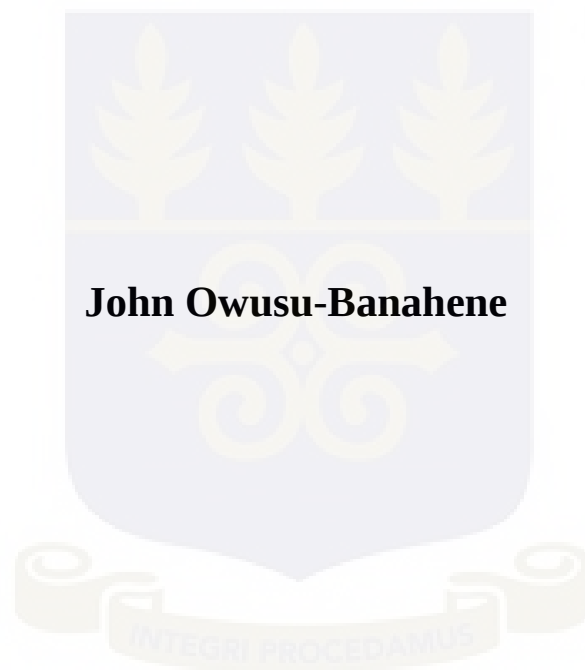


**MODELLING RADIATION DOSES TO CRITICAL ORGANS
OF PATIENTS UNDERGOING INTRACAVITARY
BRACHYTHERAPY TREATMENT AT KOMFO ANOKYE
TEACHING HOSPITAL.**



**MODELLING RADIATION DOSES TO CRITICAL ORGANS
OF PATIENTS UNDERGOING INTRACAVITARY
BRACHYTHERAPY TREATMENT AT KOMFO ANOKYE
TEACHING HOSPITAL.**

**THIS DISSERTATION IS SUBMITTED TO THE UNIVERSITY OF
GHANA, LEGON IN PARTIAL FULFILMENT OF THE
REQUIREMENT FOR THE AWARD OF PhD MEDICAL PHYSICS
DEGREE**

BY

JOHN OWUSU-BANAHENE (10191759)
BSc(HONS)(KNUST), MPhil(UG)

Department of MEDICAL PHYSICS

SCHOOL OF NUCLEAR AND ALLIED SCIENCES

UNIVERSITY OF GHANA, LEGON

JUNE, 2013

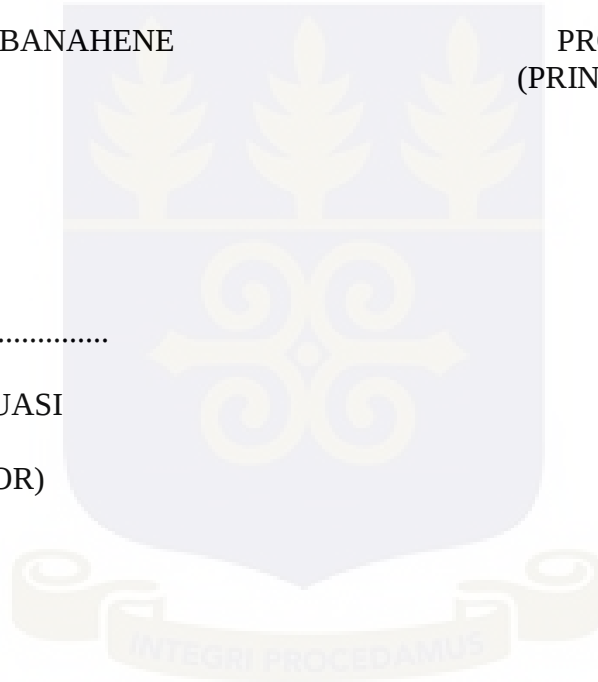
DECLARATION

I hereby declare that, except for references to other people's work, which have been duly cited, this dissertation is the result of my own research work and that it has neither in part nor in whole been presented for any degree elsewhere.

.....
JOHN OWUSU- BANAHENE
(STUDENT)

.....
PROF. E. O. DARKO
(PRINCIPAL SUPERVISOR)

.....
PROF. J. H. AMUASI
(CO-SUPERVISOR)



DEDICATION

This work is first dedicated to the Almighty God for helping me through this programme successfully and secondly to my wife Philomina Owusu-Banahene for her endless advice and encouragement.



ACKNOWLEDGEMENTS

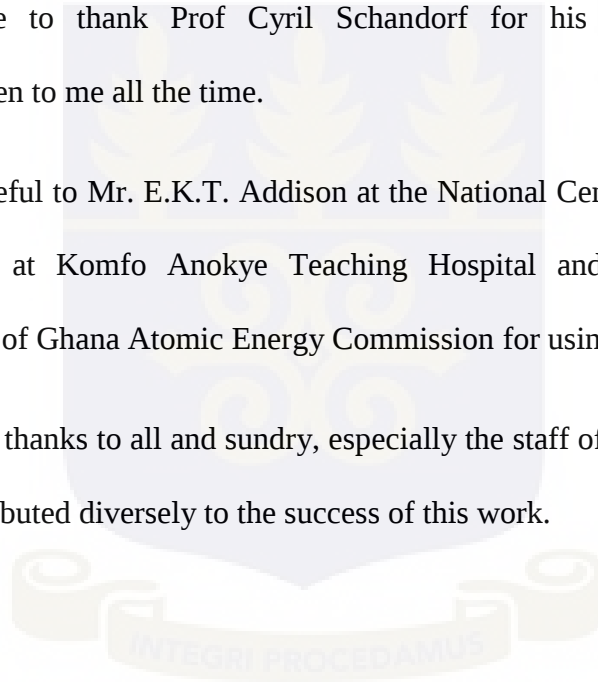
I would like to express my sincere thanks to my supervisors Prof. E.O. Darko and Prof. J. H. Amuasi for their professional guidance, encouragement and constructive criticisms.

Prof. A. W. K. Kyere, Head of Department of Medical Physics of the School of Nuclear and Allied Sciences, University of Ghana- Ghana Atomic Energy campus is hereby acknowledged for his advice, assistance and encouragement during the study.

I would also like to thank Prof Cyril Schandorf for his continuous advice and encouragement given to me all the time.

I am also very grateful to Mr. E.K.T. Addison at the National Centre for Radiotherapy and Nuclear Medicine at Komfo Anokye Teaching Hospital and also to the Radiation Protection Institute of Ghana Atomic Energy Commission for using their facilities.

Finally, my sincere thanks to all and sundry, especially the staff of the Radiation Protection Institute who contributed diversely to the success of this work.



ABBREVIATIONS

1D = One dimensional

2D = Two dimensional

3D = Three dimensional

keV = Kilo electron volts

MC = Monte Carlo

MeV = Mega electron volts

BTE = Boltzmann transport equation

PTV = Planning target volume

x,y,z = usual orthogonal axes

r = spatial coordinate, specified by coordinate (x,y,z)

Ω = direction of photon specified by angular coordinates

4π = angular domain

$\nu = R \times 4\pi$, phase space: A position in phase space as specified by (r, Ω)

t = time

$\Phi(r, \Omega, t)$ = angular photon flux at (r, Ω); the number of photons per unit area moving in the direction Ω about $d\Omega$ at r at time t

$S(r, \Omega, t)$ = volumetric source of photons at (r, Ω). The number of photons produced at r in dr at Ω in $d\Omega$ at time t

$\sum_t(r)$ = total macroscopic cross section for collision at r

$\sum_a(r)$ = total macroscopic cross section for absorption at r

$\sum_s(r, \Omega \rightarrow \Omega')$ = differential macroscopic scattering cross section at r to scatter photons from Ω to Ω'

$\sum_s(r)$ = total macroscopic scattering cross section at r

H = space of trial functions which have square integrable gradients ν

$\langle \Phi, \Psi \rangle_{\pm}$ = incoming (-) and outgoing (+) boundary inner products

$\underline{\underline{P}}$ = mass matrix in time dependent finite element approximation

$\Phi(t)$ = time dependent vector of nodal fluxes

$\dot{\Phi}(t)$ = time derivative of $\Phi(t)$

$\underline{\underline{A}}$ = matrix of coefficients

K = matrix due to collision terms

T = matrix due to transport terms

B = matrix due to boundary terms

GTV = Gross Tumour Volume

CT = Computed Tomography

MRI = Magnetic Resonance Imaging

PET = Positron Emission Tomography

CTV = Clinical Target Volume

OAR = Organs at Risk

MTD = Minimum Target Dose

KERMA = Kinetic Energy Released in Matter

FEM = Finite Element Method

LDR = Low Dose Rate

HDR = High Dose Rate

PTE = Photon Transport Equation

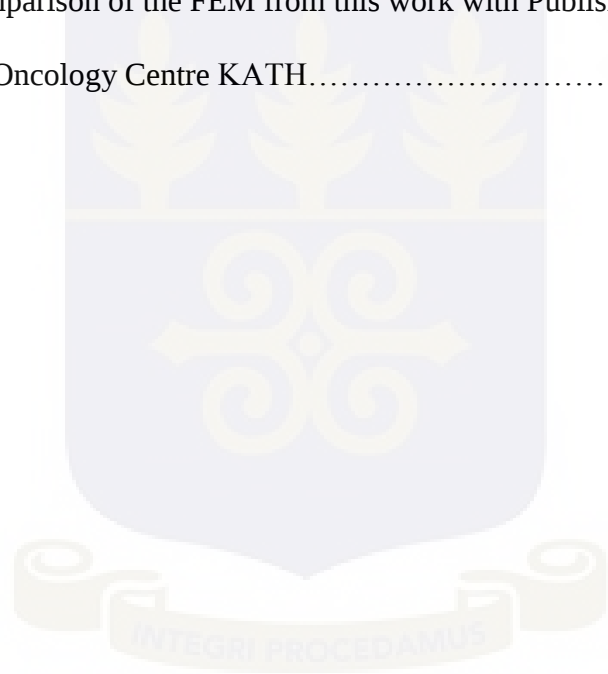
PDE = Partial Differential Equation

TPS = Treatment Planning System

KATH = Komfo Anokye Teaching Hospital

LIST OF TABLES

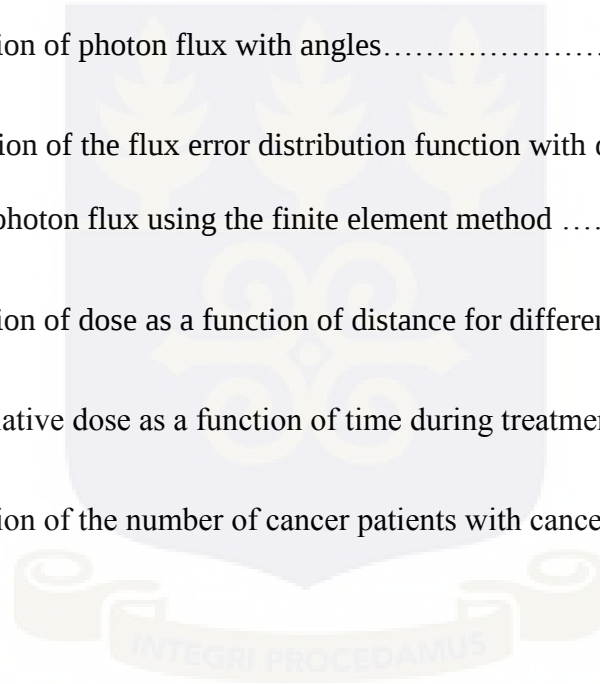
Table 2.1	Characteristics of some radionuclides used in brachytherapy.....	12
Table 2.2	Stages in cancer development.....	52
Table 2.3	Tumour Stage Grouping	53
Table 4.2	Comparison of the photon flux intensity from Green's Function with that of the model (FEM).....	90
Table 4.3	Comparison of Monte Carlo method with this work.....	91
Table 4.4	Comparison of the FEM from this work with Published data and the TPS at the Oncology Centre KATH.....	92



LIST OF FIGURES

Figure 2.1	The reference points A and B according to the Manchester system.....	14
Figure 2.2	Anatomical Structure of the human cervix.....	19
Figure 2.3	Electron undergoing a Compton scattering event.....	24
Figure 2.4	Graphical representation of volume of interests as defined in ICRU.....	33
Figure 2.5	A simplified schematic diagram of the physical simulation process showing FEM modeling terminologies.....	47
Figure 3.1	The Manchester system showing the reference points A and B and arrangement of the sources in the tandem and ovoids	57
Figure 3.2	A Cs-137 LDR afterloading unit with tube arrangements similar to Amersham ‘J-type tube.....	58
Figure 3.3	Non-homogeneous photon flux distribution around a Cs-137 source in sagittal plane.....	59
Figure 3.4	Anatomical structure of the cervix showing the target points.....	61
Figure 3.5	Diagram of a physical domain (patient) represented by a slab phantom in plane geometry.....	67
Figure 3.6	Particle trajectory from point r to the boundary ∂V along a straight line in the direction Ω	68

Figure 3.7	Polar coordinates (r, ψ, θ) indicating the direction of the particle in the standard coordinate system $x = (x, y, z)$ with $r = 1$	70
Figure 3.8	Geometry for the generation of mesh.....	73
Figure 4.1	Source strength distribution as a function of distance.....	83
Figure 4.2	Photon Flux distribution for different cancer stages as a function of distance.....	84
Figure 4.3	Variation of photon flux with angles.....	85
Figure 4.4	Variation of the flux error distribution function with distance in the solution of the photon flux using the finite element method	86
Figure 4.5	Variation of dose as a function of distance for different cancer stages.....	87
Figure 4.6	Cumulative dose as a function of time during treatment.....	88
Figure 4.7	Variation of the number of cancer patients with cancer stage.....	94



LIST OF PLATES

Plate.2.1	Fletcher-Suit-Delcos applicator.....	13
Plate.2.2	Tandem-Ring applicator.....	13
Plate.2.3	Fletcher-Suit-Delcos system in gynaecology.....	17



ABSTRACT

The main aim of radiotherapy is to destroy cancerous tissues with ionizing radiation while the other normal parts of the body are saved or spared. Intracavitary brachytherapy is a procedure in which radioactive sources are placed in the body cavities close to or inside the target volume to deliver radiation at short distances. In this mode of treatment, high radiation dose can be delivered to the tumour volume with rapid dose fall-off into the surrounding normal tissues. In brachytherapy, the dosimetry in biological tissues is a complex process. Dosimetric parameters such as the dose to critical organs and the total dose to the reference points as in the case of Manchester system are critical for patients undergoing intracavitary brachytherapy treatment. In this study, the Finite Element Method (FEM) has been utilized to solve Boltzmann Transport Equation (BTE) to determine the distribution of angular photon fluxes at various positions in the cervix of cancer patients and the dose distribution calculated for the organs of interest. The time-dependent linear BTE was used to describe the passage of ionizing radiation taking into account tissue heterogeneities and other scattering phenomena before depositing the absorbed dose in a patient. The simulation was carried out to determine doses to the critical organs, namely the rectum and bladder. Results from the study indicate doses to the rectum and the bladder to be in the range of 10.13-85.67cGy and 21.32-78.81cGy respectively for stage I to stage IV cancer patients. Comparison of the results from the model with data from published articles and dose prescriptions from the treatment planning system of the Radiotherapy Center of the Komfo Anokye Teaching Hospital in Ghana for different cancer stages indicate good agreement with standard error of $\pm 20\%$ to $\pm 34\%$.

TABLE OF CONTENTS

	Page
Declaration.....	i
Dedication.....	ii
Acknowledgement.....	iii
Abbreviations.....	iv
List of tables.....	vi
List of figures.....	vii
List of plates.....	ix
Abstract.....	x
Table of Contents.....	xi
CHAPTER ONE: INTRODUCTION	
1.1 Background.....	1
1.2 Statement of the problem.....	3
1.3 Relevance and justification of the study.....	4
1.4 Scope and objectives of the study.....	5
1.5 Structure of the dissertation.....	6

CHAPTER TWO: LITERATURE REVIEW

2.1	General overview.....	7
2.2	Principles of Brachytherapy.....	8
2.3	Importance of Low Dose Rate Brachytherapy.....	9
2.4	Clinical Brachytherapy sources.....	11
2.5	Intracavitary Brachytherapy in gynaecology.....	12
2.6	Organs at Risk (OAR).....	15
2.7	Critical organ dose monitoring in gynaecology.....	16
2.8	Anatomy of the cervix.....	17
2.8.1	Risk factors of cervical cancer.....	19
2.8.2	Symptoms of cervical cancer.....	20
2.9	Physics of ionizing radiation interaction in radiotherapy.....	20
2.9.1	Photon interactions in biological media.....	21
2.9.2	Photoelectric effect.....	22
2.9.3	Coherent and Incoherent Scattering.....	23
2.9.4	Pair Production.....	25
2.9.5	Characteristic X-rays and Auger electrons.....	27
2.9.6	Rayleigh Scattering.....	27
2.10	Linear Energy Transfer (LET).....	27
2.11	Electron Interactions.....	28
2.12	Methods for calculation of radiation doses from acquired image data.....	29
2.13	International recommendations on target and Organs at Risk.....	32
2.13.1	ICRU definitions.....	32
2.14	The importance and use of numerical methods.....	34
2.15	Dose calculations in Brachytherapy.....	35
2.16	Radiation Safety during Brachytherapy treatment.....	38
2.17	Quality Control and Quality Assurance in Brachytherapy.....	38

2.18	The photon transport theory.....	39
2.18.1	Advantages of using the transport equation.....	43
2.18.2	Disadvantages of the transport equation.....	43
2.19	The Finite Element Method (FEM).....	44
2.20	Photon dose deposition mechanisms.....	48
2.20.1	The dose deposition step.....	50
2.21	Cancer staging and Grouping.....	50
2.21.1	Stage grouping.....	53

CHAPTER THREE: MATERIALS AND METHODS

3.1	Theoretical modeling of doses to the critical organs	55
3.1.1	Governing equation.....	55
3.1.2	Source term.....	56
3.1.3	Target Geometry.....	60
3.1.4	The Photon Transport Equation	62
3.1.5	Finite Element Model.....	62
3.1.5.1	Time dependent case.....	64
3.1.5.2	Time independent case in plane geometry.....	66
3.1.5.3	Boundary condition for the photon flux.....	68
3.1.5.4	Error correction and convergence.....	70
3.1.5.5	Photon dose calculation.....	71
3.2	Model implementation and simulation.....	72
3.2.1	Assumptions.....	72
3.2.2	Mesh generation.....	72
3.2.3	System matrix	73
3.2.4	Matrix solution	74
3.2.5	Time dependent case.....	74

3.2.6 Simulation using Matlab.....	76
3.3 Optimization of dose to organs at risk.....	77
3.4 Experimental validation.....	78

CHAPTER FOUR: RESULTS AND DISCUSSION

4.1 General.....	81
4.1.1 Source term.....	82
4.1.2 Photon flux distribution.....	83
4.1.3 Error distribution function.....	85
4.1.4 Dose profile analysis.....	86
4.2 Comparison with analytical reference method.....	88
4.3 Comparison with Monte Carlo method.....	91
4.4 Comparison with Published data and Treatment Planning System (TPS) of Komfo Anokye Teaching Hospital.....	92

CHAPTER FIVE: CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion.....	95
5.2 Recommendations.....	96
5.2.1 Oncology Centre.....	96
5.2.2 Research Institutions.....	96
5.2.3 Regulatory Authority.....	97

REFERENCES.....	98
-----------------	----

APPENDICES.....	109
-----------------	-----

CHAPTER ONE

INTRODUCTION

This chapter presents the background, relevance and justification, statement of the problem, the scope and objectives of the research work and the structure of the thesis

1.1 Background

After X-rays were discovered by Wilhelm Conrad Roentgen in 1895, ionizing radiation has been used for the treatment of cancer. Nowadays, the three main modalities for cancer treatment are surgery, radiotherapy and chemotherapy. Radiotherapy consists of teletherapy and brachytherapy. In this current study, only brachytherapy is considered. The word ‘brachytherapy’ originated from a Greek word which means ‘brachos’ and it refers to a short-range therapy. Brachytherapy is the short distance treatment procedures of malignant diseases or tumours with radiations coming from encapsulated sources. The radiation sources are placed either directly into or near the treatment volume to deliver radiations at short distances (Girinsky et al, 1993). The purpose of brachytherapy treatment is to destroy the cancer cells with ionizing radiation by localizing high radiation dose in the tumour volume while the normal tissues and critical organs receive as low dose as possible (ICRU 1985; Williamson, 1988).

Brachytherapy is important for the achievement of local disease control in the treatment of cervical cancer. In this mode of treatment, high radiation dose can be delivered to the target volume with rapid dose fall-off in the surrounding normal tissues. This type of treatment is always temporal and lasting only for some few days. It should therefore be

performed under strict rules of standard source-application systems such as the Manchester system or ICRU system (ICRU 1985). These systems simply prescribe the target dose to a generic reference point or to a reference volume without identifying the target volume because the systems were established before the target volume could be readily identified geometrically. Geometric identification of the individual target volume and other regions of interest have become essential in the practice of radiotherapy, especially of intracavitary brachytherapy, for specifying treatment parameters such as clinical target volume, maximum and minimum target doses, and doses to organs at risks (Williamson, 1988). Intracavitary brachytherapy is another possibility of internal radiotherapy, in which the sources of ionizing radiation are implanted inside the tumour volume of the patient. This study considers the internal radiotherapy, in which the photon and electron beams are the most common sources of radiation used in intracavitary brachytherapy for most clinical applications. The heavy particles such as neutrons and protons are rarely used because of the enormous cost involved (Feng et al, 1995; Serkies et al, 2001, Boman et al, 2005). The treatment unit is typically an AMRA-Curiatron in which photons are made to travel through special tubes called channels to deliver the treatment doses into the tumour volume of cancer patients. In this treatment unit, the sources usually emit photons during treatment, which is considered as a stream of photons moving into the treatment volume and consequently depositing dose into the tissue. Due to the complex track geometries and various types of photon interactions with matter, dose deposition is a complex process.

Current tumour therapy techniques usually use complex optimization algorithms or calculation methods to deliver fast treatment planning and dose calculations in order to

achieve very accurate results. Some of the various methods used are Monte Carlo simulations, Sievert Integrals and AAPM-TG43 (Deshpande et al, 1997; Bobylev et al, 1998; Favorite et al, 2005). Owing to the various cost of computational problems usually encountered in the aforementioned methods or algorithms there is the need for a faster but accurate method for dose calculation algorithms and the finite element method (FEM) has attracted much attention as a golden standard method of solving the photon transport equation for dose distributions in biological media.

In this study, radiation doses to critical organs will be modelled using the FEM method in solving the photon transport equation in heterogeneous media (Santhamma et al, 1978, Schweiger et al, 1995; Arridge et al, 1993; 1995,). The photon transport in tissues is restricted to geometries that are cylindrically symmetric around the incident photon. The use of the FEM as a mathematical tool to solve the photon transport equation in an integro-differential form will therefore be a confirmatory determination of radiation doses to critical organs and the target volume. The FEM is very fast, accurate and therefore the results obtained will enhance the speed accuracy of the treatment planning system for cancer patients undergoing intracavitary brachytherapy treatment.

1.2 Statement of the problem

During intracavitary brachytherapy treatments, the specific doses to the target volumes are specified by the radiation oncologist based on clinical experience. Using the Manchester or the ICRU system and the generic reference points of protocol adopted at the oncology unit, the doses to the critical organs like pelvic wall, bladder and rectum are determined, consequently the time of implant of the radioactive source is also calculated.

The most frequent clinical complications usually encountered during intracavitary brachytherapy treatment is when portions of the critical organs like rectum and bladder receive some amount of radiation doses. Errors in calculating the treatment dose and inadequate procedures for placement of sources in the applicators have resulted in many accidents in intracavitary brachytherapy treatments. As a result, a confirmatory determination of doses to critical organs and target volume during treatment planning is highly desirable for comparison of the results before delivery of radiation doses to brachytherapy cancer patients.

1.3 Relevance and Justification of the study

In intracavitary brachytherapy treatment planning, one seeks the best localization of the sources in both the tandem and ovoids to achieve the desired dose distribution in the tumour volume and as low radiation dose as possible to the surrounding healthy tissues and critical organs. Source localization in both the tandem and ovoids is usually difficult and time consuming, and this poses a major problem leading to complications in the critical organs.

Radiation treatment planning and dose calculations are the crucial steps needed before the actual treatment is delivered. Failure to correctly plan the treatment and precisely determine the amount of treatment dose deposited in the patient according to the plan could result in catastrophe. Nowadays, the use of three dimensional (3D) imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), enable accurate determination of patient 3D imaging. This enables the use of conformal radiotherapy, in which the goals of the radiotherapy treatment are met (i.e the high dose

volume conforms to the planning target volume (PTV) and other healthy tissues and critical organs receive as low dose as possible) (ICRU 1985).

From the mathematical point of view, the radiotherapy treatment planning is an inverse problem, (i.e. the problem is to find the best source arrangements to receive the desired dose distribution within the patient). In solving the inverse problem, one needs a solution of the forward problem, (i.e. a solution for the model of the dose calculation). In the forward problem of intracavitary brachytherapy, one computes the dose distribution in a patient resulting from the localization of sources of the ionizing radiation due to both the tandem and ovoids configurations. Several models have been developed for the dose calculations in radiotherapy (Schweiger et al, 1979, Allen et al, 1986,), and one of the best models currently gaining attention is the FEM.

1.4 The scope and objectives of the study

The primary objective of this study is to model radiation doses to critical organs of cancer patients undergoing intracavitary brachytherapy treatment using the FEM.

The specific objectives of the study are

- i) to group tumour stages of patients according to the International Federation of Gynaecology and Oncology (FIGO) staging guidelines as stated or used by Radiation Oncologists
- ii) to specify the doses to the tumour volume based on the prescribed dose to the reference point
- iii) to model radiation doses to critical organs of intracavitary brachytherapy patients using the Finite Element Method to solve the photon transport equation

- iv) to assess the risk of radiation doses to both the rectum and bladder of patients undergoing intracavitary brachytherapy treatment
- v) to use the results obtained from the model to improve the speed and accuracy in treatment planning system of oncology centres.
- vi) to minimize the radiation doses to critical organs of patients undergoing intracavitary brachytherapy treatment in clinical applications using the principle of optimization.

1.5 Structure of the dissertation

Chapter 1, describes the introduction relating to the background, statement of the problem, relevance and justification of the study, the scope and objectives of the study.

In chapter 2, literature review on brachytherapy and mathematical models are discussed.

Chapter 3, describes the materials and method used in the study. Details of the dose calculations to critical organs and target volume of patients undergoing intracavitary brachytherapy is presented and this is the solution of the Boltzmann transport equation using FEM. The results and discussions are presented in chapter 4. Concluding remarks and recommendations are presented in chapter 5.

CHAPTER 2

LITERATURE REVIEW

This chapter reviews the literature relevant to radiotherapy with particular emphasis on brachytherapy. A general overview of radiotherapy, clinical brachytherapy sources and various brachytherapy applicators, organs at risk and critical organ dose monitoring, physics of ionization radiation interaction in radiotherapy, photon transport and Finite Element Method (FEM) and cancer staging and groupings are also presented.

2.1 General Overview

Cancer is one of the most deadly diseases in the world killing about seven million people every year, with about 70% of the death occurring in the developing countries (IAEA 2010). The number of cancer cases is growing globally but in developing countries they are worst hit by the cancer crisis since the resources needed to prevent, diagnose and ensure treatment are severely limited. It has been highlighted by the Programme of Action for Cancer Therapy (PACT) that these figures quoted for cancer rates are likely to double by the year 2020 and tripling nearly by year 2030 with a projection of seventeen million deaths (IAEA, 2010). Most of the developing countries have very fragile economies and budgets for health care systems are too small. Hence, any additional disease developing alongside with known disease like malaria, HIV and tuberculosis (TB), can lead to crisis.

Although cancer is a devastating disease, it is highly preventable and also curable if detected early particularly for common cancers such as breast, colorectal, prostate, cervix, head and neck. While effective treatment could increase, patient survival reduce cancer

mortality in the short term, preventive measures such as tobacco control, reduction of alcohol consumption, increased physical activity; vaccination against liver and cervix cancers, screening and awareness programmes could have a great impact on reducing the global cancer burden (IAEA, 2010)

2.2 Principles of brachytherapy

Over the last hundred years, ionizing radiation has been increasingly applied in medicine and is now firmly established as an essential tool in both diagnosis and therapy. Brachytherapy or radioactive implantation has been employed since the discovery of radioactive isotopes such as radium in 1903. In brachytherapy the sources are inserted into the treatment volume or close to the treatment volume. The different types of brachytherapy implants are intracavitary, intraluminal, interstitial, surface plaques and intravascular brachytherapy. The brachytherapy implant can either be temporal or permanent. For temporal implants, the dose is delivered over a period of time which is short as compared to the half-life of the sources (Beyer et al, 2000). The sources are also removed after the prescribed dose is reached. In the case of permanent implant, the dose is delivered over the life time of the source until the source undergoes complete radioactive decay. The main characteristic of brachytherapy is the rapid dose fall-off with distance from the radiation source whereby the tumour in contact or close to the source receive high amount of radiation dose but outside the tumour, normal tissues receive doses at considerable much lower levels (Stewart et al, 2006). The physical advantage of the effectiveness of brachytherapy as compared to teletherapy is when the tumour is small with well-defined geometry or sometimes it may be used as a

boost dose to more advanced or ill-defined tumours (Georg et al, 2008). During brachytherapy treatment, the following considerations are crucial and should always be considered; these are:

- (i) using a suitable dosimetric model for the calculation of dose distributions and treatment time.
- (ii) prevention or avoidance of geometrical misses due to accurate positioning of sources.
- (iii) using a calibrated source with its calibration traceable to a standard laboratory.

2.3 Importance of Low Dose Rate brachytherapy treatment.

There are three main advantages of Low Dose Rate (LDR) brachytherapy. These are

- (i) positioning of the source at short distances from the tumour volume, this allows a very good dose distributions in the target volume; that is good radiation dose distribution is the ability to locate radioactive sources in or close to the tumour, either by topical mold, intracavitary or interstitial implant, which represents the optimal conformal dose delivery system. Specifically, it is generally easier to compare with external beam radiotherapy to deliver high doses of radiation to target tissues, while minimizing radiobiological damage to normal adjacent tissues hence, good dose distributions sparing;
- (1) early responding normal tissues, which in external beam radiotherapy, typically produce the complications that force treatments to be prolonged over more than one month; and (2) late-responding normal tissues, which, in external beam radiotherapy, often represent the dose-limiting endpoint (Han et al, 1999).

(ii) short overall treatment times, to counter tumour repopulation; It is now generally accepted that long overall treatment times can be a significant cause of local failure in radiotherapy, because accelerated repopulation during the treatment means that tumour cells start to divide more rapidly than they can be killed (Withers et al 1988; Slevin et al 1992; Brenner, 1993). However, generally speaking, the optimal strategy for any radiotherapeutic regimen requires:

(a) short overall times to limit tumour repopulation; and

(b) long overall times to reduce early normal-tissue sequelae, especially to the skin and mucosa. Prima facie, requirements (a) and (b) are mutually exclusive; therefore, in most radiotherapeutic situations, the overall treatment time represents a compromise between short treatment times to minimize tumour repopulation and long treatment times to prevent unacceptable early complications. On the other hand, brachytherapy, because of its good dose distribution, inherently produce less early normal tissue damage. Therefore, the compromise on overall time does not have to be made, and much shorter times are tolerable in brachytherapy than could conceivably be employed in external-beam radiotherapy for a comparable effective tumour dose and

(iii) low dose rate, which results in an increased therapeutic advantage between tumour control and damage to late-responding tissues. It has been known for many decades that lowering the dose rate generally results in a reduction in radiobiological damage. Also, decreasing the dose rate will decrease late effects much more than it will decrease tumour control. Thus, the therapeutic ratio (i.e the ratio of tumour control to complications) will increase as the dose rate decreases. Therefore, the lower the dose rate, the better the

differential response that can be achieved between tumour control and late sequelae (Withers, 1985).

2.4 Clinical brachytherapy sources

Different types of sealed sources are used in brachytherapy treatment. They all contain a certain amount of a radionuclide that is encapsulated in sealed layers of a metal such as platinum or stainless steel or some kind of thin foil in the case of β -emitters. Various types of sources such as tubes, needles, wires, pellets, seeds, and a single stepping source connected to a cable, are available.

There are three different types of brachytherapy sources. These are photon, beta and neutron sources. For the photon sources, they emit gamma rays through γ -decay and possibly characteristic X-rays through internal conversion and electron capture. Some of the photon sources normally used in brachytherapy treatments are Co-60, Cs-137, Ir-192, I-125 and Pd-103. The beta sources emit electrons following β -source decay. Examples are Sr-90 and Y-90. Neutron sources emit neutrons following spontaneous nuclear fission. A typical example is Cf-252. Due to the cost implications and the relevance of the sources to this study, consideration is given to only the photon sources. The dosimetric characteristics of the sources are photon energy, half-life, half value layer (HVL) of shielding material, specific activity, source strength and inverse-square dose fall off.

Table 2.1: Characteristics of some radionuclides used in brachytherapy

Radionuclide	Average photon energy(MeV)	Half-life ($T_{1/2}$)	HVL in Pb(mm)
Co-60	1.25	5.2 years	11.0
Cs-137	0.66	30 .0 years	6.5
Au-198	0.41	2.7 days	2.5
Ir-192	0.38	73.8 days	3.0
I-125	0.028	60.0 days	0.02
Pd-103	0.021	17.0 days	0.01

2.5 Intracavitary brachytherapy in gynaecology

This is the type of brachytherapy treatment in which the applicators are inserted into a body cavity to reach the volume of the tumour. It is mainly used for the treatment of cancer of the cervix, uterine body and the vagina. Various applicators are used to hold the sources in an appropriate configuration in the tumour volume. These include the Fletcher-Suit-Delcos and the Tandem-Ring applicators as shown in Plates 2.1 and 2.2 respectively.

The most commonly used applicator for intracavitary brachytherapy treatment is the Fletcher-Suit-Delcos system which consists of a central tube called the tandem and lateral capsules also called ovoids or colpostats. The most widely used brachytherapy source for the treatment of gynaecological cancers is Cs-137. It is often necessary to use sources of different strength in order to achieve the desired dose distribution (Tanderup et al, 2010).



Plate 2.1: Fletcher-Suit-Delcos applicator



Plate 2.2: Tandem-Ring applicator

Different systems are used for dose specifications in brachytherapy treatment. These include; Stockholm, Memorial, Paris, Quimby, Manchester and the ICRU systems. The

two most commonly used systems in gynaecology are the Manchester and ICRU systems. The Manchester system uses the Fletcher-Suit-Delcos applicator and is characterised by doses to four points, namely point A, B, bladder and rectum as depicted in Figure 2.1. Ideally, point A represents the location where the uterine vessel crosses the urethra and also relates to the position of the sources. The dose at point A is very sensitive to the position of the ovoid sources relative to the tandem. Point A is defined to be 2cm superior to the external cervical end of the tandem and also 2cm lateral to the cervical canal. Point B is defined as 3cm laterally to point A or 5cm from the midline of the tandem or when the central canal is not displaced. The duration of the irradiation is based on the dose rate calculated at point A or B depending on the reference point adopted by the oncology unit.

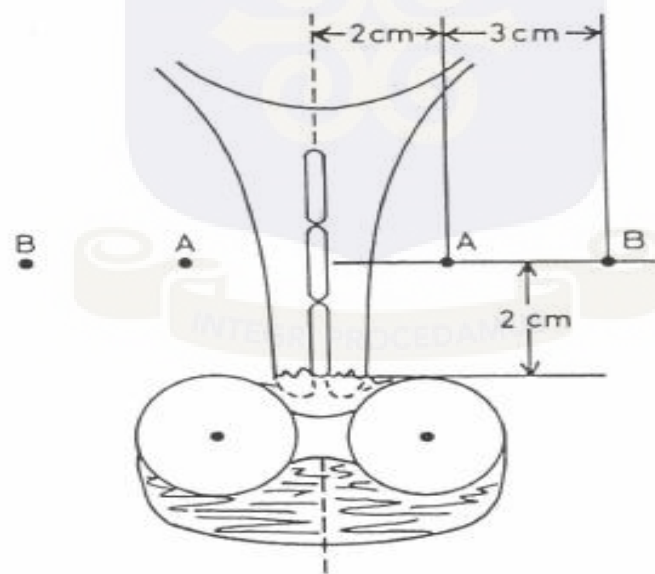


Figure 2.1: The reference points A and B according to the Manchester system

The diagram shows the reference points A and B used in intracavitary brachytherapy when using the Manchester system for the treatment of gynaecological cancers. In the ICRU system, the dose distribution is related to the target volume rather than to a specific point. The ICRU report identifies a dose level of 60Gy as the appropriate reference point for a low dose rate brachytherapy source. This result is a requirement to specify the dimensions of the pear-shaped isodose reference volume of 60Gy.

2.6 Organs at risk (OAR).

Organs at risk are sometimes called critical normal structures. They are normal structures that because of their radiosensitivity and their location close to the target volume may significantly influence the treatment planning or the prescribed dose level (ICRU, 1999). Organs at risk such as the bladder and rectum often limit the prescribed dose to the target volumes in cervical cancer in brachytherapy treatment. Therefore it is very important to accurately report OAR doses and correlate them to clinical outcome. In intracavitary brachytherapy for cervical cancer treatment, the planned tumour volume is limited to the anterior-posterior (AP) direction by the presence of bladder and rectum. The treatment is frequently planned to the maximum tolerable dose to these organs at risk. Treatment plans based on the desired dose levels, are specified for the tumour and organ at risk. The desired dose levels are chosen so that a high tumour control probability is realized and also the probability of complications in any organ at risk is very low (upper bound on dose level in healthy tissue) (Haie-Meder et al, 2005). The desired dose levels are specified in any organ which has the same harmful or beneficial effect as the actual inhomogeneous dose that is given by the radiation treatment equipment.

2.7 Critical organ dose monitoring in gynaecology

Brachytherapy of cervix carcinoma results in high doses to some surrounding critical structures such as rectum and bladder. Therefore, these structures should be closely monitored as in many cases complications are developed decreasing patient quality life and therapeutic ratio. The most related factors that could lead to the complications on these critical structures are the volume of irradiated rectum, the total dose to the rectum and the dose rate of the brachytherapy modality used (ICRU 1985; Chen et al, 2000).

In gynaecology, the most critical organs associated with intracavitary brachytherapy treatment are bladder and rectum. The most frequent clinical complications of intracavitary gynaecological radiation treatments results from a high dose delivered to portions of either the rectum or the bladder. In clinical applications, surgical gauze is used to displace the sensitive critical structures away from the applicators so as to keep the doses to the critical organs as low as possible but in most cases complications are often encountered (Chen et al, 2000; Ferrigno et al, 2001; Nag et al, 2002).

The diagram in Plate 2.3 shows the female anatomy and placement of applicators for intracavitary brachytherapy treatment in gynaecological cancers using the Manchester system.

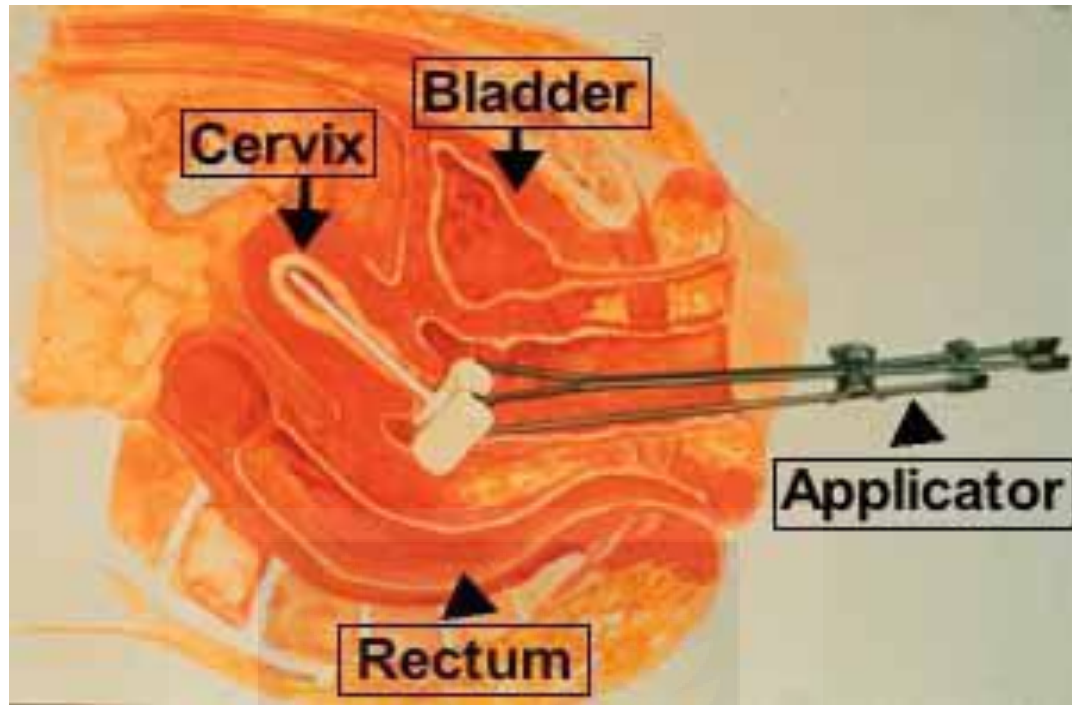


Plate 2 .3: Fletcher-Suit-Delcos system in gynaecology

Direct measurements of rectal and bladder doses have been attempted using various miniature ionization chambers, scintillation detectors and MOSFET dosimeters. It has proven that, measured data give large variability and correlate poorly with calculated values.

2.8 Anatomy of the cervix

The cervix carries out many critical functions that contribute to the overall reproductive health and wellbeing of women. The cervix is the portion of the uterus which is connected to the vaginal canal and:

1. allows the passage of menstrual fluid;
2. promotes fertility;

3. protects the uterus, upper reproductive tract, and a developing fetus from pathogens; and
4. it may play a role in women's sexual pleasure.

The cervix (Latin word meaning neck) is the lower-most portion of the uterus. Cylindrical in shape, the cervix consists of the following two major structures: the ectocervix and the endocervix. The ectocervix is the portion of the cervix which is touchable and visible through the vaginal canal. This is also the area which is swabbed during a pap smear. The endocervix is the internal, canal-like portion of the cervix which opens into the uterus. The size, shape and color of the cervix depend on a woman's age, hormonal state and whether or not she has given birth. For women who are nulliparous, or have not given birth, the cervix appears to have a small circular opening (external os) at its center. In parous women, the cervix is bulkier and the external os has a more slit like appearance.

The cervix is a small, cylindrical organ which is about several centimeters long but less than 2.5cm in diameter. It also forms part of the lower neck of the uterus. The cervix separates the body and cavity of the uterus from the vagina. There is a small canal running through the cervix which allows sperms to pass from the vagina into the uterus and during menstruation, blood passes through this same canal.

The cervical canal which forms part of birth canal during childbirth dilates widely to allow the passage of the baby. The bulk of the cervix consists of fibrous tissue with some smooth muscle. This tissue makes the cervix to form a sphincter (circular muscle) and allows great adaptability in its size and shape during pregnancy and childbirth.

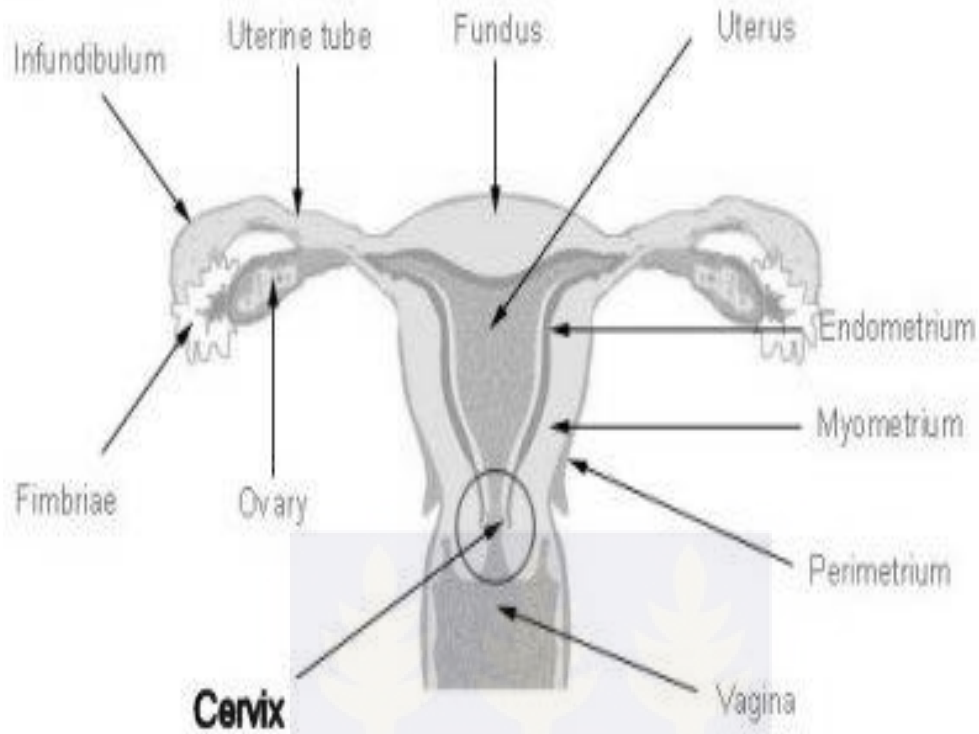


Figure 2.2: Anatomical structure of the human cervix

2.8.1 Risk Factors of cervical cancer

A person is likely to develop cervical cancer if the following practices are often indulged in

- (i) smoking processes
- (ii) starting to have sexual acts at an early stage
- (iii) having many sexual partners
- (iv) having taken contraceptive pills for longer periods
- (v) having a weakened immune system

2.8.2 Symptoms of cervical cancer

The following are some of the various associated symptoms of cervical cancer. These are

- (i) unusual bleeding between menstrual periods and also after sex
- (ii) chronic itching of the vulva
- (iii) pain in the pelvis
- (iv) persistent vaginal bleeding
- (v) post menopausal bleeding
- (vi) lower back pain

2.9 Physics of ionizing radiation interaction in radiotherapy

Ionizing radiation is used in radiotherapy treatments because of its ability to damage living tissue. The intended high local concentrations of absorbed energy can kill a cell either directly or indirectly. Ionizing radiation therefore excites and ionizes these medium atoms when traveling through the medium (Attix, 1986). It is classified as directly ionizing radiation when either electrons or positrons deliver energy to the medium directly. However, indirectly ionizing radiation, photons first transfer their energy to charged particles, which then deliver energy to the medium. In indirectly ionization radiation, there is formation of highly reactive chemical species such as free radicals in water, which are always present in a human tissue. A free radical is an atom or a compound with unpaired electrons.

Photons consist of X-rays and gamma rays named according to their mode of origin, although their properties are almost the same (Attix, 1986). Electromagnetic radiation emitted by charged particles in changing atomic energy levels is called characteristic or

fluorescence X-rays. Continuous or bremsstrahlung X-rays are emitted from inelastic collisions of charged particles in which they slow down in Coulombic force field.

Gamma rays are electromagnetic radiation emitted from the nucleus or in annihilation reactions. Annihilation radiation is emitted when there is re-combination of positron and electron. β -rays (negative or positive) and δ -rays consist of electrons and positron. β -rays are emitted from the nucleus and δ -rays are resulted from the charged particle collisions (Attix, 1986).

As photons are uncharged they travel quite a long distance in a medium without interacting with medium atoms. On the other hand, charged particles, such as electrons and positrons, travel only a small distance until they undergo interactions with medium atoms. Thus, photons undergo only few interactions until they attenuate and secondary electrons born, while electrons loose their energies in many small interactions with medium atoms along their trajectories (Attix, 1986).

Radiation therapy is primarily used to treat cancer by locally targeting radiation to the diseased tissue or cancerous cells.

2.9. 1 Photon interactions in biological media

Actually, photons by themselves do not deposit energy to matter, but during different interactions, the electrons of medium atoms obtain energy from photons and these electrons then impart that energy to matter in many interactions along their tracks (Attix,1986). Photons are individual units of energy. As photon beam passes through a medium, there are three possibilities associated with the photon; these are

- (i) it may penetrate through the matter without interacting

- (ii) it may interact with the matter and be completely absorbed hence depositing its energy
- (iii) it may interact and be scattered or deflected from its original direction and deposit part of its energy in the medium.

There are two main major interactions through which photons deposit their energy. These are photoelectric effect and Compton effect. Photon interactions are dominated by absorption and inelastic scattering collisions, in which the photon's energy is reduced. The most important interactions of photons are Photoelectric effect, Compton effect, Pair production and Rayleigh scattering.

2.9.2 Photoelectric Effect

In the photoelectric effect, an incident photon gives all its kinetic energy to a tightly bound electron, such as those in the inner shells of an atom (Attix, 1986 ; 2004). The photoelectric effect can only occur when the kinetic energy of incident photon is greater than the electron binding energy. However, the photoelectric effect is more probable in lower energies, as long as the energy is more than the binding energy of an electron. The photoelectric effect is dominant at energies below about 200keV for low Z media or materials. The energy range increases as Z increases. Photoelectric effect is an event in which an incident photon disappears and the so called photo-electron is ejected. The affected gap in the atomic shell is then immediately filled with another electron from the outer less bound atomic shell resulting in an emission of the characteristic X-ray, sometimes called fluorescence X-ray or emission of an Auger electron with kinetic energy.

The photoelectric effect is the process by which a photon with energy $h\nu$ is absorbed by an atom which, as a result, emits an electron with energy $h\nu - E_B$ where E_B , is the binding energy of the ejected electron. This process leaves the atom in an excited state and it relaxes by emitting a characteristic X-ray or subsequent Auger electron. The photoelectric effect is most likely to occur when the photon's energy is slightly greater than the electron's binding energy and low energy interactions tend to produce photoelectrons ejected at right angles while higher energy interactions will eject photoelectrons in a forward direction.

The mass attenuation coefficient for photoelectric interactions varies as Z^3 for high-Z media and as $Z^{3.8}$ for low-Z media. For low-Z materials the photoelectric effect is dominant at energies below 200 keV and varies approximately with energy as $\frac{1}{h\nu^3}$

2.9.3 Coherent and Incoherent Scattering

The most common photon interaction at therapeutic energies is scattering by electrons. There are two types of photon scatter: coherent and incoherent. Coherent, or Rayleigh scattering, involves the deflection of a photon by atomic electrons during which none of the photon's energy is converted to electron kinetic energy. Atomic electrons, subject to the electric field of an incident photon, are set into vibrational motion and the oscillations of each electron emit a particular wavelength of radiation that combine to form the wave of the incident photon, but travelling in a new direction. Rayleigh scattering is primarily forward directed and has little impact on photons with energy greater than 100 keV.

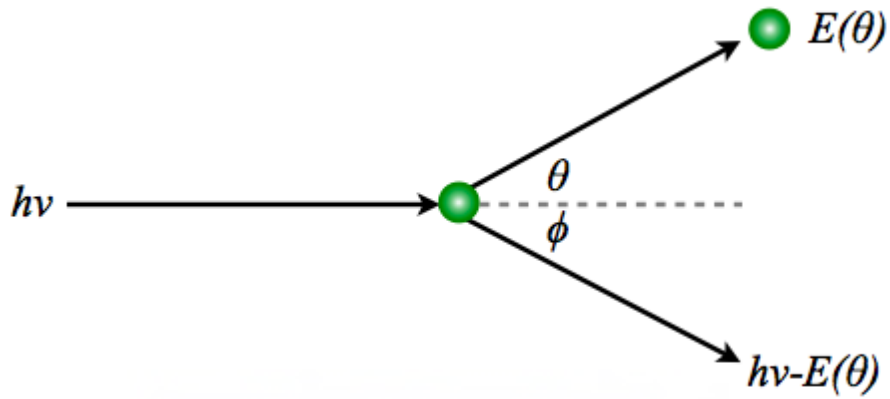


Figure 2.3: An electron undergoing a Compton scattering event.

The most significant interaction for photons between 20 keV and 5 MeV in tissue-like material is incoherent scattering, or Compton scattering, during which a photon interacts with an atomic electron and is scattered at a new trajectory while the electron is ejected with kinetic energy imparted by the incident photon. Figure 2.3 shows a schematic diagram of a Compton scattering event. The photon has initial energy $h\nu$ before colliding with the electron. Because the electron's binding energy is greatly exceeded by the energy of the incident photon, it is treated as a free electron. The electron is ejected from its orbit at some angle θ with energy $E(\theta)$ while the photon is scattered at a corresponding angle Φ with energy $h\nu - E(\theta)$.

The Klein-Nishina formula is used by EGSnrc Monte Carlo to determine the Compton cross section and is given per unit solid angle as

$$\frac{\partial \sigma}{\partial \Omega} = \frac{r_o^2}{2} (1 + \cos^2 \theta) \left\{ \frac{1}{1 + \alpha(1 - \cos \theta)} \right\}^2 \left\{ 1 + \frac{\alpha^2 (1 - \cos \theta)^2}{[1 + \alpha(1 - \cos \theta)](1 + \cos^2 \theta)} \right\} \quad (2.1)$$

where $\alpha = \frac{h\nu}{m_o c^2}$ and $m_o c^2$ is the rest energy of an electron.

If the scattered electron is emitted in the direction of the incident photon, the scattered photon will be emitted at 180° and the electron will have the maximum energy possible for a Compton electron. Conversely, a scattered electron will receive the least possible energy if the incident photon grazes by and continues nearly straight forward, emitting the scattered electron at nearly 90° .

Compton interactions are nearly independent of atomic number and decrease with increasing energy (Johns et al, 1983). The Compton effect is dominant at energies between 20keV and 30 MeV in mediums like human tissue or water (number of electrons per molecule $Z = 10$). The dominance region is narrower for high Z mediums. In Compton effect, the incident photon (energy E'_p , direction Ω'_p) collides with an electron and gives some of its energy to that electron. After the collision the incident photon energy and direction are changed to E_p and Ω_p , respectively. Also the electron has now kinetic energy E_e and direction Ω_e . If the electron is assumed to be initially at rest and unbounded, then

$E_e = E'_p - E_p$, and the relation between Ω_p' and Ω_e is obtained by kinematics.

2.9.4 Pair Production

In pair production, the incident photon with a minimum energy of $2E_o = 1.022\text{MeV}$ is absorbed and electron and positron are born or created (Attix,1986). Pair production is

more dominant at very high energies. It can only take place in a Coulomb force field, which is usually near an atomic nucleus. Sometimes, pair production can occur in the field of an atomic electron. Then the interaction is called triplet production, because the initial electron achieves also kinetic energy and thus two electrons and one positron has now a significant amount of kinetic energy. An opposite interaction to pair production is an annihilation process, in which electron and positron recombine leading to disappearance and emergence of two photons.

Pair production is the conversion of energy to mass that results when a photon is subject to the strong field of an atomic nucleus and becomes an electron-positron pair. The photon must have energy of at least 1.022 MeV to comprise the rest masses of the charged particles. Any additional energy held by the photon is distributed between the electron and positron as kinetic energy. Because the atomic nucleus plays a part in this interaction it receives a very small portion of the photon's momentum; consequently, the momentum of the electron does not uniquely predict the momentum of the positron and vice-versa. If the incident photon has energy of at least 2.04 MeV, it may interact in the field of an orbital electron to the same end, with the addition of an ejected atomic electron. This less common process is called triplet production as it produces a total of three charged particles. A positron will propagate through and ionize matter in the same manner as an electron until it slows down enough to annihilate with a free electron and produce two 0.511MeV photons which are ejected at 180° from one another. If the positron has some remaining kinetic energy when it annihilates, the angle will be nearly 180° . The incidence of pair-production interactions increases rapidly with increasing energy once the 1.022 MeV threshold has been met and the mass attenuation coefficient

increases approximately with atomic number. Pair production is the dominant photon interaction at energies in excess of 5 MeV.

2.9.5 Characteristic X-rays and Auger Electrons

Characteristic X-rays, or fluorescence X-rays, are the photons emitted when an atomic orbital vacancy is filled by an electron from a higher orbital shell. The energy of a characteristic X-ray is equal to the difference in binding energies between the orbital levels and is unique to atomic number. If a characteristic X-ray is absorbed by an outer orbit electron, that electron is ejected with the energy of the characteristic X-ray less the binding energy of the electron and is called an Auger electron (Attix, 2004).

2.9.6 Rayleigh scattering

In Rayleigh scattering, the incident photon is scattered by the combined action of the whole atom (Attix, 1986 and 2004). That is why it is also called coherent scattering. Rayleigh scattering is elastic, which means that no energy is lost in the interaction, in which the atom moves just enough to conserve momentum and initial photon is redirected in a small angle. Rayleigh scattering is more significant at low energies, in which the photon scattering angle is much bigger.

2.10 Linear Energy Transfer(LET)

The total distance an electron travels in a material before losing all its energy is referred to as its range. There are two main factors that determine the range, these are the initial energy of the electrons and the density of the material or medium. One important

characteristic of electron interactions is that all electrons of the same energy have the same range in a specific material.

The rate at which an electron transfers energy to a material is known as LET and it is expressed in terms of the amount of energy transferred per unit distance travelled in a medium.

Mathematically, it can be expressed as

$$LET = \frac{dE}{dx} \quad (2.2)$$

The S.I unit of *LET* is $\text{keV}/\mu\text{m}$

In tissue, the LET depends on the kinetic energy or velocity of the electron. Generally, the LET is inversely proportional to electron velocity. As the electron loses energy, its velocity decreases and the value of LET increases until all its energy is dissipated. Particles can lose energy continuously along their path when interacting with the matter and continuously slowing down.

When working out the impact of biological systems or matter, the amount of energy lost by the particle, then the LET is important. Particles with large LET can do a large amount of damage, but usually over a short range.

2.11 Electron interactions

Because electrons are charged particles their interaction probabilities are much higher than those of uncharged particles. For example, photons need only few interactions to dissipate all of its kinetic energy rather than electron would typically undergo several (about 10⁵) interactions before losing all of its kinetic energy (Attix, 1986 and 2004).

Because photons may pass a slab of matter without any interaction or it may lose all of its kinetic energy in a few interactions, it is impossible to predict individual photon traveling distance. On the contrary, because electrons interact almost with every atomic electron or nucleus it passes and loses its kinetic energy gradually in small friction-like process, it is customary to describe electron traveling by stopping power, range and yield. These are expectation values for a charged particle energy loss per path length, for a path length and for an electromagnetic radiation production, respectively. Due to the nature of the charged particle, it is not customary to describe charged particle interactions by total cross sections and differential cross sections, which are needed in the Boltzmann transport equation and these, are found more rarely in the literature than those for photons (Zerby et al, 1967; Zheng et al, 1992). Electron interactions are elastic scattering, inelastic scattering and radiation processes, which take place in a form of bremsstrahlung and electron positron annihilation. The bremsstrahlung process dominates at high energies where as the inelastic scattering dominates at low electron energies in high Z media. In tissue-like materials, the inelastic scattering dominates at all energies and the influence of the bremsstrahlung process is only few percents (Attix, 2004).

2.12 Methods for calculation of radiation doses from acquired image data

There are various ways of radiation-dose determination in particular, computational methods and other systems for calculating radiation doses delivered to anatomical tissues and critical structures during radiotherapy treatments. Radiation transport plays an important role in many aspects of radiotherapy and medical imaging. In radiotherapy, radiation dose distributions are accurately calculated to both the treated regions and

neighbouring organs and other structures where the dose is to be minimized. Dose calculations are commonly used in radiotherapy treatment planning and verification (Daskalov et al, 2000). The dose calculations are often repeated numerous times in the development and verification of a single patient plan. Some modalities include external beam radiotherapy, brachytherapy, and targeted radionuclide therapies.

In addition, many variations exist in beam delivery methods, including 3D conformal radiotherapy (3D-CRT), intensity modulated radiotherapy (IMRT), and stereotactic radiosurgery (SRS). Brachytherapy treatments include photon, electron and neutron sources with the use of a variety of applicators and other delivery mechanisms in delivering the required prescribed dose.

The physical models that describe radiation transport in the anatomical structures are usually complex and difficult, hence accurate methods for radiation dose determination due to radiation transport in tissues are highly needed and also of great importance in brachytherapy.

The various methods employed in radiotherapy for radiation-transport computations can be broadly grouped into three categories; these are stochastic Monte Carlo methods, deterministic and analytic or empirical methods.

Monte Carlo methods, stochastically predict particle transport through media by tracking a statistically significant number of particles. While Monte Carlo methods are recognized as highly accurate, simulations are time consuming, limiting their effectiveness for clinical applications. In most clinical applications, this method of approach is based on simplifications of results which limit its accuracy and scope of applicability.

The phrase "deterministic radiation-transport computation," refers to methods which solve the Linear Boltzmann Transport Equation (LBTE), which is known to be the governing equation of radiation transport, by approximating its derivative terms of discrete volumes. Examples of such approaches include discrete-ordinates, spherical-harmonics, and characteristic methods. However, the use of deterministic methods in radiotherapy and imaging applications has been limited to research in radiotherapy delivery modes such as neutron capture therapy and brachytherapy. This can be attributed to several factors, including methodic limitations in transporting highly collimated radiation sources, and the computational overhead associated with solving equations containing a large number of phase-space variables.

The phrase "analytic or empirical radiation-transport computation methods," refers to approaches which employ approximate models to simulate radiation transport effects; for example, using pre-defined Monte Carlo scattering or dose kernels. Examples of analytic or empirical methods include pencil beam convolution (PBC) methods and collapsed cone convolution (CCC). Due to their relative computational efficiency, PBC approaches are widely used in radiotherapy, even though their accuracy is limited, especially in the presence of narrow beams or material heterogeneities.

In radiotherapy, various uncertainties in dose delivery may translate into suboptimal treatment plans of cancer patients, and for imaging, a reduced reconstructed image quality may result. This has necessitated the need for accurate, fast, stable, generally applicable and computationally efficient method in both radiotherapy and diagnostic applications by solving the radiation transport equations using different approaches or methods.

2.13 International recommendations on target and organs at risk: ICRU-definitions

The success of Boltzmann transport equation requires the delivery of a high radiation dose directly to the tumour volume or target whilst possibly sparing to some degree, the surrounding normal tissues. The target volume must always be described, independently of the dose distribution, in terms of the patient's anatomy and tumour volume.

The gross tumour volume (GTV), may be evaluated by various diagnostic methods; clinical examination i.e. inspection and palpation, endoscopies, and image techniques such as radiography, Computer Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), ultrasound, or other techniques, depending on the location and type of pathology.

The clinical target volume (CTV), is the volume which contains the gross and subclinical disease. Clinically, it thus contains the GTV and a safety margin around the GTV to take into account (probable) subclinical involvement. The CTV may also include other anatomical areas, e.g., regional lymph nodes or other tissues with suspected (or proven) subclinical involvement.

The planning target volume (PTV), is a geometrical concept, taking into consideration the net effect of all possible geometrical variations.

The organ at risk (OAR) is normal tissue whose radiation sensitivity may significantly influence treatment planning or prescribed dose.

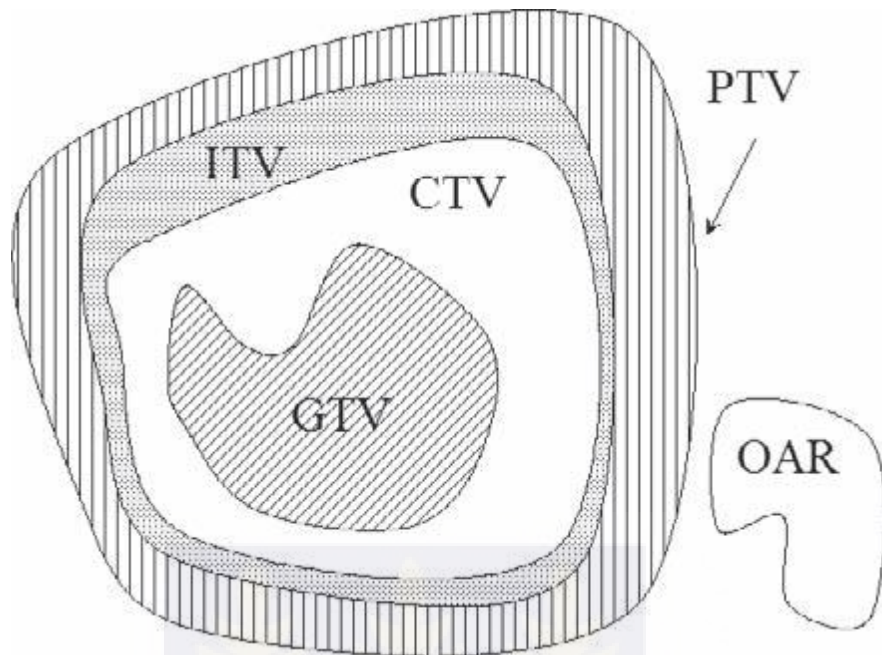


Figure 2.4: Graphical representation of the volumes of interest, as defined by ICRU (ICRU,1999).

For brachytherapy the planning target volume PTV is the same as the clinical target volume, CTV. The prescribed dose is defined as the dose which the oncologist or clinician intends to give and enters in the patient treatment chart.

The minimum target dose (MTD) at the periphery of the CTV is the minimum dose decided upon by the clinician as adequate to treat the CTV (minimum peripheral dose). MTD is approximately equal to 90% of the prescribed dose in the Manchester system.

A pear-shaped dose distribution with an extremely sharp dose gradient is usually achieved by using tandem and ovoid applicators with appropriate configuration of sources (ICRU Report 50).

2.14 The importance and use of numerical methods

Numerical methods have played important role both in science and engineering to solve and analyze problems. The solution to these problems can be achieved with the help of computers. The importance of numerical methods in analysis is due to several factors; some of them, in most natural phenomena can best be described by differential equations with varying boundary conditions, whose solutions cannot be obtained by analytical means except only in very simple cases. Great improvements have been made in developing numerical techniques so that problems could be solved at low cost and within span of short times. With the arrival of high speed computers, scientists and engineers have succeeded in exploiting a lot of numerical methods. Numerical solution of the transport equation finds application in numerous areas like nuclear reactor design, radiation shielding, semiconductor device design, radiation oncology and radiation transfer in stellar atmospheres.

Transport is the process by which particles distribute themselves within a host medium and by streaming off in various directions, interacting with other particles of the medium until they are either finally absorbed or scattered out of the system.

The transport of photons is focused on this current study of research. The photon transport was governed by the Boltzmann transport equation which was derived by Ludwick Boltzmann in connection with the kinetic theory of rare gases. It describes the distribution of photons in the host medium as a function of their position, energy, direction of motion and time.

There are two main classes of computational techniques that are used in solving the transport equation. In the first class, using deterministic methods, the transport equation is

discretized by using a variety of methods and solved directly or iteratively. Different types of discretization give rise to different deterministic methods such as spherical harmonics, discrete ordinate method, finite element method and others like Monte Carlo methods which uses stochastic techniques.

2.15 Dose calculations in brachytherapy

In brachytherapy, one or more localized radioactive sources are placed within or in close proximity to the treated region, and dose conformity is achieved by optimizing a brachytherapy source arrangement which can maximize dose to the treated region, while minimizing radiation doses to neighbouring healthy tissues and critical organs. Each of the brachytherapy sources may be represented as a point source, which is anisotropic in both angle and energy, representing the exiting photon flux on the surface of the brachytherapy source. In most brachytherapy applications spatial electron transport can be neglected, and the dose field can be obtained by a kinetic energy released in matter (KERMA) using the energy-dependent photon flux.

There are various methods of calculating doses in brachytherapy. Some of the current methods are stochastic Monte Carlo simulations and deterministic methods like the discrete ordinate method, spherical harmonics and finite element methods (Jones et al, 1994).

Nowadays, the Monte Carlo (MC) method is assumed to be the most accurate method for the dose calculation in brachytherapy (Rogers, 2006). In MC, the paths of the scattering particles are followed by randomly selecting the directions and energies of the particles. In different media, there are scattering interactions whereby some particles lose their

energy and other particles are created and finally, energy is absorbed in matter depositing the dose. With several millions particle histories MC method gives an estimate for the dose distribution. The major drawback of the MC method is the long computation time and because of this, the pencil-beam models are the most common approach which is sometimes used in treatment planning systems (Ulmer et al, 1996). In pencil-beam models, the dose distribution in a patient is achieved as a superposition of appropriately weighted dose deposition kernels. The kernels can be modeled with Monte Carlo methods, using some approximations or using empirical beam data (Strochi et al, 1999). Most of the dose calculation models have their roots in Boltzmann transport equation (BTE). The previously presented MC method uses BTE to simulate particle transport in a medium. In its original form, the BTE takes rigorously into account the patient inhomogeneity and scattering effects. It is an integro- differential equation and it is studied in many fields of physics. The linear BTE can be used in radiation therapy, because the high energy particles move nearly at the speed of light and the interactions of particles with each other are assumed to be negligible. The BTE describes particle traveling in a medium and it is based on the particle equilibrium in a small volume. The unknown function in the BTE based forward problem is the particle angular flux, from which the dose can be calculated. Instead of finding an analytical solution of the BTE, one can seek for a numerical solution, which can be stochastic or deterministic.

The solution of the BTE using deterministic methods has been carried out by many authors and several production codes have been generated in the field of radiation therapy physics (Mordant, 1986 and Williams et al, 2003). In deterministic methods, the stationary BTE is usually solved using some grid-based numerical method, in which the

phase space is discretized in spatial, angular and energy domains. The energy discretization is often done by multi-group approximation, in which the energy range is divided into energy groups and the interaction cross sections are replaced by multi-group cross sections (Allen, 1986). Most of the methods often used for angular discretization are the discrete ordinates and spherical harmonic approximations (Manteuffel et al, 2000). Finite difference and finite element methods (FEM) are usually used in spatial discretization and also for angular discretization. The finite element discretization method may be used for all variables simultaneously (Tervo et al, 1999) but sometimes the discontinuous FEM is used. Other methods, which are successfully used to solve the BTE, are the method of characteristics, the method of moments, the electron multiple scattering theory, the collocation method and hybrid collocation-Galerkin-Sn method.

Mainly due to computational problems, the BTE based on deterministic models are not often used in dose calculations in clinical applications. BTE describes particle traveling in a medium and it is based on the particle equilibrium in a small volume. The unknown function in the BTE based forward problem is the particle angular flux, from which the dose can be calculated. In the stationary case, it has six variables, three spatial, two angular and one energy variable. BTE can be solved analytically only in very simplified geometries, in which it does not have very much of practical use. Instead of finding an analytical solution of the BTE, one can seek for a numerical solution, which can be stochastic or deterministic (Tagziria, 2000).

2.16 Radiation safety during brachytherapy treatment

There is the need for radiation safety precautions when patients are implanted with radioactive sources during brachytherapy. All temporary patients undergoing low dose rate (LDR) brachytherapy treatments are hospitalized for some few days and the radiation levels in and around their room should be monitored to assure low radiation levels for personnel attending to the patient. For high dose rate (HDR) brachytherapy treatments the staff should not be allowed in the treatment room during the short time of irradiation which lasts between five to sixty minutes (Lertsanguansinchai et al, 2004).

The walls of the treatment room are designed to meet acceptable levels of exposure outside. Time, shielding and distance are common key factors used to limit exposure to staff and visitors. Sometimes, additional movable lead shields are used to lower excessively high radiation levels around implant patients. For LDR brachytherapy, visitors are allowed to see their patients. In the case of remote afterloading technique, the treatment will be interrupted but such an interruption should not take too long because of the effect on the dose and time pattern. The irradiation should not be considered as continuous pattern if the interruption exceeds 10% of the total irradiation time. If, exceptionally, the sources are in the patient during a visit, the visitor should be clearly informed of the risk and special measures like time, distance and shielding should be taken into consideration in order to minimize exposure.

2.17 Quality Control and Quality Assurance in brachytherapy

In brachytherapy, extreme attention should be given to quality control and quality assurance. The main aim of quality control and assurance is to maximize the probability

that each individual treatment is carried out consistently, accurately and safely. A very important function in brachytherapy treatment is the correct geometric localization of the applicator in order to treat the target volume adequately. The consistent applicator placement is crucially dependent on the skill of the radiation Oncologist at the facility. Following the application procedure, it is primarily the physicist's responsibility to ensure that the treatment is delivered accurately and safely in accordance with the radiation Oncologist's prescription. The treatment planning system that calculates the dose distributions must be provided with the correct data needed to perform these calculations.

Brachytherapy source arrangements consist of individual sources, but they are often grouped as strings, trajectories, or applicators. One should confirm that parameter changes that might affect the entire group of sources are correctly made. The verification of dose calculations for clinical use is a very important part of the commissioning of a treatment planning system. A comprehensive series of test cases must be planned. These tests involve measurements and calculations. The results must be analyzed before any dose calculation is used clinically.

2.18 The photon transport theory

The transport theory is used to refer to a mathematical description of transport of particles or radiations through a medium. The foundation of the transport theory lies in the kinetic theory of gases which was developed by Ludwig Boltzmann who was a renowned Austrian Physicist. There are three famous equations named after Boltzmann, these are (i) the equation of entropy, (ii) an equation concerning particles in a gravitational field, and

(iii) an equation for particle or radiation transport. The latter is sometimes called the Boltzmann transport equation.

The mechanism of photon transport in media (tissues) has been the subject of description during the last decade. If one considers photon propagation as a particle (eg. neutral particle) then the BTE provides an exact description of the photon transport. The photon transport theory may be considered as the main foundation of radiotherapy treatment. The photon transport equation is considered to be an expression governing the photon distribution in water equivalent tissue such as patient undergoing radiotherapy treatment. However, the complexity of the integro-differential equation makes the photon transport equation exceedingly difficult to solve analytically. Typically, simplifying approximations are made to reduce its complexity.

The term 'transport' can be explained as the processes in which particles distribute themselves in a host medium, by streaming off in various directions, interacting with other particle of the medium and finally being absorbed or leaked out of the system.

The transport theory has been applied to the study of many areas; some of them are as follows

- (a) neutron transport in nuclear reactors
- (b) penetration of light through the atmosphere
- (c) shielding of radioactive sources
- (d) diffusion of holes and electrons in semiconductors
- (e) photon transport through biological tissues

Despite the fact that different kinds of particles (eg neutrons, gas molecules, electrons and photons) may be involved in the transport processes, all these phenomenon can be studied and described by using the same basic transport equation.

One of the principal equations used in radiotherapy dose analysis is the transport equation, which is a linearized derivative of the equation developed by Ludwick Boltzmann for the kinetic theory of gases (Bell et al, 1970). This equation may be used to determine the photon distribution during brachytherapy treatment as a function of energy, position, direction and time. Actually, a solution for the photon source distribution is always sought in a given problem and the coupling between the two is treated externally. This study will focus on the problem of photon transport distribution in a biological media such as patients undergoing intracavitary brachytherapy treatment and the time-dependent form of the linear transport equation will be used. The photon transport equation may be presented in different forms, and simplifications are often applied to tailor the equation to the requirements for a specific application. In radiotherapy physics applications, the transport equation is often written in terms of the angular photon flux as the dependent variable. Generally, the transport equation is difficult to apply and solve analytically hence, simplifications and numerical solutions are often necessarily sought in order to apply the equation in radiotherapy applications. The photon transport equation is an integro-differential equation that cannot often be solved simply in analytical form and for this reason as an alternative; researchers have reported various computational methods such as stochastic and deterministic method which renders the PTE solvable.

The propagation of photons in matter might be seen as stream of particles, each with a localized quantum of energy. Photon transport through a turbid media can be

mathematically expressed by the Photon Transport Equation (PTE). The PTE is derived by considering the principle of conservation of energy balance of incoming, outgoing, absorbed and emitted photons of an infinitesimal volume element in the medium. The PTE is valid for an isotropic and quasi-homogeneous medium; hence it is assumed that, the inhomogeneities are small and uniformly distributed throughout the material. The tissue is assumed to be a homogeneous matrix containing absorbing and scattering centers. In this case, a tissue is represented by these parameters namely, absorption coefficient (μ_a), and scattering coefficient (μ_s). A photon propagating through a medium or a patient is affected not only by the inverse square law but also scattering and attenuation. These parameters make the dose deposition in a medium a complicated process and its determination rendering it to be a complex task.

Numerical methods are usually used to solve the photon transport equations which are divided into two forms: these are (i) stochastic (Monte Carlo) methods and (ii) deterministic techniques (Lewis et al, 1984). Even within the deterministic methods, further categorization breaks the approaches into discrete ordinates and integral transport approaches (Kavenoky, 1981). The integral transport approximations are derived from the integral form of the transport equation, in which the angular dependence of the angular flux is eliminated by integrating out all angular variables, based on an assumed order of scattering (Lewis et al, 1984). This technique can be applied to complicated, heterogeneous tumour geometries with multiple dimensions.

The discretization method is one of the most widely used method for solving the PTE in integro-differential form. The accuracy of the solution obtained by using the method of discretization is governed by the number of discretization terms used. A wide range of

different techniques to solve the PTE are available but each with its advantages and drawbacks.

The governing equation of transport theory is the transport equation, which is equivalent to the Boltzmann equation used to describe particle transport. In this particular case the particles are photons.

2.18.1 Advantages of using the transport equation

The following are some of the advantages of using the photon transport equation in the determination of absorbed dose in tissues:

- (i) The solutions are exactly reproducible from one run to another unlike that of Monte Carlo simulations
- (ii) The method lends itself well for making parameter changes easily for a given application
- (iii) When it applies, it can be more rapid than Monte Carlo simulations
- (iv) It generates a solution for all points in a given phase space

2.18.2 Disadvantages of the transport equation

The main disadvantages in using the transport model in the determination of the absorbed dose in a medium are:

- (i) Very large grids are needed for solution with sufficient accuracy
- (ii) Little progress has been made on 3-D solutions.

2.19 Finite Element Method (FEM)

A number of analytical tools such as the Sievert integral and Convolution methods are available for brachytherapy dosimetry (Williamson *et al* 1991, Carlson and Ahnesjo 2000). The AAPM TG-43 also recommends a formulation that uses parameters such as geometry factors, anisotropy functions and radial dose functions derived through Monte Carlo methods and measurements. Monte Carlo methods are known to provide very accurate results for a wide range of problems of complex geometries. The efficiency of the Monte Carlo methods starts to degrade if the detailed distribution of the results, such as three-dimensional flux or absorbed dose distributions, is computed. Since the volume needs to be divided into very small meshes for detailed distributions, obtaining enough histories contributing to such small volumes may not be quite easy (Lewis and Miller 1984).

The FEM was first used by Clough in 1960 to solve continuum problems, however in 1972 the tempo of development of FEM increased remarkably which became the most active field of interest in numerical solution of continuum problems and it has remained the dominant method till today.

The FEM is a numerical technique for solving problems which are described by partial differential equations (PDE) or can be formulated as a functional minimization; it is well-suited for approximating continuum solutions to boundary-value problems with complex geometries or domains and composed of inhomogenous materials. The FEM is based on integral formulations and is one of the computational techniques for obtaining approximate solution to partial differential equations that arise in scientific and

engineering applications. It can provide approximate solutions to many complicated problems that would be intractable by other techniques

The FEM is one of the numerical methods often used to solve the PTE. The numerical stability of the finite element model depends on the mesh resolution, error limit of the conjugate gradient method (that is, it refers to an iterative scheme for symmetric and positive definitive problems), optical properties of the simulated media and the modulation frequency (Arridge et al, 1993). When compared with Monte Carlo methods, FEM is found to be twenty (20) times faster than MC in time - domain measurements and 550 times faster than MC in the continuous intensity measurements (Lapidus and Pinder 1982).

The use of the FEM in transport problems has given geometrical flexibility to the deterministic methods which were lacking previously but are now comparable to the stochastic Monte Carlo methods. After its appearance in the late fifties, the FEM has been finding its applications in almost all branches of science and engineering. The general procedure in the FEM is to subdivide the region of interest into a finite number of sub-regions called the finite elements. Apart from its geometrical flexibility, the FEM is particularly advantageous because it gives the angular flux everywhere in the system.

The finite element method is sometimes referred to as finite element analysis. The solution approach of PDE is based either on eliminating the differential equation completely as in the case of steady state problem or rendering the PDE into an approximating system of ordinary differential equations which are solved using standard techniques such as Euler or Runge-Kutta method. It is a good choice for solving PDE

over complex domains. It is an approximate method for solving PDE by replacing continuous function by piecewise approximations defined on polygons.

In FEM, the domains of the phase space are partitioned or discretized into sub-regions which are called elements or cells. In 3D, typical elements are bricks, triangular prisms and tetrahedrons. In 2D, the elements are usually triangular or quadrilateral in shape. A one dimensional (1D) interval is divided into sub-intervals. Typically, the boundaries of the spatial elements are located near the surfaces of different materials and one can assume the material properties to be the same within an element (Chai et al, 2004). The FEM discretization is applied to a variational form (weak form) of the original equation (Johnson, 1987). The variational form is achieved by multiplying the original equation by a test function and integrating over the whole phase space domain. When applying the Green's formula, the boundary conditions can be appended in the variational form. When using any numerical approach in finding the solution, one has to ensure that the problem has a solution and it is unique. The boundedness and coercivity conditions also result in an estimate for the error of the FEM which is sometimes known as the Cea's estimate (Dautray et al, 1993).

The principal advantage of FEM is its speed and flexibility. In addition it can produce photon density everywhere and as well as photon flux on the boundary. The only disadvantage is that there is no means of deriving individual photon histories.

The spatial configuration of any system is described by its degrees of freedom (DOF). The DOF is also called generalized coordinates. If the DOF is finite, the model is called discrete and continuous otherwise. Since FEM is a discretisation method, the number of DOF is necessarily finite. The basic steps of FEM are discussed in more generality in

Figure 2.5. Although this diagram oversimplifies the way FEM is actually used, it serves to illustrate the terminology. The three key simulation steps are idealization, discretisation and solution; each step has its source of error. Considering the reverse processes, continuification and realization will not be considered under this study now, however it can be considered for another study area in solving a physical system under modelling aspects.

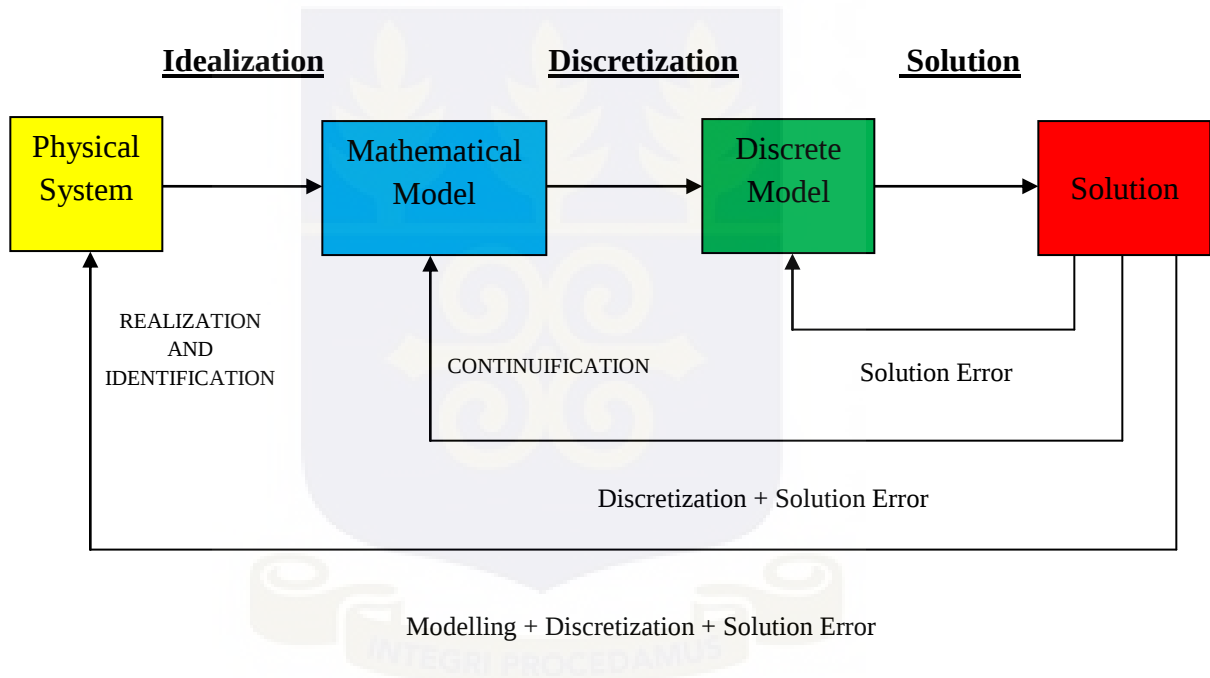


Figure 2.5: A simplified schematic diagram of the physical simulation process showing FEM modeling terminologies

Many researchers have preferred the use of FEM as it offers advantages in speed and flexibility in solving complex geometries and heterogeneous tissues (Arridge et al, 1997). The FEM is a numerical analysis technique used for obtaining solution to a wide variety of continuum problems. The basic premise of FEM is that a solution region can be

analytically modeled or approximated by replacing it with an assemblage of discrete elements. The finite discretization procedures reduce the problem to a finite number of unknown field variables in terms of assumed approximation functions within each element. The approximation functions sometimes called interpolation functions are defined in terms of the field variables at specified points called nodes or nodal points. The nodes usually lie on the boundaries where adjacent elements are connected.

In the FEM, the domain of interest is replaced by a finite number of unknown specified variables in terms of so called finite elements, such that their assemblage represents the same domain with the same properties in terms of finite number of unknowns. Within each element, nodal field variables are used to determine the approximating functions. In other words, a continuous physical problem with an infinite number of degrees of freedom (DOF) is transformed into a discretized finite element problem with a finite number of unknown nodal parameters. For a linear problem the unknowns correspond to a system of linear algebraic equations that are straightforward to solve and to determine the nodal values (Jin, 2002). Finally, the unknown fields throughout the finite elements are determined from these nodal values.

2.20 Photon dose deposition mechanisms

The dose deposition in tissue from photon beams is a two step process (AAPM Report 85, 2004).

- (1) The TERMA step: the photons interact in the medium and impart their energy to charged particles

- (2) The dose deposition step: charged particles, launched by the interacting photons, deposit their kinetic energy along their tracks

The TERMA is an acronym for Total Energy Released to Matter and it sometimes referred to as the initial photon interactions step. In the therapeutic range of photon beam energies and tissues constituting the human body the prevailing types of photon interactions, resulting in deposition of their energy in the medium, are the following: Compton effect, pair production and photoelectric absorption. The probability of Compton interaction dominates (>80%) in water-like media, but decreases for high-Z materials. Pair production becomes relevant for higher beam energies. The contribution from photoelectric absorption is negligible in water-like media, although it becomes greater in the high-Z materials (eg: prostheses or teeth implants). The probabilities of these interactions per unit distance are characterized with linear attenuation coefficients and their sum μ represents the probability of the photon removal from the beam. The attenuation coefficients are dependent both on the photon properties (energy) and tissue characteristics (density and atomic composition) which is given by the relation as

$$\mu_t(E, \rho, A, Z) = \mu_c(E, \rho, A, Z) + \mu_{pp}(E, \rho, A, Z) + \mu_{pe}(E, \rho, A, Z)$$

where:

μ_t - total linear attenuation coefficient, E - photon energy, ρ – density, A - atomic number
 Z - atomic number of element, μ_c , μ_{pp} , μ_{pe} - linear attenuation coefficient for Compton effect, pair production and photoelectric absorption respectively

2.20.1 The dose deposition step:

Due to the finite range of the charged particles released in the photon interactions, the energy absorption occurs at some distance around the interaction point. The recoil charged particles are launched with a spectrum of kinetic energies and initial directions. The multiple scatter interactions result in energy loss and deflection from the initial direction.

They dissipate their energy either locally, in multiple quasi-continuous Coulomb collisions with atomic nuclei or orbital electrons or in occasional radiative events, in which the electron is deflected from its original path and part of its energy is emitted in the form of a *bremsstrahlung* photon that carries it away from the charged particle track

2.21 Cancer Staging and Grouping.

Since the 1930s, gynaecologic oncologists have strived for a common language to facilitate making diagnoses and planning treatment for their patients. The aim was, and still is, to reach a uniform or unified terminology that is able to provide appropriate prognosis to the patients and to enhance the exchange of information among health professionals.

The first rules for classification and staging of female genital cancers adopted by the International Federation of Gynaecology and Obstetrics (FIGO) in 1958 (Creasman W. T, 2001).

Staging is a way of describing a cancer in terms of its location, where it has spread, whether it is affecting the functions of other organs in the body. There are two systems of

staging most types of cervical cancer. These are the International Federation of Gynaecology and Obstetrics (FIGO) and American Joint Committee on Cancer (AJCC).

The two systems are very similar because they both classify cervical cancer on the basis of three main factors. The factors are (i) the extent of the tumour (**T**) (ii) whether the cancer has spread to the lymph nodes (**N**) and (iii) whether the cancer has metastasized or spread to other distant sites (**M**). There are different stage descriptions for the cancer types. One most important tool the oncologist use to describe the stage of cancer is the **TNM** system. The **TNM** is an abbreviation for tumour (**T**), node (**N**) and metastasis (**M**). This system classifies the disease in stages from 0 to IV. It is based on clinical staging rather than surgical staging. This means that the extent of the disease is evaluated by the oncologist's physical examination and a few other tests that are done in some cases such as cystoscopy and protoscopy.

Using the **TNM** system, “**T**” plus a letter or number ranging from 0 to 4 is used to describe the size and location of the tumour. However, in some stages they are further divided into smaller groups that help to describe the tumour in more details. The following examples explain how the stages of the tumour are applied.

Lymph node spread (N):

N0: no spread to the nearby lymph node.

NI: the cancer has spread to the nearby lymph nodes.

Distant spread (M):

M0: the cancer has not spread to distant lymph nodes, organs or tissues.

MI: the cancer has spread to distant organs like the lungs or liver, to lymph nodes in the chest or neck

Table 2.2: Stages in cancer development

Cancer stage	Description
I	the cancer cells are only found on the surface layer of the cervix that is the layer of the cells lining the cervix without growing into the deeper tissues.
IA	there is very small amount of cancer which can be seen under a microscope.
II	the cancer has grown beyond the cervix and uterus but has not spread to the walls of the pelvis or to the lower part of the vagina.
IIA	The cancer has not spread into the tissues next to the cervix called parametria
IIA1	The cancer can be seen but it is not larger than 4 cm .
IIA2	The cancer can be seen and it is larger than 4 cm
IIB	The cancer has spread into the tissues next to the cervix (the parametria).
III	The cancer has spread to the lower part of the vagina or to the walls of the pelvis. The cancer may be blocking the ureters (tubes that carry urine from the kidney to the bladder).
IIIA	The cancer has spread to the lower third of the vagina but not to the walls of the pelvis.
IIIB	the cancer has grown into the walls of the pelvis and it blocking either one or both the ureters (this is called hydronephrosis)
IV	The cancer has spread to the bladder or rectum.

2.21.1 Stage Grouping

Combining all the information with regard to the tumour stage (**T**), lymph node (**N**) any cancer spread (**M**) assigned to the stage of the disease is called stage grouping.

Table 2.3: Tumour stage Grouping

Stage of cancer	Grouping	Description
I	TI,N0,M0	Cancer has grown into the cervix but it is not growing outside the uterus. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IA	TIA,N0,M0	This is the earliest form of stage I. There is very small amount of cancer and can be seen only under microscope. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IAI	TIAI,N0,M0	The cancer is less than 3mm deep but less than 7mm wide. The cancer has not spread to the lymph nodes (N0) or to distant sites (M0).
IB	TIB,N0,M0	This stage includes stages I cancers that can be seen without a microscope as well as cancers that can only be seen with a microscope. These cancers have not spread to nearby lymph nodes (N0) or to distant sites (M0).
II	T2,N0,M0	In this stage the cancer has grown beyond the cervix and uterus but has not spread to the nearby lymph nodes (N0) nor to the distant sites (M0).
IIA	T2A,N0,M0	the cancer has not spread to the tissues next to the cervix(called parametria). The cancer may have grown into the upper part of the vagina. It has not spread to nearby lymph nodes (N0) nor to distant sites (M0).
IIAI	T2AI,N0,M0	The cancer can be seen but it is not larger than 4cm. It has not spread to nearby lymph nodes (N0) nor to distant sites (M0)
IIB	T2B,N0,M0	The cancer has spread into the tissues next to the cervix (parametria) It has not spread to nearby lymph nodes (N0) nor

		to the distant sites (M0).
III	T3,N0,M0	The cancer has spread to the lower part of the vagina or to the walls of the pelvis. The cancer may be blocking the ureters. It has not spread to nearby lymph nodes (N0) nor to distant sites (M0).
IIIA	T3A,N0,M0	The cancer has spread to the lower third of the vagina but not to the walls of the pelvis. The cancer has not spread to the nearby lymph nodes (N0) nor to the distant sites (M0)
IIIB	T3B,N0,M0	The cancer has grown into the walls of the pelvis and has blocked one of the ureters but has not spread to lymph nodes (N0) nor to the distant sites (M0)
IVA	T4A,N0,M0	The cancer has spread to the bladder or rectum which are organs close to the cervix (T4). It has not spread to nearby lymph nodes (N0) nor distant sites (M0).
IVB	AnyT,anyN,MI	The cancer has spread to distant organs beyond the pelvic area such as the lungs or liver.

In addition to identifying the type and stage of the cancer of the cervix, the tumour's grade should also be determined. The tumour grade is based on how the tumour cells appear under microscope. If they look like normal tissue, the cancer is called a low grade tumour. If cells do not look like normal cells the cancer is classified as a high grade tumour. Knowing the grade of the tumour is important in determining whether treatment is needed after surgery.

CHAPTER 3

MATERIALS AND METHODS

This section describes the method used in this study to model doses to the critical organs of cancer patients undergoing cervical cancer treatment. The theoretical model is based on the Boltzmann's Transport Equation (BTE) for photons in biological tissues. The medium is assumed to be heterogeneous and the finite element method is used in this case to solve the BTE in order to account for the complex geometries and angular distribution of the photons. Data from literature and results from treatment planning system (TPS) of the Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana were used to compare results obtained by the method.

3.1 Theoretical Modeling of Doses to the Critical Organs

3.1.1 Governing Equation

The model described in this section is based on the solution to the Boltzmann Transport Equation (BTE) using the finite element method. The BTE can be rewritten and explained in terms of the following;

$$\left[\begin{array}{c} \text{the net number} \\ \text{of particles} \\ \text{entering} \\ \text{volume element} \end{array} \right] = \left[\begin{array}{c} \text{particles} \\ \text{source} \end{array} \right] - \left[\begin{array}{c} \text{flux of} \\ \text{particles} \\ \text{along} \\ \text{direction } \Omega \end{array} \right] - \left[\begin{array}{c} \text{scattering and} \\ \text{absorption} \\ \text{within the} \\ \text{phase element} \end{array} \right] + \left[\begin{array}{c} \text{particles at} \\ \text{position } r \text{ being} \\ \text{scattered in all} \\ \text{directions } \Omega' \\ \text{into } \Omega \end{array} \right]$$

(3.1)

The balanced Boltzmann integro-differential equation for particle j can be written mathematically as;

$$\int_{\Delta v} \left(\frac{1}{v_j} \frac{\partial \Phi_j}{\partial t} + \Omega \cdot \nabla \Phi_j + \sigma_j \Phi_j - \iint_{1 \text{ A}} \sum_{j=1}^3 \sigma_{j \rightarrow j} \Phi_j dE' d\Omega' - S_j \right) dr dE d\Omega dt = 0 \quad (3.2)$$

Thus;

$$\frac{1}{v_j} \frac{\partial \Phi_j}{\partial t} + \Omega \cdot \nabla \Phi_j + \sigma_j \Phi_j - \iint_{1 \text{ A}} \sum_{j=1}^3 \sigma_{j \rightarrow j} \Phi_j dE' d\Omega' - S_j = 0 \quad (3.3)$$

And

$$\frac{1}{v_j} \frac{\partial \Phi_j}{\partial t} = S_j - \Omega \cdot \nabla \Phi_j - \sigma_j \Phi_j + \iint_{1 \text{ A}} \sum_{j=1}^3 \sigma_{j \rightarrow j} \Phi_j dE' d\Omega' \quad (3.4)$$

Where, S_j indicates the source term, Φ_j is the photon flux distribution, E_j is the energy and Ω is the angular flux, v_j is the particle velocity, and σ_j is the interaction coefficient. $\sigma_{j \rightarrow j}$ is a phase function given by:

$$\sigma_{j \rightarrow j} = f(r, E, E', \Omega, \Omega') = \frac{\partial^2 \sigma}{\partial E \partial \Omega}(r, E, E', \Omega, \Omega') \quad (3.5)$$

3.1.2 Source term

The source geometry is represented by the Manchester system using the Fletcher-Suit Delcos applicator as shown in Figure 3.1. In Ghana, Cs-137 low dose rate (LDR) sources are used for gynaecological disorders. The Cs-137 sources are made up of spherical pellets arranged in a stainless steel encapsulation. Secondary arrangements are made in a stainless steel tube similar to the Amersham “J-Type” tube. The source arrangement is shown in Figure 3.2.

In order to relate the source strength to the specific activity of the source, the spherical sources are assumed to be multiple isotropic point sources distributed over the surface of a cylinder in a heterogeneous medium. The source to the targets is assumed to be in plane geometry.

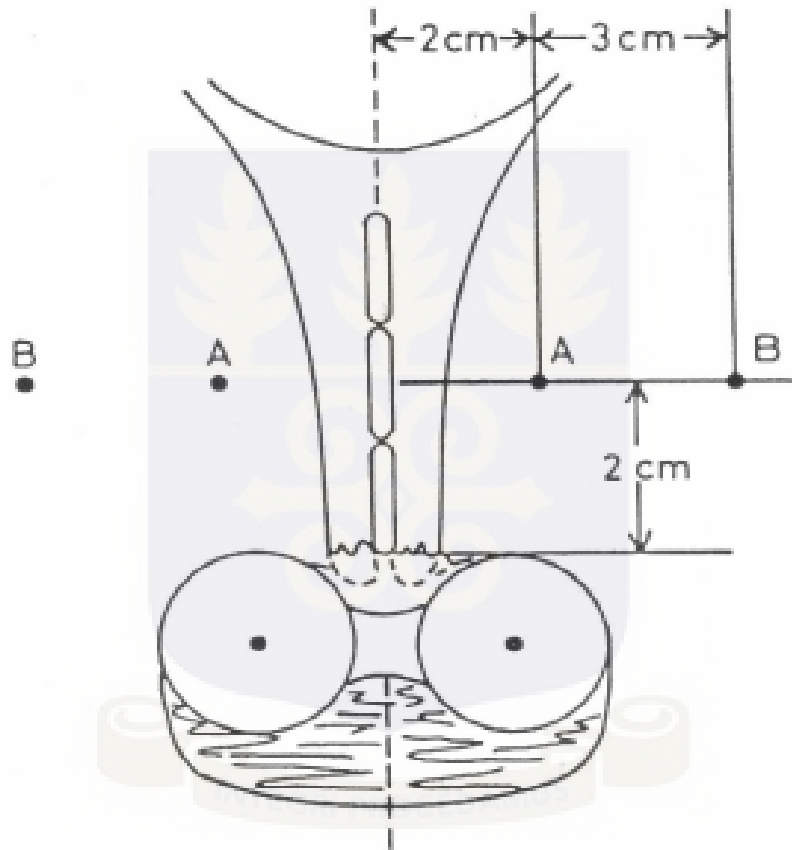


Figure 3.1: The Manchester system showing the reference points A, B and geometrical arrangement of sources in the tandem and ovoids.

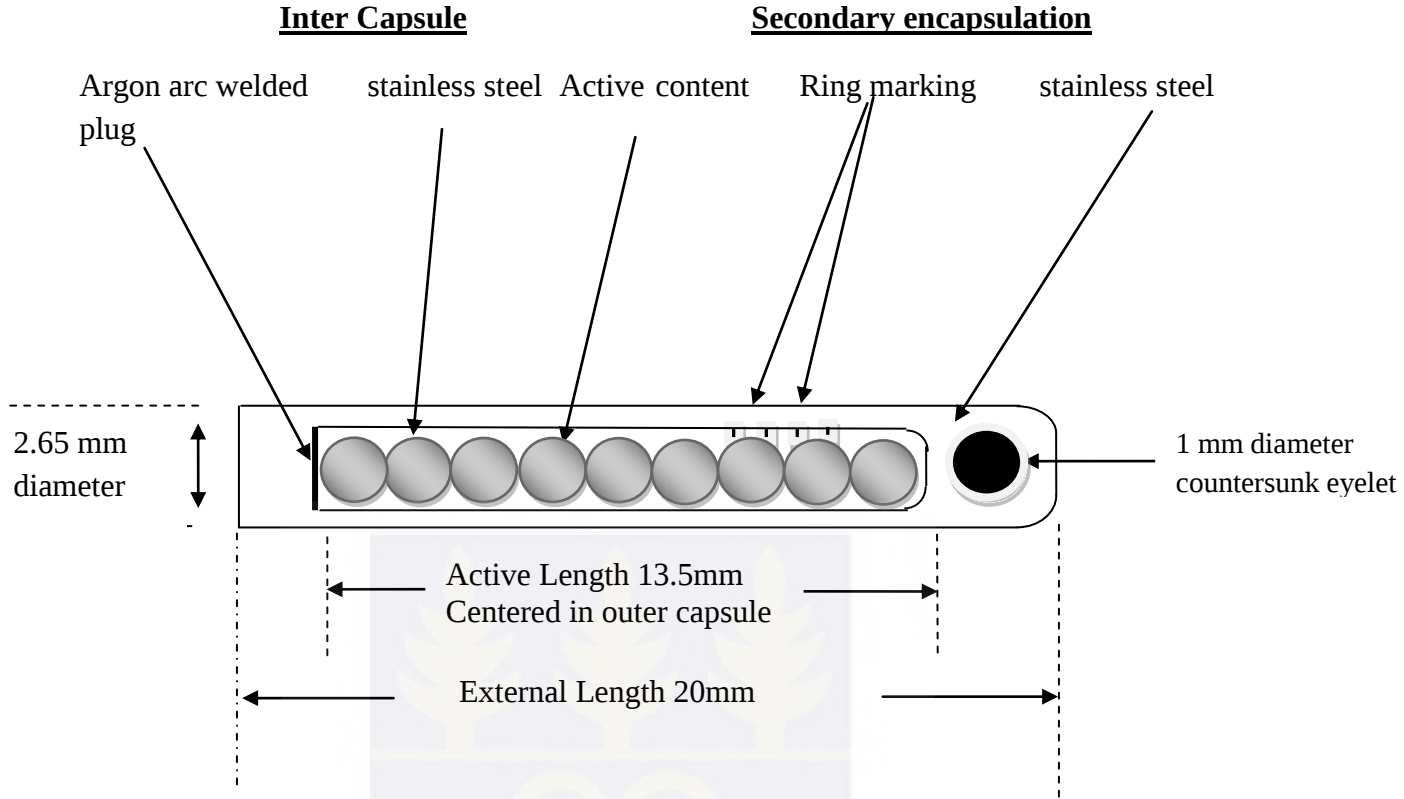


Figure 3.2: A Cs-137 LDR afterloading unit with tube arrangements similar to an Amersham “J-Type” tube (Activity: Up to 1480 MBq (40 Ci) per pellet).

The total source strength, $S(r)$, representing the activity injected into a solid angle in a unit volume per unit time is given by:

$$S(r) = \int \int_{4\pi E} S(r, \Omega, E) dE d\Omega \quad (3.6)$$

Where, $S(r, \Omega, E, t)$ is the source strength for a discrete point source, which indicates the number of photons emitted per unit time; per unit solid angle in the direction, Ω ; per unit energy interval at a location specified by the position vector, r .

Photon flux from the sources are formed by two components, namely the primary uncollided flux and the secondary scattered flux. The photons emitted by the seed form the uncollided flux and this does not include the characteristic radiation emission induced by photoelectric absorption. The flux distribution around the integrated source is as shown in Figure 3.3.

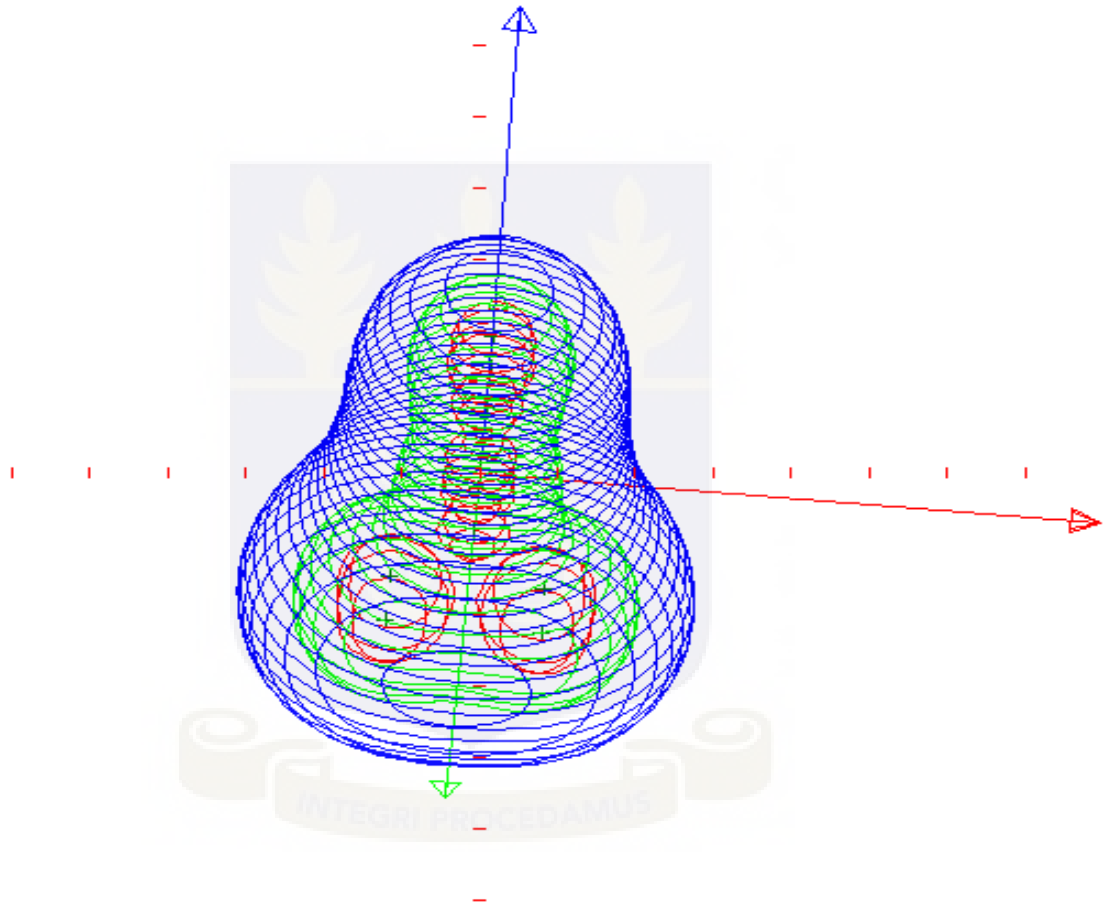


Figure 3.3: Non-homogeneous photon flux distribution around a Cs-137 source in sagittal plane

The uncollided flux is computed by taking the product of the total attenuation of each source and summing the contribution from all the sources. In this model, the source is taken as a collection of point sources. The angular flux induced by the point sources at a

point of interest, r , is subjected to attenuation along the photon path. If the angular flux is integrated over the solid angle, this provides the primary flux, $\Phi_p(r, \Omega, E)$ with the source term, S_0 , is given by

$$S_0 = 4\pi r^2 \Phi_p(r, \Omega, E) \exp \int_0^r \mu_t(r, \Omega, E) dr$$

And the primary flux is also given as follows

$$\Phi_p(r, E, \Omega) = \frac{S_0}{4\pi r^2} \exp\left(-\int_0^r \mu_t(r, \Omega, E) dr\right) \quad (3.7)$$

The scattered photon flux distribution is also given by:

$$\Phi_s(r, E, \Omega) = \int_{4\pi} \int_E^\infty \mu_s(r, E' \rightarrow E, \Omega' \rightarrow \Omega) \Phi(r, E', \Omega') d\Omega' dE' \quad (3.8)$$

Where, μ_t is the total attenuation coefficient of the tissues between the source point and the point of interest per unit solid angle per unit energy, E ; μ_s is the scattered photon attenuation coefficient; r is the spatial coordinate boundary for target boundary and photon source. $\mu_s(r, E' \rightarrow E, \Omega' \rightarrow \Omega)$ is the scattering coefficient for both coherent and incoherent scattering.

3.1.3 Target geometry

The targets are the rectum and the bladder, which can be represented by a slab phantom with specific distances from the source point depending on the patient's topography as shown in Figure 3.4. The targets represent the organs at risk (OAR), where there is the need to limit doses to avoid complications during the treatment. The thickness of the

OAR and the specific distances between the source point and the targets depends on the patient's size and weight.

The target geometry can be represented by a hollow cylindrical surface matrix. In a cylindrical coordinate system, the flux distribution over the surface geometry is given by:

$$\Phi = \frac{S_o}{4\pi} \int_0^H \int_0^{2\pi} \frac{dS}{r^2} \quad (3.9a)$$

or

$$\Phi = \frac{S_o}{4\pi} \int_0^H \int_0^{2\pi} \frac{Rd\phi dz}{r^2} \quad (3.9b)$$

where, $dS = Rd\phi dz$, and R is the radius of the cylinder and H is the height.

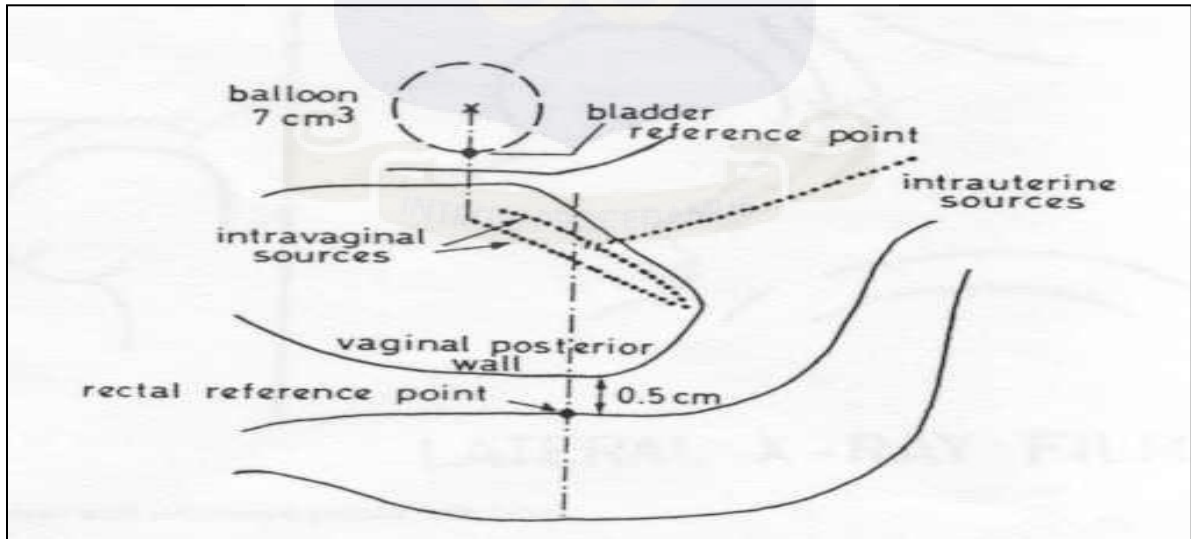


Figure. 3.4: Anatomical structure of the cervix showing the target points

3.1.4 The Photon Transport Equation

The photon transport equation is derived by considering energy conservation in a small volume and is given by the following 2D time dependent case for photons as

$$\begin{aligned} \frac{1}{c} \frac{\partial \Phi_E(r, \Omega, t)}{\partial t} = S_E(r, \Omega, t) - \Omega \cdot \nabla \Phi_E(r, \Omega, t) - \mu_t \Phi_E(r, \Omega, t) \\ + \mu_s \int_0^{2\pi} f(\Omega, \Omega') \Phi_E(r, \Omega', t) d\Omega' \end{aligned} \quad (3.10)$$

Where, r is a position vector, c is the velocity of light and Ω is a unit vector in the direction of photon propagation. $\Phi_E(r, \Omega, t)$ is the energy flux given by $\Phi_E(r, \Omega, t) = \int \Phi(r, \Omega, E, t) dE$. The source term $S_E(r, \Omega, t)$ is given by $S_E(r, \Omega, t) = \int S(r, \Omega, E, t) dE$ and represents the activity injected into a solid angle centered on Ω in a unit volume at r . The phase function $f(\Omega, \Omega')$ describes the probability that during any scattering event, a photon with direction Ω' is scattered into the direction, Ω . Where, $\mu_t = \mu_a + \mu_s$, is the total attenuation co-efficient in tissue.

3.1.5 Finite Element Model(FEM)

The Finite Element Method (FEM) is a numerical technique for solving problems which are described by partial differential equations or can be formulated as a functional minimization. It is well-suited for approximating continuum solutions to boundary-value problems with complex geometries and composed of inhomogeneous materials. In the FEM, the domain of interest is replaced by a finite number of unknowns specified in

terms of so called finite elements, such that their assemblage represents the same domain with the same properties in terms of finite number of unknowns. Within each element nodal field variables are used to determine the approximating functions. In other words, a continuous physical problem with an infinite number of degrees of freedom (DOF) is transformed into a discretized finite element problem with a finite number of unknown nodal parameters. For a linear problem the unknowns correspond to a system of linear algebraic equations that are straight forward to solve and to determine the nodal values. Finally, the unknown fields throughout the finite elements are determined from these nodal values

In the finite element method (FEM) for the Boltzmann equation, the angular flux is expressed in a finite-dimensional space X^h

$$\Phi(r, \Omega) \approx \Phi^h(r, \Omega) = \sum_{k=1}^K \Phi_k \Psi_k(r, \Omega) \quad (3.11)$$

Where, ($\Psi_k ; k=1, \dots, K$) are a set of basis functions for X^h . When applied to the first-order form of the Boltzmann equation with all the boundary conditions is natural and the resultant discretized system is again expressed as a matrix relation;

$$B\Phi = C \quad (3.12)$$

where, B represents element stiffness matrix of order $MN \times MN$ and C is the element source vector of order $MN \times 1$.

The basis function can be developed separately for the spatial and angular terms,

$$\Psi_k(r, \Omega) = u_i(r)\theta_j(\Omega) \quad (3.13)$$

This simplifies the derivation of the matrix elements B_{kk} . The spatial basis is usually taken as a piecewise polynomial just as the angular basis.

3.1.5.1 Time dependent case

Here, the finite element method is applied to solve the time dependent transport equation.

From the general photon transport equation

$$\frac{1}{c} \frac{d\Phi}{dt} + \Omega \nabla \Phi(r, \Omega, t) + \mu_t(r) \Phi(r, \Omega, t) = \int_{4\pi} d\Omega' \mu_s(r, \Omega \rightarrow \Omega') \Phi(r, \Omega', t) + S(r, \Omega, t) \quad (3.14)$$

Subject to the initial conditions

$$\Phi(r, \Omega, 0) = \Phi_o(r, \Omega,) \quad (3.15)$$

and boundary conditions

$$\Phi(r, \Omega, t) = \Phi_s(r, \Omega, t) \quad (3.16)$$

Defining the space, H , and choosing an arbitrary element $\chi \in H$ and multiplying equation (3.14) and integrate by parts over the phase space, ν , the following equation is obtained;

$$\left\langle \frac{1}{c} \frac{d\Phi}{dt}, \chi \right\rangle - \langle \Phi, \Omega \nabla \chi \rangle + \langle k\Phi, \chi \rangle + \langle \Phi, \chi \rangle_+ = \langle S, \chi \rangle + \langle \Phi_s, \chi \rangle \quad (3.17)$$

where, the inner product $\langle \Phi, \chi \rangle$ is defined as earlier.

For the time-independent case, defining a finite dimensional subspace $\delta^h \subset H$ and expanding $\Phi_n(r, \Omega)$ in terms of the following basis function for δ^h

$$\Phi_n(r, \Omega) = \sum_{j=1}^N \Phi_j \Psi_j^n(r, \Omega) \quad (3.18)$$

A similar procedure is followed for the time dependent case except that the expansion coefficients are time dependent:

$$\Phi_n(r, \Omega, t) = \sum_{j=1}^N \Phi_j(t) \Psi_j^n(r, \Omega) \quad (3.19)$$

Substitution of this expansion into equation (3.14) and requiring equation(3.14) to hold for all

$$\Psi_i^n(r, \Omega), i= 1,2,3,...,N$$

One obtains the matrix differential equation

$$\frac{1}{c} \underline{\underline{P}} \dot{\underline{\Phi}} + \underline{\underline{A}} \underline{\Phi} = \underline{\underline{S}} \quad (3.20)$$

$$\text{where } \underline{\Phi} = \begin{pmatrix} \Phi_1(t) \\ \Phi_2(t) \\ \vdots \\ \Phi_N(t) \end{pmatrix}; \quad \dot{\underline{\Phi}} = \begin{pmatrix} \dot{\Phi}_1(t) \\ \dot{\Phi}_2(t) \\ \vdots \\ \dot{\Phi}_N(t) \end{pmatrix} \text{ and } \underline{S} = \begin{pmatrix} S_1(t) \\ S_2(t) \\ \vdots \\ S_N(t) \end{pmatrix}$$

Also

$$\underline{\underline{P}} = \{P_{ij}\}; \text{ but } P_{ij} = (\Psi_j^n, \Psi_i^n)$$

and

$$\underline{\underline{A}} = \{A_{i,j}\}; \quad A_{ij} = (\Psi_j^n, \Psi_i^n)$$

writing the terms explicitly one obtains

$$A_{i,j} = T_{i,j} + B_{i,j} + k_{i,j}$$

where,

$$T_{i,j} = - \iint_{\nu} dr d\Omega \psi_j^n(r, \Omega) \Omega \cdot \nabla \psi_i^n(r, \Omega)$$

$$B_{i,j} = \int_{\Gamma^+} dr d\Omega m' \psi_i^n(r, \Omega) \psi_j^n(r, \Omega)$$

$$k_{i,j} = \iint_{\nu} dr d\Omega \sum_t (r) \psi_i^n(r, \Omega) \psi_j^n(r, \Omega) - \iint_{\nu} dr d\Omega \psi_i^n(r, \Omega) \int_{4\pi} d\Omega \sum_s (r, \Omega, \rightarrow \Omega') \psi(r, \Omega')$$

$$S_i = \iint_V dr d\Omega S(r, \Omega) \psi_j^n(r, \Omega) - \int_{\Gamma^-} dr d\Omega m' \Phi_o(r, \Omega) \psi_i^n(r, \Omega)$$

The time dependent equations result in a system of ordinary differential equations. An efficient method to solve equation (3.20) is the Crank-Nicholson scheme which approximates the time derivative with a forward difference and other time-dependent terms are averaged over the present time and the incremented time:

$$\dot{\Phi} \approx \frac{\Phi(t^{m+1}) - \Phi(t^m)}{t^{m+1} - t^m} \text{ and } S \approx \frac{S(t^{m+1}) + S(t^m)}{2}$$

Using the notation, the matrix equation (3.20) becomes

$$\frac{1}{c} P \frac{\Phi^{(m+1)} - \Phi^m}{\Delta t} + A \frac{\Phi^{(m+1)} + \Phi^m}{2} = \frac{S^{(m+1)} + S^m}{2} \quad (3.21)$$

Since equation (3.21) gives Φ^o then clearly, it can be solved for $\Phi^{(m+1)}$ in terms of Φ^m or

$$\left\langle P + \frac{\nu \Delta t}{2} A \right\rangle \Phi^{(m+1)} = \left\langle P - \frac{\nu \Delta t}{2} A \right\rangle \Phi^{(m)} + \frac{S^{(m+1)} + S^{(m)}}{2} \nu \Delta t \quad (3.22)$$

For which $\Phi^{(m+1)}$ can be solved for in terms of $\Phi^{(m)}$ and the known source term S.

Thus with $\Phi^{(o)}$ known $\Phi^{(1)}, \Phi^{(2)}, \dots, \Phi^{(m)}$, can be calculated using equation (3.21).

This is especially efficient if the LU decomposition (Cholesky method) is used to solve equation (3.20)

3.1.5.2 Time-independent case in plane geometry

In plane geometry, the general time dependent transport equation (3.8) becomes

$$\frac{1}{c} \frac{d\Phi}{dt} + \mu \frac{d\Phi}{dx} + \sum_l (x) \Phi(x, \mu, t) = \sum_{l=0}^l \frac{2l+1}{2} b_l(x) P_e(\mu) \int_{-1}^1 d\mu P_e(\mu) \Phi(x, \mu, t) + S(x, \mu, t)$$

(3.23) subject to the initial conditions

$$\Phi(x, \mu, 0) = \Phi_o(x, \mu) \quad (3.24)$$

and the boundary conditions

$$\begin{aligned} \Phi(0, \mu, t) &= \Phi_o(0, \mu, t) \\ \Phi(1, \mu, t) &= \Phi_o(1, \mu, t) \end{aligned} \quad (3.25)$$

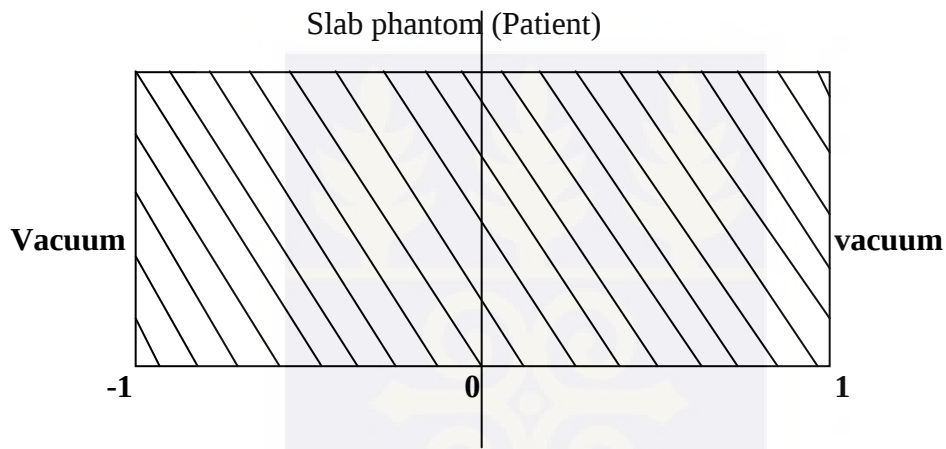


Figure 3.5: Diagram of a physical domain (patient) represented by a slab phantom in plane geometry

Applying the finite element approximation to the equivalent integral law results in the following system of ordinary differential equations (ODE's)

$$\frac{1}{c} \underline{P} \dot{\underline{\Phi}} + \underline{A} \underline{\Phi}(t) = \underline{S}(t) \quad (3.26)$$

The specific matrix elements are

$$A_{i,j} = T_{i,j} + k_{i,j} + B_{i,j} \quad (3.27)$$

$$P_{i,j} = \int_0^1 dx \int_{-1}^1 d\mu \psi_i^n(x, \mu) \psi_j^n(x, \mu) \quad (3.28)$$

The source vector is

$$S_i(t) = \int_0^1 d\mu \int_{-1}^1 d\mu S(x, \mu, t) \psi_i^n(x, \mu) + \int_0^1 d\mu \mu \Phi_0(0, \mu, t) \psi_i^n(0, \mu) - \int_{-1}^0 d\mu \mu \Phi_0(1, \mu, t) \psi_i^n(1, \mu) \quad (3.29)$$

3.1.5.3 Boundary Conditions for the Photon Flux

In intracavitary brachytherapy, the high energy particles are directed to planning target volume (PTV) from the source inserted into the cervix which is the domain V . The boundary of the domain V is typically assumed to be a free surface in which particles can only escape from the surface V , through the surface ∂V but cannot re-enter as shown in Figure 3.6.

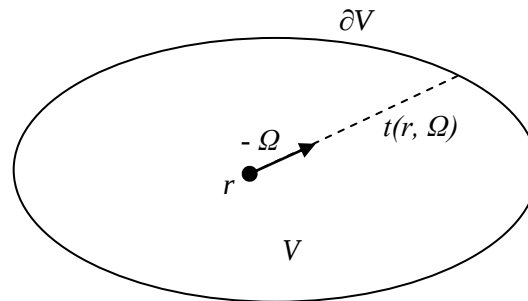


Figure 3.6: Particle trajectory from point r to the boundary ∂V along a straight line in the direction, Ω . The length of the trajectory is $t(r, \Omega)$.

The assumption is approximately valid for convex domains in which a straight line segment connecting the two points in the region, lies entirely within the region. The free surface assumption is an idealization, since particles have always some probability to return to the volume V once they leave because of scattering process (Bell and Glasstone, 1970; Duderstadt and Martin, 1979). However, the probability is negligible and it is always possible to choose the boundary to be far enough from the volume of interest so that the free surface assumption is valid (Bell and Glasstone, 1970, Duderstadt and Martin, 1979, Boman, 2007). In the following paragraph, the boundary conditions are defined for photon flux leaving the volume.

In brachytherapy, photon flux is inside the domain and enters outside to the normal organs. This photon flux can be modeled using the transport model by setting boundary conditions, which states the photon outflow at the free surface.

Let $n(r) = [n_1(r), n_2(r), n_3(r), \dots]$ be the inward unit normal vector at a point r on the boundary. The particles which fulfill the condition $n(r) \cdot \Omega > 0$ at the point r on the boundary will cross the surface in an inward direction; and the particles for which $n(r) \cdot \Omega < 0$ will cross the surface in the outward direction.

The condition $n(r) \cdot \Omega < 0$ for the outward flux gives the relation

$$n_1(r) \cos \Psi \sin \theta + n_2(r) \sin \Psi \cos \theta + n_3(r) \cos \theta < 0,$$

which is obtained by using the relation

$$\Omega = \frac{v}{u} = \cos \Psi \sin \theta; \sin \Psi \cos \theta, \cos \theta \quad (3.30)$$

where, (Ψ, θ) are standard spherical coordinates on a unit sphere $\Psi \in [0, 2\pi]$ and $\theta \in [0, \pi]$

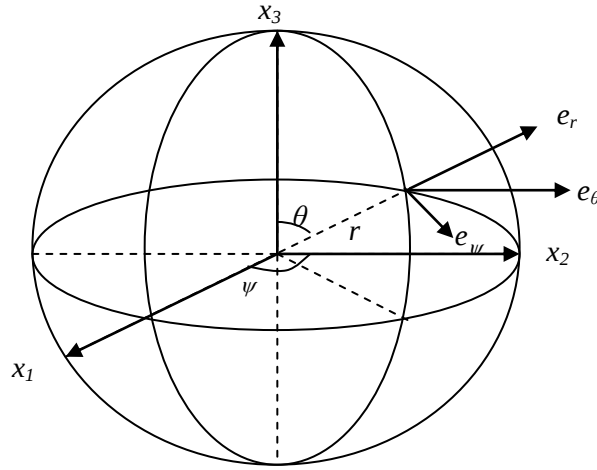


Figure 3.7: Polar coordinates (r, ψ, θ) indicating the direction of the particle in standard coordinate system $\mathbf{x} = (x_1, x_2, x_3)$ with $r = 1$

Once the outward flux is specified, it is possible to set a boundary condition for the outward flux on the boundary. The boundary condition for the outward photon angular flux is of the form

$$\Phi_o = \begin{cases} 0, & \text{for } (r, E, \Omega) \in \partial V \mid P \times I \times \xi \text{ such that } n(r) \cdot \Omega < 0 \\ \Phi_o, & \text{for } (r, E, \Omega) \in P \times I \times \xi \text{ such that } n(r) \cdot \Omega < 0 \end{cases} \quad (3.31)$$

$$\Phi_1 = \Phi_2 \text{ for } (r, E, \Omega) \in \partial V \times I \times \xi \text{ such that } n(r) \cdot \Omega < 0 \quad (3.32)$$

where, P is the patch on the surface ∂V of the domain V and Φ_o is the photon angular flux per unit area with incident on P . Thus only the outward photon angular flux on P obtains non-zero values. Elsewhere on ∂V the photon outward flux is zero. The inward flux on the particles is not constrained.

3.1.5.4 Error correction and Convergence

FEM formulation is the discretization of the original problem, the error between the exact solution and approximation is bounded by

$$\|\Phi - \Phi^h\| \leq Ch^{\min(m-1, p)} \quad (3.33)$$

where $\|\cdot\|$ denotes the Euclidean norm, h is the maximum mesh size, p is the degree of basis function and m is a measure of singularity of the problem.

In order to reduce the error, three versions of FEM are adopted, which corresponds to shortening the element size by h -adaptivity, increasing the degree of basis functions by p -adaptivity and swapping the edge and facet of the element by r -adaptivity respectively. In theory, if the maximum mesh size is sufficiently small, then the numerical solution could converge to the exact solution (Rao, 1999).

3.1.5.5 Photon Dose Calculation

The absorbed dose distribution can be computed from the solved particle flux and describes the energy absorption in the matter. For photon interaction, the spatial distribution of electrons can be neglected and the energy dependent photon flux can be used. The dose or the energy absorbed by the tissue is therefore given by the following equation

$$D(r, E) = \int_r \int_E \Phi(r, E) \frac{\mu_{en}}{\rho}(E) \partial E \partial r \quad (3.34)$$

where, $\frac{\mu_{en}}{\rho}(E)$ is the mass-energy absorption coefficient of the material or medium.

The discretized form of equation (3.34) is given by the following:

$$D(r_i, E_j) = \sum_i^r \sum_j^N \Phi(r_i, E_j) \frac{\mu_{en}}{\rho}(E_j) E_j \quad (3.35)$$

3.2 Model implementation and Simulation

The implementation of the FEM is based on the numerical algorithm of MATLAB and runs on PC/LAPTOP with a minimum of 32MB memory. For computational speed, the application is limited to fit into physical memory.

3.2.1 Assumptions

- a. The source term is assumed to be multiple isotropic point sources arranged in a line segment and with each source limited to a point $r=r'$ in space and time, $t=t'$ for the time dependent case. The depth, d , of the point source below the mesh is chosen to be equal to the mean free path before the first scattering event. i.e.

$$d = \frac{1}{\mu_s}$$

- b. No surface reflections occur for boundaries and assume Dirichlet condition, i.e. $\phi(d\Omega) = 0$, $d\Omega$ of the domain, Ω , i.e. no surface reflections
- c. The boundary, $d\Omega$, is a polygon and the general description of the FEM allows for many other forms of the boundary conditions.

3.2.2 Mesh Generation

A mesh is a collection of nodes which are points in the domain and elements are regular shapes- subset of the domain generally tetrahedral or hexahedral and having nodes and vertices. A two-dimensional slab geometry which is equivalent to a finite line source is described. The model comprises a two-dimensional rectangular mesh formed by triangular elements. For stability reasons the generated elements are regular with no internal angles greater than 90° and have approximately constant in size. The mesh

resolution is characterized by the mesh parameter, h , which is defined as the longest side of any element τ , in the mesh

$$h = \max size(\tau_i)_i \quad (3.36)$$

$$1 < i < n$$

Where, n is the number of elements. Figure 3.8 shows a rectangular mesh having elements and nodes. In order to keep the size of elements approximately constant we have a linear increase in the number of nodes per rectangular section. A finer division of elements in the boundary is used in order to increase accuracy.

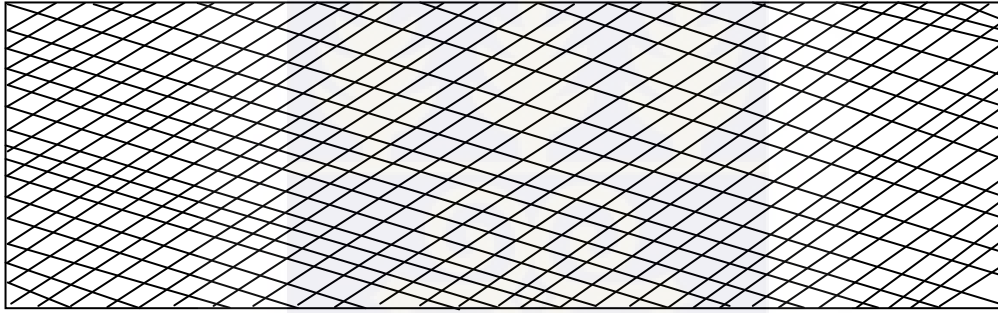


Figure 3.8: Geometry for the generation of mesh.

3.2.3 System Matrix

The construction of the system matrices is performed in two steps: first a separate set of element matrices $\mathbf{P}^e$, $\mathbf{A}^e$ of order 3×3 is formed for each element by carrying out the integrations numerically over the element domain Ω^e . Inhomogeneous properties of the tissues can be simulated by altering the element coefficients. The contributions of each element are then assembled into the system matrices $\mathbf{P}$, $\mathbf{A}$ of order $D \times D$. Note that $\mathbf{P}$, $\mathbf{A}$ are symmetric diagonal banded matrices with the semi band width W determined by the

maximal node number difference within a single element. They can be represented by matrices of order $W \times D$. As the model requires a high number of nodes it is essential to minimize W by reordering the node list prior to feeding it into the FEM processing algorithm. The source vector $\mathbf{S}$ is assembled from the element contributions $\mathbf{S}^e$.

3.2.4 Matrix solution

In the time – independent case, a simple matrix equation of the form $\mathbf{A}\Phi = \mathbf{S}$ where, $\mathbf{A}$ is a symmetric, positive definite, sparse, banded matrix. A variety of techniques exist for solving for Φ . First, $\mathbf{A}$ is reduced to the form $\mathbf{LL}^T$, where $\mathbf{L}$ is a lower triangular (banded) matrix. Then we rewrite as $\mathbf{LL}^T\Phi = \mathbf{S}$ and solve first $\mathbf{Lc} = \mathbf{S}$ (forward substitution) and then $\mathbf{L}^T\Phi = \mathbf{c}$ (backward substitution). These two procedures (i.e forward and backward substitutions) will make the computations simple. It is remarked that if all that is required is the solution for nodes near the boundary, then if these are grouped at the lower end of the vector Φ the backward substitution can be stopped after these nodes are evaluated, leading to a slight improvement in speed.

3.2.5 Time dependent case

In the time-dependent case, sparse matrix inversion is required, but in addition, a finite difference scheme is used.

The time step interval, Δt , is chosen in accordance with the node spacing, given by the mesh parameter, h , and is governed by the following equation

$$\Delta t \leq \frac{h^2 \nu}{4kc_o} \quad (3.37)$$

Where, c_o is the velocity of light in vacuum and ν is the refractive index of the tissue and

$k = \frac{c_o}{3[\mu_a(r) + (1-f)\mu_s(r)]}$. The choice of Δt is governed by the requirement that the

transport equation remains stable even for small values of t (i.e. transient behaviour). The Crank-Nicholson scheme incorporates an average of the fully explicit and fully implicit finite difference schemes. Both Crank-Nicholson scheme and the fully implicit scheme are stable for any value of time step Δt and if only the equilibrium form is required, then larger time steps could be used and approach this limit quickly. The explicit scheme is required to accommodate the early behaviour and this is only stable for the maximum value of Δt .

Application of equation (3.20) with $\theta = \frac{1}{2}$ and $S_j(t) = \Psi_j(r')\delta(t-t')$, where $\Psi_j(r')$ will have a nonzero value only when N_j is a node of the element containing the source, leading to

$$\left[\frac{1}{2}A + \frac{1}{\Delta t}M \right] \Phi_{n+1} + \left[\frac{1}{2}A - \frac{1}{\Delta t}M \right] \Phi_n = \frac{1}{\Delta t} S_n^{(\delta)} \quad (3.38)$$

where, $S_n^{(\delta)}$ is nonzero only if t' is contained in the interval (t_n, t_{n+1}) with the assumption $S_k^{(\delta)} = 0$, for all $k > 0$, and $\Phi_0 = 0$, successive solutions of Φ_n is obtained, which has the structure

$$A\Phi_{n+1} + B\Phi_n = Q_n^{(\delta)}$$

$$A\Phi_1 = Q_0^{(\delta)}$$

$$A\Phi_{k+1} = -B\Phi_k, \forall k \geq 1 \quad (3.39)$$

The matrices A and B are constant throughout the finite differencing procedure. Therefore the method requires one Cholesky decomposition for matrix A followed by another matrix multiplication applying Cholesky forward and backward decomposition per the time step.

3.2.6 Simulation using MATLAB

The photons traveling in a tissue(water) was simulated using the BTE. For a time dependent BTE, the finite element approximation in 2D is given by

$$\Phi^h(r, E, \Omega, t) = \sum \alpha_k \Psi_k(r, E, \Omega, t) \quad (3.40)$$

At the energies around several MeVs, Compton effect is the main scattering event, which slows down photons and changes them to electrons. The maximum energy of the incident photon is approximately around 10 MeV and only Compton effect can be taken into account to describe the photon interactions. The total cross section for the photons was obtained from literature (Berger et al, 2007).

The forward problem FEM simulations presented in this thesis were computed in two steps. First the smaller matrices, in which the linear system could be constructed using Kronecker tensor product, were generated using MATLAB in a normal PC (2.2 GHz Intel Core i3 with 4.0 GB memory). These matrices were then written to files in a sparse

matrix format. Then the resulted linear system was solved using portal extensible toolkit for scientific calculations (PETSc) and Krylov subspace matrix free methods. The least-squares solution algorithm without preconditioning was used from the PETSc package for solving the linear system with Krylov methods.

The first simulation was made in 2D spatial geometry in a $(-5,5) \times (0,2)$ cm² slab phantom. The incoming photon flux was located at the center of the phantom at intervals of $(-2, 2)$ cm. The number of spatial nodes was 357 and the angular domain was divided into 164 evenly distributed elements, $\theta \in (0, 2\pi)$ $N_\theta = 164$.

A MATLAB programme for the calculation of photon fluxes, photon source strength and patient doses for various tumour stages have been determined as indicated in Appendix III

3.3 Optimization of Doses to the OAR

Typically, physical or biological criteria are used in intracavitary brachytherapy treatment planning process. Here the physical criteria are considered. Similar theories can be used for biological criteria. The patient domain $V \subset R^3$ consists of a target volume T that is PTV, which includes the tumour volume and some safety margin, critical organs' region C and normal tissue's region N . Thus, the patient domain is a mutually disjoint union $V = T \cup C \cup N$. The dose $D(r)$ can be computed from the particle flux $\Phi(r, E, \Omega)$ using equation (3.34). One can assign several physical criteria for the dose. One can simply set and deduce that

$$D(r) = D_0 \quad r \in T \quad (3.41)$$

$$D(r) = 0 \quad r \notin V/T \quad (3.42)$$

where D_0 is a prescribed uniform dose in target T . The criterion in equation (3.41) is unrealistic since radiation must pass through healthy tissue to reach the tumour. That is why it is important to demand the equation (3.41) with conditions

$$D(r) \leq D_c; r \in C \quad (3.43)$$

$$D(r) \leq D_N; r \in N \quad (3.44)$$

where, D_c and D_N are the upper bounds of the dose in critical organs C and normal tissue N respectively.

Instead of condition (3.41), one can demand a feasibility condition

$$\partial_T \leq D(r) \leq D_T \quad r \in T \quad (3.45)$$

where, ∂_T and D_T are the lower and upper bounds for the dose in PTV respectively.

3.4 Experimental Validation

A very important function in brachytherapy is to obtain the correct geometric localization of the applicator in order to treat the target volume adequately. The dose distributions are totally dependent on the inverse square law effect. As a result, proper positioning of the radiation sources is very important during treatment of gynaecological malignancies. This is study of 164 patients with cervical carcinoma treated with low dose rate brachytherapy source (AMRA-Curiatron). In Appendix II, the patients characteristics with different cancer stages from stages I-IV were selected. The prescribed doses of the target volumes were in the range of 25-30Gy for each patient depending on the tumour stage. The dose reference point was placed in the target volume and normalization performed on the point to obtain the required dose distribution.

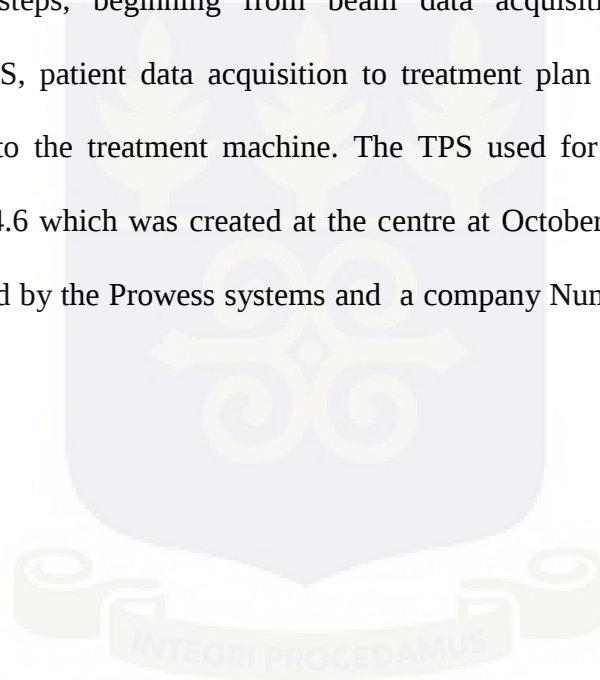
In this study, source localizations were determined from the 3D co-ordinates and orientation of each source relative to the patient anatomy. Based on the prescribed dose to tumour, the dose to reference point A and critical organs are determined using a digitizer

as shown in Appendix II. It was accomplished by at least two images (orthogonal radiographs) taken from different perspectives. In order to aid dose calculations, precise localization of the sources in three spatial dimensions (3D) and two orthogonal radiographic images are used. The dose rate distributions in relation to the tumour volume and critical structures were calculated using a Treatment Planning System (TPS) at the facility. Once the dose rate distributions and the treatment time have been accurately determined, the patient was ready for loading the sources for treatment.

Depending upon the stage of the cancer, the Oncologist determines the type of treatment modality, source configuration for the cancer patient and positions both tandem and ovoids in the cervix. Depending on the tumour stage, two orthogonal projections of radiographic films are taken using a simulator C-arm X-ray machine. The C-arm X-ray machine with model number S 06U75411 and manufactured by Siemens in Germany at July 2006 was used for this study.

The 3D source locations were input into the treatment planning computer, with the co-ordinate system being orthogonal to the x, y, and z-axis. Localization began by entering source co-ordinates on the projection image into the computer by means of digitization process. A single point in space (3D) results in two co-ordinates in each projection image (2D). The origin of the 3D co-ordinate system was taken as reference point and was chosen as a point near the centre of the applicator and as a point that can easily be identified on both projection images. After all sources have been identified, the co-ordinates of each end of a linear source on each projection image were sequentially entered into the Treatment Planning System (TPS).

Computerized TPS are used in radiotherapy to generate dose distributions with the intent to maximize tumour control and also to minimize normal tissue complications. Brachytherapy TPS is necessary to estimate the dose to the target volume and organs at risk. Patient anatomy and tumour targets are represented in 3-D models. The entire TPS process involves many steps and the medical physicist is responsible for the overall integrity of the computerized TPS to accurately and reliably produce dose distributions and associated dose calculations in radiotherapy. The entire treatment planning process involves many steps, beginning from beam data acquisition and entry into the computerized TPS, patient data acquisition to treatment plan generation and the final transfer of data to the treatment machine. The TPS used for this study was Prowess Panther version 4.6 which was created at the centre at October 2009. The digitizer was also manufactured by the Prowess systems and a company Numonics(Accu Grid model) in USA.



CHAPTER 4

RESULTS AND DISCUSSIONS

The use of radiation sources in Medical Physics is very important in diagnosis and treatment of diseased conditions. Brachytherapy has played an important role in the treatment of cervical cancer patients. Analytical and computational models of the radiative transport equation in tissues have been applied in the interpretation of procedures during treatment planning stages and in dose delivery to patients. The methods commonly applied include the Sievert Integral, Monte Carlo and AAPM (TG-43). The AAPM (TG-43) uses modular dose calculation and incorporates an anisotropy function.

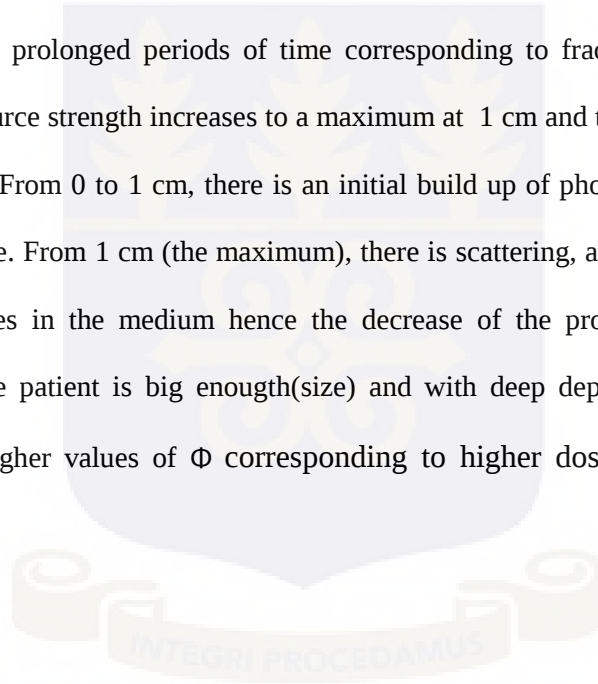
In this chapter, the results from the study are presented and discussed. The study considered the solution of the Boltzmann's Photon Transport Equation (BTE) in biological tissues using the Finite Element Method (FEM) and its application in cervical cancer treatment. The results have been compared with published data and analytical reference method as well as Monte Carlo method and the treatment planning system (TPS) of the Komfo Anokye Teaching Hospital.

4.1. General

This section discusses the source term characteristics, angular flux distribution and dose profile obtained from the study.

4.1.1. Source Term

Fig 4.1 shows the source term characteristics as a function of distance. The source was assumed to be Cs-137 spherical pellets arranged in line geometry. The source strength for the various treatment regimes corresponding to different cancer stages was determined. In the treatment of cervical cancer in brachytherapy, the same source with a specific source strength is used. The different stages of the cancer are treated by exposing the cancerous tissues to different time regimes resulting in specific photon fluxes. The photon fluxes result in specific dose distributions depending on whether the treatment is delivered over a short time for a single large dose or over prolonged periods of time corresponding to fractionated doses. Figure 4.1 shows that, the source strength increases to a maximum at 1 cm and then decreases again to zero for the next 5 cm. From 0 to 1 cm, there is an initial build up of photon particles increasing to the maximum value. From 1 cm (the maximum), there is scattering, absorption and anisotropy of the photon particles in the medium hence the decrease of the profile. In relation to patient anatomy, when the patient is big enough(size) and with deep depth tumor, it requires more photon particles(higher values of Φ corresponding to higher doses) for treatment and vice versa.



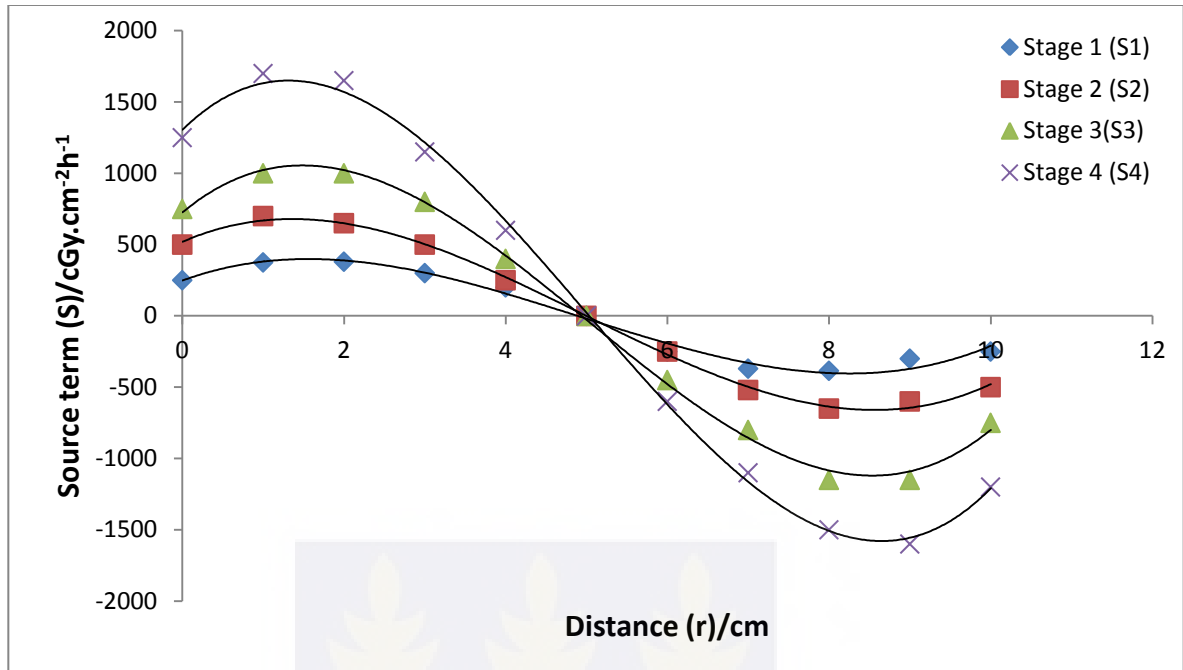


Fig 4.1: Source strength distribution as a function of distance

4.1.2. Photon Flux Distribution

The photon flux distribution as a function of distance is shown in Figure 4.2. The Figure indicates increase in the photon fluxes over a distance of 5cm and then decreases for the rest of the distance. A similar trend is observed in Figure 4.3 for the corresponding doses. In Figure 4.3 the angular distribution of the photon flux also shows an increase from $\theta = 0$ to a maximum at $\theta = \pi/2$ radians. This is followed by a decrease as one moves from $\theta = \pi/2$ to $\theta = \pi$ radians. This observation may be attributed to the interaction of the photon fluxes with the tissues, which initially results in an increase until they reach the peak, but slowly decreases when there is more scattering, anisotropy and attenuation effect.

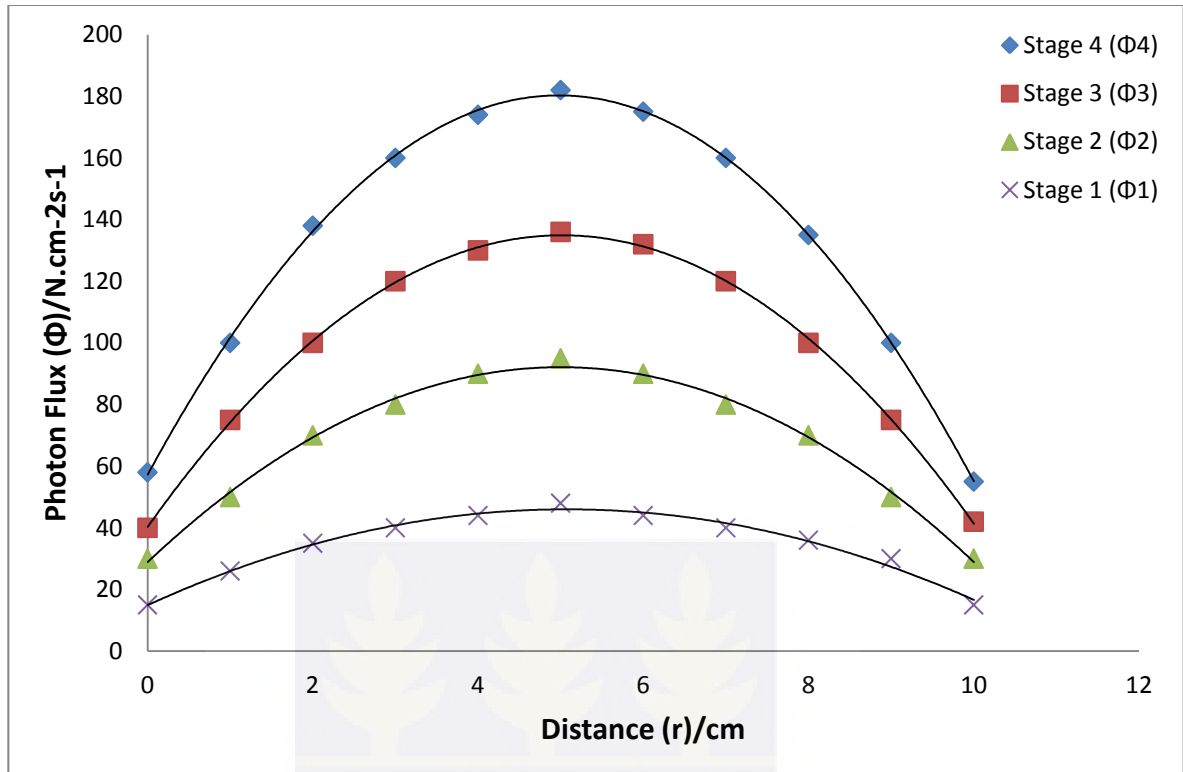


Fig 4.2: Photon Flux distribution for different cancer stages as a function of distance

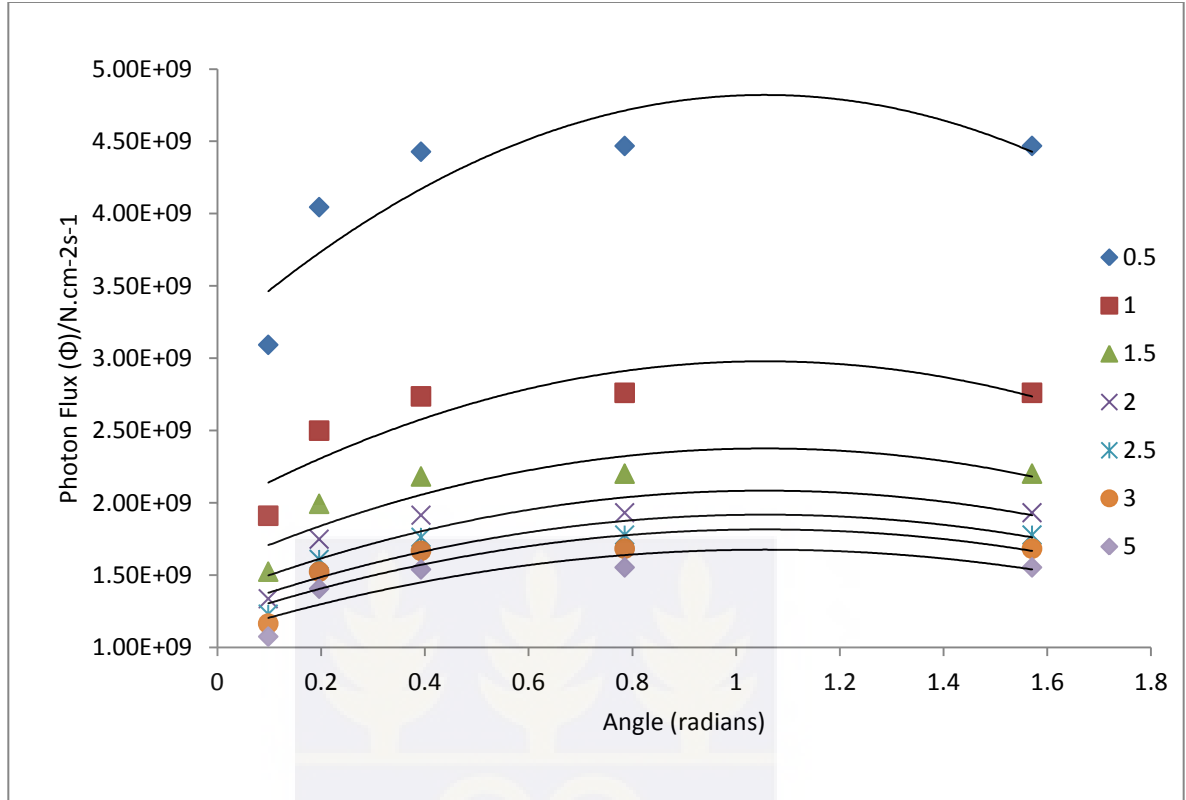


Fig 4.3: Variation of photon flux with angles

4.1.3 Error Distribution Function

The error distribution function from the solution of the FEM is shown in Figure 4.4. The error function shows a similar trend as that of the photon flux distribution in Figure 4.2. It is observed that the error increases to a maximum over a distance of 5cm and then decreases afterwards for the different values of the photon flux. This error is related to the mesh resolution and decreases as the mesh resolution increases until it converges to a certain parameter, η . For a homogeneous material, the value of $\eta \rightarrow 0$. In the application of the FEM, it is possible to overestimate the error $\|\Phi - \Phi^h\| \leq Ch^2$, where C is a constant and h represents the mesh resolution. The error can also be related to the angular distribution

of the photon flux for different mesh resolutions. Correction in the solution of the flux using Green's Function is very important in order to ensure that the uses of this method result in high degree of accuracy in addition to its speed compared to Monte Carlo method.

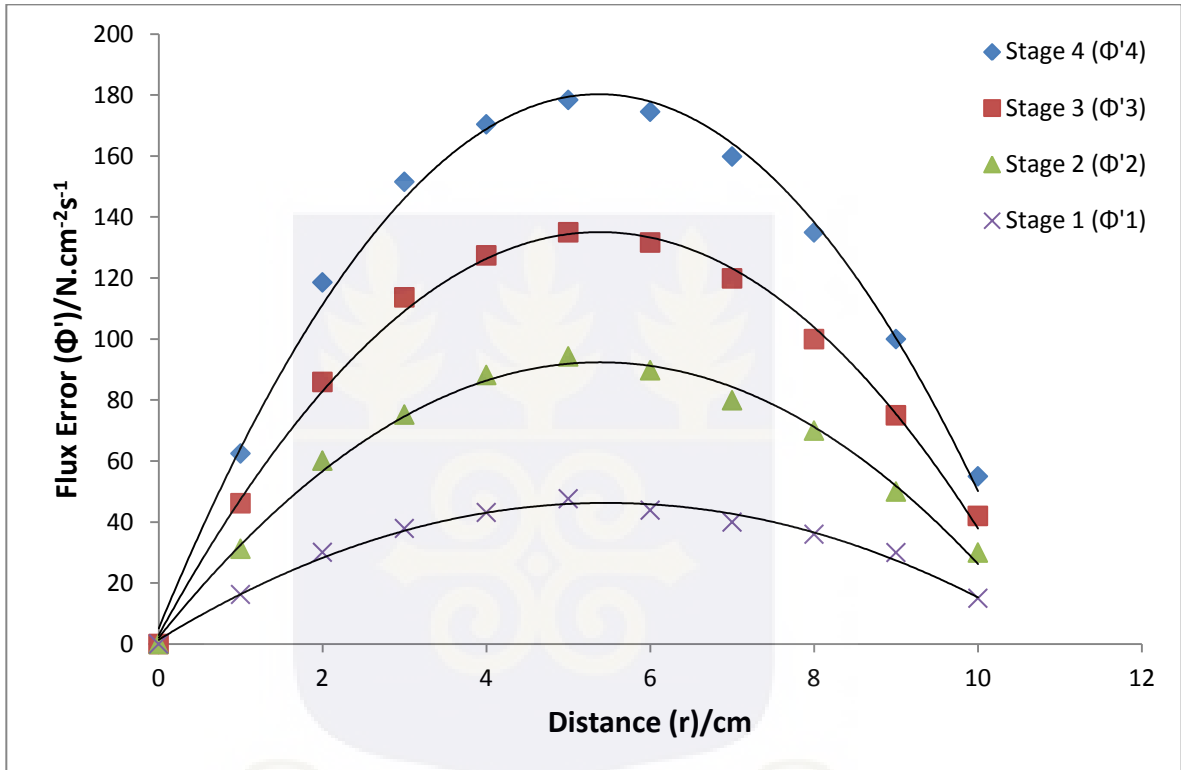


Fig 4.4: Variation of the flux error distribution function with distance in the solution of the photon flux using the FEM

4.1.4 Dose Profile Analysis

The dose distribution is shown in Figure 4.5. The distribution is characterized by an increase to a distance of 5cm followed by a decrease for the rest of the distance as it approaches the boundaries. The Figure 4.5 represents the corresponding dose due to the photon flux and therefore has similar characteristics as that of Figure 4.2. The graph gives a general overview of the relationship between the dose prescriptions for the different treatment regimes corresponding

to the different stages of cancer disease. The target volumes and the critical organs like the rectum and bladder, have specific distances from the source point depending on the patient's anatomical structure. The thicknesses of the rectum and the bladder, the specific distances between the source point and the target volumes depend on the patient's size and weight.

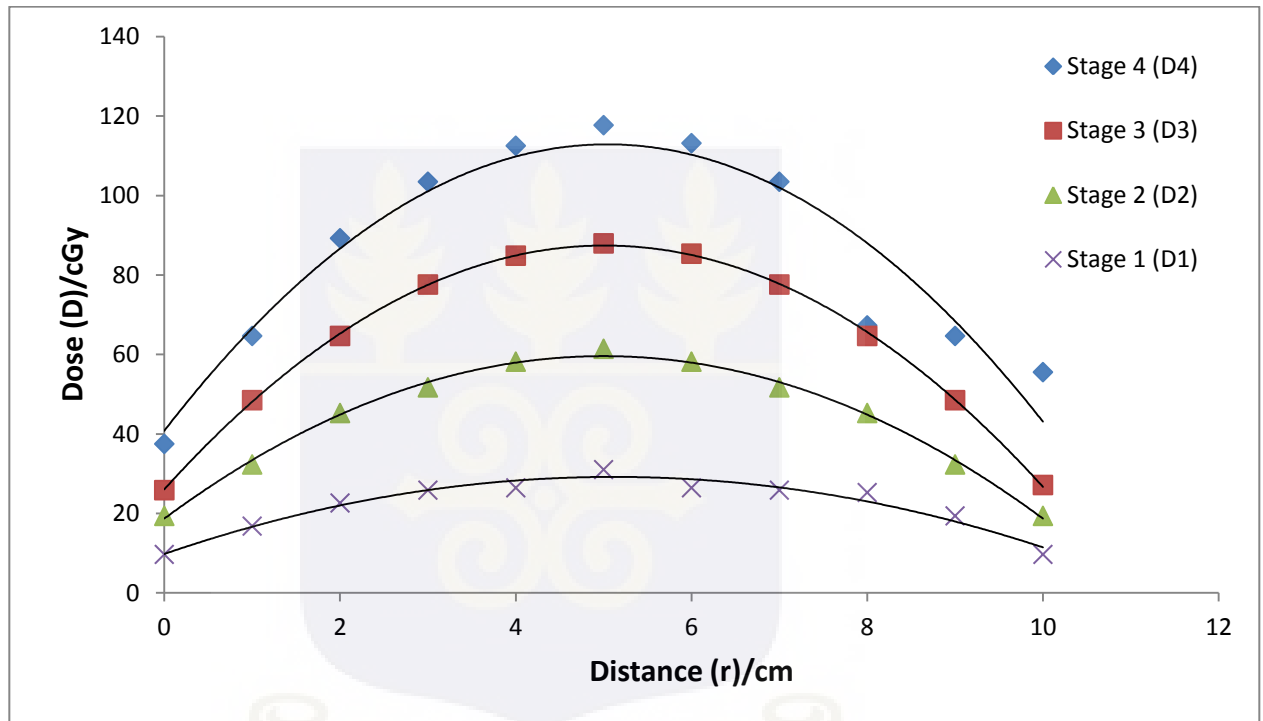


Fig 4.5: Variation of dose as a function of distance for different cancer stages

The Figure 4.6 shows a graph of the cumulative dose with time. Depending on the type and stage of the cancer, the doses are normally delivered in fractions over a period of time. Initially, during treatment the number of photons particles begin to build up in the medium given rise to the various photon interactions with the medium hence the delay for some few seconds. Also as there is more particles streaming because of the source

strength of photon particles injecting from the source term, it is later overcome and shoot up which rise to required prescribed doses for the treatment. This shows a slow rise in the dose with time followed by a rapid increase after 2 seconds.

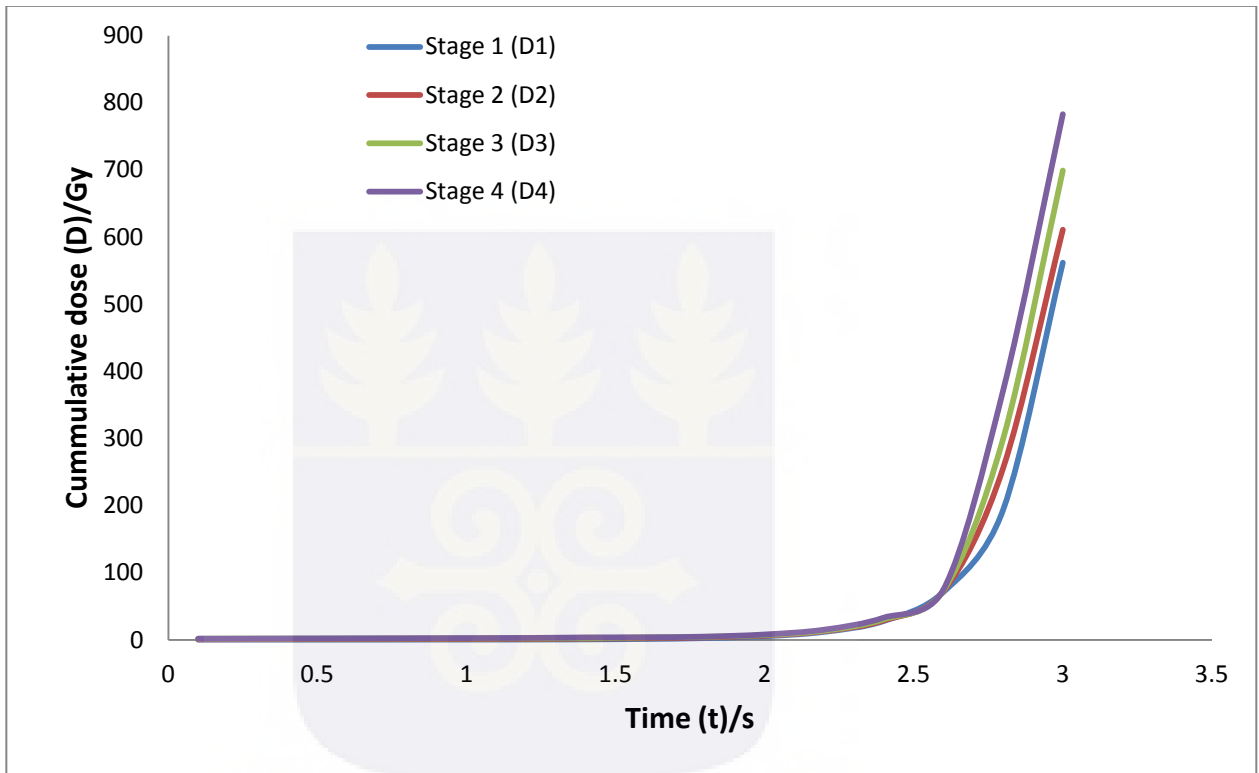


Fig 4.6 : Cumulative dose as a function of time during treatment

4.2 Comparison with analytical reference method

Solution of the transport equation for complex geometries using an analytical method provides an approximate solution with a number of assumptions, which limits the accuracy of the transport model. The FEM model is capable of dealing with very complex

heterogeneous geometries with certain discretization error. The analytic solution of the transport equation is used to calculate the discretization error of the FEM model. Exact solutions for the complex photon intensity in the homogeneous case are available for a limited number of simple geometries.

In the following analytical and FEM approximations, the integrated intensity, Φ_E and the mean time (t) have been computed for the two-dimensional circular case. The absorption coefficient $\mu_a = 0.98 \text{ mm}^{-1}$ and the scattering coefficient $\mu_s = 0.94 \text{ mm}^{-1}$ were used as values representing the human tissue, with radius $R=49 \text{ mm}$. The analytic solution for the integrated photon flux intensity, Φ_E , in units of photon number per unit length, is given by

$$\Phi_E = \frac{1}{(2\pi)^2 R} \sum_{n=-\delta}^{\delta} \cos(n\theta) \frac{I_n(\delta r')}{I_n(\delta R)} \quad (4.1)$$

where $\delta = \left(\mu_a c / k \right)^{1/2}$ and I_n is the modified Bessel function of the first kind of order n , and, $r' = R - \frac{1}{\mu_s}$, is the radial position of the source. The value of k is evaluated

using the expression $k = \frac{c}{3[\mu_a(r) + (1-f)\mu_s(r)]}$ obtained from the solution of the transport equation using P_1 approximation by the expansion of the radiative transport equation in spherical harmonics.

The expression for the mean time (t) component is given by the expression

$$\langle t \rangle = \frac{1}{2\delta k} \sum_{-\delta}^{\delta} \frac{r^1 I_n^1(\delta r^1) I_n(\delta R) - \delta I_n(\delta r^1) I_n^1(\delta R)}{I_n^2(\delta R)} \times \cos(n\theta) \left[\sum_{-\delta}^{\delta} \frac{I_n(\delta r^1)}{I_n(\delta R)} \cos(n\theta) \right]^{-1} \quad (4.2)$$

when $r < r^1$ the photon density itself is given by

$$\Phi = \frac{\delta}{\pi R^2} \sum_{-\delta}^{\delta} \cos(n\theta) I_n(\delta r) \left(K_n(\delta r^1) - \frac{I_n(\delta r^1) K_n(\delta R)}{I_n(\delta R)} \right) \quad (4.3)$$

where, K_n is the modified Bessel function of the second kind of order n .

Comparison of the analytic method with the result from this work is shown in Table 4.2.

Table 4.2: Comparison of the photon flux intensity from Green's function (GF) with that of the model (FEM)

Method	Photon Flux Intensity $\Phi(\text{Nm}^{-2}\text{s}^{-1})$	Reference
Green's Function (GF)	7.76×10^{-4}	This work
Finite Element Method (FEM)	3.27×10^9	This work

4.3 Comparison with Monte Carlo Method

Comparison of finite element data with results obtained from the analytical Green's Function shows that the FEM implementation in this study provides correct solutions of the transport equation. The FEM was also compared with the Monte Carlo (MC) model which is widely accepted as a method for simulating photon propagation in a random scattering media. The three dimensional (3D) MC model assumes a collimated point source perpendicularly incident on the surface of an infinite cylinder. The radiation emitted from the surface is given as a function of the detection angle being integrated in the direction of the cylinder axis to simulate line detector. The comparison of the rectum and bladder doses from this study and the MC values (Miguel et al 2002) are shown in Table 4.3. In general, the rectal doses from this study was lower than the MC values, while the bladder doses from this study was slightly higher than bladder dose obtained using MC simulations.

Table 4.3 Comparison of Monte Carlo method with this work

Method	Rectum (cGy)	Bladder (cGy)	Reference
Monte Carlo simulations	78.71±0.36	29.04±0.24	Miguel et al (2002)
FEM	46.92±0.15	48.49±0.13	This work

4.4 Comparison with Published Data and Treatment Planning System of Komfo Anokye Teaching Hospital

The results from the study were compared with published data using TLD and the treatment planning system (TPS) of the Komfo Anokye Teaching Hospital (KATH). The results show variations between the method and data from published articles and the KATH TPS. Data from the KATH, TPS covered one hundred and sixty-four patients who were referred to the hospital for cancer treatment. Their ages range from 20-82 years. The median age was 55 years. The general characteristics of the patients are presented in the Appendix IV.

Table 4.4: Comparison of the FEM with Published data and TPS of the Oncology centre at KATH

Method	Rectum (cGy)	Bladder (cGy)	Reference
TLD	22.13 - 63.76	-	Ahimedzie Cletus (2011)
TLD	-	18.99 - 46.36	Owusu-Kyere Reynolds (2011)
TPS	10.13 – 85.67	21.32 – 78.81	KATH Data Sheet (2012)
FEM	21.5 - 90.10	25.60 – 110.02	This work

In brachytherapy, the planning target volume (PTV) is the same as the clinical target volume (CTV). The total dose should be as high as possible and appropriate to eradicate all residual macroscopic tumour (Haie-Meder et al, 2005).

The various cervical cancer stages were grouped from stages I to IVA in accordance with FIGO guidelines,. Based on this, the most appropriate treatment modality was carefully chosen for each patient. From Figure 4.7, the most frequent stage was found to be stage IIIB and the least one is the stage IVA. This is due to early reporting at the facility for treatment or screening to assess the patient situation of the cancer before getting to the worst advanced stage. From Figure 4.7, stages IIB and IIIB are more pronounced than the rest of the stages. This agrees well with patient characteristics in Appendix IV Table 5; thus patients with stage IIIB (39.6%) followed by stage IIB (35.4%) and the stage with the least percentage is stage IV(0.6%). Of all the 164 cancer patients only one had the most worst advanced stage of tumour occurring in stage IV. It was observed that, the early cervical carcinoma for patients occurring from stage I to IIA were about 26 patients(15.85%); and the more advanced cervical cancer from IIB-IIIB were about 137 patients (83.53%). The most advanced stage IVA occurred only in one(1) patient which forms about 0.6% of the general characteristics of Table 5 in Appendix IV.

Comparison of values from the TPS at KATH with other published values (Ahimedze Cletus, 2011 and Owusu-Kyere Reynolds, 2011) can be found in Table 4.4. In general the various dose values for the bladder and rectum were comparable and found to agree with each other and acceptable.

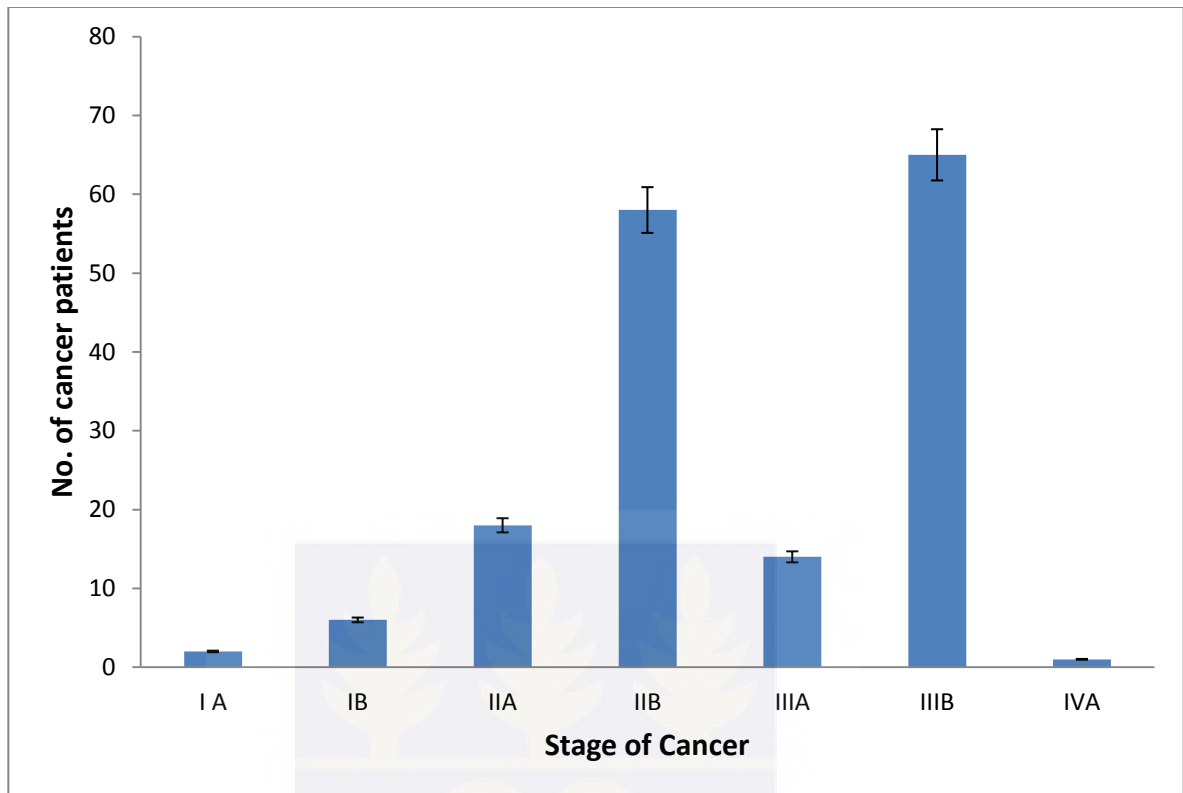


Fig 4.7: Variation of the number of cancer patients with cancer stages

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

This chapter presents the conclusion drawn from the results and the recommendations to stakeholder institutions to improve their treatment planning methods in the near future.

5.1: Conclusion

A number of theoretical and experimental methods have been applied in the treatment planning systems at various Oncology Centers. These include the AAPM (TG-43), Monte Carlo, etc. The method used in this study is based on the application of the finite element method (FEM) in the solution of the Boltzmann's transport equation in biological tissues. Doses to the rectum and the bladder were determined by simulation using MATLAB and plotted with Microsoft Excel for clarity in order to determine the relationship between the various parameters. The results show doses to the rectum and the bladder to be in the range of 10.13-85.67cGy and 21.32-78.81cGy respectively for stage I to stage IV patients. Data on dose prescriptions from the treatment planning system from the Radiotherapy Center of the Komfo Anokye Teaching Hospital in Ghana and published articles for different cancer stages were compared with the model results and were found to agree with standard error of $\pm 20\%$ to $\pm 34\%$.

Curative radiotherapy for cancer of the cervix consists of a combination of external beam radiotherapy (EBRT) and brachytherapy (BT). The intracavitary brachytherapy is used to give a high dose to the tumour or target volume because of its characteristic steep dose gradient. The most important prognostic factors are tumour size, tumour extension and lymph node involvement. With access to modern imaging technology, it is possible to exactly well define the tumour in the cervix, the target volume, the organs-at-risk and the

applicator geometry in 3D (Gerbaulet et al 2002). Doses to the target volume can be optimized whilst minimizing the doses to the organs-at risk at the same time.

5.2 Recommendations

The following recommendations are addressed to stakeholder institutions:

5.2.1. Oncology centres

The Oncology Centres can adopt this method after extensive study in order to verify their treatment planning system (TPS) to improve treatment planning systems at the hospitals(Oncology centres) and also serve as a faster way of checking the dosimetric parameters of the patients before treatment is delivered. This method could also be extended to External Beam Radiotherapy (EBRT) to determine the doses to critical organs of patients undergoing radiotherapy treatment.

5.2.2 Research Institutions

There are many aspects for future work which can be carried out at the various research institutions to enhance research work. Improvements to the model that can be investigated are the use of higher order basis for the shape functions such as quadratics; usage of a basis in time as well as space, adaptive re-meshing for error reduction. In addition to these theoretical improvements and modifications, there are also improvements to these parameters that are used to set up the model. The model can be extended to a fully 3-D. More complex boundary conditions can be incorporated and higher order differential

equation descriptions of the transport model could be used. Undoubtedly, more study is required in future to determine the applicability of the finite element method and once such results have been obtained, it is possible to adopt it as the method of choice for fast accurate investigation of complex problems of photon transport in biological tissues.

5.2.3 Regulatory Authority

It is recommended that regulators dealing with therapy facilities can employ the FEM to check patients' treatment parameters for accurate delivery of doses.



REFERENCES

AAPM Report 85. Tissue inhomogeneity corrections for megavoltage photon beams. Technical report, Medical Physics Publishing, 2004.

Allen, E.J. A finite element approach for treating the energy variable in the numerical solution of the neutron transport equation. *Transport Theor Stat*, 1986,15(4): 449-478

Arridge, S. R. and. Schweiger, M. Direct calculation of the moments of the distribution of photon time of flight in tissue with a finite-element method. *Appl. Opt.*1995,34. 2683–2687

Arridge, S. R.,. Schweiger, M., Hiraoka, M and Delpy, D. T. A finite element approach for modeling photon transport in tissue. *Med. Phys.* 1993,20: 299–309

Arridge, S.R and Hebden, J.C Optical imaging in medicine II; Modeling and reconstruction. *Phys. Med. Biol.* 1997,42: 841-853

Attix, F.H. Introduction to Radiological Physics and Radiation Dosimetry. John Wiley and Sons, Inc, 1986.

Attix,F.H. Introduction to Radiological Physics and Radiation Dosimetry. Wein- heim, Germany; Wiley-VCH Verlag GmbH & Co, 2004.

Bell, G.I and S. Glasstone, *Nuclear Reactor Theory*, Van Nostrand Reinhold Company, New York. 1970.

Berger, A.L, Caruana, R, Cohn, D, Freditag, D, and Mittal, V, Bridging the lexical chasm. Statistical approaches to answer-finding. In proceedings of SIGIR'00, 2000, Athens, Greece

Beyer, D., Nath, R., Butler, W., Merrick, G., Blasko, J., Nag, S. and Orton, C. American Brachytherapy Society recommendations for clinical implementation of NIST- 1999 standards for $^{103}\text{Palladium}$ brachytherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2000, 47: 273-275.

Bobylev A.V. and Spiga, G. On a model transport equation with inelastic scattering. *SIAM J Appl Math.* 1998, 58(4): 1128-1137

Boman, E., Tervo, J and Vauhkonen, M. Modelling the transport of ionizing radiation using the finite element method. *Phys Med Biol*, 2005, 50: 265-280

Brenner D.J. Accelerated repopulation during radiotherapy-Evidence for delayed onset: *Radiat Oncol Invest* 1993, 1:167-172.

Carlson, A.K. and Ahnesjo, A. Point kernels and superposition methods for scatter dose calculations in brachytherapy, *Phys. Med. Biol.* 2000; 45, 357-382

Case K.M and Zweifel,P.F. Fundamental in linear transport theory. Addison –Wesley, Publishing Co. MA. 1967

Chai, J.C. Hsu, P.F and Lam,Y.C. “Three-dimensional transient radiative transfer modeling using the finite-volume method’ *Journal of Quantitative Spectroscopy and Radiative Transfer*; 2004, 86: 299-313.

Chen S.W. Liang, J.A, Yang, S.N, *et al.* The prediction of late rectal complications following the treatment of uterine cervical cancer by high-dose-rate brachytherapy. *Int J Radiat On-col Biol Phys* 2000, 47: 955–961.

Cletus Ahimedzie; ‘Rectal dose estimation for cervical cancer patients at the radiotherapy department of Komfo Anokye Teaching Hospital using thermoluminescent dosimeters’ Kumasi; 2011

Creasman W.T. Controversies in FIGO staging of corpus cancer. *CME J. Gynecol. Oncol*, 2001, 6: 257-259

Daskalov, G. M, Baker R. S, Little, R. C, Rogers, D. W. O and Williamson, J. F. A two-dimensional discrete ordinates photon transport calculations for brachytherapy dosimetry applications *Nucl. Eng. Sci.* 2000; 134; 121–134

Dautray, R and Lions, J.L. 'Mathematical Analysis and Numerical Methods for Science and Technology'; Springer-Verlag, 1993

Deshpande, D.D., Shrivastav, S.K., Pradhan, A.S; Viswanathan, P.S and Dinshaw, K.A.: Dosimetry of intracavitary applications in carcinoma of cervix : rectal dose analysis. *Radiother Oncol.*1997, 42: 163-166.

Favorite J.A., and Sanchez, R. An inverse method for radiation transport. *Radiat Prot Dosim*; 2005,116(1-4): 482-485

Feng. S., Zeng, F and Chance, B. Photon migration in the presence of a single defect; a perturbation analysis. *Appl Opt.* 1995,34: 3826

Ferrigno R, Novaes PERS, Pellizzon A.C.A, *et al.* High dose rate brachytherapy in the treatment of uterine cervical cancer. Analysis of dose effectiveness and late complications. *Int J Radiat Oncol Biol Phys* 2001, 50(5): 1123–1135.

Georg, D. Kirisits, C. Hillbrand, M. Dimopoulos, J. and Pötter, R. Image-guided radiotherapy for cervix cancer: high-tech external beam therapy versus high-tech brachytherapy. *Int J Radiat Oncol Biol Phys*, 2008, 71(4): 1272-1278.

Gerbaulet A, Pötter R, Mazon J.J. Meertens H, Van Limbergen E, GEC ESTRO handbook of Brachytherapy. Cervix Carcinoma. Dose Calculating and Treatment Planning. 2002; Chapter 14:8

Girinsky, T., Rey, A., Roche, B, *et al.* Overall treatment time in advanced cervical carcinomas: A critical parameter in treatment outcome. *Int J Radiat Oncol Biol Phys.* 1993; 27. 1051– 1056

Griffiths, D. J. ‘Introduction for electrodynamics’. 3rd ed. 1998. Prentice Hall: 50.

Haie-Meder, C. Pötter, R. Van Limbergen, E et.al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): Concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiotherapy & Oncology.* 2005, 74: 235-245

Haie-Meder, C. Potter, R. Van Limbergen, E. and et al, Recommendations from the gynaecological (GYN) GEC ESTRO working group: concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiother & Oncol*, 2005,47: 115-140

Han, I. Orton, C. Shamsa, F. *et al.* Combined low-dose-rate brachytherapy and external beam radiation for cervical cancer: Experience over ten years. *Radiat Oncol Investig* 1999,7: 289– 296.

IAEA, International Atomic Energy Agency Bulletin, April 2010, 51(2): 6-7

ICRU Report No. 38. Dose and volume specification for reporting intracavitary therapy in gynaecology. International Commission on Radiation Units and Measurements (ICRU) Bethesda, MD, 1985

ICRU-Report 62, International Commission of Radiation Units and Measurements. Prescribing, Recording and Reporting Photon Beam Therapy (supplement to ICRU Report 50 November 1999). NR:62

Jin, J. The Finite Element Method in Electromagnetic. New York: John Wiley & Sons, 2nd ed., 2002.

Johns H.E. and Cunningham J.R, The Physics of Radiology. Springfield, Illinois; Thomas 4th ed; 1983

Johnson, C. Numerical solution of partial differential equations by the finite element method. Claes Johnson and Student litteratur, 1987.

Jones, B. Dale, R.G. Bleasdale, C. Tan, L.T. Davies, M.A. Mathematical model of intraluminal and intracavitary brachytherapy. Br. J. Radiol. 1994, 67: 805-812

KATH, Komfo Anokye Teaching Hospital, Treatment Planning System Data sheet
Kumasi, 2012

Kavenoky, A. "Status of Integral Transport Theory," *Proc. Int Topl. Mtg. Advances in Mathematical Methods for the Solution of Nuclear Engineering Problems*, Munich, Germany, European Nuclear Society; April 1981; 27-29.

Lertsanguansinchai P, Lertbutsayanukul, C, Shotelersuk K, *et al.* Phase III randomized trial comparing LDR and HDR brachytherapy in treatment of cervical carcinoma. *Int J Radiat Oncol Biol Phys* 2004; 59: 1424 –1431.

Lewis, E. E. and Miller, W.F. Jr., *Computational Methods of Neutron Transport*, John Wiley & Sons, New York, 1984.

Lipidus, L. and Pander, G.F. Numerical solution of Partial Differential Equations in Science and Engineering; Wiley-Interscience; 1st ed, 1982, USA

Manteuffel T.A. Ressel, K.J. and Starke, G. A boundary functional for the least squares finite-element solution of neutron transport problems. *SIAM .J. Numer Anal*, 2000; 37(2): 556-586.

Martin, W.R. and Dudesrstadt, J.J. 'Finite element solutions of neutron transport equation with applications to strong heterogeneities'. *Nucl Sci Eng*, 1977, (62): 371-390

Miguel, L. Rodriguez et al; Absorbed dose calculations in a brachytherapy phantom using Monte Carlo simulations, 2002

Mordant, M. 'Linear discontinuous finite elements for phase-space multidimensional transport calculations. Nucl Sci Eng; 1986, 92: 218-227

Nag S, Chao C, Erickson B et al, 'The American Brachytherapy Society Recommendations for Low Dose Rate Brachytherapy of the cervix'. Int. J. Radiat. Oncol. Bio. Phys. 2002, 52: 33-48

Owusu-Kyere, Reynolds. 'Bladder dose estimates using TLD for cervical cancer patients at the Radiotherapy Department of Komfo Anokye Teaching Hospital', Kumasi, 2011.

Rao, S. S. The Finite Element Method in Engineering. Butterworth-Heinemann, Boston, 3rd ed., 1999.

Rogers D.W.O. Fifty years of Monte Carlo simulations for medical physics. Phys Med. Biol; 2006, 51: 287-301

Santhamma, A.V and Das K.R. Clinical dosimetry of the rectum in cathetron applications for treatment of carcinoma uterine cervix. Clin. Radiol. 1978, 29: 343-345.

Schweiger, M., Arridge, S. R., Hiraoka, M and Delpy, D. T. The finite element model for the propagation of light in scattering media: boundary and source conditions. *Med. Phys.* 1995, 22: 1779–1792

Serkies, K., Badzio, A; Jereczek-Fossa J., Tarnawska Z., Nowak R., Szewczyk P and Jassem J. Rectal doses in intracavitary brachytherapy of gynaecological malignancies: comparison of two dosimetric methods. *Radiother. Oncol* 2001, 58: 37-41

Slevin, N.J, Hendry, J.H, Roberts, S.A, Agren-Cronqvist, A. The effect of increasing the treatment time beyond three weeks on the control of T2 and T3 laryngeal cancer using radiotherapy. *Radiother Oncol* 1992, 24: 215–220.

Stewart, A.J and Viswanathan, A.N. Current controversies in high-dose-rate versus low dose- rate brachytherapy for cervical cancer. *Cancer*, 2006, 107: 908-115

Strochi. P. R.M. van Battum, L.J and Woudstra, E. Calculation of a pencil beam kernel from measured photon beam data. *Phys Med Biol*, 1999, 44: 2917-2928.

Tagziria H. editor. Review of Monte Carlo and Deterministic Codes in Radiation Protection and Dosimetry. NPL Report Teddington, 2000.

Tanderup K, Georg D, Pötter R, Kirisits C, Grau C, and Lindegaard, J.C. *Adaptive management of cervical cancer radiotherapy*. Semin Radiat Oncol, 2010,20(2): 12-19.

Tervo, J. Kolmonen, P. Vauhkonen, M. Heikkinen, L.M and Kaipio, J.P. A finite element model of electron transport in radiation therapy and a related inverse problem. Inverse Probl, 1999,15:1345-1361.

Ulmer, W and Harder, D. Applications of a triple Gaussian pencil beam model for photon beam treatment planning; Med. Phys. 1996, 6: 68-74.

Williams, M,L; Ilas, D. Sajo, E Jones, D.B and Watkins, K.E. ‘Deterministic photon transport calculations in general geometry for external beam radiation therapy’. Med.Phys. 2000,30(12); 3183-3195

Williamson, J.F. Monte Carlo and analytic calculations of absorbed dose near Cs-137 intracavitary sources. Int.J. Radiat Oncol Biol Phys. 1988,15: 227

Williamson, J.F and Nath, R. Clinical implementation of AAPM(TG-32) recommendations on brachytherapy source strength specifications, Med. Phys, 1991,18: 439-448

Withers, H.R. Taylor, J.M.G, Maciejewski, B. ‘The hazard of accelerated tumour clonogen repopulation during radiotherapy’. Acta Oncol 1988, 27:131–146.

Withers, H.R. Biologic basis for altered fractionation schemes. *Med. Phys. Biol* 1985, 55: 2086–2095.

Zerby, C.D. and Keller, F.L. Electron transport theory, calculations and experiments. *Nucl Sci Eng*, 1967, 27: 190-218

Zheng-Ming, L and Brahme, A. High-energy electron transport. *Phys Rev B*, 1992, 46(24): 739-752.



APPENDIX I

FORMULATION OF THE BOLTZMANN TRANSPORT EQUATION

The Boltzmann Transport Equation (BTE) is an energy balanced equation and can be derived from first principles by considering particle conservation within a unit volume element of a phase space (Case and Zweifel, 1967). Here the BTE is derived for a coupled system of particles including photons, electrons and positrons assuming particle conservation. The particles are assumed to interact with only medium atoms but not with each other. The particles are assumed to travel in straight lines between interactions.

Consider a small volume Δv with surface ΔA about a point r . The number of particles dN_j of type j in this volume Δv surface ΔA with energies E and $E+dE$ in the direction Ω and $\Omega + d\Omega$ with time dt is given by integrating the time derivative of the angular density over the volume element as

$$dN_j = \int_{\Delta v} \frac{\partial \Phi_j(r, E, \Omega, t)}{\partial t} dr \quad (1)$$

where $\Phi_j(r, E, \Omega, t)$ is the angular flux.

For conservation of energy, the particles with energy between E and $E+dE$ in the direction Ω and $\Omega + d\Omega$ and time dt enter and leave the volume Δv suffer collisions or attenuated, created or born in different scattering interactions and produced by sources in Δv . Thus

$$dN_j = -N_{j,out} - N_{j,att} + N_{j,sca} + N_{j,so} \quad (2)$$

where $N_{j,out}$, is the net number of particles flowing out of the volume Δv through the surface ΔA in time dt ,

$N_{j,att}$ is the number of particles j that are attenuated in volume Δv in time dt , $N_{j,sca}$ is the number of particles j that are born in the scattering interactions with the medium atoms in Δv in time dt , and $N_{j,so}$ is the number of particles j produced by the sources inside the volume Δv in time dt . $N_{j,out}$ is obtained by integrating the angular flux $\Omega\Phi_j$ over the surface ΔA . The surface integral can be changed into volume integral using Gauss's theorem (Griffiths 1998; Case et al 1967).

Thus

$$\begin{aligned} N_{j,out} &= \int_{\Delta A} \Omega\Phi_j(r, E, \Omega, t) \cdot n dA dE d\Omega dt \\ &= \int_{\Delta v} \nabla \cdot \Omega\Phi_j(r, E, \Omega, t) dndEd\Omega dt \end{aligned} \quad (3)$$

where n is the unit outward vector normal to dA . Also equation(3) can be re-written as

$$N_{j,out} = \int_{\Delta v} \nabla \cdot \Omega\Phi_j(r, E, \Omega, t) dndEd\Omega dt \quad (4)$$

$N_{j,att}$ is obtained using the total cross-section $\sigma_j(r, E)$ which is defined as the probability per unit path length for particle j with energy E to attenuate. The attenuation frequency depends on the particle speed v_j and is given by the number of particles absorbed in unit distance travelled by the particle

$$v_j \sigma_j(r, E) \quad (5)$$

$N_{j,att}$ is also obtained by integrating the number of particles within the energy range $E+dE$ in the volume element Δv . Thus

$$N_{j,att} = \int_{\Delta v} v_j \cdot \sigma_j(r, E) \Phi_j(r, E, \Omega, t) \cdot dr dE d\Omega dt \quad (6)$$

or

$$N_{j,att} = \int_{\Delta v} \sigma_j(r, E) \Phi_j(r, E, \Omega, t) \cdot dr dE d\Omega dt$$

(7)

$N_{j,sca}$ is obtained using the differential cross-section

$$\sigma_{j' \rightarrow j} = \sigma_{j'} \rightarrow f(r, E', E, \Omega', \Omega) \\ = \frac{\partial^2 \sigma}{\partial E \partial \Omega}(r, E', E, \Omega', \Omega) \text{ which is defined as the probability per unit path length that a}$$

particle j' with energy E' and direction Ω' will produce a secondary particle j with energy E and direction Ω . Assuming the particles $j' = 1, 2, 3$ with initial photon energy E' and direction Ω' . Then the rate at which these particles are scattered to secondary particles j is given by

$$(v_1' \sigma_1 \rightarrow j f_1 + v_2' \sigma_2 \rightarrow j f_2 + v_3' \sigma_3 \rightarrow j f_3) dE d\Omega \\ = \sum_{j'=1}^3 v_j' \sigma_{j' \rightarrow j} f_j(r, E', \Omega', E) dE' d\Omega' \quad (8)$$

where $f_{j'} = f_{j'}(r, E', \Omega', t)$

$N_{j,sca}$ can therefore be obtained from the following general equations as

$$N_{j,sca} = \int_{\Delta v} \int_1 \int_{\Delta \Omega} \sum_{j'=1}^3 v_j' \sigma_{j' \rightarrow j} f_j(r, E', \Omega', t) dE' d\Omega' dt \quad (9)$$

or

$$N_{j,sca} = \int_{\Delta v} \int_1 \int \sum_{\Delta A j'=1}^3 \sigma_{j' \rightarrow j} \Phi_j(r, E', \Omega', t) dE' d\Omega' dt \quad (9a)$$

In

radiotherapy, there are no interactions that change electrons to positrons. Thus the differential cross-sections $\sigma_{2 \rightarrow 3}$ is zero for all energies and angles.

$$N_{j,so} = \int_{\Delta v} S_j(r, E, \Omega) dr dE d\Omega dt \quad (10)$$

where $S_j(r, E, \Omega)$ is the source term for particle j inside the volume Δv and Φ_j is the number of particles j per unit time at t in $dr dE d\Omega$. The balanced integro-differential equation is thus

$$\int_{\Delta v} \left(\frac{1}{v_j} \frac{\partial \Phi_j}{\partial t} + \Omega \cdot \nabla \Phi_j + \sigma_j \Phi_j - \int_1 \int_A \sum_{j'=1}^3 \sigma_{j' \rightarrow j} \Phi_{j'} dE' d\Omega' - S_j \right) dr dE d\Omega dt = 0 \quad (11)$$

Thus

$$\frac{1}{v_j} \frac{\partial \Phi_j}{\partial t} + \Omega \cdot \nabla \Phi_j + \sigma_j \Phi_j - \int_1 \int_A \sum_{j'=1}^3 \sigma_{j' \rightarrow j} \Phi_{j'} dE' d\Omega' - S_j = 0 \quad (12)$$

which is the linear Boltzmann transport equation for particle j

APPENDIX II

Patient characteristics with cancer stages ,prescribed and critical organ doses

Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA/cGy	Rectum dose /cGy	Bladder dose /cGy
001	37	IIB	2500	86.61	45.39	37.69
002	56	IIIA	3000	143.13	18.84	38.80
003	50	IIIB	3000	93.71	26.28	29.14
004	62	IIIB	3000	98.81	18.94	28.83
005	71	IIIB	3000	79.60	45.86	36.40
006	54	IIA	2500	86.10	76.45	50.01
007	62	IIB	2500	105.95	52.93	56.47
008	70	IIIB	3000	81.52	58.23	36.14
009	46	IIB	2500	84.63	38.43	30.04
010	59	IIA	2500	96.66	17.62	42.53
011	40	IIB	2500	80.60	47,03	35.09
012	38	IIA	2500	80.49	30.44	62.59
013	68	IIB	2500	80.30	72.43	68.37
014	69	IIIA	3000	107.68	27.08	38.75
015	52	IIIB	3000	85.06	57.29	26.99
016	43	IIB	2500	90.18	33.63	50.18

017	43	IIB	2500	122.94	47.30	70.90
Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA /cGy	Rectum /cGy	Bladder /cGy
018	56	IIA	2500	79.78	34.86	45.69
019	65	IIA	2500	86.16	69.54	40.47
020	45	IIIB	3000	97.21	19.26	38.97
021	48	IIB	2500	117.20	19.32	30.13
022	59	IIIB	3000	90.96	74.71	30.28
023	67	IIA	2500	69.63	23.55	56.22
024	57	IIB	2500	86.79	30.16	67.47
025	58	IIB	2500	81.31	25.22	43.22
026	47	IIA	2500	74.00	42.45	40.23
027	60	IIB	2500	81.88	62.43	50.86
028	72	IIB	2500	61.33	23.34	48.39
029	71	IIB	2500	89.94	45.87	51.77
030	67	IIB	2500	96.65	10.13	28.69
031	33	IIIA	3000	88.65	62.55	43.95
032	71	IIB	2500	94.98	22.52	61.62
033	54	IIIB	3000	94.53	51.97	30.53
034	44	IIA	2500	83.46	30.77	41.35
035	65	IIA	2500	93.57	33.01	45.53
036	48	IIIA	3000	98.39	37.33	42.44

037	49	IIIA	3000	87.47	54.46	67.05
Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA/cGy	Rectum /cGy	Bladder /cGy
038	54	IIIB	3000	88.92	50.32	36.25
039	59	IIIB	3000	87.88	53.58	38.12
040	64	IIIB	3000	90.69	75.93	59.59
041	46	IIIB	3000	91.91	34.83	43.19
042	53	IIIB	3000	84.92	54.43	37.20
043	50	IIIB	3000	72.03	42.18	30.72
044	55	IIB	2500	92.59	36.60	50.30
045	44	IIIB	3000	85.75	56.64	25.62
046	43	IIIB	3000	78.43	55.74	38.64
047	40	IIIB	3000	81.68	43.45	38.19
048	56	IIB	2500	88.28	57.10	68.66
049	63	IIIB	3000	92.18	50.97	40.76
050	71	IIB	2500	79.73	38.03	43.40
051	72	IB	2500	94.29	68.47	70.61
052	56	IIB	2500	86.77	53.30	65.24
053	61	IIIA	3000	98.36	30.36	43.90
054	40	IIIA	3000	94.87	77.47	65.95
055	40	IIA	2500	109.26	85.67	69.56
056	52	IIA	2500	92.12	57.17	44.19

057	35	IIA	2500	91.05	78.21	58.91
Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA/cGy	Rectum /cGy	Bladder /cGy
058	63	IIA	2500	97.62	43.54	78.81
059	55	IIA	2500	95.94	60.68	37.01
060	49	IIIB	3000	94.43	53.35	65.85
061	51	IIB	2500	100.43	76.05	32.94
062	70	IIIB	3000	70.25	28.85	58.78
063	45	IIIB	3000	84.17	62.11	52.82
064	53	IIA	2500	81.07	33.70	65.18
065	53	IIIA	3000	87.55	61.78	43.50
066	53	IIIA	3000	91.33	77.87	42.59
067	70	IIB	2500	92.12	37.17	24.19
068	72	IIIB	3000	86.41	42.24	68.85
069	52	IIIB	3000	82.17	26.41	40.67
070	35	IIB	2500	82.39	40.80	35.02
071	58	IB	2500	87.72	55.30	48.38
072	55	IB	2500	86.05	60.36	31.16
073	69	IIB	2500	86,63	59.57	37.52
074	48	IIIB	3000	98.05	67.54	58.88
075	80	IIIB	3000	92.40	35.57	60.07
076	61	IIIB	3000	94.87	70.79	61.46

077	62	IIB	2500	94.98	22.52	34.62
Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA/cGy	Rectum /cGy	Bladder /cGy
078	75	IIB	3000	83.13	69.20	49.06
079	48	IIIB	3000	90.26	38.19	59.48
080	50	IIIB	3000	93.83	48.37	53.43
081	52	IIIB	3000	99.40	45.07	30.16
082	43	IIIB	3000	88.71	53.09	37.68
083	46	IIIB	3000	79.93	54.64	38.84
084	72	IB	2500	112.61	75.68	38.37
085	78	IB	2500	87.43	39.62	28.68
086	53	IIIB	3000	109.12	34.77	63.41
087	45	IIIB	3000	91.02	53.88	39.07
088	35	IIA	2500	91.59	25.44	58.56
089	65	IIIB	3000	86.74	31.39	48.40
090	46	IIA	2500	82.10	28.05	32.00
091	65	IA	2000	109.09	35.31	51.32
092	44	IIIA	3000	105.46	56.74	38.24
093	53	IIB	2500	88.12	33.11	48.64
094	45	IIB	2500	97.94	45.44	63.91
095	57	IIIB	3000	87.23	39.86	51.69
096	69	IIIB	3000	91.14	39.48	21.32

097	65	IIIB	3000	103.57	33.01	45.53
Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA/cGy	Rectum /cGy	Bladder /cGy
098	55	IIIB	3000	94.27	51.51	39.26
099	70	IIB	2500	90.04	33.90	40.56
100	56	IIIB	3000	81.88	42.43	62.50
101	48	IIIB	3000	86.24	38.46	50.75
102	79	IIIB	3000	89.82	34.77	63.41
103	82	IIIB	3000	71.32	27.44	58.42
104	70	IIB	2500	128.91	28.61	35.33
105	51	IIB	2500	84.23	57.14	47.44
106	52	IIB	2500	98.13	78.52	50.28
107	61	IIIB	3000	82.50	57.11	60.02
108	70	IIIB	3000	92.31	80.40	72.99
109	63	IIB	2500	98.75	44.51	70.38
110	36	IIB	2500	106.96	52.28	33.69
111	75	IIIB	3000	86.09	34.36	56.16
112	51	IIB	2500	88.11	50.94	62.79
113	64	IIIB	3000	88.13	50.40	54.82
114	62	IIB	2500	89.15	58.34	47.89
115	65	IIIB	3000	85.82	52.28	43.39
116	45	IIIB	3000	79.86	46.06	39.87

117	46	IIIA	3000	78.87	34.80	46.54
Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA/cGy	Rectum /cGy	Bladder /cGy
118	60	IIIA	3000	74.01	38.60	54.34
119	75	IIIB	3000	95.83	44.52	68.89
120	54	IIB	2500	88.89	36.50	41.53
121	70	IIB	2500	88.51	36.39	47.84
122	70	IIB	2500	109.04	45.80	32.62
123	62	IIB	2500	89.99	54.74	67.80
124	55	IIB	2500	92.05	26.76	36.60
125	47	IIB	2500	89.91	36.70	25.64
126	57	IIB	2500	91.49	65.77	51.32
127	55	IIB	2500	93.55	41.63	53.91
128	75	IIB	2500	87.66	46.52	50.25
129	46	IIB	2500	88.57	39.93	50.03
130	61	IIIB	3000	91.85	39.25	50.79
131	39	IB	2500	89.84	33.01	43.42
132	71	IIIB	3000	91.60	58.95	44.03
133	78	IIIB	3000	83.49	66.54	56.53
134	50	IIIB	3000	89.87	55.03	60.60
135	70	IIB	2500	82.22	57.81	65.00
136	38	IIB	2500	94.01	42.68	56.68

137	75	IIB	2500	90.20	55.45	67.65
Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA/cGy	Rectum /cGy	Bladder /cGy
138	55	IIIB	3000	94.43	75.48	61.55
139	49	IIB	2500	90.32	22.47	73.73
140	77	IIB	2500	109.97	53.51	70.25
141	39	IIIB	3000	93.29	27.67	57.87
142	20	IIB	2500	92.93	64.72	43.09
143	40	IIB	2500	121.77	59.51	39.54
144	36	IIIB	3000	92.51	46.48	62.96
145	45	IA	2500	71.53	35.03	55.67
146	70	IIIB	3000	91.13	60.05	38.61
147	55	IIIB	3000	94.21	33.91	44.07
148	56	IIA	2500	81.01	27.54	51.34
149	54	III	3000	153.67	64.33	54.28
150	42	IIIB	3000	88.80	35.56	49.01
151	50	IIB	2500	89.50	40.76	34.96
152	71	IIIB	3000	92.28	49.04	56.16
153	68	IIIB	3000	105.85	65.13	42.65
154	48	IIIB	3000	125.85	63.37	47.66
155	45	IVA	3000	93.75	54.49	62.29
156	45	IIIA	3000	93.22	41.97	52.52

157	68	IIB	2500	90.98	55.55	34.29
Patient ID Number	Age/yrs	Cancer Stage	Prescribed dose to tumour /cGy	Dose to reference pointA/cGy	Rectum /cGy	Bladder /cGy
158	56	IIB	2500	93.56	54.53	60.30
159	47	IIB	2500	91.82	41.61	55.53
160	75	IIIB	3000	91.66	55.68	45.88
161	71	IIIB	3000	101.61	43.48	36.48
162	67	IIB	2500	92.29	54.53	49.92
163	68	IIIB	3000	91.99	49.63	77.70
164	55	IIIB	3000	97.91	57.99	43.68



APPENDIX III

1. Angular flux distribution with time using Matlab

```

meu = 0;
t = 0;
x = 0;
ind = 1;
for t = 0:0.25:1
for x = 0:0.25:10
    flux = -(x + 1)*(x - 11)*(5 - meu^2)*(1-t);
    f(ind)=flux;
    xt(ind)= x;
    %flux(index)=flux;
    ind = ind + 1;
end
f;
xt;
disp((f    xt'))
plot(xt,f)
grid on
end
title ('ANGULAR FLUX DISTRIBUTIONS AT TIME t')
xlabel ('DISTANCE (mm)')
ylabel ('ANGULAR FLUX')
gtext('t = 0')
gtext('t = 0.25')
gtext('t = 0.50')

```

2. CALCULATION OF THE SOURCE TERM

```

speed = 3*10^8;
meu = 1;
t = 0;
x = 0;
bo = 0.25;
b2 = 0.05;
sigmat=2;
ind = 1;
for t = 0:0.25:1
for x = 0:0.25:10
    T = (1/speed)*(x - 11)*(x + 1)*(5 - meu^2)-(2*x-10)*meu;
    G = (5 - meu^2)*(1-t)-sigmat*(x - 11)*(x + 1);
    M = (5 - meu^2)*(1-t);
    N = (14/3*bo - (meu^2-1/3)*b2)*(x - 11)*(x + 1)*(1-t);
    source = (T*G*M) + N;
    srce(ind)=source;
    xt(ind)= x;
    %flux(index)=flux;
    ind = ind + 1;
end

```

```

srce;
xt;
disp((srce    xt)')
plot(xt,srce)
grid on
end
title ('SOURCE TERM DISTRIBUTIONS AT TIME t')
xlabel ('DISTANCE (mm)')
ylabel ('SOURCE TERM')
gtext('t = 0')
gtext('t = 0.25')
gtext('t = 0.50')

```

3. % DOSE CALCULATION

```

%{
Do = Initial dose rate
t = radiation time in secs
Dcum = cumulative dose
t2 = half - life of cesium
lumbda = decay constant
%}
Dcum = 0.662;
t2 = 30
%lumbda = 0.693/30;
disp('t          Dcum')
disp('-----')
iter = 1;
for t = 1:0.2:3
    Dcum = 1.44*t2*Dcum*(1-exp(-reallog(2)*t/t2));
    disp((t Dcum))
    time(iter) = t;
    Dcumm(iter)= Dcum;
    iter = iter +1;
end
plot(Dcumm,time)
grid on
xlabel('CUMULATING DOSE (Gy)')
ylabel('TIME (s)')
title('CUMULATIVE DOSE PER TIME IN HUMAN TISSUE USING CESIUM')

```

APPENDIX IV

Table 1. The flux distribution with distance

Distance (r)	Flux			
	Φ_4	Φ_3	Φ_2	Φ_1
0	58	40	30	15
1	100	75	50	26
2	138	100	70	35
3	160	120	80	40
4	174	130	90	44
5	182	136	95	48
6	175	132	90	44
7	160	120	80	40
8	135	100	70	36
9	100	75	50	30
10	55	42	30	15

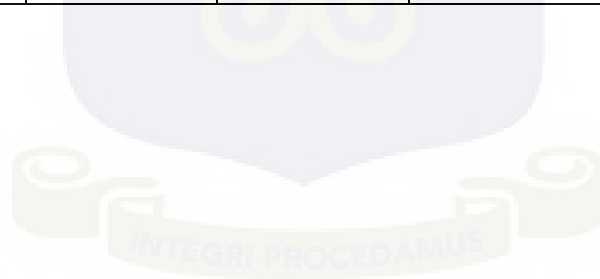


Table 2. Dose distribution with distance

Distance (r)	Doses			
	D4	D3	D2	D1
0	37.51	25.87	19.4	9.7
1	64.68	48.51	32.34	16.82
2	89.26	64.68	45.28	22.64
3	103.49	77.62	51.74	25.87
4	112.54	84.88	58.21	26.46
5	117.72	87.97	61.45	31.05
6	113.19	85.38	58.21	26.46
7	103.49	77.62	51.74	25.87
8	67.32	64.68	45.28	25.28
9	64.68	48.51	32.34	19.4
10	55.57	27.16	19.4	9.7

Table 3. The flux error with distance

Distance (r)/mm	Flux error			
	$\Phi'4$	$\Phi'3$	$\Phi'2$	$\Phi'1$
0	0	0	0	0
1	62.47	46.15	31.23	16.24
2	118.56	85.92	60.13	30.07
3	151.54	113.66	75.23	37.89
4	170.39	127.42	88.21	43.13
5	178.39	134.99	94.29	47.64
6	174.51	131.63	89.75	43.88
7	159.83	119.87	79.92	39.96
8	134.95	99.96	69.97	35.99
9	99.98	74.99	49.99	29.99
10	54.97	41.99	29.99	14.99



Table 4 Fluxes(Φ) and Error fluxes(Φ^E) with distance

Distance (r)	Φ_4	Φ_3	Φ_2	Φ_1	Φ_4^h	Φ_3^h	Φ_2^h	Φ_1^h	Φ_4^E	Φ_3^E	Φ_2^E	Φ_1^E
0	58.00	40.00	30.00	15.00	58.00	40.00	30.00	15.00	0.00	0.00	0.00	0.00
1	100.00	75.00	50.00	26.00	37.53	28.85	18.77	9.76	62.47	46.15	31.23	16.24
2	138.00	100.00	70.00	35.00	19.44	14.08	9.87	4.93	118.56	85.92	60.13	30.07
3	160.00	120.00	80.00	40.00	8.46	6.34	4.77	2.11	151.54	113.66	75.23	37.89
4	174.00	130.00	90.00	44.00	3.45	2.58	1.79	0.87	170.55	127.42	88.21	43.13
5	182.00	136.00	95.00	48.00	1.36	1.01	0.71	0.36	180.64	134.99	94.29	47.64
6	175.00	132.00	90.00	44.00	0.49	0.37	0.25	0.12	174.51	131.63	89.75	43.88
7	160.00	120.00	80.00	40.00	0.17	0.13	0.08	0.04	159.83	119.87	79.92	39.96
8	135.00	100.00	70.00	36.00	0.05	0.04	0.03	0.01	134.95	99.96	69.97	35.99
9	100.00	75.00	50.00	30.00	0.02	0.01	0.01	0.01	99.98	74.99	49.99	29.99
10	55.00	42.00	30.00	15.00	0.01	0.01	0.01	0.01	54.99	41.99	29.99	14.99

Table 5. The patient characteristics with tumour stage

Number of patients	N
	164(100%)
<u>Age</u>	
Median	55
Range	20-82
<u>Stage</u>	
IA	2 (1.2%)
IB	6 (3.7%)
IIA	18 (11.0%)
IIB	58 (35.4%)
IIIA	14 (8.5%)
IIIB	65 (39.6%)
IVA	1 (0.6%)

