COLLEGE OF BASIC AND APPLIED SCIENCES

ASSESSMENT OF DOSE VARIATION TO CRITICAL POINTS IN LOW DOSE RATE INTRACAVITARY BRACHYTHERAPY OF CERVICAL CANCER AT KOMFO ANOKYE TEACHING HOSPITAL

BY

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DECLARATION

This thesis is the result of research work carried out by Joseph Adom in the Department of Medical Physics, School of Nuclear and Allied Sciences, University of Ghana, under the supervision of Dr. Francis Hasford, Prof John Humphrey Amuasi and Mr. Eric Kotei Addison.

I hereby affirm that, no part of this work has been presented in part or whole to any other University or institution for the award of a diploma, or degree at any level. Accordingly other works and/or researches done by other researchers cited in this work have been acknowledged under references.

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ABSTRACT

For LDR brachytherapy, the time taken to deliver the dose to a patient is very long which makes the patient be on the machine for a very long period of time. Due to this long treatment time, soaking of vaginal packing and patient movement can change the applicators position. The aim of this work is to assess the dose variation to point 'A' and point 'B' as well as critical organs (i.e. bladder and rectum) for low dose rate (LDR) brachytherapy at Komfo Anokye Teaching Hospital. Forty (40) patients with invasive cervical cancer were treated with LDR brachytherapy with 30 – 35Gy prescription to point 'A'. Two pairs of orthogonal X-ray images were taken: one prior to treatment and the other after treatment. Pre- and post- treatment doses were calculated and analyzed to determine the variation in the doses to points 'A' and 'B', as well as, the critical organs. The disparity in dose to point 'A' was found to be 1.16% which is very laudable as compared to other studies that established dose variations of 2, 35, 8 and 20%. Variation in dose at point B in this work was 0.75%. In this study, average variations of 2.32 and 0.30% were found for the bladder and rectum, respectively. For quality assurance purposes the variation found between prescribed and deposited dose was 2.11%. The geometric variations between the Intracavitary Brachytherapy Treatment (ICBT) applicators and the critical organs vary during the treatment procedure and thus result in dose alterations. Since the variation is within the recommended standard levels, it can be concluded that, the practice at KATH meets the international standard.

DEDICATION

This work is dedicated to my brother Solomon Adom (of blessed memory), my wife Miriam Owusu Sekyere and my wonderful children Othniel Adom Agyapong, Ilona Kissiwaah Adom and Kennice Nyarko Adom.

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ABBREVIATIONS

2D	Two-Dimensional
3D	Three-Dimensional
3DCRT	Three-Dimensional Conformal Radiotherapy
ABS	American Brachytherapy Society
AP	Anterior-posterior
CFRMI	The French Committee on Ionizing Radiation Measurements
CT	Computer Tomography
CTV	Clinical Target Volume
DNA	Deoxyribonucleic Acid
EBRT	External Beam Radiation Therapy
GTV	Gross Tumor Volume
GTV_{LN}	Lymph Nodes Gross Tumor Volume
HDR	High Dose Rate
ICBT	Intracavitary Brachytherapy Treatment
ICRU	International Commission on Radiation Units and Measurements
IGRT	Image-Guided Radiation Therapy
IMRT	Intensity Modulated Radiation Therapy

IORT	Intra-Operative Radiotherapy
LAT	Lateral
KATH	Komfo Anokye Teaching Hospital
LDR	Low Dose Rate
MDR	Medium Dose Rate
MRI	Magnetic Resonance Imaging
NCRP	National Council on Radiation Protection and Measurements
pCTV	primary Clinical Target Volume
QUANTEC	Quantitative Analysis of Normal Tissue Effect in the Clinics
rCTV	regional Clinical Target Volume
RT	Radiotherapy
SBRT	Stereotactic Body Radiation Therapy
TBI	Total Body Irradiation TBI
TPS	Treatment Planning System
VMAT	Volumetric Modulated Arc Therapy
WHO	World Health Organization

CHAPTER ONE

1 INTRODUCTION

1.1 BACKGROUND

Cervical cancer is the fourth most occurring cancer affecting women in the world, after breast, colorectal, and lung cancers, with 528 000 new cases every year; it is most common in the lower resource countries of sub-Saharan Africa (WHO 2012). Cancer of the cervix is responsible for the death of an estimated 231000 women annually, with over 80% of these deaths occurring in developing countries (Domfeh et al. 2008). The second most prominent female malignancy in sub-Saharan Africa is cervical cancer (Parkin et al. 2003). Southern and Eastern Africa with respectively 43 per 100000 women and 37 per 100000 women reported the maximum incidence rates in the world (WHO, 2008). The corresponding mortality rates are 34 per 100000 women and 23 per 100000 women. For instance, the incidence rate for all races is 8.2 per 100000 women in the United States (Leaver and Labonte, 2010), while Makin and Kamanu (2010) note that reported mortality rates in resource rich countries seldom exceed 5 per 100,000 women. This difference between Africa and the advanced world is enormous, and the success in the latter, is attributed largely to wide spread comprehensive cervical cancer screening control programs (WHO, 2008; Adewole et al., 2005). In Africa, with a total number of 267.9 million women aged 15 years or greater, estimates are that 78897 women are diagnosed with cervical cancer annually and 61671 (78%) die from the disease (Denny, 2010). In sub-Saharan Africa, among the highest worldwide with the available age-standardized rates ranging from 19.9 per 100000 in Ibadan, Nigeria, (Parkin et al. 2003) through 35.7 per 100000 in Bamako, Mali, to 41.7 per 100000 in Kyadondo, Ugandais the cervical cancer

incidence (Parkin et al. 2002). The occurrence of cervical human papilloma virus (HPV) infection differs significantly worldwide. Population-based HPV prevalence surveys have revealed a 13-fold disparity in women who are sexually-active from ages between 15 and 65 years, with the range of 2.0% in Hanoi, North Vietnam (Anh et al. 2003), 3.0% in Barcelona, Spain (de Sanjose et al. 2003), 14.8% in Bogota, Columbia (Molano et al. 2002), through 17.7% in Concordia, Argentina (Matos et al. 2003) to the highest of 26.3% in Ibadan, Nigeria, a West African neighbor of Ghana (Thomas et al. 2004).

Radiotherapy, in the form of External Beam Radiotherapy (EBRT), brachytherapy or both, constitutes an essential aspect of treating carcinomas. Cancers such as those of the breast, prostate, cervical and skin are usually treated by combining both EBRT and brachytherapy. In Ghana, brachytherapy is usually used to manage cervical cancers and sometimes prostate cancers. Intracavitary brachytherapy (ICBT) was first performed by Margaret Cleaves in 1903 which involves placement of uterine tandem and vaginal ovoids (Koushik et al. 2010). Due to technological advancements, three types of brachytherapy have been developed; high dose rate (HDR), medium dose rate (MDR) and low dose rate (LDR) brachytherapy, with LDR and HDR commonly used. The development of after loading along with different applicators which make use of newer radioisotopes with a range of specific activities(resulting in varied dose rates), has increased flexibility in brachytherapy for the modern radiation oncologist (Datta et al. 2001). Furthermore, the readiness of modern imaging devices for better tumor localization and newer treatment planning systems has provided options for altering patient treatment (Datta et al. 2001). Again, technological advancements in dosimetry, treatment planning, treatment delivery-units and tumor imaging have aided the radiation oncologist and physicist to individualize treatment.

Unlike brachytherapy, this has been accepted and put into practicing teletherapy. In Ghana, both HDR and LDR are used in the two national radiotherapy facilities. For a better and effective treatment delivery and reduction in the risk of complications, the proper insertion of the intracavitary applicator is paramount to the success of the treatment. Thus, a higher dose will be delivered to the main tumor while sparing surrounding healthy tissues. In treating cervical cancer with brachytherapy, a high dose rate (HDR) or low dose rate (LDR) therapy machine may be deployed depending on its availability to the radiotherapy department. In using continuous LDR brachytherapy, the displacement and motion of the applicator as a result of prolonged treatment time and unavailability of rigid applicator fixation is one of the most major problems (Ljunggren et al, 1987). Other authors have found that there is a significant inter-fraction motion of the reference points as the International Commission on Radiation Units and Measurements, ICRU Report 38 (ICRU, 1985) defined with regards to the bony pelvis between the first and second intracavitary applications. This movement causes a variation in the dose to the prescription point from 233 to 135% (Grigsby et al. 1993).

1.2 STATEMENT OF THE PROBLEM

The clinical decision to determine the radiation amount given to a patient undergoing LDR intracavitary brachytherapy is determined by the radiation dose the critical organs (i.e. the rectum and the bladder) receive. The position of the applicators (i.e. the vaginal ovoids and the uterine tandem) are very crucial in the delivery of radiation dose to the diseased area. In some cases, only two ovoids are used, that is, when the patient has undergone total or partial hysterectomy. For LDR brachytherapy, the time taken to deliver the dose to a patient

is very long which makes the patient be on the machine for a very long period of time. Low dose rate intracavitary brachytherapy involves delivery of radiation at a continuous rate of 0.4-2 Gy/hr and this means, delivering 30 to 35 Gy will take around 30 to 50 hours. Due to this long treatment time, soakage of vaginal packing and patient movement can change the applicators position. These changes go a long way to defeat the intent of the oncologist and makes most of the patients have some complications such as fistula after treatment. In view of this, there is the need to evaluate the dose variation to the rectum and bladder as a result of the patient delay on the machine.

1.3 OBJECTIVES

The principal objective of this work was to determine the variation of dose to the critical organs (i.e. rectum and bladder) resulting from prolonged treatment periods for cervical cancer patients undergoing brachytherapy. This objective was to be achieved by:

- Evaluating the geometric movement of the fixed reference points in LDR brachytherapy patients.
- Determining the actual dose difference, in turn to critical structures and the clinical outcome.

The specific objectives are to:

- Evaluate rectal and bladder doses in pre-treatment planning.
- Evaluate rectal and bladder doses in post-treatment planning.
- Assess dose variations between pre- and post-treatment plans.

1.4 RELEVANCE AND JUSTIFICATION

LDR brachytherapy takes a very long time to deliver a specific dose to a target during a brachytherapy procedure. Dose variation assessment is, therefore, required before and after treatment to evaluate the dose delivered to the target as a result of patient movement due to the longer stay on the machine. It also helps the radiation oncologist to make an informed decision on whether to fractionate or give full dose. Dose variation assessments in LDR brachytherapy treatments have the potential to ensuring accurate and precise treatment in radiotherapy centres.

1.5 SCOPE AND LIMITATION

The research study covers the steps below:

- Acquisition of orthogonal X-ray images of patients reporting for cervical brachytherapy procedures. The radiographs obtained on the patients are digitized into a treatment planning system and planned to determine the absorbed doses and dose to the rectum and blabber.
- Acquisition of orthogonal X-ray images of patients after undergoing cervical brachytherapy to determine absorbed doses and dose to rectum and bladder.
- Comparison between the forecasted and delivered doses is made to measure the effect of movements and changes in applicator positions on the treatment delivered.

1.6 STRUCTURE OF THE THESIS

This thesis is presented in five main chapters:

- Chapter one gives an introduction to the research topic, explains the purpose of this study, as well as, its importance; and the importance for checking the dose variation in LDR intracavitary brachytherapy treatment technique;
- Chapter two provides an overview of the literature associated to the study, what other researchers have done, theoretical approaches used in the past and how they are applied in practice;
- Chapter three explains materials used for the study and the techniques applied in all the needed calculations;
- Chapter four presents the results generated and the successive discussions, giving an understanding of the outcomes and their inference; and
- Chapter five is the conclusion of the work, providing a general summary of the thesis, lessons learned and recommendations based on the results available.

CHAPTER TWO

2 LITERATURE REVIEW

2.1 BACKGROUND

Cancer is a disease that occurs at the cellular deoxyribonucleic acid (DNA) level. It is an uncontrolled growth of human cells, making them able to spread to surrounding and remote tissues. Cancer has the potential to invade other body parts through the hematopoietic and/or lymphatic systems. There are over one hundred types of cancers and are mostly named by the organ or kind of cell they attack (cancer that begins in melanocytes of the skin is melanoma). Cervical cancer begins in cells lining of the cervix. The squamous cells and glandular cells are the two main forms of cells covering the cervix. The meeting place of these types of cell is known as the transformation zone. Early detection of the tumor makes its treatment quite easier and effective. If there is an uncontrolled cell growth, it will end up in death of the individual (Chaffer et al., 2011). The past years have observed a great development towards the treatment and understanding of the previous proposed cancer hallmarks (Hanahan and Weinberg, 2000) and with improvements in early detection and in the different treatment modalities, many cancers have become curable (Pollack et al., 2009). In treating cancers (depending on the stage and grade), surgery, chemotherapy or radiation therapy are considered. Radiotherapy involves the use of high energy radiations (i.e. photons and particles) to treat illness (usually cancers). After Wilhelm Röntgen had discovered X-rays in 1895, its clinical usefulness, by way of cancer treatment was first appreciated. Furthermore, about half of all cancer patients will undergo radiotherapy in their course of illness

(Delaney et al., 2005; Begg et al., 2011) with an estimation that radiotherapy contributes to around 40% towards curative treatment (Barnett et al., 2009).

2.2 PRINCIPLES OF RADIATION THERAPY

Radiation is the emission of energy as electromagnetic waves or as moving subatomic particles, especially high energy particles which cause ionization. In radiotherapy, the radiations used to kill the cancer cells are known as ionizing radiation. These ionizing radiations form ions and deposit energy in the tissue cells they pass through. This energy deposited can cause genetic changes resulting in cancer cell death. The DNA is damaged by a high energy radiation and the cell loses its ability to divide and proliferate further (Jackson and Bartek, 2009).Even though radiation causes damage to both normal cells as well as cancer cells, the therapeutic goal is to cause lethal damage to cancer cells and minimize radiation dose to normal cells. Table 2.1 shows a list of common cancers treated with radiotherapy. Radiation can be delivered in two ways, which are external beam radiation where radiation is delivered from outside the body by aiming high-energy rays to the location of the tumor; and brachytherapy, where the source is placed directly into the tumor.

Table 2.1 Examples of cancers treated with radiation therapy.

Early cancers curable with radiation therapy alone	**Cancers curable with radiation therapy in combination with other modalities**
Skin cancers (Squamous and Basel cell)	Breast carcinomas
Prostate carcinomas	Rectal and anal carcinomas
Lung carcinomas (non-small cell)	Locally advanced cervix carcinomas
Cervix carcinomas	Locally advanced head and neck carcinomas
Lymphomas (Hodgkin's and low grade Non-Hodgkin's)	Locally advanced lung carcinomas
Head and neck carcinomas	Advanced lymphomas
	Bladder carcinomas
	Endometrial carcinomas
	CNS tumors
	Soft tissue sarcomas
	Pediatric tumors

2.3 RADIATION THERAPY TECHNIQUES

2.3.1 Fractionation.

Radiotherapy administered in a fractionated regime is dependent on the different radiobiological properties of both cancer and various normal tissues. In general, these regimes increase the survival advantage of normal tissues over malignant cells, mostly based on the fact that, normal cells have a better sub lethal damage repair of radiation

damage than cancer cells. Normal cells have more time to repair damage before replication than the cancer cells. In the 1920s, initial effects of fractionated radiotherapy finally led to the development of regimes comparing various treatment schedules based on overall dose, number of fractions and total treatment time (Bernier et al., 2004). Current regimes are based on the linear-quadratic formula which takes care of the time-dose factors for individual tumor types and normal tissues (Ellis, 1969). A typical radiation therapy regime now includes daily fractions of 1.5 to 3Gydelivered over several weeks.

2.3.2 External Beam Radiation Therapy (EBRT)

This is the most commonly used form of radiation therapy, and most often uses photon beams. The radiation originates from an external source and is focused on the tumor. High energy X-rays and/or gamma rays are used to deposit radiation doses to the tumor to damage the cancerous cells and, with careful treatment planning, healthy cells are spared. During EBRT sessions, patients are made to lie on a treatment couch in one position for every fraction of treatment. For every fraction, more than one radiation beams from several gantry angles are focused on the patient. A cobalt-60 therapy machine or linear accelerator (LINAC) is usually used for EBRT. Before the start of radiotherapy treatment procedure, a treatment plan is designed and is done by arranging beams at angles to deliver dose at the site of the tumor(s). This is done by taking a CT scan to get a 3-dimensional image of the body of the patient. Treatment Planning Systems (TPSs) are used to generate beam shapes and dose distributions with the intent to maximize tumor control and minimize normal tissue complications. Ideally, EBRT would destroy a cancerous cell/tissue every time if a big enough dose could be given to the cancer. The therapeutic goal is to deliver a very high

dose to the cancer cells whiles minimizing radiation to the normal cells. But in reality, this is not possible therefore there is a compromise between sparing healthy tissues from damage and killing the cancerous ones, and therefore, radiotherapy techniques need to be improved.

Several techniques of EBRT exist and these are employed depending on several factors like availability of technology and the treatment option. These techniques include three-dimensional conformal radiotherapy (3DCRT), intensity modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), image guided radiotherapy (IGRT), stereotactic body radiation therapy (SBRT), radiosurgery, proton therapy, adaptive radiotherapy, intra-operative radiotherapy (IORT), molecular radiotherapy, and total body irradiation (TBI).

2.3.3 Brachytherapy

This is a term which describes the short distance treatment of cancer with radiation from small, encapsulated radionuclide sources. These sources are directly placed into or near the tumor. The dose can be delivered either by temporal or permanent implants. Photon emitting sources are commonly used in brachytherapy; however, there are few specialized cases where beta or neutron emitting sources are used. Brachytherapy treatment is divided into two main types;

- Intracavitary, where sources are placed in body cavities close to the tumor volume;
- Interstitial, where sources are implanted within the tumor volume.

There are other common forms of brachytherapy treatments which include surface plaque, intraoperative, intravascular and intraluminal source applications, where either gamma or

beta emitting sources are used. The advantage of brachytherapy treatments over external beam radiotherapy is its ability to localize the delivered dose to the target volume. (Suntharalingam et al., 2005). The disadvantage is that brachytherapy can only be used in cases where the tumor is well localized and relatively small. In a typical radiotherapy department about 10–20% of all radiotherapy patients undergo brachytherapy (Suntharalingam et al., 2005). Several factors must be considered when delivering brachytherapy, especially, how the sources are positioned relative to the volume to be treated. Tables 2.2–2.5 summarize brachytherapy treatment techniques with regard to the type of implant, duration of implant, method of source loading and dose rate according to the ICRU (ICRU, 1985)..

Table 2.2 Various types of brachytherapy implant

Type of implant	**Description**
Intracavitary	Sources are placed into body cavities close to the tumor volume
Interstitial	Sources are implanted surgically within the tumor volume
Surface (mould)	Sources are placed over the tissue to be treated
Intraluminal	Sources are placed in a lumen
Intraoperative	Sources are implanted into the target tissue during surgery
Intravascular	A single source is placed into small or large arteries

Table 2.3 Brachytherapy treatments classified with respect to dose rate

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

2.3.3.1 Brachytherapy Applicators

Several applicators used in brachytherapy are accessible for gynecologic applications; nevertheless, the supremacy of one over another cannot be promoted. A model gynecological brachytherapy applicator should have the following features: Simple, comfortable for patient, high tensile strength, economical, robust, nontoxic, ease of sterilization, and adaptability. Apart from its physical features, an applicator should be easily "image-able" using different modalities, comprising CT and MRI, with marginal image artefact (Suntharalingam et al., 2005).

2.3.3.2 Applicator Fixation and Immobilization

Patient immobilization and organ fixation are renowned as critical to the radiation therapy outcome. In brachytherapy, the outcome also could be determined by the maintenance of the relative position of the applicator to the target and organs of concern. Vaginal packing and simple waistbands are mutual efforts at fixation. During LDR brachytherapy an initial and final check should be carried out in order to assess changes in the applicator positions (Suntharalingam et al., 2005).

2.3.3.3 Cs-137 Brachytherapy Source

Caesium-137 was used to substitute radium-226 for short-term interstitial/intracavitary low dose rate brachytherapy due to its stable daughter product and improved radiation protection features. It is 'readily' acquired from fission of uranium-235 in a nuclear reactor. The half-life of ^{137}Cs is 30.1 years. The radioactive material is then doubly encapsulated in stainless steel, with each layer soldered closed.

2.3.4 Definition of Organs at Risk

The description of healthy tissue volumes at risk is set on the basis of the MRI outcomes. Imaging is done with the patient in the treatment position, with all other treatment settings replicated as meticulously as possible. In cases where patients lie in supine with the knees slightly raised, patient imaging is done in the exact position. In the imaging process, an MRI-compatible treatment applicator is placed, along with a Foley catheter in the bladder. A rectal marker, if used, must be MRI compatible. Imaging of the bladder is duplicated as closely as possible for the treatment conditions. The anterior and superior walls of the bladder move away from the treatment applicator when the bladder is filled, thereby minimizing the dose. Under some conditions, filling of the bladder may push the posterior and inferior walls closer to the applicator, thereby increasing the dose to these areas (Nag et al., 2004).

Just like the bladder, filling of the rectum during the time of imaging and treatment should be the same. Sometimes, some late complications emanate as a result of dose to the small bowel after many years of treatment.

2.4 BRACHYTHERAPY SYSTEMS

Brachytherapy systems are specific systems containing radioisotope(s) that have spatial distribution in an applicator to deliver a specific dose to a designated region. Specification of treatment in terms of dose, timing, and administration is very crucial within every system in order to make prescriptions in a reproducible manner. In the treatment of the cervix, various systems have been developed for dose specification but the two systems mostly used are the Manchester and the ICRU systems. Others include Stockholm and the historical Paris system.

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2.4.1 ICRU System

The system recommended by the ICRU relates the dose distribution to the target volume rather than to a specific point (ICRU, 1985).

2.4.2 Manchester System

This system was formerly developed as a practical system for interstitial, mould, and intracavitary radiotherapy using radium. It gives rules that state how the radium is to be distributed, and tables which allow either the amount of radium required, or the treatment time to be calculated. The system has also successfully been used with other radionuclides. The source strength of those radionuclides with a long half-life and a short half-life is specified conveniently by the radium equivalent mass and the initial activity, respectively. A numerical factor, determined by the exposure rate constant, the actual total treatment time and the half-life, is used to estimate the equivalent radium milligram hours.

Mass, equivalent mass, and activity are all acceptable statements of the source content and, therefore, of source strength. Alternatively, the strength of a source may be specified in the form of the radiation emission. The use of exposure rate at a specified distance was recommended by the National Council on Radiation Protection and Measurement and has been discussed in papers by Wambersie et al (1973), and Dutreix and Wambersie (1975). Since then, exposure and exposure rate have been substituted in modern radiation dosimetry by air kerma and air kerma rate. The French Committee on Ionising Radiation Measurements proposed, and the British Committee on Radiation Units and Measurements formally recommended that brachytherapy source strength should be identified in terms of air kerma rate at 1 m and that the unit used should be the microgray per hour (μGyh^{-1}) (Massey et al., 1985). The Manchester system is characterized by doses to four points: 'A', 'B', bladder and rectum (ICRU, 1985). Point 'A', which is located 2 cm superior to the cervical orifice and 2 cm lateral to the cervical canal determines the duration of implant. Point 'B' is 3 cm laterally to point 'A' only when there is displacement in central canal, otherwise it remains fixed at 5 cm from the midlines. A radiation survey is then performed in areas within and around the patient's room after the implantation of the sources in the patient. Radiation levels are measured and recorded in order to assist in maintaining minimum exposure of hospital staff and visitors.

2.5 MAGNITUDE OF DISPLACEMENTS OF APPLICATORS

Corn in the 1980s first estimated the magnitude of variation of applicators, showing several dislocation of applicators in the lateral direction on an average of 3 mm (Corn et al., 1993). Other oncologists, such as, Pham et al. (1998) and Bahena et al. (1998) also found that the

displacements were not only in lateral, but also in antero-posterior and superio-inferior directions. In the study of Koushik et al. (2010), the normal dislocations in the lateral and antero-posterior directions were 3 and 1 mm, respectively. It kowtows to the above cited studies. Glenn et al.(1993) have assessed the geometric movement of the fixed brachytherapy reference points comparative to the bony pelvis, all through the time interval of the first and the second gynecologic intracavitary implants. Using a Fletcher-Suit-Delclos applicator in 40 successive patients, they detected movement of the absolute position of ICRU report 38 reference points between the first and the second applications, leading to substantial variances in the absolute dose rates to these reference points in two insertions. Kim et al. (1997) studied the major geometric disparities between multiple HDR applications of brachytherapy in 17 consecutive patients of carcinoma cervix treated with Gammamed (Isotopen Technik, Hann, Germany) or the Nucletron (Nucletron International, Veenendaal, The Netherlands) HDR systems. The geometric disparities studied involved an assessment of axis, length and slippage in the tandem placement and separation, vaginal packing and slippage in colpostat placement. Major disparities between applications were detected more commonly in the colpostat placement than in the tandem placement. For tandems, the rates of disparity stated by them were: 5.7% in axis, 4.3% in length, and 1.4% in slippage. For colpostat, the rates of variations were: 7.1% in separation, 25.7% in vaginal packing, and 7.1% in slippages.

2.5.1 Dose Variations Due to Change in Applicator Position

The variation of dose to point ‘A’ has been studied by many researchers such as Corn et al. (1993) and Hoskin et al. (1996). These studies revealed different levels of dose

variations such as 2, 35, 8 and 20%. These variations are widely ranged for the fact that some of the studies were done using radium source and several with iridium and cesium sources. According to the study of Koushik et al. (2010), they found an average variation of 14% which is well within the results shown in the above mentioned studies. They also assessed the variation in dose at point 'B' and point 'P' in order to make out the differences at the lymph node areas. In the study they found variations of 2 and 1% at point 'B' and point 'P', respectively. Corn et al. (1993) also observed this variation to be 1.7 and 0.9%, respectively. As per the guidelines, researchers usually use only one rectal point, but in Koushik et al' (2010) tried to include two rectal points in order to assess rectal morbidity. Studies done by Corn et al. and Pham et al. have shown certain dissimilarity of 3 and 10%, respectively (Corn et al., 1993; Pham et al., 1998). Koushik et al found 3.5% variation in the dose to rectum. For bladder dose variation, Koushik et al, presented on an average estimate of 9.3% (Koushik et al.,2010) and the results of other studies by Corn et al. and Pham et al. were 1.9% and18% respectively (Corn et al., 1993; Pham et al., 1998).

CHAPTER THREE

3 METHODOLOGY

3.1 MATERIALS

In this study, materials used for patient set up and absorbed dose calculations include Fletcher type brachytherapy applicators, Varian Acuity simulator, Prowess Panther treatment planning system (TPS) and Cs-137 LDR brachytherapy system.

3.1.1 Fletcher Type Brachytherapy Applicators

The Fletcher type brachytherapy applicators employed in this work comprise of a tandem and two vaginal ovoids. The diameter are 0.6 and 2 cm for the tandem and ovoids, respectively, with an active source length of 1.72 cm. The applicators are simple to use, comfortable for patients and have a high tensile strength. It is also economical, robust, non-toxic and easier to sterilize. The tandem and ovoids are made from titanium. The Fletcher type brachytherapy applicators are shown in Figure 3.1.

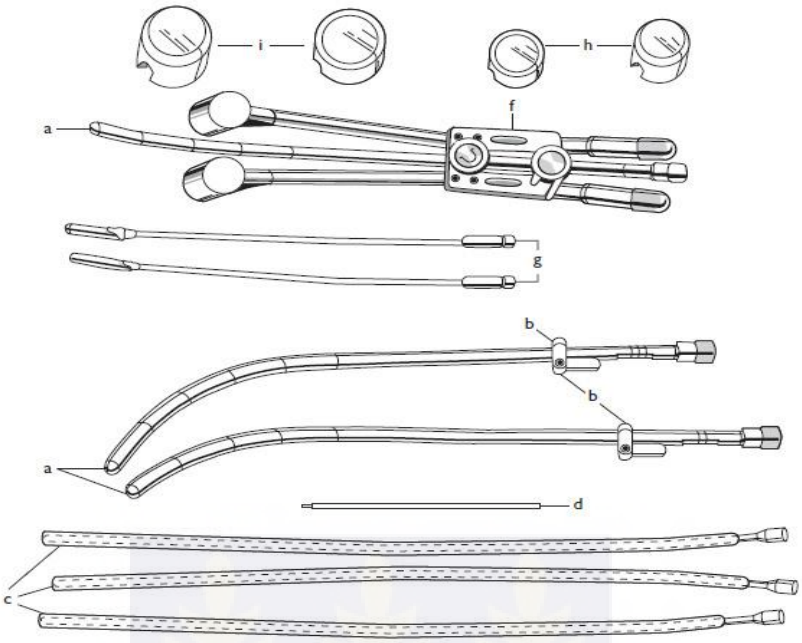


Figure 3.1 Fletcher type brachytherapy applicators.

3.1.2 Varian Acuity Simulator

The Acuity simulator is a highly valued verification and simulation system and is designed to work alongside CT simulators. This system can also be used to plan and simulate brachytherapy patients. This allows the whole process to be done in a single room without having to utilize multiple rooms within the department. The stable gantry gives Acuity the maximum isocentric accuracy specification in its field. It supports both two-dimensional (2D) and three-dimensional (3D) imaging. Figure 3.2 shows a Varian Acuity simulator.

Figure 3.2 Varian Acuity Simulator

3.1.2 Prowess Panther Treatment Planning System

Prowess® has a competitive advantage by offering Panther 3D conformal therapy on the familiar and most user-friendly Windows® platform. Users can generate treatment plans quickly due to the familiar Windows®. The version used in this work is v.4.31. Figure 3.3 shows an interface of the Prowess® Panther TPS at Komfo Anokye Teaching Hospital.

Figure 3.3 Interface of Prowess® Panther TPS

3.1.3 Cs-137 LDR Brachytherapy System

The treatment machine used in the study is AMRA-Curietron with model number CA: 9610, which is a LDR brachytherapy machine and manufactured by Cis-Bio International (Germany). The maximum activity of the source was 259 GBq. The system has five channels and is a remote afterloader as shown in Figure 3.4. In the Curietron treatment machine, the ovoids are marked with the letter "V" which represents channels 1 and 5, respectively. For the tandem, there are three channels which are marked by the letter "U." In this instance, there are three channels for "U"; these are channels 2, 3, and 4.

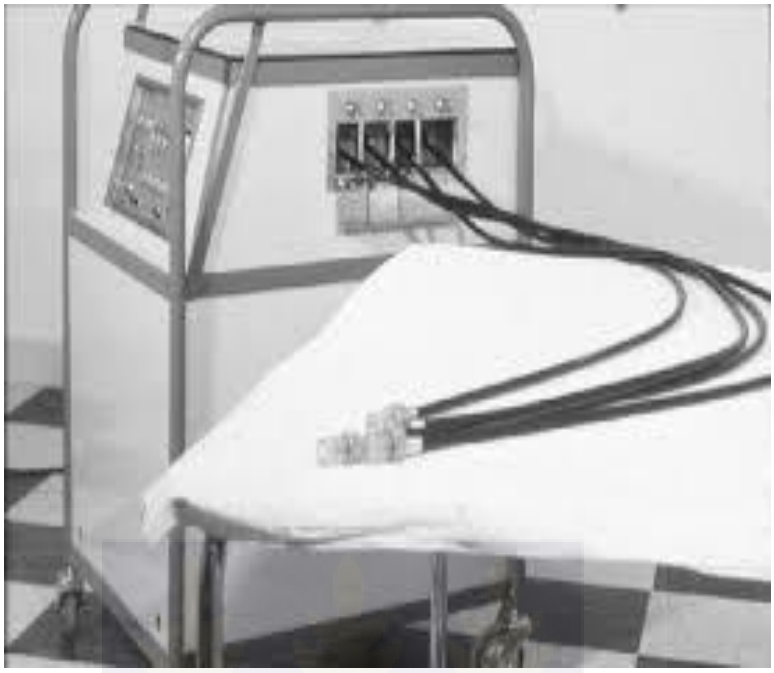


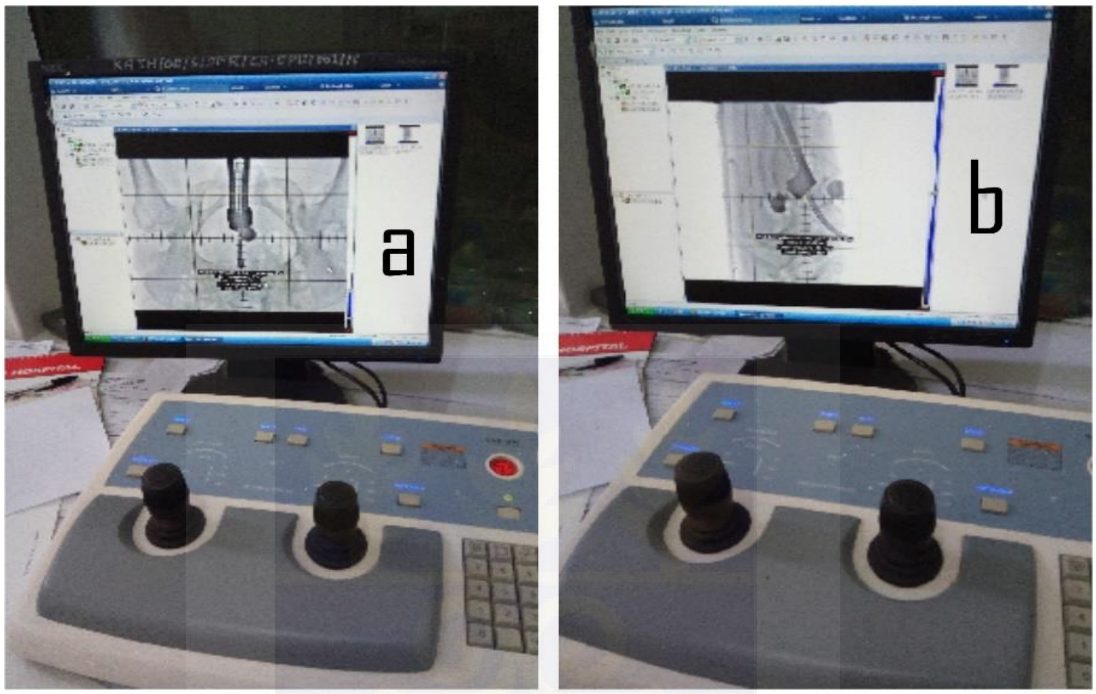
Figure 3.4 Cs-137 LDR Brachytherapy System

3.2 METHOD

3.2.1 Patient Imaging

The age group of adult patients for the study was between 25 and 60 years all being females with the tumor stages I-IV at KATH. Orthogonal images of anterior-posterior (AP) and lateral (LAT) were taken for every patient. In each case, two sets of orthogonal images (before and after treatment) were considered to decide on various parameters relating to the applicator geometry and its spatial relation to the bony pelvis as described in Figures 3.5(a) and 3.5(b). In order to see the bladder and rectum, Urografin (radio-opaque substance) was passed through a catheter into the organs. Gauze was packed into the vagina in order to stabilize the applicators. Reference planes (x, y, z) were also defined for each set of images by using the patient's bone landmarks to evaluate changes in positioning of

applicators relative to fixed bony landmarks of the patient. To ensure the same patient positioning for the post treatment images, marks were made on the patients.



a b

Figure 3.5 (a) AP image of the pelvis of a patient (b) LAT image of the pelvis of a patient

3.2.2 Patient Treatment

The Curietron LDR brachytherapy treatment machine has five channels to which the ovoids (marked ‘V’) and tandem (marked ‘U’) connect. During treatment, only one channel of the "U" was selected and used depending upon the measured length of the tandem that protruded. It has been found clinically that if the measured length (L) of the protruded tandem is ≤ 4 cm, then channel 2 is required to be used. Alternatively, if the measured length of the protruded tandem is between 4 and 5 cm, then channel 3 is required to be

used. If the measured length of the protruded tandem is found to be >5 cm, then channel 4 is required to be used.

In this study, four source arrangements or channel combinations were used, namely 1-2-5, 1-3-5, 1-4-5, and 1-5. The channel 1-5 combination was used when the patient had undergone total or partial hysterectomy. After the various combinations, the Cs-137 radioactive sources in the brachytherapy system were called in (moved into treatment positions) from their respective storage locations. The time at which the sources were called was noted. Figure 3.6 shows a schematic diagram of the source arrangement.

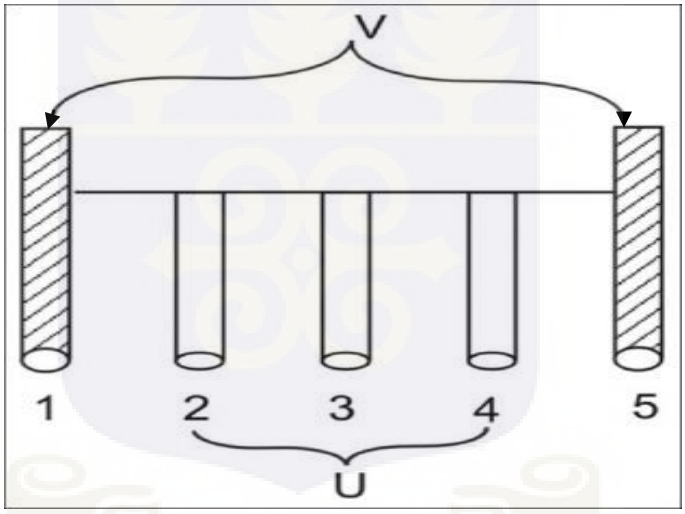


Figure 3.6 A schematic diagram of channel arrangement in AMRA-Curietron intracavitary brachytherapy system.

3.2.3 Brachytherapy Treatment Planning

3.2.3.1 Planning Process

The treatment was planned using the AP and LAT images obtained. Outline shape of the ovoid (on the lateral image) was obtained and the centre was located. The new diameters of ovoid and tandem on the image were measured (I), with the original diameter of 20 mm

and 6 mm for the ovoid and tandem, respectively. Equation 3.1 was used to estimate the magnification of the images (given tandem d_{tandem} = 6 mm, d_{ovoid} 20 mm).

$$Magnification\ (M) = \frac{Image\ size}{Object\ size} \qquad 3.1,$$

$$M_{tandem} = \frac{I}{6}\ \ M_{ovoid} = \frac{I}{20} \qquad 3.2,$$

The average of the magnifications of ovoid and tandem was then estimated and taken as the magnification factor of the lateral image M_{lat}.

$$M_{lat} = \frac{M_{tandem} + M_{ovoid}}{2} \qquad 3.3,$$

The active source length (17.2 mm) was then multiplied by the image magnification, to obtain the active source length which was used for the treatment planning.

$$source\ length_{apparent} = M_{lat}\ x\ 17.2\ mm \qquad 3.4,$$

The centre of the tandem was identified and the sources were allocated on it using a pair of vernier callipers including the interval between sources (given actual interval 3.1 mm).

$$interval_{apparent} = M_{lat}\ x\ 3.1\ mm \qquad 3.5.$$

A perpendicular line was drawn through the last point of the line source. One active source length ($source\ length_{apparent}$) was subtracted from ovoid length (apparent), then the average was found. A vernier callipers was used to demarcate the points from both ends of ovoid. The centre between two sources was noted and a perpendicular line drawn through, which was parallel to the perpendicular line drawn through the last point source. Point 'A' was located 2 cm above the intersection of the ovoid and the perpendicular line passing through the centre of the source located in ovoid and traced adjacent to the tandem. Point 'B' was located 3 cm away from point A lateral to the tandem on the AP image. Both points 'A' and 'B' were located on the image as multiples of the image magnification.

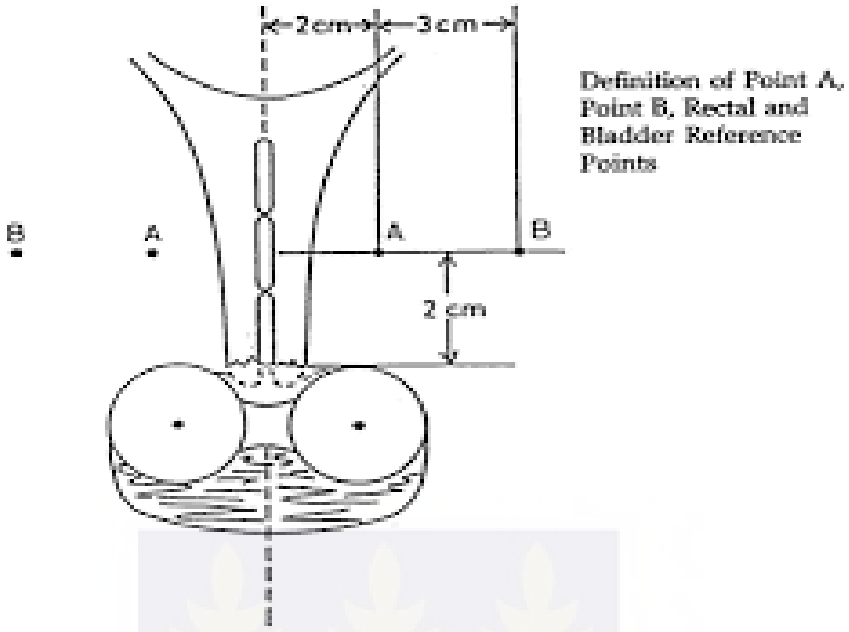


Figure 3.7. The position of dosage points A and B.

3.2.3.2 Digitization and Dose Computations

The LAT and AP X-ray images were digitized to generate a plan for treatment delivery. Beginning with the lateral, then to the AP, the points on the images were transferred unto the TPS. Data were input into the treatment planning computer, optimized, and dwell times and dose distribution calculated. The data were entered into the computer, based on information from the prescription by the physician who did the insertion and localization films. Figure 3.7 shows the planning, digitizing and dose computation phases in the study.

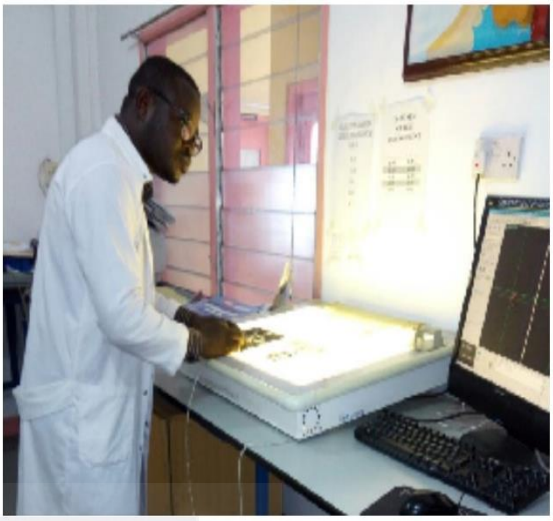


Figure 3.7a b

c

Figure 3.7a. Brachytherapy planning

Figure 3.7b. Digitizing the brachytherapy plan onto the TPS

Figure 3.7c. Dose calculation of the brachytherapy procedure.

Then absorbed dose to tissue/medium is given by,

$$D_{med} = D_{air}\left(\frac{\mu_{en}}{\rho}\right)_{air}^{med} \qquad 3.6$$

$$D_{med} = X\left(\frac{W_{air}}{e}\right)\left(\frac{\mu_{en}}{\rho}\right)_{air}^{med} \qquad 3.7$$

Where, $\left(\frac{W_{air}}{e}\right) = \frac{33.97J}{C}$;$\left(\frac{\mu_{en}}{\rho}\right)$ is the mass energy absorption coefficient, and X been exposure rate in the air. The mathematical equation for the treatment time is given as;

$$t = \frac{D}{\dot{D}} \qquad 3.8$$

where D = Prescribed dose,

$\dot{D}$ = Dose rate of cesium-137

D_{med} =absorbed dose to tissue/medium,

D_{air} = absorbed dose in air,

μ_{en} = energy absorption coefficient,

ρ = density of the medium,

3.2.4 Analysis

Calculations made in this study were done using Microsoft Excel which forms part of the Microsoft Office 2013 Suite. The variation in doses to point "A" and point "B" as well as the critical organs were determined by the use of the software. Tables and graphs for data analysis were also done using the same software.

CHAPTER FOUR

4 RESULTS AND DISCUSSION

4.1 DOSE VARIATIONS

Variability in doses to points 'A', 'B', bladder and rectum resulting from change or movement of applicators has been studied for forty (40) patients. Thirty-four (34) of the patients had their cervix present whiles six (6) patients had undergone hysterectomy. The variations were studied in terms of: (a) difference in pre and post treatment calculated doses and; (b) difference in prescribed and delivered doses, as shown in appendices C-F.

4.1.1 Dose Variations at Point 'A'

The geometrical point 'A' often occurs in a high gradient region of the pear-shaped volume of isodose distribution, based on the anatomy of the patient's pelvic region in the geometrical arrangement of the radioactive source. The slightest change in position can result in large differences in delivered dose. The dose variations at point 'A' for 34 patients with their cervix present is shown in Figures 4.1, 4.2 and 4.3 and in tabular form in Appendix A1.

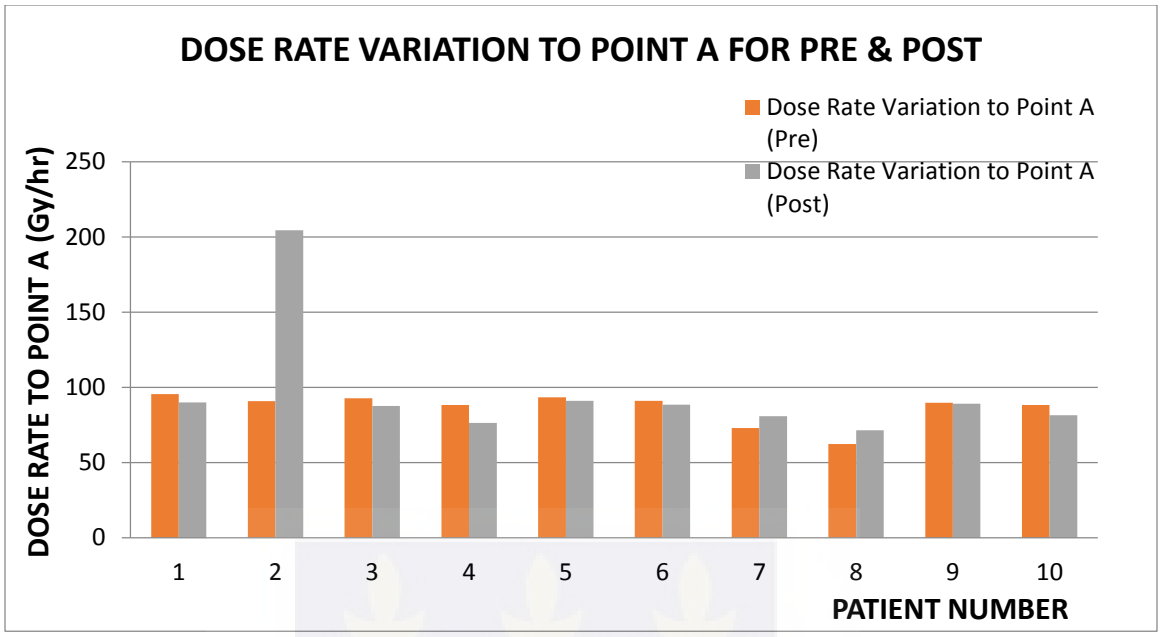


Figure 4.1A bar chart of dose rate variation to point 'A' for pre & post treatment for first 10 patients

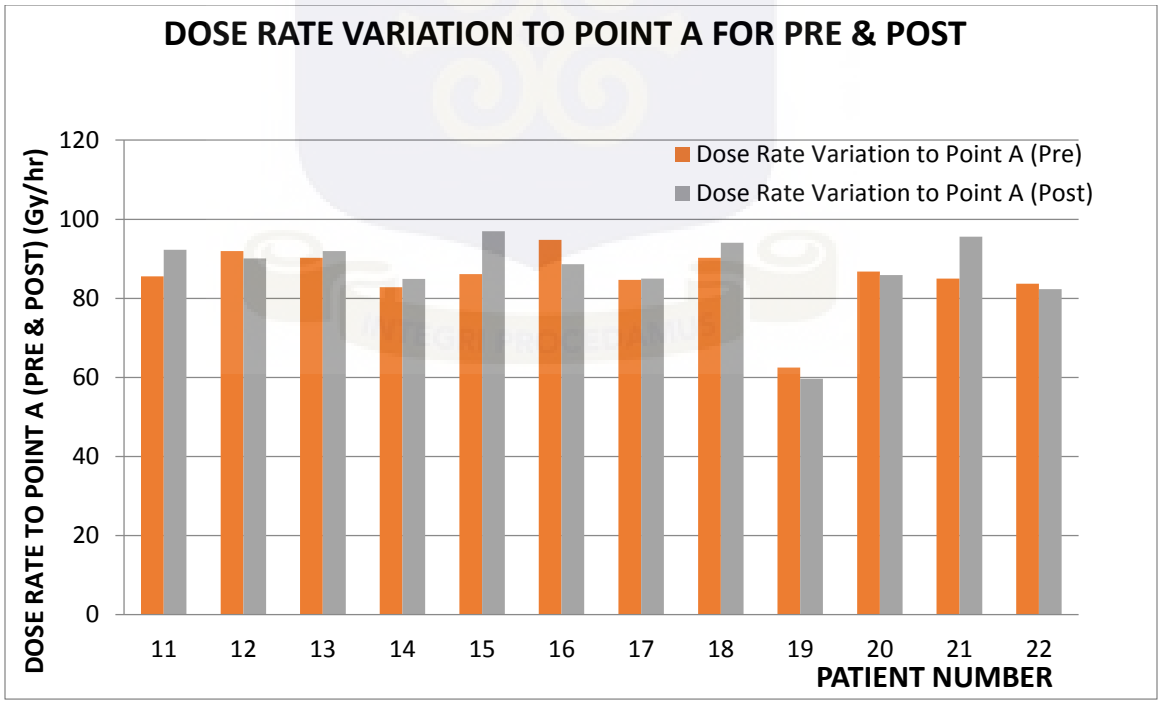


Figure 4.2 A bar chart of dose rate variation to point 'A' for pre & post treatment for next set of 12 patients

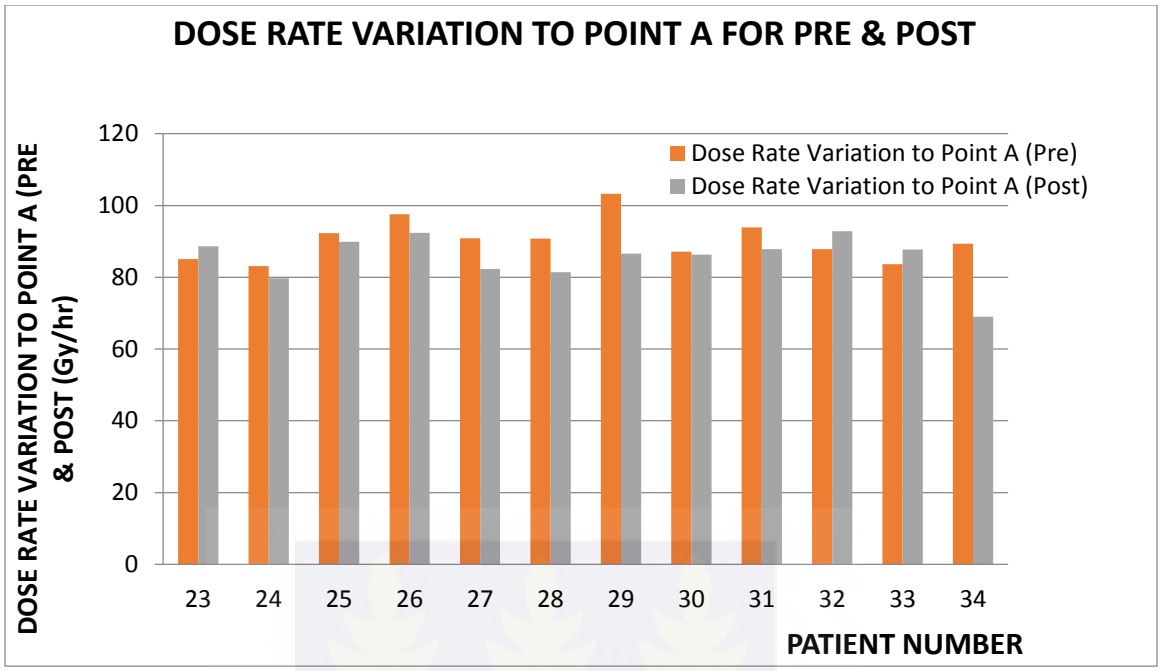


Figure 4.3 A bar chart of dose rate variation to point 'A' for pre & post treatment for last 12 patients

From Figures 4.1, 4.2 and 4.3 above, it was observed that there was minimum deviation between most of the pre-treatment calculated dose and post-treatment calculated dose. Patients 2, 4, 7, 8, 15, 21, 29 and 34 showed large deviations of 125, 13, 11, 15, 13, 12, 16 and 23%, respectively. The deviations occurred due to loose packing of the applicators, transport of patient from simulator room to brachytherapy room and instability of patients during the treatment. Patient 2 in Figure 4.1 showed an outrageous deviation, with more than 100% dose increment. It was observed that the tandem turned to the opposite direction making it move closer to the point 'A', thereby doubling the dose received. Patient 19 also showed a sharp decline in both pre- and post-treatment calculated dose (from Figure 4.2). This was as a result of a short tandem used which had only 2 source allocations, thereby reducing the dose rate to point 'A'.

Figure 4.4 and Appendix A2 show the dose variation at point A for 6 patients who had undergone hysterectomy.

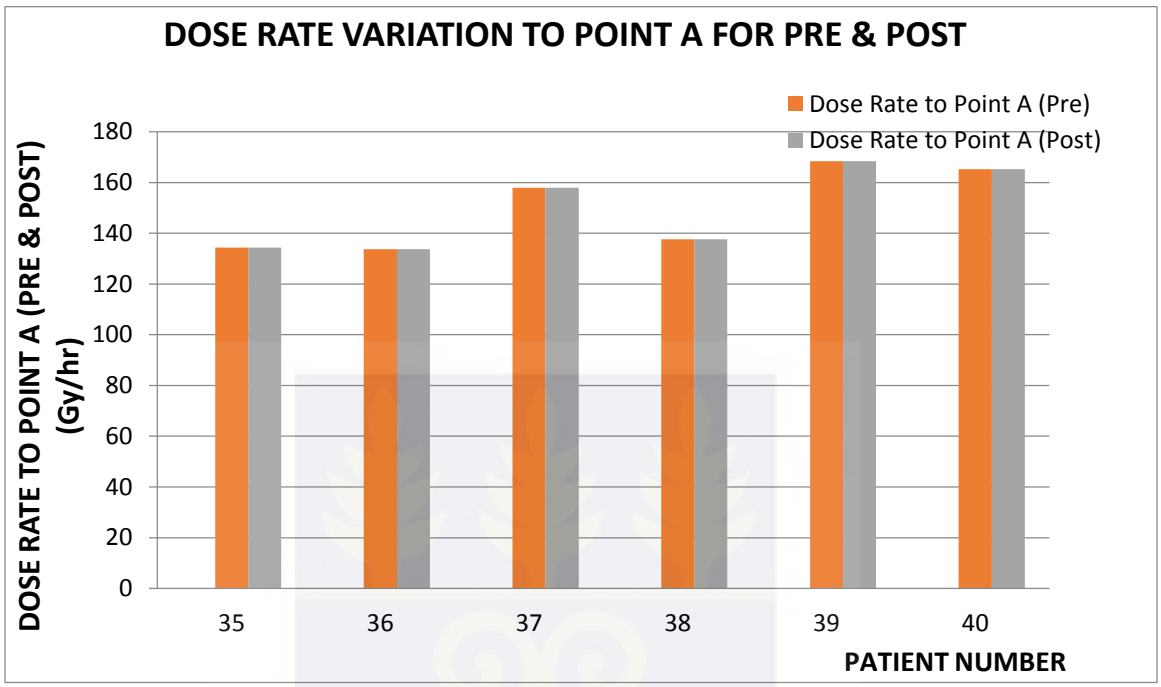


Figure 4.4 A bar chart of dose rate variation to point 'A' for pre & post treatment for 6 hysterectomy patients

The dose rates to point 'A' for pre- and post-treatment calculated doses do not differ much (since the time taken for treatment is shorter) for the patients who had undergone total or partial hysterectomy. For hysterectomy patients, point 'A' is located in the middle of the vaginal ovoids which are within the source. Therefore as the dose increases the time also becomes shorter resulting in less movement of the patient during treatment. Two patients (i.e. Patients 39 and 40) showed a 10% deviation which was the highest for the hysterectomy patients.

4.1.1.1 Difference in Prescribed Dose and Delivered Dose

In brachytherapy, doses are prescribed to point 'A' by clinicians since it is usually located within the tumor. Doses prescribed to point 'A' are usually 30 or 35Gy. Variation in doses prescribed and delivered is shown in Figures 4.5 and 4.6 and in tabular form in Appendix B. High variation between doses prescribed and delivered to point 'A' is not of much concern (i.e. when it does not lead to under dose of the tumor) since it is delivered to the tumor itself other than the organs at risk.

From Figures 4.5, it was observed that patients 2showed a delivered dose twice as much as the prescribed dose. This was not of much concern since further investigations of the same patient showed no alarming increase of the doses to the organs at risk. Even though the dose to point 'A' doubled, but, was within the tumor. The total bladder dose for the same patient after treatment was 65.05 Gy whiles that of rectum was 69.55 Gy. QUANTEC dose limit for LDR BT for bladder is 80 Gy, whiles that of rectum is 75 Gy. Some patients also showed lesser delivered doses than prescribed which was also not of concern since it did not lead to under dosing of the tumor.

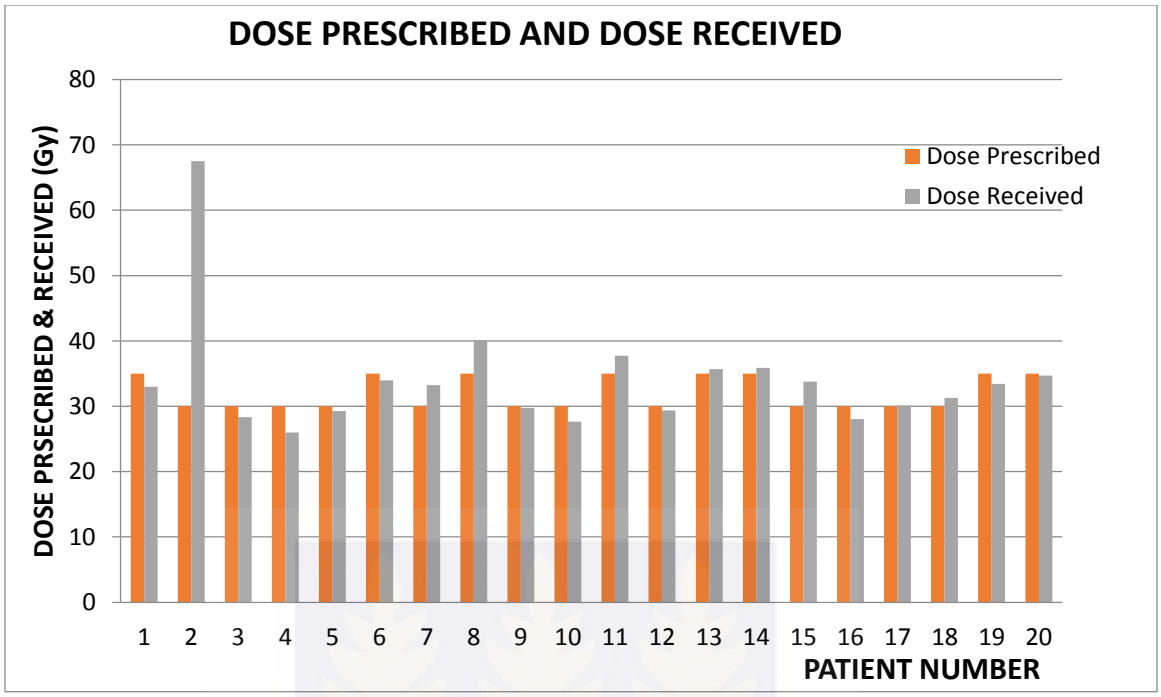


Figure 4.5A bar chart of dose prescribed and received for the first 20 patients

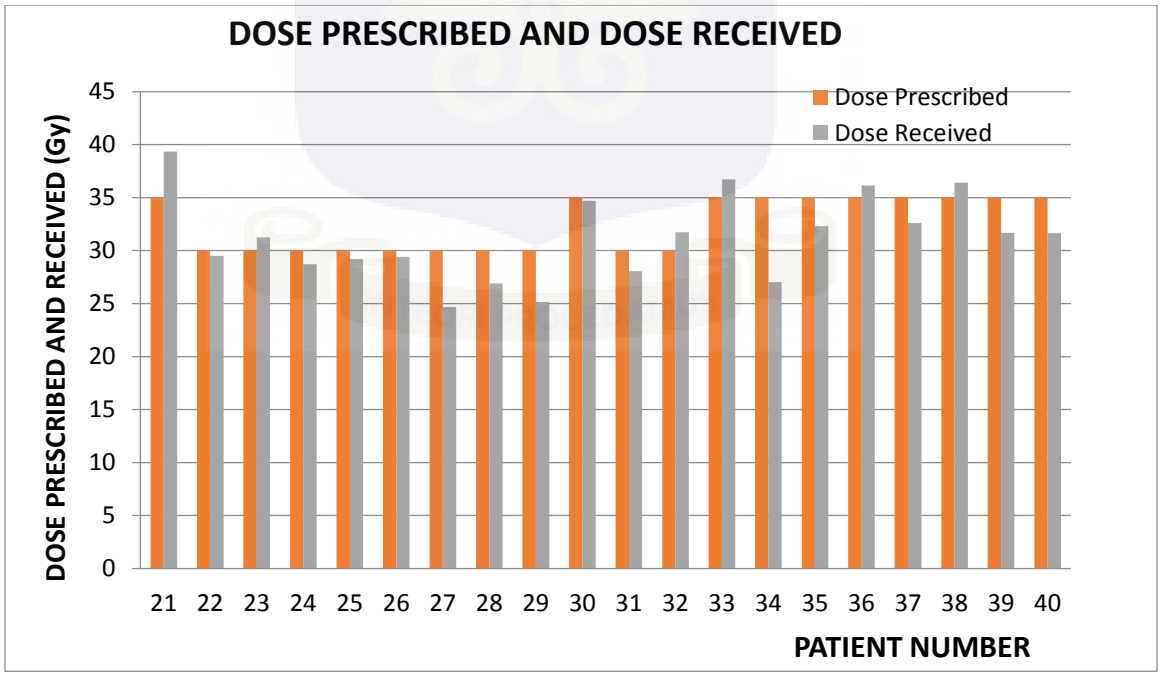


Figure 4.6 A bar chart of dose prescribed and received for the last 20 patients

4.1.2 Dose Variations at Point 'B'

Point 'B' is 5cm lateral from the midline at the same level as point 'A'. The dose variations at point 'B' for 34 patients with their cervix present is shown in Figures 4.7, 4.8 and 4.9 and in tabular form in Appendix G1.

The point 'B' does not rotate hence very small deviation is observed between the pre and post-treatment calculated doses. The dose rate to this point was very low compared with that of the critical organs. This was assessed to find out the difference at the lymph node area. From Figures 4.7, 4.8 and 4.9, Patients 15 and 18 showed very high deviations (12% and 21% respectively). This deviation is attributed to movement of the applicators due to loose packing.

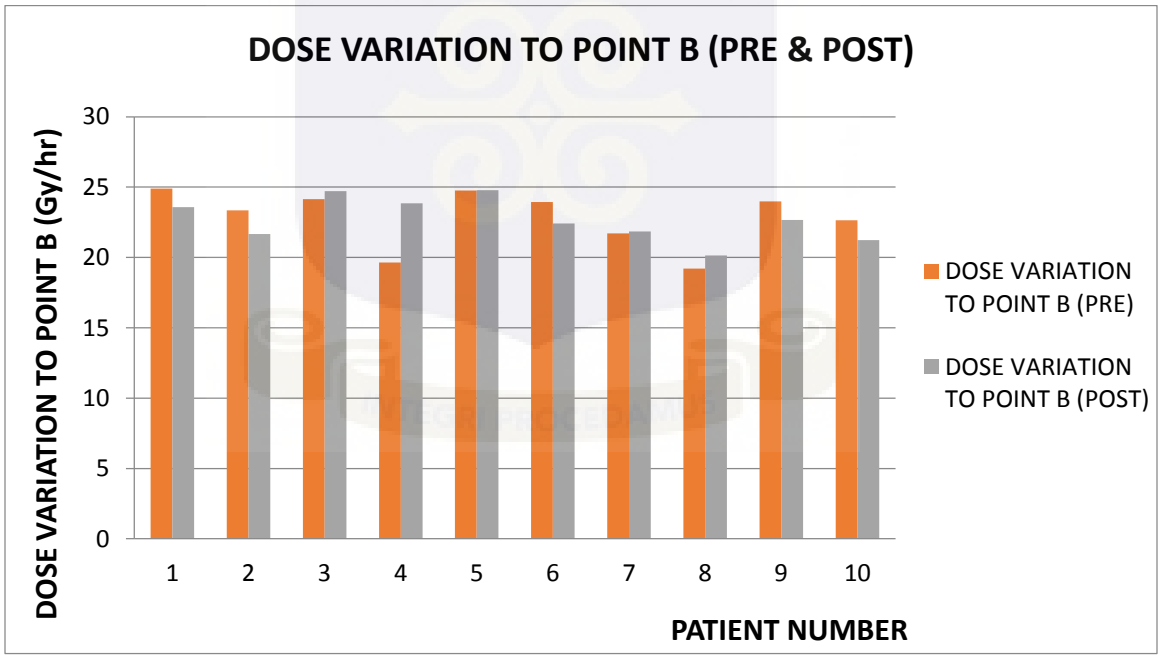


Figure 4.7 A bar chart of dose rate variation to point 'B' for pre & post treatment for first 10 patients

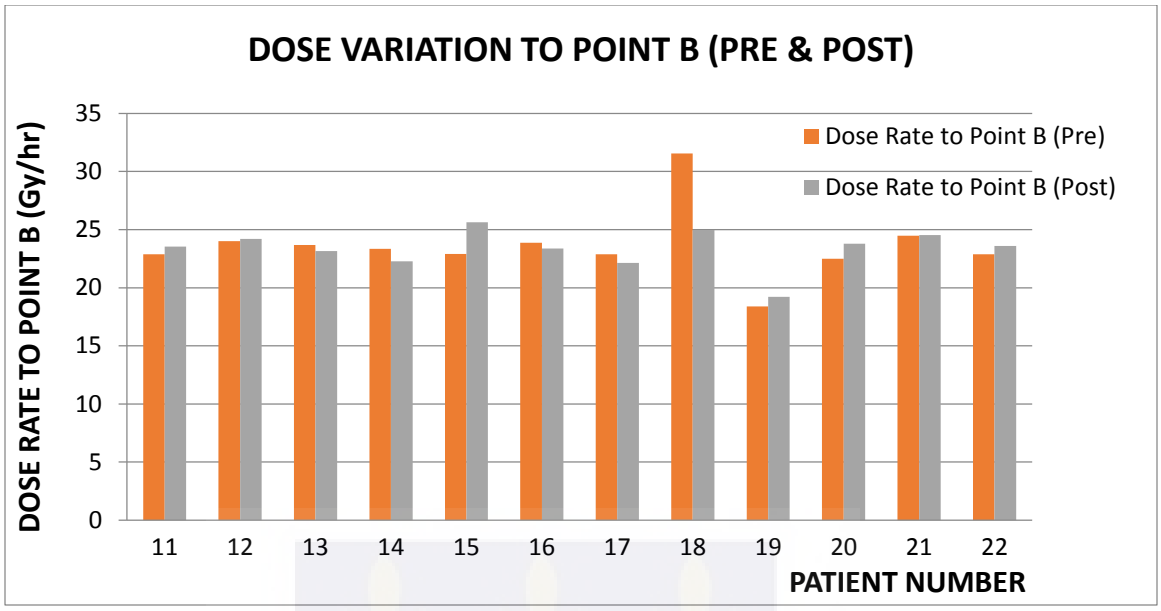


Figure 4.8 A bar chart of dose rate variation to point 'B' for pre & post treatment for next set of 12 patients

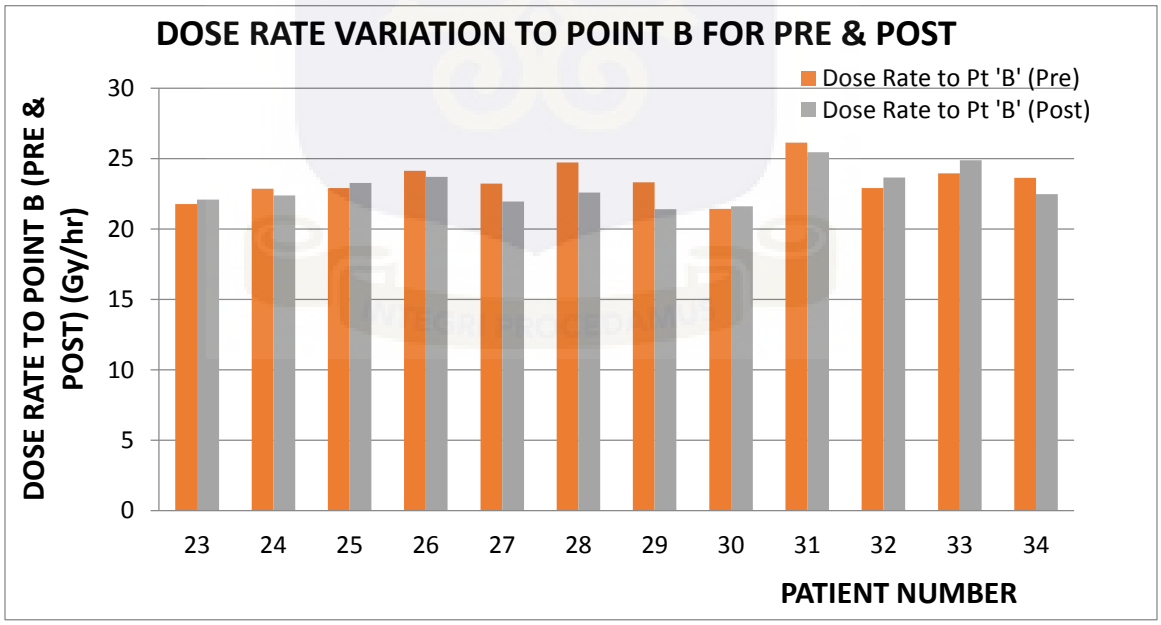


Figure 4.9 A plot of dose rate variation to point 'B' for pre & post treatment for last 12 patients

4.1.3 Variation of Doses at the Critical Organs

The bladder and rectum are the organs of interest during a cervical brachytherapy procedure. Particular interest is given to these organs to ensure that they do not exceed the acceptable limits of radiation exposure which is based on the volume of that organ receiving a particular dose. The American Brachytherapy Society (ABS) has given recommendations on the acceptable levels of radiation exposure to these organs at risk (Nag et al., 2002).

4.1.3.1 Dose Variation at the Bladder

The quantitative analysis of normal tissue effect in the clinics (QUANTEC) has set 80Gy as the bladder tolerance dose for the purpose of LDR brachytherapy (Viswanathan et al., 2009). The dose variation to the bladder is shown in Figures 4.10 and 4.11 and in Appendix H1 in tabular form.

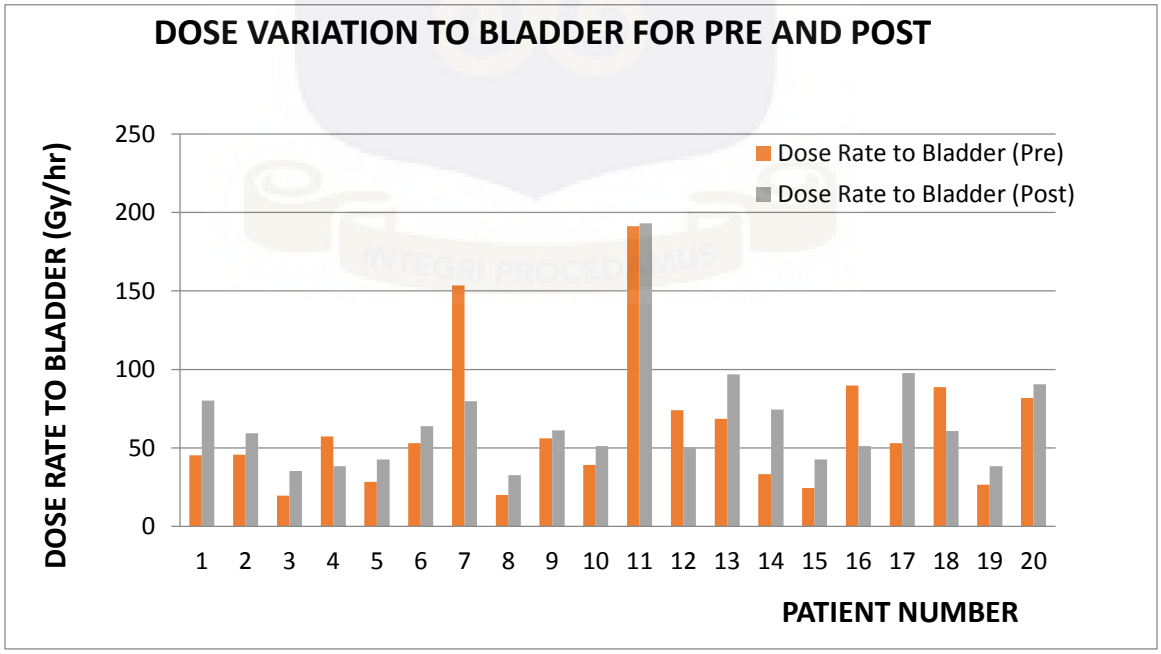


Figure 4.10 A bar chart of total dose received to bladder for pre- &post treatment calculation for first 20 patients

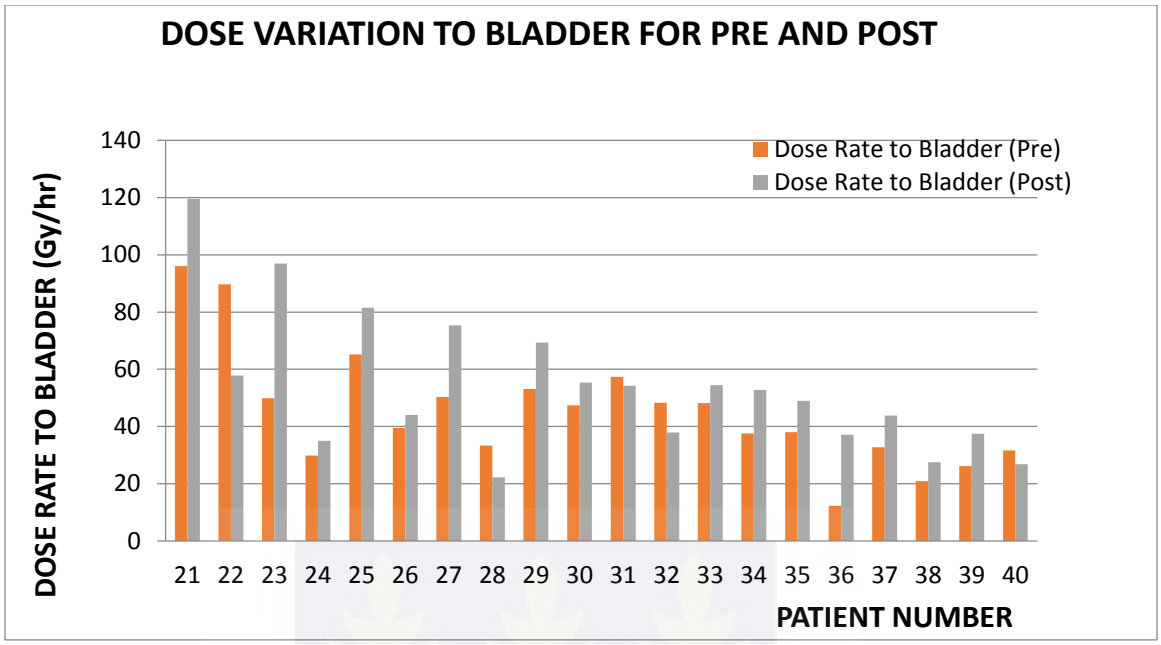


Figure 4.11 A bar chart of total dose received to bladder for pre- & post-treatment calculation for last 20 patients

From Figures 4.10 and 4.11 above, Patients 11 and 21 have their doses calculated for both pre- and post-treatment exceeding the bladder dose limit set by QUANTEC. According to Sheybani et al. (2013), the filling of the bladder, packing with gauze and the anatomy of the patient can lead to increase doses to the bladder. This may explain why Patients 11 and 21 had both pre and post doses being high. Patients 7, 16 and 26 also had their pre-treatment calculated doses above the tolerance level, but their post-treatment calculated doses showed a reduction of the doses (lower than the tolerance level). Comparing the pre and post-treatment images of the patients showed that the bladder had moved further away from the applicators which in effect reduced the dose to the bladder. On the contrary, Patients 17 and 23 had their pre-treatment calculated doses below the tolerance level, but their post-treatment calculated doses showed an increase in the doses (higher than the tolerance level). Comparing the pre and post-treatment images of the patients showed that the bladder

had moved closer to the applicators which in effect increased the dose to the bladder. Average doses of 69.26Gy and 71.09Gy were obtained for the pre- and post-treatment with an average deviation of 2.32%.

4.1.3.2 Dose Variation at the Rectum

The quantitative analysis of normal tissue effect in the clinics (QUANTEC) has set 75Gy as the rectum tolerance dose for the purpose of LDR brachytherapy (Viswanathan et al., 2009). The dose variation to the rectum is shown in Figures 4.12 and 4.13 and in Appendix H2 in tabular form.

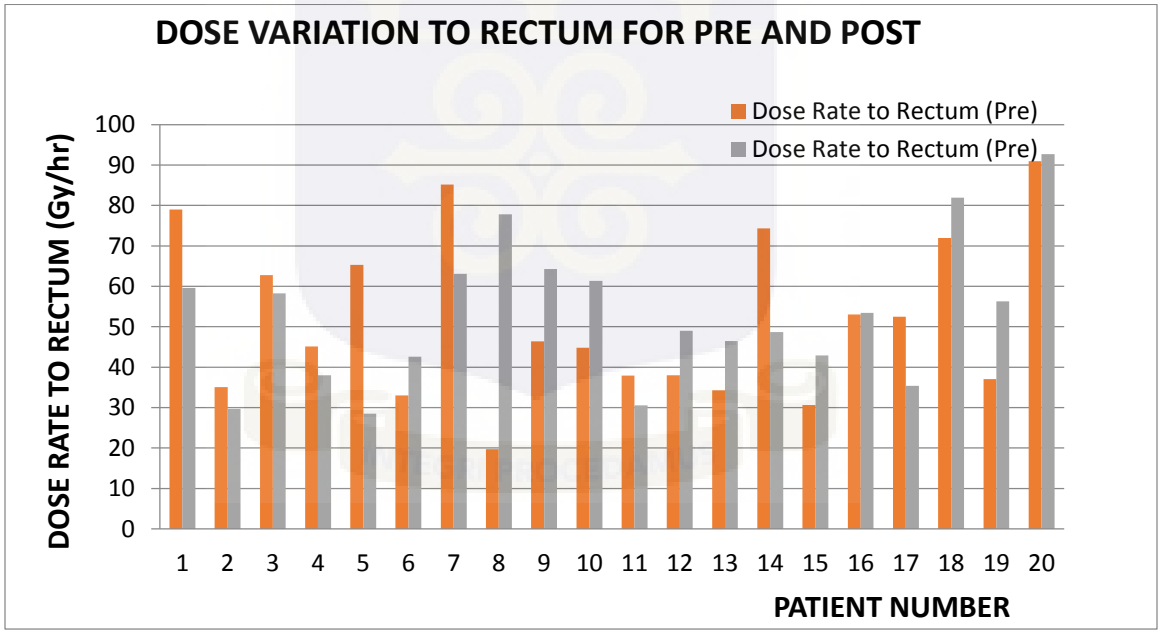


Figure 4.12 A bar chart of total dose received to rectum for pre- and post-treatment calculation for first 20 patients

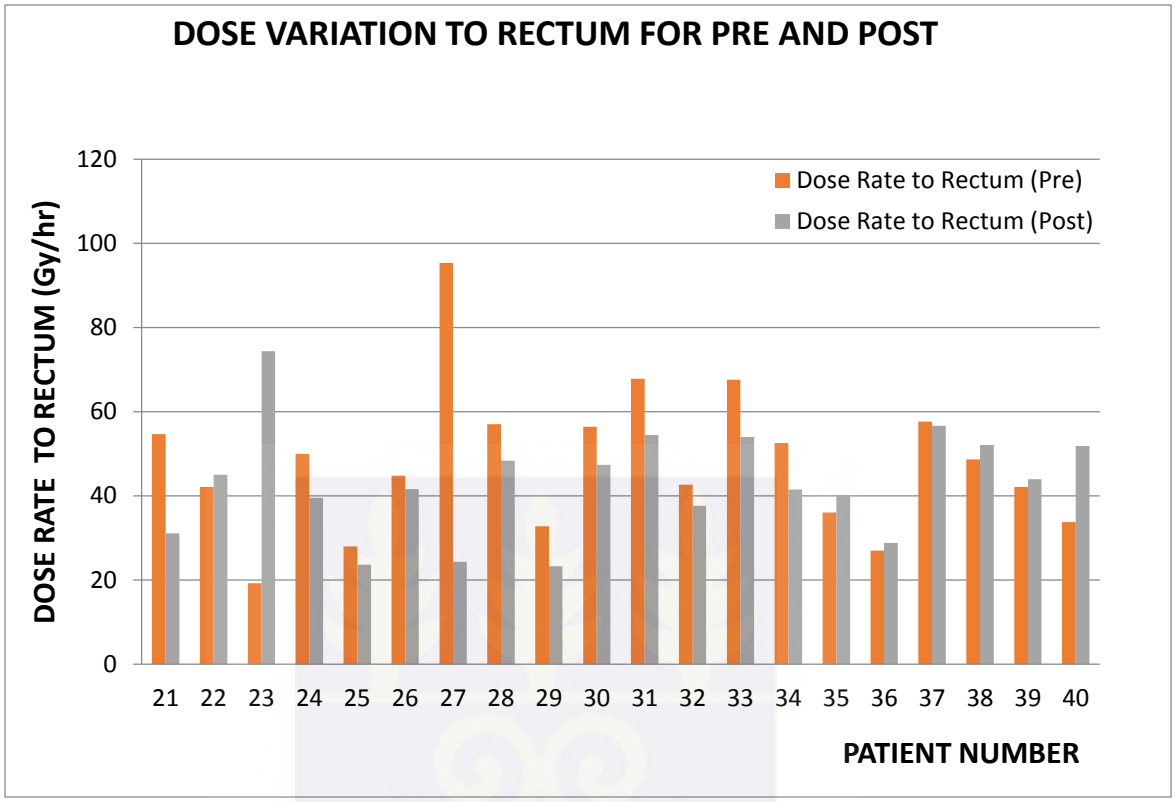


Figure 4.13 A plot of total dose received to rectum for pre- and post-treatment calculation for last 20 patients

From Figures 4.12 and 4.13 above, Patient 31 had the dose calculated for both pre and post-treatment exceeding the rectum dose limit set by QUANTEC. According to Sheybani et al. (2013) the filling of the rectum with gauze and the anatomy of the patient can lead to increased doses to the rectum, and this may explain why Patient 31 had both pre and post doses been high. Patients 7, 14, 20, 27 and 33 also had their pre-treatment calculated doses above the tolerance level, but their post-treatment calculated doses showed a reduction of the doses (lower than the tolerance level). Comparing the pre- and post-treatment images of the patients showed that the rectum had moved further away from the applicators, which in effect reduced the dose to the rectum. On the contrary, Patients 8, 18, 19 and 20 had their

pre-treatment calculated doses below the tolerance level, but their post treatment calculated doses showed an increase in the doses (higher than the tolerance level). Comparing the pre and post- treatment images of the patients showed that the rectum had moved closer to the applicators which in effect increased the dose to the rectum. An average dose of 67.02 Gy and 66.64 Gy were obtained for the pre- and post-treatment with an average deviation of 0.30%.

CHAPTER FIVE

5 CONCLUSION AND RECOMMENDATION

5.1 CONCLUSION

Applicator displacement, such as the tandem and ovoids, can have a substantial influence on patient dosimetry. The geometric relationships between intracavitary brachytherapy applicators and the critical structures differ significantly during the course of LDR BT. Source movement results in considerable dose alterations to the critical organs which can generate an increased rate of complications that can influence the cure rates. The disparity in dose to point 'A' was found to be 1.16 % which is very laudable as compared to other studies that established dose variations of 2, 35, 8 and 20% (Corn et al., 1993). This wide range is due to the fact that the studies were performed with radium, iridium, and cesium sources. Variation in dose at point 'B' in this work was 0.75%; while (Corn *et al*., 1993) showed this variation to be 1.7%. As per the guidelines there was only one rectal point chosen by most researchers, but in this study three rectal and bladder points were respectively used in order to assess rectal and bladder mobility. Studies done by Corn and Pham have found dose dissimilarities in the rectum and bladder of 3 and 10%, respectively (Corn et al., 1993; Pham et al., 1998). In this study, an average variations of 2.32 and 0.30% were found for the bladder and rectum respectively. For quality assurance purposes, the variation found between prescribed and deposited dose was 2.11%

From the results obtained and the observations made from this work, it can be concluded that most of the findings agreed with literature and works done by other researchers. Since

the variation is within the established dose variation, it can be concluded that, the practice at KATH meets the international standard.

5.2 RECOMMENDATION

The recommendations made to the various stakeholders in cancer management at the KATH Radiotherapy Department as well as the research community as a whole are as follows:

HDR brachytherapy be considered as a viable option for a short treatment time. Apart from the fact that HDR BT has the short treatment time, it has several advantages over the LDR BT such as:

- Outpatient treatment,
- Short administration time,
- Standard source strength,
- Source easily available,
- Intravenous conscious sedation feasible,
- Possibility to reassess tumor size after multiple fractions,
- Dose optimization of normal tissues,
- Minimal staff exposure and applicator stabilized by board during treatment.

It is also recommended that further studies are carried out for patients who have undergone hysterectomy in order to assess the veracity of the dose deviations observed in this study.

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APPENDIX

APPENDIX A **Data measurements for Pre and Post Treatment doses to Point A**

APPENDIX A1 **Patients with cervix intact**

Patient Number	Dose Rate to Point 'A'(Pre) (Gy/hr)	Dose Rate to Point 'A' (Post) (Gy/hr)	Mean Dose Rate (Gy/hr)	Treatment time (hr)	Deviation (%)
1	95.47	90.04	92.75	36.66	0.06
2	90.84	204.45	147.64	33.027	-1.25
3	92.66	87.55	90.10	32.378	0.06
4	88.18	76.42	82.30	34.023	0.13
5	93.37	91.10	92.23	32.132	0.02
6	91.10	88.37	89.73	38.421	0.03
7	72.95	80.76	76.85	41.127	-0.11
8	62.26	71.40	66.83	56..216	-0.15
9	89.78	89.03	89.40	33.417	0.01
10	88.32	81.38	84.85	33.969	0.08
11	85.57	92.27	88.92	40.90	-0.08
12	91.98	90.10	91.04	32.62	0.02
13	90.26	91.98	91.12	38.78	-0.02
14	82.84	84.94	83.89	42.25	-0.03
15	86.10	96.93	91.52	34.84	-0.13
16	94.75	88.66	91.70	31.66	0.06
17	84.71	85.01	84.86	35.42	-0.004
18	90.25	94.08	92.16	33.42	-0.04
19	62.46	59.68	61.07	56.04	0.05
20	86.74	85.86	86.30	40.35	0.01
21	85.03	95.57	90.30	41.16	-0.12
22	83.73	82.34	83.03	35.83	0.02

APPENDIX A1 Continued

Patient Number	Dose Rate to Point 'A'(Pre) (Gy/hr)	Dose Rate to Point 'A' (Post) (Gy/hr)	Mean Dose Rate (Gy/hr)	Treatment time (hr)	Deviation (%)
23	85.07	88.67	86.87	35.27	-0.04
24	83.09	79.68	81.38	36.02	0.04
25	92.26	89.85	91.05	32.52	0.03
26	97.59	92.43	95.01	30.74	0.05
27	90.87	82.27	86.57	33.02	0.10
28	90.74	81.41	86.08	33.06	0.10
29	103.27	86.61	94.94	29.05	0.16
30	87.14	86.37	86.75	40.17	0.01
31	93.87	87.80	90.83	31.95	0.07
32	87.80	92.86	90.33	34.17	-0.06
33	83.64	87.79	85.71	41.85	-0.05
34	89.35	68.98	79.17	39.17	0.23

APPENDIX A2 Patients who have undergone Hysterectomy

Patient Number	Dose Rate to Point 'A'(Pre) (Gy/hr)	Dose Rate to Point 'A' (Post) (Gy/hr)	Mean Dose Rate (Gy/hr)	Treatment time (hr)	Deviation (%)
35	134.36	124.06	129.21	26.04	0.08
36	133.72	138.07	135.90	26.17	-0.03
37	158.02	147.22	152.62	22.15	0.07
38	137.71	143.36	140.53	25.42	-0.04
39	168.43	152.47	160.45	20.78	0.10
40	165.26	149.38	157.32	21.18	0.10

APPENDIX B **Prescribed and Received doses**

APPENDIX B1 **Patients with Cervix intact**

Patient Number	Dose Prescribed (Gy)	Dose Received (Gy)	Mean (Gy)	Deviation (%)
1	35	33.00	34.00	0.06
2	30	67.52	48.76	-1.25
3	30	28.34	29.17	0.06
4	30	25.99	28.00	0.13
5	30	29.27	29.64	0.02
6	35	33.95	34.48	0.03
7	30	33.21	31.61	-0.11
8	35	40.13	37.57	-0.15
9	30	29.75	29.88	0.01
10	30	27.64	28.82	0.08
11	35	37.73	36.37	-0.08
12	30	29.38	29.69	0.02
13	35	35.66	35.33	-0.02
14	35	35.88	35.44	-0.03
15	30	33.77	31.89	-0.13
16	30	28.06	29.03	0.07
17	30	30.10	30.05	-0.003
18	30	31.27	30.64	-0.04
19	35	33.43	34.22	0.05
20	35	34.69	34.85	0.01
21	35	39.34	37.17	-0.12
22	30	29.50	29.75	0.02

APPENDIX B1 Continued

Patient Number	Dose Prescribed (Gy)	Dose Received (Gy)	Mean (Gy)	Deviation (%)
23	30	31.26	30.63	-0.04
24	30	28.70	29.35	0.04
25	30	29.21	29.61	0.03
26	30	29.41	29.71	0.02
27	30	24.68	27.34	0.18
28	30	26.91	28.46	0.10
29	30	25.16	27.58	0.16
30	35	34.69	34.85	0.01
31	30	28.05	29.02	0.07
32	30	31.73	30.87	-0.06
33	35	36.73	35.87	-0.05
34	35	27.02	31.01	0.23

APPENDIX B2 Patients who have undergone Hysterectomy

Patient Number	Dose Prescribed (Gy)	Dose Received (Gy)	Mean (Gy)	Deviation (%)
35	35	32.30	33.65	0.08
36	35	36.13	35.57	-0.03
37	35	32.60	33.80	0.09
38	35	36.43	35.72	-0.04
39	35	31.68	33.34	0.10
40	35	31.63	33.32	0.10

APPENDIX C **Data measurements for Pre and Post Treatment doses to Bladder**

APPENDIX C1 **Patients with cervix intact**

Patient Number	Dose to Bladder (Pre) (Gy)	Dose to Bladder (Post) (Gy)	Mean(Gy)	Deviation (%)	TDR (Pre)(Gy)	TDR (Post)(Gy)
1	16.59	29.33	22.96	-0.77	66.59	79.33
2	15.05	19.55	17.30	-0.30	65.05	69.55
3	6.34	11.39	8.87	-0.80	62.34	67.39
4	19.47	13.05	16.26	0.33	65.47	59.05
5	9.07	13.66	11.37	-0.51	59.07	63.66
6	20.34	24.48	22.41	-0.20	70.34	74.48
7	63.15	32.78	47.97	0.48	109.15	78.78
8	11.23	13.39	12.31	-0.19	57.23	59.39
9	18.76	20.41	19.59	-0.09	68.76	70.41
10	13.27	17.35	15.31	-0.31	59.27	63.35
11	78.24	78.97	78.61	-0.01	128.24	128.97
12	24.15	16.36	20.26	0.32	74.15	66.36
13	26.58	37.52	32.05	-0.41	76.58	87.52
14	14.00	31.40	22.70	-1.24	60.00	77.4
15	8.47	14.81	11.64	-0.75	58.47	64.81
16	28.40	16.22	22.31	0.43	84.40	72.22
17	18.74	34.56	26.65	-0.84	64.74	80.56
18	29.50	20.21	24.86	0.32	79.50	70.21
19	14.83	21.47	18.15	-0.45	60.83	67.47
20	33.00	36.55	34.78	-0.11	79.00	82.55
21	39.53	49.21	44.37	-0.25	85.53	95.21
22	32.14	20.71	26.43	0.36	78.14	66.71

APPENDIX C1 Continued

Patient Number	Dose to Bladder (Pre) (Gy)	Dose to Bladder (Post) (Gy)	Mean(Gy)	Deviation (%)	TDR (Pre)(Gy)	TDR (Post)(Gy)
23	17.57	34.17	25.87	-0.95	63.57	80.17
24	6.74	12.61	9.68	-0.87	56.74	62.61
25	21.18	26.49	23.84	-0.25	71.18	76.49
26	30.14	13.53	21.84	0.55	86.14	69.53
27	16.63	24.87	20.75	-0.50	66.63	74.87
28	11.00	7.35	9.18	0.33	61.00	57.35
29	15.44	20.14	17.79	-0.30	65.44	70.14
30	19.03	22.22	20.63	-0.17	65.03	68.22
31	18.33	17.32	17.83	0.06	78.33	77.32
32	16.50	12.95	14.73	0.22	66.50	62.95
33	20.16	22.78	21.47	-0.13	71.76	74.38
34	14.71	19.11	16.91	-0.30	66.71	71.11

APPENDIX C2 Patients who have undergone Hysterectomy

Patient Number	Dose to Bladder (Pre) (Gy)	Dose to Bladder (Post) (Gy)	Mean(Gy)	Deviation (%)	TDR (Pre)(Gy)	TDR (Post)(Gy)
35	9.89	12.75	11.32	-0.29	61.89	64.75
36	3.23	9.72	6.48	-2.01	53.23	59.72
37	7.25	9.7	8.48	-0.34	53.25	55.70
38	5.32	6.97	6.15	-0.31	56.32	57.97
39	5.42	7.78	6.60	-0.44	57.02	59.38
40	6.70	5.67	6.19	0.15	56.70	55.67

APPENDIX D **Data measurements for Pre and Post Treatment Doses to Rectum**

APPENDIX D1 **Patients with cervix intact**

Patient Number	Dose to Rectum (Pre) (Gy)	Dose to Rectum (Post) (Gy)	Mean(Gy)	Deviation (%)	TDR (Pre)(Gy)	TDR (Post)(Gy)
1	28.95	21.84	25.40	0.25	78.95	71.84
2	11.58	9.79	10.69	0.16	61.58	59.79
3	20.32	18.87	19.60	0.07	76.32	74.87
4	15.34	12.92	14.13	0.16	61.34	58.92
5	20.98	9.16	15.07	0.56	70.98	59.16
6	12.67	16.35	14.51	-0.29	62.67	66.35
7	35.03	25.94	30.49	0.26	81.03	71.94
8	11.10	43.93	27.52	-2.96	57.1	89.93
9	15.50	21.48	18.49	-0.39	65.5	71.48
10	15.21	20.85	18.03	-0.37	61.21	66.85
11	15.51	12.49	14.00	0.20	65.51	62.49
12	12.40	15.98	14.19	-0.29	62.40	65.98
13	13.30	18.00	15.65	-0.35	63.30	68.00
14	31.40	20.56	25.98	0.35	77.40	66.56
15	10.67	14.95	12.81	-0.40	60.67	64.95
16	16.78	16.92	16.85	-0.01	72.78	72.92
17	18.59	12.53	15.56	0.33	64.59	58.53
18	23.92	27.24	25.58	-0.134	73.92	77.24
19	20.76	31.52	26.14	-0.52	66.76	77.52
20	36.71	37.40	37.06	-0.02	82.71	83.40
21	22.49	12.80	17.65	0.43	68.49	58.80
22	15.09	16.12	15.61	-0.07	61.09	62.12

APPENDIX D1 Continued

23	6.76	26.22	16.49	-2.88	52.76	72.22
24	17.99	14.22	16.11	0.21	67.99	64.22
25	9.09	7.69	8.39	0.15	59.09	57.69
26	13.75	12.77	13.26	0.07	69.75	68.77
27	31.48	8.03	19.76	0.75	81.48	58.03
28	18.84	15.98	17.41	0.15	68.84	65.98
29	9.51	6.76	8.14	0.29	59.51	56.76
30	22.67	19.01	20.84	0.16	68.67	65.01
31	21.67	17.38	19.53	0.20	81.67	77.38
32	14.56	12.84	13.70	0.12	64.56	62.84
33	28.29	22.60	25.45	0.20	79.89	74.2
34	20.58	16.24	18.41	0.21	72.58	68.24

APPENDIX D2 Patients who have undergone Hysterectomy

Patient Number	Dose to Rectum (Pre) (Gy)	Dose to Rectum (Post) (Gy)	Mean(Gy)	Deviation (%)	TDR (Pre)(Gy)	TDR (Post)(Gy)
35	9.37	10.47	9.92	-0.12	61.37	62.47
36	7.06	7.54	7.30	-0.07	57.06	57.54
37	12.76	12.55	12.66	0.02	58.76	58.55
38	12.35	13.23	12.79	-0.07	63.35	64.24
39	8.74	9.13	8.94	-0.05	60.34	60.73
40	7.15	10.97	9.06	-0.53	57.15	60.97

APPENDIX E **Data measurements for Pre and Post Treatment Dose Rate to Bladder**

APPENDIX E1 **Patients with cervix intact**

Patient Number	Dose Rate to Bladder (Pre) (Gy/hr)	Dose Rate to Bladder (Post) (Gy/hr)	Mean(Gy/hr)	Deviation (%)
1	45.27	80.02	62.65	-0.77
2	45.57	59.21	52.39	-0.30
3	19.59	35.19	27.39	-0.80
4	57.25	38.37	47.81	0.33
5	28.25	42.53	35.39	-0.51
6	52.95	63.74	58.34	-0.20
7	153.56	79.71	116.64	0.48
8	19.98	32.49	26.24	-0.63
9	56.14	61.10	58.62	-0.09
10	39.07	51.09	45.08	-0.31
11	191.30	193.08	192.20	-0.01
12	74.05	50.16	62.11	0.32
13	68.55	96.76	82.66	-0.41
14	33.16	74.33	53.74	-1.24
15	24.33	42.53	33.43	-0.75
16	89.71	51.24	70.48	0.43
17	52.94	97.59	75.27	-0.84
18	88.77	60.82	74.80	0.32
19	26.47	38.33	32.40	-0.45
20	81.79	90.59	86.19	-0.11
21	96.04	119.57	107.80	-0.25
22	89.71	57.81	73.76	0.36

APPENIX E1 Continued

23	49.83	96.91	73.37	-0.95
24	29.82	35.01	32.42	-0.17
25	65.16	81.49	73.32	-0.25
26	39.50	44.04	41.77	-0.12
27	50.37	75.35	62.86	-0.50
28	33.27	22.23	27.75	0.33
29	53.15	69.36	61.26	-0.31
30	47.38	55.33	51.36	-0.17
31	57.38	54.23	55.81	0.06
32	48.29	37.92	43.11	0.22
33	48.18	54.45	51.32	-0.13
34	37.57	52.84	45.20	-0.41

APPENDIX E2 Patients who have undergone Hysterectomy

Patient Number	Dose Rate to Bladder (Pre) (Gy/hr)	Dose Rate to Bladder (Post) (Gy/hr)	Mean(Gy/hr)	Deviation (%)
35	37.98	48.97	43.48	-0.29
36	12.36	37.18	24.77	-2.01
37	32.74	43.80	38.27	-0.34
38	20.97	27.46	24.22	-0.31
39	26.13	37.49	31.81	-0.44
40	31.65	26.82	29.24	0.15

APPENDIX F Data measurements for Pre and Post Treatment Dose Rate to Rectum

APPENDIX F1 Patients with cervix intact

Patient Number	Dose Rate to Rectum (Pre) (Gy/hr)	Dose Rate to Rectum (Post) (Gy/hr)	Mean(Gy/hr)	Deviation (%)
1	78.97	59.58	69.28	0.25
2	35.07	29.66	32.37	0.15
3	62.79	58.30	60.54	0.07
4	45.10	37.98	41.54	0.16
5	65.31	28.51	46.91	0.56
6	32.99	42.56	37.78	-0.29
7	85.20	63.08	74.14	0.26
8	19.75	77.80	48.77	-2.94
9	46.39	64.29	55.34	-0.39
10	44.79	61.38	53.09	-0.37
11	37.92	30.55	34.23	0.19
12	38.02	49.02	43.52	-0.29
13	34.31	46.43	40.37	-0.35
14	74.32	48.66	61.49	0.35
15	30.64	42.92	36.78	-0.40
16	53.02	53.47	53.25	-0.01
17	52.52	35.40	43.96	0.33
18	71.98	81.97	76.98	-0.14
19	37.06	56.25	46.66	-0.52
20	90.98	92.70	91.84	-0.02
21	54.65	31.11	42.88	0.43
22	42.11	45.00	43.56	-0.07

APPENDIX F1 Continued

23	19.19	74.36	46.77	-2.88
24	49.95	39.5	44.72	0.21
25	27.96	23.66	25.81	0.15
26	44.75	41.57	43.16	0.07
27	95.37	24.32	59.85	0.75
28	57.01	48.36	52.68	0.15
29	32.75	23.28	28.02	0.29
30	56.45	47.35	51.90	0.16
31	67.84	54.42	61.13	0.20
32	42.63	37.59	40.11	0.12
33	67.62	54.01	60.82	0.20
34	52.56	41.48	47.02	0.21

APPENDIX F2 Patients who have undergone Hysterectomy

Patient Number	Dose Rate to Rectum (Pre) (Gy/hr)	Dose Rate to Rectum (Post) (Gy/hr)	Mean(Gy/hr)	Deviation (%)
1	35.99	40.24	38.12	-0.12
2	26.99	28.83	27.91	-0.07
3	57.64	56.67	57.16	0.02
4	48.62	52.08	50.35	-0.07
5	42.10	43.94	43.02	-0.04
6	33.77	51.82	42.80	-0.54

APPENDIX G **Data measurements for Pre and Post Treatments Dose Rate to Point 'B'**

APPENDIX G1 **Patients with cervix intact**

Patient Number	Dose Rate to Point 'B'(Pre) (Gy/hr)	Dose Rate to Point 'B' (Post) (Gy/hr)	Mean(Gy/hr)	Deviation (%)
1	24.91	23.57	24.24	0.05
2	23.35	21.67	22.51	0.07
3	24.15	24.71	24.43	-0.02
4	19.64	23.86	21.75	-0.22
5	24.76	24.79	24.77	-0.001
6	23.95	22.42	23.18	0.06
7	21.72	21.85	21.78	-0.01
8	19.2	20.14	19.67	-0.05
9	23.99	22.68	23.33	0.06
10	22.65	21.23	21.94	0.06
11	22.87	23.55	23.21	-0.03
12	24.01	24.21	24.11	-0.01
13	23.68	23.15	23.41	0.02
14	23.34	22.28	22.81	0.05
15	22.91	25.62	24.27	-0.12
16	23.87	23.36	23.62	0.02
17	22.89	22.14	22.52	0.03
18	31.55	24.97	28.26	0.21
19	18.40	19.22	18.81	-0.05
20	22.48	23.78	23.13	-0.06
21	24.47	24.53	24.50	-0.003
22	22.88	23.60	23.24	-0.03

APPENDIX G1 Continued

23	21.78	22.09	21.93	-0.02
24	22.87	22.39	22.63	0.02
25	22.92	23.27	23.09	-0.02
26	24.15	23.71	23.93	0.02
27	23.24	21.96	22.60	0.06
28	24.73	22.59	23.66	0.09
29	23.32	21.41	22.36	0.08
30	21.43	21.62	21.52	-0.01
31	26.14	25.45	25.79	0.03
32	22.91	23.66	23.28	-0.03
33	23.95	24.88	24.42	-0.04
34	23.65	22.49	23.07	0.05

APPENDIX H Variation of doses to Critical Organs

APPENDIX H1 Bladder

Patient Number	Total Bladder Dose (Pre) (Gy)	Total Bladder Dose (Post) (Gy)	Deviation (Gy)	% Deviation
1	66.59	79.33	-0.1606	-16.06
2	65.05	69.55	-0.0647	-6.47
3	62.34	67.39	-0.0749	-7.49
4	65.47	59.05	0.1087	10.87
5	59.07	63.66	-0.0721	-7.21
6	70.34	74.48	-0.0556	-5.56
7	109.15	78.78	0.3855	38.55
8	57.23	59.39	-0.0364	-3.64
9	68.76	70.41	-0.0234	-2.34
10	59.27	63.35	-0.0644	-6.44
11	128.24	128.97	-0.0057	-0.57
12	74.15	66.36	0.1174	11.74
13	76.58	87.52	-0.1250	-12.50
14	60	77.4	-0.2248	-22.48
15	58.47	64.81	-0.0978	-9.78
16	84.4	72.22	0.1687	16.87
17	64.74	80.56	-0.1964	-19.64
18	79.5	70.21	0.1323	13.23
19	60.83	67.47	-0.0984	-9.84
20	79	82.55	-0.0430	-4.30
21	85.53	95.21	-0.1017	-10.17
22	78.14	66.71	0.1713	17.13
23	63.57	80.17	-0.2071	-20.71
24	56.74	62.61	-0.0938	-9.38
25	71.18	76.49	-0.0694	-6.94
26	86.14	69.53	0.2389	23.89
27	66.63	74.87	-0.1101	-11.01
28	61	57.35	0.0636	6.36
29	65.44	70.14	-0.0670	-6.70
30	65.03	68.22	-0.0468	-4.68
31	78.33	77.32	0.0131	1.31
32	66.5	62.95	0.0564	5.64
33	71.76	74.38	-0.0352	-3.52
34	66.71	71.11	-0.0619	-6.19

APPENDIX H1 Continued

35	61.89	64.75	-0.0442	-4.42
36	53.23	59.72	-0.1087	-10.87
37	53.25	55.7	-0.0440	-4.40
38	56.32	57.97	-0.0285	-2.85
39	57.02	59.38	-0.0397	-3.97
40	56.7	55.67	0.0185	1.85
Average	**69.26**	**71.09**	**-0.0232**	**-2.32**

APPENDIX H2

Patient Number	Total Bladder Dose (Pre) (Gy)	Total Bladder Dose (Post) (Gy)	Deviation (Gy)	% Deviation
1	78.95	71.84	0.09	9.01
2	61.58	59.79	0.03	2.91
3	76.32	74.87	0.02	1.90
4	61.34	58.92	0.04	3.95
5	70.98	59.16	0.17	16.65
6	62.67	66.35	-0.06	-5.87
7	81.03	71.94	0.11	11.22
8	57.10	89.93	-0.58	-57.50
9	65.50	71.48	-0.09	-9.13
10	61.21	66.85	-0.09	-9.21
11	65.51	62.49	0.05	4.61
12	62.40	65.98	-0.06	-5.74
13	63.30	68.00	-0.07	-7.43
14	77.40	66.56	0.14	14.01
15	60.67	64.95	-0.07	-7.06
16	72.78	72.92	-0.001	-0.19
17	64.59	58.53	0.09	9.38
18	73.92	77.24	-0.05	-4.49
19	66.76	77.52	-0.16	-16.12
20	82.71	83.40	-0.01	-0.83
21	68.49	58.80	0.14	14.15
22	61.09	62.12	-0.02	-1.69
23	52.76	72.22	-0.37	-36.88
24	67.99	64.22	0.06	5.55
25	59.09	57.69	0.02	2.37
26	69.75	68.77	0.01	1.41

APPENDIX H2 Continued

27	81.48	58.03	0.29	28.78
28	68.84	65.98	0.04	4.16
29	59.51	56.76	0.05	4.62
30	68.67	65.01	0.05	5.33
31	81.67	77.38	0.05	5.25
32	64.56	62.84	0.03	2.66
33	79.89	74.20	0.07	7.12
34	72.58	68.24	0.06	5.98
35	61.37	62.47	-0.02	-1.79
36	57.06	57.54	-0.01	-0.84
37	58.76	58.55	0.003	0.36
38	63.35	64.24	-0.01	-1.41
39	60.34	60.73	-0.01	-0.65
40	57.15	60.97	-0.07	-6.68
Average	67.03	66.64	0.003	-0.30