MODERATOR, COLLIMATOR AND SHIELDING STUDIES FOR BNCT RESEARCH AT MALAYSIAN NUCLEAR AGENCY

by

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TABLES OF CONTENTS

Page

CHAPTER II – THEORY AND LITERATURE REVIEW

CHAPTER III – MATERIALS AND METHODS

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOLS

α	Alpha
β	Beta
γ	Gamma
n	Neutron
μ	Linear attenuation coefficient
ρ	Density
g	Geometrical factors
∅	Fluence
E	Energy
F	Fluorine
f	Fission
Gy	Gray
H	Hydrogen
^{4}He	Helium-4
Ar	Argentum
$B^{4}C$	Boron carbide
Bi	Bismuth
C	Carbon
^{252}Cf	Californium-252
3D	Three dimension
$D^{2}O$	Deuterium oxide
I	Intensity
INP	Input file
k	Boltzmann's constant
^{7}Li	Lithium-7
Mg	Magnesium
N	Nitrogen
N	Number of histories
p	Proton
Pb	Lead

R	Relative error
s	Second
Sv	Sievert
T	Absolute temperature
T	Time
U	Uranium
W	Watt
Z	Atomic number

LIST OF ABBREVIATIONS

ACTI	Advanced Computational Technology Initiative
ACTL	Activation Library
BNCT	Boron Neutron Capture Therapy
BNL	Brookhaven National Laboratory
BPA	Boronophenylalanine
BSA	Beam shaping assembly
BSH	Borane sulfhydryl
$BWhr^{-1}$	Body weight per hour
CD	Compact disc
CEM	Cascade-Exciton Model
CF	Calibration factor
COV	Coefficient of variation
CT	Computed tomography
ECC	Element correction coefficients (sensitivity factor)
ENDF	Evaluated Nuclear Data File
ENDL	Evaluated Nuclear Data Library
EPDL	Evaluated Photon Data Library
FF	Fission fragment
FOM	Figure of Merit
GBM	Glioblastoma
HCC	Hepatocellular carcinomas
HFR	High Flux Reactor
IAEA	International Atomic Energy Agency
ICP-AES	Inductively coupled plasma-atomic emission spectrometry
ICRP	International Commission on Radiological Protection
IE	Institute for Energy
INEEL	Idaho National Engineering & Environmental Laboratory
LAQGSM	Los Alamos Quark-Gluon String Model
LET	Linear energy transfer
MCA	Multichannel analyser

MCNP5	Monte Carlo N-Particle Transport Code, Version 5
MeV	Mega electron volt
MIT/H	Massachusetts Institute of Technology with the New England Deaconess-Beth Israel Medical Center of Harvard University
nC	Nano coulomb
NPS	Number per second
OS	Overall survival
RBE	Relative biological effectiveness
RSICC	Radiation Safety Information Computational Center
TFC	Tally fluctuation chart
TLD	Thermoluminescent dosemeter
TRR	Tehran Research Reactor
UV	Ultraviolet
VisEd	Visual editor
VOV	Variance of the variance

KAJIAN MODERATOR, KOLIMATOR DAN PERISAIAN UNTUK PENYELIDIKAN BNCT DI AGENSI NUKLEAR MALAYSIA

ABSTRAK

Objektif penyelidikan ini adalah untuk mengkaji pengoptimunan susun atur bagi kemudahan *Boron Neutron Capture Therapy* (BNCT) pada garisan alur neutron yang melalui kolum termal pada Reaktor TRIGA MARK II Malaysia. Belum ada penyelidikan sebegini dilakukan di kolum termal tersebut dan ciri setiap reaktor TRIGA adalah berbeza. Ciri alur neutron yang diperlukan adalah neutron yang bertenaga terma dengan fluk sebanyak 10^9 $cm^{-2}s^{-1}$ dan alurnya berdiameter 15 cm. Kolimator, moderator dan komponen perisaian bersama teras reaktor dan kolum termal disimulasi menggunakan *Monte Carlo N-Particle Transport Code*. Fluk neutron dan foton dikira bersama dengan tenaga masing-masing menggunakan perisian yang sama. Selepas itu kolimator dan perisai telah dibina. *Polyethylene* dan air telah digunakan sebagai perisai neutron laju dan neutron epiterma. Plumbum pula digunakan sebagai perisai sinar gama. Kolimator diperbuat dari paip *polyethylene* berdiameter 8 cm dan disikan dengan lilin. Pengukuran neutron dan sinar gama di dalam Graphite Stringer tengah (G7) pada kolum termal telah dilakukan menggunakan pengesan TLD. Pada kuasa reaktor 1 MW, kadar dos sinar gama adalah 30.67 $Svjam^{-1}$ dan fluk neutron adalah 1.69×10^{10} $cm^{-2}s^{-1}$. Pengukuran fluk neutron dan sinar gama di dalam kotak perisai telah dilakukan menggunakan pengesan TLD juga. Kadar dos sinar gama adalah 1.41 $Svjam^{-1}$. Fluk neutron adalah 3.00×10^7 $cm^{-2}s^{-1}$ iaitu lebih rendah dari fluk neutron yang diperlukan. Untuk mengkaji penembusan neutron ke dalam tubuh

manusia, ujikaji menggunakan fantom air telah dijalankan. Fluk neutron pada 0.0 cm adalah 5.00×10^6 $cm^{-2}s^{-1}$ dan 3.00×10^7 $cm^{-2}s^{-1}$ pada kedalaman 0.8 cm kemudian berkurang kepada 1.00×10^6 $cm^{-2}s^{-1}$ pada kedalaman 8.1 cm. Pengukuran spektrum neutron telah dilakukan menggunakan spektrometer MICROSPEC-2. Spektrum yang diperoleh adalah menepati jangkaan. Hitungan spektrum tertinggi adalah pada neutron bertenaga terma dan spektrum berkurang bila tenaga neutron bertambah. Pengukuran diteruskan dengan meletakkan plat kadmium, plat B_4C, plat plumbum, air didalam bekas aluminium dan ais didalam bekas aluminium di hadapan MICROSPEC-2. Ais telah menghasilkan 0.05 bilangan per saat neutron terma. Air pula menghasilkan 0.04 bilangan per saat. Kesimpulan yang boleh dibuat daripada kajian ini adalah kolum termal pada reaktor TRIGA MARK II Malaysia sesuai untuk digunakan dalam rawatan kanser berdasarkan kaedah BNCT.

MODERATOR, COLLIMATOR AND SHIELDING STUDIES FOR BNCT RESEARCH AT MALAYSIAN NUCLEAR AGENCY

ABSTRACT

The objective of this research is to optimally study an arrangement for BNCT facility at a beam line through the thermal column of Malaysian TRIGA MARK II Reactor. There is no similar research had been done at this thermal column and all TRIGA reactors have different characteristics. The characteristics of the neutron beam needed are thermal neutron with a flux of 10^9 $cm^{-2}s^{-1}$ and the diameter of the beam is 15 cm. Collimator, moderator and shielding components with reactor core and thermal column were simulated with Monte Carlo N-Particle Transport Code. Fluxes of neutron and photon were calculated together with their energies with the same software. After that, collimator and shielding are fabricated. For fast and epithermal neutron shielding, a polyethylene and water were used. For gamma-ray shielding, lead was used. The collimator is made from polyethylene pipe with 8 cm of diameter filled with paraffin. Neutron and gamma-ray measurement in a Central Graphite Stringer (G7) of thermal column was done with TLD detectors. At 1 MW of reactor power, gamma-ray dose rate was 30.67 $Svhr^{-1}$ and neutron flux was 1.69×10^{10} $cm^{-2}s^{-1}$. Neutron and gamma-ray fluxes in shielding box were measured with TLD also. Gamma-ray dose rate was 1.41 $Svhr^{-1}$. Neutron flux was 3.00×10^7 $cm^{-2}s^{-1}$ which is lower than needed neutron flux. In order to study neutron penetration in human body, an experiment with water phantom was conducted. Neutron flux was 5.00×10^6 $cm^{-2}s^{-1}$ at 0.0 cm depth and 3.00×10^7 $cm^{-2}s^{-1}$ at the depth of 0.8 cm and then decreased

to 1.00×10^6 $cm^{-2}s^{-1}$ at the depth of 8.1 cm. Neutron spectrum measurement was done with MICROSPEC-2. The spectrum obtained was as expected. The highest spectrum count was around thermal neutron energy and decreasing as neutron energy increased. The experiment is continued with a cadmium plate, B_4C plate, lead plate, water in aluminium case and ice in aluminium case were placed at the front of MICROSPEC-2. Ice had produced thermal neutron of 0.05 counts per second. Water produced 0.04 counts per second. The conclusion of this study is that the thermal column of Malaysian TRIGA MARK II reactor is sufficient to be used in cancer treatment based on BNCT method.

CHAPTER I

INTRODUCTION

Cancer is one of the major causes for human death. Cancer patients are reported spending more than $18,000 on care (Bach *et al*., 2012). There are numerous studies conducted around the world to help in curing cancer. Some of the methods as reported by American Cancer Society (2015) to treat cancer are surgery, chemotherapy, targeted therapy, immunotherapy, hyperthermia, photodynamic therapy, laser therapy and radiation therapy.

Surgery can be used to diagnose, treat, or even help prevent cancer in some cases. Surgery often offers the greatest chance for cure, especially if the cancer has not spread to other parts of the body. The second option is chemotherapy which is the use of medicines or drugs to treat cancer. The third choice is targeted therapy which is a newer type of cancer treatment that uses drugs or other substances to more precisely identify and attack cancer cells, usually while doing little damage to normal cells. Targeted therapy is a growing part of many cancer treatment regimens. The other approach is immunotherapy which is a treatment that uses body's own immune system to help fight cancer. The idea of using heat to treat cancer had gived mixed results (National Cancer Institute, 1992). Today, newer tools allow more precise delivery of heat, and hyperthermia is being studied for use against many types of cancer. Stem cell transplants are also used to treat cancer. Photodynamic

therapy (PDT) is a treatment that uses special drugs, called photosensitizing agents, along with light to kill cancer cells. The drugs only work after they have been activated or "turned on" by certain kinds of light. The lasers treatment can be used in two ways to treat cancer either to shrink or destroy a tumor with heat or to activate a chemical (known as a photosensitizing agent) that kills only the cancer cells. Though lasers can be used alone, they are most often used with other cancer treatments, such as chemotherapy or radiation. Lasers are also being studied for treating or preventing side effects of common cancer treatments. For instance, some studies are looking at how low-level laser therapy (LLLT) might be used to prevent or treat severe mouth sores caused by chemotherapy, and how they may be used to treat the swelling (lymphedema) that can result from breast surgery (National Cancer Institute, 1992). Finally, radiation therapy which uses high-energy particles (e.g. proton, alpha, beta and neutron) or ionising electromagnetic radiation (e.g. X-rays and gamma-rays) to destroy or damage cancer cells. It is one of the most common treatments for cancer, either by itself or along with other forms of treatment.

One type of radiation therapy commonly used involves photons. X-rays were the first form of photon radiation to be used to treat cancer. Depending on the amount of energy they possess, the rays can be used to destroy cancer cells on the surface of or deeper in the body. The higher the energy of the X-ray beam, the deeper the X-rays can go into the target tissue. Gamma are another form of photons. Gamma are produced spontaneously as certain elements (such as radium, uranium, and cobalt) release radiation as they decompose, or decay. Each element decays at a specific rate and gives off energy in the

form of gamma and other particles. X-rays and gamma have the same effect on cancer cells (National Cancer Institute, 1992).

Neutron therapy uses beams of neutrons to attack cancer cells. There are two advantages in using neutrons instead of electrons or photons. The first is that neutron beams have much more power. They deposit about 20 to 100 times as much energy into the target tissue as other radiation therapy does. The second is that neutron beams have a higher probability to damage both strands of a cell's DNA, whereas regular radiation in general damages only one strand. This makes it harder for cells to repair neutron beam damage and harder for them to survive the treatment. So neutron therapy is a good choice in cases when tumors are resistant to other radiation (Seattle Cancer Care Alliance, 2015).

An alternative cancer treatment that can treat cancer using neutron beams is called Boron Neutron Capture Therapy (BNCT). It is a very promising cancer treatment using the neutron radiation which can be obtained from either a low-flux nuclear research reactor or neutron generator and it is the interest of this study. BNCT exploits the selective deposition in tumor cells of boron carriers, boronophenylalanine (BPA) and sulfhydryl borane (BSH), enriched with ^{10}B isotope, and the high thermal neutron capture cross-section of ^{10}B. When a high boron concentration ratio between tumor and healthy tissue is reached, the patient is irradiated with low energy neutrons either thermal neutron or epithermal neutron (Durisi, 2007). When the tumor is irradiated with thermal neutrons a

capture nuclear reaction is induced in ^{10}B converting it to ^{11}B, which decays by emission of an alpha particle (Faião-Flores *et al*., 2010). BNCT is a binary radiation therapeutic modality for cancer treatment. As a binary treatment modality, BNCT is based on the reaction between the non-radioactive isotope ^{10}B and thermal neutrons. Neutron is a particle contained and formed the nucleus and is neutral because it does not have electrical charge. Neutrons, especially thermal neutrons can be absorbed by atomic nuclei that they collide with, creating a heavier isotope of the chemical element as a result. In BNCT, ^{10}B will capture thermal neutron and became unstable. It will then change to ^{7}Li isotope after emitting α and γ each with respectively linear energy transfer (LET). BNCT is done by firstly, a stable isotope of boron-10 (^{10}B) is administered to the patient via a carrier drug and then the patient is irradiated with a neutron beam. ^{10}B will then undergo the capture reaction $^{10}B(n, \alpha)^{7}Li$ where ^{10}B capture cross-section for thermal neutrons is 3840 barn (Valda *et al.*, 2005). This is why thermal neutron is used in BNCT.

LET is a measure of the force acting on a charged ionizing particle travelling through matter. The LET or restricted linear collision stopping power of charged particles in a medium is the quotient of dE by dl, where dl is the distance traversed by the particle and dE is the mean energy-loss due to collisions. LET depends on the velocity, charge and mass of the particle (International Commission on Radiation Units and Measurements, 1970). A high LET of emitted charged particles in BNCT are lethal only to the cells in close proximity to the reaction point because their range is ~10 μm (Valda *et al.*, 2005) this is the mean cell diameter. Therefore, BNCT treatment is a very much localized procedure which make this treatment a real advantage over others.

BNCT is a radiation therapy for the treatment of cancers like melanoma and glioblastoma multiforme. As for the two common cancers studied for BNCT, Burton *et al.* (2007) has defined melanoma as a highly malignant tumour of melanin-forming cells, the melanocytes. Such tumour usually occurs in the skin but are also found in the eye and the mucous membranes. They may contain melanin or be free of pigment. Spread of this cancer to other parts of the body, especially to the lymph nodes and liver, is common. The response rate to conventional chemotherapy is poor.

Glioblastoma is described as the most aggressive type of brain tumour derived from non-nervous (glial) tissue (Burton *et al.*, 2007). Its rapid enlargement destroys normal brain cells, with a progressive loss of function, and raises intracranial pressure, causing headache, vomiting, and drowsiness. Treatment is never curative and the prognosis is poor. The evident from data compiled andsummarized by Barth *et al.* (2012), had shown that the clinical results obtained in treating patients with either primary or recurrent high grade gliomas, there has been significant progress in improving the clinical results. Specifically, increasing the dose of BPA and administering it over a longer time period or combining BNCT with a photon boost, as has been carried out in Japan, have resulted in the best survival data obtained to date using BNCT to treat patients with gliomas.

Kreiner *et al.* (2014) had made a comparison of variety of possible charged-particle induced nuclear reactions and the characteristics of the resulting neutron spectra are discussed along with the worldwide activity in suitable accelerator development.

Endothermic $^{7}Li(p,n)^{7}Be$ and $^{9}Be(p,n)^{9}B$ and exothermic $^{9}Be(d,n)^{10}B$ are compared. Be as a target leads to stable products. This is a significant advantage for a hospital-based facility. $^{9}Be(p,n)^{9}B$ needs at least 4–5 MeV bombarding energy to have a sufficient yield, while $^{9}Be(d,n)^{10}B$ can be utilized at about 1.4 MeV, implying the smallest possible accelerator. This reaction operating with a thin target can produce a sufficiently soft spectrum to be viable for accelerator-based BNCT (AB-BNCT). The machines considered are electrostatic single ended or tandem accelerators or radiofrequency quadrupoles plus drift tube linear accelerator (Linacs).

There are many studies on BNCT using research reactors. Long term goal for this research is to develop a cancer treatment facility which is safe and practical by using neutron emitted by a low flux research reactor. Firstly, it needs to establish a suitable flux of neutron beams. For TRIGA types research reactors, thermal column is mainly design to produce thermal/epithermal neutrons which can be utilized for BNCT. It is, therefore, the thermal column of Malaysian TRIGA MARK II Reactor was used to produce thermal neutron source for this research. In order to build a BNCT facility outside the reactor, neutron collimator, neutron moderator and shielding for neutron and gamma-ray were required to ensure the safety and practicality of the procedure.

Collimator is needed to collimate neutron beam from thermal column and sending them to the target area outside the reactor wall. Material used in collimator must not either absorb or slowing down the neutron. Clark *et al.* (2009) had defined collimator as any

device for producing a parallel beam of radiation. Neutron moderator is needed to reduce the velocity of fast and ephitermal neutrons which means reducing their energy to thermal energy producing more thermal neutron. Clark *et al.* (2009) had defined moderator as a substance that slows down free neutrons in a nuclear reactor, making them more likely to cause fissions of atoms of uranium-235 and less likely to be absorbed by atoms of uranium-238. Moderators are light elements, such as deuterium (in heavy water), graphite, and beryllium, to which neutron can impart some of their kinetic energy on collision without being captured. Neutrons that have had their energies reduced in this way are said to have been thermalized or to have become thermal neutrons. Neutron shielding is needed to avoid unwanted exposure of patient and radiation worker to the neutron. It is the same for gamma-ray. Clark *et al.* (2009) had defined shielding as a barrier used to surround a source of harmful or unwanted radiations.

1.1 PROBLEM STATEMENT

BNCT treatment was studied around the world and Finland has already conducted treatments because the conventional treatments are not totally successful in curing cancer (Auterinen and Kankaanranta, 2001). Despite recent improvements in multimodal therapies that include surgery, radiotherapy and chemotherapy, glioblastoma (GBM) patients in particular continue to have a short median overall survival (OS) time of less than 18 months (Hopewell *et al*., 2010a).

Mallick (2014) defined OS as a term that denotes the chances of staying alive for a group of individuals suffering from a cancer. It denotes the percentage of individuals in the group who are likely to be alive after a particular duration of time. At a basic level, the overall survival is representative of cure rates. 5-year rates are reported for many cancers including high grade lymphomas because those who survive 5 years are quite likely to be cured of their disease. In some slow growing and low grade malignancies like follicular lymphoma where late relapses are common, the 10 year overall survival is more representative of cure rates.

Dose escalation studies using conventional radiation or late stereotactic irradiation have been intensively investigated; however, there is no randomized study which supports the survival benefit of these methods at a high evidential level. The current standard care of GBM is maximal safe surgical resection, conventional radiation and chemotherapy using temozolomide, by which the life expectancy is 15 months. BNCT however had produced a median overall survival time of 17.6 months (Hopewell *et al*., 2010a).

The volume of tumor with decrease diffusion analyzed by Hiramatsu *et al*. (2013) for two days was the highest indicator of patient survival time for BNCT. Most of hepatocellular carcinomas (HCC) are thought to be incurable by many medical practitioners, and also

limited surgical operation, even chemotherapy, or radiation therapies are available for a prolonged survival (Yanagie *et al.*, 2010).

Malaysia shares the same problems. Treatments used such as surgery, anti-cancer drugs and radiotherapy (Ibrahim, 2004) are not successful enough in curing cancer. The traditional approach has not achieved the desired results as far as oncology and radiotherapy is concerned (Ibrahim, 2004). There is neither simulation nor measurement done for neutron and gamma-ray beam outside Malaysian TRIGA MARK II Reactor's thermal column. Neutron collimator and shielding are not fabricated to use outside the thermal column. The available beamport are underused. This situation is so unfortunate because Malaysian TRIGA MARK II reactor is believed to be able to supply a sufficient neutron beam for BNCT treatment. This study will optimize the usage of Malaysian TRIGA MARK II Reactor.

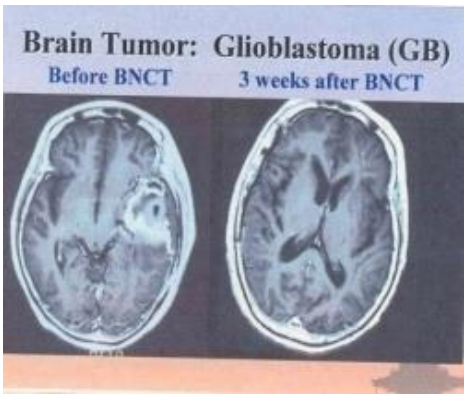
1.2 SIGNIFICANCE OF RESEARCH

There are interesting successful results from BNCT research conducted around the world. Two hundred and one (201) patients whom suffered with brain tumors, where eighty one (81) patients suffered with glioblastoma, forty five (45) patients suffered with anaplastic astrocitomas, eight (8) patients suffered with brain stem gliomas, six (6) patients suffered with meningiomas and the rest suffered with other tumors had been

treated with BNCT in Japan. It was found that forty (40) patients out of two hundred and one (201) patients were alive at the end of three (3) years and ten (10) patients survived more than ten years (Hatanaka *et al.*, 1991).

Other successful results for BNCT are: firstly, an ex-glioblastomas patient, 68 years old, lived 18 years and is in good shape. Secondly, there is a man who was operated on for astrocytoma was given a course of accelerator radiation, then underwent BNCT, has survived 12 years and his mind is still clear (Hatanaka *et al.*,1991). Thirdly, a young woman lived normally for 9 years after her treatment for a grade III astrocytoma which was a huge tumor with 9 cm in diameter in the right frontal lobe. This was because she has no trace of surgery or radiation damage in her appearance or performance (Hatanaka *et al.*, 1991).

Figure 1.1 shows a few results from BNCT treatment reported by Shiroya (2005). There is also 1 and 2 years patient survival rates of 80.0% and 53.3%, respectively and the 3 years patient survival rates of 26.6% was reported by Shirakawa *et al.* (2010).



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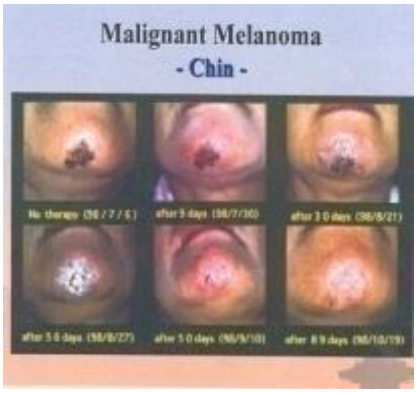

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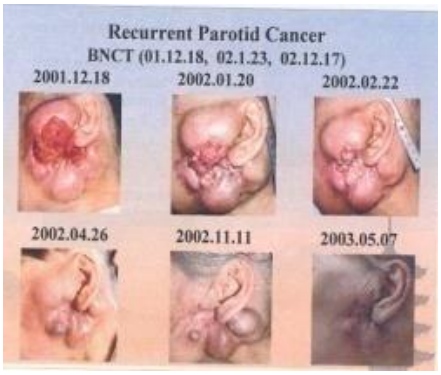

(d)

Figure 1.1: A few results of BNCT treatment (Shiroya, 2005).

The advantage of BNCT as a high LET radiation and tumor-selective radiation without serious damage of surrounding normal-tissue, BNCT is effective and safe in the patients whom with inoperable, locally advanced head and neck cancers even if that recur at previously irradiated sites. As a result, eleven (11) patients showed complete remission and seven (7) patients showed partial remission of irradiated site. The effective rate was

90%. No severe, acute or chronic normal tissue reactions were observed in any patients (Aihara *et al.*, 2010).

There are many other advantages in applying BNCT to head and neck cancers. The first advantage is the head and neck has many important physiological and cosmetic functions. Therefore, organ preservation is one of the most important things. The second advantage is there are many patients that recur after intensive treatment including surgery and chemoradiotherapy, and locally advanced that cannot be controlled by conventional cancer therapy. The third advantage is that head and neck cancers exist superficially and are not very far from the skin surface (Aihara *et al.*, 2010). The other results from clinical study are overall survival rates of 1 and 2 years were 53.8% and 32.3 %, respectively, and the disease free survival rates of 1 and 2 years were 34.2% and 0 %, respectively. However, the loco-regional progression-free survival rates of 1 and 2 years were 58.8% and 47.7%, respectively. The loco-regional progression-free survival rate of one year was 100% and overall survival rate was 100% at 18 months (Aihara *et al.*, 2010). Three (3) years and six (6) years survival rate was 40%, and 24% respectively by using Kaplan-Meier analysis (Kato *et al.*,2001).

Twelve (12) patients with cancer of the head and neck that had recurred at the same place after a surgery and conventional radiation therapy had been treated again with BNCT in Finland. Ten (10) patients, or 83%, had responded well to BNCT, and two (2), or 17%, had tumor growth stabilization for 5.5 and 7.6 months, respectively. The average duration

of response was 12.1 months and four (4) patients, or 33%, were alive without recurrence with a median follow-up of 14 months (Volkin and Dargan, 2007).

In other clinical study, ten (10) patients received two treatments of BNCT, and two (2) patients received one treatment conducted in Finland. The results were shown that seven (7) of the patients, or 58%, had achieved a complete response, while three (3), or 25%, had experienced a partial response. A stabilized disease had been achieved for the remaining two (2) patients (17%) for a period of 5.5 and 7.6 months. Overall, the median time to disease progression was 9.8 months, while median survival was 13.5 months (Nelson, 2007).

In a clinical study of the other cancer, the mean survival times of the patients with glioblastoma multiforme treated at Brookhaven, United States of America, were 15 months in protocol group 1, and more than 10 months in groups 2 and 3; the corresponding times for conventional therapy are 10.5 months in group 1 and similar to those seen so far in the other groups (Feinendegen, 1998). Most of aged-GBM patients tend to be suffering from cognitive function after conventional radiotherapy therefore BNCT can contribute in the improvement of clinical outcome in such aged patients (Kageji *et al.*, 2001). Increasing of radiation dose can achieve complete remission of GBM with BNCT (Nakagawa *et al.*,2003).

From light microscopy analysis conducted for BNCT, the result is BNCT had selectively damages tumor blood vessels, but had spare precancerous and normal tissue vessels. Selective tumor lethality would thus result from selective blood vessel damage rather than from selective uptake of the boron compound (Trivillin *et al.*,2006).

BNCT treatment was expanded further to treat liver cancer. BPA-BNCT had induced significant partial remission of experimental implanted colorectal tumor nodules in the liver 2 and 3 weeks post irradiation. The absence of acute normal liver changes had proved a safe escalation of the radiation dose (Pozzi *et al*., 2013). The potential clinical advantage of BNCT towards otherforms of radiotherapy is the possibility to selectively deliver higher radiation doses to cancerous tissue, without damaging healthy tissue involved (Schütz *et al.*, 2010).

Metastatic malignant melanomas are largely refractory to existing therapies so new treatment strategies are urgently needed and BNCT is the best option (Rossini *et al.*, 2015). The human neuroblastoma cell lines (SH-SY5Y cells) are irradiated by ^{7}Li ions and by means of the clone-forming method and flow cytometry; the damage effects of neurocytes are analyzed. The cells survival fraction in the consequence of ^{7}Li irradiation reduces obviously when compared with γ-rays irradiation (Yiguo *et al.*, 2010).

No acute symptoms were reported during or after irradiation of BNCT for malignant meningioma. No treatment related deaths occurred and no deaths have occurred in the follow up time of 14 months. It was concluded that BNCT is safe and effective in the treatment of recurred malignant meningioma patients (Kankaanranta *et al.,* 2001).

From five (5) patients treated with BNCT for cutaneous malignant melanoma, again there is no toxic or adverse effects. The treated cancer nodules in the skin responded well, and, depending on size, were seen to fully disappear with no recurrence in one (1) patient 2.5 years after BNCT. The normal skin showed lower radiation effects than are normally seen after conventional radiotherapy. The convenience of a single BNCT treatment, versus multiple treatments over about two months required by current conventional radiotherapy, considered to improve the quality of life (Feinendegen, 1998).

The geometrical factors, g, from the BNCT plans, which describes target volumes receiving doses under the prescribed doses and normal brain volume covered by the prescribed doses, were lowest compared to those for the other modalities. For the BNCT plans, maximum dose escalation up to 2.08 times the prescribed dose was possible without exceeding normal brain tolerance dose (Jung *et al.,* 2010).

From the measurements and with MONTE CARLO verification for neutron flux at the thermal column of Malaysian TRIGA MARK II reactor done by Munem (2007), it was

clear that there is sufficient neutron flux for BNCT treatment in Malaysian TRIGA MARK II reactor at Nuclear Malaysia. The quality of the neutron flux is as good as is required for standard BNCT treatment. The next step is to direct these neutrons outside the reactor to be used in BNCT treatment with full safety precautions. The availability of the neutron flux and the support from Malaysian Nuclear Agency had given the opportunity for this research to be done. This research will produce neutron and gamma beam data from MCNP code simulation together with experimental data. Neutron beam research set-up outside thermal column will be developed to include a good neutron collimator and a safe neutron and gamma shielding.

The other reasons for the interest in BNCT studies in Malaysia are (Shukri, 2005):

i. The result for development of new compounds that can accumulate into tumours with a ratio of greater than three (3).
ii. The newer method for measuring boron concentration in tissues and in tumours.
iii. The availability of computer based dose calculation algorithm which allow accurate determination of dose in boron-containing tissues.
iv. BNCT also does not produce a mental retardation as occurred in conventional radiotherapy.

1.3 OBJECTIVES OF RESEARCH

1. To simulate a BNCT treatment for Malaysian Training, Research, Isotope Production, General Atomic MARK II (TRIGA MARK II) reactor and then calculate the fluxes of neutron and gamma-ray.

2. To establish a neutron beam collimator as well as neutron and gamma-ray shielding set-up where the neutron collimator and neutron and gamma-ray shielding will be test together with neutron moderator.

3. To compare between the results from TLD, Fission Chamber and NP-100 detectors with simulation results.

1.4 SCOPE OF RESEARCH

This study will be confined to investigate the availability, suitability and quality of thermal neutron beam exiting from thermal column of Malaysian TRIGA MARK II reactor. This thermal neutron beam is prepared to be used in BNCT treatment. Collimator and shielding were fabricated to be used in neutron and gamma-ray measurement. For fast and epithermal neutron shielding, a polyethylene and water were used. For gamma-ray shielding, lead was used. The collimator is made from polyethylene pipe with 8 cm of

diameter filled with paraffin. Thermal neutron flux were measured with TLD, Fission Chamber and NP-100 detectors. Data obtained were compared with simulation results from MCNP code that was done earlier.

There are a lot of constraints and obstacles in this study. Time constraints had prevent the repetation of measurements conducted. Budget constraints had highly limited the use of materials and instruments. Best materials and equipments are unaffordable. Available materials and instruments in Universiti Sains Malaysia and Malaysian Nuclear Agency were mostly used throughout this study. Safety issue had limited research activities and studies that can be done. This study must not change the structure of the reactor because it will affect other reactor usage. At this stage of study, all the collimator, moderator and shielding were fabricated as a portable equipments as not to disturb the other operations of the reactor.

1.5 STRUCTURE OF THESIS

The work summarizes in this thesis describes the characterization of neutron beam exiting from thermal column of Malaysian TRIGA MARK II reactor. Generally, the content of this thesis is organized as follows:

Chapter 1 highlights a general introduction on the BNCT treatments and the importance of BNCT treatment in Malaysia and around the world. In addition, the problem statement and objectives of this thesis are listed out.

Chapter 2 contains the theoretical background of BNCT treatment. The quality of neutron beam needed is presented with the examples from other studies around the world. The process and procedure in BNCT treatments are discussed with the list of all facilities needed and most importantly the safety precautions. Literature review is also included in this Chapter.

Chapter 3 discusses the materials and methodology of this work. In this Chapter, all materials used in fabrication of collimator, shielding and moderator and in experiment done are discussed in detail. Methodology used in simulation, fabrication and neutron and gamma-ray measurements are also discussed.

In Chapter 4, the results and discussions of simulation and calculation of neutron and gamma flux are presented. This Chapter also discusses the results of neutron and gamma measurements done with fabricated collimator and shielding. The discussion is extended further with the result of moderators investigated in this research. Finally, in Chapter 5, the conclusions of this thesis and recommendations for future works are presented.

CHAPTER II

THEORY AND LITERATURE REVIEW

2.1 THEORY OF BNCT

BNCT is a binary radiation therapeutic modality for cancer treatment. As a binary treatment modality, BNCT is based on the reaction between the non-radioactive isotope ^{10}B and thermal neutrons. The thermal neutron absorption cross-section for ^{10}B is 3837 barn and with 94% probability, the capture reaction $^{10}B(n, \alpha)^{7}Li$ yields 1.47 MeV of kinetic energy for ^{4}He and 0.84 MeV of kinetic energy for ^{7}Li. The range of energy release is 9 and 5 μm, respectively, which is around one cell diameter for about 10 μm (Liu *et al.*, 2001).

2.1.1 Neutron and Its Properties

In the interaction between neutrons and nuclei, the kinetic energy of the neutron determines the nature of the interaction. A characteristic quantity is the reduced de Broglie wave length $\lambda\!\!\!^{-} = \lambda/2\pi$ of the neutron-nucleus center-of-mass system, defined by

$$\lambda\!\!\!^{-} = \sqrt{\frac{\hbar^2}{2ME}} \qquad 2.1$$

where M is the reduced mass, E the kinetic energy in the center of mass frame, and $\hbar = h/2\pi$ is the reduced Planck constant. If the nucleus has a mass A times that of the neutron m_n, then

$$M = \frac{A}{A+1} \times m_n \qquad 2.2$$

at very low neutron energies, typcially in the meV range and below, this wavelength has a size of the order of the spacing between the nuclei in their material, for example, a crystalline structure (Cacuci, 2010).

Fully thermalized neutrons behave like an ideal gas and can, therefore, be described in good approximation by Maxwell–Boltzmann statistics. The neutron density, that is, the number of neutrons per unit of volume, has a Maxwell–Boltzmann velocity distribution $n_v(v)$ of the form

$$n_v(v) = 4\pi \left(\frac{m}{2\pi kT}\right)^{3/2} v^2 exp\left(-\frac{mv^2}{2kT}\right) \qquad 2.3$$

where k is the Boltzmann constant, m the neutron mass, and T the temperature. This distribution shows a maximum at $v = \sqrt{2\mathrm{kT/m}}$ corresponding to a kinetic energy of $E_{max} = kT$. For a velocity of 2200 ms^{-1}, used as a reference for thermal neutrons, this gives E_{max} = 25.3 meV, λ = 0.18 nm, and $T = mv^2/2k$ = 293.6 K, which is practically room temperature (Cacuci, 2010).

From the velocity distribution $n_v(v)$ one can obtain the distribution $n_E(E)$ of the kinetic energy E, the distribution $n_t(t)$ of the time-of-flight t, and the distribution $n_\lambda(\lambda)$ of the wavelength λ using the relation

$$n_v(v)dv = n_E(E)dE = n_t(t)dt = n_\lambda(\lambda)d\lambda \quad (2.4)$$

where dv, dE, dt, and $d\lambda$ are obtained from taking the derivates of the expressions

$$E = \frac{1}{2}mv^2 = \frac{1}{2}m\frac{L^2}{t^2} \quad (2.5)$$

and

$$\lambda = h/mv = ht/mL \quad (2.6)$$

where L is the length or distance.

Accurate knowledge of the thermal neutron capture and fission cross sections are of paramount importance for many applications and considerable experimental as well as evaluation effort was expended in obtaining precise and consistent constants at a neutron energy of 0.0253 eV (velocity v = 2200 ms^{-1}) (Cacuci, 2010).

Neutron interaction with matter can be divided into two classifications which are absorption and diffraction. In diffraction interaction, neutron is still free after collision even though its energy is decreased. In absorption interaction, neutron is captured by a nucleus and secondary particle will be produced. Thermal cross section is equal to the sum of the scattering cross section and the absorption cross section. The absorption cross

section typically varies as $1/v$ where v is the velocity of the neutron. The scattering cross section can be more complex as solid state effects take place. Neutrons can undergo Bragg scattering by any crystalline material present, undergo paramagnetic scattering with the target nuclei and neutrons can be up-scattered or down-scattered in energy from the thermal motion of the nuclei they interact with.

2.1.1.1 Absorption

Neutron absorption of a nucleus will make the nucleus to be excited then emit particles and radiations return to its initial state. Thermal neutron can experience four types of absorption interaction with a nucleus of an atom which are

i. (n,γ) reaction: Nucleus of an atom will capture neutron and became excited with excessive energy. The nucleus will then emit gamma and therefore will be back to stable state.
ii. (n,α) reaction.
iii. (n,p) reaction.
iv. Fission: Nucleus of an atom can absorb neutron and became unstable. The nucleus then splitted into two parts. Substances that can produce fission are ^{233}U, ^{235}U and ^{239}Pu.

The probability of neutron reaction with a nucleus is determined by neutron reaction cross-section. Consider one mono-energy neutron source that is moving toward a nucleus. The number of neutron per unit time per unit area that moving toward the nucleus is called neutron flux (φ) and given by an equation (Wagiran, 1997),

$$\varphi = nv \qquad 2.7$$

where n is the number of neutron per unit volume and v is neutron velocity. When the target material contain N atom per unit volume for a width of dx, the number of nucleus per unit area is $N \cdot dx$.

If C is neutron absorption per unit area, neutron cross-section is given by the equation (Wagiran, 1997),

$$\sigma = \frac{C}{\varphi N dx} \qquad 2.8$$

For a system with neutrons of multiple energy where $n(E)$ is neutron intensity in energy range of dE, the number of neutron in energy range from E to $(E + dE)$ is $N(E)dE$. The total neutron flux from all those energy where $v(E)$ is their velocity at energy E is (Wagiran, 1997),