DOSIMETRY VERIFICATION FOR HIGH DOSE RATE BRACHYTHERAPY OF CERVICAL CANCER USING CO-60 SOURCE AT THE KORLE-BU TEACHING HOSPITAL

A THESIS PRESENTED TO THE UNIVERSITY OF GHANA, LEGON IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF MASTER OF PHILOSOPHY DEGREE

BY

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DECLARATION

Student's Declaration:

I hereby declare that, with the exception of references to other people's work which have been duly acknowledged, this work is the result of my own research undertaken under supervision, and either in whole or in part has not been presented for any other degree at another university elsewhere.

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ABSTRACT

Transition from the low dose rate brachytherapy to high dose rate brachytherapy at the National Center for Radiotherapy and Nuclear Medicine, Korle-Bu Teaching Hospital, Accra, Ghana necessitated the performance of dose verification test, which serves an end-to-end quality assurance procedure to verify and validate dose delivery in intracavitary brachytherapy of the cervix and the vaginal walls based on the Manchester system. An in-house water phantom was designed and fabricated from Perspex (poly methyl acrylate) sheets to represent the cervix region of a standard adult patient. The phantom was used to verify the whole dose delivery chain such as the calibration of the cobalt -60 source in use, applicator and source localization method, output of treatment planning with the dedicated treatment planning system and the actual dose delivery process. Since the above factors would influence the final dose delivered, doses were measured at various points within the in-house phantom for a number of clinical implants that were likely to be used to treat a patient based on departmental protocol. The measured doses were compared to those of the treatment planning system. The various implants were immersed into the phantom filled with water, and the doses were measured with samples of calibrated Gafchromic EBT3 films. The Gafchromic film was calibrated against output of a 0.6 cc cylindrical ionization chamber having traceability to a secondary standard dosimetry laboratory with beams from a cobalt-60 teletherapy machine using the International Atomic Energy Agency technical report series 398 protocol. The discrepancies between the measured doses and their corresponding calculated doses obtained with the treatment planning system ranged from - 28.75% to 42.19% (mean of ±12.50). These compared favourably well with those reported in other related publications.

DEDICATION

I first and foremost dedicate this study to God Almighty. Secondly, to my mother Madam Georgina Afeafa Sapaty for the support she is shown me throughout my study.

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To God is the glory for His strength, wisdom, protection, guidance and divine favour given me throughout this research study to reach a successful end.

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ABBREVIATION

AAPM	American Association of Physics in Medicine
BIPM	Burreau International de Poids et Mesure
BT	Brachytherapy
Co-60	Cobalt-60
CT	Computed Tomography
Cs-137	Cesium-137
EBRT	External Beam Radiotherapy
Gy/h	Gray/hour
HDR	High Dose rate
IAEA	International Atomic Energy Agency
ICBT	Intracavitary Brachytherapy
ICRP	International Commission on Radiological Protection
ICRU	International Commission on Radiation Units and Measurements
Ir-192	Iridium-192
ISBT	Interstitial Brachytherapy
IVD	In vivo dosimetry
KBTH	Korle-Bu Teaching Hospital
LDR	Low Dose Rate
MBDCA	Model based dose calculation algorithm
MBq	Megabecquerel

MDR	Medium Dose Rate
MeV	Mega-electron Volts
MOSFET	Metal-oxide semi-conductor-field-effect-transistor
MP1	One dimensional water phantom
MR	Magnetic Resonance
NCRNM	National Center of Radiotherapy and Nuclear Medicine
NIH	National Institute of Health
OAR	Organ at Risk
PDR	Pulse Dose Rate
PMMA	Poly-methyl methacrylate
QA	Quality Assurance
QC	Quality Control
ROI	Region of Interest
SSD	Source to skin distance
Sv	Sievert
SSDL	Secondary Standard Dosimetry Laboratory
TLD	Thermoluminescence dosimeter
TPS	Treatment Planning System
TG	Task Group
USA	United States of America

CHAPTER ONE

INTRODUCTION

1.1 Background

Brachytherapy (BT) has become the fundamental treatment approach in the treatment of early tumour in several countries. Brachytherapy is a radiation therapy treatment modality commonly used for the treatment of cancer. The term 'brachy' implies short distance treatment as opposed to external beam radiation therapy (EBRT), or teletherapy, where treatment is delivered from a distance.

The practice of brachytherapy first began following the discovery of radium by Marie Curie in 1898, where patients were treated using small quantities of radium placed on or implanted into tumours (Wilkinson, 2013; Golden, 1988). Brachytherapy has evolved over the years with the introduction of a variety of new radionuclides for brachytherapy, the use of remote after loading units and computer based dose calculation systems.

The electronic brachytherapy which is a latest technological BT model uses a smaller electronic X-ray source which generates radiations with low energy at a high dose rate.

Brachytherapy makes use of discrete, encapsulated gamma sources that can be placed into or immediately adjacent to the tissue to be treated, allowing the delivery of a highly localized radiation dose in the tumour. The intensity of the source decreases according to the inverse square law resulting in a rapid dose fall off at short distances from the sources. The significance of the rapid dose fall off in brachytherapy is that a highly

localized dose can be delivered directly to the tumour, while the surrounding normal tissue receives only a small fraction of the total dose. For this reason, brachytherapy allows higher doses per fraction to be delivered to the tumour (Wilkinson, 2013). In brachytherapy, most radionuclides used are photon emitters however; beta or even neutron emitting sources are also used for source applications.

There are several sources that depicts that BT treatment results in the minimization of tumour occurrence and improves the rate of survival (Eifel et al, 1994). For BT treatment to meet its set targets, there is the need to increase the dose to the tumour volume and reduce the chance as low as possible to the surrounding normal tissues.

Brachytherapy is classified on the basis of source placement, intensity of radiation and duration. With source placement, brachytherapy is divided into interstitial and intracavitary. Interstitial brachytherapy (ISBT) is when the source is placed directly in the target tissue of the site, example, is used for breast and/or for prostate. For intracavitary brachytherapy (ICBT), the radiation source is placed next to the affected tissue. ICBT could be further divided into;

a. An intracavity placement such as in uterus, cervix or vagina

b. An intraluminal placement as in oesophagus or trachea

c. A surface placement such as in the skin

d. An intravascular placement for coronary in-stent restenosis.

Low dose rate (LDR), medium dose rate (MDR), and high dose rate (HDR) are the three BT procedures classified based on intensity of radiation given. Dose rate refers to the

amount of dose given per time. The unit of measurement for dose rate is Gy/h. The LDR BT is a brachytherapy modality where less than 2 Gy/h rate of dose is delivered. Several tumours are treated using LDR BT. Among these tumours include cancer of the oral cavity, prostate, oropharynx and sarcomas. Medium dose rate BT emit doses at a rate between 2 Gy/h and 12 Gy/h. For HDR BT, the rate of dose is more than 12 Gy/h. This BT approach (HDR BT) is used to treat several tumours. They include tumours of cervix, prostate, lungs and breast. Brachytherapy can be classified in two ways based on treatment duration. These are permanent brachytherapy and temporary brachytherapy. Permanent BT is an approach of treatment where implants containing sources are permanently placed into tumour targets (area of treatment). Prostate tumour is one of the fundamental tumours being treated through this BT approach. For temporary BT, the implants are placed at the affected area of treatment for a shorter period of time compared to the permanent BT.

High dose rate (HDR) brachytherapy is now widely accepted in the treatment of cancer. The HDR BT has a unique advantage over the LDR BT, such that the former (HDR) is used to treat a lot more patients. This feature of the HDR BT enables it to be used in clinical centers with less facilities. Before, the Iridium-192 (Ir-192) was recognizably used for HDR procedures than the cobalt-60 source because smaller amounts of Ir-192 were produced for BT insertions (Chao et al., 2000).It is now possible to produce smaller sizes of cobalt-60 sources for HDR applications. The dosimetric and physical features of the smaller sized cobalt-60 has been shown to compare with Ir-192 (Ballester et al, 2005).

Many areas of BT should be considered when giving BT treatments. Among these is the quality assurance/control done during everyday BT treatment to ensure optimal

treatment delivery process. In BT treatment, errors may occur at times which has adverse effects on the overall treatment outcome; no matter the level of errors. The error types during brachytherapy treatments and their occurrence rates are not well known. The type of treatment errors that occur in BT dose delivery and how these errors occur are not well identified. The lack of knowledge is due to the fact that when treatment is in progression, there are no independent verification systems. There are uncertainty factors that do also occur during BT procedure; these include the source calibration uncertainty, source-to-detector uncertainty and organ-applicator movement uncertainty. The presence of these uncertainties and probable errors have adverse effect on the treatment delivery process. As a result of these, there are the need to develop QA protocols within the BT set up to boost the confidence in the treatment delivery process.

Brachytherapy treatment in Ghana has evolved from the use of LDR systems to HDR, particularly at the National Center for Radiotherapy and Nuclear Medicine (NCRNM), Korle-Bu Teaching Hospital (KBTH). Modern brachytherapy is increasingly based on remote afterloading (for HDR BT), the use of three-dimensional imaging and treatment planning systems (TPSs). These developments have reduced manual procedures, which are well known to be the most frequent sources of errors (Lopez et al, 2000; World Health Organisation, 2008).

In the 1930, before the introduction of planning computers, treatment planning was carried out by following a set of rules according to dosimetry systems, such as Manchester system (Tod and Meredith, 1938). In spite of this, manual procedures such as catheter applicator insertion, treatment planning and treatment delivery is used in BT

than in EBRT. Also, verification systems are less advanced in BT than in EBRT. Therefore, BT may be more prone to errors than in EBRT (Kertzscher et al, 2014).

Technological advances in afterloading of computerized planning using planar radiographic imaging were being implemented in an attempt to verify the applicator or catheter positions and calculate patient specific dose. Alongside these advances, the need to compare patient's treatment with those from other treatment centers were being recognized as an important scientific standardization of treatment (ICRU 38 Report, 1985; ICRU 58 Report, 1997). However, this study highlights quality assurance protocols and the confidence that comes with it in ensuring highly accurate and precise dose delivery during the HDR BT procedure at NCRNM.

During treatment of patients, the radiation oncologist prescribes a treatment which is intended to cure or control the disease while minimizing complication to healthy tissues. The planning team relies on published clinical and experimental results to know that the response to radiation by tumour and normal tissues are different. With every detected tumour, there are surrounding tissues and their tolerance level to radiation. The gap for optimal treatment in brachytherapy can be quite narrow therefore the radiation dose must be delivered accurately and precisely. The International Commission on Radiation Units and Measurements recommends that the dose delivered should be within an allowable margin of error of the prescribed dose (ICRU 24 Report, 1976).

1.2 Statement of Problem

The aim of radiotherapy is to give maximal dose to the tumour whilst reducing dose as much as possible to the normal surrounding tissues. Treatment delivery set targets are tempered when the dose delivered does not get to the required affected area (tumour target). During radiation treatment, the prescribed dose and irradiation geometry must be translated into physical machine and beam parameters. An error in the calculations or machine settings can have adverse effect on the intended treatment outcome. After the change of the use of a LDR machine to a HDR system at the NCRNM, there is the need for quality assurance on brachytherapy procedures to boost the confidence level on the accuracy of dose delivery. The change in source type from cesium-137 (Cs-137) to cobalt-60 (Co-60) and the mode of treatment calls for the need to review some parameters used in cervical cancer BT treatment. Moving from a type of machinery requires a lot of quality assurance checks and dosimetric quantity evaluation which justifies the need to develop BT treatment for cervical cancer protocols for accurate and precise dose delivery and treatment planning to meet clinical needs.

This study is targeted at using a locally fabricated water phantom to aid in the studies of

a. The dosimetry aspects (dose calculation, accuracy of dwell positions, beam calibration and dose distribution of the BT system.

b . Treatment planning dose verification with estimated doses.

1.3 Research objectives

The main goal of this study is to develop and implement a dosimetry protocol to bring about an accurate and precise dose delivery in BT at the NCRNM. The study is focused

on the dosimetry verification of HDR BT for cancer of cervix using Co-60 source. The specific objectives are to design and fabricate a water phantom to aid in the following;

a. The dosimetry aspects of the HDR Co-60 BT system

b. Treatment planning dose verification with estimated doses.

1.4 Relevance and Justification of Research

The HDR unit at the NCRNM is situated in a well-shielded room where necessary procedures needed for its commissioning were met. This work was aimed at building a baseline for the operation and to enhance the treatment planning outcomes. The work is aimed at meeting the clinical need of assuring accurate and precise dose delivery in the hospital. Accuracy evaluation is a necessity in radiation treatment as a whole because radiation delivered during patient treatment is irreversible. The building of a water phantom was to assess and verify dosimetric quantities that play an important role in error detection.

The QA program is targeted at the advancement of BT verification systems and improvement of QA and quality control (QC) measurements used in cervical cancer BT.

The findings of this research work serve as a guide and protocol for oncologists, radiographers, medical physicists, dosimetrist and other related medical professionals at the Korle- Bu Teaching Hospital (KBTH).

The International Atomic Energy Agency (IAEA) has projects among its member States including Ghana that seeks to strengthen radiological protection of patients; hence findings from this study will be of relevance nationally and internationally.

1.5 Scope and delimitation

This work was carried out at KBTH in Accra, Ghana. It was limited to HDR cervical cancer brachytherapy system at the radiotherapy department of the hospital.

The research and protocol development included calibration of gafchromic EBT3 film for dose measurement, measured dose verification and calculated dose verification.

1.6 Organization of thesis

This research work write up covers five chapters. Chapter one focuses on the introduction to the study. Chapter two reviews existing literature relating to the research problem.

Chapter three focuses on the materials and methodology of the study. Chapter four contains the results and discussions, while chapter five provides the conclusions and recommendations from the research findings. The references section contains all the relevant works cited throughout the thesis.

CHAPTER TWO

LITERATURE REVIEW

This chapter focuses on the review of existing literature relevant to this research work.

2.1 High dose rate brachytherapy compared with Low dose rate brachytherapy

There is the need to know which brachytherapy procedure to use (whether LDR or HDR) before starting any BT procedure. Historically, LDR sources were exclusively used for cervical BT which made patients to be immobilized for longer hours running into days. However, HDR became increasingly adopted since the early 2000s. The HDR BT allows for the protection of personnel during treatment delivery procedure and avoids patients being hospitalized for long (Wang et al, 2010 ; Park et al, 2002).

2.2 Errors and uncertainties during HDR BT treatment

During everyday BT treatments, there are possibilities of errors and uncertainties which have adverse effects on the overall treatment outcome. As a result of this, there is the need for quality assurance procedures to be done to boost the confidence in the treatment delivery process.

2.2.1 Errors during HDR BT

The knowledge about BT treatment errors comes from published reports (Lopez et al, 2000; Ashton et al, 2004) and databases, such as radiation oncology safety information system (ROSIS), safety in radiation oncology (SAFRON) (Holmberg et al, 2010; IAEA,

2014) and irradiation accidents (ACCIRAD), and is limited to the information that clinics are willing and able to share. As demonstrated through phantom and computer-simulated error scenarios (Andersen et al, 2009; Therriault-Proulx et al, 2011; Kertzscher et al, 2014; Kertzscher et al, 2011), several of the reported BT error types could have been detected with real-time in vivo dosimetry, for example, for the reported case of an HDR unit malfunction, where the BT source had broken loose from the guide wire and remained inside the patient (Cunningham et al, 2010). If real-time in-vivo dosimetry (IVD) was more frequently implemented in the clinical workflow routine, in addition to consensus recommendations for image-guided BT (Haie-Meder et al, 2005; Hellebust et al, 2010; Potter et al, 2006; Dimopoulos et al, 2012), our knowledge about BT errors and their occurrence rates could improve, provided the reporting is open and honest.

2.2.2 Uncertainties during BT

Uncertainties cover various aspects of BT treatment workflow. Uncertainties related to treatment planning arise partly from source calibration uncertainties (DeWerd et al, 2011) and imperfections of the dose calculation protocols. Present treatment planning systems (TPSs) incorporate the American Association of Physicists in Medicine Task Group (TG)-43 dose calculation protocol, (Rivard et al, 2004), which assumes that a patient is made of water and disregards tissue heterogeneities and inter-source dose attenuation. In addition, present TPSs are subject to uncertainties related to source parameters and the implementation of dose calculation protocols (DeWerd et al, 2011; Rivard et al, 2004). Treatment planning uncertainties are further enhanced by inter-observer variability in the volumetric delineation of clinical targets and organ at risk (Kirisits et al, 2007; Hellebust

et al, 2012; Petric et al, 2013) and by systematic effects of source positioning and applicator reconstructions (Hellebust et al, 2007; Hellebust et al, 2010).

Shortcomings of the TG-43 dose calculation protocol (Rivard et al, 2004) are targeted by developments of model-based dose calculation methods, which is in contrast to the TG-43 account for tissue heterogeneities and individualized patient anatomy (Beaulieu et al, 2009).

Although dosimetric uncertainties in BT have been well described, there has been a limited overview of how the impact of clinical uncertainties relate to, for example, contouring, treatment planning and organ movements affect the treatment outcome. However, recently, a number of investigations have been published, which improve the possibilities to describe BT uncertainty budgets that encompass the entire treatment workflow from source calibration to treatment delivery (Tanderup et al, 2013; Kirisits et al, 2013). These investigations point towards the importance of geometric variations induced by organ and applicator movements (Nesvacil et al, 2013) which complicate and potentially compromise accumulated dose calculations in the organs. The AAPM TG 46 recommendation declared an uncertainty of ±15% in the delivery of dose for intracavitary brachytherapy (Hanson et al., 1994).

Inter- and intra-fraction deformations of prostate, bladder and rectum have been studied (Buchali et al, 1999; Cherpak et al, 2013), and the dosimetric impact owing to more general anatomical variations has been evaluated in a multicenter comparison of cervix BT (Nesvacil et al, 2013). Organ-applicator movements occurring between patient imaging and treatment delivery stages have been identified as a major source of

uncertainty (DeLeeuw et al, 2009; Hoskin et al, 1996; Beriwal et al, 2009) and their impact further analysed (Anderson et al, 2013; Rey et al, 2013). In cervical cancer BT, inter- and intra-fraction uncertainties owing to organ movements and deformations account for 20-25% of the minimum dose to the most irradiated 2 cm^3 per fraction and is the most essential component in the uncertainty budget for organs at risk (OARs) (Tanderup et al, 2013).

2.2.3 Fixed and statistical discrepancy criterion

Errors may be declared if monitored treatment parameters, for example, measured dose rates or source positions, differ from expected values by a pre-defined fixed discrepancy level. Such fixed discrepancy criteria have been implemented during patient measurements and phantom experiments (Waldhausl et al, 2013; Therriault-Proulx et al, 2011). Waldhäusl et al, (2013) performed IVD in the rectum and bladder during intracavitary BT and compared measured and expected doses calculated based on image reconstructed distances between the source applicators and dosimeter probe positions and the dwell times defined in the treatment plan. The BT treatments were investigated in detail if measured and expected doses differed by >10%. Therriault-Proulx et al, (2011) simulated real-time IVD in the rectal wall and urethra during phantom experiments of HDR BT treatment plans where positioning errors were imposed. The numbers of true and false errors detected were investigated for individual source dwell positions for fixed discrepancy criteria between 3% and 20%.

For statistical based discrepancy criteria, the discrepancy between measured and expected treatment parameter values is expressed in terms of all known sources of uncertainty, for example, the number of measured and calculated standard uncertainties added in quadrature. The dominating source of uncertainty in BT is the positional uncertainty (Andersen et al, 2009; Kertzscher et al, 2011), which depends on the source-to-detector distance, and should therefore not be excluded from the uncertainty budget.

Andersen et al, (2009) performed real-time IVD in the tumour region during interstitial pulsed dose rate (PDR) BT for cervical cancer and compared measured dose rates with calculations based on the treatment plan. The comparison was based on the statistical discrepancy criterion, which declared a treatment error if the dose rate difference was >2.58 standard deviations, which corresponded to a *p*-value of 0.01. Similar concepts have been implemented during phantom measurements (Therriault-Proulx et al, 2011; Therriault-Proulx et al, 2013; Reniers et al, 2012; Kertzscher et al, 2011; Able et al, 2013). Nakano et al, (2003) adapted statistical based discrepancy criteria during phantom experiments using HDR BT sources, where the discrepancy was based on measured and expected source coordinates rather than on dose rates.

2.2.4 Optimal error detection criterion

In BT, the relative magnitudes of measurement and positional uncertainties depend on the source-to-detector distance (Andersen et al, 2009). For instance, dose rate uncertainties for individual source dwell positions may range between 3% and 26% in a single treatment plan owing to the impact of the positional uncertainties for the source and

dosimeter probe (Kertzscher et al, 2011). Fixed discrepancy criteria would declare an error whenever the discrepancy between measured and expected treatment parameter values exceed the pre-defined limit, for example, 10%. As by stated (Kertzscher et al, 2011) such an error criterion is more susceptible to false-positive error declarations when the source-to-detector distance is small and where the uncertainties are potentially >10% and to false-negative error declarations when the distance is large and the uncertainties are potentially <10%. As a result, statistical discrepancy criteria provide more confidence in the error declaration for IVD during BT than do fixed discrepancy criteria.

Error criteria based on treatment progression snapshots would be able to detect potential treatment errors that have occurred up to the instance of monitoring and would not be sensitive to errors that could occur at a later stage during treatment. Real-time IVD can monitor the agreement between measured and planned parameter values, hence statistical discrepancy criteria would be more suitable for BT than would treatment progression snapshots.

Treatment errors could be declared if too large doses were measured at International Commission on Radiation Units and Measurements (ICRU) reporting rectal and bladder points (Chassagne et al, 1985; Potter et al, 2011). For instance, a statistical discrepancy criterion could be defined in order to monitor the dose at reporting points. However, dose estimates at ICRU reporting points have been shown to be unreliable given practical difficulties to position the dosimeter probe accurately in the steep dose gradient regions (Waldhausl et al, 2013; Clark et al, 1994; Datta et al, 2003). A further argument against error criteria based on dose rates at ICRU reporting points is that modern BT is adapting

volumetric dosimetry during treatment planning (Pelloski et al, 2005; Tanderup et al, 2010).

2.3 Radionuclides used in HDR brachytherapy

For HDR cervical brachytherapy, there are two radionuclides that can be used, the Ir-192 and the Co- 60 source. The Ir-192 used to be mostly used for HDR BT. Recently, cobalt-60 has emerged to be used since its geometric and physical features compare well to Ir-192 source. In low resource settings like what we have in Ghana at NCRNM, and to the relevance of this paper Co-60 is more economical due to its long half life and as such is the main source used at the Center (NRCNM).

2.3.1 Iridium - 192 source

Iridium - 192 has a half life of 73.8 days and 4.7% decays through electron capture and 95.3% through beta - minus transitions, followed by gamma transitions and K - and L - shell x-rays. The weighted average energy of an Ir - 192 brachytherapy source is 397kev (Goetsch et al, 1991). With a high maximum - activity concentration of 330 GBqmm^{-3}, Ir-192 is suitable for high - activity afterloading sources; it is available in the form of seeds and flexible wires. In wire form it is produced by reactor irradiation of a 75% / 25% iridium / platinum alloy, which is usually provided as a wire, clad with 0.1 mm of pure platinum. The iridium / platinum wire is available with 0.3mm and 0.6mm overall diameter.

2.3.2 Cobalt - 60 source

The earlier sizes of cobalt-60 was larger than Ir-192 and as a result of that, was not really in use as it is now. Smaller sizes of cobalt-60 sources are produced currently which has similar geometric and physical characteristics as Ir-192 (Ballester et al, 2005).

Co-60 is now considered to be the choice for treating several tumours. These include tumours of the cervix, prostate, breast, skin and other parts of the body.

The mean energy of cobalt-60 is 1.25 MeV compared to 0.39 MeV of Ir-192. Due to this, treatment delivery with cobalt-60 results in less dose to organ at risk since there is less scatter. The NCRNM at the Korle - Bu Teaching Hospital (KBTH) uses Co- 60 as the source for therapy as indicated above.

A radioactive isotope that has high activity is needed to achieve HDR and small source size essential for intracavitary and interstitial brachytherapy. Cobalt is used because of its high activity of 74 GBq with air kerma rate constant of 0.306 μ $Gym^2/h/MBq$ (Michael et al, 2012). Most HDR have the same active source length approximately 3.5 mm, and an active diameter of 0.5 mm. The encapsulated source is approximately 5 mm long (some sources may be up to 10 mm long) and less than 1.5 mm in diameter. The source is welded to the end of a drive cable that is transferred to dwell positions in the applicators and held in place for programmed duration using motor driven system.

2.4 Source localization and real-time applicator construction

Time-resolved source localization methods have been developed for the localization of moving sources and BT seeds by means of real-time dosimetry technology (Tanderup et

al, 2006; Therriault-Proulx et al, 2013; Cartwright et al, 2010; Nakano et al, 2003; Nakano et al, 2005). These methods are mainly used for BT QA protocols, although some of them have also been implemented for real-time IVD probes during phantom experiments.

3D localization of a moving Ir-192 HDR BT source was performed in a water phantom by Therriault-Proulx et al (2013), with single fibre three-point mPSD and an algorithm based on the weighted dosimeter light outputs of the individual scintillator elements. The parallel dosimeter probe and source catheters were positioned from 1 to 5 cm in the radial direction, and the source dwelled at positions along the longitudinal detector axis. The source localization accuracy was better than 1 and 2 mm from 69% and 87% of the dwell positions, respectively. Furthermore, the mPSD measured the uncertainty of the source position in the longitudinal direction to be 0.32 ± 0.06 mm in the fixed water phantom geometry, leading to the conclusion that 0.5 mm lower limit of source localization accuracy should be expected when using this technique in vivo.

Source localization techniques have been employed for BT QA protocols (Rosenfeld et al, 2004; Duan et al, 2001; Espinoza et al, 2013; Batic et al, 2009), however they have an interesting potential for IVD implementations in BT with the state of the art dosimetry technology and should therefore be further investigated. For instance, Nakano et al (2003) suggested methods of backscatter and tissue heterogeneity corrections using multiple dosimeter points, which could be relevant if the dosimeter probe had been calibrated under irradiation conditions significantly different from the in vivo scenario.

Palvolgyi (2006) used multi-parametric fit techniques (Nelder and Mead, 1965) to develop methods to reconstruct intracavitary and interstitial applicators. The techniques were based on pre-determined applicator template files and specific reference points of the applicators (for example tandem tips and needle base) identified with C-arm radiograph. The same techniques could be employed for source applicator reconstructions if source localization coordinates in individual applicators acquired with real-time IVD were used as applicator reference points. Therefore IVD could potentially provide an independent verification of target-applicator reconstruction uncertainties in the treatment planning (Tanderup et al, 2006).

2.5 Dosimeters used in HDR QA

A dosimeter is used to detect the amount of radiation delivered to a system. It is used as a measurement tool in medical facilities and for human radiation protection. Reliable comparative dosimetry data is of significant importance for the purpose of clinical quality control. There are various studies done using several different detectors such as semi-conductor dosimeter(diodes and metal-oxide semi-conductor-field-effect-transistor), thermoluminescence dosimeter (TLD), fibre-coupled dosimeter, ionization chamber, radiometric films (gafchromic film) etc.

2.5.1 Semi-conductor dosimetry

Semi-conductor dosimetry in BT, as in EBRT, is based on diodes and MOSFET detectors. Diodes have been incorporated for IVD during BT (Waldhausl et al, 2005;

Tanderup et al, 2006; Seymour et al, 2011; Alecu and Alecu, 1999), in the bladder (3-mm outer probe diameter) and/ or rectum (7-mm outer probe diameter) manufactured by PTW Fruiberg, Freiberg, Germany. Compared with diode-based dosimeters, the MOSFET detector is a relative new dosimeter technology in RT. MOSFET detectors are based on miniature n-or p-type silicon devices with small dosimetric sensitive volumes, of submicron thickness. The small sensitive volume allows for dosimetry in steep dose gradients as well as cases of electronic disequilibrium, which are common conditions in BT. It also allows for the construction of small dosimeter probes with approximately 1.3-mm outer diameters that can fit inside small catheters in or near the tumour region.

Common disadvantages of semi-conductor dosimeters are temperature and energy dependences in radiation fields.

The temperature dependence of diodes has been reported to range between 0% $K^{-1}$and 0.6%K^{-1}(Walhausl et al, 2005; Van Dam et al, 1990; Grussel and Rikner, 1986). Temperature instability in MOSFETS can be compensated electronically by using a read out current corresponding to the thermostable point (Buehler and Blaes, 1993) or a dual-MOSFET-dual-bias device, as realized in the Best Medical Canada (Ottawa, Ontario) commercial MOSFET (Soubra et al, 1994). However some MOSFET arrays may still exhibit temperatures between 20 and 37^0C.

Energy dependence in semi-conductor devices can be minimized by calibration of the detectors in a reference radiation field of a similar energy as used in patient measurements. Comparisons between MOSFET responses and reference dose rates obtained with Monte Carlo simulations were made for Ir-192 source irradiation in water

at various angles and radial distances from the point of interest (Zilio et al, 2006). If an energy correction coefficient was applied, the results agreed within 5%, which corresponds to experimental uncertainties. Reniers et al (2012), measured the variation of the MOSFET response with distance used a linear fit through the measurements as an energy correction factor.

2.5.2 Fibre-coupled dosimetry

Fibre-coupled dosimeter probes are composed of a detector that is coupled to a fibre optic cable. The detector emits light in proportion to the absorbed dose in the detector volume. Fibre-coupled dosimetry for BT sources has been performed with detectors composed of organic scintillation materials (Therriault-Proulx et al, 2011; Suchowwerska et al, 2011; Lambert et al, 2006), aluminum oxide crystal ($AL_2O_{3:}C$) (Andersen et al, 2009) and Ce^{3+} doped SiO_2 (Carrara et al, 2013). The small (1 mm) outer diameter of the dosimeter probes and their flexibility allows for IVD, example in urethra (Suchowerska et al, 2011) and BT needles (Andersen et al, 2009).

The main disadvantages of fibre-coupled dosimeters are temperature dependence and the stem signal. The stem signal corresponds to irradiation -induced emission of fluorescence and Cerenkov light in the fibre optic cable and is a significant source of background when the source irradiates near the fibre optic cable and relatively far from the detector. The stem signal can be suppressed efficiently using a chromatic removal technique, originally developed fibre-coupled scintillator dosimetry for EBRT by Fontbonne et al (2002) which has been adapted for BT with scintillator (Therriault-Proulx et al, 2011) and $AL_2O_{3:}C$ dosimetry (Kertzscher et al, 2011).

Recently, Bedder (2012) pointed to new evidence for temperature dependence of plastic sensitivity. The results were confirmed in two other studies (Bedder, 2012; Buranurak et al, 2013), which demonstrated that the response decreases linearly with increasing temperatures. The studies revealed that the responses of blue BCF-12 and green BCF-60 scintillators from Saint Gobain, Paris France, decreased with temperature by $0.05\%K^{-1}$ or $0.09\%K^{-1}$ and $0.55\%K^{-1}$ or $0.5\%K^{-1}$ respectively. The studies also that the stem signal was not significantly temperature dependent.

Edmund and Andersen (2007), showed that the Ce^{3+} doped SiO_2 response increases by $0.2\%K^{-1}$. Whereas scintillation and Ce^{3+} doped SiO_2 detectors do not exhibit energy dependence for high-energy BT sources, AL_2O_3:C dosimeter probes have shown some energy response artifacts (Andersen et al, 2009) demonstrated that a dosimeter probe placed inside a stainless steel needle would over-respond with respect to water with magnitudes depending on the source-to-detector distance at an approximately constant rate.

However, in this study the gafchromic film was the detector used. The decision of using the film was as a result of the unavailability of the various dosimeters/detectors during the study. The gafchromic film was available and that made the choice for usage much more easy. It is of low cost and easy to use as well. It is a favourable 2D dosimeter due to its radiological tissue equivalency and real time development. The gafchromic film is a practical dosimeter for phantom studies because it can be cut in any shape and size for placement in a specially designed or custom made dosimetry phantom.

2.5.3 Significant challenges for in vivo dosimetry

Widespread implementation of high-precision IVD systems in the clinical routine is limited by the potential introduction of added risks and discomfort to the patient as well as the extra workload and potential interference with the existing clinical workflow. The extra workload is linked to dosimeter calibration, reconstruction of dosimeter position in patient images, and placement and securing of dosimeter probe etc. The accepted extra workload depends on the user. One clinic may consider a daily 20-min dosimeter calibration routine acceptable, whereas another would require a maximum 5-min investment for all IVD-related stages. Also, BT clinics would most likely require that the implementation of the IVD system did not reduce or disturb the focus on patient care.

A common problem in IVD is the poor knowledge of the exact dosimeter position. For instance, discrepancies >30% between measured and expected dose rates have been observed during IVD (Andersen et al, 2009; Suchowerska et al, 2011;Kertzscher et al, 2014; Seymour et al, 2011; Allahverdi et al, 2012) and have been attributed to poor correspondence between the dosimeter position during the patient image acquisition and that during the treatment delivery owing to patient movements during the transfer between imaging and treatment locations (Suchowerska et al, 2011; Kertzscher et al, 2014; Allahverdi et al, 2012). Since BT dose distributions are characterized by steep gradients, the uncertainties in the detector position may generate substantial dose uncertainties. Positional uncertainties <1.5 mm for the dosimeter and individual source positions are required in order to be able to detect source displacement errors of 5 mm (Kertzscher et al, 2011). However, with some substandard image quality and potential geometric variations in the anatomy, it is not trivial to achieve positional uncertainties

better than 1.5 mm during IVD measurements. As a result, IVD implementations must incorporate unrestrictive error criteria in order to avoid false alarms, which in turn allows only for the detection of gross errors of >50% and can lead to situations where smaller errors are undetected and may cause harm to the patient.

Compromised dosimeter positions, where the position during the treatment delivery did not correspond to that acquired from patient images, have been indicated during IVD in the urethra (Waldhausl et al, 2005), the rectum (Waldhausl et al, 2005; Tanderup et al, 2013; Seymour et al, 2011; Allahverdi et al, 2012; Haughey et al, 2011), and source applicators (Andersen et al, 2009; Kertzscher et al, 2014). Compromised dosimeter positions may be caused by erroneous reconstructions owing to poor image quality and/or by dosimeter shifts from their initial placement with respect to the adjacent tissue, for example, owing to patient movements during transport between locations. Such dosimeter shifts are difficult to model and can result in too optimistic uncertainty budgets. In addition, compromised dosimeter positions make it difficult, if not impossible, to relate measured dose rates with planned dose rate calculations. As a result, false error alarms may be generated if comparisons between measured and planned dose rates rely on a static *a priori* reconstruction of the dosimeter position. In-vivo dosimetry (IVD) would therefore provide only limited warranty for a treatment termination unless risks of such false errors are eliminated.

The extra workload and potential interference with the clinical workflow are linked to manual procedures of the IVD implementation and the lack of automated dosimetry procedures. For instance, most *in vivo* measurements require a manual insertion of the

dosimeter probe into source applicators or catheters placed in OARs. Although the dosimeter placement procedures may be straightforward, they may require preparations by the doctor in the operating theatre (Andersen et al, 2009; Kertzscher et al, 2014), and thus reduce the dissemination of IVD in BT.

In vivo dosimetry is a QA approach which is done to ensure error free treatment delivery process. In this study the water phantom was used to account for the challenges involved with the in vivo dosimetry to boost the overall confidence in the treatment delivery process.

2.6.1 Quality Assurance of high dose rate brachytherapy

Quality assurance in brachytherapy is not much different from that of external beam therapy. There are different aspects of QA procedures and these have been identified in several publications. Among these include AAPM TG53 report on QA (Fraass et al., 1998) and Code of Practice for BT physics (Nath et al., 1997).

Quality Assurance is a total procedure performed in the clinical setting to ensure that all necessary aspects are in a good condition and state. In the brachytherapy setting, QA is performed on the equipments to ensure that dose delivery is accurate and precise with minimal level of uncertainty. Education and training of clinical staffs forms part of the QA procedure.

The use of a remote afterloader with a long half-life source (Co-60) at KBTH is different from the use of manual iridium wire or seed in another clinic hence QA in the

centers should be different. It is reasonably clear that the QA program should suite the type of application done by a particular hospital.

2.6.2 Effects of treatment verification systems on the quality of treatment process

During the developments of high dose rate brachytherapy systems, there have been a couple of major researches done to enhance the knowledge of treatment modalities and accuracy of treatment delivery.

The International Commission on Radiological Protection (ICRP) reports 38 (ICRP, 1983) and 58 (ICRP, 1997) require the same steps to be considered for dose specification and documentation; description of volume, description of method and technique, specification of source strength, description of source distribution and source pattern, reference dose and dose distribution and fractionation.

This specification clarifies the relevance of dose distribution and accuracy of treatment concerns. It is known that quality control during treatment delivery includes the verification of position of applicators used, the connecting tubes and the way the treatment unit responds to the treatment console. It is very relevant to go through a quality assurance test before treatment is delivered accurately. A publication made by Shanta et al.,2008 talks about individual dose verification systems and how they can improve the quality of treatment through the checking of doses delivered through the treatment planning system in high dose rate planning procedures.

The study indicates that "The use of formalisms that are complex enables dose to be computed and result in localisation of source, which is significant to ensure that the dose

delivered is planned". Manual dose calculation is difficult when implants used for a particular BT procedure have complex geometry of source and increased number of foci. Therefore manual dose verification is hardly reported . This shows there is a call for such quality assurance of machines to be made (Shanta, 2008).

There has been challenges through the use of mathematical formulas for dose estimation before treatment and hence the necessity of the verification of the Medical Physicist plans before delivery. Kubo (1992), in his work on verification due to the irreversible damage being caused out of 500 to 1000 cGy in a matter of minutes during treatment (Kubo, 1992).

Moura et al. (2004) used a phantom to validate high- dose - rate brachytherapy treatment planning systems with heterogeneous algorithms. TLD- 100^{TM}, Gafchromic EBT3 film, and an $Extradin^{TM}$ A1SL ionisation chamber were the instruments used during the process to mimic a heterogeneous medium, Virtual $Water^{TM}$(VM), BR $50/50^{TM}$, cork and aluminium.

The findings were that " the difference in the relative response as high as 11.5% were found from the homogeneous materials were inserted into the experimental phantom. The discrepancy between the Brachytherapy $Vision^{TM}$, $Acuros^{TM}$, and TG-43 dose responses in the phantom described by this work exceeded 12% for certain set ups". It was concluded that the phantom used had good agreement with the TPS Calculations using the $Acuros^{TM}$ algorithm (Moura et al, 2015).

CHAPTER THREE

3.0 MATERIALS AND METHODS

Chapter three focuses on materials and the methodology that was used for this study.

3.1.1 One dimensional manual water phantom (MP1 manual water phantom)

The MP1 water tank is a small one dimensional (1D) phantom that is used to assess the qualities of dose and to identify absolute doses which is in accordance with the international dosimetry standards. The tank also assesses absorbed doses at reference conditions which meets the IAEA TRS 398 and AAPM TG51 protocols. The tank has a vertical moving range of 254 mm and external horizontal phantom dimensions of 320 mm x 370 mm.

There is a tap at the bottom edge of the phantom that is used in draining out water after its being used. Also easy set up is ensured due to the presence of alignment and fill lines on the phantom. The one dimensional water phantom used to calibrate the gafchromic EBT3 film strip during this study is shown in Plate 3.1.1.

Plate 3.1.1: One dimensional water phantom (MP1 manual water phantom)

3.1.2 Gafchromic EBT3 film (Lot number: 04201601)

Gafchromic EBT3 films are made of 2 layers that are polyester coated. These two layers are held together by an active layer. A film scanner is used with the gafchromic film. The response of the film is increased when its absorbance compares favourably with the spectral response of the scanner. The range at which the EBT3 film response to radiation is between 50 KeV to MV, which is quoted by the manufacturer. These energy ranges include that emitted by cobalt-60 HDR source (Uniyal et al., 2012). The film can be used in dose range of 1 cGy to 10 Gy due to its high level of sensitivity.

There are several scanners that are of high quality, which are available to digitize coloured films. The Epson 10000XL PHOTO flatbed colour scanner, which is designed to digitze film 20.32 x 25.40 cm^2 in size, and even as large as 30.48 x 40.64 cm^2 in size,

is recommended to scan EBT3 film. In this study, 20.32 x 25.40 cm^2 size gafchromic film was used.

There are factors which affect the response of the gafchromic EBT3 film. These factors are said to be facility specific. They include the range of radiation energy used, the film scanner available and the time when exposure and measurement elapses. Therefore, it is important to know the measurement standards and facility protocols before estimating density-dose response of the film.

The most attractive feature of the EBT3 film to be used for HDR brachytherapy are its high spatial resolution required to assess doses in steep gradient regions about the source, usable with water phantom and its overall effective atomic number (Z_{eff}) is 6.8, which makes it near tissue equivalent (Z_{eff} of tissue 6.5) (Uniyal et al, 2012). Plate 3.1.2 shows a picture of the gafchromic film strip used in this study.

Plate 3.1.2: Gafchromic EBT3 film strip (lot #: 04201601)

3.1. 3 Co-60 teletherapy Machine

Gamma ray treatment machines are known as teletherapy units. The components of a Co-60 EBRT machine (plate 3.1.3) are ;

a. A radioactive source, in this case Co-60, which is housed in a steel capsule.

b. Source housing, which includes the primary beam collimator to prevent unwanted radiation emission. The source housing can also shift the source to allow gamma rays to exit the unit through the collimator aperture.

c. A patient support assembly or patient couch to be positioned in the desired position.

d. A machine console outside the bunker which allows therapists to operate the machine remotely.

When the source is not in use, it is located in the 'off ' position that prevents significant dose from exiting the treatment head. Some radiation leaks out of the head, which must be less than 0.02 mSv/h to comply with radiation safety standards. Typically a light field is generated when the source is in the off position which allows visualisation of the radiotherapy field prior to treatment.

The source is rotated or slid into the treatment position when dose delivery is desired. An emergency shut off is required in the event of power failure. Dose delivery is measured by treatment time as opposed to monitor units, as the time required to deliver a dose increases when the source activity decreases. A primary timer and back up secondary timer are used to control treatment time.

Fields are defined by secondary collimators and range from 5x5 cm^2 to 35x35 cm^2 at an source-surface distance (SSD) of 80 cm. The geometric penumbra of the beam is dependent on the source size (limited for cobalt 60 units to about 1cm) and typically wider than that for a linear accelerator. Penumbra trimmers, a beam accessory, can be placed closer to the patient surface to provide additional collimation and reduce the effect of the finite source size.

The teletherapy Co-60 source was used in this study to expose the gafchromic EBT3 film strip with known doses for calibration purposes.

Plate 3.1.3: Co-60 teletherapy Machine

3.1.4 The PTW UNIDOS Electrometer

The PTW UNIDOS electrometer (TM10008 ; SN: 081102) (Plate 3.1.4) is a high performance secondary standard and reference class dosimeter or electrometer used universally for either radiological or electrical measurements. The electrometer (PTW UNIDOS) is calibrated at the PTW laboratory. The PTW-Freiburg is a member of the Secondary Standards Dosimetry Laboratory (SSDL) network that is known by IAEA and as such are accredited. Obviously, calibration is based on the primary protocols of the Institute of German Physics and the Bureau International de Poids et Mesure, Paris (BIPM).There are detectors that can be connected to the electrometer during clinical procedures. These include the ion chambers and solid-state detectors. The electrometer shows the values of dose measured, the rate of dose, electric charges and electric currents. Values of dose and dose rates are measured in gray (Gy), Sievert (Sv), Rontgen (R), gray per minute (Gy/min), Sievert per hour (Sv/hr), Rontgen per minute (R/min) or

Gy·m; whiles those of electrical charges and currents are measured in coulomb (C) and ampere (A) respectively. The device includes an automatic leakage compensation, an automatic built-in system test and an RS232 interface. It features both on mains (power supply) and battery operation. The electrometer (Plate 3.1.4) was used to calibrate the film against the ion chamber during the study.

Plate 3.1.4: The PTW UNIDOS electrometer

3.1.5 The ionization chamber system (0.6cc ionisation chamber)

An ion chamber (TM30001-01; SN: 00820) is made up of a collecting electrode and a polarizing electrode between which there is a gas filled cavity. A potential difference is applied between the two electrodes resulting in an electric field inside the cavity. When the chamber is irradiated, secondary electrons are produced thus ionizing the gas within

the cavity. The resulting positive and negative ions will move to their respective electrodes due to the presence of the electric field. The total charge collected, or the current produced at the collecting electrode is measured and displayed using an electrometer. The potential difference between the two electrodes must be set at a value low enough to minimize charge amplification whilst being large enough to avoid charge recombination. There are different types of ionisation chambers, but in this study a 0.6cc ion chamber manufactured by PTW Freiburg, Germany was used. The ionisation chamber (Plate 3.1.5) used was calibrated against a source of known beam quality at the IAEA Secondary Standard Dosimetry Laboratory (SSDL).

Plate 3.1.5: 0.6cc ionisation chamber

3.1.6 ImageJ software

ImageJ (Plate 3.1.6) is a Java-based image processing program developed at the National Institutes of Health (NIH) (Collins, 2007). ImageJ was designed with an open

architecture that provides extensibility via Java plugins and recordable macros (Vijayalakshima and Girish, 2004). User-written plugins make it possible to solve many image processing and analysis problems (Elicieri and Rueden, 2005). ImageJ's plugin architecture and built in development environment has made it a popular platform (Burger and Burge, 2007; Dougherty, 2005) and therefore was employed for analyzing the optical density of the scanned films in this study.

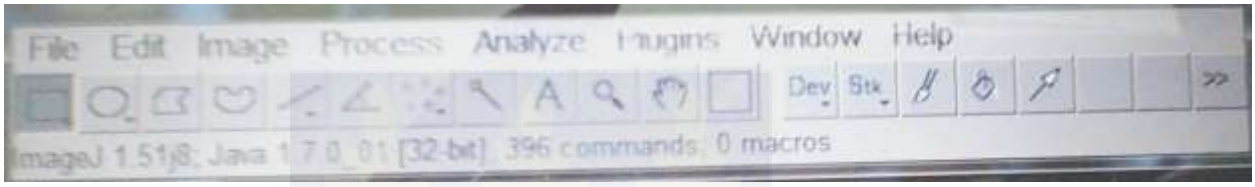

Plate 3.1.6: An opened view of imageJ user interface.

3.1.7 Epson scanner

There are several scanners that are of high quality standard, which are used to scan coloured films. The Epson scanner is used to scan films of various sizes. The film sizes are 20.32 x 25.40 cm^2 and 30.48 x 40.64 cm^2 (which is larger size).The scanner provides sensitive response for EBT3 film at doses up to 8 Gy in the red colour. The EBT3 film has a unique marker dye in its active layer. This improves the automatic uniformity of the film in the blue channel range. Doses from 8 Gy to 40 Gy are measured by the green channel. The landscape orientation is required for scanner. The Epson scanner (Plate 3.1.7) was therefore used to scan the gafchromic film strips during calibration procedure.

Plate 3.1.7: Epson scanner flatbed scanner document

3.1.8 Fabricated cervix water phantom

A self built manual cervix water phantom (Plate 3.1.8) was used during this research. This phantom was manufactured from poly-methyl methacrylate (PMMA) material. The PMMA was cut and joined into an open top box with dimensions of 30x30x30 cm reference of dimension.

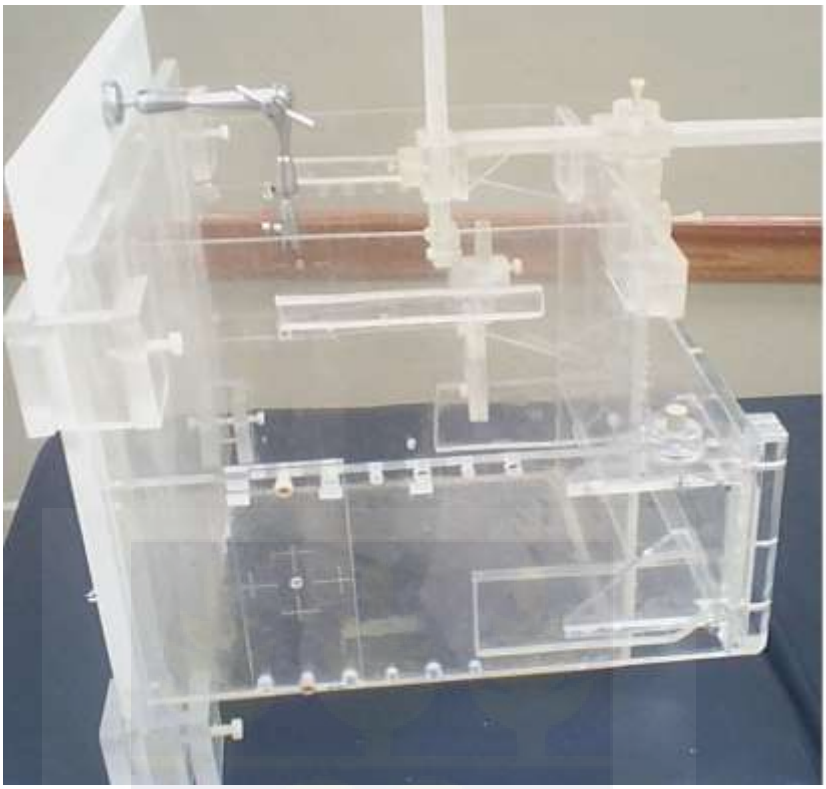

Plate 3.1.8: Cervix water phantom (in-house)

The phantom was constructed in a way to prevent more scatter although scatter is known not to be eliminated totally. A holder was also designed which forms part of the phantom design. This holder was designed with a thin slab of PMMA with sliding sides for easy movement and rigid holding capabilities.

This holder was designed to hold the gafchromic EBT3 film strip during absorbed dose measurement procedure. An external slab provided by the manufacturer was used for holding of the applicators used for this experimental work.

The cervix water phantom (Plate 3.1.8) was used to measure absorbed dose to the film strips at different distances from applicators.

3.2 METHODOLOGY

3.2.1 Calibration of gafchromic film for dose measurement

Gafchromic films with dimensions 20.32 x 25.40 cm^2, batch number of 04201601; Ashland Inc., USA, were cut into strips each having dimensions of 7.8 cm x 5.4 cm, so that they can be accommodated in a locally designed holder, which formed part of the fabricated phantom to represent the cervix region. The films were cut such that the longest length of the strip corresponded to that of the main film. This was done to ensure that the strip films were scanned in the same direction during the analysis process.

The film strips were irradiated with known doses of : 0 Gy, 3 Gy, 5 Gy, 6 Gy, 7 Gy, 9 Gy, 10 Gy and 15 Gy respectively using beams from the Co-60 teletherapy machine. During the irradiation process the films were held by the locally designed holder and mounted on the detector holder of the one dimensional water phantom. The films were each irradiated with beam having field size of 10 cm x 10 cm, such that the films were central to the irradiation field. The measurements were done at a depth of 5 cm employing source-to-surface (SSD) irradiation technique. Prior to the irradiation, it was ensured that the water surface in the phantom as well as the film holder were levelled for normal beam incidence. A spirit level and levelling knobs at the base of the phantom were used to achieve the levellng.

The doses to which the films were irradiated to, were obtained through the following procedures; firstly, the teletherapy machine output was measured (or calibrated) for a reference field size of 10 x 10 cm^2 at depth of 5cm using SSD irradiation technique.

The measurement was done in the one dimensional water phantom with a 0.6cc ionisation chamber (TM 30001-01; SN: 00820; PTW Freiburg, Germany) which was connected to a UNIDOS E electrometer (T10008-081102; PTW Freiburg, Germany) employing International Atomic Energy Agency (IAEA) TRS 398 protocol. The ion chamber and the electrometer have traceability to a Secondary Standard Dosimetry Laboratory (SSDL). Absorbed dose to water per minutes (Dose rate) measuring depth was calculated based on the TRS 398 protocol. Secondly, the dose rate obtained was used to compute irradiation time (treatment time) for the various doses to which the films were irradiated. The treatment times obtained were also confirmed with the TPS in use at the department. This was done by creating a phantom having the same dimensions as the one in which the films were irradiated, and the irradiation process simulated with the TPS. Doses to be given to the film were prescribed to the corresponding point of measurement within the phantom and the dose distributions within the phantom calculated to obtain corresponding treatment times (irradiation times) for the various doses. These treatment times were set on the console of the teletherapy machine during the irradiation process. The films after exposure were marked with the dose they had received to help with identification. The marks were placed closed to the edges of the film. The exposed films were allowed to stay for a period of 3 days (post-irradiation time), after which they were scanned in a batch with EPSON flatbed document scanner.

The scan was done in 24 bit colour mode with a resolution of 72 dpi. No colour corrections were applied. The scanned images were saved as JPEG image format and imageJ software was used to analyze the scanned images. During the analysis, a square region of interest (ROI) which covers about 2/3 (two-third's) of the film area was

analysed. The ROI was placed central to the film (scanned film). This ROI was replicated on all the scanned films and the optical density within the region of interest per film determined. The analysis were done per colour channel (red, blue and green) to see which channel gives the optimal sensitometry curve.

A graph of dose (Gy) against optical density was plotted for the various channels on the same axis. The correlation equation and its related regression (R^2) of the line of best fit was determined for each channel.

Plate 3.2.1 which shows a picture of the set up of the one dimensional water phantom with the necessary parameters in place. Plate 3.2.1.1 shows the film holder which was used in supporting the film strips in this study. Plates 3.2.1.1a and 3.2.1.1b shows the respective settings which were used in scanning the films.

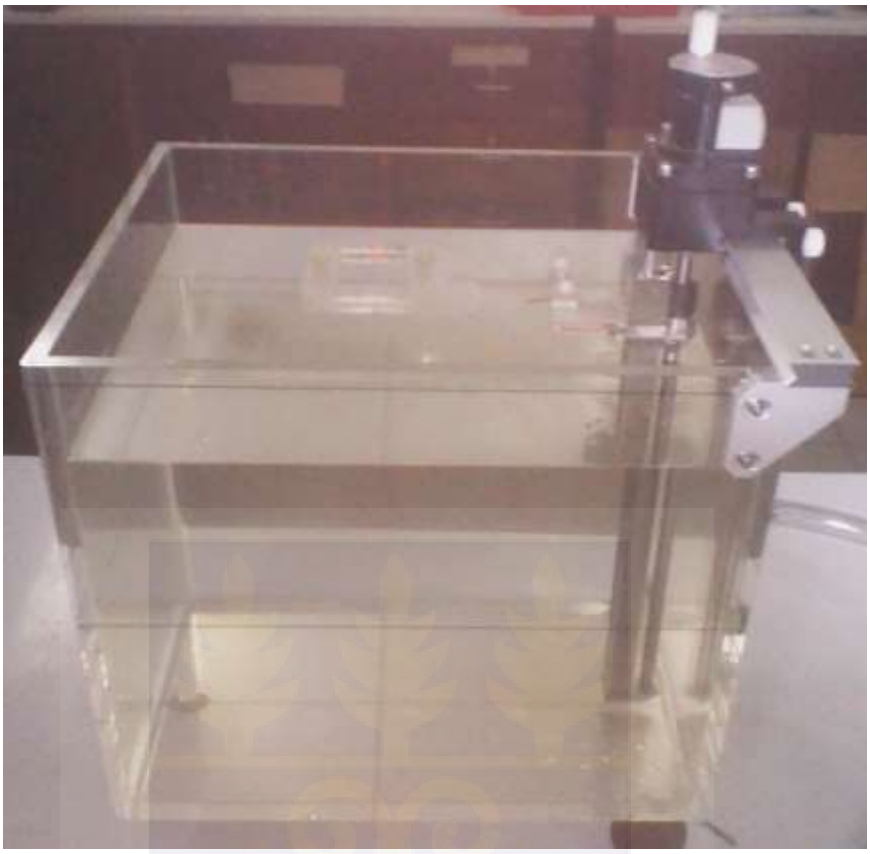

Plate 3.2.1: Set up of the one dimensional water phantom on the couch of equinox 100 teletherapy machine

Plate 3.2.1.1: Film holder (in-house manufactured)

The film holder has the same dimensions as the film strip. It was used to hold the film strips in steady position during exposure.

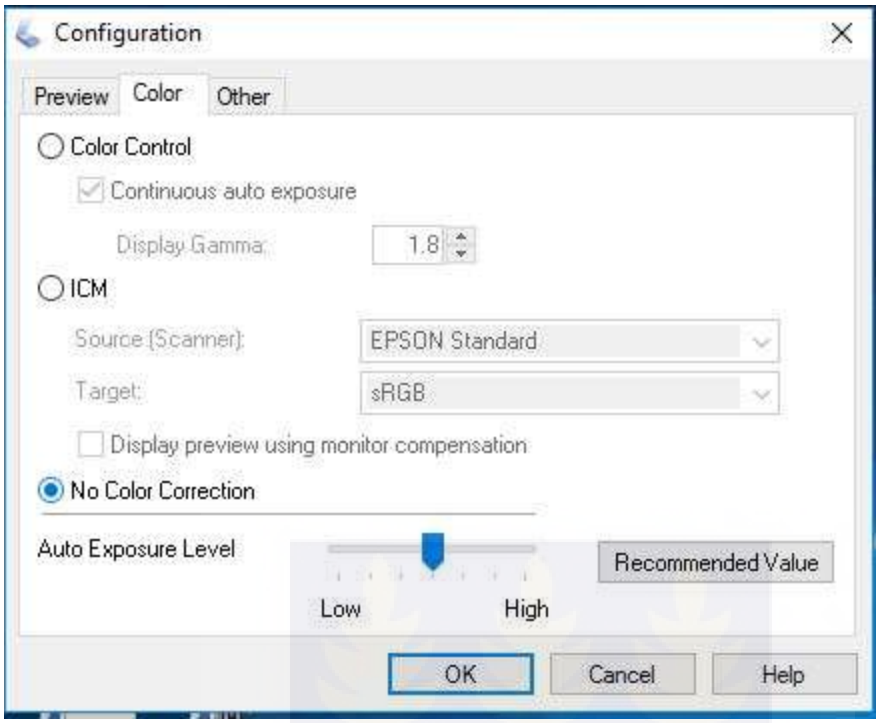

Plate 3.2.1.1a: Settings on the Epson flatbed scanner used in scanning film strips.

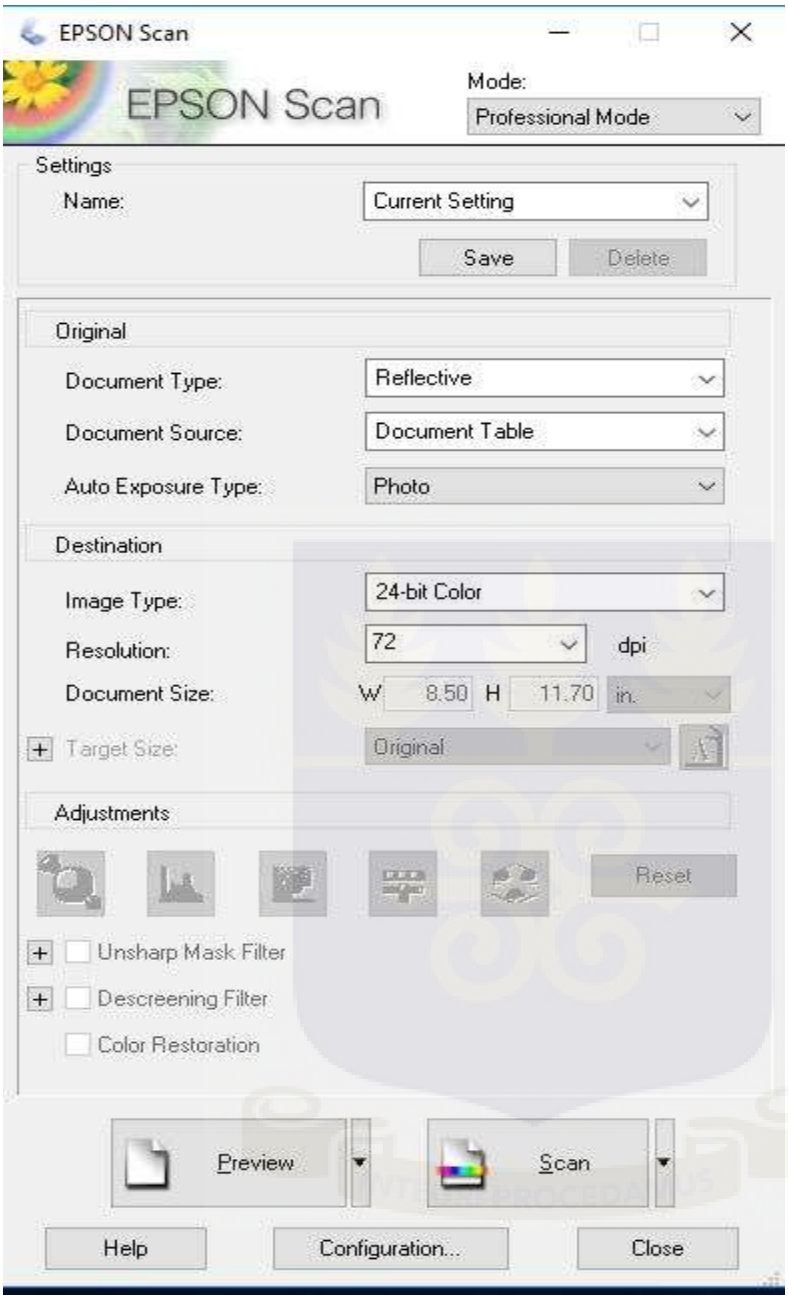

Plate 3.2.1.1b: Set up settings used in scanning the gafchromic film strips

A uniformity test was performed by scanning unexposed film strips and were analysed using the imageJ software to obtain the mean optical densities. This was a precautionary

test done to check the transmission of light on the surface of the scanner would be the same as on the surface of the film.

3.2.2: Brachytherapy Treatment Planning System

The NCRNM uses HDR source of Co-60 to treat cervical cancer. In this study, a phantom was locally designed to mimic the cervical region. Before the procedure, a card white in colour was designed which had dimensions of 7.8 cm x 5.4 cm so that could fit firmly in the locally designed film holder. The card was used to mark the center of the images.

The fabricated cervix phantom was filled with water to the brim with a reconstruction box firmly placed around it which has fiducial markers. The cervix phantom was placed on a bed to replicate normal patient set up.

With the use of the C-arm, different orthogonal images were taken which were used for the high dose rate brachytherapy. The C-arm movements were limited to three directions only between the orthogonal images: the C-rotation, the up-down, and the left-right directions. The designed card was positioned firmly in the film holder and immersed gently into the water in the phantom and applicators of different forms available at the Department were also positioned and immersed into water each time imaging was done. Available applicators in the Department which were used were LCT05.01/LC330.02 (whether the latter is the ovoid applicator and former is a tandem applicator), LCT06.01/LC330.02 (LCT06.01 is the most curved of the tandem applicators used in the Department), LCT05.01/LC0330.01 and LCR01.01 (cylinder applicator).

The film holder with the card was positioned at various points around the immersed applicators at each time when imaging was to be done. These points included the bladder points, rectal points and measuring points around the applicators.

The C-arm was used to obtain images at various positions of the card around the applicators at each imaging time. The C-arm was used to obtain images of the card in the film holder from the anterior end and the lateral ends of the cervix water phantom. The fluoroscopy images were then captured on the phone camera and transferred to the planning computer through a DICOM network.

The C-arm was repeatedly used to obtain images at the bladder points, rectal points and other measuring points with the applicators also being repeatedly varied based on the available applicators in use at the Department.

The images that were transferred to the planning computer were merged such that the anterior images merged with the lateral end images and planned respectively. In planning the images, doses were prescribed to Manchester point A, 0.5 cm of the ovoid surface and 0.5 cm at the surface of womb based on the Departmental protocol. Doses which were prescribed to these points included 5 Gy, 7 Gy, 7.41 Gy, 8 Gy and 18.5 Gy. These doses were used in this study based on the departmental prescription protocols. Plates 3.2.2a and 3.2.2b shows the set ups used for imaging and planning respectively.

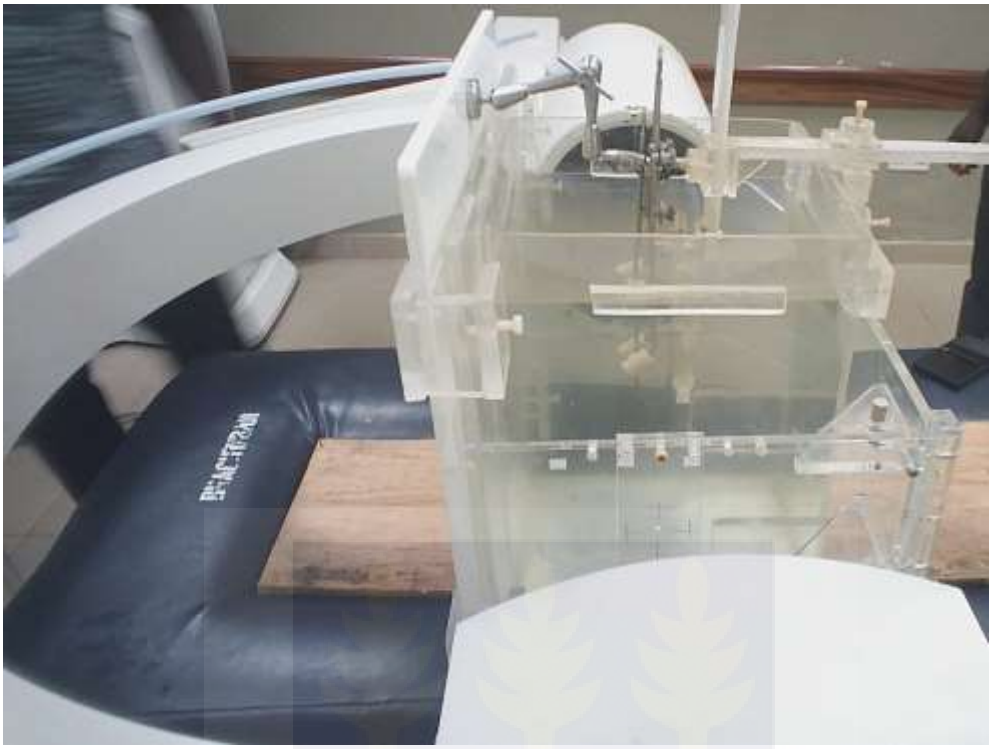

Plate 3.2.2a: Set up showing the imaging using the C-arm with card in the holder

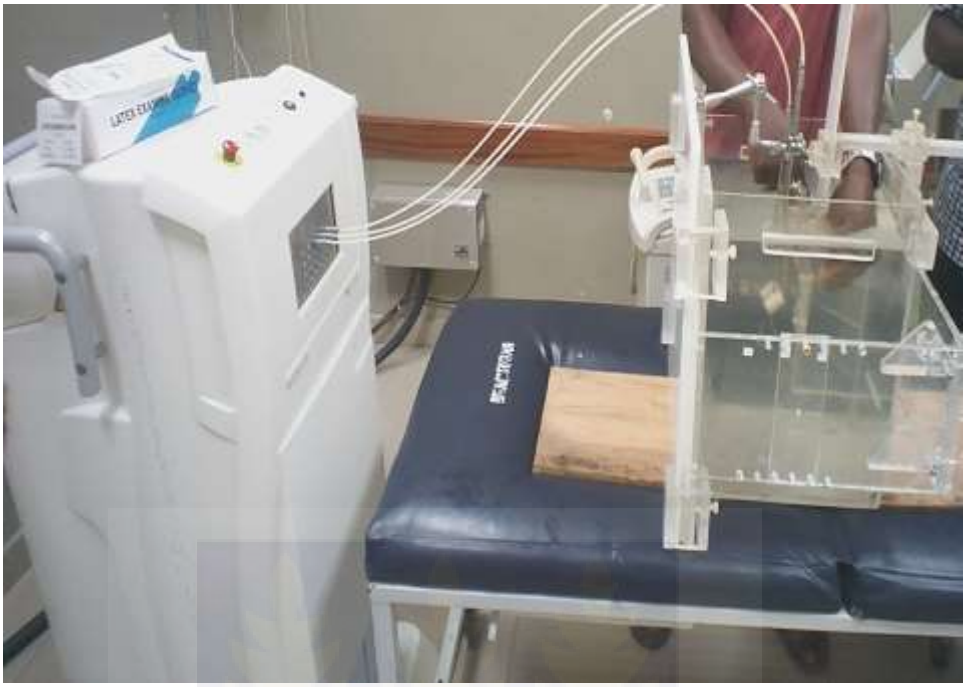

Plate 3.2.2b: Set up showing change of card in holder and putting film in for dose delivery

3.2.3: Dose verification

The planning computer of the BT TPS (HDR multisource TPS, Eckert and Ziegler, Germany) was used to generate calculated doses (which were automatically generated by the TPS) during the treatment planning. Each of the planning treatment times were generated which were used to expose gafchromic film strips.

When each imaging and planning was done, the card in the film holder was removed and replaced with a film of dimensions of 7.8 cm x 5.4 cm and the applicators were connected to the HDR multisource unit to deliver doses to the gafchromic film strip. This was repeated several times after imaging and planning was done.

The films exposed by the brachytherapy Co-60 source were allowed to have post-irradiation time beyond 48 hours. This was so to enable all the films be scanned at the

same time. The films were scanned after the post-irradiation time with the Epson flatbed document scanner. The imageJ was used to analyze the films respectively. In scanning the exposed films, there were always two unexposed films which were scanned with the exposed films.

The optical density values of the exposed films, were evaluated with the imageJ. The optical density values of the unexposed values were known as the zero values since they were not exposed with any treatment dose. These zero values were added and their mean was divided by the zero value of the mean optical density of the blue channel of 73.720. The value obtained was multiplied to the optical density values of the exposed films.

In plotting the graph of the optical density against the doses, the blue channel gave better correlation and as such had a regression (R^2) of 0.9988. The blue channel equation of $y(blue)= 0.127x^2-3.7985x + 73.951$ was used to manually compute the measured doses. This was done by respectively computing the optical density values of the exposed films against the polynomial equation of the blue channel as stated above. Thus the measured doses were compared to their calculated counterparts (which was generated by the TPS, Eckert and Ziegler, Germany). The percentage deviations/uncertainties in each case was determined between the measured and the TPS calculated doses. This was done by substracting the TPS calculated dose values from the measured dose for each cases performed and then dividing by the TPS calculated doses, all expressed as percentage. The percentage absolute deviations are absolute values of the negative and positive values obtained. Plates 3.2.3a (fluoroscopy image of applicator positions), 3.2.3b1 (volume drawn showing the isodose lines on the treatment planning system) and plate

3.2.3b2 (treatment planning 3D generated volume) shows the volumes drawn during the brachytherapy planning section in this study.

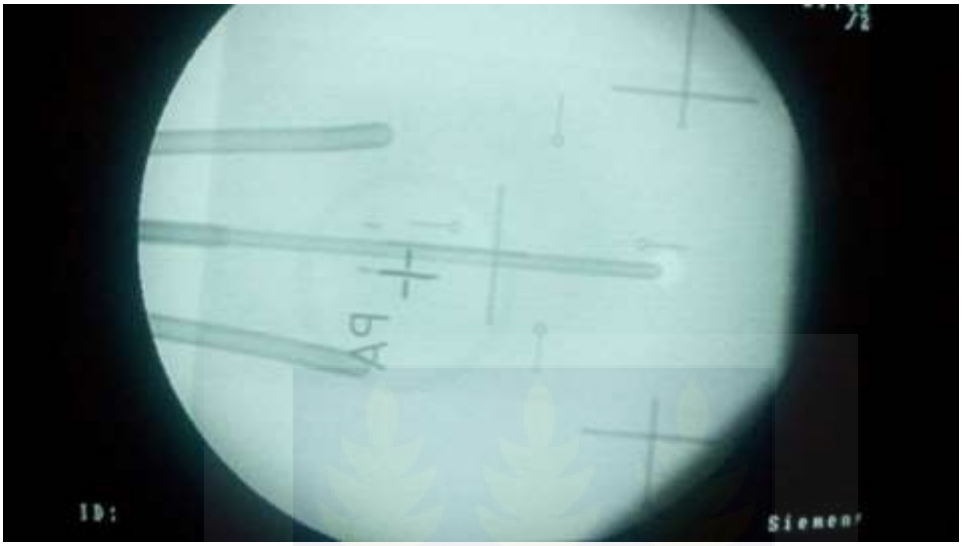

Plate 3.2.3a: Fluoroscopy images of applicator positions

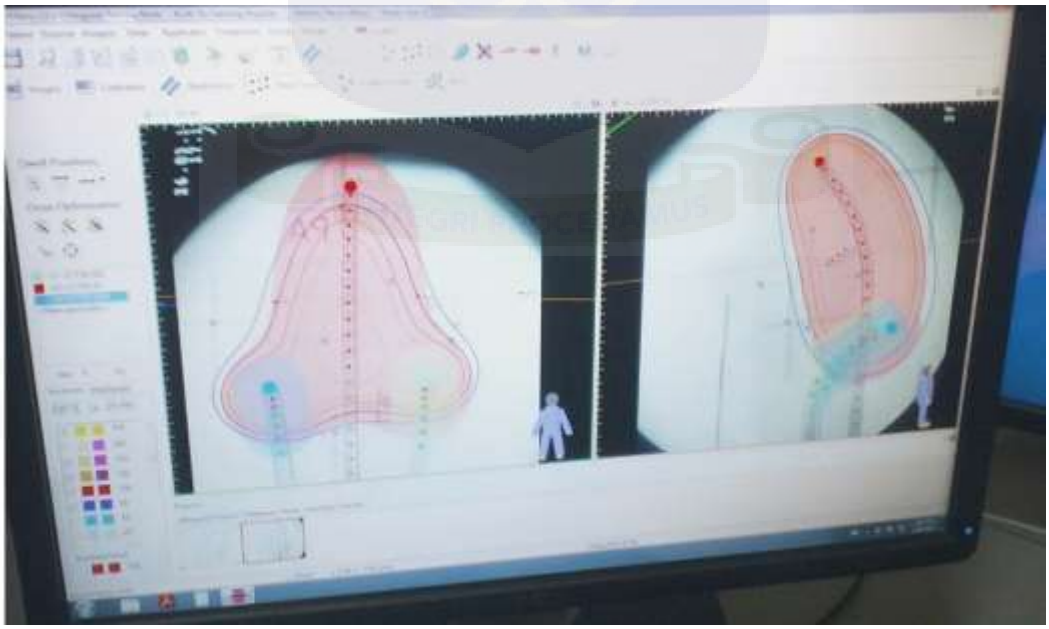

Plate 3.2.3b1: Treatment planning Dose volume Histogram (DVH)

Plate 3.2.3b2: Treatment planning 3D generated volumes

CHAPTER FOUR

4.0 RESULTS AND DISCUSSION

In this chapter, the analysis of the results obtained and discussions are presented. The results are grouped into calibration of the gafchromic films and dosimetry.

4.1 Calibration of gafchromic film for dose measurement

The sensitometry graph (Fig.4.1) shows the three colour channels namely, red channel, the blue channel and the green channel. The graph shows a plot of the mean optical density values against dose (Gy). On the graph, the various regressions R^2 was respectively shown for the three colour channels. The equations of the RBG-channels are also clearly outlined such that the ordinate indicated as Y representing the colour.

From Fig.4.1, the blue channel had a better correlation with a regression value approaching 1 and had its line of best fit passing through all the points. As a result of

this, measurements were done in this colour range (blue channel).

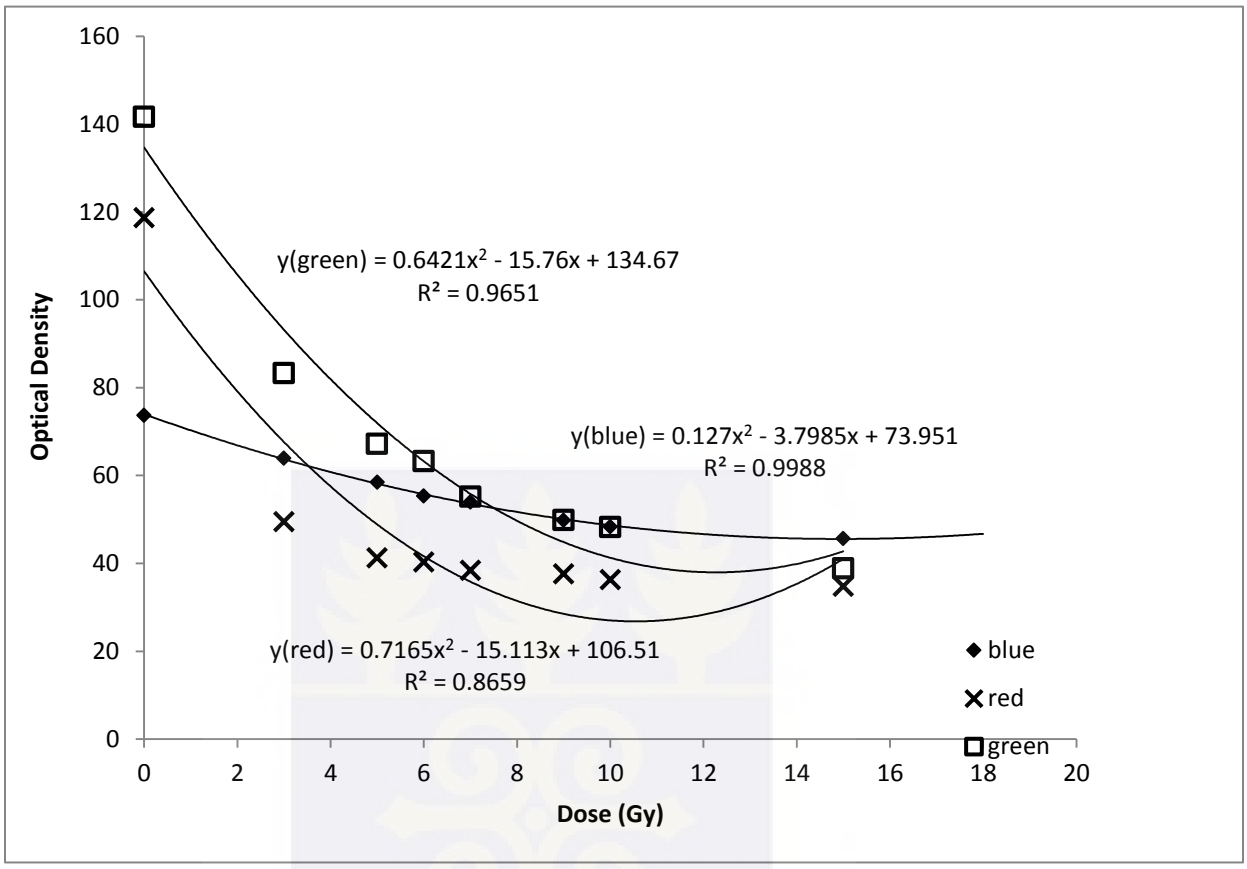

Figure 4.1: Sensitometry curve showing the RBG Colour channels

4.1.1 Sensitometry curve of the Blue channel

The Fig.4.1.1 shows the sensitometry curve (dose response curve) of the blue channel where measurements were done respectively.

The sensitometry curve between the mean optical density value and dose obtained for the calibrated Gafchromic EBT3 film is presented in figure 4.1.1. It was observed that as the mean optical density value increases, the dose decreases exponentially. The dose read from the calibrated films yielded deviations between -0.19% which corresponds to mean optical density of 45.707 and 0.31% which corresponds to mean optical density of 73.720, where these values are shown in Appendix C.3. The range of deviations obtained

may have occurred due to mishandling of the films and also the unavailability of the appropriate illumination for film storage. The polynomial equation generated from the dose response curve was used for brachytherapy measurement as indicated earlier. From Fig.4.1.1 the curve shows a regression R^2 and also gives a polynomial equation used in this study for dose measurement. The equation is preceded with y which represent the blue channel.

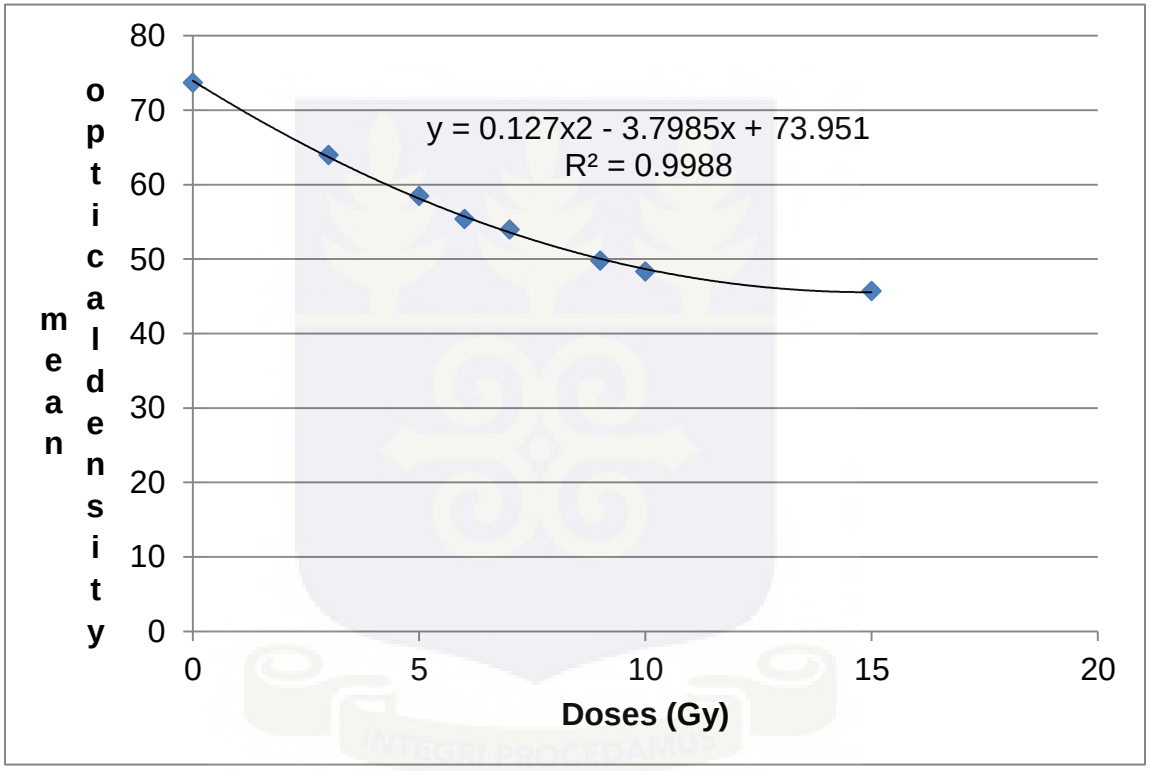

Figure 4.1.1: Sensitometry curve showing the blue channel used in dose measurement

4.2 Uniformity test

Uniformity test was performed by scanning seven (7) unexposed films. These films were analyzed and the mean optical density was evaluated. This test was done to check if the transmission of light on the surface of the scanner would not be same on the surface of the film. The test was also done to check if within the scan region of the scanner the transmission of light will not be the same and this could result in nonuniform response of the readout due to the light scattering of the scanner lamp caused by particles in the film active layer.

In analysing the films, a percentage error ranging between -0.98% and 0.86% was obtained and standard error of 0.5%. The optical density values and the relative percentage deviations are tabulated in Appendix B.2.

4.3: Comparison of the measured doses with calculated doses of brachytherapy implants

Table 4.3: Results of comparison of the measured doses and the calculated doses of brachytherapy implants

cases#	measured doses (Gy)	calculated doses (Gy)	%difference (%)	Absolute % difference(%)
1	3.45	3.57	-3.36	3.36
2	5.67	7.00	-19.00	19.00
3	3.07	2.65	16.41	16.41
4	4.07	4.00	1.75	1.75
5	4.55	3.20	42.19	42.19
6	4.05	3.20	26.56	26.56
7	4.50	4.27	5.39	5.39
8	4.00	4.27	-6.32	6.32
9	3.52	3.23	8.98	8.98
10	1.86	2.47	-24.70	24.7
11	2.17	2.11	2.84	2.84
12	2.38	2.32	2.59	2.59
13	3.05	3.57	-14.57	14.57
14	5.25	7.00	-25.00	25.00
15	2.57	2.65	-3.02	3.02
16	3.57	4.00	-10.75	10.75
17	3.02	3.23	-6.50	6.50
18	1.76	2.47	-28.75	28.75
19	2.12	2.11	0.47	0.47
20	2.30	2.32	0.86	0.86

The Table 4.3 displays the measured doses and the corresponding TPS calculated doses counterparts. It also shows the relative percentage uncertainties between the measured dose and the TPS calculated doses. The difference between the measured and the TPS

calculated dose range from - 28.75% to 42.19%. The mean difference is ±12.50% (Standard deviation of ±11.72%).

Comparing the mean difference of ±12.50% to the acceptable action level uncertainty by AAPM TG 46 which declared ±15% (for phantom measurement) in the delivery of prescribed dose for intracavitary brachytherapy (Hanson et al., 1994), it implies that the ±12.50% was within that of ±15% uncertainty level documented in AAPM TG 46. Also comparing the mean difference of ±12.50% (SD of ±11.72%) to that of Gholami et al., (2013), on dosimetry verification for cervical brachytherapy where cervix phantom combined with gafchromic films were used for dose verification test, it is observed that the mean uncertainty of this study is better than that of Gholami et al. Gholami et al estimated an uncertainty of ±23.4%.

Comparing the uncertainty of ±12.50% in this study to that of AAPM TG 46 and that of Gholami et al., 2013,the findings of this study shows cervix phantom measurements were within the acceptable variations. It also showed that the locally fabricated phantom was a valuable tool for QA program as well as verification of brachytherapy treatment system even for non-standard conditions. Thus this aims at achieving a desired level of accuracy and precision and boost the confidence in cervical brachytherapy dose delivery at the NCRNM, Korle-Bu.

4.4 Limitations of the study

a. In the construction of the cervix water phantom; the distance between the source applicator and the dosimeter (film) was not close enough as it should be.

b. The film holder was not marked at its four ends to match that of the gafchromic film strips hence shifts occur which interfere with point dose.

CHAPTER FIVE

CONCLUSION

This chapter presents conclusions from this study on dose verification of HDR BT for cancer of the cervix using cobalt-60 source and associated recommendations.

5.1 Conclusion

Dose measurements were carried out in fabricated phantom for various cervical brachytherapy insertions that could be used clinically to assess the accuracy of doses computed by the HDR brachytherapy treatment planning system in use at the Oncology Department of the Korle-Bu Teaching Hospital. The BT insertions were based on Manchester system, and the doses at specific points within the phantom measured with calibrated gafchromic films for a particular insertion. Doses to the specified points within the phantom were also estimated with the TPS.

The measured doses were compared to their corresponding calculated doses obtained with the TPS. The mean difference between the measured and the TPS calculated doses, which was expressed as a percentage was ±12.50% (standard deviation of ±11.27%). The uncertainty in this study of ±12.50% compares well with ±15% obtained by Hanson et al., 1994 and with ±23.4% of Gholami et al., 2013. The mean value uncertainty in this study deviates from that Hanson et al., (1994) because in that study the phantom used for dose verification has homogeneous and heterogeneous components compared to homogeneous component present in the phantom designed. Thus the heterogeneity resulted in difference in deviation. For Gholami et al., (2013), real patient was used which also have both heterogeneous and homogeneous component which contributed to

the high deviation obtained in that study. The results of this study provide a good evidence for agreement in dose distribution in a definite clinical condition regarding doses to the specific points in the phantom with a non-significant difference in accuracy.

The study can therefore be used as a quality assurance tool to evaluate the entire procedures involved with the BT treatment. Not-withstanding this, the experimental procedure may be repeated with other dosimeters such as TLD due to the inherent errors associated with film dosimetry.

5.2 Recommendations

The following are the recommendations for various stakeholders based on the findings of the study.

5.2.1 National Center for Radiotherapy and Nuclear Medicine

It is recommended that the Management of the Center should establish a QC committee with the following objectives/goals:

a. Establish a QA/QC program for periodic evaluation of the performance of cervix brachytherapy system and verification of treatment planning and dosimetry accuracy using the findings of this study as baseline information for quality improvement.

b. Establish a mechanism for monitoring and evaluation of the effectiveness of the treatment with cervix brachytherapy system and its associated Treatment Planning System

c. Recommends purchasing of accompanying QC kits and phantoms when acquiring new equipments.

5.2.2 Nuclear Regulatory Authority, Ghana

a. Provide a regulatory guidance performance standards, safe and effective use of the cervix brachytherapy system and its associated Treatment Planning System.

5.2.3 Future research studies

a. It is recommended that the use of another dosimetric system such as TLD aside the gafchromic film should be used to verify the TPS dose.

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APPENDIX

APPENDIX A: CALIBRATION OF GAFCHROMIC FILM MEASUREMENTS

A1. GAFCHROMIC FILM MEASUREMENTS

cases#	doses(Gy)	blue channel	red channel	green channel
1	0	73.720	118.706	141.650
2	3	63.968	49.530	83.303
3	5	58.474	41.242	67.177
4	6	55.385	40.300	63.283
5	7	53.966	38.429	55.188
6	9	49.801	37.611	49.876
7	10	48.358	36.331	48.299
8	15	45.707	34.809	38.850

B.2 UNIFORMITY TEST MEASUREMENT

film #	optical density	% error
1	74.208	0.776
2	72.928	-0.962
3	74.271	0.862
4	73.971	0.455
5	72.917	-0.978
6	73.593	0.059
7	73.568	0.093
		MEAN= 0.598

C.3 BLUE COLOUR CHANNEL MEASUREMENTS

cases#	doses(Gy)	blue channel(O.D)	% error
1	0	73.720	0.312
2	3	63.968	0.139
3	5	58.474	0.041
4	6	55.385	-0.014
5	7	53.966	-0.039
6	9	49.801	-0.113
7	10	48.358	-0.139
8	15	45.707	-0.186

D.1 DOSE VERIFICATION TEST MEASUREMENT

Cases#	optical density
1	62.369
2	56.150
3	63.080
4	60.230
5	59.268
6	60.632
7	59.415
8	60.762
9	62.165
10	67.331
11	66.298
12	65.616
13	63.724
14	57.505
15	64.435
16	61.585
17	63.520
18	68.686
19	67.653
20	66.971