



2D Brachytherapy Planning versus 3D Brachytherapy Planning For Patients With Cervical Cancer

*Submitted in fulfillment of the requirements of the degree of
Master of Technology: Radiography
In the Faculty of Health Sciences at
Durban University of technology*

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August 2014

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ACKNOWLEDGEMENTS

My sincere gratitude to the following:

- *My Lord and Saviour, Jesus Christ, for His never failing love that gave me the strength and knowledge to achieve success. Philippians 4:3, 'Study to show yourself approved'*
- *My family, for their love, support and motivation – my sunshine and clear skies in the midst of life's many storms*
- *All the individuals who volunteered for this research project*
- *My supervisor, Mrs S. Naidoo, for her guidance and encouragement*
- *My co-supervisor, Dr P. Govender, for his support*

DEDICATION:

This dissertation is dedicated to my precious family:

My mum: Una Govender

My late dad: Mr J. Govender

My brother: Luvendren Govender

and

My husband: Wayne Keagan Rajagopaul

ABSTRACT

Keywords

Google: HDR brachytherapy, cancer of the cervix, bladder, rectum, effects of brachytherapy, 2D planning, 3D planning

Research Aims

The purpose of this study is to compare 2D HDR Brachytherapy planning and 3D HDR Brachytherapy planning in terms of dose distribution in order to accurately determine bladder and rectal doses. Further research questions were explored to determine whether relationships existed between Computer Tomography volumes and bladder and rectum dose.

Methodology

The 30 female patients that volunteered for the study were conveniently selected. Their age and ethnic group did not contribute to their selection.

All participants were prepared for cervical HDR Brachytherapy. The Brachytherapy templates were computer generated and treatments were given based on the templates. They then had a Computer Tomography (CT) scan (3D data set) of the pelvis. The computer generated templates for 2D Brachytherapy planning were applied to the CT data set i.e. 2DBP. The plans were optimised to take into consideration the dose to the bladder and the rectum i.e. 3DBP. The 2DBP and the 3DBP were then evaluated in order to determine which method of planning yielded more acceptable dose distributions to the bladder and rectum.

Results

Significant differences in dose distribution were noted on comparison of 2DBP and 3DBP. A significant relationship was noted in respect of bladder mean dose and rectum mean dose. 3DBP proved to be more efficient in yielding lower mean dose to the bladder and the rectum. Whilst a significant relationship was noted in respect of bladder maximum dose, an insignificant relationship was noted for rectum maximum dose. Therefore, the efficiency of 3DBP to yield lower bladder maximum dose was established but its efficiency to yield lower rectum maximum dose is questionable. This has implications for the management of patients' with cervical cancer who require cervical Brachytherapy.

Recommendations

It is imperative that imaging modalities be used for the accurate planning of cervical Brachytherapy. This study recommends that CT be used for HDR Brachytherapy planning by proving its greater efficiency compared to template planning.

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A	KwaZulu-Natal Department of Health: Permission to conduct research
B	Inkosi Albert Luthuli Central Hospital: Permission to conduct research
C	Patient Information sheet

D	Informed consent
E	Ethics approval

LIST OF ABBREVIATIONS

2DBP	Two dimensional high dose rate Brachytherapy planning using computer generated templates
3DBP	Three dimensional high dose rate Brachytherapy planning using computer tomography scans
B CT volume 2D	Bladder Computer Tomography volume for 2D HDR Brachytherapy planning using computer generated templates
R CT volume 2D	Rectum Computer Tomography volume for 2D HDR Brachytherapy planning using computer generated templates
B CT volume 3D	Bladder Computer Tomography volume for 3D HDR Brachytherapy planning using Computer Tomography scans
R CT volume 3D	Rectum Computer Tomography volume for 3D HDR Brachytherapy planning using Computer Tomography scans
B Mean 2D	Bladder mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates
R Mean 2D	rectum mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates

B Mean 3D	Bladder mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans
R Mean 3D	Rectum mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans
B Max 2D	Bladder maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates
R Max 2D	Rectum maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates
B Max 3D	Bladder maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans
R Max 3D	Rectum maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans
Cc	The abbreviation used for cubic centimeter (Bentel, 1996)
Gray (Gy)	The International System of units of absorbed ionizing radiation equal to the dose of one joule of energy absorbed per kilogram of matter (Podgorsak, 2010: 402)

CHAPTER ONE

BACKGROUND OF THE STUDY

1.1 Introduction

Cancer of the cervix is one of the most common malignancies in women (Jain, Singh, Shrivastava, Saumsundaram, Sarje, and Jain, 2007:212; Jamema, Saju, Mahantshetty, Pallad, Deshpande, Shrivastava and Dinshaw, 2008:3). External beam radiotherapy, that is, radiation treatment and high dose rate (HDR) Brachytherapy is effective in the treatment of patients with cancer of the uterine cervix. However, the benefits of HDR Brachytherapy may be coupled with the potential side effects of this type of treatment; hence there is a need to improve the methods which are used to perform this treatment. This study investigates two dimensional (2D) and three dimensional (3D) Brachytherapy planning.

Eich, Haverkamp, Micke, Prott, and Müller, (2000:62-66) emphasise the need to lower the radiation dose to the normal tissue structures in order to minimise the radiation induced side effects. The study by Eich *et al* (2000:62-66) state that it is advantageous to utilise (3D) Brachytherapy planning to determine the radiation dose to structures prior to treatment delivery in order to ensure that the dose to the normal tissue structures are within the tolerance values. A more recent study conducted by Jain *et al*, (2007:212) further state that the success of Brachytherapy is dependent on the delivery of a high radiation dose to the tumour while sparing as much as possible of the surrounding normal tissue. While there are various techniques employed to achieve this response; this study will focus on two techniques, namely two dimensional (2D) HDR Brachytherapy planning (using computer generated templates) and three dimensional (3D) HDR Brachytherapy planning (using Computer Tomography scans). The routine protocol at Inkosi Albert Luthuli

Central Hospital (IALCH) employed the 2D method of HDR Brachytherapy planning using computer generated templates whilst the method that was investigated in this research employed the 3D method of HDR Brachytherapy planning using Computer Tomography scans (CT), that is, 3D data set. Whilst there has been many larger studies over the years based on this topic, this study serves to test and possibly prove the efficiency of 3D Brachytherapy planning, in order to benefit local institutes on the global trends surrounding this issue.

Therefore, the purpose of this study is to compare 2D HDR Brachytherapy planning using computer generated templates with 3D HDR Brachytherapy planning using CT scans in terms of dose distribution in order to determine which method results in more accurate (reduced) bladder and rectal doses, thereby resulting in fewer side effects.

1.2 Motivation and Significance

In HDR Brachytherapy for patients with cervical cancer, the radiation source is in close proximity to the target area and inevitably to the bladder and rectum, as will be discussed in chapter two. This results in high radiation dose being delivered to these critical structures as indicated by Wachter-Gerstner, Wachter, Reinstadler, Fellner, Knocke, Wambersie, and Pötter (2003:269) therefore, it is imperative to determine the most efficient technique for the application of Brachytherapy in order to reduce radiation dose to the bladder and the rectum. Nag (2006:164) emphasises the necessity to accurately plan Brachytherapy by employing the most technically advanced imaging modality available. Oinam, Goda, Dubey, Bhardwaj and Patel (2008:156) write that the International Commission on Radiation Units and Measurements report – 38 (ICRU 38) is a comprehensive report which

gives reasonable estimates on dose-volume relationships in intracavitary Brachytherapy for carcinoma of the cervix. However, with the implementation of more advanced diagnostic tools, such as CT scans, there has been a shift towards 3D Brachytherapy planning which individually adapts the dose distribution to the target area.

Hellebust, Dale, Skjonsberg, and Olsen, (2001:274) address the need for dose distributions that accurately reflect the dose received by the bladder and rectum in order to reduce these dose whilst optimising the target dose. Further studies conducted by Yoshioka, Nishimura, Kamata, Harada, Kanazawa, Fuji, and Murayama, (2005:317) and Shin, Kim, Cho, Kim, Park, Park, Kim, Chie, Pyo, and Cho, (2006:197-204) state that 3D based treatment planning for HDR Brachytherapy may be more useful to achieve reduced radiation dose to the bladder and rectum than 2D Brachytherapy planning. According to Al-Booz, Boiangiu, Appleby, French, Coomber, Humphery, and Cornes, (2006:156), conformity of the dose to the target point (Point A as per the Manchester system) will not only permit normal tissue (bladder and rectum) sparing but it will also allow possible dose escalation to the target point enabling a greater rate of tumour control. Studies by Chajon, Dumas, Touleimat, Magné, Coulot, Verstraet, Lefkopoulos, and Haie-Meder, (2007:955) and Lindegaard, Tanderup, Nielsen, Haack, and Gelineck, J. (2008:756) illustrate the fact that the use of 3D methods produce dose distributions of improved significance. This study investigates the significance of a 3D method, that is, HDR Brachytherapy planning using CT scans. Bahadur, El-Sayed, El-Taher, Zaza, Moftah, Hassouna, and Ghassal (2008:1) go on to discuss that CT allows for accurate and reliable means of delineation and calculation of the dose to normal tissue.

Bomford, Kunkler and Sherriff (2001:411), state that side effects of HDR Brachytherapy include irritation of the bladder with dysuria which tends to

occur one to ten years after treatment. The authors maintain that haematuria (blood in the urine) may occur as a result of telangiectasia (dilation of the capillaries) at the bladder base and the bladder may contract as a result of scarring and infection of the submucosal and muscle layers. Rectal ulceration, haemorrhage, fistulae, rectal urgency, tenesmus, constipation and diarrhea are potential side effects that may affect the rectum (Huh, Lim, Ahn, Lee, Kang, Shin, Shin, Kim, Park and Han, 2003:191.). Due to these side effects that may be caused (Wachter-Gerstner *et al*, 2003:269), dose received by the target area are generally limited to the tolerance dose of the bladder and rectum (Shrivastava, Umbarkar, Sarje and Singh, 2009:93).

Chapter two, the literature review, provides an overview of the anatomy and physiology of the cervix, rectum and bladder. A discussion on the radiation complications to the rectum and the bladder due to HDR Brachytherapy of the cervix has been included. The dosimetry and biological effects of HDR Brachytherapy will be briefly described as well. The chapter will end with a summary and state the research aim and questions. Chapter three describes the methods and design, the sample population and the inclusion and exclusion criteria that were used in the selection of the research patients. It also describes the Brachytherapy techniques that were compared in this study. Chapter four documents the data analysis and results. Descriptive and inferential statistics are presented on the research questions. Chapter five focuses on the discussion based on the results. Chapter six concludes this study by emphasising the significance of the results and makes recommendations for areas of future research in the treatment of cervical cancer using HDR Brachytherapy.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

This chapter provides an overview of the anatomy and physiology of the cervix in order to demonstrate an understanding of the relationships between the cervix, the rectum and the bladder. An insight into the anatomy and physiology of the rectum and bladder has also been included in this chapter in order to facilitate an understanding of the radiation induced complications of these organs. Only the female bladder has been included in this chapter in order to adhere to the scope of this research study. The nerve and blood supply, and the lymph and venous drainage, will not be discussed as these are not directly relevant to this study.

The radiotherapy technique used to treat cancer of the cervix which is investigated in this research study is HDR Brachytherapy. Its definition, as well as its dosimetry and biological effects will be described in this chapter. Similar research will also be discussed in this chapter. This chapter concludes with a summary and states the aim and research questions of this dissertation.

2.2 Anatomy and Physiology of the Cervix

There are various methods of treating cervical cancer, all of which take into consideration the anatomy of the cervix and its location in relation to surrounding organs. Khan (1994:303) describes the cervix as the lower third, narrow cylindrical portion of the uterus. The cervix derives its name from the

Latin word meaning neck (Fox, 1996:630). The cervix is divided into two parts, namely the vaginal and the supravaginal parts (Khan, 2006:303). Khan (2006:303) further states that upper limit of the cervix is the internal os, which is an anatomically and histologically ill-defined junction of the muscular uterine fundus and the denser, fibrous cervical stroma, as illustrated in Figure 2.1.

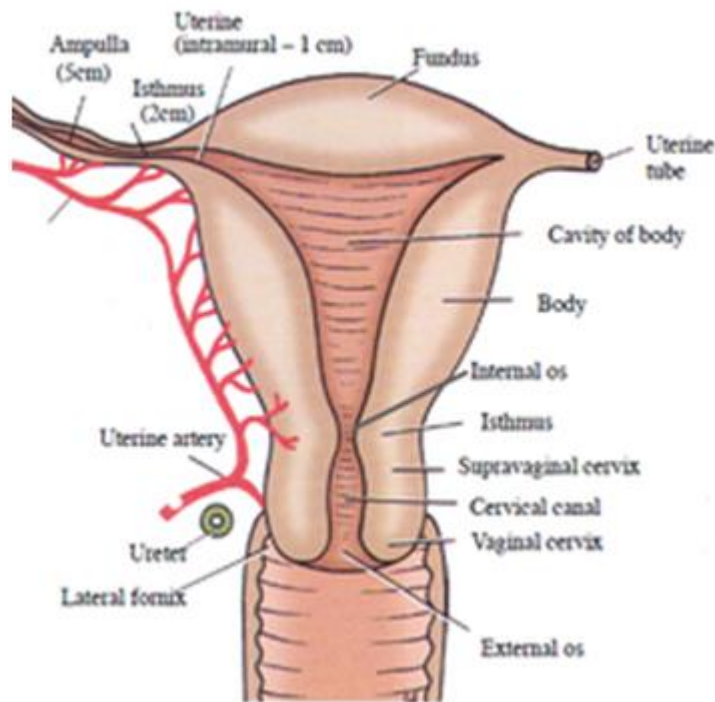


Figure 2.1: Parts of the uterus including the cervix (Quizlet – use permitted)

The cervix protrudes through the upper anterior vaginal wall. The portion projecting into the vagina is referred to as the portio vaginalis (Droegemuller, Herbst, Michell, and Stendever, 1987:50). The portion of the cervix exterior to the external os is called the ectocervix and the passageway between the external os and the endometrial cavity is referred to as the endocervical canal (Khan, 1994: 303). The size and shape of the cervix varies widely with age, hormonal state, and parity (Khan, 2006: 303).

The postero-inferior surface of the bladder is closely related to the anterior wall of the supravaginal cervix (Khan, 1994:303). The bladder and the cervix are separated by the vesicouterine pouch whilst the rectum lies posterior to the cervix and is separated by a weak rectouterine pouch (Moore and Agur, 1995:172). Due to the close relation of the cervix with the surrounding organs, as illustrated in Figure 2.2, care needs to be taken when selecting and administering the methods of treatment for cervical cancer in order to minimise subsequent damage to these surrounding organs (Dox, Melloni, Eisner and Melloni, 2001:118).

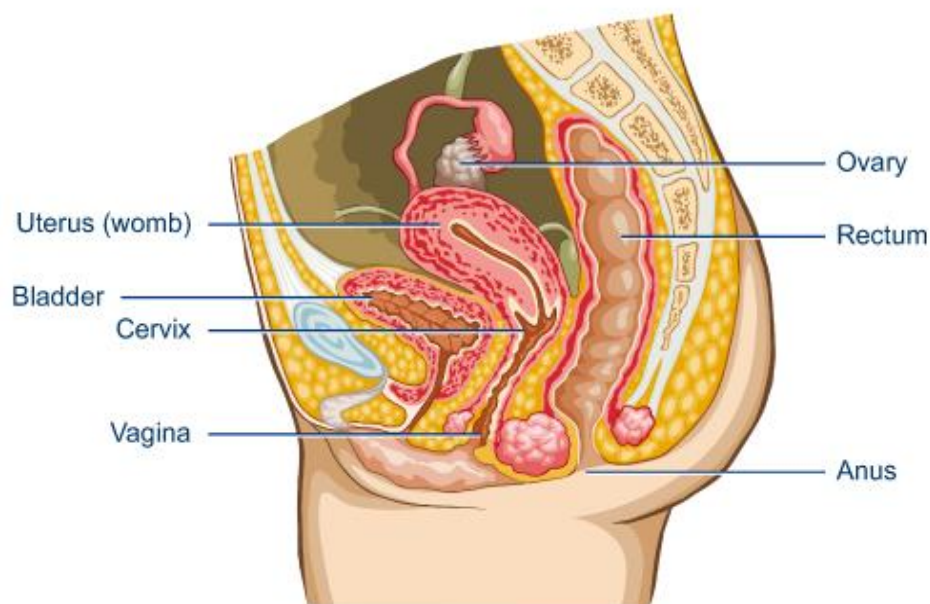


Figure 2.2: The cervix and its relations (About Brachytherapy – use permitted)

2.2.1 Staging of Carcinoma of the Cervix

Eligibility for entry to the study was restricted to patients with carcinoma of the cervix Stage II A, II B, III A and III B non-bulky disease as per the International Federation of Gynaecologists and Obstetricians (FIGO) clinical staging system (Boardman; 2013). Only these stages of the disease will be explained in this dissertation.

Stage II is less extensive than stage III in terms of region (Khan, 1994:303). Each stage is further classified where A is associated with vaginal spread and B is associated with parametrial spread which is more ominous (Bomford, Kunkler and Sherriff, 2001:405). Khan (2006:303) describes stage II A as vaginal involvement to the upper two thirds of the vagina but not its lower third whereas stage III A is vaginal involvement including the lower third of the vagina, and stage II B is parametrial involvement excluding the lateral pelvic wall whereas stage III B is parametrial involvement including the pelvic wall.

2.3 Anatomy and Physiology of the Bladder

Lewis (2000) states that an empty bladder comprises of a fundus, a vertex, a superior and an inferior surface. Dox *et al*, (2001:75) describes the urinary bladder as a musculomembranous sac which holds fluid.

Moore and Agur (1995:159) state that the peritoneum is carried from the vertex of the bladder on to the abdominal wall to form the middle umbilical fold and the anterior part of the bladder is in contact with the coils of the small intestine. According to Lewis (2000) the triangular fundus is directed downward and backward where it is merely separated from the rectum by the rectovesical fascia whilst the vertex is directed forward toward the upper part of the symphysis pubis. The superior surface of an empty bladder is triangular, bounded on either side by a lateral border which separates it from the inferior surface, and behind by a posterior border, represented by a line joining the two ureters, which intervenes between it and the fundus (Lewis, 2000), as illustrated in Figure 2.3. The postero-superior surface is directed upward and backward (Ashton-Miller, Howard and DeLancey, 2001). The lower parts of the lateral surfaces of the bladder are in contact with the lateral

walls of the pelvis as stated by Ashton-Miller, Howard and DeLancey (2001). The summit is directed upward and forward above the point of attachment of the middle umbilical ligament, and hence the peritoneum which follows the ligament, forms a pouch of varying depth between the summit of the bladder, and the anterior abdominal wall (Rackley, 2013).

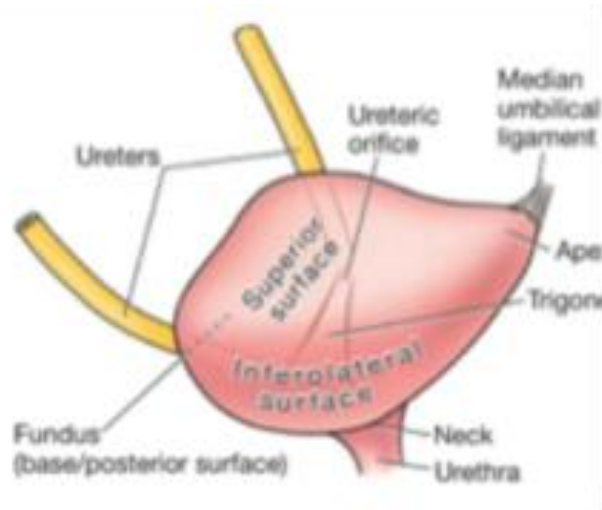


Figure 2.3: Female Bladder (Quizlet – use permitted)

In the female, the fundus is closely related to the anterior vaginal wall and cervix (Moore and Agur, 1995: 157). The posterior aspect of the bladder is in relation with the uterus and the upper part of the vagina. It is separated from the anterior surface of the body of the uterus by the vesicouterine excavation, but below the level of this excavation it is connected to the front of the cervix uteri and the upper part of the anterior wall of the vagina by areolar tissue (Lewis, 2000). The position of the bladder varies with changes of the rectum, being pushed upward and forward when the rectum is distended (Lewis, 2000). When the bladder is empty the uterus rests upon its superior surface. Bomford, Kunkler and Sherriff (2001: 425) states that the bladder is related to the pubic symphysis anteriorly, as illustrated in Figure 2.4. Inferiorly, the bladder is related to the levator ani muscle and superiorly it is related to the

small intestine and sigmoid colon (Rackley, 2013).

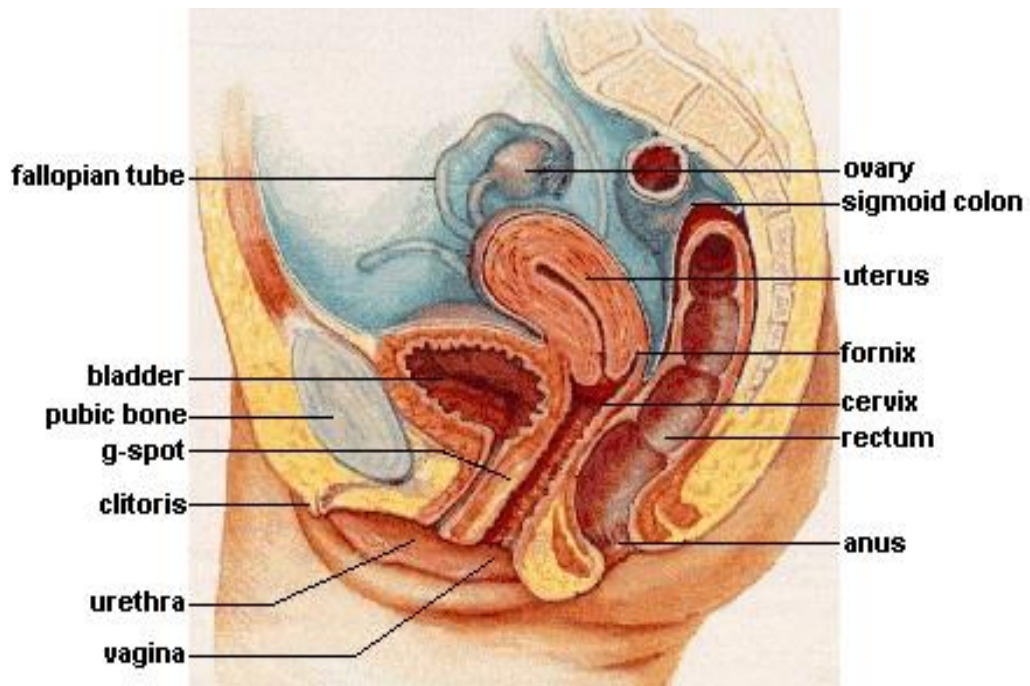


Figure 2.4: Median section of female pelvis (Kim, Brandner, Saiful Huq and Beriwal, 2011 – open access article)

The bladder expands superiorly to the level of the umbilicus as it fills (Moore and Agur, 1995: 157). According to Lewis (2000) the bladder size, position, and relations vary according to the amount of fluid it contains. However, the fundus undergoes little alteration in position when the bladder is full; being only slightly lowered (Ashton-Miller, Howard and DeLancey, 2001 and Fowler, Griffiths and de Groat, 2008:454). This is an important fact as it has a direct implication on the doses that are received by the bladder in this research. It has been observed in this research that when the bladder is in close proximity to the target area, the bladder receives a higher dose.

2.3.1 Radiation Induced Complications of the Bladder

Fujikawa, Miyamoto, Ihara, Matsui and Takeuchi (2001:21) indicate that many patients experience radiation induced complications of the organs adjacent to the radiotherapy target volume. Fujikawa *et al* (2001:21) report that the incidence of spontaneous rupture of the bladder is particularly high in Japan as their study concluded that this spontaneous rupture might be due to the use of HDR Brachytherapy. Bomford, Kunkler and Sherriff (2001:411) advised that the possibility of a high incidence of severe complications must be considered when using HDR Brachytherapy. According to Kaplan and Wolf (2009:641) radiation induced cystitis is a common deficiency affecting patients post Brachytherapy.

The symptoms of radiation cystitis include an alteration of the voiding pattern, bladder inflammation, bleeding that can range from minor to severe, bladder pain and an urgency to urinate (Crew, Jephcott, and Reynard, 2001:118). Further studies indicate that the symptoms of this deficiency may occur immediately after Brachytherapy or up until ten years after treatment (Wong-You-Cheong, Woodward, Manning, and Davis, 2006:1852). The rate of complications of radiation induced cystitis depends on the volume and area of the bladder affected by radiation, the dose rate of radiation, dose per fraction and the total dose of radiation. The most severe radiation induced complications include bladder necrosis, incontinence and fistula formation (Kaplan and Wolf, 2009:642).

2.4 Anatomy and Physiology of the Rectum

According to Moore and Agur, (1995:173), the rectum begins anterior to the level of the third sacral vertebrae, forming an S-shape as it follows the curve of the sacrum and coccyx. The rectum is continuous proximally with the sigmoid colon and extends 13 cm to 15 cm to the anus (Moore and Agur, 1995:173). The internal cavity of the rectum is divided into three or four chambers (Moore and Agur, 1995:173). Each chamber is separated from the other chambers by permanent transverse folds (valves of Houston) that help to support the rectal contents. A sheath of longitudinal muscle surrounds the outside wall of the rectum, making it possible for the rectum to shorten in length (O'Rahilly, 2008), as illustrated in Figure 2.5. The pelvic diaphragm, which is a muscular sheet, runs perpendicular to the juncture of the rectum and anal canal and serves as a constriction between these two segments of the large intestine (Encyclopaedia Britannica, 2011). Kapoor (2013) describes the rectum as the terminal segment of the digestive system in which faeces accumulate just prior to excretion.

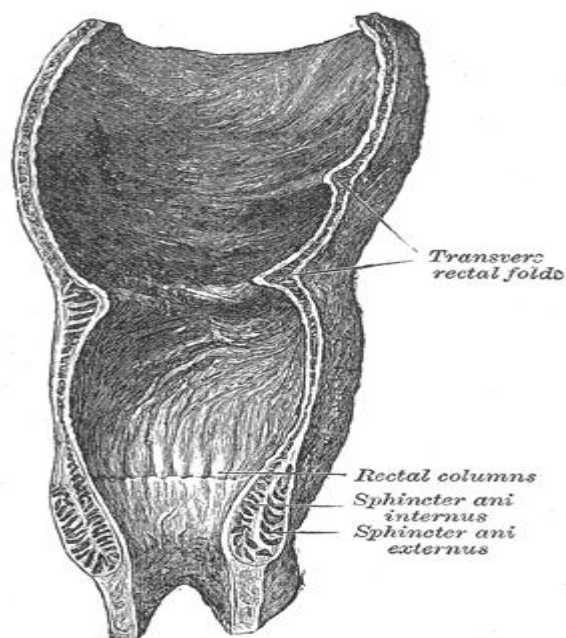


Figure 2.5: Medial section of the rectum (Kapoor, 2013 – open access site)

Waste products are stored in the sigmoid colon until they are ready to be excreted from the body. As the faecal material enters the rectum, the walls distend to accommodate the material (Moore and Agur, 1995:173). The dilated terminal part of the rectum is called the rectal ampulla. The rectum ends antero-inferior to the tip of the coccyx by turning posterior-inferiorly to become the anal canal (Encyclopaedia Britannica, 2011).

The anterior and lateral surfaces of the superior third of the rectum are covered by peritoneum, whilst only the anterior surface of the middle third is covered by peritoneum (Moore and Agur, 1995:173). According to O'Rahilly (2008), no surface of the lower third of the rectum is covered by peritoneum. Kapoor (2013) states that in females, the peritonem reflects from the rectum to the posterior fornix of the vagina and the cervix where it forms the floor of the rectouterine pouch.

2.4.1 Radiation Induced Complications of the Rectum

Clark, Souhami, Roman, Evans and Pla (1994) found in their study, that patients who received higher doses to the rectum presented with serious rectal complications four months post treatment, so recommended lower doses. This recommendation was reiterated in the study by Clark, Souhami, Roman, Chappell, Evans and Fowler (1997) who documented the late rectal complications of patients treated with HDR Brachytherapy for cancer of the cervix. Sakata, Nagakura, Oouchi, Nakata, Shido, Koito, Sagae, Kudo and Hareyama (2002) observed in their study that there was a drastic increase in rectal complications after the maximal rectal dose was exceeded by 60 Gray. This demonstrates the importance of making every effort to ensure that rectal doses are kept to a minimum or at least within its tolerance dose.

Almost all patients receiving radiation to their pelvis will show signs of acute enteritis as indicated by Quade (2004). The information supplied by Quade (2004) also states that intracavitary Brachytherapy can cause a decrease in vascular flow to the anterior rectal wall behind the posterior vaginal fornix and impair rectal mobility, increasing the chance of radiation injury. Hendry, Jeremic and Zubizarreta (2006:151-152) explain the cause of these side effects by stating that radiation has the potential to cause various degrees of damage to normal tissue therefore recommend limiting the dose administered to a patient in order to have a curative effect. Shrivastava *et al* (2009:95) further stress the importance of decreasing the dose to the rectum as they observed an increased morbidity even in successfully treated patients who received higher rectal doses.

Andreyev (2007:1009) estimates that ninety percent of patients develop a permanent change in their bowel habits after pelvic radiotherapy and fifty percent of that group has an associated reduction in their quality of life. Andreyev (2007:1015) further states that pelvic Brachytherapy can cause injury to the small bowel, terminal ileum, caecum, transverse colon and rectosigmoid colon. Late onset bowel dysfunction post Brachytherapy is increasingly common according to the study conducted by Henson (2010:363). Henson (2010:359) states that fifty percent of patients develop bowel symptoms post a course of radiotherapy including Brachytherapy, affecting the patient's quality of life negatively. Henson (2010:365) concludes that there is an adjustment required to the treatment of patients receiving pelvic radiotherapy, as well as the need for further research, in order to minimise this late side effect. Huang (2011:66) discusses the concept of bladder distension in order to decrease the volume of the small bowel receiving dosage from Brachytherapy. Distention increases the risk of exposure to radiation. Huang's study showed a statistically significant reduction in dose to the bladder wall as well as the rectum with reduced

distention. This has relevance to this study as patients were advised not to eat or drink anything for six hours prior to the treatment.

Puetz (2008) demonstrated that chronic radiation proctitis was a common complication experienced in patients receiving pelvic radiotherapy. Vorvick, Longstreth and Zieve (2011) state that Brachytherapy has the potential to cause proctitis, a condition where there is inflammation of the rectum which causes discomfort, bleeding painful bowel movements and a discharge of mucous or pus. Proctitis can cause further complications including anal fistula, recto-vaginal fistula and severe bleeding which may result in anaemia (Vorvick, Longstreth and Zieve, 2011).

The rate of complications may also depend on the radiation dose per fraction delivered to the patient. Moore, Magrino, and Johnstone (2000:216) stated that the use of 3D treatment techniques aids in the reduction of the amount of rectum within the treated volume as smaller volumes of rectum have the ability to tolerate a higher dose. This theory forms part of the investigations of this study as a 2D technique is compared to a 3D technique.

2.5 Brachytherapy

According to Suntharalingam, Podgorsak and Tölle (2005:451), Brachytherapy is the term used to describe the short distance treatment of cancer with radiation from small encapsulated radionuclide sources. The author maintains that the treatment is administered by placing radioactive sources directly into or near the region to be treated. The current study focused on intracavitary Brachytherapy, in which the radioactive sources are placed in the body cavity (cervical canal) close to the tumour volume.

Jameme *et al* (2008:3) state that the use of Brachytherapy plays a vital role in case management as it aids in disease control as well as toxicity. Crucial to the study by Jamema *et al* (2008:3) was the ability of intracavitary Brachytherapy to deliver very high doses to the tumour whilst delivering lower doses to the surrounding normal tissue structures; however, due to the sensitivity of the bladder and rectum to radiation, the latter act as dose-limiting structures. The bladder and rectum are critical organs due to their close location to the vagina. Haie-Meder, Dumas, Paumier, Lessard, Kanoun, Morice and Lhommé (2008:526) discuss the fundamental role of Brachytherapy in the treatment of patients with carcinoma of the cervix, emphasising the role of imaging in the improvement of knowledge of the tumour and surrounding normal tissue structures.

There are different classifications for intracavitary Brachytherapy. According to the ICRU 38, treatment dose rates fall into three categories (ICRU 38: 1985:4). Low dose rate (LDR) Brachytherapy which ranges between 0.4 Gy and 2 Gy per hour, has the compatibility to be performed with both manual and automatic afterloading techniques. Medium dose rate (MDR) Brachytherapy ranges from 2 Gy to 12 Gy per hour and may also be delivered by manual or automatic afterloading. High dose rate (HDR) Brachytherapy delivers the dose at 12 Gy per hour or more and only automatic afterloading can be used due to the high source activity (Mazeron, Scalliet, Van Limbergen and Lartigau: 2008:95).

The current study focused on high dose rate (HDR) intracavitary Brachytherapy which was performed using an automatic remote afterloader. HDR has many advantages over other techniques as it minimise a shorter treatment time, the patients suffer less discomfort from prolonged treatment sessions, it eliminates radiation exposure of staff, patients do not need to be hospitalised and the risk of applicator movement during treatment is reduced

(Lee, Huh, Park, Lim, Ahn, Park, Kim, Bae, Lee, Park, Kim, Lim, Chung, Lee, and Shim, 2004:225). HDR Brachytherapy means that the numerical value of the dose rate at the dose specification points (e.g. Point A as per the Manchester System) are greater than 12 Gray per hour (Suntharalingam, Podgorsak and Tölle, 2005:454). Automatic afterloading describes the placement of the applicator into the target position, which is inserted into the patient. The radioactive sources are then loaded mechanically into the applicators (Suntharalingam, Podgorsak and Tölle, 2005:454). The remote system such as the one used for this study allows for the source insertion and removal from a control panel situated a distance away from the patient, eliminating the exposure to staff (ICRU 3; 1985:5).

The Manchester system as per ICRU 38 was used for dose specification in this study. As per the ICRU 38 (1985:1-2), the Manchester system delivers a constant dose rate to defined points near the cervix. These points are specified in terms of dose and location. Whilst it is optional to relate Point A to the geometry of the source, this study relates Point A to anatomical references in the patients (ICRU 38; 1985:1).

There are various techniques that may be employed to achieve the desired outcome; however this study focused on two techniques, namely 2D Brachytherapy planning, via template planning, and 3D Brachytherapy planning, via CT planning. Two-dimensional (2D) refers to an object, or in the case of this study, the patient, that is viewed on the vertical plane (x axis) and horizontal plane (y axis) only; whereas three dimensional (3D) views the patient in the horizontal plane and the vertical plane, taking into consideration the depth (z axis) of the patient, that is, viewing the patient as a sphere (Khan, 1994:304-305). For 2D Brachytherapy planning, algorithms were programmed by the physicist to calculate the dose distribution simply by considering the length (vertical plane) and the width (horizontal plane) to

be treated as specified by the oncologist post a clinical examination. For 3D Brachytherapy planning, the dimensions to be treated are determined post clinical examination and a CT scan so that the organs at risk can be visualized for effective Brachytherapy planning.

2.5.1 Dosimetry for Intracavitary Brachytherapy

Of the few radioactive nuclides used today, Iridium-192 is used at IALCH for Brachytherapy. The Iridium-192 are sealed sources and are made available as seeds (Bentel, 1996:537). Bentel (1996:537) states that these sources are doubly encapsulated with an outer sheath of stainless steel. The capsules serve several purposes which include containing the radioactivity, providing source rigidity, and absorbing any alpha rays from the photon emitting source and beta radiation produced through the source decay (Suntharalingam, Podgorsak and Tölle, 2005:455 – 457). The choice of photon emitting nuclide depends on the photons penetration into tissue and its radiation protection requirements. Dose distributions in tissue within a short treatment distance are not influenced much by photon scattering when photon energies are above 300 kilo electron volt (KeV), due to the attenuation by tissue being compensated for by scatter build-up of the dose. For photon energies of 30KeV and below, the tissue attenuation is highly significant. It is for this reason that Iridium-192 is used, as it has an approximate photon energy of 0.38 mega electron volt (MeV) (Suntharalingam, Podgorsak and Tölle, 2005:457).

Dosimetry for intracavitary Brachytherapy for cervical cancer at IALCH is performed using the Manchester System. According to Suntharalingam, Podgorsak and Tölle (2005:460), the Manchester System is characterised by Point A. Point A is the prescription point, that is, the point that receives the prescribed radiation dose. Point A is located 2 cm superior to the cervical os

and 2 cm lateral to the cervical canal or from the axis of the central intrauterine applicator (Jamema *et al*, 2008:4). The duration of the treatment is based on the dose rate at Point A.

ICRU 38 (1985:7) also relates the dose distribution to the target volume rather than a specified point and it contributes to reaching a consensus between centres (Feller, Pötter, Knocke and Wambersie; 2001:57 and Suntharalingam, Podgorsak and Tölle, 2005:460).

The results of the study by Kim, Shen and Duan (2007: 189) reveal that the ICRU point dose for the bladder was markedly underestimated when compared to that of 3D Brachytherapy planning whilst the ICRU point dose for the rectum did not differ significantly to that of 3D Brachytherapy planning. This is contrary to Wang, Kwon, Zhu, Yeo and Henson (2009:246) who established in their study that the dose to the target volume and the dose to the bladder correlated between the 3D Brachytherapy plan and ICRU reference points; however the dose to the rectum did not correlate significantly. The study conducted by Gao, Albuquerque, Chi and Rusu (2010:57) demonstrated that the point of the prescribed dose did not correlate to the target area when the 2D plan was applied to a 3D volume. This lends itself to the conclusion that 2D plans do not deliver the prescribed dose efficiently and affirms the requirement for improved planning methods, such as 3D Brachytherapy, which is demonstrated in this study.

In order for Point A to receive the prescribed dose, the bladder and the rectum receives unwanted yet unavoidable radiation dose resulting in complications including rectal and urinary side effects that hinder the patients' quality of life (Lee *et al*, 2004:222). Therefore, intracavitary Brachytherapy requires careful placement of the sources in respect to the

target volume and the surrounding normal tissue structures as this will affect the dose distribution (Kirisitis, Pötter, Lang, Dimopoulos, Wachter-Gerstner, and Georg; 2005:911). Clinical guidelines and protocols should be set so as to deliver adequate dose to the target volume and minimise dose to the surrounding normal tissue structures. Furthermore, the dose volume histograms (standard statistical description of a distribution in terms of dose verses volume) constraints, produced by 3D planning methods, for the normal tissue structures allow reproducible treatment plans that help to detect and avoid severe overdosage (Pötter, Haie-Meder, Van Limbergen, Barillot, De Brabandere, Dimopoulos, Dumas, Erickson, Lang, Nulens, Petrow, Rownd and Kirisits; 2006:72).

2.5.2 The Biological Effects of Brachytherapy

It is crucial to view Brachytherapy radiobiologically, as dose delivery has the potential to result in complex dose rate effects that may influence the therapeutic outcome (Bentel, 1996:8-9). The continuous delivery of dose will influence the repair of sublethal and lethal damage, cell proliferation and other cell kinetics (Suntharalingam, Podgorsak and Tölle, 2005:453). These effects will modify the radiation response of the tumour (target volume) and normal tissues (Khan, 2006:268). Mazon (2008:96) state that the repair of sublethal damage to the tumour depends on the radiosensitivity and radiocurability of the tumour, therefore the stage of cancer has implications on the effectiveness of Brachytherapy. Cell proliferation of normal tissue has a protective effect whilst cell proliferation of tumour cells has a detrimental effect (Mazon *et al*; 2008:97).

Ionising radiation has the ability to affect the chemical state of a material and cause changes which are biologically significant (Bentel, 1996:8-9). The biological effects of ionising radiation originate primarily from damage to the

deoxyribonucleic acid (DNA) of a cell or cells (Gallagher, 2001). There are four basic effects of ionizing radiation on DNA. Radiation may pass through the cell without doing any damage, the radiation may damage the cell but this damage may be repaired by the cell, the radiation may damage the cell so that the cell fails to repair itself and reproduces itself in a damaged form or the radiation may cause cell death (Khan, 2006:271-273). Biological changes due to the interaction with ionising radiation depends on the stage of cell cycle at the time of irradiation (Mazeron *et al*; 2008:96-97). According to Mazeron *et al* (2008:97), cells are most resistant during synthesis and most radiosensitive during mitosis.

2.6 Summary and Main Aim

Brachytherapy is a complex treatment option, which would be highly successful if the ionising radiation causes tumour cell death only and is able to pass through the normal tissue cells without causing any damage. However, this may not be possible due to the sensitivity of the bladder and rectum to ionising radiation. It is inevitable that these organs will experience some degree of damage resulting in side effects which have the potential to affect the patient's quality of life. However, by adequate and efficient planning, the amount of ionisation radiation exposure can be reduced. Reduction in exposure may possibly facilitate normal cell repair or at least minimise normal cell damage.

Therefore, the aims of this study:

The purpose of this study is to compare 2D HDR Brachytherapy planning (using computer generated templates) and 3D HDR Brachytherapy planning (using Computer Tomography scans) in terms of dose distribution in order to accurately determine bladder and rectal doses. Further research questions

are explored to determine whether relationships exist between CT volume of the bladder and the dose received by the bladder as well as the relationship between CT volume of the rectum and the dose received by rectum.

Research questions emanating from the Aim are as follows:

- Procedure 1: Is there a significant relationship between the mean dose obtained for the bladder from 2D HDR Brachytherapy planning using computer generated templates and the mean dose obtained for the bladder from 3D HDR Brachytherapy planning using Computer Tomography scans
- Procedure 2: Is there a significant relationship between the mean dose obtained for the rectum from 2D HDR Brachytherapy planning using computer generated templates and the mean dose obtained for the rectum from 3D HDR Brachytherapy planning using Computer Tomography scans
- Procedure 3: Is there a significant relationship between the maximum dose obtained for the bladder from 2D HDR Brachytherapy planning using computer generated templates and the maximum dose obtained for the bladder from 3D HDR Brachytherapy planning using Computer Tomography scans
- Procedure 4: Is there a significant relationship between the maximum dose obtained for the rectum from 2D HDR Brachytherapy planning using computer generated templates and the maximum dose obtained for the rectum from 3D HDR Brachytherapy planning using Computer Tomography scans
- Procedure 5: Is there a significant relationship between the bladder CT volume obtained from 2D HDR Brachytherapy planning using

computer generated templates and bladder mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates

- Procedure 6: Is there a significant relationship between the rectum CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and the rectum mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates
- Procedure 7: Is there a significant relationship between the bladder CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the bladder mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans
- Procedure 8: Is there a significant relationship between the rectum CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the rectum mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans
- Procedure 9: Is there a significant relationship between the bladder CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and the bladder maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates
- Procedure 10: Is there a significant relationship between the rectum CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and rectum maximum dose obtained

from 2D HDR Brachytherapy planning using computer generated templates

- Procedure 11: Is there a significant relationship between the bladder CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the bladder maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans
- Procedure 12: Is there a significant relationship between the rectum CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the rectum maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans

CHAPTER THREE

RESEARCH METHODS AND DESIGN

3.1 Introduction

This chapter describes the research study population and explains the inclusion and exclusion criteria that were employed for selection of the sample. Included in this chapter is a description of the research parameters that were used for this research study, as well as the reasons for their use. The chapter concludes with a description of the data analysis methods used.

3.2 Research Design

This research study was a prospective study as it looked at future events; therefore, information was collected over time to assess relationships between the outcomes and the variables (Dox *et al*, 2001:533). Furthermore, it was a quantitative study because the data could be analysed using conventional statistical methods which employed models (graphs depicting bladder and rectal doses) to evaluate results (Peat, 2002:16). In addition to being a quantitative study, the study was also an experimental study because the effect of an intervention was tested i.e. the bladder and rectal doses were measured, evaluated and analysed on a 2D planning technique and then on a 3D planning technique and the results were compared (Peat, 2002:16). The evidence yielded from this study was dependent on the consequences observed, and the data produced by this study was testable by using observations or experiments; therefore, this study was an empirical study (Ramlaul, 2010 glossary).

3.3 Permission to Perform the Study

This study was conducted at IALCH in KwaZulu-Natal, South Africa. Permission was obtained from the Department of Health (DoH) for the research to be conducted at this provincial hospital (Appendix A). Permission was also obtained from the hospital manager and the head of department of Radiation Oncology for the research to be performed within the department (Appendix B). The researcher was a member of staff at the time of data capture.

3.4 Invitation to Patients

Patients scheduled for HDR Brachytherapy at the research venue were invited to participate in this study. Patients' participation was voluntarily and they were permitted to withdraw from the study at any time without any obligations.

3.5 Sponsors

The use of the equipment required for this research study was sponsored by IALCH.

3.6 Data Collection

Primary data was collected over a period of eight months, commencing in July 2010, as patients were scheduled for HDR Brachytherapy at the research venue.

The primary data collected consisted of:

- personal and demographic data of the research patients
outputs of 2D HDR Brachytherapy planning using computer generated templates
- outputs of 3D HDR Brachytherapy planning using Computer Tomography scans

3.7 Patient Information Sheet and Informed Consent

The patient information sheets (Appendix C) and informed consent forms (Appendix D) were designed by the researcher and approved by the Durban University of Technology Research Ethics Committee (Appendix E). These forms were made available to patients in English and Zulu. Patients were requested to participate in this study post approval of the research proposal by the Durban University of Technology Faculty of Health Research committee, the KwaZulu-Natal Department of Health Research Committee (Appendix A), the Medical Manager of IALCH and the Head of Department of Radiation Oncology of IALCH (Appendix B).

All patients were requested to read, understand and then sign the patient information sheet, acknowledging that it was understood and that their questions about the study were answered. They then read, understood and signed the informed consent form. All forms were also signed by a witness.

The researcher ensured confidentiality by not disclosing the identity of the patients that participated in this study. All computer files were coded with the patients HDR Brachytherapy data. This data was stored with no names.

3.8 Selection of Research Population

Patients were recruited as they were easily available for the study, therefore it can be said that the convenience sampling method was employed. This method was used instead of random selection in order to reduce the time for recruitment. According to Dorak (2009), random sampling is the basic sampling technique where a group of subjects are selected for study from a larger group. Each individual is chosen entirely by chance and each member of the population has an equal chance of being included in the sample. Every possible sample of a given size has the same chance of selection. It is an unbiased method that may prove to be very time consuming, therefore convenience sampling was utilised in this research study.

Patients were recruited for participation in this research study due to them being selected by their Oncologist to receive 9 Gy cervical HDR Brachytherapy as part of their treatment prescription as per the protocol used at IALCH. All patients also received external beam radiotherapy to a total dose of 55.8 Gy (1.8 Gy per fraction for 31 fractions).

The first 30 female patients receiving cervical HDR Brachytherapy at IALCH were selected to participate in this research study. The following were inclusion and exclusion criteria that were used for this study.

3.8.1 Inclusion Criteria

The criteria for a patient to be recruited for this study were:

- Female patients with cervical cancer
- Any age or ethnic group

- Patients with stage II A, II B, III A and III B non-bulky disease, according to the International Federation of Gynaecologists and Obstetricians (FIGO) clinical staging system (Boardman; 2013)
- Patients receiving 9 Gy cervical HDR Brachytherapy
- Stainless steel and titanium applicators were used for Brachytherapy at IALCH, however, only those inserted with the titanium applicators were considered for this study as it has been found that titanium applicators do not cause image artefacts as do stainless steel (Wei, Chen, Sandison, Liang and Xu; 2004: 5416). Haie-Meder, Pötter, Van Limbergen, Briot, De Brabandere, Dimopoulos, Dumas, Hellebust, Kirisits, Lang, Muschitz, Nevinson, Nulens, Petrow and Wachter-Gerstner (2005:235) state that CT compatible applicators allow for an improved assessment of the target area and the critical structures therefore it was best to consider this in this study.

3.8.2 Exclusion Criteria

- Patients presenting with bulky disease
- Patients presenting with fistulas or deemed not to be amenable for Brachytherapy as per the Oncologist's decision

3.9 Radiation Dosage

All patients had a treatment scheme that consisted of a combination of external beam radiotherapy and HDR Brachytherapy. External beam radiotherapy comprised of a conformal plan with four fields, the commonly termed 'Box Technique'. The 'Box Technique' included an anterior-posterior (AP), posterior-anterior (PA) and two lateral fields. Treatment was planned to the planning tumour volume (PTV) where the superior border of the fields

was the junction of the fourth and fifth lumbar vertebrae. The inferior border was at the bottom of the obturator foramina of the pubic bones; unless the target area was to include the lower third of the vagina, then the inferior border was at the bottom of the ischial tuberosities. The lateral borders were 2 cm lateral to the pelvic brim. The anterior border was at the tip of the symphysis pubis and the posterior border was the junction of the second and third sacral vertebrae. External beam radiotherapy was administered in 1.8 Gy daily dose for 31 fractions to a total dose of 55.8 Gy, five fractions per week. PTV received 50.4 Gy and the gross tumour volume (GTV) received 5.4 Gy. Considering the anatomical level of the bladder and rectum as discussed in Chapter 2.3 and Chapter 2.4 respectively, it can be assumed that these critical structures would receive a substantial amount of the prescribed dose which would contribute to the radiation induced complications discussed in Chapter 2.3.1 and Chapter 2.4.1. This lends itself to the caution required during HDR Brachytherapy to reduce the dose to the critical structures. HDR Brachytherapy was delivered on completion of external beam radiotherapy. Patients received cervical HDR Brachytherapy of 9 Gy in one fraction.

3.10 Reasons for Choice of Research Parameters

According to Huang (2011:62), the bladder and rectal dose is an exceptionally important consideration in HDR Brachytherapy planning, as these are the two normal tissue structures most affected by the radiation dose delivered. In dose analysis, the dose to the bladder and rectum from external beam radiotherapy should also be considered as this cumulative dose contributes to the severity of side effects. Due to large tumour volumes for external beam radiotherapy, the dose to the bladder and rectum are quite high, therefore, it becomes imperative to, by all means possible, minimise the dose to the bladder and rectum during HDR Brachytherapy. It is for these

reasons that the doses to the bladder and the rectum have been chosen for evaluation in this study.

The technique employed at IALCH at the time of the study, i.e. 2D HDR Brachytherapy planning via computer generated template planning is not the best option available as can be seen from the literature reviewed in Chapter 2.5.1 of this dissertation. The researcher proposes in this study an improved method of planning i.e. 3D HDR Brachytherapy planning via Computer Tomography planning. Three dimensional planning was seen as a practical approach to a more conformed method of HDR Brachytherapy planning as the department had its own dedicated scanner within the department for radiotherapy planning.

3.11 Research Parameters

The test methodologies that were employed for the purposes of this research are described in the following sections.

3.11.1 Two-Dimensional Planning

Two-dimensional (2D) refers to an object, or in the case of this study, the patient/applicator, that is viewed on the vertical plane (y axis) and horizontal plane (x axis) only. The depth of the patient (z axis) is not taken into consideration (Khan, 1994:304-305). The critical structures are not viewed and the dose is prescribed to a point. The applicators are viewed in terms of their length and width. Doses to the bladder and rectum are not considered as the dose to Point A is the prescribed dose.

3.11.1.1 Patient Preparation

The same procedure for applicator insertions, which were inserted by the oncologist, was followed for each patient and was as follows. Patients were advised not to eat or drink anything six hours prior to the treatment. Applicator insertion was completed under light sedation, which for the purpose of this study was Midazolam Hydrochloride. The vagina was packed with gauze to push the bladder and rectum away from the target area and stabilise the applicators (Jain *et al*, 2007:213 and Frere, 2008). HDR Brachytherapy dose specification at IALCH was calculated by employing the Manchester System therefore this system was used for this research study. Remote afterloading was automatic. This procedure was part of the normal protocol followed at IALCH.

Equipment

- Automatic remote after loader - Iridium 192 - MDS Nordion Varian GammaMed Treatment unit
- BrachyVision vs.8.6 (Brachytherapy planning system)
- Siemens Somatom Sensation Open CT scanner
- Titanium (CT compatible) Fletcher-style applicator set (flexible geometry)
 - A cervical applicator consists of a central probe (tandem) and lateral capsules (ovoids) (Suntharalingam, Podgorsak and Tölli, 2005:460).

3.11.1.2 2D Brachytherapy Plan

Once patients had been prepared for HDR Brachytherapy i.e. applicators (central and ovoid probes) inserted as illustrated in Figure 3.1, the patients were planned for HDR Brachytherapy using the computer generated templates. The Manchester system was used to define Point A. Dose to the

critical structures was not considered. The patients were then treated using the automatic remote after loader.

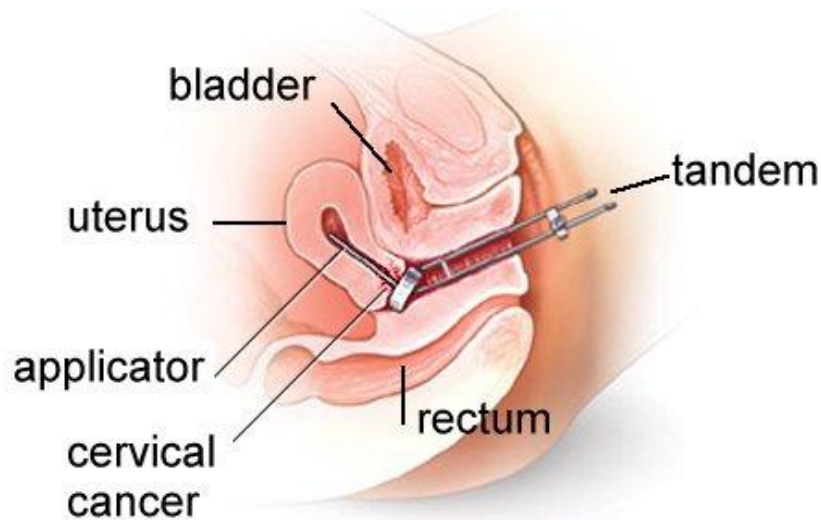


Figure 3.1: Patient inserted with Brachytherapy applicators (About Cancer – no copyright)

Imaging Modalities

- CT scans (this was completed as part of the investigation for this research)

After the Titanium Fletcher-style applicator set was inserted in the patients, the researcher performed a CT scan with the Siemens Somatom Sensation open CT scanner. The CT scans were performed to a 5 mm slice thickness from the level of the fifth lumbar vertebrae superiorly to the level of the anus inferiorly. The CT images were transferred to the Brachytherapy planning system digitally. Thereafter, two techniques of planning were applied to the CT data set i.e. 2D HDR Brachytherapy planning via computer generated templates (2DBP) and 3D HDR Brachytherapy planning via Computer Tomography (3DBP). All planning was done by the researcher using BrachyVision vs. 8.6.

The same parameters; i.e. dwell position times, as that of the 2D HDR Brachytherapy planning method were applied to the CT data set. External contours for the bladder and rectum were delineated in order to compute the corresponding doses. The entire bladder was contoured and the rectum was contoured from the recto-sigmoid junction superiorly to the ischial tuberosity inferiorly. The use of CT facilitates reasonably accurate delineation (Wachter-Gerstner *et al*, 2003:269). The doses to Point A were noted but were not adjusted in any way so as to determine resultant doses to the bladder and the rectum. For the purpose of this study the plan produced i.e. 2D HDR Brachytherapy plan was called the 2DBP. Cumulative dose-volume histograms (DVH) were computed based on the external contours of the bladder and rectum from 2D HDR Brachytherapy planning using computer generated templates (2DBP). The DVH were evaluated for each plan in order to determine the maximum and mean dose to the bladder and the rectum were recorded as well the volume of the bladder and rectum receiving the corresponding dose. Bahadur, El-Sayed, El-Taher, Zaza, Moftah, Hassouna, and Ghassal (2008:1) state that a DVH provides accurate estimation of the dose in relation to the normal tissue structures.

3.11.2 Three-Dimensional Planning

Three dimensional (3D) views the object in the horizontal plane (x axis) and the vertical plane (y axis), taking into consideration the depth (z axis) of the object i.e. viewing the object as a sphere (Khan, 1994:304-305). The critical structures were delineated and viewed as a volume. In this study the dose was prescribed to a point (Point A as per the Manchester System) for a more accurate comparison of bladder and rectal doses between the two techniques discussed. Ideally, the prescribed area should be defined in 3D as well.

3.11.2.1 Patient Preparation

The same procedure for patient preparation was observed as explained in Section 3.11.1.1.

3.11.2.2 3D Brachytherapy Plan

A 3D HDR Brachytherapy plan was prepared for each patient utilising the same CT scan used for the 2DBP. The 3D HDR Brachytherapy plan took into consideration the doses to Point A, as well as the doses to the bladder and the rectum. Constraints were set for the bladder and rectum to aid the planning process in order to achieve bladder and rectal doses that did not exceed 80 percent of the dose prescribed to Point A. Since the applicators that were used for the study were of flexible geometry, a variety of dose distributions were generated from a given applicator simply by adjusting the length of time, that is dwell time, which the source dwells at any location along the applicator, that is dwell position. The optimal sequences of dwell times were related to the unique clinical situation of each patient. This sequence of dwell times defines the volume and shape of the dose distribution and the treatment outcome (UCSF Comprehensive Cancer Center, 2006:3). A 3D HDR Brachytherapy plan was considered acceptable when Point A received the prescribed dose as best possible whilst the bladder and rectal doses did not exceed 80 percent of the dose prescribed to Point A as per the International Commission for Radiation Units (ICRU) Report 38 (Thomadsen, 2008).

The DVH were computed based on the external contours of the bladder and rectum from 3D HDR Brachytherapy planning using Computer Tomography scans (3DBP). The DVH were evaluated for each plan in order to determine the maximum and mean dose to the bladder and the rectum were recorded

as well the volume of the bladder and rectum receiving the corresponding dose. Doses to the rectum and bladder of the 3DBP were compared with the doses to these structures via 2DBP.

3.12 Ethical Considerations

The Ethics Form (Appendix E) adhered to the ethical considerations requirements of this study. An information sheet (Appendix C) was made available to each patient to ensure that the patient understood what was required. The information sheet included the radiation risks involved in the procedures. Informed consent (Appendix D) was obtained from all patients.

3.13 Statistical Analysis

The process of primary data collection involved the retrieval of the data that was printed once HDR Brachytherapy planning was completed for analysis and comparison. Primary data collection included personal and demographic data of the patients as protocol of IALCH, CT scans, computer generated template planning outputs and CT planning outputs. Demographic data is not reported on as it serves as irrelevant to this study. This primary data that was collected, in the form of results, included the rectum dose and the bladder dose. The statistical programme, SPSS Analysis without Anguish version 12.0 for Windows was used for primary data entry and analysis. Statistical tests were performed by the researcher and a statistician independently, who then compared and discussed the results. Data is represented in the form of graphs and tables.

The following statistical tests were conducted:

- Descriptive statistics - mean, median, mode, standard deviation
- Inferential statistics - Pearson product-moment correlation coefficient and independent groups t-test

All the raw data were assessed for normality, as this is a prerequisite for using inferential statistics. The assumption of normality was assessed using tests for standardised skewness and standardized kurtosis. The Kolmogorov-Smirnov statistic with a Lilliefors significance level was also used for testing normality. Descriptive statistics were necessary as this would explore the data and summarise and describe the observations. Mean and median values were used as the measures of central tendency. The measures of variability included range and standard deviation.

The types of inferential statistical tests used were the paired sample T-Test and the Pearson product-moment correlation coefficient. The T-Test was used to determine if there was a relationship between the categorical independent variables and the dependent variables. The Pearson product-moment correlation coefficient was used for describing the relationship between the dependent variables.

CHAPTER FOUR

RESULTS

4.1 Introduction

The main aim of this research was to compare the bladder and rectal doses yielded from the two techniques studied, i.e. 2D HDR Brachytherapy planning using computer generated templates and 3D HDR Brachytherapy planning using Computer Tomography scans, to determine which technique yields lower yet more accurate doses. Further research questions were used to determine if the relationships existed between the doses to the critical structures (bladder and rectum) and the volume of that structure being irradiated.

This chapter documents the results of the data analysis. 2DBP is the abbreviation used in this chapter to represent 2D HDR Brachytherapy planning using computer generated templates and 3DBP is the abbreviation used in this chapter to represent 3D HDR Brachytherapy planning using Computer Tomography scans.

The independent variables were:

- bladder Computer Tomography volume for 2D HDR Brachytherapy planning using computer generated templates, that is, B CT volume 2D;
- rectum Computer Tomography volume for 2D HDR Brachytherapy planning using computer generated templates, that is, R CT volume 2D,

- bladder Computer Tomography volume for 3D HDR Brachytherapy planning using Computer Tomography scans, that is, B CT volume 3D; and
- rectum Computer Tomography volume for 3D HDR Brachytherapy planning using Computer Tomography scans, that is, R CT volume 3D.

The dependent variables were:

- bladder mean dose from 2D HDR Brachytherapy planning using computer generated templates, that is, B Mean 2D;
- rectum mean dose from 2D HDR Brachytherapy planning using computer generated templates, that is, R Mean 2D;
- bladder mean dose from 3D HDR Brachytherapy planning using Computer Tomography scans, that is, B Mean 3D;
- rectum mean dose from 3D HDR Brachytherapy planning using Computer Tomography scans, that is, R Mean 3D;
- bladder maximum dose from 2D HDR Brachytherapy planning using computer generated templates, that is, B Max 2D;
- rectum maximum dose from 2D HDR Brachytherapy planning using computer generated templates, that is, R Max 2D;
- bladder maximum dose from 3D HDR Brachytherapy planning using Computer Tomography scans, that is, B Max 3D; and
- rectum maximum dose from 3D HDR Brachytherapy planning using Computer tomography scans, that is, R Max 3D.

4.2 Descriptive Statistics

Statistical tests were performed with and without the outliers and it was found that there were insignificant differences in the statistical outputs whether the outliers were included or not. In order to maintain an accurate representation

of the results, statistical outputs without the outliers will be included in chapter 5. However, chapter 4 will show where there was a presence of outliers and the repeated test without those outliers. Outliers were present in some of the data ranges. This may be due to the Oncologist accepting higher doses to the bladder and the rectum for some of the patients.

It is essential to perform normality testing as this is a prerequisite for further analytical statistics, certain statistical test can only be performed if the range is said to be 'normal'. The Kolmogorov-Smirnov statistic with a Lilliefors significance level for testing normality can be produced.

$p > 0.05$ indicates that normality can be assumed for that range.

The boxplot indicates if any outliers are found within the range and was used to describe the distribution. Outliers indicated by a circle with the number were accepted because it strayed only slightly from the trend whilst an outlier indicated by a star with the number was unaccepted because it marginally differed from the trend.

4.2.1 Descriptive Statistics - Independent Variables

4.2.1.1 B CT Volume 2D

- Table 4.1: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Bladder CT Volume 2D (Template) Planning	.110	30	.200 [*]

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

$p(0.200) > 0.05$ therefore normality was assumed.

- The mean ± 1 standard deviation of the B CT volume 2D was $60.99\text{cc} \pm 29.38\text{cc}$. At the 95 percent level of confidence the B CT volume 2D varied between 31.61cc and 90.37cc .
- Figure 4.1 is the histogram illustrating skewness and kurtosis. Skewness = 0.114 therefore the curve was skewed to the left. Kurtosis = 1.028 indicating a peaked distribution.

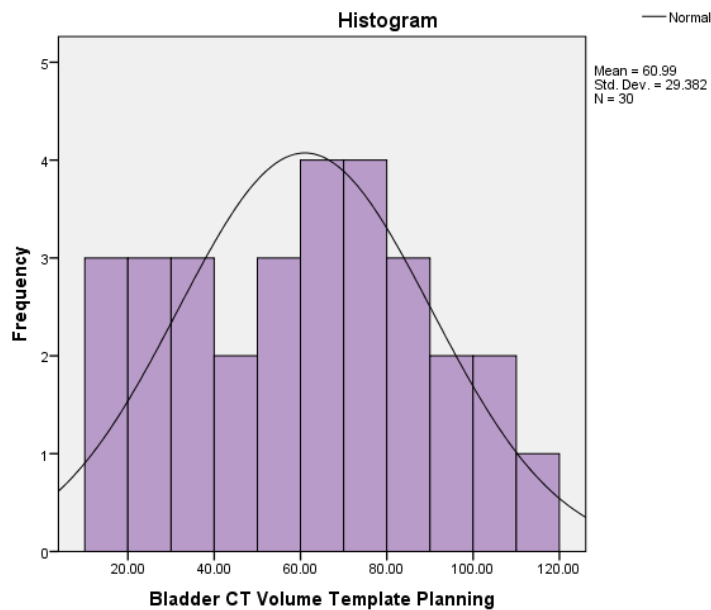


Figure 4.1: Histogram: B CT Volume 2D

- Figure 4.2 is the boxplot illustrating that there were no outliers present within the range.

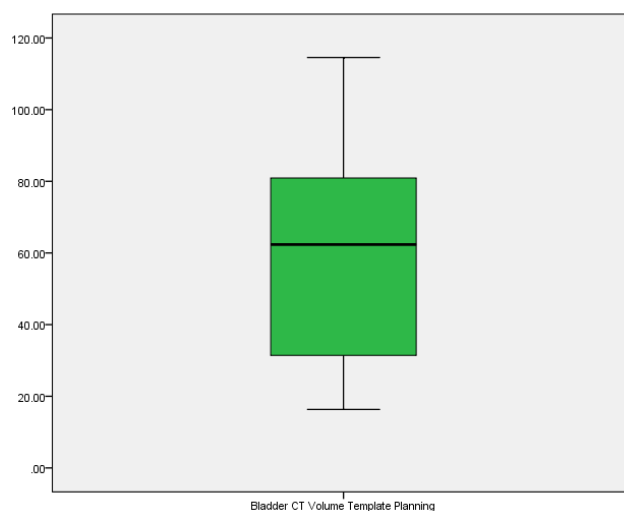


Figure 4.2: Boxplot: B CT Volume 2D

- Figure 4.3 is the Normal Q-Q plot indicating that there was normality, even though the circles did not lie exactly on the straight line curve, their distribution above and below the straight line curve normalised the distribution.

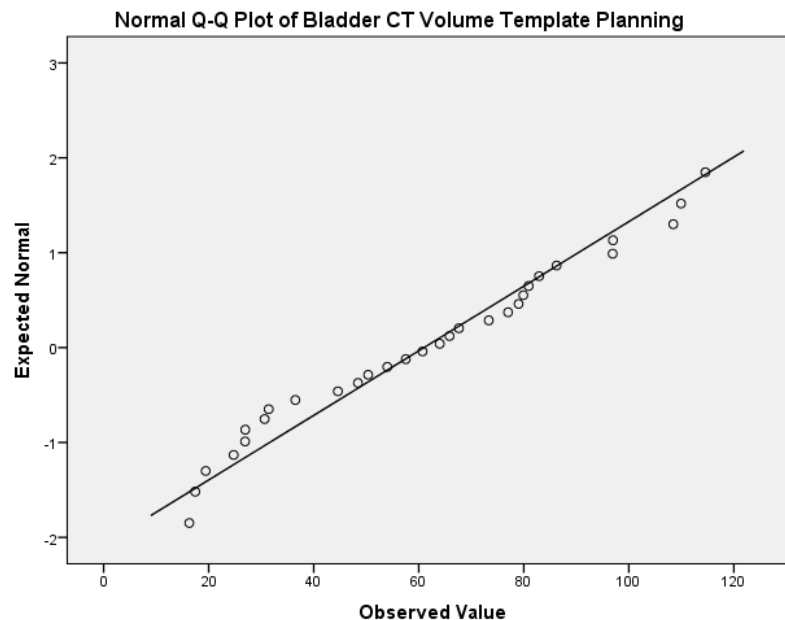


Figure 4.3: The normal Q-Q plot: B CT Volume 2D

4.2.1.2 R CT Volume 2D

- Table 4.2: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Rectum CT Volume 2D (Template) Planning	.134	30	.178

a. Lilliefors Significance Correction

p (0.178) > 0.05 therefore normality was assumed.

- The mean cc \pm 1 standard deviation of R CT volume 2D was 47.3cc \pm 18.33cc. At the 95 percent level of confidence R CT volume 2D varied between 28.97cc and 65.63cc.

- Figure 4.4 is the histogram illustrating skewness and kurtosis. Skewness = 0.456 therefore the curve was slightly skewed to the left. Kurtosis = -0.582 indicating a flattened distribution.

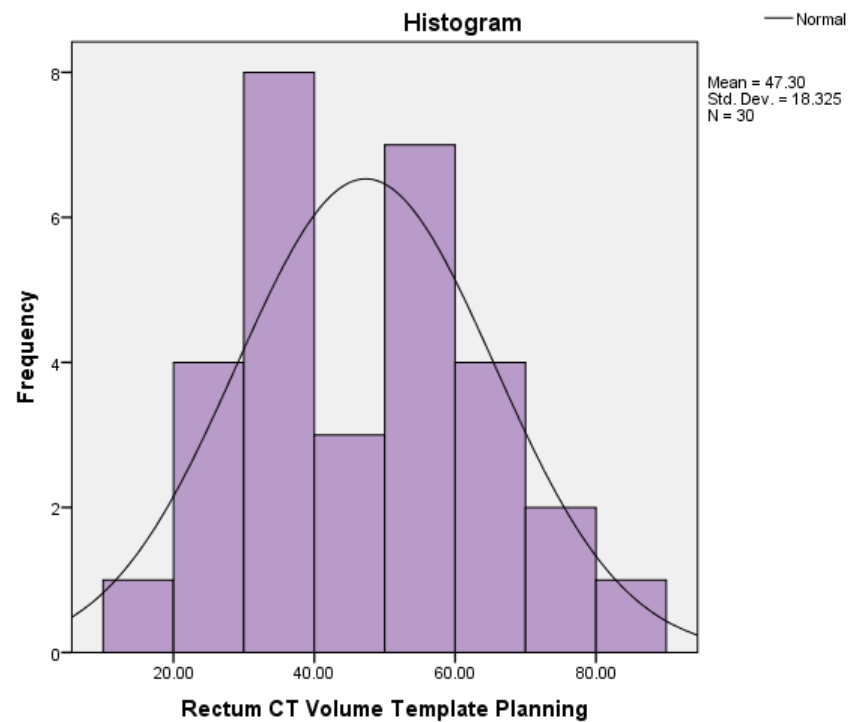


Figure 4.4: Histogram: R CT Volume 2D

- Figure 4.5 is the boxplot illustrating that there were no outliers present within the range.

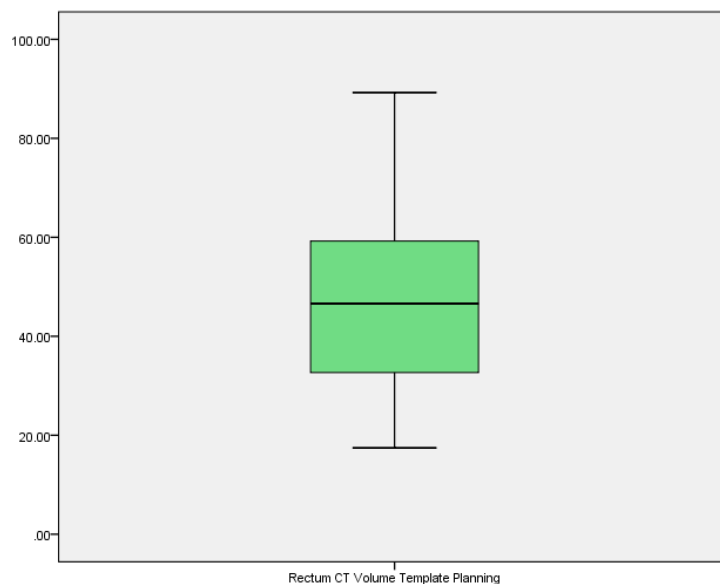


Figure 4.5: Boxplot: R CT Volume 2D

- Figure 4.6 is the Normal Q-Q plot indicating that there was normality, even though the circles did not lie exactly on the straight line curve, their distribution above and below the straight line curve normalised the distribution.

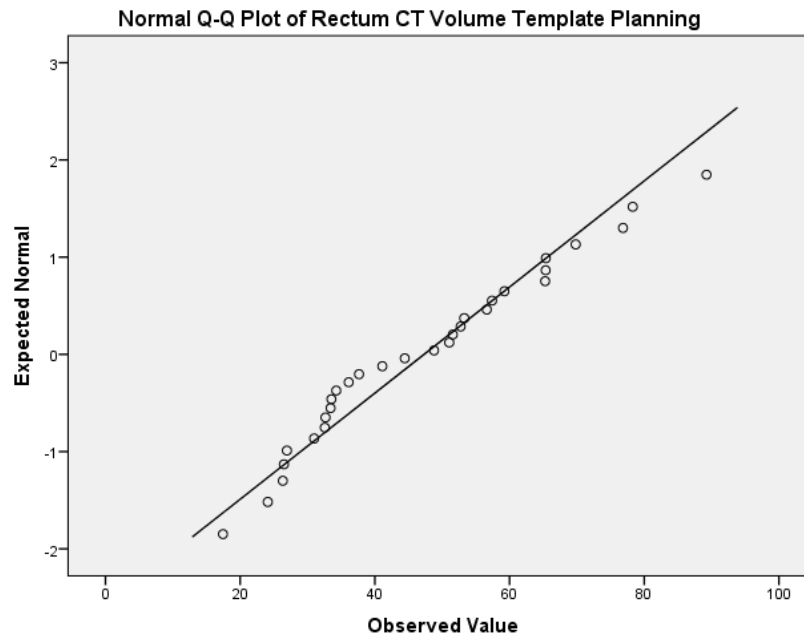


Figure 4.6: The Normal Q-Q Plot: R CT Volume 2D

4.2.1.3 B CT Volume 3D

- Table 4.3: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Bladder CT Volume 3D (CT) Planning	0.162	30	0.413

a. Lilliefors Significance Correction

$p(0.413) > 0.05$ therefore normality was assumed.

- The mean cc \pm 1 standard deviation of the B CT volume 3D was 40.09cc \pm 16.1cc. At the 95 percent level of confidence the B CT volume 3D varied between 23.99cc and 56.19cc.

- Figure 4.7 is the histogram illustrating skewness and kurtosis. Skewness = -0.545 therefore the curve was skewed to the right. Kurtosis = -0.789 indicating a flattened distribution.

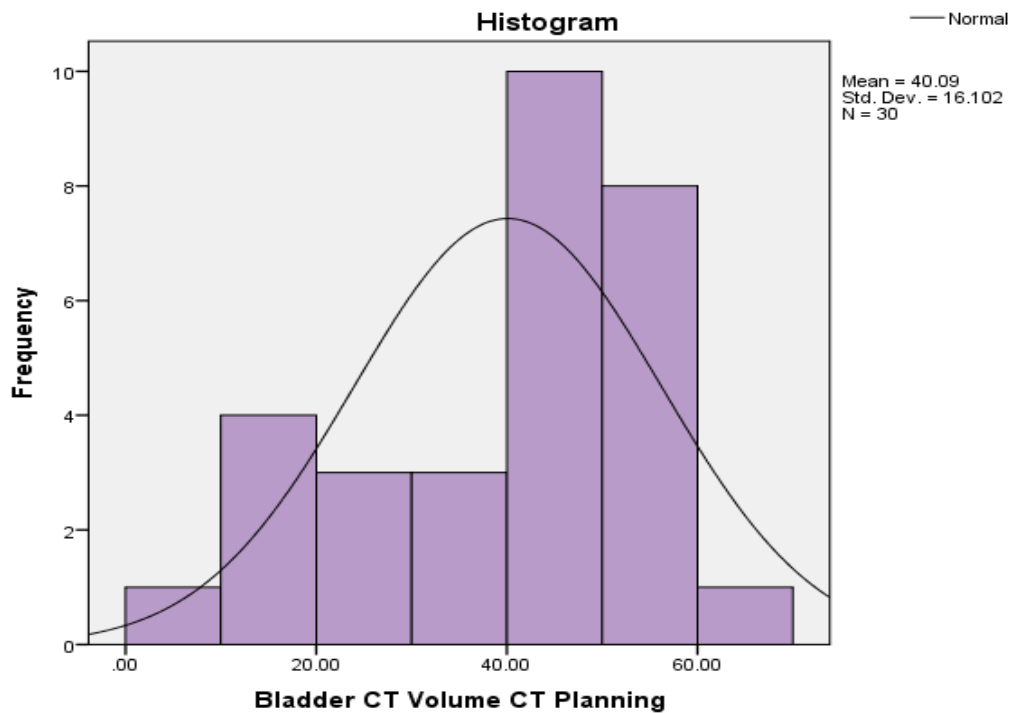


Figure 4.7: Histogram: B CT Volume 3D

- Figure 4.8 is the boxplot illustrating that there were no outliers present within the range.

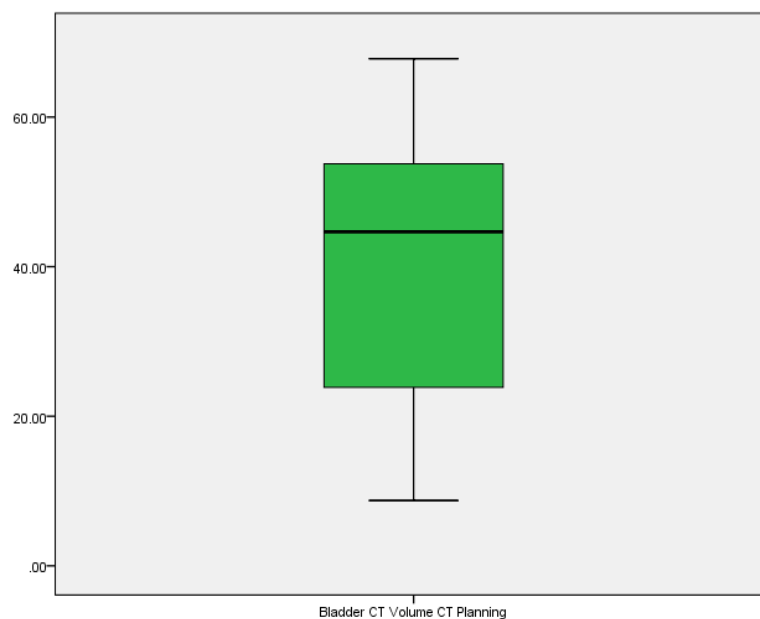


Figure 4.8: Boxplot: B CT Volume 3D

- Figure 4.9 is the Normal Q-Q plot indicating that there was normality, even though the circles did not lie exactly on the straight line curve, their distribution above and below the straight line curve normalised the distribution.

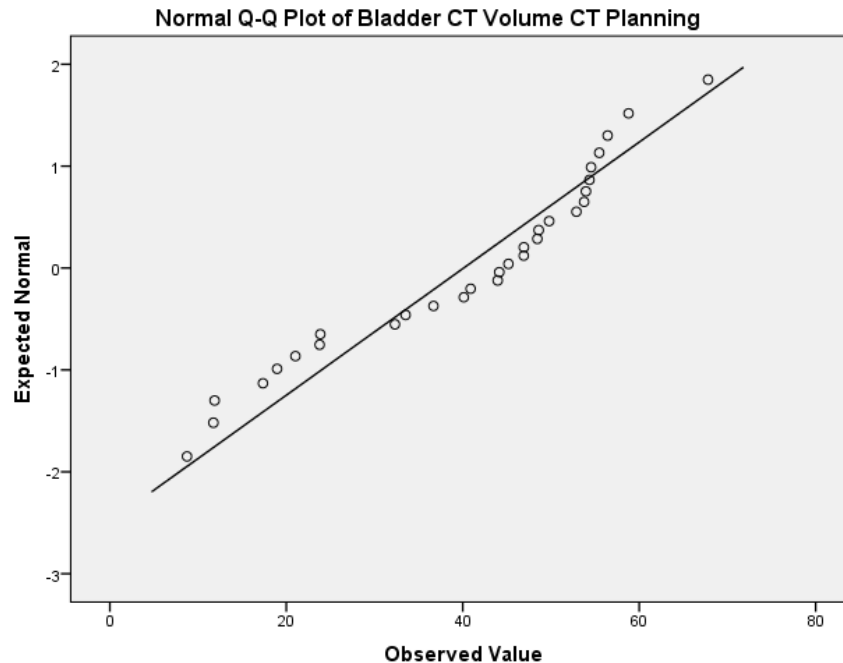


Figure 4.9: The Normal Q-Q Plot: B CT Volume 3D

4.2.1.4 R CT Volume 3D

- Table 4.4: Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Rectum CT Volume 3D (CT) Planning	.142	30	.124

a. Lilliefors Significance Correction

$p(0.124) > 0.05$ therefore normality was assumed.

- The mean cc \pm 1 standard deviation of R CT volume 3D was 38.19cc \pm 17.48cc. At the 95 percent level of confidence R CT volume 3D varied between 20.71cc and 55.67cc.

- Figure 4.10 is the histogram illustrating skewness and kurtosis. Skewness = 0.653 therefore the curve was skewed to the left. Kurtosis = 0.427 indicating a peaked distribution.

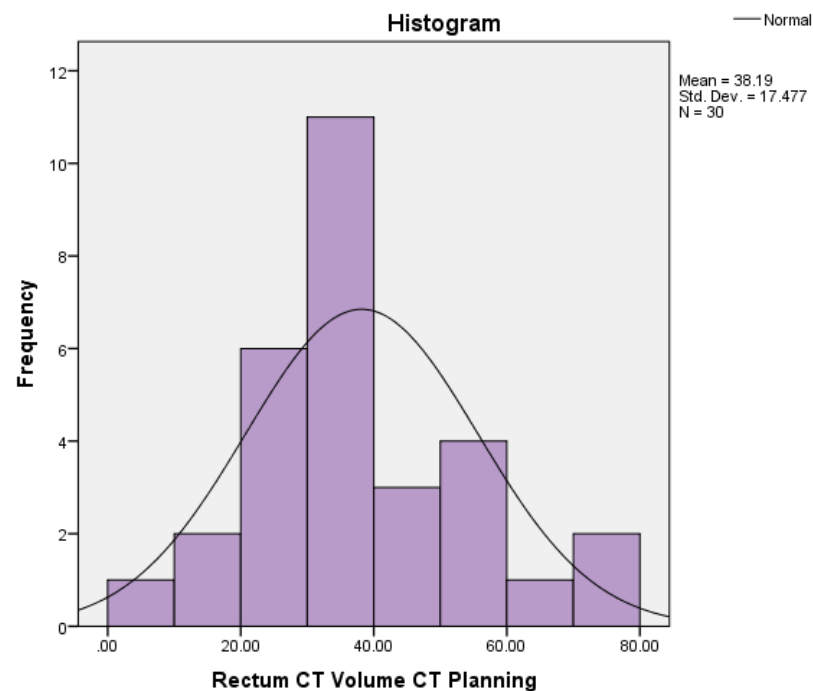


Figure 4.10: Histogram: R CT Volume 3D

- Figure 4.11 is the boxplot illustrating that there were no outliers present within the range.

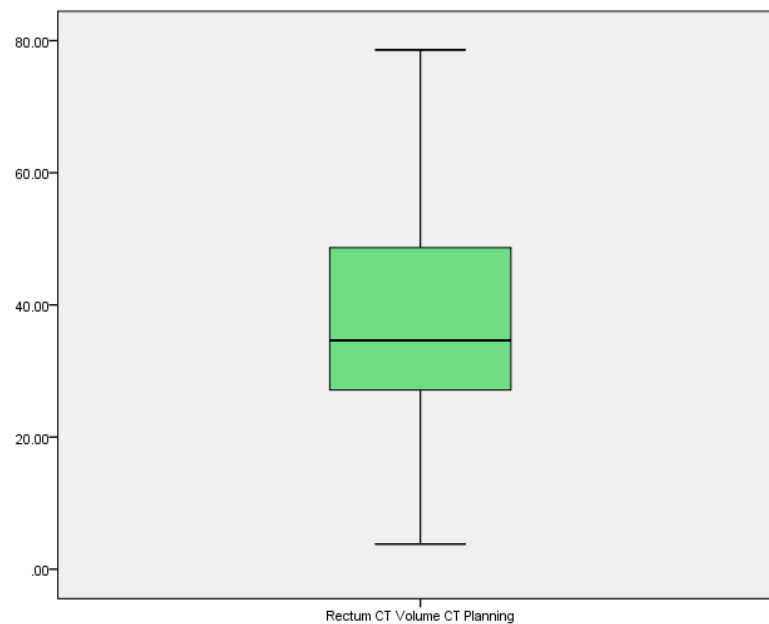


Figure 4.11: Boxplot: R CT Volume 3D

- Figure 4.12 is the Normal Q-Q plot indicating that there was normality, even though the circles did not lie exactly on the straight line curve, their deviation was not drastic.

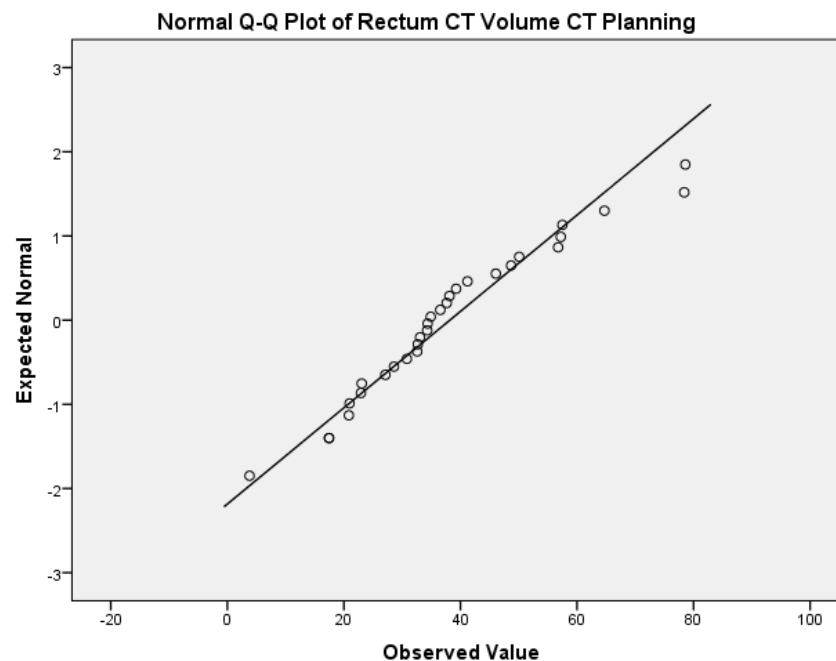


Figure 4.12: The Normal Q-Q Plot: R CT Volume 3D

4.2.2 Descriptive Statistics - Dependent Variables

4.2.2.1 B Mean 2D

- Table 4.5: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Bladder Mean Dose 2D (Template) Planning	.141	30	.132

a. Lilliefors Significance Correction

$p(0.132) > 0.05$ therefore normality was assumed.

- The mean Gy \pm 1 standard deviation of B mean 2D was 3.67Gy \pm 0.98Gy. At the 95 percent level of confidence B mean 2D varied between 2.69Gy and 4.65Gy.
- Figure 4.13 is the histogram illustrating skewness and kurtosis. Skewness = -0.029 therefore the curve was skewed to the right. Kurtosis = 0.009 indicating a slightly peaked distribution.

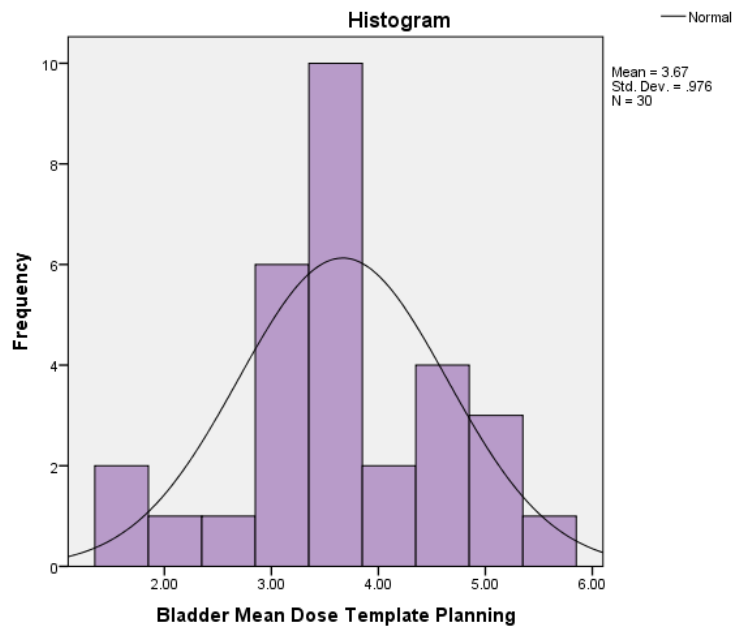


Figure 4.13: Histogram: B Mean 2D

- Figure 4.14 is the boxplot illustrating that there were no outliers present within the range.

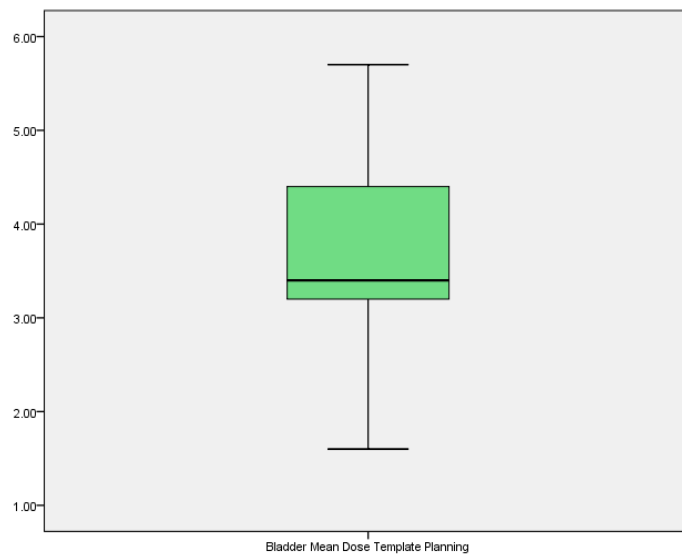


Figure 4.14: Boxplot: B Mean 2D

- Figure 4.15 is the Normal Q-Q plot indicating that there was normality, even though the circles did not lie exactly on the straight line curve, their distribution above and below the straight line curve normalised the distribution.

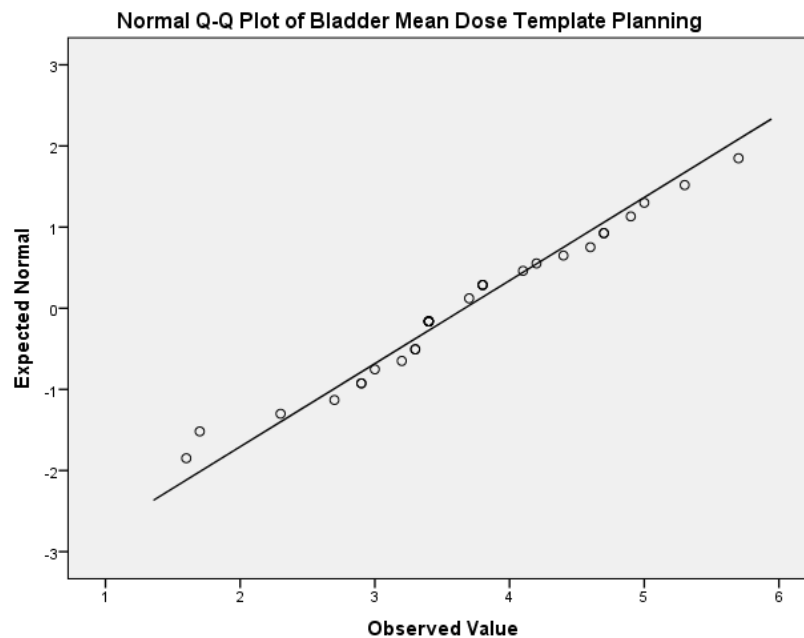


Figure 4.15: The Normal Q-Q Plot: B Mean 2D

4.2.2.2 R Mean 2D

- Table 4.6: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Rectum Mean Dose 2D (Template) Planning	.134	30	.179

a. Lilliefors Significance Correction

$p (0.179) > 0.05$ therefore normality was assumed.

- Figure 4.16 is the histogram illustrating skewness and kurtosis. Skewness = -0.545 therefore the curve was skewed to the left. Kurtosis = -0.789 indicating a flattened distribution.

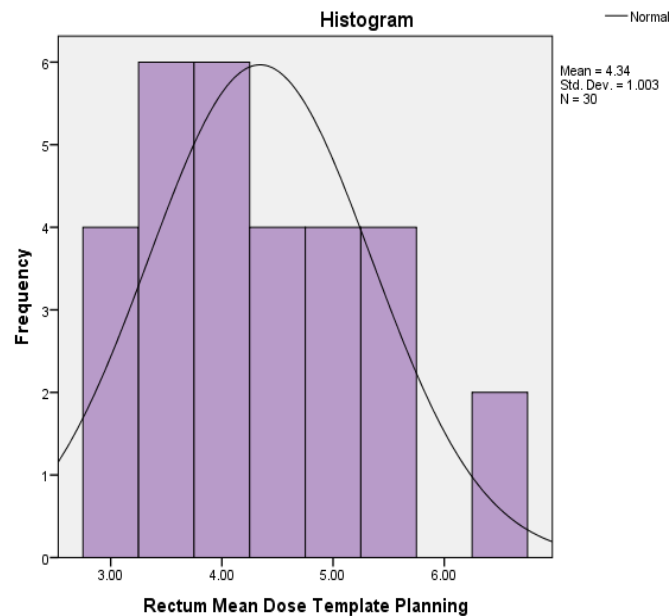


Figure 4.16: Histogram: R Mean 2D

- The mean Gy \pm 1 standard deviation of R mean 2D was 4.34Gy \pm 1Gy. At the 95 percent level of confidence R mean 2D varied between 3.34Gy and 5.34Gy.
- Figure 4.17 is the boxplot illustrating that there were no outliers present within the range.

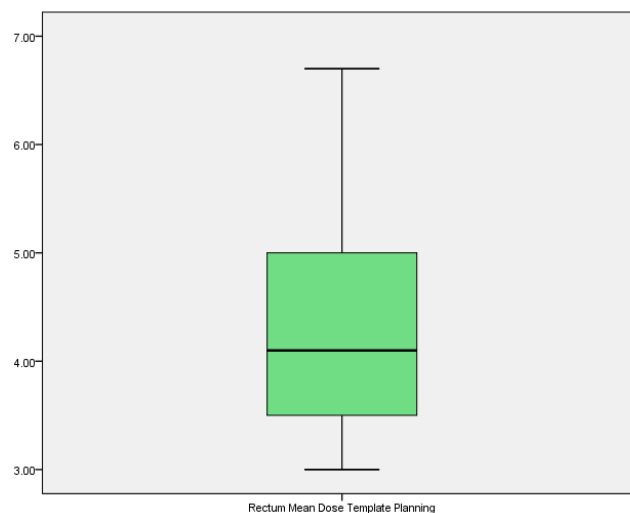


Figure 4.17: Boxplot: R Mean 2D

- Figure 4.18 is the Normal Q-Q plot indicating that there was normality, even though the circles did not lie exactly on the straight line curve, their distribution was not drastically deviated from the straight line curve.

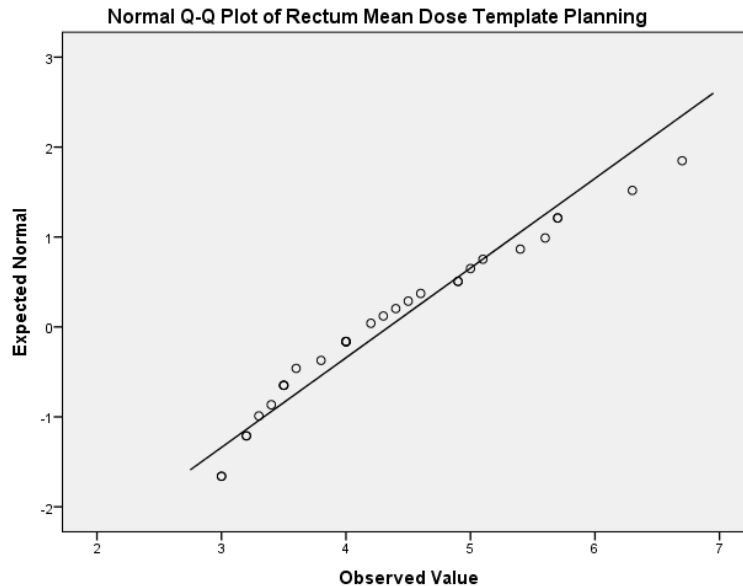


Figure 4.18: The Normal Q-Q Plot: R Mean 2D

4.2.2.3 B Mean 3D

- Table 4.7: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Bladder Mean Dose 3D (CT) Planning	.121	30	.200 [*]

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

$p(0.200) > 0.05$ therefore normality was assumed.

- Figure 4.19 is the histogram illustrating skewness and kurtosis. Skewness = 0.180 therefore the curve was skewed to the left. Kurtosis = 0.485 indicating a peaked distribution.

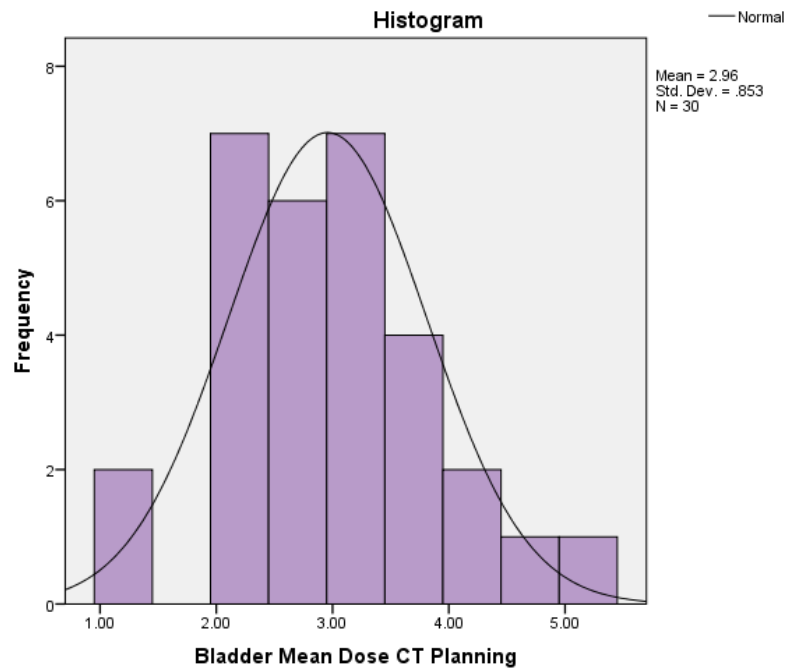


Figure 4.19: Histogram; B Mean 3D

- The mean Gy \pm 1 standard deviation of the B mean 3D was 2.96Gy \pm 0.85Gy. At the 95 percent level of confidence B mean 3D varied between 2.11Gy and 3.81Gy.
- Figure 4.20 is the boxplot illustrating that there were no outliers present within the range.

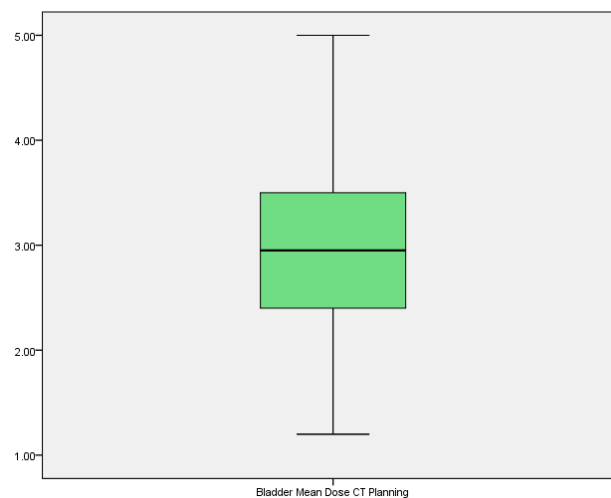


Figure 4.20: Boxplot: B Mean 3D

- Figure 4.21 is the Normal Q-Q plot indicating that there was normality, even though the circles did not lie exactly on the straight line curve, their distribution above and below the straight line curve normalised the distribution.

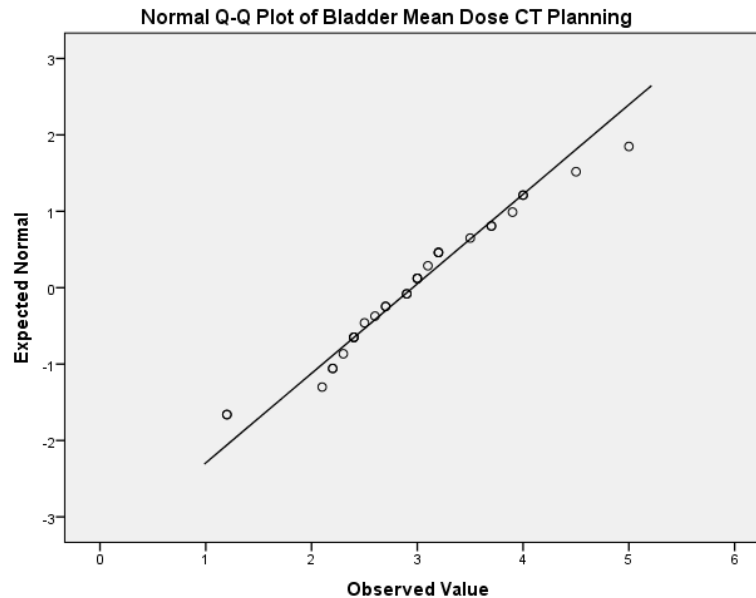


Figure 4.21: The Normal Q-Q Plot: B Mean 3D

4.2.2.4 R Mean 3D

- Table 4.8: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Rectum Mean Dose 3D (CT) Planning	.119	30	.200 [*]

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

$p(0.200) > 0.05$ therefore normality was assumed.

- Figure 4.22 is the histogram illustrating skewness and kurtosis. Skewness = 0.115 therefore the curve was skewed to the left. Kurtosis = -0.103 indicating a flattened distribution.

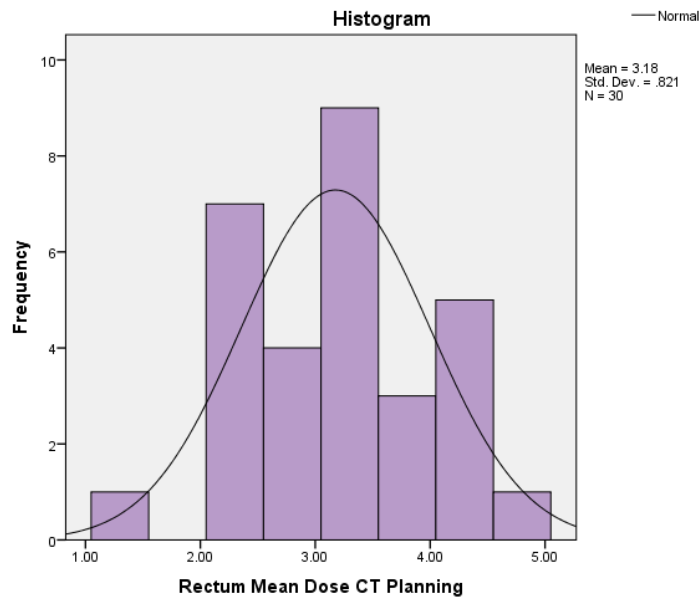


Figure 4.22: Histogram: R Mean 3D

- The mean Gy \pm 1 standard deviation of R mean 3D was 3.18Gy \pm 0.82Gy. At the 95 percent level of confidence R mean 3D varied between 2.36Gy and 4Gy.
- Figure 4.23 is the boxplot illustrating that there were no outliers present within the range.

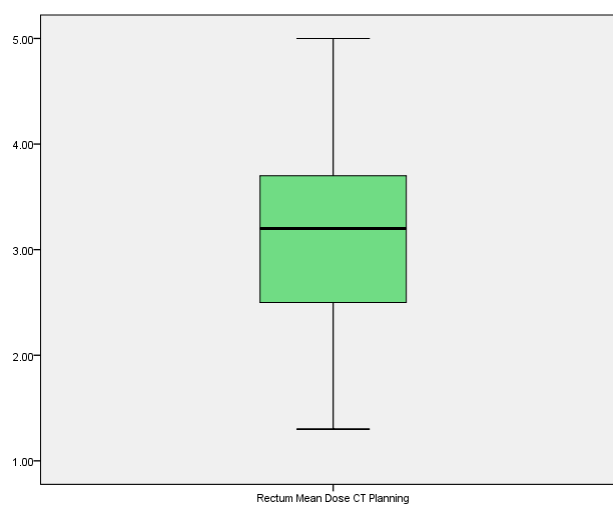


Figure 4.23: Boxplot: R Mean 3D

- Figure 4.24 is the Normal Q-Q plot indicating that there was normality, even though the circles did not lie exactly on the straight line curve, their distribution above and below the straight line curve normalised the distribution.

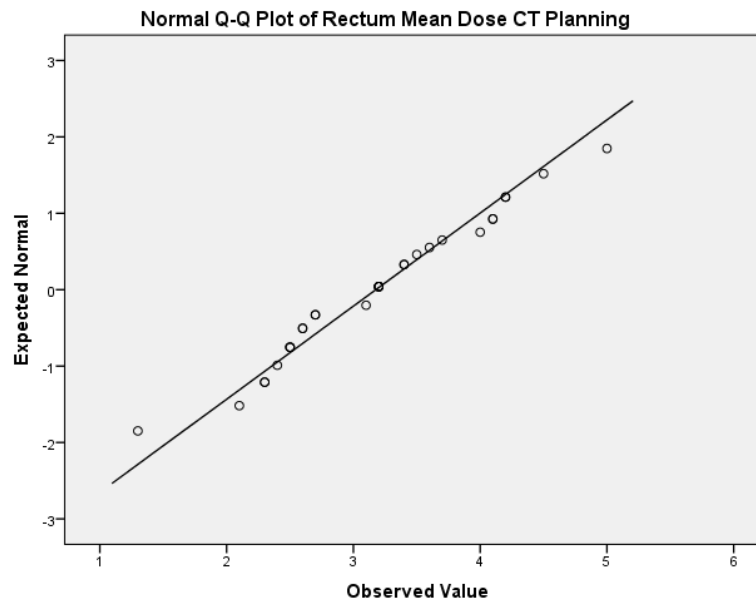


Figure 4.24: The Normal Q-Q Plot: R Mean 3D

4.2.2.5 B Max 2D

- Table 4.9: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Bladder Maximum Dose 2D (Template) Planning	.223	30	.001

a. Lilliefors Significance Correction

$p(0.001) < 0.05$ therefore normality was not assumed.

Table 4.10: The outliers were removed in order to establish normality.

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Bladder Maximum Dose 2D (Template) Planning Outliers Removed	.067	27	.200 [*]

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

p (0.200) > 0.05 therefore normality was now assumed.

- The mean Gy \pm 1 standard deviation of B max 2D was 13.47Gy \pm 6.59Gy. At the 95 percent level of confidence of B max 2D varied between 6.88Gy and 20.06Gy. The mean Gy \pm 1 standard deviation was recalculated with the three outliers removed according to the Boxplot. The mean Gy \pm 1 standard deviation then changed to 11.51Gy \pm 2.87Gy; and 95 percent level of confidence now varied between 8.64Gy and 14.38Gy.
- Figure 4.25 is the histogram illustrating skewness and kurtosis. Skewness = 0.999 therefore the curve was skewed to the left. Kurtosis = 3.898 indicating a peaked distribution.

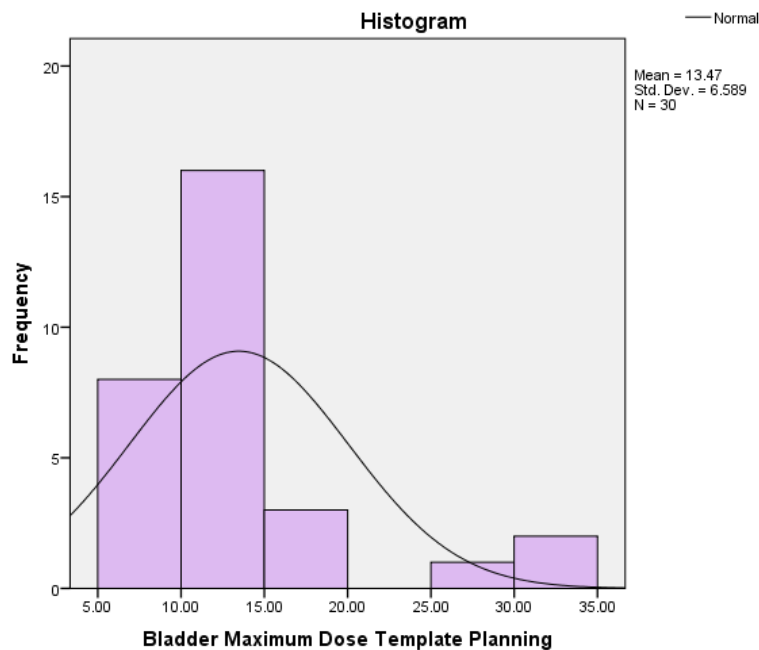


Figure 4.25: Histogram: B Max 2D (with outliers)

- Figure 4.26 is the histogram, with the outliers removed, illustrating skewness and kurtosis. Skewness = -0.144 therefore the curve was slightly skewed to the right. Kurtosis = -0.473 indicating a flattened distribution.

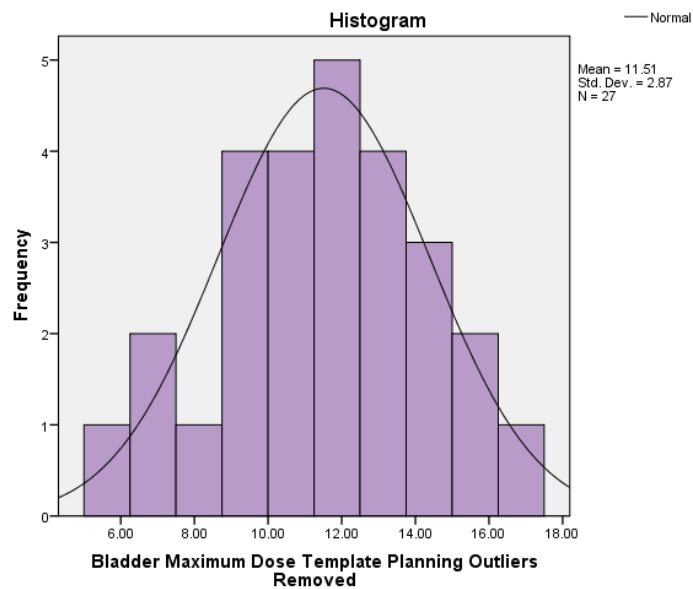


Figure 4.26: Histogram: B Max 2D (outliers removed)

- Figure 4.27 is the boxplot illustrating that there were three outliers present within the range. The outlier shown with the circle was a minor outlier and was ignored; however the two outliers shown with a star could not be ignored and was therefore included in the analysis.

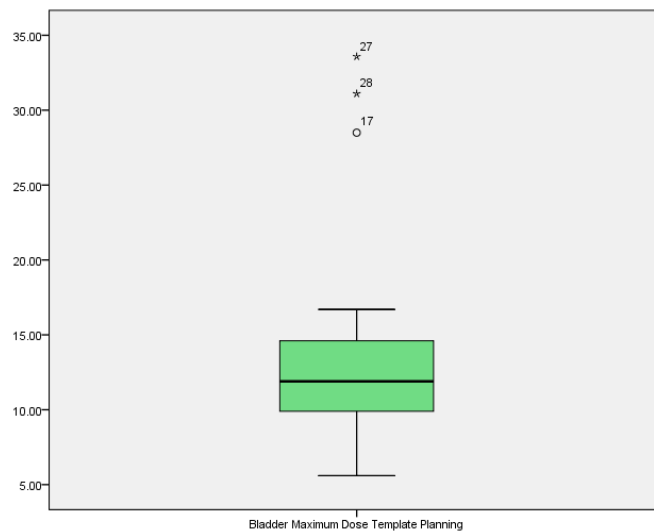


Figure 4.27: Boxplot: B Max 2D (with outliers)

- Figure 4.28 is the boxplot, with the outliers removed, illustrating that there were no outliers present within the range.

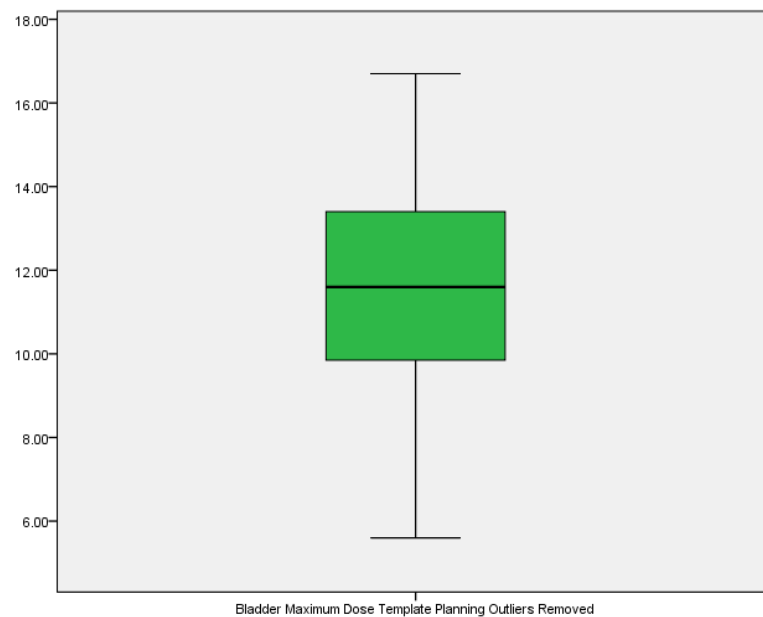


Figure 4.28: Boxplot: B Max 2D (outliers removed)

- Figure 4.29 is the Normal Q-Q plot indicates that there was an absence of normality. The three outliers could be seen as they were located at a distance from the straight line curve.

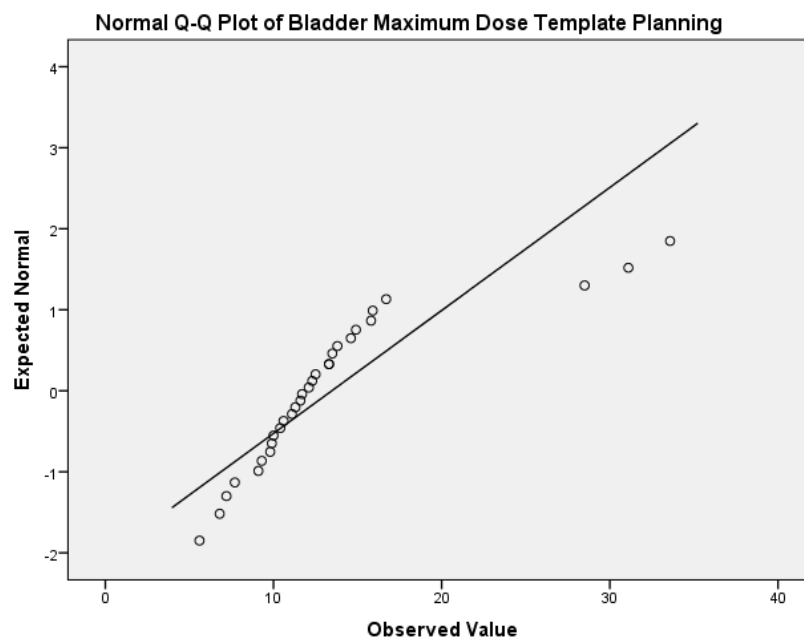


Figure 4.29: The Normal Q-Q Plot: B Max 2D (with outliers)

- Figure 4.30 is the Normal Q-Q plot, with the outliers removed, indicating that there was normality as the circles lie along the straight line curve.

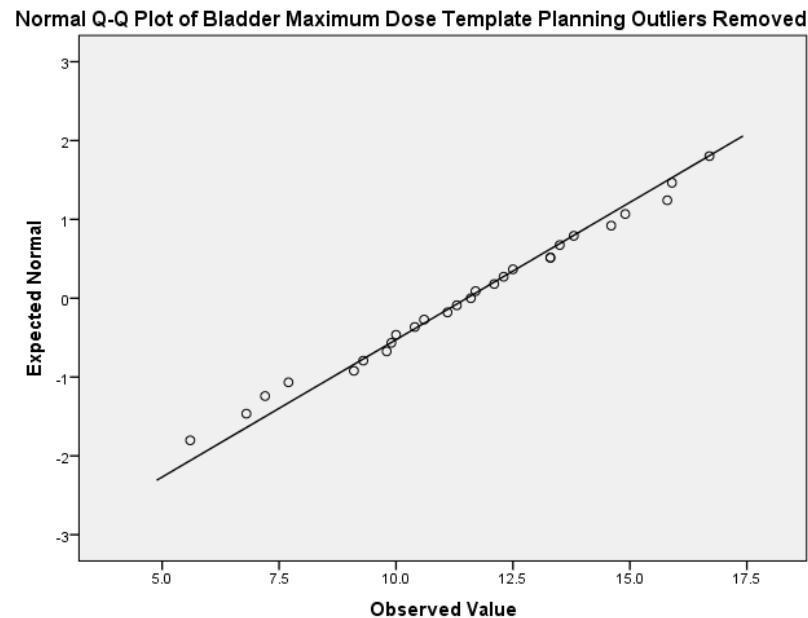


Figure 4.30: The Normal Q-Q Plot: B Max 2D (outliers removed)

4.2.2.6 R Max 2D

- Table 4.11: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Rectum Maximum Dose 2D (Template) Planning	.218	30	.001

a. Lilliefors Significance Correction

$p(0.001) < 0.05$ therefore normality was not assumed.

Table 4.12: The outliers were removed in order to establish normality.

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Rectum Maximum Dose 2D (Template) Planning Outliers Removed	.129	27	.200 [*]

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

p (0.200) > 0.05 therefore normality was now assumed.

- The mean Gy \pm 1 standard deviation of the R max 2D was 17.14Gy \pm 7.77Gy. At the 95 percent level of confidence the R max 2D varied between 9.37Gy and 24.91Gy. The mean Gy \pm 1 standard deviation was recalculated with the two outliers removed according to the Boxplot. The mean Gy \pm 1 standard deviation then changed to 14.98Gy \pm 3.84Gy; and 95 percent level of confidence now varied between 11.14Gy and 18.82Gy.
- Figure 4.31 is the histogram illustrating skewness and kurtosis. Skewness = 2.015 therefore the curve was skewed to the left. Kurtosis = 4.310 indicating a peaked distribution.

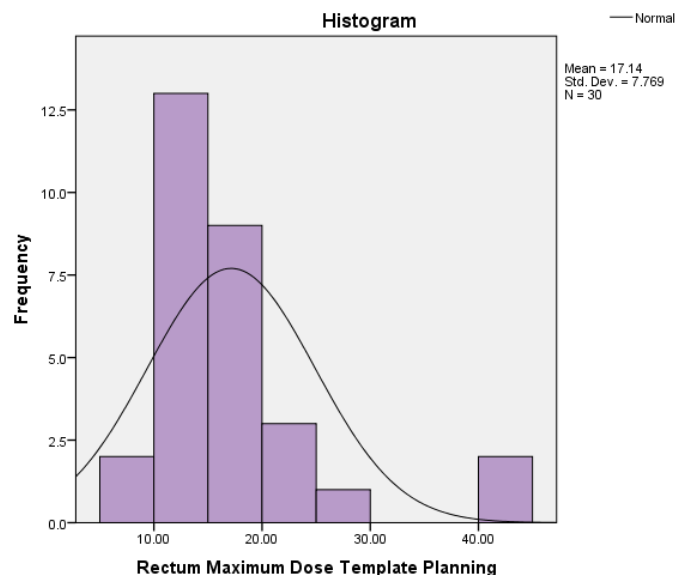


Figure 4.31: Histogram: R Max 2D (with outliers)

- Figure 4.32 is the histogram, with the outliers removed, illustrating skewness and kurtosis. Skewness = 0.437 therefore the curve was skewed to the left. Kurtosis = -0.444 indicating a flattened distribution.

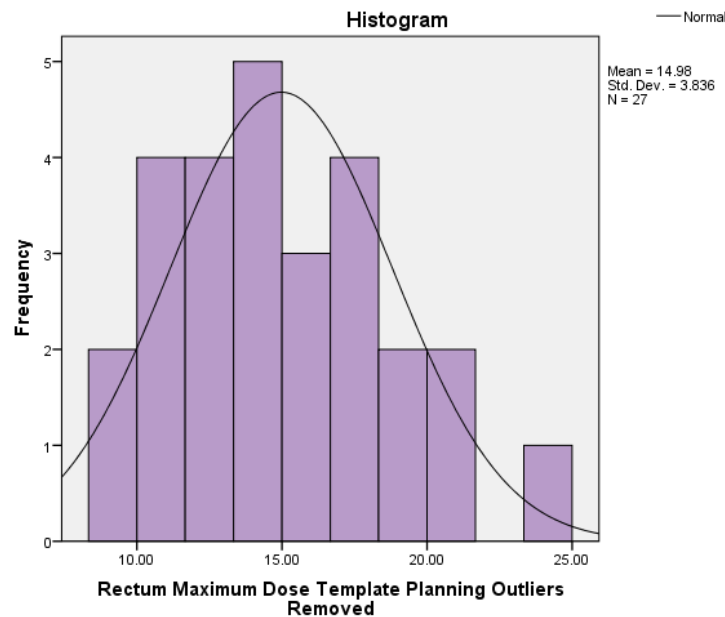


Figure 4.32: Histogram: R Max 2D (outliers removed)

- Figure 4.33 is the boxplot illustrating that there were two outliers present within the range. Both the outliers were shown with a star indicating that they were major outliers which could not be ignored.

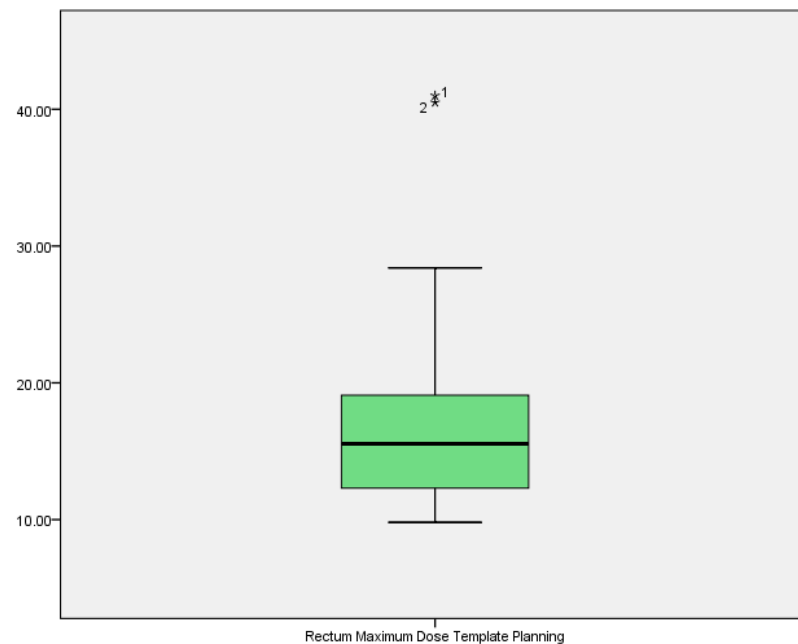


Figure 4.33: Boxplot: R Max 2D (with outliers)

- Figure 4.34 is the boxplot, with the outliers removed, illustrating that there were no outliers present within the range now.

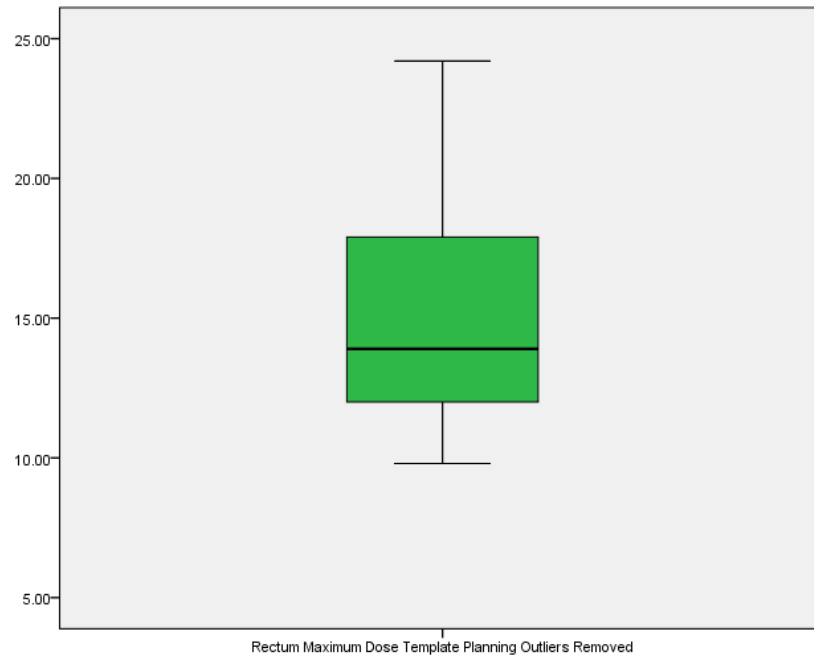


Figure 4.34: Boxplot: R Max 2D (outliers removed)

- Figure 4.35 is the Normal Q-Q plot indicating that there was an absence of normality; the circles did not lie along the straight line curve.

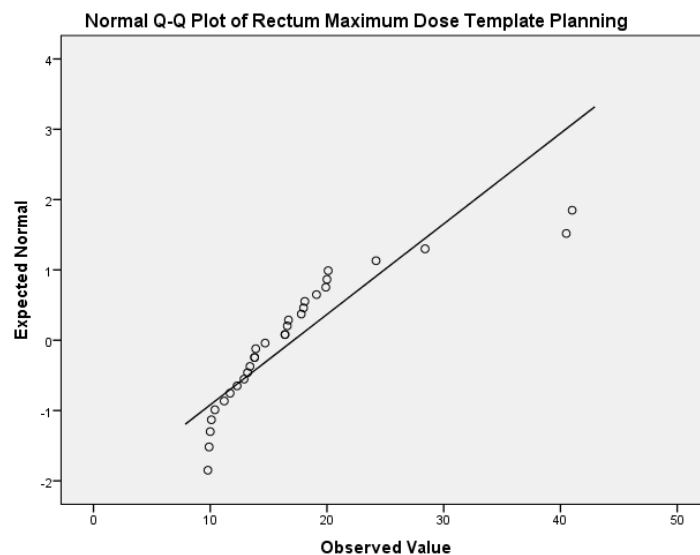


Figure 4.35: The Normal Q-Q Plot: R Max 2D (with outliers)

- Figure 4.36 is the Normal Q-Q plot, with the outliers removed, indicating that there was normality since the circles lie more or less along the straight line curve. The circles that lie above the straight line curve normalise those circles that lie below the straight line curve.

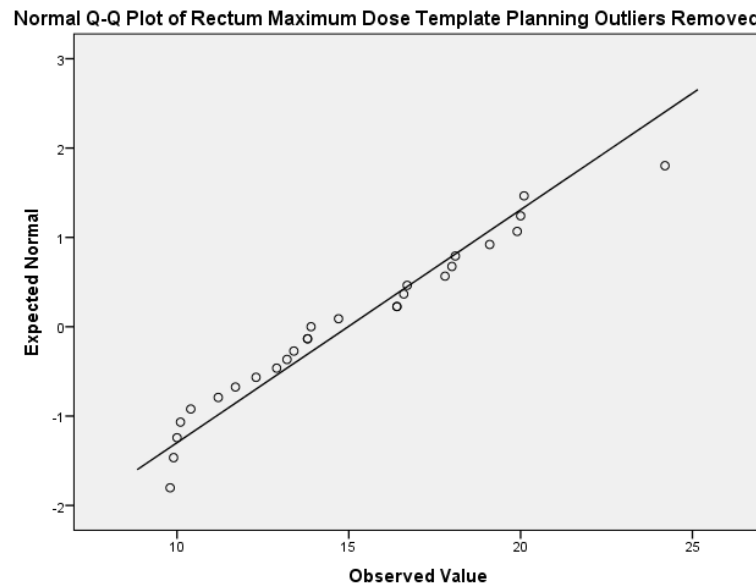


Figure 4.36: The Normal Q-Q Plot: R Max 2D (outliers removed)

4.2.2.7 B Max 3D

- Table 4.13: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Bladder Maximum Dose 3D (CT) Planning	.145	30	.109

a. Lilliefors Significance Correction

$p(0.109) > 0.05$ therefore normality was assumed.

- Figure 4.37 is the histogram illustrating skewness and kurtosis. Skewness = 1.368 therefore the curve was skewed to the left. Kurtosis = 3.088 indicating a peaked distribution.

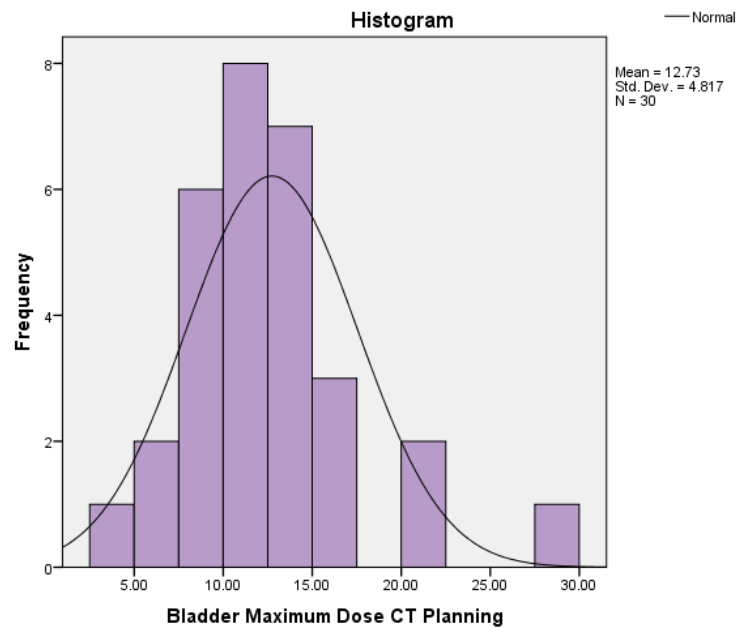


Figure 4.37: Histogram: B Max 3D

- The mean Gy \pm 1 standard deviation of B max 3D was 12.73Gy \pm 4.82Gy. At the 95 percent level of confidence B max 3D varied between 7.91Gy and 17.55Gy.
- Figure 4.38 is the boxplot illustrating that there was an outlier present within the range. This was a minor outlier as it was denoted with a circle and could be ignored.

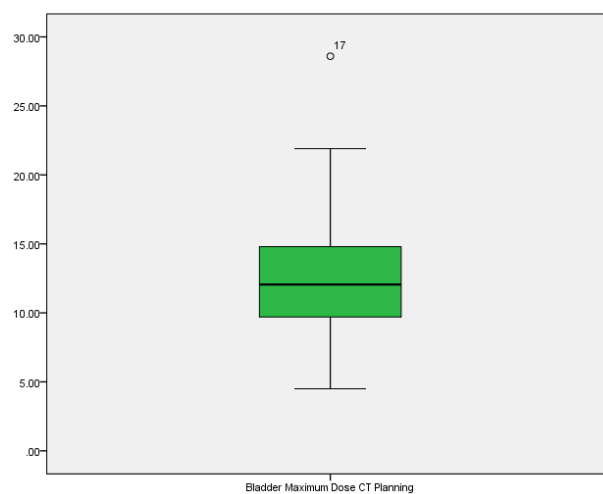


Figure 4.38: Boxplot: B Max 3D

- Figure 4.39 is the Normal Q-Q plot indicating normality as the circles lay more or less on the straight line curve, however there was a circle that lay away from the straight line curve and it accounted for the outlier as indicated by the boxplot.

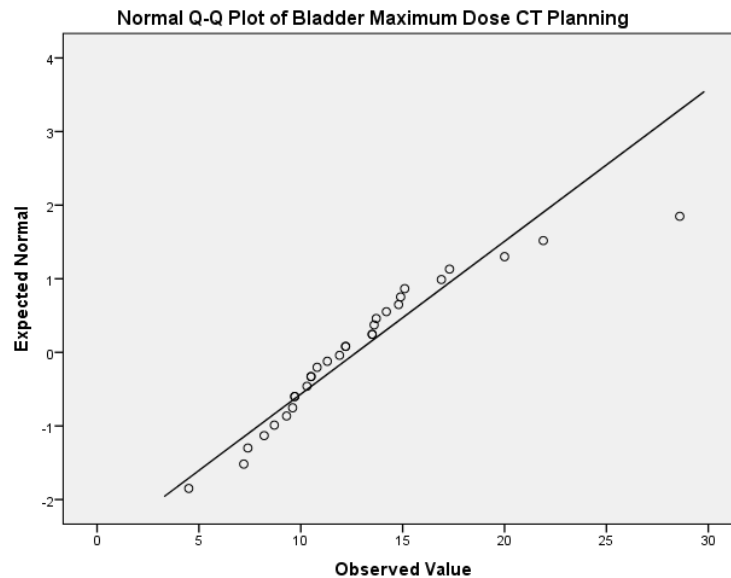


Figure 4.39: The Normal Q-Q Plot: B Max 3D

4.2.2.8 R Max 3D

- Table 4.14: The Kolmogorov-Smirnov statistic with a Lilliefors significance level

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Rectum Maximum Dose 3D (CT) Planning	.257	30	.000

a. Lilliefors Significance Correction

$p(0) < 0.05$ therefore normality was not assumed.

Table 4.15: The outliers were removed in order to establish normality.

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
Rectum Maximum Dose 3D (CT) Planning Outliers Removed	.118	27	.200 [*]

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

p (0.200) > 0.05 therefore normality was now assumed.

- The mean Gy \pm 1 standard deviation of the R max 3D was 12.6Gy \pm 7.71Gy. At the 95 percent level of confidence the R max 3D varied between 4.89Gy and 20.31Gy. The mean Gy \pm 1 standard deviation was recalculated with the three outliers removed according to the Boxplot. The mean Gy \pm 1 standard deviation then changed to 10.32Gy \pm 2.7Gy; and 95 percent level of confidence now varied between 7.62Gy and 12.59Gy.
- Figure 4.40 is the histogram illustrating skewness and kurtosis. Skewness = 2.565 therefore the curve was skewed to the left. Kurtosis = 6.655 indicating a peaked distribution.

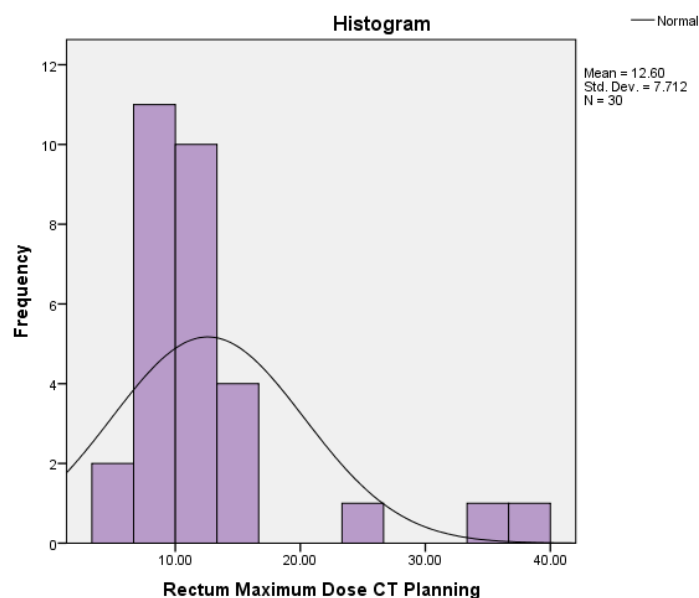


Figure 4.40: Histogram: R Max 3D (with outliers)

- Figure 4.41 is the histogram, with the outliers removed, illustrating skewness and kurtosis. Skewness = 0.195 therefore curve was skewed to the left. Kurtosis = -0.061 indicating a flattened distribution.

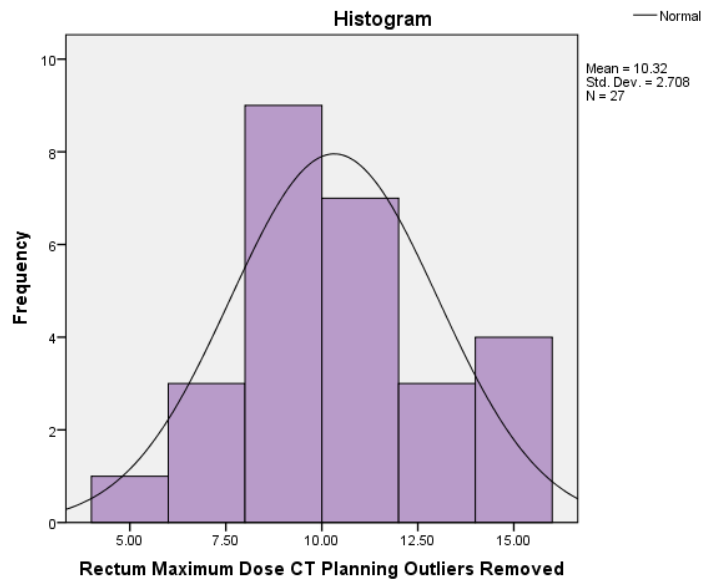


Figure 4.41: Histogram: R Max 3D (outliers removed)

- Figure 4.42 is the boxplot illustrating that there were three outliers present within the range. One outlier was considered minor as it was shown with a circle and the other two were major outliers as they were shown with a star.

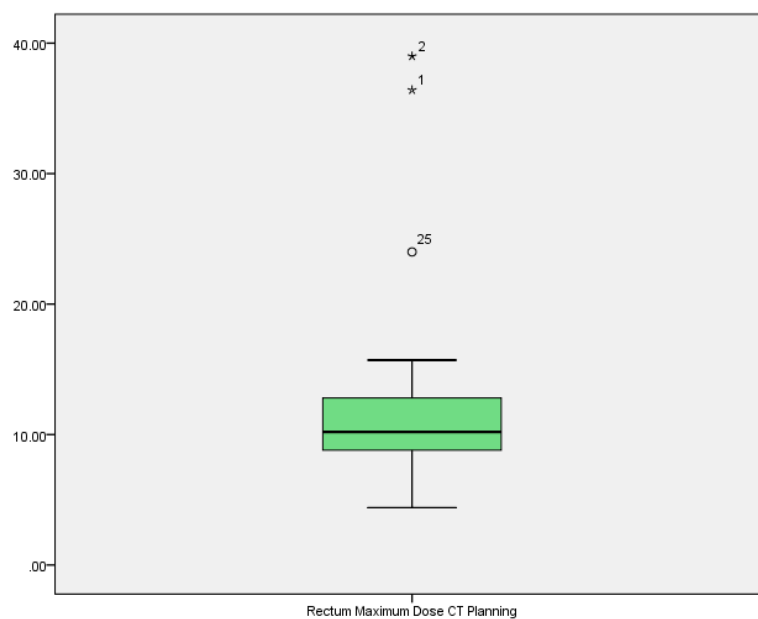


Figure 4.42: Boxplot: R Max 3D (with outliers)

- Figure 4.43 is the boxplot illustrating that there were no outliers present now.

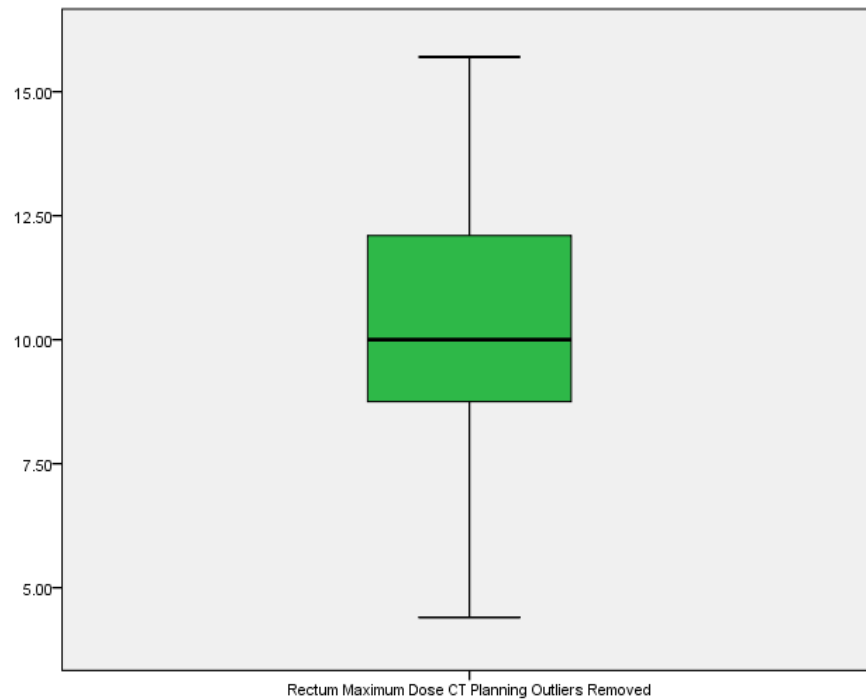


Figure 4.43: boxplot: R Max 3D (outliers removed)

- Figure 4.44 is the Normal Q-Q plot indicating that there was an absence of normality as the circles did not lie along the straight line curve.

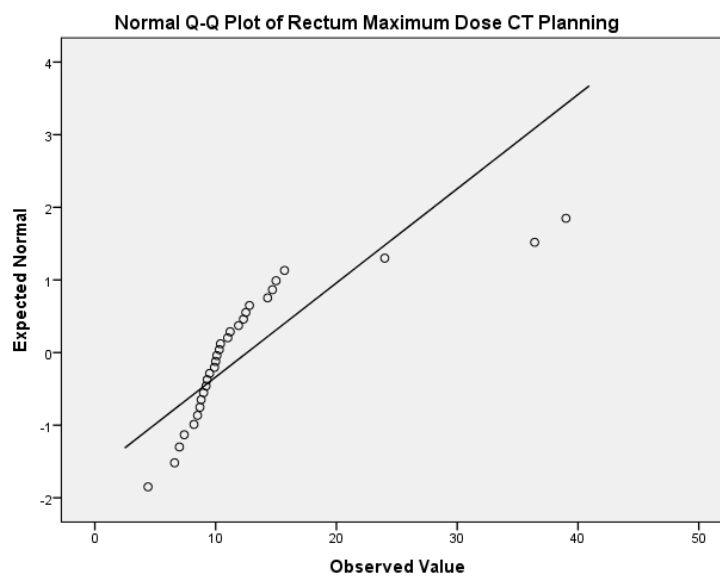


Figure 4.44: The Normal Q-Q Plot: R Max 3D (with outliers)

- Figure 4.5 is the Normal Q-Q plot, with the outliers removed, indicating that there was normality as the circles lay along the straight line curve.

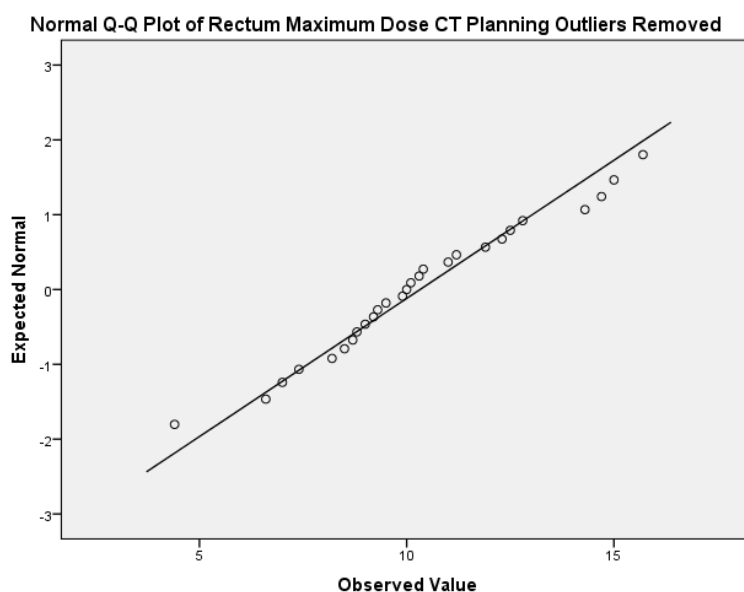


Figure 4.45: The Normal Q-Q Plot: R Max 3D (outliers removed)

4.3 Inferential Statistics

The Pearson product-moment correlation coefficient was used for describing the relationship between the dependent variables. The paired sample T-Test was used to determine if there was a relationship between the independent variables and the dependent variables.

4.3.1 Procedure 1

Research Question

Is there a significant relationship between the mean dose obtained for the bladder from 2D HDR Brachytherapy planning using computer generated templates and the mean dose obtained for the bladder from 3D HDR Brachytherapy planning using Computer Tomography scans?

Test used

Pearson-product-moment correlation

Sample

N = 30

Null hypothesis

The bladder dose obtained from 2D HDR Brachytherapy planning using computer generated templates is the same as that obtained from 3D HDR Brachytherapy planning using Computer Tomography scans.

Assumption testing

- Related pairs – data were collected from related pairs
- Scale of measurement – data was interval in nature
- Normality – Scores for each variable were normally distributed
- Linearity – the relationship between the two variables were linear
- Homoscedasticity – scores clustered uniformly around the regression line

Decision rule

$p < 0.05$ indicates statistical significance

Decision

$p = 0$ ($r = 0.834$, $p < 0.05$). The significance level indicates that $p < 0.05$ and thus was significant. A significant relationship did exist between B Mean 2D and B Mean 3D indicating that there was a significant relationship between the mean dose obtained for the bladder from 2D HDR Brachytherapy planning using computer generated templates and the mean dose obtained for the bladder from 3D HDR Brachytherapy planning using Computer Tomography scans, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that 2D HDR Brachytherapy planning

using computer generated templates yields higher doses to the bladder than 3D HDR Brachytherapy planning using Computer Tomography scans.

4.3.2 Procedure 2

Research Question

Is there a significant relationship between the mean dose obtained for the rectum from 2D HDR Brachytherapy planning using computer generated templates and the mean dose obtained for the rectum from 3D HDR Brachytherapy planning using Computer Tomography scans?

Test used

Pearson-product-moment correlation

Sample

N = 30

Null hypothesis

The rectum mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates is the same as that obtained from 3D HDR Brachytherapy planning using Computer Tomography scans.

Assumption testing

- Related pairs – data was collected from related pairs
- Scale of measurement – data was interval in nature
- Normality – Scores for each variable were normally distributed
- Linearity – the relationship between the two variables were linear
- Homoscedasticity – scores clustered uniformly around the regression line

Decision rule

$p < 0.05$ indicates statistical significance

Decision

$p = 0$ ($r = 0.708$, $p < 0.05$). The significance level indicates that $p < 0.05$ and thus a significant relationship did exist between R Mean 2D and R Mean 3D. There was a significant relationship between the mean dose obtained for the rectum from 2D HDR Brachytherapy planning using computer generated templates and the mean dose obtained for the rectum from 3D HDR Brachytherapy planning using Computer Tomography scans, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that 2D HDR Brachytherapy planning using computer generated templates yields higher doses to the rectum than 3D HDR Brachytherapy planning using Computer Tomography scans.

4.3.3 Procedure 3**Research Question**

Is there a significant relationship between the maximum dose obtained for the bladder from 2D HDR Brachytherapy planning using computer generated templates and the maximum dose obtained for the bladder from 3D HDR Brachytherapy planning using Computer Tomography scans?

Test used

Pearson-product-moment correlation

Sample

$N = 26$ (four outliers were removed)

Null hypothesis

The maximum bladder dose obtained from 2D HDR Brachytherapy planning using computer generated templates is the same as that obtained from 3D HDR Brachytherapy planning using Computer Tomography scans.

Assumption testing

- Related pairs – data was collected from related pairs
- Scale of measurement – data was interval in nature
- Normality – Scores for each variable were normally distributed
- Linearity – the relationship between the two variables were linear
- Homoscedasticity – scores clustered uniformly around the regression line

Decision rule

$p < 0.05$ indicates statistical significance

Decision

$p = 0$ ($r = 0.689$, $p < 0.05$). The significance level indicates that $p < 0.05$ and thus was significant. A significant relationship did exist between B Max 2D and B Max 3D. There was a significant relationship between the maximum dose obtained for the bladder from 2D HDR Brachytherapy planning using computer generated templates and the maximum dose obtained for the bladder from 3D HDR Brachytherapy planning using Computer Tomography scans, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that 2D HDR Brachytherapy using computer generated templates yields higher bladder maximum doses than 3D HDR Brachytherapy planning using Computer Tomography scans.

4.3.4 Procedure 4

Research Question

Is there a significant relationship between the maximum dose obtained for the rectum from 2D HDR Brachytherapy planning using computer generated templates and the maximum dose obtained for the rectum from 3D HDR Brachytherapy planning using Computer Tomography scans?

Test used

Pearson-product-moment correlation

Sample

N = 26 (four outliers removed)

Null hypothesis

The rectum maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates is the same as the rectum maximum doses obtained from 3D HDR Brachytherapy planning using Computer tomography scans.

Assumption testing

- Related pairs – data was collected from related pairs
- Scale of measurement – data was interval in nature
- Normality – Scores for each variable were normally distributed
- Linearity – the relationship between the two variables were linear
- Homoscedasticity – scores clustered uniformly around the regression line

Decision rule

$p < 0.05$ indicates statistical significance

Decision

$p = 0.121$ ($r = 0.312$, $p < 0.05$). The significance level indicates that $p > 0.05$ and thus was not significant. A significant relationship did not exist between R Max 2D and R Max 3D. There was an insignificant relationship between the maximum dose obtained for the rectum from 2D HDR Brachytherapy planning using computer generated templates and the maximum dose obtained for the rectum from 3D HDR Brachytherapy planning using Computer Tomography scans, therefore the null hypothesis was accepted that the rectum maximum dose obtained from 2D HDR Brachytherapy planning was the same as that obtained from 3D HDR Brachytherapy planning using Computer Tomography scans.

4.3.5 Procedure 5

Research Question

Is there a significant relationship between the bladder CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and bladder mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates?

Test used

Paired sample t-test

Sample

$N = 30$

Null hypothesis

As the bladder CT volume 2D fluctuates, the bladder mean dose 2D remains the same.

Assumption testing

- The data were at the interval level of measurement.
- The scores have been randomly sampled from the population of interest.
- The scores were normally distributed

Decision rule

$p < 0.05$ indicates statistical significance

Decision

The t-value with 29 df was -10.74, $p = 0$. The two-tail significance indicates that $p < 0.05$ and thus was significant. The bladder CT volume 2D did have a significant relationship with B Mean 2D. There was a significant relationship between the bladder CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and bladder mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that the bladder mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates fluctuates as the bladder CT volume from 2D HDR Brachytherapy planning using computer generated templates fluctuates.

4.3.6 Procedure 6

Research Question

Is there a significant relationship between the rectum CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and the rectum mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates?

Test used

Paired sample t-test

Sample

N = 30

Null hypothesis

As rectum CT volume 2D fluctuates, the rectum mean dose 2D remains the same.

Assumption testing

- The data were at the interval level of measurement.
- The scores have been randomly sampled from the population of interest.
- The scores were normally distributed

Decision rule

$p < 0.05$ indicates statistical significance

Decision

The t-value with 29 df was -12.72, $p = 0$. The two-tail significance indicates that $p < 0.05$ and thus was significant. The rectum CT volume 2D did have a significant relationship with R Mean 2D. There was a significant relationship between the rectum CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and the rectum mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that the rectum mean dose obtained from 2D HDR Brachytherapy planning using computer generated templates fluctuates as the rectum CT volume from 2D HDR Brachytherapy planning using computer generated templates fluctuates.

4.3.7 Procedure 7

Research Question

Is there a significant relationship between the bladder CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the bladder mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans?

Test used

Paired sample t-test

Sample

N = 30

Null hypothesis

As the bladder CT volume 3D fluctuates, B Mean 3D remains unchanged.

Assumption testing

- The data were at the interval level of measurement.
- The scores have been randomly sampled from the population of interest.
- The scores were normally distributed

Decision rule

$p < 0.05$ indicates statistical significance

Decision

The t-value with 29 df was -12.82, $p = 0$. The two-tail significance indicates that $p < 0.05$ and thus was significant. The bladder CT volume 3D did have a significant relationship with B Mean 3D. There was a significant relationship between the bladder CT volume obtained from 3D HDR Brachytherapy

planning using Computer Tomography scans and the bladder mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that the bladder mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans fluctuates as the bladder CT volume from 3D HDR Brachytherapy planning using Computer tomography scans fluctuates.

4.3.8 Procedure 8

Research Question

Is there a significant influence between the rectum CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the rectum mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans?

Test used

Paired sample t-test

Sample

N = 30

Null hypothesis

As the rectum CT volume 3D fluctuates, R Mean 3D remains unchanged.

Assumption testing

- The data were at the interval level of measurement.
- The scores have been randomly sampled from the population of interest.
- The scores were normally distributed

Decision rule

$p < 0.05$ indicates statistical significance

Decision

The t-value with 29 df was -11.16, $p = 0$. The two-tail significance indicates that $p < 0.05$ and thus was significant. The rectum CT volume 3D did have a significant relationship with R Mean 3D. There was a significant relationship between the rectum CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the rectum mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that the rectum mean dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans fluctuates as the rectum CT volume from 3D HDR Brachytherapy planning using Computer tomography scans fluctuates.

4.3.9 Procedure 9**Research Question**

Is there a significant relationship between the bladder CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and the bladder maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates?

Test used

Paired sample t-test

Sample

$N = 27$ (three outliers removed)

Null hypothesis

As the bladder CT volume 2D fluctuates, B Max 2D remains unchanged.

Assumption testing

- The data were at the interval level of measurement.
- The scores have been randomly sampled from the population of interest.
- The scores were normally distributed

Decision rule

$p < 0.05$ indicates statistical significance

Decision

The t-value with 26 df was -8.85, $p = 0$. The two-tail significance indicates that $p < 0.05$ and thus was significant. The bladder CT volume 2D did have a significant relationship with B Max 2D. There was a significant relationship between the bladder CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and bladder maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that the bladder maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates fluctuates as the bladder CT volume from 2D HDR Brachytherapy planning using computer generated templates fluctuates.

4.3.10 Procedure 10

Research Question

Is there a significant relationship between the rectum CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and rectum maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates?

Test used

Paired sample t-test

Sample

N = 27 (three outliers removed)

Null hypothesis

As rectum CT volume 2D fluctuates, the rectum maximum dose 2D remains the same.

Assumption testing

- The data were at the interval level of measurement.
- The scores have been randomly sampled from the population of interest.
- The scores were normally distributed

Decision rule

$p < 0.05$ indicates statistical significance

Decision

The t-value with 26 df was -9.18, $p = 0$. The two-tail significance indicates that $p < 0.05$ and thus was significant. The rectum CT volume 2D did have a significant relationship with R Max 2D. There was a significant relationship

between the rectum CT volume obtained from 2D HDR Brachytherapy planning using computer generated templates and the rectum maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that the rectum maximum dose obtained from 2D HDR Brachytherapy planning using computer generated templates fluctuates as the rectum CT volume from 2D HDR Brachytherapy planning using computer generated templates fluctuates.

4.3.11 Procedure 11

Research Question

Is there a significant relationship between the bladder CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the bladder maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans?

Test used

Paired sample t-test

Sample

N = 28 (two outliers removed)

Null hypothesis

As bladder CT volume 3D fluctuates, the bladder maximum dose 3D remains the same.

Assumption testing

- The data were at the interval level of measurement.
- The scores have been randomly sampled from the population of interest.

- The scores were normally distributed

Decision rule

$p < 0.05$ indicates statistical significance

Decision

The t-value with 29 df was -10.25, $p = 0$. The two-tail significance indicates that $p < 0.05$ and thus was significant. The bladder CT volume 3D did have a significant relationship with B Max 3D. There was a significant relationship between the bladder CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the bladder maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that the bladder maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans fluctuates as the bladder CT volume from 3D HDR Brachytherapy planning using Computer tomography scans fluctuates.

4.3.12 Procedure 12

Research Question

Is there a significant relationship between the rectum CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the rectum maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans?

Test used

Paired sample t-test

Sample

$N = 27$ (three outliers were removed)

Null hypothesis

As rectum CT volume 3D fluctuates, the rectum maximum dose 3D remains the same.

Assumption testing

- The data were at the interval level of measurement.
- The scores have been randomly sampled from the population of interest.
- The scores were normally distributed

Decision rule

$p < 0.05$ indicates statistical significance

Decision

The t-value with 26 df was -9.18, $p = 0$. The two-tail significance indicates that $p < 0.05$ and thus was significant. The rectum CT volume 3D did have a significant relationship with R Max 3D. There was a significant relationship between the rectum CT volume obtained from 3D HDR Brachytherapy planning using Computer Tomography scans and the rectum maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans, therefore the null hypothesis was rejected and the alternate hypothesis was accepted that the rectum maximum dose obtained from 3D HDR Brachytherapy planning using Computer Tomography scans fluctuates as the rectum CT volume from 3D HDR Brachytherapy planning using Computer tomography scans fluctuates.

CHAPTER FIVE

DISCUSSION

5.1 Introduction

The data collected were described, analysed and presented in the form of tables, graphs and text as depicted in Chapter Four. The trends and patterns depicted in the data are discussed in this chapter referring to the main aim as stated in Chapter Two.

2DBP is the abbreviation used in this chapter to represent 2D (Template) Brachytherapy planning and 3DBP is the abbreviation used in this chapter to represent 3D (Computer Tomography) Brachytherapy planning.

5.2 The Research Aim of this Study

The purpose of this study was to compare 2DBP and 3DBP in terms of dose distribution in order to accurately determine bladder and rectal doses. The main aim was to determine which planning technique yields more favourable doses to the bladder and rectum. This led to the research question of whether any significant relationship exists between:

- (a) bladder dose resulting from 2DBP and 3DBP
- (b) rectal dose resulting from 2DBP and 3DBP

5.3 Bladder Dose

5.3.1 Is there a significant relationship between the bladder CT volume and the bladder dose?

Evaluation of the mean Gy \pm 1 standard deviation of the bladder CT volume irradiated indicates that a smaller CT volume of the bladder was irradiated in 3DBP (40.09cc \pm 16.1cc) as compared to 2DBP (60.99cc \pm 29.38cc). This corresponds to a lower dose to B mean 3D due to a smaller volume (B CT volume 3D) being irradiated as compared to the dose to B mean 2D due to a larger volume (B CT volume 2D) being irradiated. The bladder receiving a lower dose is supported by the descriptive statistics for bladder mean dose. This indicates that with a plan that produces conformity, the bladder can potentially receive lower doses facilitating fewer radiation complications. Conformity was only possible, in this case, with the introduction of CT scanning (3D visualisation of the anatomy).

A statistically significant relationship did exist between the B mean 2D and B CT volume 2D ($p = 0$). The dose to the bladder was not considered for 2DBP. As B CT volume 2D increased the dose was not changed accordingly, that is, the volume of bladder being irradiated did not influence the dose received by the bladder. This correlates to the study performed by Jamema *et al* (2008) which compared CT planning with plans prepared using plain radiographs.

5.3.2 Does 2DBP or 3DBP yield more favourable bladder mean doses?

The Pearson-product-moment correlation shows a significant difference in the bladder mean doses as the p value ($p = 0$) is less than the level of significance of 0.05. This serves as evidence that a relationship does exist between B mean 2D and B mean 3D. In view of the results it is deduced that 2DBP yields higher doses to the bladder than 3DBP. The results indicate that

3DBP is a superior method of planning in order to yield better doses to the bladder in order to minimise radiation induced complications to the bladder. Similar results were obtained by Bahadur *et al* (2008) in their study that compared CT planning and plain radiograph planning methods where they concluded that CT based planning is more ‘... reliable and accurate for the delineation and calculation ...’ of the dose to the critical structures. This implies that the normal surrounding tissue may be more adequately visualised with the utilisation of CT, allowing for accuracy in terms of the calculation of dose to these tissue. This will further allow for the dose to be minimised to the normal tissue.

5.3.3 Does 2DBP or 3DBP yield more favourable bladder maximum doses?

The Pearson-product-moment correlation indicates a significant relationship between B max 2D and B max 3D ($p < 0.05$). The correlation value is positive ($p = 0$), therefore this indicates a proportional relationship. This indicates that as the bladder CT volume increases so did the doses for 2DBP and 3DBP, however 3DBP yielded a lower dose than 2DBP. This result was similar to the results achieved by Bahadur *et al* (2008) and Jamema *et al* (2008).

There is a significant difference between the mean values of the variables (B max 2D and B max 3D) as the p-value is less than the level of significance of 0.05 (that is, $p = 0$). This can be seen in Figure 5.1.

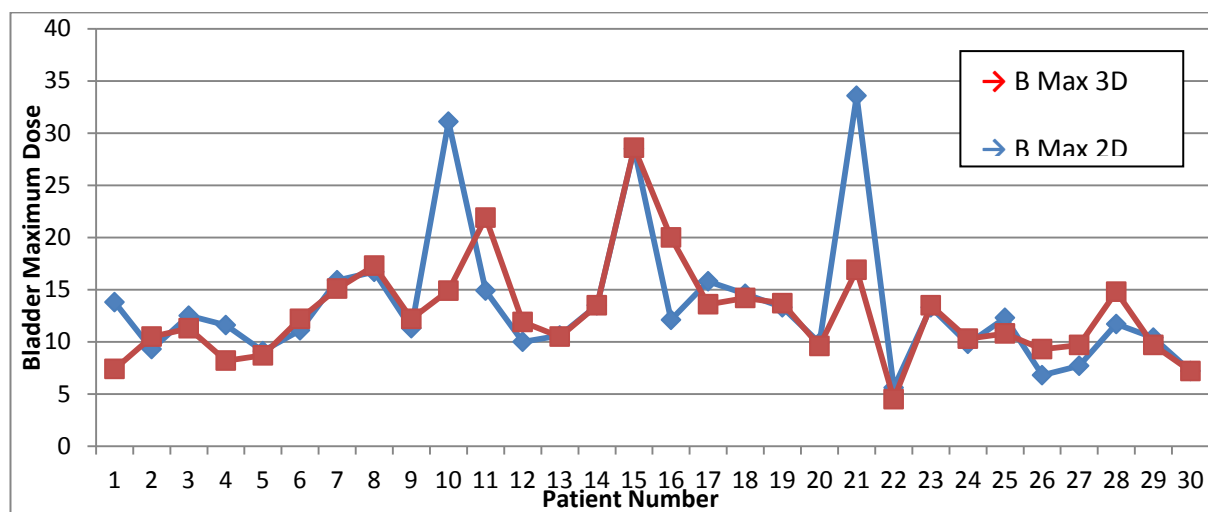


Figure 5.1: Comparison of Bladder Maximum Doses for 2DBP and 3DBP

The linear relationship graph for bladder maximum dose is plotted below. As can be seen from Figure 5.2, the best fitting straight line drawn through the curves illustrates the linear nature of the relationship.

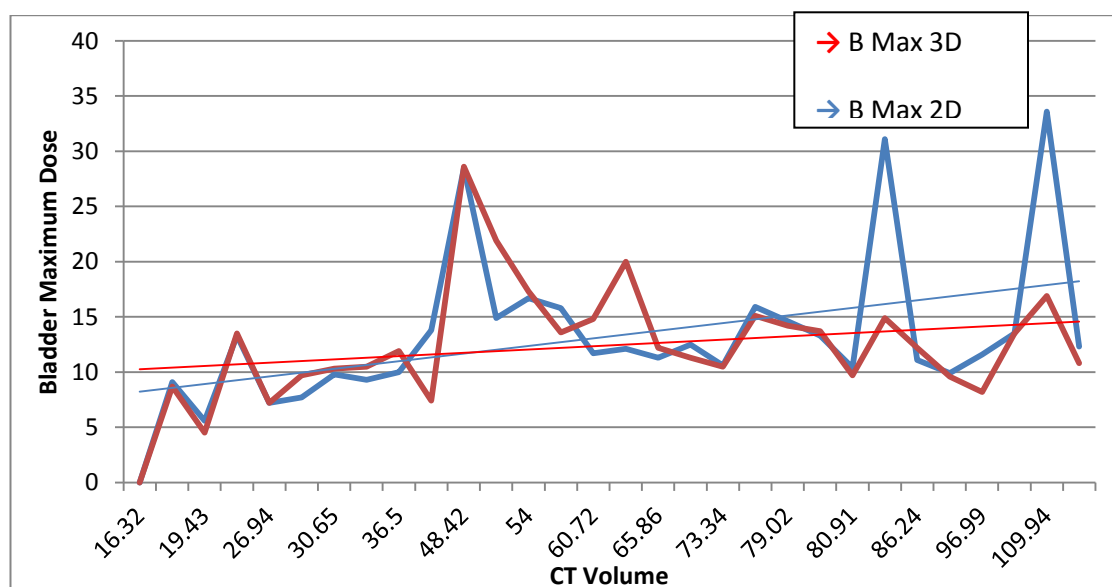


Figure 5.2: Linear Relationships between Bladder Maximum Doses for 2DBP and 3DBP

A proportional relationship for 2DBP is demonstrated in Figure 5.2. This implies that as the bladder CT volume 2D increased so did the doses for B max 2D. Therefore in terms of the maximum bladder dose, 3DBP did prove to be more efficient than 2DBP in terms of yielding lower bladder maximum doses. Figure 5.2 also illustrates that B max 3D is greater at smaller bladder CT volumes than B max 2D. This result was subject to the Oncologist advice at IALCH for 3DBP. On the advice of the Oncologist, higher bladder maximum doses were accepted for smaller bladder CT volumes. In some instances these bladder maximum doses were merely the dose to a point.

5.4 Rectal Dose

5.4.1 Is there a significant relationship between the rectum CT volume and the rectal dose?

Evaluation of the mean Gy \pm 1 standard deviation indicates that a smaller CT volume of the rectum was irradiated in 3DBP (R CT volume 3D = 38.19cc \pm 17.48cc) as compared to 2DBP (R CT volume 2D = 47.3cc \pm 18.33cc), which corresponds to a lower dose to the rectum as indicated by the descriptive statistics for R mean 2D and R mean 3D. This indicates that with a plan that has better conformity the rectum can potentially receive lower doses facilitating fewer radiation complications. In this study, conformity was improved through the introduction of CT scanning (3D visualisation of the anatomy).

A relationship did exist between the R mean 2D and R CT volume 2D; however, this relation was proven to be statistically significant ($p = 0$). The dose to the rectum was not considered for 2DBP. Evaluation of Figure 5.3 demonstrates the linear relationship between R mean 2D and R CT volume 2D. It can be seen that as the rectum CT volume increases the dose to the

rectum remains unchanged. The result was expected as the dose to the rectum was not considered for 2DBP. This result differs from the studies performed by Jamema *et al* (2008) and Bahadur *et al* (2008) which compared CTP with plans prepared using plain radiographs as their studies revealed that the mean dose to the rectum fluctuated with variations in the volume of rectum irradiated. This difference in the results obtained may be attributed to the different methods of Brachytherapy planning that were employed.

Figure 5.3 is a plot for the variables that constitute R mean 2D and its correlation to R CT Volume 2D.

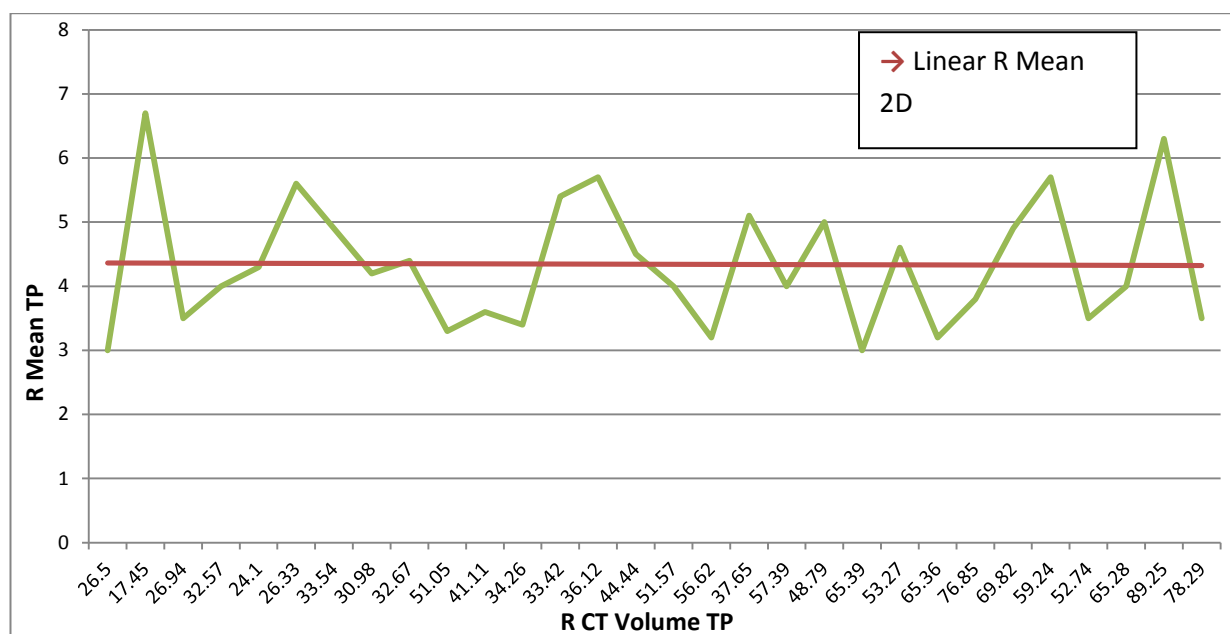


Figure 5.3: 2DBP - R Mean 2D vs. R CT Volume 2D

5.4.2 Does 2DBP or 3DBP yield more favourable rectum mean doses?

The Pearson-product-moment correlation used for analysis of the R mean 2D and R mean 3D. The Pearson-product-moment correlation shows a significant difference in the mean values as the p value ($p = 0$) is less than the level of significance of 0.05. This serves as evidence that a relationship

does exist between R mean 2D and R mean 3D. In view of the results it is deduced that 2DBP yields higher doses to the rectum. This proves that 3DBP is a more efficient method of planning in order to yield lower dose to the rectum.

5.4.3 Does 2DBP or 3DBP yield more favourable rectum maximum doses?

The Pearson-product-moment correlation indicates an insignificant relationship between R max 2D and R max 3D ($p > 0.05$). The correlation value is positive ($p = 0.121$), therefore this indicates a proportional relationship. This indicates that as the volume increases so did R max 2D and R max 3D. This result was similar to the results achieved by Bahadur *et al* (2008) and Jamema *et al* (2008).

There is an insignificant difference between the mean values of the variables (R max 2D and R max 3D) as the p-value is greater than the level of significance of 0.05 (that is, $p = 0.121$). This can be seen in Figure 5.4.

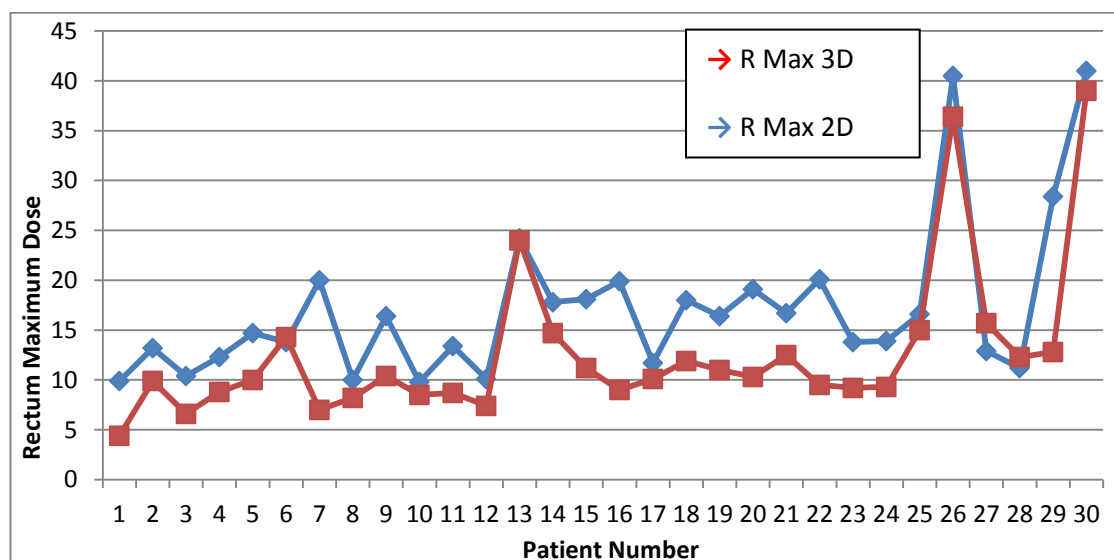


Figure 5.4: Comparison of R Max 2D and R Max 3D

As the correlation coefficient values are strongly positive, it demonstrates a proportional relationship. This implies that as the volume increases the dose increases for 2DBP and 3DBP therefore in terms of the rectum maximum dose, 3DBP did not prove to be more efficient than 2DBP.

The linear relationship graph is plotted below. As can be seen from Figure 5.5, the best fitting straight line drawn through the curves illustrates the linear nature of the relationship between R max 2D and R max 3D.

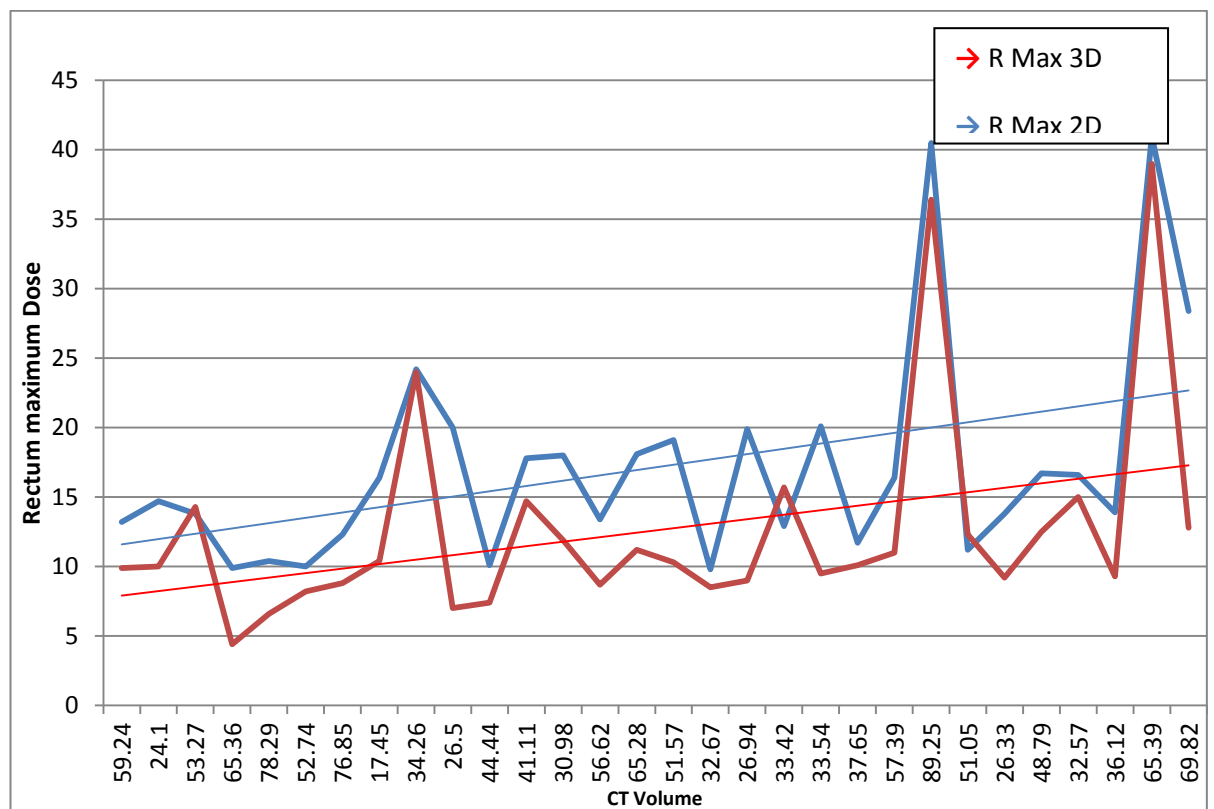


Figure 5.5: Linear Relationship between R Max 2D and R Max 3D

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Introduction

The data presented in this dissertation represents a comprehensive study comparing two planning techniques that may be applied to HDR Brachytherapy for patients with cancer of the cervix. The main finding serves as evidence that 3D HDR Brachytherapy planning using Computer Tomography scans is an improved planning method compared to 2D HDR Brachytherapy planning using computer generated template planning in terms of bladder and rectum doses determination. This investigation has added to the global evidence for the advantages of utilising more advanced HDR Brachytherapy techniques. Kim, Shen and Dan (2007) and Wang *et al* (2009) achieved significant correlation for bladder dose and insignificant correlation for rectal dose when comparing 2D and 3D Brachytherapy planning. Gao *et al* (2010) concluded that 2D Brachytherapy planning underestimates the dose to the bladder as compared to 3D Brachytherapy planning, however dose to the rectum was relatively similar for both planning techniques. The results achieved by the above mentioned studies differ from those of this research. The results of this research demonstrated a significant dose correlation for rectal dose and a significant correlation for bladder dose. The differences in the doses to the rectum and bladder were significant in this research demonstrating the effectiveness of 3D HDR Brachytherapy planning, where as in the previous studies mentioned; only significance was demonstrated for bladder dose. This may be attributed to experience in 3D Brachytherapy HDR planning, hospital protocols or even Oncologist/radiotherapist perspectives. However, the end result of this research demonstrated relevance to the global research for 2D Brachytherapy planning versus 3D Brachytherapy planning.

6.2 Conclusion and Significance

This research study demonstrated that 3D HDR Brachytherapy planning using Computer Tomography scans is an improved method of planning compared to 2D HDR Brachytherapy planning using computer generated templates as it provides a more accurate means of determining the doses to the rectum and bladder. Once these doses are accurately determined, methods can be established to reduce these doses even further in order to minimise side effects and allow patients to experience an improved quality of life. Brachytherapy planning utilising 3D methods such as CT planning, as used in this study, facilitates improved dose conformity facilitating accuracy and effectiveness of intracavitary HDR Brachytherapy.

It is the author's opinion that whilst template Brachytherapy planning may save time in terms of Brachytherapy planning, it is out-weighed by the potential benefits of 3D Brachytherapy planning in terms of reduced side effects. Efforts should be made to improve protocols and procedures in local Brachytherapy facilities, as well as global centres, directing practices towards utilising the technology at hand or that may be available. The dynamic environment of radiography as whole should be taken advantage of so that a multidisciplinary approach may be applied to Brachytherapy planning.

6.3 Summary of Contributions/Recommendations

- ICRU 38 recommendations should be strictly adhered to in order to reduce late complications caused by intracavitary HDR Brachytherapy (Shrivastava *et al*, 2009:93). In this study, these recommendations were adhered to for 3D HDR Brachytherapy planning.

- Shrivastava *et al* (2009:96) suggests that the volume of rectum and bladder within the treatment area should be decreased. In this study the vagina was packed with gauze in order to move the rectum and the bladder away from the target area and to stabilise the applicators. Further means of decreasing the volume of rectum and bladder within the treatment area may be investigated.
- Accurate delineation of the irradiated volume is warranted. Henry, Jeremic and Zubizarreta (2006:152) advice that the irradiated volume should be reduced as a smaller volume can tolerate higher dose. In this study the dose was prescribed to a point (Point A). Prescribing the dose to a volume will allow for more accurate treatment planning and possibly reduce the irradiated volume.
- Huang (2011:66) discusses the concept of bladder distension in order to decrease the volume of the small bowel receiving dose from Brachytherapy. Their study also demonstrated statistical significance in the reduction in dose to the bladder wall as well as the rectum. This has relevance to this study as patients were advised not to eat or drink anything for six hours prior to the treatment. Following the suggestion from Huang (2011:66) it is recommended that patients are advised to consume at least 2 glasses of water prior to treatment in order to reduce dose to the critical structures facilitating a decrease in side effects.

6.4 Limitations

- This is a contextual study. Many studies surrounding this topic have been performed over the years globally. Whilst this study benefits local practices by demonstrating the effectiveness of utilising imaging, in the

case of this study, CT, this point has already been established worldwide.

6.5 Future Research

- Ogino, Kitamura, Okamoto, Yamasita, Aikwaw, Okajima and Matsubara (1995) concluded their study by suggesting that late rectal complications arising from HDR intracavitary Brachytherapy may be reduced by improving the technique of inserting the intracavitary Brachytherapy apparatus. Therefore, it is recommended that in future an investigation be conducted to evaluate the different techniques available for inserting the intracavitary Brachytherapy apparatus.
- Brooks, Bownes, Lowe, Bryant, and Hoskin (2005:938) and Pötter, Dimopoulos, Georg, Lang, Waldhäusl, Wachter-Gerstner, Weitmann, Reinthaller, Knocke, Wachter, and Kirisits (2007:152) discuss improvement in local control without increasing the side effects by prescribing the target dose to a volume instead of a point (Point A), as well as considering the critical structures in 3D. They found this method of dose prescribing significantly improved the therapeutic ratio. In the provincial hospitals in KwaZulu-Natal, the target dose is being prescribed to Point A. Investigation of prescribing the target dose to a volume instead of a point is warranted.
- As proposed by Kim, Shen and Dan (2007:193) in their study, the proximal rectum and sigmoid colon should be evaluated as organs at risk of radiation side effects due to cervical Brachytherapy. In their study they found that these organs received a significant radiation dose and could therefore affect the patients' quality of life.

- An investigation exploring the use of cone-beam CT for Brachytherapy planning is recommended in order to determine whether this is a more convenient alternative to CT based planning due to the advantage of minimizing applicator motion (Al-Halabi, Portelance, Duclos, Reniers, Bahoric and Sohami; 2010: 1097).

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cards%2F&ei=87OAU5i9MqbL0AXbooCgBA&psig=AFQjCNGTp7nvakcjNcR
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APPENDIX

A

**KZN DEPARTMENT OF HEALTH
PERMISSION TO CONDUCT
RESEARCH**



HEALTH
KwaZulu-Natal

Health Research & Knowledge Management sub-component

10 – 103 Natalia Building, 330 Langalibalele Street

Private Bag x9051

Pietermaritzburg

3200

Tel.: 033 – 3953189

Fax.: 033 – 394 3782

Email.: hrkm@kznhealth.gov.za

www.kznhealth.gov.za

Reference : HRKM074/10
Enquiries : Mrs G Khumalo
Telephone : 033 – 3953189

25 May 2010

Dear Ms N Govender

Subject: Approval of a Research Proposal

1. The research proposal titled **'2D Brachytherapy Planning vs 3D Brachytherapy Planning for patients with cervical cancer'** was reviewed by the KwaZulu-Natal Department of Health.

The proposal is hereby **approved** for research to be undertaken at **Inkosi Albert Luthuli Central Hospital**.

2. You are requested to take note of the following:
 - a. Make the necessary arrangement with the identified facility before commencing with your research project.
 - b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.
3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mrs G Khumalo on 033-3953189.

Yours Sincerely

Dr S.S.S. Buthelezi

Date: 02/06/2010

Chairperson, Health Research Committee
KwaZulu-Natal Department of Health

uMnyango Wezempilo . Departement van Gesondheid

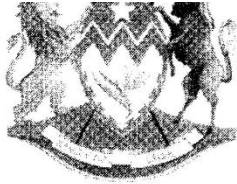
Fighting Disease, Fighting Poverty, Giving Hope

APPENDIX

B

INKOSI ALBERT LUTHULI CENTRAL
HOSPITAL

PERMISSION TO CONDUCT RESEARCH



PROVINCE OF KWAZULU-NATAL
INKOSI ALBERT LUTHULI CENTRAL HOSPITAL

OFFICE OF THE MEDICAL MANAGER
800 Bellair Road, Mayville, 4058
Private Bag X03, Mayville, 4058
Tel.: 031 240 1042 Fax. 031 240 1050
Email. Philisiwemaz@ialch.co.za

22 April 2010

Ms Natalie Govender
Dept of Radiotherapy
IALCH

Dear Ms Natalie Govender

**Re: Ref No: FHSEC 054/09 2D Brachytherapy planning VS 3D Brachytherapy
planning for patient with cervical cancer.**

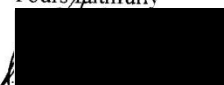
As per the policy of the Provincial Health Research Committee (PHRC), you are hereby granted permission to conduct the above mentioned research once all relevant documentation has been submitted to PHRC inclusive of Full Ethical Approval.

Kindly note the following.

1. The research should adhere to all policies, procedures, protocols and guidelines of the KwaZulu-Natal Department of Health.
2. Research will only commence once the PHRC has granted approval to the researcher.
3. The researcher must ensure that the Medical Manager is informed before the commencement of the research by means of the approval letter by the chairperson of the PHRC.
4. The Medical Manager expects to be provided feedback on the findings of the research.
5. Kindly submit your research to:

The Secretariat
Health Research & Knowledge Management
330 Langaliballe Street, Pietermaritzburg, 3200
Private Bag X9501, Pietermaritzburg, 3201
Tel: 033395-3123, Fax 033394-3782

Yours faithfully


Dr M E L Joshua
Medical Manager





Inkosi Albert Luthuli Central Hospital (IALCH)
800 Bellair Road
Mayville
4091

Dear Sir/Madam

RE: REQUEST FOR PERMISSION TO CONDUCT STUDY

I am presently registered as a Masters student at the Durban University of Technology in the Department of Radiography as I aim to obtain a Masters degree in Radiography. My current qualifications include a National Diploma in Radiography (Therapy) and a B. Tech in Radiography (Therapy).

The proposed title of my research project is: 2D Brachytherapy planning vs. 3D Brachytherapy planning for patients with cervical cancer

Approximately 30 patients will be selected for the study. This study will in no way alter the patients' prescribed course of treatment. I intend to evaluate and compare the technique used for cervical Brachytherapy (2D planning) with Computed Tomography (CT) aided Brachytherapy (3D planning), therefore my subject group will include those patients referred for cervical Brachytherapy. I intend to commence data collection in December 2009 and complete the project by December 2010. Primary data collection will include personal and demographic data of the participants, CT scans, 2D outputs and 3D planning outputs.

A Radiation Oncologist has offered me his supervisory support for the project. This study will benefit the patients, doctors and radiographers in terms of planning accuracy in order to improve patients' quality of life. Brachytherapy is a promising radiation treatment modality that delivers a curative dose directly to the tumour. Due to the high doses being delivered to the target, the need for precision arises (UCSF Comprehensive Cancer Center. 2006). At Inkosi Albert Luthuli Central Hospital Radiation Oncology, Brachytherapy are planned using templates. In some centres in our country and in most centres if not all the centres worldwide Brachytherapy are being planned using CT scans. My research aims to boost the use of the technology at hand in provincial radiotherapy centres in KwaZulu-Natal thereby providing an improved treatment technique.

During irradiation of the pelvis, the bladder and rectum are critical structures that require much attention as their preservation is essential to maintain or improve the patient's quality of life. Malfunction or complications of these organs, e.g. incontinence, compromises their quality of life. It is for this reason that it becomes vital to optimally delineate the bladder and rectum for Brachytherapy planning in order to accurately determine the doses received by these organs to untimely reduce the doses received (Baucal, Babić and Kuzmanović, 2002:253). The results of the study will evaluate the efficiency and precision of 2D and 3D Brachytherapy. It will highlight the necessity for precise delineation of the bladder and rectum to decrease side effects whilst achieving adequate doses to the target volume. The results will also determine the accuracy of both techniques so that the feasibility of the techniques may be established.

I hereby request your permission to conduct a research project at your institute which will include the use of the CT scanner and planning equipment at IALCH Radiation Oncology Department. My research proposal has been reviewed and approved by the Research committee of the Faculty of Health Sciences at the Durban University of Technology. I have also obtain the necessary ethical approval. There will be no additional costs to the patient.

My research proposal has been attached for your appraisal. Your support and permission to conduct the study at IALCH Radiation Oncology Department will by appreciated.

Yours sincerely
Natalie Govender

.....
Student number: 20200608

Internal Supervisor: Ms S. Naidoo (Master of Applied Science (MRT))

.....
External Supervisor: Dr P. Govender (Oncologist)

.....
Permission Granted
.....
Mrs B. Rasool (HOD - Radiation Ongology)

If permission not granted, please explain:

Permission Granted:

.....
V 21/04/10 (CEO - IALCH)

If permission not granted, please explain:

APPENDIX

C

PATIENT INFORMATION SHEET



PATIENT INFORMATION SHEET

Title: 2D Brachytherapy planning vs. 3D Brachytherapy planning for patients with cervical cancer

Researcher: Natalie Govender

Contact

Details: nataliegov@ialch.co.za / 0827870646

Purpose: You are asked to volunteer for a research project that will compare two methods of Brachytherapy (radiation treatment) and evaluate which is the best technique to be used. There are about 30 people that will volunteer for this project. They are patients from Inkosi Albert Luthuli Central Hospital. Your participation is once off and will occur during your scheduled Brachytherapy appointment time so as not to inconvenience you in any way.

Procedures: You will have an x-ray of the pelvis for the purpose of this research.

Preparation: You cannot eat or drink anything for 6 hours before the treatment.

Risks/

Discomforts: You will not experience any additional risks or discomforts as part of this research.

Benefits: This research may benefit patients in the future.

Confidentiality: All information concerning you will be kept private and confidential.

Participation: Your participation is voluntary and you may withdraw from the study at any stage.

Ethics

Approval: This study has been approved by the Faculty of Health Sciences Research Committee.

Signatures: A copy of this form will be given to you. Your signature below indicates that you have read and understood the contents of this form and that the researcher has answered all of your questions to your satisfaction, and that you volunteer for this study.

Subject's Signature: _____

Researcher's Signature: _____

Witness's Signature: _____

Date: _____



ULWAZI OLUBALULEKILE LWEZIGULI

Isihloko: Inhlololuvo eqhathanisa indlela yokulapha nge 2D kanye ne 3D Brachytherapy isifo somhlavuza wesibeheletho

Iomcwoningi: Natalie Govender

Contact

Details: nataliegov@ialch.co.za / 0827870646

Inhloso: Uyacelwa ukuthi uvolontiyi kucwaningo oluzoqhathanisa izindlela zokulapha nge brachytherapy, nokuhlaziya kanye nokuthi iyiphi indlela engcono. Kunabantu ababalelwa ku-30 obazovolontiya kulolucwaningo. Kuzoba neziguli zase- Inkosi Albert Luthuli Hospital. Ukuvolontiya kuzoba kanye(1) uma isikhathi se-Brachytherapy sizovumelana nawe.

Izinqubo: Kuyothathwa izithombe zesibeheletho uma kwenziwa lolucwaningo.

Ukulungiselela: Uyacelwa ukuthi ungadli futhi ungaphuzi lutho amahora ayisithupha ayisithupha ngaphambi kokulashwa.

Ubungozi/Ukuhlukumezeka:

Akukho okuzokuhlukumeza noma okuzokuphatha kabi uma kwenziwa lolucwaningo.

Inzuzo: Lolucwaningo lungakwenza uzuze esikhathini esizayo.

Imfihlo: Ulwazi lonke luzoba imfihlo lungatshelwa muntu.

Ukuzibandakanya: Ukuvolontiya kuzoba sothandweni lakho futhi ungaphuma noma inini uma ungasathandi.

Imvume

Yokuziphatha: Lesisifundo sivunyelwe ngabakwa-Faculty of Health Science Research Committee

Ukusayina: Uzonikwa ikhophi yalelifomu. Ukusayina kwakho kuchaza ukuthi uyifundile futhi wayiqonda imininingwane equkethwe yilelifomu, umcwaningi uyiphendule ngokwanelisayo yonke imibuzo yakho nokuthi uvumile ukubandakanya kulolucwaningo.

Umcwaningi: _____

Umhloli sayina: _____

uFakazi sayina: _____

Usuku: _____

APPENDIX

D

INFORMED CONSENT



INFORMED CONSENT FORM

I, hereby voluntarily give consent to participate in the research titled:
2D Brachytherapy planning vs. 3D Brachytherapy planning for patients with cervical cancer

Researcher: Natalie Govender
Internal Supervisor: Mrs S. Naidoo
External Supervisor: Dr P. Govender

Please circle the appropriate answer:

- | | |
|---|---------------------|
| 1. Have you read and understood the information sheet? | <div>YES / NO</div> |
| 2. Have you had the opportunity to ask questions? | <div>YES / NO</div> |
| 3. Have you had the opportunity to discuss the study? | <div>YES / NO</div> |
| 4. Who have you spoken to? | |
| 5. Have you received satisfactory answers to your questions? | <div>YES / NO</div> |
| 6. Do you understand that you can withdraw from the study at any time without a reason? | <div>YES / NO</div> |
| 7. Do you understand that should you withdraw from the study, your medical care or legal rights will not be affected? | <div>YES / NO</div> |
| 8. Do you understand that there are no financial implications on you to participate in the study? | <div>YES / NO</div> |
| 9. Do you understand and agree to voluntarily participate in the study? | <div>YES / NO</div> |
| 10. Do you agree not to discuss this research project with any other individuals, except your family members? | <div>YES / NO</div> |

If you have answered NO to any of the above, please obtain any necessary information before signing.

Natalie Govender _____

Name of Researcher Date Signature

Name of Participant Date Signature

Name of Witness/Interpreter Date Signature

INFOMU LEMVUME

Mina, ngiyovuma ukuzibandakanya nocwaningo olusihloko:

Inhloluluvo eqhathanisa indlela yokulapha nge 2D kanye ne 3D Brachytherapy isifo somhlavuza wesibeetho

Umcwoningi: Natalie Govender

Umhloli ongaphakathi: Mrs S. Naidoo

Umhloli ongaphandle: Dr P. Govender

Uyacelwa ukuthi uzungeze impendulo efanele:

1. Usulifundile waliqonda ikhasi lolwazi?

YEBO / CHA

2. Ubenalo ithuba lokubuza imibuzo?

YEBO / CHA

3. Ubenalo ithuba lokuxoxa ngaloluphenyo?

YEBO / CHA

4. Ukhulume nobani?

5. Izimpendulo ozitholile ziyagculisa na?

YEBO / CHA

6. Uyazi ukuthi ungahoxa kuloluphenyo noma nini ngaphandle kokunika isizathu?

YEBO / CHA

7. Uyazi ukuthi uma uhoxa kuloluphenyo usizo lokwelashwa kanye nama lungelo akho angeke athinteki?

YEBO / CHA

8. Uyaqonda ukuthi isimo sakho sezimali angeke sithinteki uma uzibandakanya kuloluphenyo?

YEBO / CHA

9. Uyaqonda futhi uyavuma ukuzibandakanya kuloluphenyo ngokuthanda?

YEBO / CHA

10. Uyavuma ukuthi angeke uxoxe ngaloluphenyo ngaphandle kwamalunga omndeni wakho?

YEBO / CHA

Uma uphendule cha kokukodwa kulemibuzo engaphezulu, uyacelwa ukuthi uthole ulwazi oludingekayo ngaphambi kokuba usayine.

Natalie Govender _____

Igama lomcwaningi

Ilanga

Signature

Igama lobambe iqhaza

Ilanga

Signature

Igama lomtoliki/uFakazi

Ilanga

Signature

APPENDIX

E

ETHICS APPROVAL

ETHICS CLEARANCE CERTIFICATE

Student Name	NATALIE GOVENDER	Student No	20200608
Ethics Reference Number	FHSEC 054109	Date of FRC Approval	02 NOVEMBER 2009
Qualification	MASTER'S DEGREE RADIOGRAPHY: THERAPY		
Research Title:	2D BRACHYTHERAPY PLANNING VS 3D BRACHYTHERAPY PLANNING FOR PATIENTS WITH CERVICAL CANCER IN TERMS OF DELINEATION ACCURACY IN ORDER TO DETERMINE BLADDER AND RECTUM DOSE ACCURATELY		

In terms of the ethical considerations for the conduct of research in the Faculty of Health Sciences, Durban University of Technology, this proposal meets with Institutional requirements and confirms the following ethical obligations:

1. The researcher has read and understood the research ethics policy and procedures as endorsed by the Durban University of Technology, has sufficiently answered all questions pertaining to ethics in the DUT 186 and agrees to comply with them.
2. The researcher will report any serious adverse events pertaining to the research to the Faculty of Health Sciences Research Ethics Committee.
3. The researcher will submit any major additions or changes to the research proposal after approval has been granted to the Faculty of Health Sciences Research Committee for consideration.
4. The researcher, with the supervisor and co-researchers will take full responsibility in ensuring that the protocol is adhered to.
5. **The following section must be completed if the research involves human participants:**

	YES	NO	N/A
❖ Provision has been made to obtain informed consent of the participants	X		
❖ Potential psychological and physical risks have been considered and minimised	X		
❖ Provision has been made to avoid undue intrusion with regard to participants and community	X		
❖ Rights of participants will be safe-guarded in relation to:	X		
- Measures for the protection of anonymity and the maintenance of Confidentiality.			
- Access to research information and findings.	X		
- Termination of involvement without compromise	X		
- Misleading promises regarding benefits of the research	X		

SIGNATURE OF STUDENT/RESEARCHER

SIGNATURE OF SUPERVISOR

SIGNATURE OF CO-SUPERVISOR

SIGNATURE OF HEAD OF DEPARTMENT

SIGNATURE: CHAIRPERSON OF RESEARCH ETHICS COMMITTEE

02/12/2009

DATE

3/12/09

DATE

02/12/09

DATE

3/12/09

DATE

7/12/09

DATE