors were 1, 3.2, and 1.3 for photon, neutron, and alpha, respectively. These discrepancies could affect the dose calculations considerably. Although the ADDR and the irradiation time of our system were based on the assumption that the DD neutron flux was sufficient for treatment, the in-air FOMs, the AD and the AR demonstrated that the optimized neutron beam possessed the appropriate dosimetric properties for BNCT of the brain.
Table 3.5 Comparison of the in-phantom FOMs and the irradiation time with different types of BNCT sources.

<table>
<thead>
<tr>
<th>Source</th>
<th>AD (cm)</th>
<th>AR</th>
<th>ADDR (cGy/min)</th>
<th>Irradiation time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIT FCB\textsuperscript{88}</td>
<td>9.7</td>
<td>5.7</td>
<td>170</td>
<td>7</td>
</tr>
<tr>
<td>THOR\textsuperscript{89}</td>
<td>8.9</td>
<td>5.6</td>
<td>50</td>
<td>25</td>
</tr>
<tr>
<td>Yanch et al\textsuperscript{90}</td>
<td>8.5</td>
<td>4.1</td>
<td>7.9</td>
<td>32</td>
</tr>
<tr>
<td>Birmingham\textsuperscript{91}</td>
<td>10.3</td>
<td>5.6</td>
<td>5.5</td>
<td>220</td>
</tr>
<tr>
<td>Han et al\textsuperscript{92}</td>
<td>9.1</td>
<td>5.6</td>
<td>9.9</td>
<td>822</td>
</tr>
<tr>
<td>Proposed system</td>
<td>12.5</td>
<td>4.4</td>
<td>20.8</td>
<td>60</td>
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</tbody>
</table>

The most difficult IAEA recommendations to satisfy were the epithermal flux and the fast neutron dose. While thicker moderators and filter could further suppress the fast neutron and photon doses, the epithermal neutron flux would suffer as well. Thinner moderator would increase not only the epithermal flux but also the neutron and photon doses, inevitably. Therefore, the trade-off between the epithermal flux and the contamination radiation doses needed to be balanced. The final moderator combination was chosen due to its acceptable in-air FOMs and balance between the epithermal fluence and the fast neutron dose. While our results did not satisfy the IAEA commendations, it is important to note that the FOMs of our system agreed with those of existing BNCT facilities.

The materials investigated for the moderator component were largely based on literature search\textsuperscript{62,64,67,93,94}. The approach was a trial-and-error and time-consuming process. We attempted to find a more systematic method by computing and comparing the neutron cross sections of different materials. An ideal moderator should have a high scatter cross section and low absorption. Figure 3.10 illustrates the neutron cross sections for various moderator materials that were found to be either a good or poor moderator for 2.45-MeV
neutrons. The cross sections included the total scatter, elastic scatter, inelastic scatter, and absorption at 2.45 MeV. All the materials had relatively negligible absorption cross sections. However, none of the materials had a prominent scatter cross section. The simulation results showed that LiF and MgF\textsubscript{2} were the optimal materials for fast neutron moderation, but their scatter cross sections were comparable to those of other materials. Materials that were found to have better moderating ability (e.g. Al and Fluental\textsuperscript{TM}) had lower scatter cross sections than those that were poor moderators (e.g. CF\textsubscript{2} and TiF\textsubscript{3}). Further investigation is needed to identify the common characteristics among the moderator materials and to have a better understanding of epithermal neutron interaction with matter.

![Figure 3.10 Neutron cross sections for various moderator materials at 2.45 MeV.](image)

To satisfy the epithermal recommendation by the IAEA, the DD neutron generator would require a neutron yield of $5.1 \times 10^{13}$ n/s. On the other hand, according to the in-
phantom FOMs and the irradiation time of 1 hour, the neutron yield should be $3.6 \times 10^{13}$ n/s. With the lower neutron flux, the epithermal flux would be just shy of the IAEA criterion. Therefore, the desired DD neutron intensity should be the higher value, $5.1 \times 10^{13}$ n/s, which would reduce the treatment time from 60 to 42 minutes. While the flux of our current generator is $5 \times 10^9$ n/s, study has found that by increasing the deuterium beam current, along with other technical adjustments, the neutron yield could be enhanced to $10^{12}$ n/s.\textsuperscript{93} In addition, Adelphi Technology Inc. is in the process of developing a multi-beam system that combines multiple DD neutron generators to produce a higher neutron intensity.

The simulated neutron source configuration had been simplified as a point source in a vacuum casing before the arrival of the actual DD neutron generator in our lab. The model did not consider the other components of the actual generator, such as a layer of polyethylene in the beam direction for grounding. This may have an effect on the neutron spectrum and, therefore, BSA optimization. In order to assess the possible effect of the simplification, a separate simulation was done using a more complicated neutron source model. Figure 3.11 shows the neutron spectrum when the additional components were added to the neutron source model while the BSA remained the same as in Figure 3.7. Compared to Figure 3.8, the neutron spectrum has an energy peak at a higher energy, 22 keV, and more fast neutrons. The epithermal neutron flux was reduced to $3.1 \times 10^4$ n/cm\textsuperscript{2}-s; the thermal-to-epithermal neutron ratio increased to 0.06. The fast neutron dose and the photon dose increased to $3.6 \times 10^{12}$ cGy-Eq/n\textsubscript{epi} and $3.5 \times 10^{-13}$ cGy-Eq/n\textsubscript{epi}, respectively. By modifying the source configuration, the neutron output was affected considerably, and the in-air FOMs no longer meet the IAEA recommendations or were in agreement with
other BNCT neutron sources. It indicates that further simulations should be performed using the updated source configuration to investigate if a different BSA layout would better optimize the neutron beam output.

![Neutron spectrum simulated using the actual DD neutron source layout with the optimized BSA layout.](image)

In this MCNP study, the goal was to determine a BSA layout that would moderate the 2.45-MeV DD neutrons to the desired energy range for BNCT of the brain. The neutron output produced from the optimized layout was evaluated in air at the beam aperture and in a head phantom. The in-air FOMs either met the IAEA recommendations or were within the range of existing BNCT facilities, except for the epithermal neutron flux. The in-phantom parameters were comparable to those of other BNCT systems. The resulting peak skin dose was 0.59 Gy-Eq, which was well below the dose tolerance of 18 Gy-Eq.
According to the results, the DD neutron yield would need to reach $5.1 \times 10^{13}$ n/s to satisfy the epithermal neutron flux requirement and complete irradiation within a reasonable amount of time. The proposed system showed encouraging results and was capable of producing a neutron beam with acceptable dosimetric characteristics. Further efforts are underway to improve the neutron yield to make DD neutron generators a competitive BNCT neutron source for clinical use.
CHAPTER 4. MCNP DOSE DISTRIBUTIONS

4.1 Introduction

While the in-air and in-phantom FOMs provided insights into the properties of the produced neutron beam of the optimized DD-based BNCT system, the dose distributions within tissues are still unclear. Previous simulations applied mathematical head phantoms to assess tissue doses; however, the accuracy of MCNP simulations greatly depend on the modeling of the phantom and the environment. The MIRD phantom has been used extensively in the health physics and radiotherapy communities, but the human anatomy is far too complex to be simplified into several mathematical equations. A more realistic phantom model will substantially improve MCNP dosimetry calculations and provide more accurate results. In addition to the average dose and the maximum dose that the tumor and normal tissues receive, it is also essential to obtain information on what percentage of the normal tissues receive a certain dose and what the tumor dose coverage looks like. With an improved phantom model, a dose-volume histogram will provide a better understanding of the dosimetric characteristics of the DD-based neutron beam. The objective of this study was to examine the dose distributions in a cadaver-based phantom in MCNP.

4.2 Materials and Methods

4.2.1 VIP-Man

While the MIRD phantom allowed simulation modeling to benchmark beam parameters and characteristics, it is important to use a more realistic phantom model for clinical applications. VIP-Man is an imaged-based, whole-body adult male model, developed by the National Library of Medicine in the Visible Human Project for Monte
Carlo dose calculations (Figure 4.1). The images were of a male cadaver that was representative of a large population and were implemented into Monte Carlo codes. The VIP-Man phantom models the anatomical organs that are not represented in the MIRD phantom and closely resembles an actual human body compared to mathematical models. There was a total of over 5 million voxels in the whole-body phantom, and the voxel size was $4 \times 4 \times 4 \text{ mm}^3$. While the region of interest in this study was the brain only, the rest of the phantom could potentially affect particle transports and was kept intact. The brain region of the VIP-Man was separated into multiple compartments, which were combined and tallied together to determine the dose to the whole brain in MCNP. The tissues consisted of caudate nuclei, lentiform nuclei, thalamus, white matter, lateral ventricle, corpus callosum, pons, fornix, cerebellum, and gray matter. The total brain region was comprised of 19,926 voxels and had a volume of $1275.3 \text{ cm}^3$. 
4.2.2 Dose Distribution

The optimized BSA from the previous chapter (Figure 3.7) was used as the neutron source in this study. The source was positioned behind the VIP-Man phantom. Figure 4.2
shows a lateral view of the posterior-anterior beam setup. The doses to all 19,926 voxels were determined and used to generate a dose volume histogram (DVH). The calculated dose from MCNP were in unit of Gy-Eq per source neutron and were then normalized to the maximum brain tolerance dose of 12.5 Gy-Eq. Simulations were performed using MCNP6 version 1.0, instead of MCNPX, due to the greater limit on the number of histories in MCNP6.

![Figure 4.2 Lateral view of the simulation setup for a posterior-anterior beam angle.](image)

4.3 Results

Figure 4.3 shows the DVH for the whole brain. The dose was normalized to the maximum tolerance dose of 12.5 Gy-Eq. The minimum dose that the brain obtained was 1.2 Gy-Eq. The average brain dose was 5.3 Gy-Eq.
4.4 Discussion and Conclusion

The purpose of this chapter study was to examine the dose distributions in a realistic boy phantom from BNCT irradiation with the DD-based BNCT system optimized in the previous chapter. The DVH for the brain was normalized to the tolerance dose of 12.5 Gy-Eq. The results showed that the maximum brain dose was, thus, 12.5 Gy-Eq, the minimum dose was 1.2 Gy-Eq, and the average dose was 5.3 Gy-Eq.

The main disadvantage of determining dose distributions in MCNP is that it is very time-consuming and computationally expensive. Despite using Purdue’s high-performance research computing system with 10-core Intel processors, it still took approximately 200 hours to tally all the voxels in the brain. Due to the small size of the voxels (4 x 4 x 4 mm$^3$), some of the relative errors in the voxels were significantly greater than 5%. To reduce the uncertainties to an acceptable level, the number of histories would need to increase by at
least one order of magnitude, potentially increasing the computational time to 2,000 hours. Instead of using the conventional central processing units, graphics processing unit (GPU) may improve the efficiency in computationally intensive tasks, such as MCNP. GPU-based MCNP has been shown to be 69 to 87 times faster than the conventional CPU-based and generated results that were in agreement with CPU-based. Another alternative is to increase the voxel size, or combine several voxels into one, hence the number of particles per voxel is higher and the statistical uncertainty is reduced. The downside of this method is that, with large voxels, the contour of the internal organs may not be well preserved, which may in turns affect the dose calculations. It is also hard to manipulate or change the VIP-Man input file due to the large number of voxels involved. A phantom with variable voxel sizes may be more advantageous for reducing the computational time. The “multi-voxel” model has smaller voxels, or higher resolution, near the beam entrance and larger voxels, or coarse resolution, distant from the beam entrance. This approach will allow more accurate dose calculations in regions of interest and increase efficiency by reducing the computational effort in the surrounding regions.

Due to the long computational time, only the brain DVH was obtained. Future works can expand to other normal tissues, such as the scalp and the cranium. It would be ideal to have tumor tissues incorporated in the phantom model to examine the dose distribution within the tumor as well. However, the VIP-Man has only normal tissues, and the user will have to introduce a voxel or voxels of tumor within the brain. It is difficult to objectively decide what size and location of the tumor to use in the simulations and may require numerous simulations to cover different scenarios. Actual patient data from CT or
MRI images would be beneficial but will require converting and importing those data into MCNP format.
CHAPTER 5. DISCUSSION

While the current standard of care for glioblastoma patients is well established and proven to improve patient survival compared to decades ago. However, the median survival remains dismal and has not changed significantly in recent years. BNCT offers a biological component to the treatment and allows targeting of the microscopic tumor cells that conventional treatments are unable to eradicate. The two major challenges that BNCT currently encounters are the development of B-10 compounds and the lack of a clinically appropriate neutron source, hindering research progress and interest in BNCT. The dilemma between the two issues of B-10 drug improvement and neutron source development is that they are interconnected, meaning that each side is dependent on the other to show progress. The two clinical compounds, BPA and BSH, have been demonstrated to provide promising B-10 delivery and preferential accumulation in the tumor cells. While continuous progress is still underway to further improve the drugs, the B-10 compound issue is the less pressing of the two. The focus of this dissertation work was to help resolve the neutron source problem that is troubling the BNCT community.

A DD neutron generator offers several advantages over nuclear reactors and large particle accelerators in terms of cost, size, installation and modification process. Although the construction of proton accelerators continues to expand, the cost to build and maintain the facility is several orders of magnitude greater than that for a DD neutron generator. Accelerators also face technical difficulties that are yet to be overcome. With less capital expenses and space, DD neutron generators can be more widespread, accessible to patient populations, and offered to all forms of clinics and institutions. As more systems are installed, data collection and patient recruitment will be enhanced as well.
The simulation results of the optimized DD neutron generator-based BNCT system demonstrated that DD neutron generators could produce comparable dosimetric properties as nuclear reactors and large accelerators. Based on the in-air evaluation, the epithermal neutron flux was insufficient by four orders of magnitude. However, this was based on several assumptions, including that the tumor-to-brain boron ratio was 3.5 and only one field, one fraction was applied. The required increase of four orders of magnitude is not solely dependent on the neutron flux alone. If further compound development is able to increase the boron ratio to 10 or if multiple fields or fractions are applied, the DD neutron flux requirement will be reduced by half or more. The in-phantom parameters presented similar results as other BNCT neutron sources, except for the dose rate, which is also due to the inadequate DD neutron flux. The AD of the proposed system was 12.5 cm, suggesting that the neutron beam could treat tumors up to 12.5 cm deep. However, since the dimension of a typical human head is 20 cm long, beam penetration greater than 10 cm may be redundant because parallel-opposed beams can be used. The maximum skin dose delivered by the proposed system was 0.6 Gy-Eq, which was substantially lower than the tolerance limit. Early clinical trials reported that patients exhibited radiation dermatitis of the scalp, and the results from this work demonstrated that radiation-induced toxicities in the skin would not be an issue.

Although the proposed system produced comparable dosimetric characteristics as other BNCT types of neutron sources, the neutron flux of DD neutron generators is still lackluster. While system and software development of DD neutron generators is beyond the scope of this dissertation, feedbacks and suggestions are provided to the manufacturer. Currently BNCT clinical trials have not shown a significant advantage in the median
survival of glioblastoma patients treated with BNCT. However, this innovative technique could be administered in conjunction with surgery or other treatment modalities. Study has found that BNCT with radiotherapy significantly increased patient survival.98

The overall goal of this dissertation is to investigate and design the use of a compact DD neutron generator for BNCT of the brain. Given the present challenges that BNCT encounters, this dissertation presented an alternative neutron source that is clinically feasible and friendly. With sufficient development and research, DD neutron generators can become a competitive neutron source that can help address deficiencies in current clinical practice and stimulate industrial interest and institutional commitment.
CHAPTER 6. OVERALL CONCLUSION

The overall objective of this dissertation research was to design a DD neutron generator-based BNCT system and to examine the dosimetric properties of the neutron output. In the first specific aim, the effect of neutron beam energy on tissue dose was investigated. Epithermal neutrons between the energy of 0.5 eV and 10 keV were the optimal energy for BNCT of brain tumors. In terms of tumor dose, epithermal neutrons were able to utilize the advantages of the high LET particles to the maximum while fast neutrons delivered radiation dose via neutron particles. With epithermal neutrons, approximately half of the brain dose originated from photons. However, as the neutron energy increased to the MeV range, both the brain and the tumor obtained the same amount of dose from neutrons. The dose ratio between the tumor and the brain was found to be maximized in the epithermal energy range as well as the AD and AR.

The second specific aim was to design a BSA for a DD neutron source to moderate the 2.45-MeV DD neutrons to the epithermal range as well as reducing the levels of background radiation. The optimized BSA layout had the following configuration: 45 cm of Li\textsuperscript{7}F and 10 cm of MgF\textsubscript{2} for the moderator, 30 cm of lead for the reflector, 10 cm of lead for the collimator, and 0.02 cm of Cd-113 for the thermal filter. Comparing the in-air FOMs with the IAEA recommendations, the epithermal neutron flux was insufficient by about four orders of magnitude, but the thermal-to-epithermal neutron ratio, the fast neutron dose per epithermal neutron, and the photon dose per epithermal neutron were acceptable. The in-phantom FOMs, e.g. AD and AR, were comparable to data from existing BNCT facilities. While the ADDR was lacking compared to others, however, if the DD neutron generator had adequate neutron flux, the ADDR would be in agreement with or higher than
some of the current facilities. For the DD neutron generator to be a feasible BNCT neutron source, the neutron flux would need to be at least $5.1 \times 10^{13}$ n/s.

The goal of the third specific aim was to examine the dose distributions from irradiations with the neutron beam of the optimized BNCT system. The phantom model was the VIP-Man, which was an imaged-based, whole-body model based on a male cadaver. The DVH for the brain showed that the maximum dose was 12.5 Gy-Eq, the minimum dose was 1.4 Gy-Eq, and the average dose was 5.3 Gy-Eq.

In the future, the BSA layout for our most current DD neutron generator can be further optimized to account for any structural differences that the simulation model did not include. Since this dissertation research focused on computer simulations of the DD neutron generator, experiments to verify the simulation results would be beneficial, such as dose measurements in air and in phantom, and neutron spectrum determination using activation foils. Future work may also investigate methods to reduce the MCNP computational time without sacrificing the accuracy of the results.
APPENDIX MCNP BSA INPUT FILE

c Male Adult Head

c BSA moderator: 45 cm LiF, 10 cm MgF₂

c Cadmium filter

c 30 cm Pb reflector

c Pb collimator

c --------------------------- Cells of the phantom -------------------------

1 0 999 $void

5 1 -0.001205

(-999 ((2203 3805 -2202):((2207 -2206):(2206 2207)) 2202 -2205)

:(2107 2205)) #15 #20 #8 #10 #11 #12 #30 #40 #41 #42 #43 #44)

:(-999 -3805 #15 #20 #8 #10 #11 #12 #30 #40 #41 #42 #43 #44) $air in sphere

c ----------------------------- Neutron Generator --------------------------

15 2 -2.6989 (11 -12 201 -202 -14 13)

20 2 -2.6989 (102 -12 202 -110 13 -14):(11 -101 202 -110 13 -14)

:(11 -12 202 -110 -14 104):(11 -12 202 -110 13 -103)

:(11 -12 110 -10 13 -14)

8 0 (101 -102 202 -110 103 -104)

c ------------------------------- Moderators --------------------------------

10 8 -3.148 (11 -12 13 -14 105 -106) #40 #41 #42 #43 #44

11 12 -2.65 (11 -12 13 -14 106 -201) #40 #41 #42 #43 #44

c ------------------------------- Reflector --------------------------------

12 9 -11.34 (-11 108 31 -111 112 -113):(12 -109 31 -111 112 -113)
: (11 -12 31 -111 14 -113): (11 -12 31 -111 -13 112)

: (11 -12 10 -111 13 -14)

c ---------------------------------- Filter -----------------------------------

30 4 -8.65 (11 -12 30 -105 13 -14)

c ------------------------------- Collimator -------------------------------

40 9 -11.34 (43 -44 31 -14 -40) $Upper yz$

41 9 -11.34 (43 -44 31 13 42) $Lower yz$

42 9 -11.34 (-12 -45 31 46 -47) $Upper xy$

43 9 -11.34 (11 48 31 46 -47) $Lower xy$

44 9 -11.34 (11 -43 31 -41 -14 47 -49): (-12 44 31 -41 -14 47 50)

: (11 -43 31 -41 13 -46 51): (-12 44 31 -41 13 -46 -52) $Corner quadrants$

c --------------------------------- Phantom --------------------------------

100 7 -1.03 ((-2201 3805 -2202):

(((-2207 -2206): (2206 -2204) 2202 -2205): (-2209 2205))

# 141 # 471

# 224 # 225 # 226

# 700 # 701 # 702 # 703 # 704 # 705 # 706 # 707 # 708 # 709 # 710

# 711 # 712 # 713 # 714 # 715 # 716 # 717 # 718 # 719 # 720 # 721

# 722 # 723 # 724 # 725 # 726 # 727 # 728 # 729 # 730 # 731 # 732 $normal tissue$

141 15 -1.04 (-1402 2205 # 700 # 701 # 702 # 703 # 704 # 705 # 706 # 707 # 708 # 709

# 710 # 711 # 712 # 713 # 714 # 715 # 716 # 717 # 718 # 719 # 720 # 721 # 722

# 723 # 724 # 725 # 726 # 727 # 728 # 729 # 730 # 731): (-1404 -1408 -2205)

# 700 # 701 # 702 # 703 # 704 # 705 # 706 # 707 # 708 # 709
#710 #711 #712 #713 #714 #715 #716 #717 #718 #719 #720 #721 #722
#723 #724 #725 #726 #727 #728 #729 #730 #731 #732 $\text{brain}$
224 6 -1.09 2201 -2203 -2202 3805 $\text{neck skin}$
225 6 -1.09 2204 -2207 2206 -2205 2202 #732
226 6 -1.09 2209 -2107 2205 #732 $\text{scalp}$
471 16 -1.61 (4701 -2209 2205):(-2205 4703 -4704 -4707)
:(-2205 4706 -4707 -4703) $\text{Cranium}$
c ------------------------------ Tally cells -------------------------------
700 15 -1.04 (-7000 -7001 7002)
701 15 -1.04 (-7000 -7002 7003)
702 15 -1.04 (-7000 -7003 7004)
703 15 -1.04 (-7000 -7004 7005)
704 15 -1.04 (-7000 -7005 7006)
705 15 -1.04 (-7000 -7006 7007)
706 15 -1.04 (-7000 -7007 7008)
707 15 -1.04 (-7000 -7008 7009)
708 15 -1.04 (-7000 -7009 7010)
709 15 -1.04 (-7000 -7010 7011)
710 15 -1.04 (-7000 -7011 7012)
711 15 -1.04 (-7000 -7012 7013)
712 15 -1.04 (-7000 -7013 7014)
713 15 -1.04 (-7000 -7014 7015)
714 15 -1.04 (-7000 -7015 7016)
82

715 15 -1.04 (-7000 -7016 7017)
716 15 -1.04 (-7000 -7017 7018)
717 15 -1.04 (-7000 -7018 7019)
718 15 -1.04 (-7000 -7019 7020)
719 15 -1.04 (-7000 -7020 7021)
720 15 -1.04 (-7000 -7021 7022)
721 15 -1.04 (-7000 -7022 7023)
722 15 -1.04 (-7000 -7023 7024)
723 15 -1.04 (-7000 -7024 7025)
724 15 -1.04 (-7000 -7025 7026)
725 15 -1.04 (-7000 -7026 7027)
726 15 -1.04 (-7000 -7027 7028)
727 15 -1.04 (-7000 -7028 7029)
728 15 -1.04 (-7000 -7029 7030)
729 15 -1.04 (-7000 -7030 7031)
730 15 -1.04 (-7000 -7031 7032)
731 15 -1.04 (-7000 -7032 7033)
732 6 -1.09 (2209 -2107 7034 -7035 2205 -7037 2206)
    :(2204 -2207 7034 -7035 -2205 7036 2206)  $Skin tally

$-------------------------------- Surfaces of the phantom ---------------------$

999 so 300  $MCNP compatible$

$c -------------------------- Neutron Generator ---------------------------$
117  pz -1

c -------------------------------- Filter ------------------------
30  py 0.98
31  py 1

c ------------------------- Collimator ---------------------
40  p 0 1.2637 -1 -4.7363
41  py 11
42  p 0 -1.2637 -1 4.7363
43  px -6
44  px 6
45  p -1 1.15895 0 -4.84105
46  pz -6
47  pz 6
48  p -1 -1.15895 0 4.84105
49  p 126.37 146.4565115 -115.895 -1307.1334885
50  p 126.37 -146.4565115 115.895 1307.1334885
51  p -126.37 -146.4565115 -115.895 1307.1334885
52  p -126.37 146.4565115 115.895 -1307.1334885

c --------------------------- Brain --------------------------
1401  sq .026699 .014945 .057233 0 0 0 -1 0 -13 0   Supper surface of inner side
1402  sq .019726 .011866 .037268 0 0 0 -1 0 -13 0
1403  sq .026699 .014945 .035870 0 0 0 -1 0 -13 0   Slower surface of inner side
1404  sq .019726 .011866 .025356 0 0 0 -1 0 -13 0
1407 p 0 -0.645477 -1 13.671431 Inner surface of the plane
1408 p 0 -0.684069 -1 15.172207

----- Head -----
2201 c/z 0 -11.8 5.81 Neck, cylindrical surface
2202 pz -12.8 Neck, upper z plane
3805 pz -18 Neck, lower z plane
2203 c/z 0 -11.8 6.01 Skin of neck
2204 sq 0.016692 0.010412 0 0 0 0 -1 0 -13 0 Face, cylindrical surface
2205 pz 0 Face, upper z plane
2206 py -8.2 Face, right y plane
2207 sq 0.015862 0.01 0 0 0 0 -1 0 -13 0 Skin of face
2209 sq 0.016692 0.010412 0.029727 0 0 0 -1 0 -13 0 Top of head
2107 sq 0.015862 0.01 0.027778 0 0 0 -1 0 -13 0 Skin of top head
4701 sq .019237 .011637 .036006 0 0 0 -1 0 -13 0 Inner upper skull
4703 sq .019237 .011637 .024645 0 0 0 -1 0 -13 0 Inner lower skull
4704 sq 0.016692 0.010412 .021004 0 0 0 -1 0 -13 0 Outer lower skull
4706 p 0 -0.687163 -1 15.301489 Inner skull plane
4707 p 0 -0.704082 -1 16.052246 Outer skull plane

----- Tally cells -----
7000 c/y 0 0 1
7001 py -4
7002 py -4.5
7003 py -5
| 7004 | py -5.5   |
| 7005 | py -6     |
| 7006 | py -6.5   |
| 7007 | py -7     |
| 7008 | py -7.5   |
| 7009 | py -8     |
| 7010 | py -8.5   |
| 7011 | py -9     |
| 7012 | py -9.5   |
| 7013 | py -10    |
| 7014 | py -10.5  |
| 7015 | py -11    |
| 7016 | py -11.5  |
| 7017 | py -12    |
| 7018 | py -12.5  |
| 7019 | py -13    |
| 7020 | py -13.5  |
| 7021 | py -14    |
| 7022 | py -14.5  |
| 7023 | py -15    |
| 7024 | py -15.5  |
| 7025 | py -16    |
| 7026 | py -16.5  |
mode n p a

c ----------------------------------------- Air -----------------------------------------
c ------------------------------------------------------------------------------------------------
c ----------------------------------------------- Cadmium (8.65 g/cm^3) ----------------------------------
c ----------------------------------- ICRU skin with boron (22.5 microg/g of tissue) ------------------
c
m1 6000 -.0001 7014 -.7553 8016 -.2318 18000 -.0128 gas=1

c ------------------------------------------------------------------------------------------------
c
m2 13027.70c -1 $ Aluminum

c ---------------------------------------------- Cadmium (8.65 g/cm^3) -------------------------------
c
m4 48000 -1

c ---------------------- ICRU skin with boron (22.5 microg/g of tissue) ----------------------
c
m6 1001 -.10

5010 -.0000225

6000 -.204
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</table>

| m9  | 82000 | -1 |

---

- ICRU soft tissue with boron (15 microg/g of tissue)
- MgF2 (3.148 g/cm³)
- Lead (11.34 g/cm³)
\[ \text{c} \quad \text{------------------------ LiF (2.65 g/cm}^3\text{) ------------------------} \]

\[ m_{12} \quad 3007 \quad 0.5 \]
\[ \quad 9019 \quad 0.5 \]

\[ \text{c} \quad \text{---------- ICRU brain tissue with boron (15 microg/g of tissue) ----------} \]

\[ m_{15} \quad 1001 \quad -.107 \]
\[ \quad 5010 \quad -.000015 \]
\[ \quad 6000 \quad -.145 \]
\[ \quad 7014 \quad -.022 \]
\[ \quad 8016 \quad -.712 \]
\[ \quad 11023 \quad -.002 \]
\[ \quad 15031 \quad -.004 \]
\[ \quad 16032 \quad -.002 \]
\[ \quad 17000 \quad -.003 \]
\[ \quad 19000 \quad -.003 \]

\[ \text{c} \quad \text{------------------------ ICRU cranium ------------------------} \]

\[ m_{16} \quad 1001 \quad -.05 \]
\[ \quad 6000 \quad -.212 \]
\[ \quad 7014 \quad -.04 \]
\[ \quad 8016 \quad -.435 \]
\[ \quad 11023 \quad -.001 \]
\[ \quad 12000 \quad -.002 \]
\[ \quad 15031 \quad -.081 \]
\[ \quad 16032 \quad -.003 \]
20000 -.176
c ------------------------------------ Source Card -----------------------------------
c ---------------------------------- Source Position ---------------------------------
sdef par=n x=d1 y=d2 z=d3 erg=2.45
si1 -1.905 1.905
sp1 0 1.0
si2 56.8175 57.0715
sp2 0 1.0
si3 -1.905 1.905
sp3 0 1.0
imp:n,p,a,e 0 1 51r
cut:a j 0
prdmp j j -1
c ------------------------------------- Tallies --------------------------------------
fc114  Photon fluence to photon kerma in cGy_Zamenhof
f114:P 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716
  717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732
sd114  1.57 31r 0.035
de114  1E-3 2E-3 5E-3 1E-2 2E-2 5E-2 1E-1 2E-1 5E-1 1 2 5 10 20
dfl14  5.99E-8 1.8E-8 3.24E-9 7.75E-10 1.75E-10 3.42E-11 4.04E-11
   9.46E-11 2.63E-10 4.94E-10 8.29E-10 1.52E-9 2.48E-9
   4.38E-9
fc124  Neutron fluence to alpha kerma in cGy/ppm_Caswell
f124: N 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716
717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732
sd124 1.57 31r 0.035
   .2E-5 .36E-5 .63E-5 .11E-4 .2E-4 .36E-4 .63E-4 .11E-3
   .2E-3 .36E-3 .63E-3 .11E-2 .2E-2 .36E-2 .63E-2 .11E-1
   .2E-1 .36E-1 .63E-1 .82E-1 .86E-1 .9E-1 .94E-1 .96E-1
   .105 .115 .125 .135 .145 .155 .165 .175 .185 .195 .21
   .23 .25 .27 .29 .31 .33 .35 .37 .39 .42 .46 .5 .54 .58
   .62 .66 .7 .74 .78 .82 .86 .9 .94 .98 1.05 1.15 1.25
   1.35 1.45 1.55 1.65 1.75 1.85 1.95 2.1 2.3 2.5
dfl24 7.95E-12 6.75E-12 5.1E-12 3.85E-12 2.86E-12 2.13E-12 1.61E-12
   1.22E-12 9.05E-13 6.75E-13 5.1E-13 3.84E-13 2.85E-13 2.12E-13
   1.6E-13 1.21E-13 8.95E-14 6.65E-14 5E-14 3.78E-14 2.8E-14
   2.08E-14 1.57E-14 1.19E-14 8.9E-15 6.8E-15 5.4E-15 4.84E-15
   4.11E-15 3.73E-15 4.49E-15
fc134  Neutron fluence to neutron kerma in cGy

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<th>700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716 717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732</th>
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</table>

**nps 1e9**
REFERENCES


VITA

EDUCATION

Purdue University, West Lafayette, IN  August 2018
   Ph.D. in Medical Physics
The University of Texas at Houston, Houston, TX  August 2014
   M.S. in Medical Physics
Purdue University, West Lafayette, IN  May 2012
   B.S. in Radiological Health Science
   Minor in Physics

CERTIFICATION

American Board of Radiology, Part I in Therapeutic Medical Physics  August 2013

RESEARCH EXPERIENCE

Purdue University  2014 – 2018
Graduate Research Assistant; Advisor: Dr. Linda Nie

• Determine the radiation dose to the relevant structures from boron neutron capture therapy (BNCT) of the brain
• Develop a BNCT beam shaping assembly for a deuterium-deuterium (DD) neutron generator
• Generate treatment plans in MCNP for BNCT of the brain

University of Texas at Houston  2012 – 2014
Graduate Research Assistant; Advisor: Dr. Laurence Court

• Examined the use of TrueBeam LINAC to treat patients with lung and H&N
cancers in an upright position
  • Developed clinical IMRT treatment plans using converted, upright CT images of actual patients
  • Performed end-to-end testing and QA to assess the efficacy and integrity of the upright treatment protocols

Purdue University 2010 – 2011

Undergraduate Research Assistant; Mentor: Dr. Raji Sundararajan
  • Determined and compared the tolerance levels of various cancer cell lines to irreversible electroporation (IR)
  • Established IR protocols for each cancer cell type to achieve effective tumor ablation
  • Wrote a conference proceeding for the Electrostatics Society of America Annual Meeting

CLINICAL EXPERIENCE

Radiation Therapy Physics Rotation, MD Anderson Cancer Center 2013
  • Performed treatment planning for each oncology service to generate clinically acceptable plans
  • Participated in conventional and special treatment procedures

Diagnostic Imaging Rotation, MD Anderson Cancer Center 2013
  • Operated diagnostic imaging equipment in clinical setting to achieve desired image quality
  • Performed measurements and calculations required for accreditation and quality control of imaging equipment

Medical Physics Intern, Clarian Arnett Cancer Center 2012
  • Performed monthly QA on linear accelerators and a conventional CT simulator
  • Completed daily QA on an HDR unit and patient-specific IMRT QA tests
  • Worked with radiation oncologists, dosimetrists, and therapists to achieve desired patient
PUBLICATIONS


PRESENTATIONS


HONORS AND AWARDS

Purdue University Incentive Award 2017
AAPM Expanding Horizon Travel Grant 2016
Purdue Graduate Student Government (PGSG) Travel Grant 2016
Compton Graduate Research Travel Award 2016
Purdue University Incentive Award 2015
PGSG Travel Grant 2015
UT Houston Graduate School of Biomedical Sciences Travel Award 2014
UT Houston Robert Shalek Fellowship 2012
Purdue University Dean’s List and Semester Honors 2008-2012
Purdue University Trustees Scholarship 2008-2012

PROFESSIONAL ORGANIZATIONS

Member, American Association of Physicists in Medicine 2014 – Present