

**Comparative Studies on Permanent Prostate Brachytherapy: Pre-Plan and Real-Time Transrectal Ultrasound Guided Iodine-125 Seed Implants at Korle-Bu Teaching Hospital, Ghana**

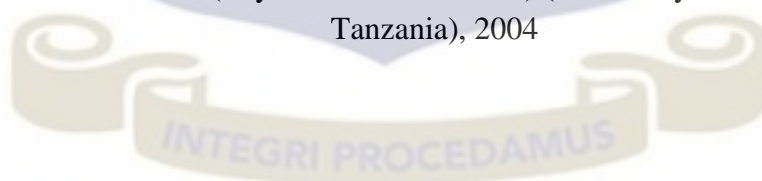
A thesis presented to the:

Department of Medical Physics  
School of Nuclear and Allied Sciences  
University of Ghana-Legon

By

TEGEMEA LAWRENCE KALOLO  
(10361094)

Bachelor of Science (Physics & Mathematics) (University of Dar-es-salaam,  
Tanzania), 2004



In partial fulfilment of the requirements for the degree of

MASTER OF PHILOSOPHY

in

MEDICAL PHYSICS

June, 2013

## DECLARATION

Candidate's Declaration:

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

.....  
TEGEMEA LAWRENCE KALOLO  
(STUDENT) DATE

.....  
PROF. A. W. K. KYERE  
(PRINCIPAL SUPERVISOR) DATE

.....  
PROF. J.H.AMUASI  
(CO – SUPERVISOR) DATE

.....  
MR. S.N.A.TAGOE  
(C0- SUPERVISOR) DATE

## ABSTRACT

This research was carried out to investigate and compare the real-time and pre-plan implant at the Radiotherapy Department of the Korle-Bu Teaching Hospital, Ghana. Prowess Panther 4.5 treatment planning system and Variseed 7.2 software were used for pre-plan and real-time implant respectively. The study was conducted for eighty - three (83) patients treated for prostate cancer through real-time implant brachytherapy between September, 2008 to April, 2013. Thirty one patients (31) whose Ultrasound images were available were selected for the pre-plan study. The slices of ultrasound images were re-drawn on transparent A-4 sheets and later on scanned, contoured and registered in the treatment planning system (Prowess 4.5) .After planning, the volume to be implanted, total number of needles, seeds and the total activity of the source were displayed. Comparison was done with the pre-plan and real-time implant. In both cases the variation was below 5% as recommended in dosimetry. About 30-40% of the imported seeds were left un-used due to over-estimation of seeds ordered from the manufacturer (BARD Company-USA) .Hence this work (pre-plan) aims to solve this problem. The comparison for dosimetric parameters was assessed for prostate, urethra and rectum as (V95%, V100%,V150%, D90Gy, D90%) , (D90Gy, D90%, D30Gy , D30%) and ( V100% , D30Gy and D30%) respectively and the variation were within the limit of  $\pm 5\%$ . Comparison of dosimetric values for this work were done with other institutions, like Karolinska university hospital, Sweden, The institute of Curie / hospital Cochin Group Paris-France and European recommendations. The values reported at Korle-Bu teaching hospital (this work) were in good agreement with the international guidelines.

## DEDICATION

To my parents Mr. and Mrs. Lawrence Kalolo who taught me the importance of education, learning, and doing that which should be done.

To my lovely wife, Elizabeth. K. Njelekela and our children: Freeman Kalolo (Son), Hellen Kalolo (Daughter) and Wenceslaus Kalolo (Son).



## ACKNOWLEDGEMENTS

-To God be the Glory, the creator of the universe for blessing me with knowledge, wisdom and will-power which has enabled me complete this work successfully.

-I wish to express my profound gratitude to my supervisors professor A.W.K.Kyere (Head of department), Professor J.H. Amuasi (Retired Director-SNAS) and Mr S. N. A. Tagoe (Head of medical physics department-KBTH) for their directives and guidance without which I would not have produced this work.

-I am grateful to the Acting director Dr. V. Vanderpuye and staff of National Centre for Radiotherapy and Nuclear Medicine for warm reception accorded me. Also my appreciation should go to Mr Francis Doughan, Evans Sasu and Michael Nyamadi for their assistance and guidance during planning. Likewise Ms Theresa Derry for editing this work.

-My sincere thanks go to the International Atomic Energy Agency (IAEA) and the Government of the United Republic of Tanzania for making it possible (Financially) to undertake this master of philosophy Degree Programme (MPhil).

-My heartfelt appreciation goes to the Management of Ocean Road Cancer Institute (ORCI), Director General, Dr. T. Ngoma, Dr. D. Msemo, Mr.Azizi Mwangolombe (Programme coordinator) and members of Medical Physics Department, Mr. Y.Shaid and Mr. J. D. Kisukari who opened my mind toward Medical Physics programme.

-My endless thanks go to my Parents, brothers, sisters and my mother -in- law (Bibi Njelekela) for taking care of my family doing my absence.

-Finally, I humbly express my gratitude's to all lectures of SNAS and all staff for their cooperation. I say God bless you all abundantly.

## TABLE OF CONTENTS

DECLARATION.....	ii
ABSTRACT.....	iii
DEDICATION.....	iv
ACKNOWLEDGEMENT.....	v
LIST OF FIGURES.....	xi
LIST OF TABLES.....	xiii
LIST OF PLATES.....	xiv
LIST OF ABBREVIATIONS.....	xvi
LIST OF SYMBOLS AND CONSTANTS.....	xix

### CHAPTER ONE: INTRODUCTION

1.1 Background.....	1
1.2 Statement of the problem.....	6
1.3 Objective of the study.....	7
1.4 Relevance and justification.....	7
1.5 Scope and delimitation.....	8
1.6 Organization of thesis.....	8

### CHAPTER TWO: LITERATURE REVIEW

2.1 Dosimetry associated with brachytherapy.....	9
2.1.1 Interstitial treatments .....	9
2.1.2 Dose distributions around sources.....	10
2.1.3 AAPM TG 43 algorithm.....	10

2.2 Radioisotopes used in prostate brachytherapy.....	12
2.2.1 Classification of brachytherapy sources.....	12
2.2.2 Description of brachytherapy sources used in prostate cancer.....	13
2.2.2.1 Iodine -125.....	13
2.2.2.2 Iridium-192.....	14
2.2.2.3 Palladium-103.....	15
2.2.2.4 Caesium -131.....	16
2.2.2.5 Cobalt -60.....	16
2.2.2.6 Gold-198.....	16
2.3 Treatment selection criteria according to ESTRO/ EAU/EORTC guidelines.....	17
2.3.1 Gleason grade.....	17
2.3.2 Prostate specific antigen (PSA).....	18
2.3.3 Digital rectum examination.....	19
2.3.4 International prostate system score (IPSS).....	20
2.3.5 Transurethral resection of the prostate .....	21
2.3.6 Pubic arch evaluation.....	22
2.4 International guidelines toward prostate cancer brachytherapy implant.....	22
2.4.1 The ESTRO/ EAU/ EORTC guideline.....	22
2.4.2 The American Brachytherapy Society (ABS) guidelines.....	23
2.5 Treatment modalities for prostate cancer patients.....	24
2.5.1 Hormone therapy.....	24
2.5.2 Chemotherapy treatment.....	24
2.5.3 Cryotherapy treatment.....	25
2.5.4 External radiation treatment (Teletherapy).....	26

## CHAPTER THREE: MATERIALS AND METHOD

3.1 Part one: Real-time implant at KBTH.....	28
3.1.1 Descriptions and application of each of the material used during real -time implant in the theatre at KBTH.....	28
3.1.1.1 The implant needle.....	29
3.1.1.2 Ultrasound unit, rectal probe and gel.....	29
3.1.1.3 The stepper and template grid.....	32
3.1.1.4 Mick applicator .....	33
3.1.1.5 Survey metre.....	34
3.1.1.6 Anaesthesia.....	35
3.1.2 Real-time implant procedure.....	36
3.1.2.1 Volume study.....	36
3.1.2.2 Needle identification.....	38
3.1.2.3 Needle placement.....	39
3.1.2.4 Delivery of seeds.....	40
3.1.2.5 Dose planning.....	42
3.1.2.6 Radiation protection (Restrictions to treated patients).....	43
3.2 Part two: Pre-plan implant planning.....	44
3.2.1 Description of transparent A4-sheets and pre-evaluated ultrasound images.....	44
3.2.2 Marker-pen.....	45
3.2.3 Treatment planning system (Prowess 4.5 panther).....	46
3.2.4 Patient characteristics.....	47
3.2.4.1 Profile of patients treated with brachytherapy.....	47

3.2.4.2 Profile of patients according to the year of treatment.....	49
3.2.4.3 Patients distribution according to their ages.....	50
3.3 Planning procedure.....	50
3.3.1 Drawing and contouring the prostate volume slices.....	50
3.3.2 Selection of parameters in the TPS.....	52
3.3.3 Pubic arch.....	52
3.3.4 Seed distribution.....	54
3.3.5 Dose margin .....	58

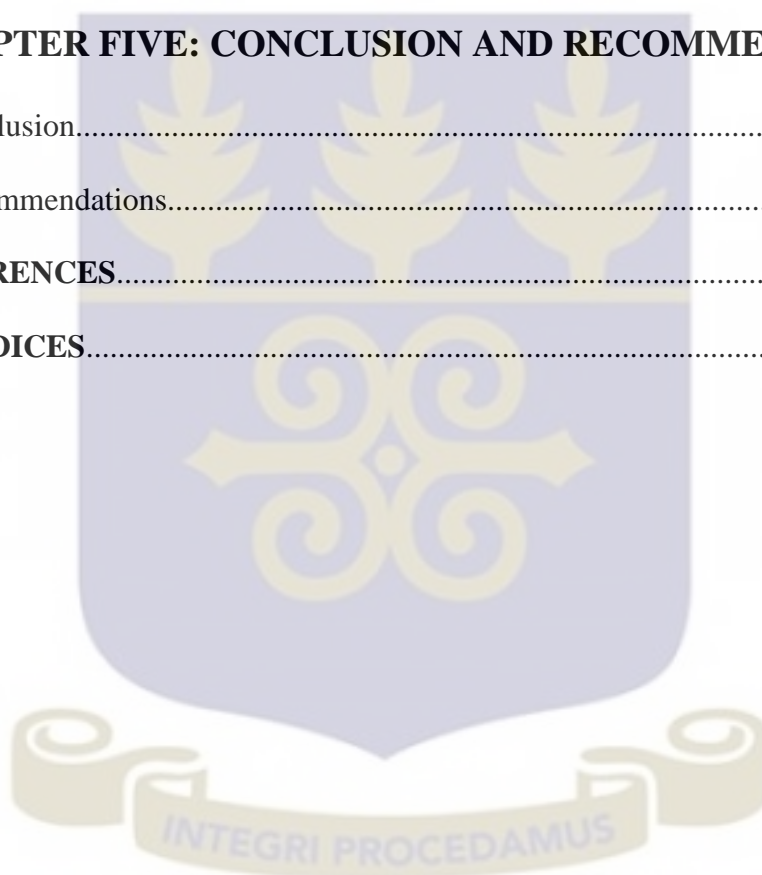
## **CHAPTER FOUR: RESULTS AND DISCUSSION**

4.1 Comparison of prostate volume, number of needles and amount of seeds implanted.....	61
4.1.1 Prostate volume.....	61
4.1.2 Number of needles.....	61
4.1.3 Number of seeds.....	62
4.2 Dosimetric parameters reported.....	62
4.2.1 The implant data obtained from pre-plan using prowl 4.5 panther at KBTH.....	62
4.2.2 The implant data obtained from real-time implant using Variseed Software at the theatre.....	64
4.3 Comparison of dosimetric parameters.....	66
4.4 Comparison of Graphs.....	66
4.4.1 The graphical presentation of numbers of seeds against prostate volume ( cc).....	66

4.4.2 The graphical presentation of total activity (mCi) against prostate volume (cc).....	67
4.5 Clinical data results compared with international guidelines.....	69
4.5.1 Data comparison with European recommendations (EAU/ESTRO and EORTC).....	69
4.5.2 Data comparison with other published work.....	72

## **CHAPTER FIVE: CONCLUSION AND RECOMMENDATIONS**

5.1 Conclusion.....	77
5.2 Recommendations.....	77
<b>REFERENCES</b> .....	79
<b>APPENDICES</b> .....	85



## LIST OF FIGURES

Figure 2.1: Geometry used in the -TG 43 protocol.....	10
Figure 2.2: I-125 seeds 6711 model.....	14
Figure 2.3: The decay scheme of I-125.....	14
Figure 2.4: Schematic diagram of palladium-103 seeds (200 model).....	15
Figure 2.5: Demonstration of digital rectal examinations (DRE).....	19
Figure 2.6: Transurethral resection of the prostate (TURP).....	21
Figure 3.1: The bar graph for patient treated between 2008 to April, 2013.....	49
Figure 3.2: The distribution of patients according to their ages.....	50
Figure 4.1: Real - time implant graph Seeds Vs. prostate volume (cc).....	66
Figure 4.2: Pre-plan implant graph seeds Vs. prostate volume (cc) .....	67
Figure 4.3: Real-time implant graph, Total activity ( $Gm^2/hr$ ) Vs. prostate volume.....	68
Figure 4.4:Pre-plan implant graph, Total activity ( $Gm^2/hr$ ) against prostate volume.....	68
Figure 4.5: Comparison of dosimetric parameters between KBTH and Sweden on Prostate doses.....	70

Figure 4.6: Comparison of dosimetric parameters between KBTH and Sweden on Urethra doses.....70

Figure 4.7: Comparison of dosimetric parameters between KBTH and Sweden on Rectum doses .....71

Figure 4.8: Comparison of median values treated with permanent seed implants in Ghana and Sweden hospitals.....73



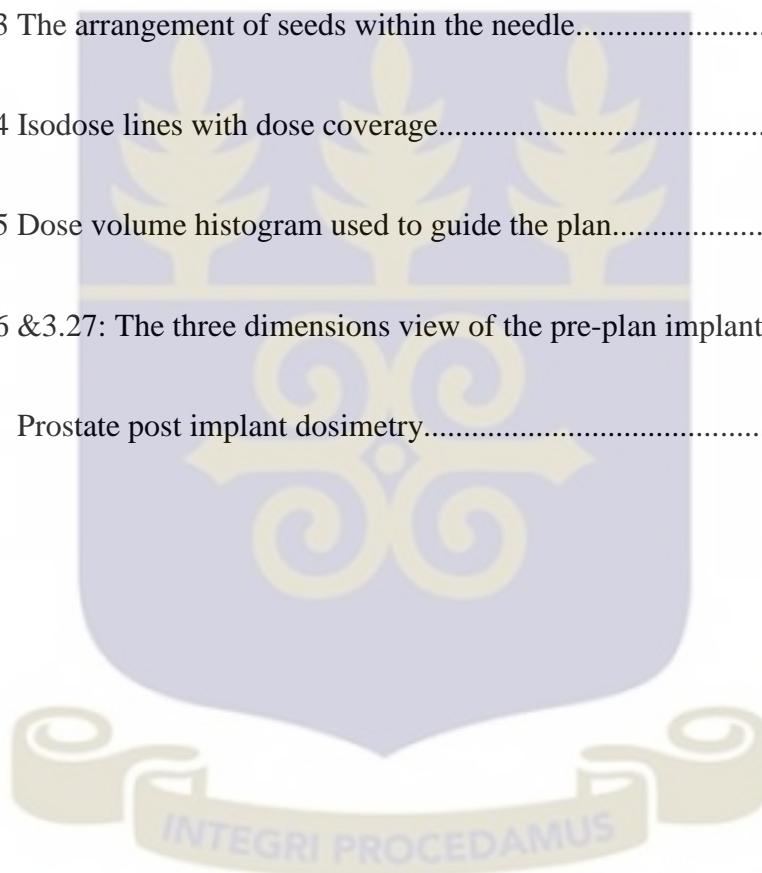
## LIST OF TABLES

Table 1.1: Half-life and energy range of the radionuclide's used for brachytherapy....	6
Table 2.1: Brachytherapy treatments classified with respect to dose rate.....	12
Table 2.2: Some characteristics of isotopes used in brachytherapy .....	17
Table 2.3: The criteria for the patients qualified for prostate brachytherapy.....	22
Table 2.4: ESTRO/ EAU/EORTC recommendations for pre- implant dosimetry.....	23
Table 3.1 Dose limits for prostate brachytherapy at KBTH.....	43
Table 3.2: Characteristics of 31 selected patients for the study.....	48
Table 4.1: The median dose values received from Prowess Panther 4.5 .....	63
Table 4.2: The median dose values received from Variseed 7.2.....	64
Table 4.3: Comparison of dosimetric parameters for prostate, urethra and rectum.....	65
Table 4.4 Comparison of dosimetric parameter between KBTH and Europe recommendation.....	69
Table 4.5: Comparison of median values between Ghana and Sweden.....	72
Table 4.6: Comparison of this work and other publications.....	74
Table 4.7: The mean comparison for needles, seeds and total activity.....	76

## LIST OF PLATES

Plate 3.1 The picture of needles/obturator system .....	29
Plate 3.2 Ultrasound probe with contrast used during volume study.....	31
Plate 3.3 Real-time: Implant facilities, Ultrasound components.....	31
Plate 3.4 Real-time: Implant facilities, stepper.....	33
Plate 3.5 Real-time implant facilities, Mick applicator, Magazine.....	34
Plate 3.6 A pictorial view of a survey metre.....	34
Plate 3.7 Anaesthesia machine .....	36
Plate 3.8 The dorsal lithotomy position of the patient.....	37
Plate 3.9 Ultrasound image, showing number of slices.....	38
Plate 3.10 Real-time, needle/catheter distribution.....	40
Plate 3.11 Real time, template guides needles during implant.....	41
Plate 3.12 Real-time, ultrasound isodose and dose distribution.....	42
Plate 3.13 A picture of A4-sheet with ultrasound traced images used in the study.....	45
Plate 3.14 Pictures of ACCU-LINER marker-pen used in the study .....	45
Plate 3.15 Pre-plan: Prowess 4.5 TPS.....	46
Plate 3.16 Pre-plan: Planning console.....	47
Plate 3.17 A scanner (Canon 5600 F) used to scan ultrasound images.....	51

Plate 3.18 One of the scanned and registered slices in the TPS.....	52
Plate 3.19 The contoured volumes for prostate, urethra and rectum.....	52
Plate 3.20 Pubic arch study demonstration.....	54
Plate 3.21 A countoured sliced of prosatte with 2mm margin.....	55
Plate 3.22 Arrangement of slices from base to apex.....	57
Plate 3.23 The arrangement of seeds within the needle.....	57
Plate 3.24 Isodose lines with dose coverage.....	57
Plate 3.25 Dose volume histogram used to guide the plan.....	59
Plate 3.26 &3.27: The three dimensions view of the pre-plan implant.....	60
Plate 5.1 Prostate post implant dosimetry.....	78



## LIST OF ABBREVIATIONS

AAPM	American Association of Physicists in Medicine
ABS	American Brachytherapy Society
AP	Anterior - Posterior
ASTRO	American Society of Therapeutic Radiology and Oncology
Au	Gold
AUA	American Urological Association
CaP	Cancer of prostate
cc	Cubic centimetre
cGy	Centigray
Co	Cobalt
CPU	Central Processing Unit
Cs	Caesium
CT	Computed Tomography
CTV	Clinical Target Volume
D30	Dose that cover 30% of the organ
D90	Dose that cover 90% of the organ
DRC	Democratic Republic of Congo
DRE	Digital rectum examination
DVH	dose volume histogram
e.g	For example
EAU	European Association of Urology
EBRT	External beam radiation therapy
EORTC	European Organisation for the Research and Treatment of Cancer

ESTRO	European Society for Therapeutic Radiology and Oncology
$\gamma$	Gamma
GBq	Giga Becquerel
GHz	gigahertz
HDR	High dose rate
HVL	half value layer
I	Iodine
IAEA	International Atomic Energy Agency
ICRU	International Commission on Radiation Units and Measurements
IGRT	Image guided radiation therapy
IMRT	Intensity modulated beam radiation therapy
IORT	Intra-operative radiation therapy
IPSS	International prostate symptom score
Ir	Iridium
KBTH	Korle-Bu Teaching Hospital
KeV	Kilo electron Volts
LAT	Laterally
LDR	Low dose rate
mCi	milli curie
MDR	Medium dose rate
Mev	mega electron volts
mm	millimetre
MRI	magnetic resonance imaging
ng	nano gram
PBRT	proton beam radiation therapy

Pd	Palladium
PSA	Prostate specific antigen
PTV	Planning target volume
QOL	quality of life
RAM	Random Access Memory
RD	Rectal dose
RIT	radio immunotherapy
T	Tumor
Te	Tellurium
TG	Task group
TPS	Treatment planning software
TRUS	Transrectal Ultrasound
TURP	Transurethral resection of the prostate
UrD10	Dose that cover 10% of the urethra
UrD30	Dose that cover 30% of the urethra
UrD90	Dose that cover 90% of the urethra
US	Ultrasound
USA	united States of America
Vs.	Versus
V100	Percentage of the organ that receive 100% of the dose
V150	Percentage of the organ that receive 150% of the dose
V95	Percentage of the organ that receive 95% of the dose
Xe	Xenon
$\alpha$	Alpha
$\beta$	Beta

## LIST OF SYMBOLS AND CONSTANTS

$P(r_0, \theta_0)$	Reference point that lies on the transverse bisector of the source at a distance of 1 cm from the origin
$D(r, \theta)$	The dose rate at point, $r$ , in the medium from a radioactive source
$G(r, \theta)$	Geometry factor
$F(r, \theta)$	Anisotropy function
$S_k$	Air kerma strength of the source
$\Lambda$	Dose rate constant
$\theta$	Angle
$g(r)$	Radial dose function
$r_0$	Reference point on the transverse axis



## CHAPTER ONE

### INTRODUCTION

#### 1.1 Background

Brachytherapy is a term used to describe the short distance treatment of cancer with radiation from small, encapsulated radionuclide sources. This type of treatment is given by placing sources directly into or near the volume to be treated. The dose is then delivered continuously, either over a short period of time (temporary implants) or over the lifetime of the source to a complete decay (permanent implants). Most common brachytherapy sources emit photons; however, in a few specialized situations beta or neutron emitting sources are used. There are generally two main types of brachytherapy treatment; intracavitary in which the sources are placed in body cavities close to the tumour volume and interstitial, in which the sources are implanted within the tumour volume (Podgorsak et al., 2005).

There are also two types of brachytherapy that are used in the treatment of prostate cancer: permanent low dose radiation (LDR) and temporary high dose radiation (HDR). LDR brachytherapy uses iodine-125 and palladium-103 stored in titanium cases usually referred to as brachytherapy seeds. As the name permanent brachytherapy suggests, the seeds are permanently left inside the prostate gland. Over the course of their radioactive lives, the seeds will continuously emit low radiations until they decay completely. HDR brachytherapy uses a single radioactive seed made of iridium-194 which is sometimes referred to as an iridium wire. Soft flexible plastic catheters are inserted through the perineum and into the prostate gland. HDR brachytherapy entails an overnight stay in the hospital during which a patient undergoes two or three treatments with the wire through each catheter. In LDR brachytherapy, tiny radioactive particles each of the size  $3.8 \times 0.5 \text{ mm}^2$  are implanted

directly into the site of the tumour. These particles are known as 'seeds', and they can be inserted linked together as strands, or individually into the prostate. Because the seeds are inserted or implanted directly into, or very close to, the tumour, they deliver high doses of radiation to the tumour with minimum effect to the normal healthy tissues around it. This means that the procedure is less damaging than conventional radiation therapy where the radioactive beam irradiates other organs (Khan, 2003; Podgorsak et al., 2005).

Brachytherapy has gained wide acceptance as a treatment modality for early stage prostate cancer, in which the disease is confined to the prostate gland. According to Jakub Pritz (2011), treatment of prostate cancer with brachytherapy began when Pasteau and Degrais (1914) inserted radium into the prostate through the urethral catheter (Pasteau et al., 1914). Interstitial implantation of radium needles was first used by Barringer (1917). By the mid 1970's, modern interstitial brachytherapy for the treatment of prostate cancer developed its formalism, after the discovery of  $^{125}\text{I}$  radionuclide in the early 1970's. The delivery of the  $^{125}\text{I}$  radioactive isotopes was done through needles inserted retropublically. Depth coordinates for the needles were determined through palpation of the prostate through the rectal cavity (Holm et al., 1981). Since 1972, several improvements have been made to the implantation process and radiation delivery of permanent seed implant brachytherapy (Whitmore et al., 1917). The first brachytherapy planning was optimized through use of patient images obtained either through transrectal ultrasound probes or CT scans. Using the patient images sets as well as dose calculation software (such as Variseed), better dose delivery by permanent seeds could be performed.

Prostate cancer has the highest prevalence of any nonskin cancer in the human body, with similar likelihood of neoplastic foci found within the prostates of men

around the world regardless of diet, occupation, lifestyle, or other factors. Essentially all men with circulating androgens will develop microscopic prostate cancer if they live long enough. The factors that determine the risk of developing clinical CaP are not well known, although a few have been identified. There are three well-established risk factors for CaP which includes, increasing age, heredity and ethnicity (Heidenreich et al., 2012). According to age, the older a man is, the greater his risk for getting prostate cancer especially at the age above fifty (50) years. Family history (genetically) certain genes (the functional and physical units of heredity passed from parent to offspring) that a son inherited from the parents may influence the prostate cancer risk. Currently, no single gene is sure to raise or lower the risk of getting prostate cancer. However, a man with a father, brother, or son who has had prostate cancer is two to three times more likely to develop the disease himself. The highest incidence rates for prostate cancer in the world are among African- American men, who have a higher risk of prostate cancer than white American men. However, racial differences may reflect differences in access to care (exogenous factors), differences in the decision-making process of whether to seek medical attention and follow- up, and differences in allelic frequencies of microsatellites at the androgen receptor (AR) locus or polymorphic variation (Bostwick et al., 2004).

Some findings indicate that there are other exogenous factors affect the risk of progression from so-called latent CaP to clinical CaP. Factors such as food consumption ( Diets high in animal fat, especially polyunsaturated fat ), pattern of sexual behaviour(men who had suffered from sexual transmitted diseases like gonorrhoea and syphilis are at high risk (Howard et al., 2001), exposure to ultraviolet radiation, chronic inflammation (Nelson et al.,2003 ) and occupational exposure (Exposures reported to be associated with prostate cancer are pesticides especially

herbicides), cadmium, aluminium, polycyclic aromatic hydrocarbons, engine emissions (particularly diesel exhaust), and mineral oil (Boers et al., 2006) may also lead to the development of prostate cancer.

Different criteria are considered before a patient is admitted for prostate cancer implant. These include, the prostate volume less than 50cc (if larger and otherwise suitable, 3 months of neo-adjuvant hormone treatment will usually bring the volume down to 50cc or less). Those patients with a volume of greater than 50 to 60 cc should have hormonal cytoreduction if they are to be considered as candidates for brachytherapy. This does not always reduce the risk of side effects but it is necessary to achieve a satisfactory implant (Ash et al., 2000). Disease confined within the prostate capsule i.e no metastases from DRE review and bone scan should be negative. Gleason score which is a pathological grading system for measuring the degree of differentiation of prostate tumours should be less than 7 (Gleason, 1977). A prostate specific antigen (PSA) test is also performed to find the concentration of the PSA protein within the patient's blood and this should be less than 20ng/mL (Heidenreich, 2012; Thomson et al, 2004). The international prostate system score (IPSS) should be less than 12. Those with a score of 0 to 8 do well with a low risk of acute retention and prolonged urethritis (Ash et al., 2000). Also a DRE is performed to check for any abnormalities. Patients not meeting these requirements may be candidates for a combination of brachytherapy with external radiation therapy, including intensity-modulated radiation therapy (IMRT) or conformal External beam radiotherapy (EBRT). There is also evidence that enlarged prostates can be successfully implanted.

Several treatment options exist for early stage prostate cancer, these include; hormone therapy, chemotherapy, cryotherapy, permanent seed implant brachytherapy,

external beam radiation therapy and prostatectomy (Heidenreich et al., 2012). Each form of treatment has its own associated risks and side effects. Urinary incontinence and impact on sexual function (impotence) may occur after prostatectomy. Sexual dysfunction and irritative gastrointestinal and genitourinary side effects are commonly reported following external radiation treatment for early stage prostate cancer. In permanent seed implant brachytherapy complications such as urinary retention, urinary incontinence, and radiation proctitis may arise (Ash et al, 2000; Stone et al., 2002). At the present time the monotherapy seed implant technique is used to deliver the prescribed dose to the tumours (Ash et al., 2000).  $^{125}\text{I}$  and  $^{103}\text{Pd}$  are the most common radioactive isotopes used for prostate seed implant. Based on their decay rates,  $^{125}\text{I}$  or  $^{103}\text{Pd}$ , has been prescribed to tumours considered slow-growing and fast-growing as designated by their Gleason grade, respectively (Ling et al., 1995). However, prescribing an isotope based on Gleason score has been criticized since no advantages have been observed. Nevertheless, differences in long-term complications between the two isotopes have been reported: a grade III-IV complication rate with  $^{103}\text{Pd}$  (2%) compared to  $^{125}\text{I}$  (6%) (Peschel et al; 1999) .Similarly the increased risk of proctitis when  $^{125}\text{I}$  is used compared to  $^{103}\text{Pd}$  and radiation prostatitis (Herstain et al., 2005).

Even though  $^{125}\text{I}$  and  $^{103}\text{Pd}$  are the two most frequently used isotopes in permanent seed implantation, other radionuclides like gold-198, caesium-131, and iridium-192 have been in use for LDR and HDR respectively.  $^{125}\text{I}$  has a half-life of 60 days, this means that significant radioactive decay will therefore occur over one year following the implant. About eight-seven per cent (87.5%) of the dose will decay after six months following the implant .With a half-life of 17 days,  $^{103}\text{Pd}$  seeds have a higher dose rate than  $^{125}\text{I}$  at the time of implantation with 99.9 % of decay occurring

during the first six months. However, overall, no difference in efficacy between  $^{125}\text{I}$  and  $^{103}\text{Pd}$  has been shown and there is no evidence that caesium-131 seeds, which have recently been introduced, offer any advantage over either  $^{125}\text{I}$  or  $^{103}\text{Pd}$  (Cha,1999 ,Khan ,2003 ).

At Korle-Bu Teaching Hospital, the radionuclide iodine-125 is used for prostate brachytherapy treatments. Palladium-103 is an alternative nuclide for the treatment but only  $^{125}\text{I}$  is currently used in Ghana. The priority for opting Iodine-125 seeds is because it has a low photon energy which is convenient for storage as it requires less shielding .As well as the longer half-life of the isotope is more appropriate for clinical use (Khan, 2003).

**Table 1.1: Half-life and energy range of emitted photons for the radionuclides used for brachytherapy ((Mayles et al., 2007; Khan, 2003).**

Radionuclide	Iodine-125	Paladium-103	Caesium-131
Half-life (days)	59.4	17.0	10
Energy range (keV)	27-36	20-23	29-34

## 1.2 Statement of the problem.

The accuracy and efficiency in the treatment of prostate cancer under brachytherapy has been a topic of discussion for many decades. In brachytherapy the treatment of cancer demands very high accuracy in dose calculation and distribution with adverse radiobiological effects if there is a significant deviation from the actual prescribed dose. Although the treatment of the prostate brachytherapy has been in existence since 1901 (Degrais et al., 2006), there has not been a uniform method of defining and calculating the dose. This makes it difficult to compare values reported

by different researchers on permanent seed implants and the significant dosimetric parameters. Hence this work aims to assess the treatment planning software (TPS) by doing pre-plan implant prior to the real-time implant so as to maintain the accuracy of the dose delivered to the patients. The selection of treatment modality is based on the later advantage, therefore more research helps to produce data that will enable us to develop and utilize an optimal protocol for treatment of prostate cancer under brachytherapy in Ghana as no such work has been done before.

### **1.3 Objective of the study.**

The main objective of this work is to compare the pre-plan against real-time plan for patients undergoing prostate brachytherapy at Korle-Bu Teaching Hospital using patient images captured during pre-evaluation study prior to the order of seeds.

The specific objectives to be addressed are to:

- (i) assess the number of seeds and needles ordered from the manufacturer prior to implantation.
- (ii) assess the dose optimization prior to implant so as to speed up the implant procedure.
- (iii) check the correlation between the real-time plans and the pre-plans.
- (iv) Make the relevant recommendations to ensure patient safety during and after implant of seeds.

### **1.4 Relevance and justification.**

This work provides guidelines to prostate cancer patients treated with brachytherapy. It also help to assess the accuracy of the treatment planning system (TPS) at Korle-Bu Teaching Hospital using data and information obtained from the study.

Currently the amount of seeds to be implanted into the patient are ordered in excess from the manufacturer and this increases the cost to the patient. This pre-plan work will present the exact amount of seeds needed before the implant. Hence minimizing the cost to patients while increasing the accuracy during implant, and simultaneously minimizing the duration of implant to the theatre. Dose optimization will be achieved since the exact allocation of needles and seeds will be known as guided by the template. Finally the work will serve as a data base for prostate cancer patients at the centre.

### **1.5 Scope and delimitation.**

This study was carried out at the Korle-Bu Teaching Hospital in Accra, Ghana. The study was limited to patients who had undergone prostate brachytherapy from the period between August, 2008 to April 2013.

### **1.6 Organization of Thesis**

This research work would be in chronological order of five chapters. Chapter one focuses on overview of the current state of knowledge relevant to the study. Chapter two reviews existing literature relating to the research problem. Chapter three focuses on the material used and methodology of the study. Chapter four contains results and discussion while Chapter five, provides conclusions and recommendation from the findings.

## CHAPTER TWO

### LITERATURE REVIEW

This chapter provides an overview on prostate cancer, cancer treatment modalities, and international guidelines.

#### **2.1 Dosimetry associated with brachytherapy.**

Radiation dose roughly falls off with the inverse square of the distance from the source. Therefore placing the source very close to the target gives the target a very high dose. If some distance can be kept from neighboring normal tissue structures, then the dose will be lower there hence sparing them from injury.

##### **2.1 .1 Interstitial treatments**

The dosimetry information recommended in ICRU Report No. 58 for reporting of interstitial implant treatments consists of;

- i. A description of clinical target volumes.
- ii. The sources, technique and implant time, the total reference air kerma.
- iii. A description of the dose: prescription point/surface, prescription dose, reference doses in the central plane, mean central dose and peripheral dose.
- iv. A description of the high and low dose region and dose uniformity indices and dose–volume histograms (DVHs).

The report emphasizes the need to report, as a minimum, four different dose related quantities to adequately describe an implant treatment. In addition to the total reference air kerma, the next significant parameter is the mean central dose, which is representative of the plateau dose region inside the target volume. The minimum dose is important in tumour control — hence the need to report the peripheral dose. To help

correlate dose and any late damage, high dose regions ( $>150\%$  of the mean central dose) and low dose regions ( $< 90\%$  of the peripheral dose) are also to be reported.

### 2.1.2 Dose distributions around sources

Dose calculations are presented in this study for photon emitting sources only. The dose calculations are divided into two categories: The first category represents the AAPM TG 43 formalism, which can be considered as the most complete formalism available today. This approach is used in modern TPSs and is suitable as a method for commissioning and the second category (Independent protocol developed on the centre) may be used for quick checks and verification of treatment plans.

### 2.1.3 AAPM TG 43 algorithm

In 1995 the AAPM introduced in TG 43 a dose calculation formalism to establish the 2-D dose distribution around cylindrically symmetric sources. It is based on measured quantities such as, dose rate constant, geometry factor, anisotropy function, radial dose function and air kerma strength.

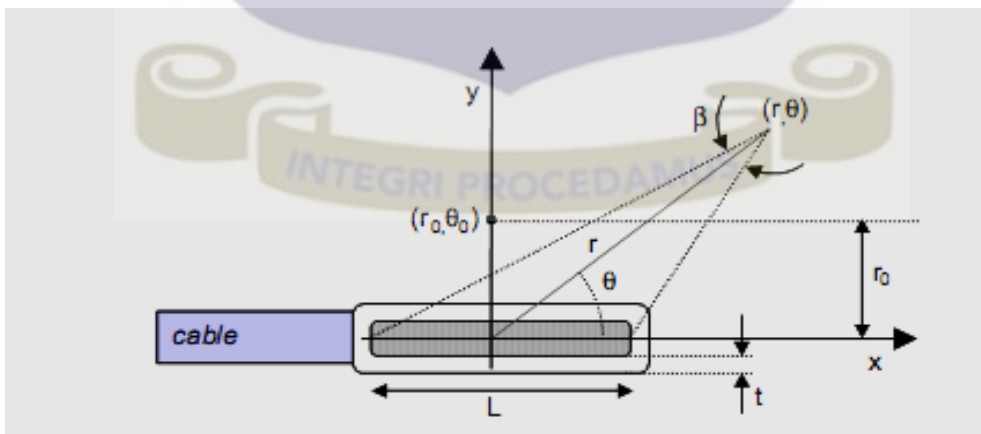


Figure 2.1: The geometry and the definitions used for the TG 43 protocol.

The quantities used in the calculation of absorbed dose in the TG – 43 formalism is measured for the specific type of source. This implies that, aside the photon spectrum and medium, the TG – 43 depends on source construction and geometry as well. Figure 2.1 summarizes the geometry and coordinate definitions used in the TG 43 dosimetry protocol. A source of an active length,  $L$ , the encapsulation geometry and the guidance wire are shown. This is the usual configuration of a PDR iridium source. The origin of the coordinate system is positioned at the centre of the active core of the source. The z-axis is along the tip of the source. A cylindrical symmetry for the activity distribution within the core is here assumed. The point of interest,  $P$ , is at a radial distance,  $r$ , from the origin and has a polar angle coordinate,  $\theta$ , in the cylindrical coordinate system.

According to the protocol, the dose rate at a point  $P(r, \theta)$  in water can be expressed as

$$\dot{D}(r, \theta) = S_K \Lambda \frac{G(r, \theta)}{G(r_0, \theta_0)} g(r) F(r, \theta) \dots \dots \dots 2.1$$

Where  $r$  is the distance from origin to the point of interest  $P$ , and  $\theta$  is the angle with respect to the long axis of the source, as shown in Figure 2.1  $\theta_0$  defines the source transverse plane and is equal to  $\theta/2$  radians,  $S_k$  is the air kerma strength of the source,  $\Lambda$  is the dose rate constant in water,  $G(r, \theta)$  is the geometry function,  $g(r)$  is the radial dose function, and  $F(r, \theta)$  is the anisotropy function (Ravinder and Jeffrey, 1995).

## 2.2 Radioisotopes used in prostate brachytherapy.

### 2.2.1 Classification of brachytherapy sources.

Brachytherapy developed largely through the use of sealed radium and radon sources. In the 1950s, alternative artificially produced nuclides became available, and gradually radium and radon were replaced with  $^{137}\text{Cs}$ ,  $^{192}\text{Ir}$ ,  $^{60}\text{Co}$ ,  $^{198}\text{Au}$ , and  $^{125}\text{I}$  sources (Godden, 1988). Although radium and radon are no longer used, many of the techniques that are used currently are based on the clinical experience gained with those sources over more than sixty years. Brachytherapy sources are classified into three categories, the first category is based on source loading where we have hot loading (LDR only such as  $^{125}\text{I}$ ,  $^{131}\text{Cs}$  and  $^{103}\text{Pd}$ ) sources and after loading (both HDR & LDR are applicable) sources. The second category is based on the treatment duration which specifies the temporally dose rate and permanent dose rate. The third category is named with respect to dose rate as high dose rate sources (HDR) in which high energy photons emitters such as  $^{192}\text{Ir}$ ,  $^{98}\text{Au}$ ,  $^{137}\text{Cs}$  and  $^{60}\text{Co}$ , are used.

**Table 2.1: Brachytherapy treatments classified with respect to dose rate (Podgorsak et al., 2005).**

Dose rate	Numerical value of the dose rate at the dose specification point(s)
Low dose rate (LDR)	0.4–2 Gy/h
Medium dose rate (MDR)	2–12 Gy/h
High dose rate (HDR)	>12 Gy/h

Brachytherapy sources are available in various forms such as seeds, wires, needles and pellets. They are commonly used as sealed sources. The sources are doubly encapsulated in order to provide adequate shielding against the alpha ( $\alpha$ ) and beta ( $\beta$ )

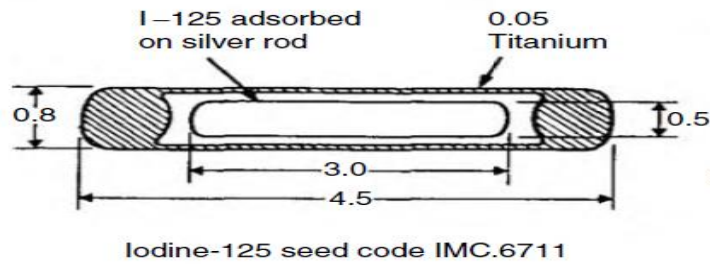
radiation emitted from the source and to prevent any leakage of the radioactive material.

### **2.2.2 Description of brachytherapy sources used in prostate cancer.**

The use of radioactive material for diagnostics and therapy purpose has been in the field of medicine since the 19<sup>th</sup> century, however more innovations came up along the way since some of the radioactive sources have very long half-life and higher energy hence not suitable for clinical use and difficult for radiation protection. Thus, it is necessary to have a detailed description of these radioisotopes. The commonly prostate brachytherapy sources are described in the next sections.

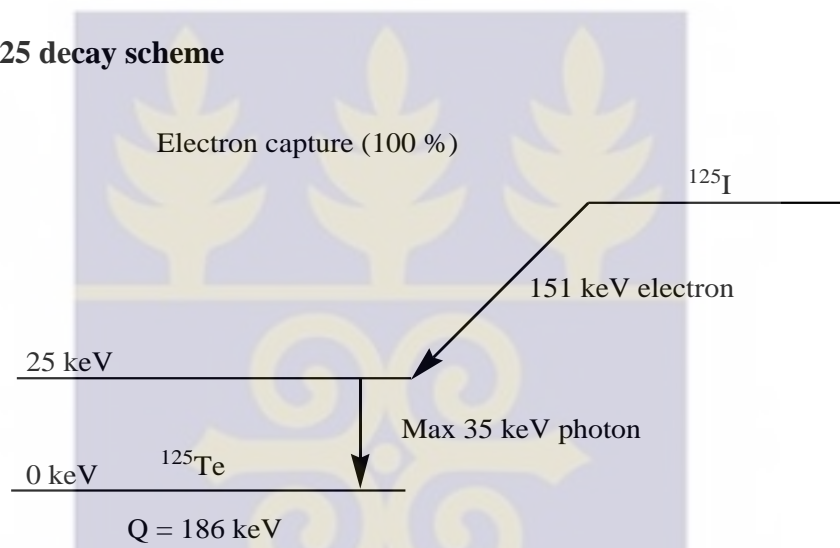
#### **2.2.2.1 Iodine-125.**

$^{125}\text{I}$  decays exclusively by electron capture to an excited state of  $^{125}\text{Te}$ , which spontaneously decays to the ground state with the emission of a 35.5 KeV photon (Figure 2.3). Characteristic x-rays in the range of 27 to 35 KeV also are produced due to the electron capture and internal conversion processes (Khan, 2003). The isotope is produced by thermal neutron irradiation of  $^{124}\text{Xe}$ ; activity concentrations as high as  $3.7\text{ GBq mm}^{-3}$  can be obtained by encapsulating an iodide-activated ion exchange bead (Mayles et al., 2007). Titanium encapsulation serves to absorb liberated electrons and x-rays with energies less than 5 KeV. The model 6711 seed emits two additional photons at 22.1 KeV and 25.2keV energies. These are fluorescent (characteristic) x-rays produced by the interaction of  $^{125}\text{I}$  photons with the silver wire (Khan, 2003). When implanted to the patients, it takes 204 days for 90% of the prescribed dose to decay (Rivard et al., 2007). Figure 2.2 shows the structure of I-125 seeds with its encapsulation.



**Figure 2.2:** An example of I-125 seeds 6711 model used currently for prostate brachytherapy implant (Mayles et al., 2007 ). The seeds used at KBTH are supplied by BARD Company from USA

### Iodine-125 decay scheme



**Figure 2.3:** The decay scheme of I-125 (Nucleide, 2013).

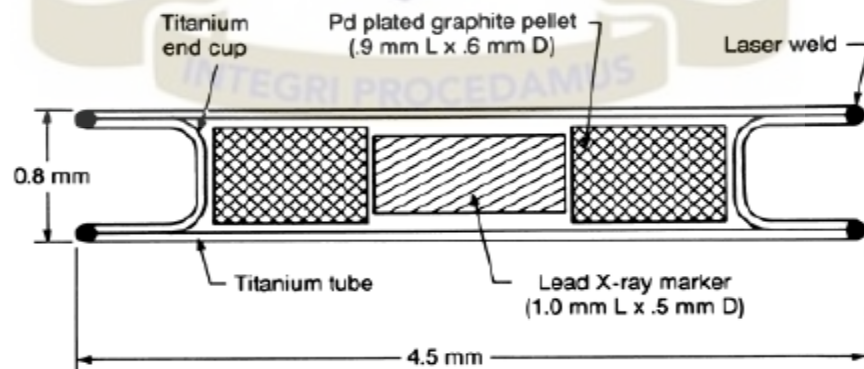
#### 2.2.2.2 Iridium-192.

$^{192}\text{Ir}$  has a half-life of 73.8 days and emits gamma photons with energies ranging from 9 KeV to 884.5 keV, but the weighted average energy of a  $^{192}\text{Ir}$  brachytherapy source is 397 keV (Goetsch et al., 1991). With a high maximum-activity concentration of  $330 \text{ GBq mm}^{-3}$ ,  $^{192}\text{Ir}$  is suitable for high-activity afterloading sources; it is also available in the form of seeds and flexible wires. In wire form it is produced by reactor irradiation of 75%/25% iridium/platinum alloy which is usually provided as wire, clad with 0.1 mm of pure platinum. Pure iridium is very hard and

brittle, and is difficult to fabricate. The iridium/platinum wire is available with 0.3 mm and 0.6 mm overall diameter. European manufacturers also produce wires with a 0.5 mm diameter. The wire should be cut to the required length by means of special cutters which are designed to minimise particulate contamination. For clinical use, wires are often sheathed in plastic tubing.

### 2.2.2.3 Palladium-103.

$^{103}\text{Pd}$  seed has a half-life of 17 days, It decays by electron capture with the emission of characteristic X-rays in the range of 20 to 23 Kev (average energy of 20.9 Kev) and Auger electrons (Khan, 2003). The palladium-103 seed model 200 consists of a laser-welded titanium tube of 0.8 mm diameter and 4.5 mm long, containing two graphic pallets plates with laser welded end caps. The lead marker between the pallets provides radiographic identification. Absorption of incident photons by the titanium wall and the lead marker, and the self-shielding by palladium, result in an anisotropic emission pattern with an axial fluence much lower than the fluence along the transverse axis (Chiu-Tsao and Anderson, 1991). Figure 2.4 shows the structure of palladium-103 seeds with its encapsulation.



**Figure 2.4: Schematic diagram of palladium-103 seeds (200 model)**  
(Mayles et al, 2007).

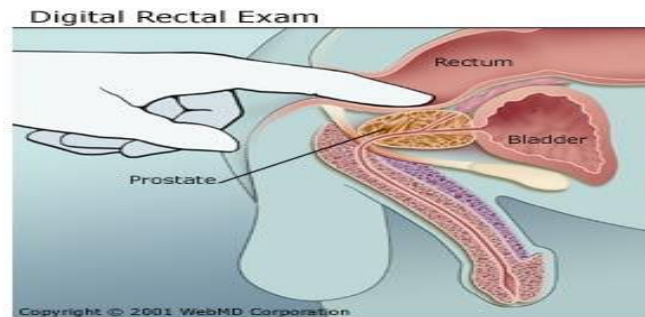






### 2.3.3 Digital Rectal Examination (DRE)

A digital rectal examination (DRE), performed as part of an annual physical check-up, is one of the most important tests for the early detection of prostate cancer. Because the prostate gland is located just in front of the rectum, it cannot be felt from the outside of the body.



**Figure 2.5: Demonstration on how digital rectal examinations (DRE) are taken (Wax, 2012)**

During the DRE, a doctor inserts a lubricated, gloved finger into the patient's rectum to feel for lumps, enlargements, or areas of hardness that might indicate prostate cancer. The procedure lasts for less than minute and, while uncomfortable, should cause no pain. However, a painful examination could indicate the presence of other, benign conditions, such as prostatitis. To help detect prostate cancer in its early stages, the American Cancer Society recommends that men talk to their doctors about the benefits, risks, and limitations of prostate cancer screening before deciding whether to be tested. For most men at average risk, screening is started at age 50. However, some doctors recommend that men at higher risk of prostate cancer - African-American men or men with a family history of prostate cancer start screening earlier. The American Urological Association (1997) recommends a first-time test at age 40, with the schedule of follow-up testing to be determined on an individual basis.











































































































































































































