

**Sudan University of Science and
Technology
College of Graduate Studies**

**Designing a Protocol for Radiotherapy
Planning for Prostate Carcinoma in
Sudan**

تصميم نظام تخطيطى للعلاج بالأشعة لسرطان البروستاتا فى

السودان

*Thesis for fulfillment of the requirements of the PhD degree in
Medical Radiation Physics*

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Abstract

This study aimed at finding an optimal approach for the distribution of the standard radiation dose to the prostate gland and in the same time the reduction of the radiation dose to the rectum , urinary bladder and skin , by using a medium energy (1.25 MV) cobalt -60 machine , alongside with the use of CT images of 55 patients undergoing radiotherapy planning for the distribution of the radiation dose via several fields (3,5,7) , in order to find out an agreed upon protocol and a standard method to substitute the images in the future (whenever they are not feasible), during the planning the study concluded that the use of five radiation fields with wedge angles 45° for oblique fields (anterior , right anterior oblique, left anterior oblique , right posterior oblique and left posterior oblique) through 0, 60 , 300, 120,240 degrees respectively, can help provide a radiation dose with ratio of 98% to the prostate gland with a reduced dose of 76.7%,96% and 71% to the rectum , urinary bladder and skin respectively. The study also concluded that a standard planning of CT images could be used as a substitute to the manual contour of the mean dimensions (AP separation 23.4 cm, lateral separation 41.4cm), to replace any other planning within the range 15.2cm to 26.1cm for the AP separation and the range 30cm to 48.4 cm for the lateral separation. This approach will cancel the need for the CT scans of any patient within this range, as there is no significant difference when comparing the distribution of radiation dose through the application of a contour depending on CT scans

for each patient with the application of the standard contour derived from the CT scans.

المستخلص

هدفت هذه الدراسة إلى إيجاد طريقة مثلى لتوزيع الجرعة الإشعاعية الأنموذج لغدة البروستاتا مع تقليل الجرعة الإشعاعية للمستقيم والمثانة والجلد باستخدام جهاز الكوبات -60 ذى الطاقة المتوسطة ((M 1.25 مع الإستعانة بـ صور الأشعة المقطعية لعدد 55 مريض فى التخطيط العلاجى لتوزيع الجرعة عبر عدة حقول 3,5,7 للوصول لنظام متفق عليه وإيجاد نموذج قياسى- للإستعاضة عن صور الأشعة المقطعية مستقبلا (متى ما تعذر ذلك) فى التخطيط. خلصت هذه الدراسة إلى أن إستخدام 5 حقول إشعاعية (حقل أمامى, حقل أمامى مائل, حقل أمامى مائل اخر, حقل خلفى مائل وحقل خلفى مائل اخر بزوايا 0,60,300,120,240 على التوالي) تمكن من إيصال جرعة إشعاعية بنسبة 98% لغدة البروستاتا مع جرعات أقل بنسب مختلفة 76.7%, 96% , 71 لكل من المستقيم, المثانة والجلد على التوالي. كما خلصت أيضا إلى أنه يمكن إستخدام مخطط قياسى من صور الأشعة المقطعية بدلا عن الكنتور اليدوى لمتوسط الأبعاد (فرق أمامى خلفى 23.4 سم فرق جانبي 41.4 سم) للإستعاضة به عن أى مخطط اخر فى المدى من 15.2 سم إلى 26.1 سم للفرق الأمامى الخلفى و فى المدى من 30 سم إلى 48.4 سم للفرق الجانبي مما

يترتب عليه عدم الحاجة لصور أشعة مقطعية من أى مريض وفق هذا المدى, نسبة لعدم وجود فرق ذى أهمية عند المقارنة بين- توزيع الجرعة الإشعاعية بإستخدام كنتور من صور الأشعة المقطعية لكل مريض و إستخدام الكنتور القياسى من صور الأشعة المقطعية .

Dedication

إلى أمى الغالية التى كانت و مازالت نبعا ومعينا لا ينضب

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**List abbreviation
The statement**

Abbreviat ion	The statement	Page No
IAEA	International Atomic Energy Agency	4
PACT	Programme of Action for Cancer Therapy	4
PSA	prostate specific antigen	5
MENA	Middle East and North Africa	6
NCCN	National Comprehensive Cancer Network	6
UAE	United Arab Emirates computed	9
MRI	Magnetic Resonance Image	9
KSA	kingdom of Saudi Arabia	9
3D	Three Dimensions	9
IMRT	Intensity-Modulated Radiation Therapy	9
CRT	Conformal Radiotherapy	9
UCSF	University of California, San Francisco	16
UK	United Kingdom	16
PIN	Prostatic intraepithelial neoplasia	17
PIA	Proliferative inflammatory atrophy	18
TURP	transurethral resection of the prostate	20
DRE	digital rectal examination	21
CAT	computed axial tomography	26
BPH	benign prostatic hypertrophy	30
GS	Gleason score	32
IMRT	Intensity Modulated Radiotherapy	32
IGRT	Image Guide Radiotherapy	32
EBRT	External Beam Radiation Therapy	32
NCAD	neoadjuvant, concurrent and adjuvant androgen deprivation	34
RT	radiation therapy	34
SVs	seminal vesicles	36
US	ultrasound	36
RUG	Retrograde urethrography	36
GTVs	gross tumor volumes	37
CTV	clinical target volume	38

PTV	planning target volume		38
MLC	multileaf collimator		39
3DCRT	three dimensions conformal radiotherapy		39
OAR	organ at risk		39
SSD	source skin distance		42
SARs	scatter air ratios		42
SAD	source axis distance		44
DMLC	dynamic multileaf collimation		54
CRT	conformal radiotherapy		55
HT	hormonal therapy		55
CHT	concomitant hormonal therapy		55
NAHT	neoadjuvant hormonal therapy		55
EORTC	European Organization for Research and Treatment of Cancer		55
RTOG	Radiation Therapy Oncology Group		55
HDR	High dose rate		56
DVH	Dose Volume Histogram	59	58
GAI	Gamma Agreement Index	59	59
CTCAE	Terminology Criteria of Adverse Effects scale	59	59
DICOM	Digital Imaging and Communications in Medicine	60	60

Chapter1

Introduction

Chapter1

Introduction

1.1 Burden of Cancer in Developing Countries

Although data on cancer cases and deaths in developing countries are more limited and less accurate than in developed countries, researchers do know that patterns and types of cancer differ considerably between the world's richer and poorer nations. In developing countries, the top cancers among women, in order of incidence, are breast, cervical, stomach, lung, and colorectal cancer (Figure 1.1) cervical cancer accounts for the greatest number of deaths. (Jamison et al, 2007).

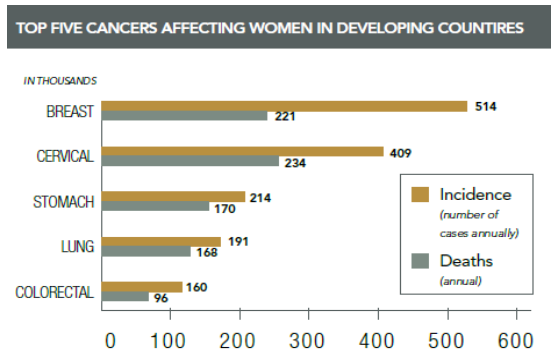


Figure (1-1)
top five

cancers affecting women in developing countries Adopted from (Jamison et al, 2007).

The top five cancers affecting men are shown in (Figure 1.2).The higher incidence of infection-related cancers (stomach, liver, and cervical) in developing countries reflect weak public health

systems that cannot control contamination, bacteria, and viruses, and the lack of effective preventive and screening services. Cancer of the esophagus may reflect in part the consumption of traditional beverages while extremely hot. Cancers that are becoming increasingly common in developing countries—lung, breast, and colorectal cancers— reflect longer life expectancies, the adoption of Western diets, and the globalization of tobacco markets(Jamison et al, 2007).

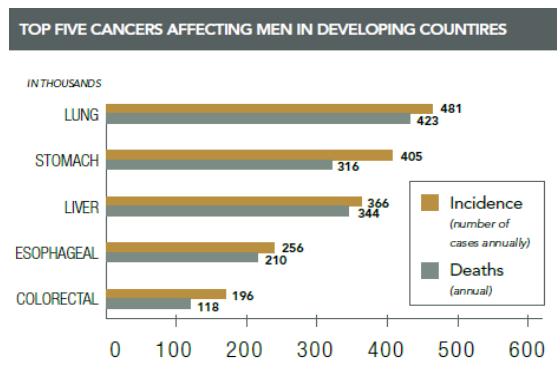


Figure (1-2), top five cancers affecting men in developing countries. A dopted from (Jamison et al, 2007).

The treatment protocols and equipment modeled on the best developed countries seldom can be applied directly to developing countries owing to financial constraints and lack of qualified personnel. A comprehensive national cancer control programmed including preventative and early detection measures, coupled with a judicious mixture of treatment by surgery, radiotherapy and chemotherapy now results in the cure of 45% of all cancers in

advanced countries. That is a target to which developing countries also aspire. (Levin et al. 2001)

The earliest applications of nuclear technology were diagnostic radiology and the treatment of cancer using radiation. The discovery of X-rays in November 1895 was followed by the first diagnostic “skiagrams” published in January 1896. Simultaneously, in January 1896, two patients, one with breast cancer, commenced treatment in Chicago; in February, a nasopharyngeal cancer was treated in Hamburg and a stomach cancer in July in Lyon. In November 1896, a 4 year-old child was the first patient treated in Vienna. What is more remarkable is that she was seen for clinical follow-up 70 years later in excellent health. (Levin et al. 2001)

This X-ray technique developed into the radiotherapy discipline referred to as “teletherapy”. Significant improvement in clinical results was achieved with the introduction of high-energy teletherapy. Cobalt-60 teletherapy was first used in October 1951, almost 50 years ago. Megavoltage accelerators for the production of high energy X-rays became increasingly more reliable from the 1970s. Radium was identified and isolated in 1898, but the first documented successful use for cancer treatment was in St. Petersburg in 1903. The application of radium evolved into the discipline of “brachytherapy” the application of sealed radioactive material directly adjacent to a tumor. There has been rapid worldwide acceptance of radiotherapy as both a curative and palliative modality in the management of cancer. Many countries,

designated as developing, initiated radiation therapy under general radiology in the early 1900s, but separated this growing discipline from diagnostic radiology in the 1950s. However, there was a severe shortfall of facilities compared to the best developed countries. (Levin et al. 2001)

The last decade has seen an acceleration of the acquisition of equipment by developing countries. For example, the whole of Africa had 63 megavoltage teletherapy machines in 1991; this number rose to 155 machines by the end of 1998. During the past few years, there has been a corresponding increased demand from the IAEA's Member States for assistance, including the provision of radiation sources and equipment, in establishing radiotherapy programmes for the treatment of cancer patients through technical cooperation projects. The activities have ranged from the initiation of radiation oncology in a country without any prior facilities to upgrading deficiencies in existing radiotherapy centers. The objective has been to nurture the radiotherapy technology until the internationally accepted standards for the centers of competence are achieved and sustained in those member States where this technology is appropriate. (Levin et al. 2001)

The IAEA has adopted a systematic approach for the provision of this assistance and equipment. The aim is to ensure that clinical, dosimetric, safety and maintenance aspects have been included, which otherwise could jeopardize the outcome of patient treatment, or contribute to accidents. All technical cooperation

projects carried out with IAEA assistance have been implemented in compliance with The International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources. The transfer of radiotherapy technology has been addressed through national and regional projects in Africa, Asia, Eastern Europe, and Latin America. (Levin et al. 2001)

1.2 cancers in Sudan

In one of Africa's largest countries, Sudan, the cancer rate among its population is rising. Since the country's health authorities are noting an increasing incidence of breast, cervical and prostate cancer, the IAEA's Programme of Action for Cancer Therapy (PACT) was requested by Sudan's Federal Ministry of Health to conduct an impact review, a comprehensive assessment of the country's cancer control capacity and needs. (IAEA, April 2012)

1.3 Prostate carcinoma in the world

Prostate cancer is the second most frequently diagnosed cancer in men, with 903,500 new cases estimated to have occurred in 2008. Nearly three-quarters of these cases were diagnosed in economically developed countries. Incidence rates of prostate cancer vary by more than 70-fold worldwide. The highest rates are recorded primarily in the developed countries of Europe, North America, and Oceania, largely because prostate specific antigen (PSA) testing is widely used and detects clinically important

tumors, as well as other slow-growing cancers that might otherwise have escaped diagnosis. The lowest rates are in many parts of Asia (Figure 1-3). (Center Melissa et al 2008)

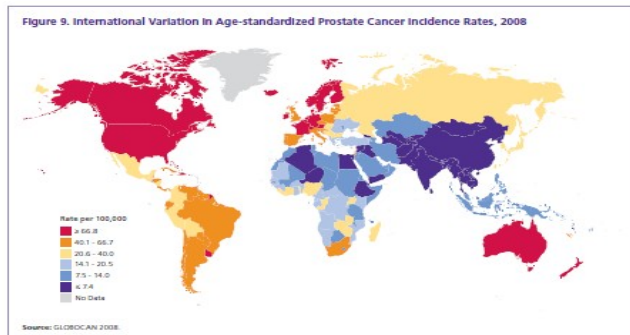


Figure (1-3) international variation in Age-standardized prostate cancer incidence rate, 2008 adopted from (Center Melissa et al 2008).

Deaths: With an estimated 258,400 deaths in 2008, prostate cancer was the sixth leading cause of cancer death in men worldwide. Men of African descent in the Caribbean region have the highest prostate cancer mortality in the world, with age-standardized rates more than four times higher than those in the US and more than 15 times higher than those in the Middle East and Eastern Asia. The reason for the high prostate cancer risk among some populations of African descent is still poorly understood, though it may in part reflect differences in genetic susceptibility. (Center Melissa et al, 2008)

Global trends: Temporal trends in prostate cancer death rates are easier to interpret than trends in incidence rates because they are less affected by changes in PSA screening rates. Incidence trends

follow a consistent pattern in countries with higher uptake of PSA, such as Australia, Canada, and the United States, with a rapid rise in incidence in prostate cancer in the early 1990s soon after the introduction of PSA testing followed by a sharp decline. In other high-income countries with low prevalence of PSA testing, such as Japan and the United Kingdom, the dramatic peak in incidence is not observed, though rates continue to increase slightly. Death rates for prostate cancer have been decreasing in many developed countries, including Australia, Canada, Finland, France, Israel, Italy, The Netherlands, Norway, Portugal, Sweden, the United Kingdom, and the United States. (Baade PD et al, 2009).

In contrast, mortality rates are rising in some Asian and Eastern European countries, such as Japan, Singapore, and Poland. While the decrease in prostate cancer death rates in Western European and North American countries has been attributed mainly to improved treatment, the increase in Asian and Eastern European countries has been thought to reflect westernization, including increased consumption of animal fat, obesity, and physical inactivity. (Center Melissa et al 2008.)

1.4 Prostate carcinoma in the Africa

Prostate cancer is a significant source of morbidity and mortality in the West, and remains the second leading cause of death from a solid malignancy in men in the United States. However; its effect on populations in the Middle East and North Africa (MENA) region is not completely known. A prostate cancer committee was established to modify the NCCN Clinical Practice Guidelines in

Oncology (NCCN Guidelines) on Prostate Cancer for adaptation and implementation in the MENA region. The objective was to enhance the multidisciplinary approach to the treatment of prostate cancer. The committee, comprising regional experts in the fields of urologic, medical, and radiation oncology, reviewed the 2009 version of the NCCN Guidelines on Prostate Cancer and suggested modifications based on the unique needs of the region determined through published evidence and local expertise. The committee identified several areas in the NCCN Guidelines that they believed required modification, which are presented in this article. The treatment of prostate cancer in the MENA region has numerous challenges. The hope is that this effort to modify the NCCN Guidelines on Prostate Cancer for practical use in the MENA region will improve regional awareness and patient care. (Jazieh Abdul -Rahman et al , 2010)

For the purposes of this section, the MENA region refers to Afghanistan, Algeria, Armenia, Egypt, Ethiopia, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Oman, Pakistan, Qatar, Kingdom of Saudi Arabia (KSA), Somalia, Sudan, Syria, Tunis, Turkey, United Arab Emirates (UAE), and Yemen. This collection of countries is obviously extremely heterogeneous in terms of economic resources and health care infrastructure. Although generalizations are difficult, some pertinent issues and challenges are broadly applicable to this region. (Jazieh Abdul -Rahman et al, 2010)

Although the exact incidence of prostate cancer in the MENA region is unknown, the reported incidence is approximately 5.8

cases per 100,000, with a mortality rate of 4.9 cases per 100,000.² The accuracy of these data is not clear, however, because they are derived from unweighted averages from other regions. In general, prostate-specific antigen (PSA) screening is not routine, and therefore whether the lower incidence rate is secondary to the absence of screening or from a truly lower prevalence in the population is unknown. Smaller regional cancer databases, however, suggest that the true impact of this disease may be more significant than generally perceived (Jazieh Abdul - Rahman et al , 2010)

Young reported on regional cancer data bases from 8 countries in the MENA region (Jordan, Egypt, Bahrain, KSA, Kuwait, Qatar, Oman, and UAE), and found that prostate cancer ranked among the top 4 malignancies in terms of frequency in 5 countries. Shamseddine et al. reported that prostate cancer represented the most frequently reported malignancy in Lebanese men (Jazieh Abdul -Rahman et al, 2010)

In general it is the committee's perception that most patients present with late-stage disease because of the lack of PSA screening. It is also important to consider that the MENA region population is approximately 750 million. Because 65% of the population is currently younger than 30 years, even if the incidence of prostate cancer is lower than that of the West, the scope of the problem will only become more significant over the next 20 years as the population ages and presumably has access to improved medical care.(Jazieh Abdul -Rahman et al , 2010)

Because PSA screening is not routine in the MENA region, patients tend to present with more advanced disease. A general lack of primary care exists in the health systems of the region, which represents a challenge to timely diagnosis. Transrectal sonography is not routinely available except in regional centers, and experience with Transrectal sonographic biopsy of the prostate also seems to be limited to regional centers. Similarly, experience with the pathologic diagnosis of prostate cancer (including the nuances of grading) is also limited to referral centers. Although CT and nuclear bone scans are generally available, MRI has more limited availability. The definitive and palliative treatment of prostate cancer has multiple regional challenges. Definitive treatment typically involves either surgery or radiotherapy, and experience in the management of this disease is generally lacking. A brief poll of urologists, for example, found that awareness of the existence of NCCN Guidelines on Prostate Cancer varied between 5% and 86%. Adequate experience in the surgical management of prostate cancer has been shown to improve outcomes.⁶ A lack of surgical experience in the localized management of prostate cancer generally exists, even in referral centers, and radiation therapy has similar issues. According to the International Atomic Energy Agency (IAEA), only 93 machines are capable of delivering greater than 10 mV of energy in a region of 730 million people.⁷ More importantly, 70 machines are clustered in 3 countries (Turkey, Egypt, and KSA), leaving 23 machines to service the needs of 19 countries. Only 30

of 93 machines are capable of delivering CT dosimetry and planning. Furthermore, the costs of neoadjuvant hormonal therapy in combination with radiation therapy are so challenging, and experience with brachytherapy is limited. Similar issues arise when addressing the management of advanced disease, although the cost of hormone ablation is prohibitive, bilateral orchiectomy is a viable option and available. Access to systemic chemotherapy is limited, palliative care specialists are few, and the availability of narcotics tends to be limited. (Jazieh Abdul-Rahman et al, 2010)

1.5 **Radiotherapy in prostate carcinoma**

Radiotherapy is a suitable treatment for men of any age and is as effective at treating localized prostate cancer as surgery to remove the prostate (radical prostatectomy), given external beam radiotherapy alongside brachytherapy or high dose rate brachytherapy (internal radiotherapy). This increases the total amount of radiation, which can improve the effectiveness of treatment, but may also increase the risk of side effects. Radiotherapy is one of the treatments that can be used to treat cancer that is still contained within the prostate gland (localized prostate cancer). Radiotherapy may also be suitable for some men whose cancer has spread to the area just outside the prostate (locally advanced prostate cancer). (Gledhill Richard , 2012)

The aim of radiotherapy is to destroy prostate cancer cells, while limiting any damage to normal cells. High energy X-ray beams are

directed at the prostate gland from outside the body. These beams damage the cells and stop them from dividing and growing. Cancer cells are not able to recover from this damage and die, but normal healthy cells can repair themselves more easily. The whole prostate is treated. In some cases, the area surrounding the gland may also be treated. This is to try and treat all cancer cells, including any that may have spread to the area just outside the prostate. The treatment is painless but there may experience some side effects.). (Gledhill Richard, 2012)

As early as 1980's, it was realized that a basic port film is definitely required to confirm reproducibility of treatment fields, and also execution of treatments with good immobilization techniques. Seldom have these techniques been implemented in most of the existing centers, which make it difficult for critical analysis of beam quality differences in the treatment outcomes. Without firm base and infrastructure, the clinical application of radiotherapy beams cannot produce optimal results. A more optimistic statement may be that about 50% of existing scenario needs intervention and correction. 3D visualization methods and computed tomography (CT) imaging have become basic need for treatment planning both for localization and staging of disease. Basic localization, selection of beam center and field placement is possible with simple projected simulator radiograph, which also accounts for beam divergence simulating beam's eye view. If 3D delineated contour is not available, there is nothing better achieved with a multi-leaf collimator. In addition, if immobilization

is not proper, a 3D treatment execution and beam direction cannot produce better treatment outcome in radiotherapy. In this context, for documentation of correct treatment plans, the role of a therapy simulator cannot be dispensed with. The ratio of sophisticated to simple treatments will be about 30:70 in the total number of patients and therefore it may be worthwhile to suggest one tele-cobalt machine for simple treatments and one low energy linac for conformal, 3D, intensity-modulated radiation therapy (IMRT) treatments. (Ravichandran,2009)

Therefore, with judicious treatment planning and intelligent executions of treatments, proper results could be achieved with tele-cobalt machines if basic facilities such as simulator and mould room are available. Reddy made an analysis and indicated that low energy linacs (6 MV) are preferred to tele-cobalt machines, the main argument was related to cost of replacement of ^{60}Co sources and management of decayed sources. Experience in the past has shown that replacements of magnetrons/klystrons also should be considered in linacs, along with increased maintenance costs. Management of decayed sources is possible by planning cascade loadings to a similar machine, so that higher dose rates with one machine could be possible, at the same time the life of the source could be prolonged. Attempts to obtain flattened isodose curves from telecobalt machines, adopting multi-leaf collimators, execution of tomotherapy with telecobalt machines have added improvement of beam applications regarding the science of ^{60}Co teletherapy. .(Ravichandran,2009)

The most common type of external beam radiotherapy for prostate cancer is called 3D conformal radiotherapy (3D-CRT). The radiotherapy machine directs the beams to fit the size and shape of the prostate. This helps to avoid damaging the healthy tissue surrounding the prostate and so reduces the risk of side effects. A new type of 3D-CRT called intensity modulated radiotherapy (IMRT) is available in some treatment centers. With IMRT, the radiation beams can be adjusted to give different doses to different parts of the area being treated. This means that a higher dose of radiation can be given to the prostate gland without increasing the risk of damage to surrounding tissues. (Gledhill Richard, 2010)

1.6 **Cobalt -60 unit**

Decay of radioactive materials can produce high - energy gamma rays that may be used for teletherapy treatments. Currently, only one source, cobalt -60, remains in regular use. Cobalt - 60 can be produced by placing cobalt - 59 in a strong neutron field, the nucleus absorbing a neutron to form ^{60}Co . As soon as it is formed ^{60}Co starts to undergo radioactive decay to nickel - 60 with a half -life of 5.26 years. The emissions are a β particle with an energy of 0.31MeV (max) and two gamma rays with energies of 1.17 MeV and 1.33 MeV.

The cobalt source is situated in a doubly encapsulated steel container, to prevent any leakage of cobalt; this also acts to filter out the unwanted β particles. The cobalt is usually in the form of discs 2 mm thick and 17 mm in diameter stacked on top of each

other until the desired air kerma rate is reached. Any spare space is filled with blank discs to prevent movement of the discs within the container when the treatment unit moves around the patient.

The unit in which the source is sealed is simple in construction and as such is very reliable. There are two basic types of unit: the moving source and fixed source. In the moving source unit the source moves from a safe position to a position just behind the primary collimator. As the source is continually emitting gamma rays when this movement occurs, the beam effectively switches on. In the fixed source unit the cobalt source is stationary, the primary collimator rotates opening up a passage for gamma rays to emerge.

Over a period of time the number of radioactive ^{60}Co atoms decrease, and as a result so will the dose rate. As a result of this the time needed to treat a patient gradually lengthens and eventually, when the treatment time becomes excessive, the source has to be replaced, which should occur approximately every 3 years. (Pamcherry and Angela Duxbury, 2009).

1.7 . **linear accelerators unit**

Linear accelerators are machines that consist of a number of discrete components functioning together to accelerate electrons to a high energy using radiofrequency (RF) waves before the electrons ' hit ' a target to produce X - rays. After this the X -ray profile is flattened, shaped (collimated) and measured before clinical use. Linear accelerators are now also capable of producing X -ray beams of different energy (multi - energy units) and/or

producing both X - rays and electrons (multimodal units). (Pamcherry and Angela Duxbury, 2009).

1.8 . Problem statement:

The prostate cancer is the most common male cancers in Sudan; patients usually present with either locally advance or metastases. Radiation therapy is the main modality of treatment for majority of patients. Dose escalation over 50 Gy is usually not possible due to the limiting radiation therapy facilities available in Sudan.

1.9 Objectives:

The main objective of this study is to design a protocol system for treatment planning of prostate carcinoma using limited radiation therapy facilities available in Sudan.

Specific objectives

-To develop standard CT-base anatomy model for radiation therapy planning of prostate carcinoma

-To develop protocol system for optimization of radiation dose distribution using

Optimum multiple fields

Optimum field's arrangement

Optimum fields weighting factors

Optimum beam modifiers

1.10 importance of the study:

This study is conducted to improve the quality of radiotherapy treatment in Sudan by providing information about the possibility of using the limited facilities such as cobalt 60 machine to obtain a similar result using linear accelerator machine.

1.11 Overview of the study

This study falls into 5 chapters where chapter one includes general introduction while chapter two literature review (theoretical background and previous studies) in chapter three the materials and methods, chapter four, the discussion of the data, chapter five , results ,conclusions and recommendations.

Chapter 2

Literature review

Chapter 2

Literature review

2.1 Background theory

2.1.1 Prostate

The prostate is a walnut-sized organ located below the bladder and in front of the rectum in the male reproductive system that normally feels like the ball portion of the palm of a man's hand. It surrounds part of the urethra, the tube that carries urine from the bladder to outside the body. The gland's main function is to produce fluid for semen, which nourishes and transports sperm cells. (UCSF, 2009)

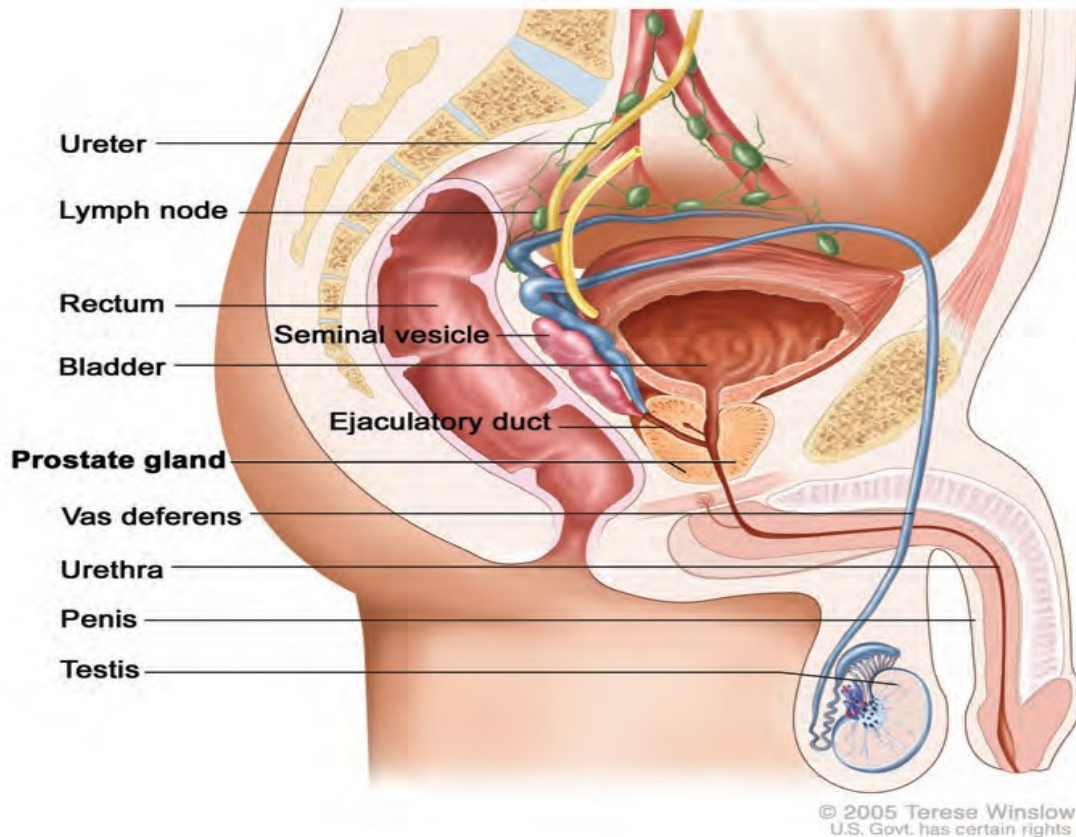


Figure 2.1 location of prostate and surrounding structures adopted from www.pcf.org [Accessed 8.5.2012]

2.1.1.1 Anatomy and physiology

The term "prostate", originally derived from the Greek word *prohistani* which means "to stand in front of," has been attributed to Herophilus of Alexandria who used the term in 355 B.C.E. to describe the small organ located in front of the bladder. The prostate gland is a small firm organ, about the size of a chestnut, located below the bladder and in front of the rectum. The urethra, the channel through which urine is voided, passes from the bladder and through the prostate and penis. The primary function of the prostate gland, which contracts with ejaculation, is to provide enzymes to maintain the fluid nature of seminal fluid and to nourish sperm as they pass through the prostatic and penile urethra to outside the body. (Kirby et al, 1996.)

Contraction of the smooth muscle expels the contents from the gland and provides part of the propulsive force needed to ejaculate the semen. The thin, milky-colored prostatic secretion assists sperm cell motility as a liquefying agent, and its alkalinity protects the sperm in their passage through the acidic environment of the female vagina. The prostate also secretes the enzyme acid phosphates, which is often measured clinically to assess prostate function. The discharge from the prostate makes up about 40% of the volume of the semen.

Blood is supplied to the prostate from branches of the middle rectal and inferior visceral arteries. The venous return forms the prostatic venous plexus, along with blood draining from the penis. The prostatic venous plexus drains into the internal iliac veins.

The prostate has both sympathetic and parasympathetic innervations arising from the pelvic plexuses.

2.1.1.2 Types of prostate cancers and stages

When cells grow abnormally and become a mass, it is called a tumor. Some tumors are benign (not likely to be life-threatening) and others are malignant (cancerous and potentially life threatening). Over time, some prostate cells may become cancerous. Sometimes, the cancer can be very small, localized, and confined within the prostate. Most often, however, the cancer is present in more than one site, often on both sides of the gland. Through a process called metastasis, the cancer cells can spread outside the prostate to nearby lymph nodes or organs in the pelvic area. They eventually can spread to more distant parts of the body, through the blood and lymph systems, most often to the bones. Determining whether the cancer is confined to the prostate, or whether it has spread either locally or to more distant sites, is very important in selecting treatment. (UCSF, 2009)

Prostate cancer is predominantly a disease of older men but around 20% of cases occur in men under the age of 65 years. Over the past 10 to 15 years there have been a number of significant advances in prostate cancer management but also a number of major controversies, especially about the clinical management of men with early, non-metastatic disease. These uncertainties clearly cause anxieties for men with prostate cancer and their families (Cancer Research UK (2007))

2.1.1.2.1 Types of prostate cancers

Several types of cells are found in the prostate, but almost all prostate cancers develop from the gland cells. Gland cells make the prostate fluid that is added to the semen. The medical term for a cancer that starts in gland cells is a adenocarcinoma. Other types of cancer can also start in the prostate gland, including sarcomas, small cell carcinomas, and transitional cell carcinomas. But these types of prostate cancer are so rare that if you have prostate cancer it is almost certain to be a adenocarcinoma. The rest of this document refers only to prostate a adenocarcinoma. Some prostate cancers can grow and spread quickly, but most grow slowly. In fact, autopsy studies show that many older men (and even some younger men) who died of other diseases also had prostate cancer that never affected them during their lives. In many cases neither they nor their doctors even knew they had it. Possible pre-cancerous conditions of the prostate some doctors believe that prostate cancer starts out as a pre-cancerous condition, although this is not yet known for sure. (American Cancer Society, 2009)

Prostatic intraepithelial neoplasia (PIN) ;In this condition, there are changes in how the prostate gland cells look under the microscope, but the abnormal cells don't look like they are growing into other parts of the prostate (like cancer cells would). Based on how abnormal the patterns of cells look, they are classified as: Low-grade PIN: the patterns of prostate cells appear almost normal.(American Cancer Society,2009)

High-grade PIN: the patterns of cells look more abnormal PIN begins to appear in the prostates of some men as early as their 20s. Almost half of all men have PIN by the time they reach 50. Many men begin to develop low-grade PIN at an early age but do not necessarily develop prostate cancer. The importance of low-grade PIN in relation to prostate cancer is still unclear. If a finding of low-grade PIN is reported on a prostate biopsy, the follow-up for patients is usually the same as if nothing abnormal was seen. (American Cancer Society,2009)

If high-grade PIN has been found on your prostate biopsy, there is about a 20% to 30% chance that you also have cancer in another area of your prostate. This is why doctors often watch men with high-grade PIN carefully and may advise them to have a repeat prostate biopsy, especially if the original biopsy did not take samples from all parts of the prostate. (American Cancer Society,2009)

Proliferative inflammatory atrophy (PIA); this is another finding that may be noted on a prostate biopsy. In PIA, the prostate cells look smaller than normal, and there are signs of inflammation in the area. PIA is not cancer, but researchers believe that PIA may sometimes lead to high-grade PIN, or perhaps to prostate cancer directly.(American Cancer Society,2009)

2.1.1.2.2 Grading and Staging

2.1.1.2.2.1 Grading of cancer

If cancer is found in the prostate biopsy sample, it is graded to estimate its aggressiveness. The most commonly used prostate cancer grading and scoring system is called the Gleason system. The pathologist examines the cancer cells under a microscope and evaluates how closely the arrangement of the cancer cells matches that of normal prostate cells. For each sample, two grading assessments are made. The first is an estimate of the most common cancer cell pattern, and the second is of the next most common cancer cell pattern. These are done on a scale of 1 (most like normal cells) through 5 (least like normal cells). (UCSF, 2009)

The two grades are then added (e.g., $3+2=5$) to give the Gleason score or sum, with a range of 2 to 10. The Gleason score is essential for treatment planning and decision-making. Every prostate cancer patient should know his Gleason score. Those with low scores (6 or less) are more likely to have a less aggressive, slower growing cancer. Gleason 6 is the most common score. Gleason 7 indicates intermediate risk; a Gleason 3+4 may be a less aggressive cancer than a 4+3, so knowing both the primary and secondary grades is helpful. Gleason scores of 8 to 10 indicate high-risk cancers that could grow and spread more rapidly. Since the most accurate grading of the cancer is, in part, a function of the skill and experience of the pathologist, it may be appropriate to get a second opinion for the Gleason score. Ideally, the pathology report should provide for each of the biopsy cores containing cancer tissue the following information (which

can help in evaluating cancer and planning treatment).(UCSF, 2009)

2.1.1.2.2.2 Staging of cancer

A prostate cancer's stage indicates how far it has spread, and is very important in selecting treatments and in predicting prognosis or the future of the disease. The commonly used staging system is the TNM system. This describes the extent of the primary tumor (T), the absence or presence of metastasis to nearby lymph nodes (N) and the absence or presence of distant metastasis (M). (UCSF, 2009)

There are two types of T classifications for prostate cancer. The clinical stage is based on the digital rectal examination, and imaging findings. The pathological stage is based upon surgical removal of the entire prostate gland, the seminal vesicles (which are two small sacs that store semen), and sometimes nearby lymph nodes. The clinical stage is used in making treatment decisions. This is the best estimate short of surgery, but may underestimate the extent of cancer development and spread. (UCSF, 2009)

The pathological stage determination is more thorough, and therefore more accurate in making a prognosis and indicating the need for further treatment. However, it can be determined only with patients who have had a radical prostatectomy or a biopsy of tissue confirming the presence of disease beyond the prostate (e.g. Seminal Vesicles). (UCSF, 2009)

T1 - Refers to a tumor that is not felt during a digital rectal exam. T1a (5% or less of specimen involved in tumor) and T1b (more than 5% tumor involved) describe cancers found incidentally during a TURP (transurethral resection of the prostate, a surgical procedure done to relieve symptoms of benign prostatic hyperplasia), where examination of the removed prostate tissue reveals cancer. T1c cancers are those detected by an elevated PSA only and which are then diagnosed with a biopsy. T1c is now the most common stage for newly diagnosed men.(UCSF, 2009)

T2 - Refers to a cancer that is felt by the doctor during the digital rectal examination, or is seen with imaging studies, and is believed to be confined within the prostate gland. If the cancer is in one half or less of only one side of the prostate, the stage is T2a. If the cancer is in more than one half of only one side of the prostate, the stage is T2b. If the cancer is in both sides of the prostate, the stage is T2c.(UCSF, 2009)

T3 - Refers to a cancer that has extended beyond the capsule of the prostate and/or to the seminal vesicles, as indicated by imaging studies or biopsy. If the cancer can be felt during a DRE, and extends outside the prostate on one side, but not to the seminal vesicles, the stage is T3a. If the cancer has spread to the seminal vesicles, the stage is T3b.(UCSF, 2009)

T4 - The cancer has spread to other organs next to the prostate, such as the bladder's external sphincter (which helps control urination), the rectum, and/or the wall of the pelvis. Imaging tests

are usually necessary to detect this more advanced tumor stage. (UCSF, 2009)

N Categories - N0 means the cancer has not spread to any lymph nodes. N1 or N+ indicates spread to one or more regional pelvic lymph nodes. (Nx indicates that regional lymph nodes have not been assessed.)(UCSF, 2009)

M Categories - M0 means the cancer has not metastasized beyond the regional nodes. M1a means metastases are present in distant lymph nodes. M1b means the cancer has spread to the bones. M1c means the cancer has spread to other distant organs such as the lungs, liver, or brain, with or without bone disease. The site(s) of the metastases may be specified. (Mx indicates that distant metastases have not been assessed.)(UCSF, 2009)

2.1.1.3 Diagnostic work up

Early detection of PCa is a key to survival. Unfortunately, routine medical tests like measuring blood concentration of prostate specific antigen (PSA), digital rectal examination (DRE), transrectal ultrasound (TRUS), and biopsy. (Ski Jacek, 2010)

Prostate cancer diagnosis begins with a digital rectal examination (During this examination, a doctor inserts a gloved, lubricated finger into a man's rectum to feel for any irregular or abnormally firm area in the prostate. Most prostate cancers cannot be detected this way). (A special program of Project Cure Foundation, 2007)

Additional tests such as a Transrectal or transperineal needle biopsy can detect small prostatic nodules or more advanced

cancerous growth. Transrectal ultrasound is also used for both diagnosis and to help guide needle biopsy. Serum acid phosphatase levels can be elevated when there is local extension or metastasis of disease. However, other conditions such as benign prostatic hyperplasia, multiple myeloma, Gaucher's disease, and hemolytic anemia can also raise these levels. (A special program of Project Cure Foundation, 2007)

Radioimmunoassay analysis of prostate-specific antigen (PSA) is a protein in the blood that is produced only by prostate cells. PSA reflects the volume of both normal and cancerous prostate tissue. The higher the PSA level, the more likely prostate cancer is present. The PSA test results are reported as nanograms per milliliter (ng/ml). (A special program of Project Cure Foundation, 2007)

In the past, results of less than or equal to 4.0 ng/ml were considered normal, and values above that were regarded as high) has become a standard test for diagnosing both localized as well as metastasized stages of the prostate cancer. Though controversial, PSA is the most sensitive marker for monitoring disease and is elevated in 25 to 92% of patients with prostate cancer. However, it is also raised in 30 to 50% of those with BPH. (A special program of Project Cure Foundation, 2007)

Prostate cancer often leads to osteoblastic (bone-formation cells) bony metastases, which are often detected on bone scans or x-rays of prostate cancer patients. Physicians often have difficulty in identifying what types of prostate cancers will spread and become

dangerous. A new protein called KAI-1 has been identified as a marker for disease. If significant levels of KAI-1 are found in cancerous tissues, the cancer is not likely to spread. If the protein is not found, cancer typically spreads. (A special program of Project Cure Foundation, 200 7)

Prostate cancer has been classified into four stages: Stage A. The tumor is not found by normal tests but during surgery for a different prostate condition. Stage B. The tumor can be palpated during rectal examination but it has not spread beyond the prostate Stage C, Cancer has spread to tissues outside of the prostate. Stage D, The cancer has metastasized to the lymph nodes of the pelvis or to other parts of the body, especially the bones.(A special program of Project Cure Foundation, 200 7)

2.1.1.3.1 Biopsy

The aim of prostate biopsy is to detect prostate cancers with the potential for causing harm rather than detecting each and every cancer. Men with clinically insignificant prostate cancers that are unlikely to cause symptoms or affect life expectancy may not benefit from knowing that they have the disease. Indeed, the detection of clinically insignificant prostate cancer should be regarded as an under-recognized adverse effect of biopsy. (National Institute for Health and Clinical Excellence, 2008)

2.1.1.3.1.1 Needle biopsy

Making a formal diagnosis of prostate cancer requires a needle biopsy. The samples obtained from the prostate are then

examined by a pathologist in a laboratory to confirm the diagnosis.(UCSF, 2009)

2.1.1.3.1.2 Transrectal ultrasound (TRUS) guided biopsy

A TRUS uses sound waves produced by a small probe placed in the rectum to create an image of the prostate on a video screen. The transrectal ultrasound also can sometimes provide valuable information about whether the cancer has reached the edge of or broken through the capsule of the prostate gland. It also provides an estimate of the size of the prostate. While the image can reveal suspicious areas that should be sampled, multiple other areas of the prostate should be sampled for tumors that do not show on ultrasound. An instrument called a biopsy gun quickly inserts and removes narrow needles, obtaining cores of tissue about one half inch long that are sent to the laboratory for examination. A minimum of 8 cores and up to 20 should be removed from different areas of the prostate and especially from the more suspicious locations. The patient should not fear this procedure. It usually causes only mild discomfort, a little bleeding, and takes less than half an hour. An antibiotic is usually given prior to and following the procedure to reduce the risk of infection. (UCSF, 2009)

2.1.1.3.2 Imaging

The clinical presentation and the treatment intent influence the decision about when and how to image an individual. Men with localized prostate cancer are stratified into risk groups according to their risk of recurrence (see table 2.1).

PSA		Gleason score		Clinical stage	
Low risk	< 10 ng/ml	and	≤ 6	and	T1-T2a
Intermediate risk	10-20 ng/ml	or	7	or	T2b-T2c
High risk	> 20 ng/ml	or	8-10	or	T3-T4

Table 2.1 Risk stratification for men with localized prostate cancer adopted from (National Institute for Health and Clinical Excellence, 2008)

Healthcare professionals should determine the provisional treatment intent (radical or non-radical) before decisions on imaging are made. Imaging is not routinely recommended for men in whom no radical treatment is intended. Computerized tomography (CT) of the pelvis is not recommended for men with low- or intermediate-risk localized prostate cancer (see table 2.1). (National Institute for Health and Clinical Excellence, 2008)

Men with high-risk localized (see table 2.1) and locally advanced prostate cancer who are being considered for radical treatment should have pelvic imaging with either magnetic resonance imaging (MRI), or CT if MRI is contraindicated. Magnetic resonance spectroscopy is not recommended for men with prostate cancer except in the context of a clinical trial. Isotope bone scans are not routinely recommended for men with low-risk localized prostate cancer. Isotope bone scans should be performed when hormonal therapy is being deferred through watchful waiting in asymptomatic men who are at high risk of

developing bone complications. Positron emission tomography imaging for prostate cancer is not recommended in routine clinical practice. (National Institute for Health and Clinical Excellence, 2008)

2.1.1.3.2.1 Bone Scan

A radionuclide bone scan can show whether the cancer has spread from the prostate to the bones. Some low level radioactive material is taken into the body by injection and will be taken up by diseased bone cells. This allows the location of diseased bone to be seen on the total body bone scan image. These areas may suggest that metastatic cancer is present, but arthritis and other bone diseases could create a similar pattern. Very small metastases may not be detected by this scan. Usually, a bone scan is not ordered unless there are signs of aggressive disease such as an elevated PSA level (>15ng/ml), a high Gleason grade (a prostate cancer grading system described later in the guidelines), a large tumor, or bone pain.(UCSF, 2009)

2.1.1.3.2.2 Computed Tomography (CT scan or CAT scan)

Using; a rotating X-ray beam to create a series of pictures of the body from many angles that can be put together into a detailed cross-sectional image. This can help reveal abnormally enlarged pelvic lymph nodes, or spread of the cancer to other internal organs. A CT scan usually isn't ordered unless there is an elevated PSA (>20ng/ml), a high Gleason score or primary Gleason grade of 4, or evidence of a large tumor.(UCSF, 2009)

2.1.1.3.2.3 Magnetic Resonance Imaging (MRI)

It is like a CT scan except that magnetic fields are used instead of X-rays to create the detailed images of selected areas of the body. These scans are not effective in revealing microscopic-sized cancers, although an MRI using an endorectal coil is superior to a routine pelvic MRI as it images the prostate gland itself better. (UCSF, 2009)

2.1.1.3.2.4 Color Doppler Ultrasound

This is a refinement of the standard transrectal ultrasound, which produces only black and white images. The Color Doppler machine can detect blood flow patterns; cancerous areas sometimes show an increase in the density of the blood vessels. Only the prostate gland and immediate adjoining tissues are imaged.(UCSF, 2009)

2.1.1.1.3.2.5 Magnetic Resonance Spectroscopy Imaging (MRSI)

This is a refinement of the endorectal MRI. Magnetic resonance spectroscopy detects the levels of certain compounds that are present in different amounts in benign and cancerous prostate tissues. These are then mapped on a regular MRI image to indicate possible cancer sites. This method can produce findings for the prostate gland, but does not image the lymph nodes. This study may be useful in monitoring the prostate after radiation therapy as well. Currently, it remains investigational.(UCSF, 2009)

2.1.1.4 Types of prostate carcinoma treatments

Prostate cancer that is localized is typically treated with radiation therapy or radical prostatectomy (excision of part or all of the prostate gland). This operation is performed through incision in the perineum, into the bladder, or through the urethra. Libido is typically unaffected by prostatectomy but some 30% of patients become impotent after the procedure.(A special program of Project Cure Foundation, 200 7)

A more common complication following a radical prostatectomy is the development of urinary incontinence. When disease has significantly progressed beyond this stage, or when the patient is very old or in poor health, these treatment approaches may not be used. These patients may be treated with irradiation, hormone therapy, or the surgical removal of the testicles. One of the hormonal therapies, oral diethylstilbestrol, has been given to prostate cancer patients in doses of 1 to 3 mg/day and has demonstrated some success over long periods of time. Long-term use of such estrogen therapies increases the risk of developing thromboembolic (blocking of a blood vessel by a thrombus) complications. Additional adverse effects caused by estrogen therapies can include breast tenderness, breast enlargement, nausea, vomiting and loss of sexual desire, impotence, and water retention. Short-term use of agents such as high-dose diethylstilbestrol diphosphate can lead to substantial relief in patients within days.(A special program of Project Cure Foundation, 200 7)

A variety of agents are used to decrease testosterone levels circulating in the body. These agents include flutamide, cyproterone acetate, ketoconazole, aminoglutethimide, and analog agents of luteinizing hormone-releasing hormone. Surgical removal of the testicles is sometimes performed when the disease has advanced or when hormone therapy has failed. The use of local radiation therapy has been found to be effective in relieving pain associated with cancer metastasis into the bones. Local radiation therapy can also help limit disease to the prostate. Chemotherapy has generally not been effective once hormonal therapy has failed. It is also associated with severe adverse effects such as nausea, vomiting, lowered blood and immune system factors, and hair loss.(A special program of Project Cure Foundation, 200 7)

Prostate cancer, unlike cancers of other sites, often has a very indolent natural history. Whereas patients with any other curable cancer would automatically be offered radical treatment, “watchful waiting” has been a recognized approach to managing prostate cancer, with acceptable results in selected patients(Albertsen PC, Hanley JA, Gleason DF, et al. Competing risk analysis of men aged 55 to 74 years at diagnosis managed conservatively for clinically localized prostate cancer. In fact, the first good evidence that some men benefit from radical treatment of localized prostate cancer has only recently become available. (Chris Parker, 2004)

2.1.1.4.1 Radiotherapy

The extent of the irradiation area (field size) is an important issue, because the larger the area treated, the more normal tissues are incidentally irradiated, and the more frequent and severe the side effects (conversely, the smaller the field size, the more likely that the entire tumor will not be adequately treated). Field size is driven both by clinical decisions about the extent of disease, as well as by technical factors regarding prostate visualization and prostate motion. Many technological advances in radiation therapy focus on minimizing the treated volume to minimize toxicity. Prostate cancer typically arises in multiple foci within the prostate gland, and thus far no imaging methods have been able to reliably identify involved areas of the prostate. For now, the entire prostate gland typically serves as the target for radiation. For some prostate tumors, there can be subclinical microscopic extension outside of the prostate into the surrounding tissues, seminal vesicles, and regional lymph nodes. There is no definitive evidence available to guide radiation oncologists on when to treat just the prostate gland, when to irradiate some of the surrounding tissues, when to irradiate the seminal vesicles, and when to treat the lymph nodes. First efforts at targeting the prostate used plain x-rays for visualization. Unfortunately, the prostate gland cannot be reliably distinguished from the surrounding soft tissues on plain films. This method of treatment planning is called two-dimensional planning. Development of CT scans for treatment

planning in the 1980's resulted in better visualization of the prostate gland and the lymphatic drainage. (Stanley et al, 2010)

Prostate cancer is now the commonest cancer in men, accounting for almost 25 per cent of all new male cancer diagnoses and is the second most common cause of cancer related death in men. There has been a huge rise in the recorded incidence of prostate cancer with the use of prostate-specific antigen (PSA) and surgery for benign prostatic hypertrophy (BPH), but this is not reflected in increased mortality rates. There are almost 32 000 new cases and 10 000 deaths from prostate cancer a year in the UK. However, most men die with their prostate cancer rather than from it and management must balance the potential toxicity of active treatment, with the chances of benefit in a disease with a long natural history. (Barrett Ann et al , 2009)

Advances in diagnosis and screening policies with the use of PSA have led to a stage migration so that prostate cancer is now detected at earlier stages with better prognostic features. The most common type of prostate cancer is a adenocarcinoma (95 per cent). Tumours are graded using the Gleason scoring system which evaluates architectural details of individual cancer glands and describes five distinct growth patterns from Gleason 1 (well differentiated) to Gleason 5 (poorly differentiated). The two commonest growth patterns seen are summated to give a final Gleason score (GS) ranging from 2 (1 + 1) to 10 (5 + 5). There are other rarer types of prostate carcinoma such as ductal, intralobular acinar, small cell and clear cell. There is less evidence

to guide treatment of other pathological subtypes. Prostate cancer is staged using the AJCC and TNM staging. (Barrett Ann et al , 2009)

Tumours are stratified by T stage, GS and PSA into three prognostic groups of low, intermediate and high risk:low risk: T1-T2a and PSA \leq 10 ng/mL and GS \leq 6 ,intermediate risk: T2b or PSA 10-20 ng/mL or GS 7 ,high risk: T2c-T4 or PSA \geq 20 ng/mL or GS 8-10.The risk is higher in an intermediate risk patient who has GS 4 \geq 3 than with GS 3 \leq 4. Patients can be offered appropriate treatment options by a multidisciplinary team, according to stage of disease, prognostic risk group and estimated survival taking into account performance status and co morbidity. (Barrett Ann et al , 2009)

2.1.1.4.1.1 Curative radiotherapy

External beam radiation therapy, interstitial brachytherapy and surgery are options for the curative treatment of localized prostate cancer with equivalent outcomes but different side effects. Factors that influence the choice include PS, other medical illnesses, likelihood of progression to symptomatic disease, life expectancy, morbidity of treatment (particularly on sexual function) and patient preference.(Barrett Ann et al , 2009)

In general patients should have a life expectancy of greater than 10 years before radical treatment is recommended. Men younger than 75 with other major illnesses such as ischaemic heart disease and diabetes may not live 10 years and men over 75 with no other illnesses may live into their nineties. There is evidence

that radical radiotherapy in fit men over 75 is very well tolerated and just as effective. It is the role of the multidisciplinary team to identify patients who will benefit from radical treatment and counsel the patient on the different options available. Radical treatments with surgery, EBRT or brachytherapy have similar outcomes and the patient should be informed of the different side effects of each treatment. Factors that influence the final choice for an individual patient include lower urinary tract symptoms, sexual function, likelihood of infertility, and risks of anaesthesia and surgery. (Barrett Ann et al , 2009)

2.1.1.4.1.3 Pelvic lymph node radiotherapy

Selected patients may benefit from radiotherapy to the pelvic lymph nodes with the prostate and seminal vesicles. A randomized trial has shown that patients with a risk of lymph node involvement between 15 per cent and 35 per cent may benefit from pelvic lymph node irradiation. However, although pelvic radiotherapy has shown a trend to improved 5-year progression-free survival, but not overall survival, this benefit is only seen in patients receiving neoadjuvant, concurrent and adjuvant hormone therapy. This has to be balanced with the increased toxicity associated with WPRT. With modern techniques, including IMRT and IGRT, this balance may become more favourable. (Barrett Ann et al, 2009)

2.1.1.4.1.4. Adjuvant and salvage radiotherapy

Adjuvant radiotherapy is not given routinely when PSA levels are undetectable after surgery to avoid overtreatment of the majority

of patients already cured. If the PSA is persistently raised following surgery, it may indicate local or metastatic disease. After negative staging investigations, metastases are still likely if the PSA doubling time is ≥ 9 months, and local radiotherapy is therefore not recommended. Seminal vesicle or lymph node involvement, especially with a high Gleason score, also correlates with risk of metastases and makes radical local radiotherapy inappropriate. If there is a persistently raised PSA with a doubling time ≥ 9 months and there are positive margins at the site of extra capsular extension, local radiotherapy should be considered. Results are better with early salvage radiotherapy when the PSA is ≥ 1.2 ng/mL (or 0.2 with the supersensitive assay). In patients in whom PSA later rises on three consecutive occasions (ASTRO definition of biochemical failure), salvage radiotherapy is also offered. Clinical trials of radiotherapy may be appropriate for patients with high risk factors for local recurrence but undetectable PSA. (Barrett Ann et al, 2009)

2.1.1.4.2.5 Palliative radiotherapy

Prostate and pelvis patients with extensive local disease in the prostate and/or pelvis may benefit from a course of palliative EBRT to relieve symptoms. Bleeding from the prostate may also be alleviated by EBRT. (Barrett Ann et al , 2009)

2.1.1.4.1.5.1 Bone and lymph node metastases

External Beam Radiation Therapy (EBRT) is an excellent treatment for palliation of pain from symptomatic bone metastasis. A single fraction of 8 Gy is very effective with few side effects. A fractionated course of EBRT may be used to treat spinal cord compression, and is given postoperatively following orthopaedic fixation of pathological fractures. Symptoms from lymph node and visceral metastases can also be relieved by EBRT. (Barrett Ann et al, 2009)

Radionuclide therapy; Patients with metastatic bone disease and multiple painful sites can be difficult to treat with EBRT to localised areas. The radionuclides strontium and samarium have been shown to be beneficial in reducing symptoms from bone metastases. This treatment is only considered for patients with good bone marrow reserve, no imminent risk of cord compression and no nodal or visceral metastases.(Barrett Ann et al , 2009)

2.1.1.4.1.5.2. Breast buds

Gynaecomastia is a major problem for patients on long-term anti-androgen and oestrogen therapy. Superficial X-ray or electron therapy (9-12 MeV) to the breast bud area using a 7-9 cm diameter circular field has been shown to reduce the incidence significantly when used prophylactically. In established cases, radiotherapy can reduce symptoms.(Barrett Ann et al, 2009)

2.1.1.4.1.6 External beam radiation therapy and hormone therapy

Hormone therapy before, during and after EBRT (neoadjuvant, concurrent and adjuvant androgen deprivation [NCAD]) has been proven to increase local control, disease-free survival and overall survival for selected patients with prostate cancer. Androgen deprivation reduces the size of the prostate by 30 per cent and the number of tumour cells, possibly through synergistic apoptotic mechanisms. Six months NCAD can be used with EBRT for low and intermediate risk disease to reduce the target volume and allow safer dose escalation. Treatment must be started at least 2 months before radiotherapy. (Barrett Ann et al, 2009)

2.1.1.4.1.7. External beam radiation therapy and brachytherapy boost

High Dose Rate and Low Dose Rate brachytherapy may be used as a boost after EBRT to escalate dose to the prostate. Radionuclide therapy to patients with metastatic bone disease and multiple painful sites can be difficult to treat with EBRT to localised areas. The radionuclides strontium and samarium have been shown to be beneficial in reducing symptoms from bone metastases. This treatment is only considered for patients with good bone marrow reserve, no imminent risk of cord compression and no nodal or visceral metastases. (Barrett Ann et al, 2009)

2.1.1.4.2 Radiotherapy techniques and planning in prostate carcinoma

Advances in image-based treatment planning and localization have contributed to better targeting of the prostate. External

beam radiation therapy (EBRT) leads to outcomes equivalent to those of radical prostatectomy and brachytherapy when case selection factors and quality of treatment delivery are controlled. Newer radiation therapy (RT) techniques that allow better targeting of the prostate and greater sparing of normal tissues have led to an improved therapeutic ratio. Lowering doses to surrounding critical structures and simultaneous safe target dose escalation have become possible. This review will detail the practical elements of radiation dose delivery, including patient setup and immobilization, target volume definition, treatment planning, treatment delivery methods, and tools to verify target localization during a course of EBRT.(Abdel-WahabMay,2011)

2.1.1.4.2.1 Patient Immobilization

Immobilization devices are widely used to allow the use of smaller margins, thus reducing the dose to the surrounding normal tissues .Although some studies suggest that they significantly reduce large day-to-day setup errors are significantly reduced with the use of patient immobilization devices, this conclusion is not universal .The average deviation of the isocenter position from the time of simulation-to-treatment has been shown to be smaller when patients are immobilized as compared to anon immobilized control group.(Abdel-WahabMay,2011)

A well-thought-out and simple device that allows a comfortable and reproducible setup can reduce large errors. The commonly used immobilization devices are constructed of a melted plastic mold material, a solidified foam mold, or a reusable inflatable

mold device. Furthermore, it is important to note that in the era of image guidance, the need for rigid fixation devices has been questioned. Alternative options such as leg and ankle support, which may be more comfortable to the patient, have been suggested when positioning is later confirmed by image guidance. (Abdel-WahabMay,2011)

2.1.1.4.2.2 Patient Positioning

Patient position during simulation treatment has been extensively studied. More recent studies have confirmed that there is no benefit to using the prone position as compared to the supine position. In the prone position there may be greater rectal sparing, particularly in patients with large seminal vesicles (SVs). However, a larger percentage of the bladder may be included, which slightly increases the probability of complications. There may also be more patient setup movement errors because some patients find the prone position less comfortable. Furthermore, the prone position appears to be associated with greater prostate motion from normal breathing. The increased intra-abdominal pressure associated with breathing in a prone position results in significant movement of the prostate and SVs evaluated the impact of breathing on the position of the prostate gland in four patients treated in four different positions in whom radiopaque markers were implanted in the periphery of the prostate using transrectal ultrasound (US) guidance prior to simulation. (Abdel-WahabMay,2011)

2.1.1.4.2.3 Retrograde Urethrography

Retrograde urethrography (RUG) was commonly used in the past to help determine the level of the prostatic apex. However, it is no longer widely used, due to the possibility of complications and apex displacement, even though a carefully administered RUG does not significantly alter the position of the prostate gland. Magnetic resonance imaging (MRI) has largely superseded urethrography as a tool to help delineate the prostatic apex. Nevertheless, RUG sometimes used in conjunction with CT scanning if an MRI is not available or in patients with contraindications to MRI (eg, pacemakers). (Abdel-Wahab May, 2011)

2.1.1.4.2.4 Computed Tomography-Based Prostate Localization

CT simulators are readily available in most radiation oncology departments. Typically the location of the apex can be resolved to two or three CT slices obtained at 3-5 mm intervals and, in the hands of experienced radiation oncologist, the use of CT may be adequate. Furthermore, inter observer variations can be reduced by learning to define the prostate on CT after studying the common sites of target definition errors using MRI prostate volumes defined by an expert radiologist. The radiation oncologist should use multi planar reconstructions to facilitate prostate definition on a treatment planning CT and image registration of MRI images with CT images can aid apex definition on a CT scan. (Abdel-Wahab May, 2011)

2.1.1.4.2.5 Magnetic Resonance Imaging-Based Prostate

2.1.1.4.2.5.1 Localization

MRI may be more accurate in delineating the prostate and SVs than CT. CT overestimates the size of the gland approximately 27%-32%. The greatest systematic discrepancy between the gross tumor volumes (GTVs) is that the posterior apical prostate border was 3.6 mm more posterior on MRI than on CT-defined contouring. Furthermore, MRI was found to be superior to CT or urethrography for localizing the prostatic apex. Endorectal MRI may detect extra capsular tumor extension, SV invasion, or neurovascular bundle involvement with greater sensitivity, specificity, and accuracy than clinical findings alone. Magnetic resonance spectroscopy (MRS) can detect variable concentrations of citrate, choline, and creatine in prostate tissue and improve the accuracy of detecting and localizing prostate cancer. MRI may also allow better identification of structures adjacent to the prostate that are associated with erectile function. (Abdel-WahabMay,2011)

2.1.1.4.2.6 Defining the Gross Tumor Volume and the Clinical Target Volume

The entire gland is commonly considered the GTV for radiation treatment planning purposes because prostate cancer is often found to be multifocal at the time of radical prostatectomy. The clinical target volume (CTV) may expand the GTV to account for direct extension, or the CTV can be extended to encompass adjacent organs or regions of spread. In prostate cancer, the CTV

may encompass the SVs and possibly the regional pelvic lymph nodes. (Abdel-WahabMay, 2011)

GTV (gross tumor volume): Tumor only, no margin. The entire prostate gland as determined by a CT scan commonly defines the GTV. Gross extension beyond the gland in a patient with a clinical stage T3-4 cancer should be included as the GTV.

CTV (clinical target volume): Includes margin around the GTV for regions of microscopic risk. This can include adjacent regions at risk of having subclinical disease, such as the SVs or pelvic lymph nodes.

PTV (planning target volume): Includes margin around the CTV to allow for patient movement, setup nerror, and organ movement.(Abdel-WahabMay,2011) ref9

2.1.1.4.2.7 Planning Target Volume Margins

The magnitude of the PTV margin depends on several factors. Treatment setup errors can vary by the method of patient positioning and immobilization. Internal organs, including the prostate gland, can shift because of variable filling of the rectum and bladder. The shifts can be asymmetric, with most movement occurring in the AP directions. In order to assure that an adequate radiation dose treats the CTV, an appropriate PTV margin must be added. However, the method of localization must be taken into account when determining the PTV margin. Methods that allow corrections for intra-fraction motion may allow smaller PTV margins. In addition, visual display tools in planning systems allow visualization of multileaf collimator (MLC) in respect to PTV. The MLC's position to define beam apertures in 3DCRT or to create

intensity maps in IMRT can be estimated on beam eye view. The magnitude of OAR sparing or PTV coverage can be visualized and judged accordingly.(Abdel-WahabMay,2011)

2.1.1.4.2.8 Localization for Prostate Radiation Therapy

High precision is extremely important in limiting toxicity after dose escalation. IMRT has emerged as the most current available treatment planning technology. IMRT planning begins in nearly an identical manner to that of forward planned 3DCRT; however, patient positioning and reproducibility are far more critical due to the sharp dose gradients that can be seen with this modality. (Abdel-WahabMay,2011)

Every effort is made to maintain accuracy while decreasing margin. The daily target localization method is critical in patients receiving IMRT for prostate cancer. Suitable methods include transabdominal US, intraprostatic fiducial markers with daily megavoltage portal or radiographic imaging, endorectal balloon immobilization, or daily in-room CT imaging. IMRT treatment planning requires defining dose constraints for the target and each critical structure. IMRT creates more heterogeneity of dose than 3DCRT, and the planning prescription needs to define a minimum dose to cover a predetermined volume of the PTV as well as a maximum dose to a small volume inside the PTV. Dose limits to OAR need to take into account both upper dose limits and the volume of those organs that are allowed to exceed those limits. By definition, PTV accounts for setup error and internal organ motion. Many studies have used different tools to define

the optimum PTV margin, and this margin depends on the tracking technology used, as well as the method used to adapt to this motion.(Abdel-WahabMay,2011)

Use of IGRT in prostate cancer has improved results and allowed safe and effective dose escalation. The quality assurance strategy differs by method of localization and institutional preference. New strategies to reduce the uncertainty in daily treatment delivery and the magnitude of the PTV margin have been introduced. These methods employ daily imaging of the prostate in the treatment room. Setup correction using bony landmarks, as opposed to skin marks, were the acceptable standard before wide use of implantable fiducial markers.(Abdel-WahabMay,2011)

Care should be taken when adapting to prostate motion while pelvic lymph nodes are treated, as this may lead to degradation of the dose to pelvic lymph node PTV. Deformation of prostate shape, radiation exposure as well as inability to visualize OAR is some of the limitations of using fiducials alone for tracking. (Abdel-WahabMay,2011)

2.1.1.4.2.8 Transabdominal Ultrasound

Transabdominal US has been used to localize the prostate for treatment planning and during daily RT delivery with accuracy parallel to that of CT scanning of the pelvis. (Abdel-WahabMay, 2011)

2.1.1.4.2.9 Computed Tomography

Imaging with position correction can reduce the magnitude of systematic setup errors in daily EBRT. Tomographic volumetric imaging capabilities allow daily capture of 3D image data. Both megavoltage and kilovoltage CT reconstructions can display the daily position of the prostate and adjacent OAR, thereby allowing treatment position to be adjusted to ensure that the entirety of the target is in the daily treatment volume. It is important to note that CT-based methods of image guidance (whether kilovoltage or megavoltage) provide a spectrum of image quality and exposure levels that depend on the method used. These differences in image quality are due to the range of energies and geometries that subsequently lead to various levels of soft-tissue contrast and spatial resolution. Furthermore, differences in imaging doses to the patient are also seen. In general, higher doses need to be applied to the patient when using megavoltage systems to achieve the same image quality seen with some kilovoltage systems. Day-to-day organ position and shape changes may require adaptation of the dosimetry of the old plan or even development of a new plan. With the exception of electromagnetic transponder methods, all other methods only correct for interfraction and not intrafraction prostate motion, which is largely dependent on rectal filling. (Abdel-WahabMay,2011)

2.1.2 Types of radiotherapy machines

2.1.2.1Cobalt 60 machine

The cobalt-60 machines were first used for patient treatment in 1951 in Canada. Although megavoltage x-ray units had been available for some years prior to this date, they were not in widespread use, whereas, cobalt units became the mainstay of external beam therapy for the next 30 years or so world-wide. Cobalt-60 sources are produced by irradiating cobalt-59 in a high neutron flux nuclear reactor. The main reasons for its suitability for teletherapy are the availability of relatively small, high specific activity, sources that minimize the beam penumbra; its relatively long half-life (5.27 years); and the almost monochromatic high-energy photon emission (photons of 1.173 MeV and 1.333 MeV in equal quantity). (Mayles et al 2007).

Compared to modern linear accelerators, cobalt units offer poorer geometrical precision in treatment because of a larger penumbra and greater mechanical inaccuracy. Coupled with the fact that cobalt beams are less penetrating than those from linacs and that cobalt units lack the flexibility in the control of the radiation output offered by linacs, cobalt can no longer provide the basis for contemporary sophisticated radiation therapy. However, commercially available cobalt units may be quite adequate for many non-radical treatments, and there are even some applications where cobalt sources have been used in specially designed equipment to give a performance that could be argued to be superior to that obtainable from a conventional linac, for example stereotactic radiosurgery with the Elekta Gamma Knife

and total body irradiation with custom-designed extended source skin distance (SSD) units. (Mayles et al 2007).

In countries where facilities for the maintenance of linear accelerators are lacking, cobalt-60 therapy may be the most appropriate choice for radiotherapy. Many of the major techniques and advances in the physics of external beam therapy were developed on cobalt units including arc therapy; conformal therapy; transmission dosimetry; the development and measurement of tissue air ratios and the subsequent derivation of scatter air ratios (SARs); and differential SARs and the associated algorithms for treatment planning based on the separation of primary and secondary radiation. More recently, Poffenbarger and Podgorsak have investigated the possibility of using an isocentric unit for stereotactic radiosurgery, and Warrington and Adams have shown that conformal therapy, and even IMRT, could be adequately delivered with a cobalt-60 unit except for the most deep-seated tumours. That generally makes them inherently reliable. Nevertheless, care must be taken to ensure that they are robustly built and carefully maintained to minimize the potential hazards from the high activity source and the associated heavy shielding. (Mayles et al 2007).

A sectional drawing of a modern cobalt unit treatment head is shown in Figure 2.4. As with any item of radiotherapy equipment, it is essential that the physicists responsible for its performance understand the way that the unit is constructed and operates so that they will be aware of its capabilities and limitations. This

knowledge will also help them to appreciate what routine safety measures should be put in place and also the possible causes when there are malfunctions or the performance deteriorates. (Mayles et al 2007).

The cobalt source usually consists of a series of either millimetre-size cylindrical pellets or thin, metallic discs sealed within a double capsule of stainless steel and manufactured to meet certain standards regarding protection from impact, corrosion, and heat. Active source diameters are generally in the region of 15mm to 20 mm, being a compromise between achieving a high enough activity to obtain a reasonable output and keeping the source small enough to minimize the beam penumbra. The source length may be longer than the diameter, but this is not such a critical dimension because the photons from there are of the source contributed relatively less to the clinical beam than those from the front. (Mayles et al 2007).

In atypical source, about 25% of the primary photons are lost due to self-attenuation. The space behind the active cobalt material in the capsule must be tightly packed with blank discs to eliminate movement. The low-energy β -ray emission from the source is filtered out by the capsule walls. The head of a cobalt unit has three basic functions: to shield the source, to expose the source as required, and to collimate the beam to the correct size. Shielding is achieved by surrounding the source and exposure mechanism with lead and, in many designs, with alloys of a higher density metal such as tungsten in order to reduce the

volume. In some earlier designs, depleted uranium alloy (with a high percentage of U-238, density approximately $19.0 \times 10^3 \text{ kg m}^{-3}$) was used, but this has been discontinued because of the problems with stability of the alloy as some of it became powdery and also because of the difficulties associated with eventual disposal. (Mayles et al 2007).

The source exposure mechanism is usually one of two types where either the source is moved between a safe and exposed position (as shown in Figure 2.4) or where the source remains stationary, and a moving shutter opens or closes the beam. The latter solution, implemented on earlier machines is now obsolete. In the former solution, the source movement is either a translation (as in Figure 2.4) or a rotation. (Mayles et al 2007).

Various beam collimator designs exist to give variable rectangular fields with sides ranging in length, typically, from 4 cm to 30 cm or even up to 40 cm on isocentric units with a source axis distance (SAD) of 100 cm. Each of the four collimator leaves is usually focused on the edge of the source proximal to it so as to avoid cut-off of the primary beam and minimize penumbra. Distances from the source to the far edge of the collimators are typically between 40 cm and 50 cm for machines designed for 80 cm SSD, but this distance may be increased by penumbra trimmers that are particularly desirable when the machine is to be used for 100 cm SSD treatment. With careful design of the collimation system and a 15 mm diameter source, a penumbra of no more than 10 mm (distance between the 20% and 80%

decrement lines) may be achieved at 5 cm depth for field sizes with an area of less than 400 cm².(Mayles et al 2007).

Modern cobalt units are manufactured in a standard isocentric configuration, with a source axis distance of 80 cm being the most common, to obtain a reasonable compromise between output, depth dose, and clearance around the patient. Units with an SAD of 100 cm are also practical if high activity sources can be afforded and offer the advantages of greater depth dose, larger field sizes, greater clearance around the patient, and geometrical compatibility with linacs. To increase their versatility, isocentric units have often been made with the ability to swivel the head about a horizontal axis through the source. This swivel motion keeps the beam axis in a vertical plane, and when used with an appropriate gantry angle, may be useful for extended SSD treatments or for treating immobile patients in a bed or chair. (Mayles et al 2007).

Some non-isocentric cobalt units have been manufactured with the head held by a yoke on a vertical stand, and these are particularly useful for giving single field palliative treatments. Where an isocentric unit has the swivel facility, great care must be taken to ensure that its position is accurately reset before the equipment is used for normal isocentric use since the slightest angulation of the head swivel will create a large deviation of the beam axis from the mechanical isocentre . Some isocentric units use slip rings for the supply of all power and control signals to the gantry and this allows continuous gantry rotation. Coupled with

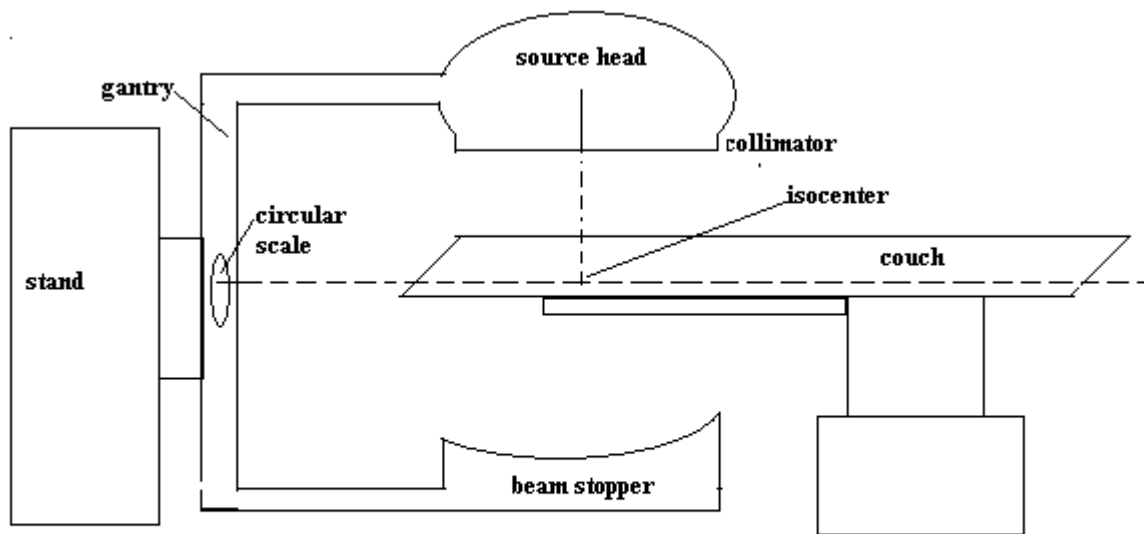
the guaranteed constant output from the source as the unit rotates, such a versatile and simple rotation mechanism provides an ideal unit for arc or full rotation therapy when this technique is required. Although beam flattening filters can, in principle, be successfully used on cobalt units, they are rarely employed in practice because of the consequent reduction in output. (Mayles et al 2007).

Without a flattening filter, the beam homogeneity is relatively poor across a large area beam, especially at greater depths, because of scattering in the tissue and the greater distance from the source to the field edges compared to the centre for a constant depth. Users should be aware of this fact when using such fields, even for palliative applications, as the 90% decrement level will be much farther inside the beam than for a similar field on a linac. Fixed wedge filters may be inserted into the beam below the end of the collimator to give a range of wedge angles, typically between 15° and 60°. These wedges will usually incorporate a certain amount of beam flattening, giving a somewhat straighter isodose curve within the central portion of the beam than for an open field. Wedge filters inevitably reduce the dose rate at the centre of the beam and this is more of a problem with a cobalt machine than with a linear accelerator. (Mayles et al 2007).

The reduction in output may be minimised by making the wedge shape always begin at the field edge by linking the toe end of the wedge to the collimator so that wedging always begins at the

edge of the beam. With this system, the wedge factor will be different for each field size, so modern units usually have a fixed relationship between the centre of the wedge and the centre of the field with perhaps different wedges for different ranges of field size. In principle, there is no reason why a virtual wedge could not be created by dynamically moving one collimator during treatment in a similar fashion to that employed on linacs. Such a system has not yet been commercially produced and would probably require a different design for the collimators to allow them to travel across the beam axis, but it would have the advantage of minimizing the increase in treatment time associated with the use of a wedge. Other beam modifiers and accessories such as the beam-defining light, range finder, accessory tray, laser positioning system, front and back pointers, etc., will be very similar to those employed on linacs (Mayles et al 2007).

Figure 2-2



The telecobalt machine

2.1.2.2 Linear accelerator machine

Linear accelerator (linac) designed for radiotherapy; electrons gain energy by interacting with a synchronized radio-frequency electromagnetic field rather than by acceleration by direct potential. In free air, electromagnetic waves travel at the speed of light, but in a suitably designed waveguide, the speed of propagation of the waves can be substantially reduced. The accelerating waveguide (or accelerator structure) consists of a long cylindrical tube Figure 2.5, containing a series of circular baffles. These are designed so that speed of propagation of the microwaves increases in the first part of the accelerating tube until it eventually reaches velocities close to the speed of light. Bunches of electrons generated in the gun are injected into the guide in synchronism with pulsed microwave radiation and are

carried down the guide in a manner analogous to riding the crest of a wave (i.e. surfing). (Mayles et al 2007).

The high energy electron beams, typically 6 MeV or above, can be directly used for therapy and have a number of advantages compared to kilovoltage x-ray beams. Their depth dose curves are characterized by initial skin sparing followed by several centimeters of uniform dose (depending on energy) and then a rapid fall-off in dose.(Mayles et al 2007).

Electron beams from linear accelerators are useful for treatment of tumours up to about 70 mm deep, but for more deep-seated tumours, it is better to use photon beams. If the electron beam is to be used for therapy, the originally narrow beam of electrons must be broadened by scattering the electrons. In photon mode, the electrons are focused onto a high-atomic-number thick target, and their energy loss is converted into bremsstrahlung radiation. (Mayles et al 2007).

At megavoltage energies, the principal direction of bremsstrahlung emission is in the forward direction. In the simplest accelerators, the target is fixed and the accelerating structure is coaxial with the emerging x-ray beam (i.e. it is parallel to the direction of travel of the electrons so that no bending of the electrons takes place) and is perpendicular to the cranio-caudal axis of the patient. However, for energies above 6 MeV, the length of the accelerator tube is such that it makes this impracticable. In order for the radiation beam to be brought in to irradiate the patient from any angle, it becomes necessary to

bend the beam. Electrons are easily deflected in a magnetic field, and it is convenient to bend them through about 90°.(Mayles et al 2007).

The challenge for accelerator design is to produce a stable monoenergetic high current electron beam concentrated onto a small focal spot that will ensure that a sharply focussed x-ray beam can be produced. The x-ray beam must be modified to allow uniform irradiation of the intended treatment area of the patient, which can vary from a very small area up to a maximum of about 40 cm!40 cm. It is also of considerable benefit to be able to choose the beam energy to suit the tumour being treated. Modern accelerators are the result of a complex design process with different emphases being placed by different manufacturers. In the following pages, the issues relating to the different components will be considered. (Mayles et al 2007).

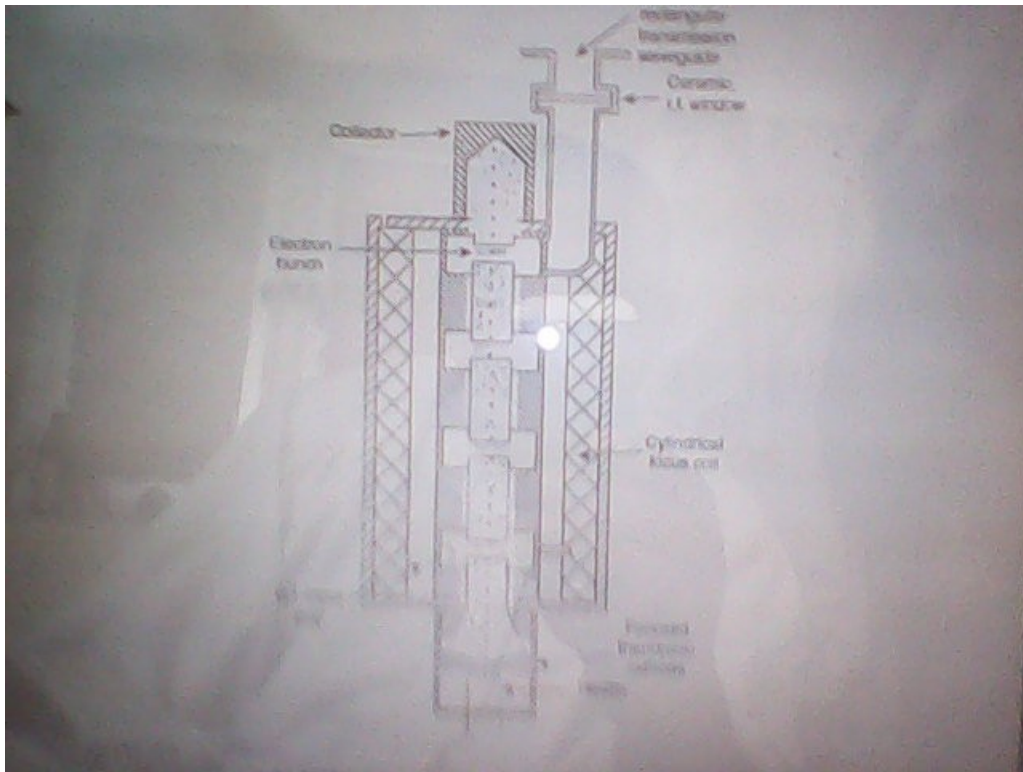


Figure 2-3 linear accelerator components

2.1.2.3 Cobalt 60 machine versus linear accelerator machine

First application of x-rays for therapeutic purpose was made on Jan.29, 1896 in Chicago by Grubbe for treatment of breast carcinoma (Van Dyk, Battista, J.J. 1996). The first case of cure of malignant tumour by radiotherapy alone was reported on a patient with a histologically confirmed squamous cell carcinoma of the nose. In mid 1930s, radiotherapy was beginning to be used as an adjuvant to radical mastectomy. Cobalt 60 Unit: In 1951, Cobalt 60 teletherapy was first put to clinical use in London, Ontario. Cobalt-60 Gamma radiation typically has energy of about 1.2 MV, D-max being 0.5 cm. and a percentage depth of 55% at 10 cm (Van Dyk et al, 1996).

Cobalt-60 units over the last several decades have remained static in design and there has been very little change in ancillaries and accessories. The major problem with these units is the decaying source, reduced output resulting in increased treatment times which in turn will effectively reduce the patient output. The source needs to be replaced every 5-7 years and is becoming more and more expensive and is also hard to get. In the first few decades after discovery of x-rays only low energy x-rays were available and they were used predominantly for palliative treatment. From the technology of World War II radars give the ability to produce high energy microwaves. This field advanced with the development of high energy microwave tubes known as Klystrons or Magnetrons which are still at the heart of today's' modern Linear Accelerators. (VanDyk et al,1996).

The First medical Linear Accelerator was created and used in England in 1953 followed by USA (Van Dyk et al,1996).

Basically the Linear accelerator (Linac) is a device that uses high frequency electromagnetic waves to accelerate charged particles such as electrons to high energies through a linear tube. In the '60s & '70s Cobalt Unit has largely been replaced by Linear Accelerators in most of the radiation oncology departments in the developed countries. Low, medium and high energy Linacs are now available which can generate not only x-rays but also electrons for treatment. (VanDyk et al,1996).

Several arguments have been put forward both for and against Cobalt Units as well as Linear accelerators. These arguments relate to physics, clinical advantages and more importantly, the cost consideration. The following table compared the co 60 with linear accelerator (VanDykj et al,1996).

Feature	Linear accelerator	Cobalt 60	Linac vs Co 60
Dose rate	600 MU/Min	Reducing dose In Cobalt units dose will starts at 200r/min Dose decrease with time (max dose 250 cGy/ min)	In Cobalt units dose will reduce because of decay, and depends on source activity. whereas with Linear Accelerator one has the guarantee of constant dose rate
Energy Source DIA	<2mm	20mm	Penumbra effect is higher in cobalt machines

Source change	None	Every 5-7 years	at the time of change of source one has to send the decayed source back to the manufacturer, which is very expensive.
D- max	1.5 cm	0.5cm	Linear accelerator with 6 MV, photon, we are able to get D-max 1.5 cm. This is very useful for deep seated tumours. Skin sparing is better with Linac (6 MV).
Minimum field size	0.5x0.5 cm	5 x 5 cm	In cobalt one cannot treat field size less than 5x5cm.

Table 2-2 Co60 machine versus linear accelerator adopted from (Van Dykj et al,1996).

Cobalt 60 units provide relatively high energy gamma rays for radiotherapy which are ideally suited for treatment of head and neck cancers and other superficially located tumours like breast cancers and soft tissue sarcomas of extremities. They are not adequate for treatment of deep seated tumours and have the added disadvantage of decreasing output with decay of source. Disposal of decayed source is another major concern. (VanDykJ et al,1996).

The beam characteristics when compared to 6MV Linacs are inferior and fewer ancillaries are available for cobalt machines as compared to Linacs. High energy Linacs in addition to giving two or three x-ray energies can also generate variable energy electron beam for treatment. While such high energy Linacs are expensive, 6 MV Linacs compare favorably in terms of cost with the Cobalt 60 units. Even though the initial cost appears to be high, over a ten year period maintenance costs are less as it does not require change of source. It is stressed that service contracts with performance guarantees for 5-10 years have to be built into the contracts while procuring the equipment. To summarize Linear accelerators have several advantages: Very high energy beams can be created with a machine that is not very bulky or cumbersome to use, the edges of the beams are much more sharply defined than those of a cobalt machine, allowing additional precision in dose delivery and electron beams can be created (with high energy linacs) that is of particular value in treating superficial lesions and the dose rate per minute is variable and can be turned up very high allowing the patient to be located at substantial distance from the machine in order to create large fields necessary for total skin or total body irradiation while still maintaining adequate dose rate. With cobalt, the rate is determined by the amount of cobalt source in the machine and cannot be regulated. (Reddy, 2011)

2.2 Previous studies

The simplicity of cobalt units gives the advantage of reduced maintenance, running costs and downtime when compared with linear accelerators. The advantages of cobalt units are well known to the radiotherapy community. Several studies had been carried out concerning using of linear accelerator machines to treat prostate carcinoma in different ways of planning, despite the using of Co-60 machines although it has been recently improved in their facilities.

Dirk et al 2002 studied Considerations on treatment efficiency of different conformal radiation therapy techniques for prostate cancer , their study carried out Three major classes of intensity-modulated radiation therapy (IMRT) delivery as well as a conformal rotation technique have been evaluated: sequential tomotherapy, dynamic multileaf collimation (DMLC) with conventional MLC, DMLC with miniMLC and dynamic field shaping arc. Treatment planning for the IMRT techniques has been performed with inverse planning. Forward planning was used for the dynamic arc technique. The four techniques have been compared to treat two different prostate cases with a conservative target dose of 70 Gy: a convex shaped target volume and one containing concavities formed by the bladder and rectum. Cumulative dose volume histograms, tumor control probability and normal tissue complication probability, conformity index and dose heterogeneity, and finally efficiency of treatment delivery have been evaluated. Their results were for the convex shaped target, all treatment modalities met the desired treatment

goals, although the conventional MLC delivered more doses to the bladder. Compared to the dynamic arc modality, both tomotherapy and the conventional MLC technique needed a tenfold higher number of monitor units per target dose, and the miniMLC a twofold higher number. The same trend has been observed for the concave target, yet the dynamic arc did not meet the desired dose reduction for the rectum. The miniMLC configuration represented the best compromise for both targets with respect to treatment goals and delivery efficiency. Sequential tomotherapy performed adequately with respect to conformity at the cost of efficiency.

İlknurÇetin et al 2004 studied a comparison of conventional external radiotherapy technique and conformal radiotherapy technique in terms of acute toxicity with regard to hormonal treatment, their studied carried out Seventy-five patients diagnosed with localized prostate cancer were treated with primary radiotherapy (RT) between March 1997 and July 2002, 47 with EBRT and 28 with CRT. 23 patients (31%) did not receive HT, 22 patients (29%) received concomitant HT (CHT) and 30 patients (40%) received neoadjuvant HT (NAHT). The patients were observed for at least 3 months and the acute toxicity was evaluated by EORTC/RTOG (European Organization for Research and Treatment of Cancer / Radiation Therapy Oncology Group) scale. Their results were there was no grade III-IV acute urinary and rectal toxicity. The percentage of grade I and II acute urinary toxicity was determined as 30% and 23%, respectively in the

EBRT group. The ratios were 61% and 18%, respectively in the CRT group ($p=0.025$). Grade II urinary toxicities were 13% in patients who did not receive HT and who received NAHT, 41% in patients who received CHT ($p=0.02$). Grade II rectal toxicities were 30% for EBRT and 7% for CRT group ($p=0.022$).

Roca 2006 studied that the role of external-beam radiation therapy in the treatment of clinically localized prostate cancer, his curried out that the treatment of clinically localized prostate cancer is controversial. Options include radical prostatectomy, external-beam radiation therapy (EBRT), brachytherapy, cryotherapy, and watchful waiting. The author reviews EBRT as treatment for clinically localized prostate cancer, with particular emphasis on the technological advances that have allowed dose escalation and fewer therapy-related side effects. His results were Technological advances in the last two decades have significantly improved the delivery of EBRT to the prostate. This has resulted in an overall increase in the total dose that can be safely delivered to the prostate, which has led to modest improvements in biochemical outcome. An alternative approach of combining androgen suppression therapy and EBRT has also been successful in improving clinical outcomes. However, establishing the optimal therapy for prostate cancer remains controversial. Recent progress has led to improvements in clinical outcomes in patients treated with EBRT for prostate cancer. It is hoped that the next decades will bring continued advances in the development of biological that will further improve current clinical outcomes.

Brenner et al 1999 studied that, fractionation and protraction for radiotherapy of Prostate carcinoma, they analyzed two mature data sets on radiotherapeutic tumor control for prostate cancer, one using EBRT and the other permanent seed implants, to extract the sensitivity to changes in fractionation of prostatic tumors. The standard linear-quadratic model was used for the analysis. Their results were Prostatic cancers appear significantly more sensitive to changes in fractionation than most other cancers. The estimated a/b value is 1.5 Gy [0.8, 2.2]. This result is not too surprising as there is a documented relationship between cellular proliferative status and sensitivity to changes in fractionation, and prostatic tumors contain exceptionally low proportions of proliferating cells. High dose rate (HDR) brachytherapy would be a highly appropriate modality for treating prostate cancer. Appropriately designed HDR brachytherapy regimens would be expected to be as efficacious as low dose rate, but with added advantages of logistic convenience and more reliable dose distributions. Similarly, external beam treatments for prostate cancer can be designed using larger doses per fraction; appropriately designed hypofractionation schemes would be expected to maintain current levels of tumor control and late sequelae, but with reduced acute morbidity, together with the logistic and financial advantages of fewer numbers of fractions.

Pesce et al 2010 studied that early clinical experience of radiotherapy of prostate cancer with volumetric modulated arc therapy, they carried out Forty-five patients with a median age of

72 ± 3, affected by prostate carcinoma (T1c: 22 patients, T2a-b: 17 patients, T3a-b: 6 patients. N0: 43 patients, N1-Nx: 2 patients, all M0), with initial PSA of 10.0 ± 3.0 ng/mL, were treated with Rapid Arc in a feasibility study. All patients were treated with single arc using 6MV photons. Dose prescription ranged between 76 (7 patients) and 78 Gy (38 patients) in 2Gy/fraction. Plan quality was assessed by means of Dose Volume Histogram (DVH) analysis. Technical parameters of arcs and pre-treatment quality assurance results (Gamma Agreement Index, GAI) are reported to describe delivery features. Early toxicity was scored (according to the Common Terminology Criteria of Adverse Effects scale, CTCAE, scale) at the end of treatment together with biochemical outcome (PSA). Their results were From DVH data, target coverage was fulfilling planning objectives: V95% was in average higher than 98% and V107%~0.0%(D2%~104.0% in average). Homogeneity D5%-D95% ranged between 6.2 ± 1.0% to 6.7 ± 1.3%. For rectum, all planning objectives were largely met (e.g. V70Gy = 10.7 ± 5.5% against an objective of < 25%) similarly for bladder (e.g. D2% = 79.4 ± 1.2Gy against an objective of 80.0Gy). Maximum dose to femurs was D2% = 36.7 ± 5.4Gy against an objective of 47Gy. Monitor Units resulted: MU/Gy = 239 ± 37. Average beam on time was 1.24 ± 0.0 minutes. Pretreatment GAI resulted in 98.1 ± 1.1%. Clinical data were recorded as PSA at 6 weeks after RT, with median values of 0.4 ± 0.4 ng/mL. Concerning acute toxicity, no patient showed grade 2-3 rectal toxicity; 5/42 (12%) patients experienced grade 2 dysuria; 18/41

(44%) patients preserved complete or partial erectile function. Rapid Arc proved to be a safe, qualitative and advantageous treatment modality for prostate cancer.

ANNIE et al 2007 studied that a study of image-guided intensity-modulated radiotherapy with fiducials for localized prostate cancer including pelvic lymph nodes. They carried out Five patients with prostate cancer in whom prostate and pelvic nodes were irradiated with IMRT were studied. Dose was prescribed such that 95% of the prostate planning target volume (PTV) and 90% of the nodal PTV were covered. Random and systematic prostate displacements in the anterior posterior, superior-inferior and left-right directions were simulated to shift the original isocenter of the IMRT plan. The composite dose during the course of treatment was calculated. Their results were compared with a static setup, simulating random shifts reduced dose by less than 1.5% for nodal hotspot (*i.e.*, dose to 1 cm³), by less than 1% for the 90% nodal PTV coverage, and by less than 0.5% for the nodal mean dose. Bowel and femoral head hotspots were reduced by less than 1.5% and 2%, respectively. A 10-mm systematic offset reduced nodal coverage by up to 10%. The use of prostate fiducials for daily localization during IMRT treatment results in negligible changes in dose coverage of pelvic nodes or normal tissue sparing in the absence of a significant systematic offset. This offers a simple and practical solution to the problem of image-guided radiotherapy for prostate cancer when including pelvic nodes.

Tsalafoutas et al 2009 studied that A method for calculating the dose length product from CT DICOM images, they carried out In this study a method for the calculation of these quantities from digital imaging and communication in medicine (DICOM) CT images is presented that allows an objective audit of patient doses. This method was based on software that has been developed to enable the automatic extraction of the DICOM header information of each image (relating to the parameters that affect the aforementioned quantities) into a spreadsheet with embedded functions for calculating the contribution of each image to the CTDI volume and DLP values. The applicability and accuracy of this method was investigated using data from actual examinations carried out in three different multi slice CT scanners. These examinations have been performed with the automatic exposure control systems activated, and therefore the tube current and tube loading values varied during the scans. Their results were the calculated DLP values were in good agreement (5%) with the displayed values. The calculated average CDTI volume values were in similar agreement with the displayed CTDI volume values but only for two of the three scanners. In the other scanner the displayed CTDI volume values were found to be overestimated by about 25%. As an additional application of this method the differences among the tube modulation techniques used by the three CT scanners were investigated.

Falco et al 2010 studied that Preliminary experience of a predictive model to define rectal volume and rectal dose during the treatment of prostate cancer. They carried out that Patient set-up was verified using a volumetric three-dimensional CBCT scanner; 9-14 CBCT scans were obtained for each patient. Images were transferred to a commercial treatment planning system for offline organ motion analysis. The shape of the rectums were used to obtain a mean dose-volume histogram (,DVH.), which was the average of the DVHs of the rectums as they appeared in each verification CBCT. A geometric model of an average rectum (AR) was produced using the rectal contours delineated on the CBCT scans (DVHAR). To check whether the first week of treatment was representative of the whole treatment course, we evaluated the DVHs related to only the first five CBCT scans (,DVH5. and DVHAR5). Finally, the influence of a dietary protocol on the goodness of our results was considered. Their results were in all six patients the original rectal DVH for the planning CT scan showed higher values than all DVHs. Although the application of the model to a larger set of patients is necessary to confirm this trend, reconstruction of a representative volume of the rectum throughout the entire treatment course seems feasible.

Chapter 3

Materials and Methods

Chapter 3

Materials and Methods

3.1 Introduction

The planning in radiotherapy passes through many phases, firstly: traditional phase in which the oncologists depend on their anatomical experience to guess the location tumor site with help of plain radiographs, secondly :conventional simulator phase to visualize and localize the site of the tumor and organs at risk , thirdly : virtual simulation phase in which combine between conventional simulation and CT images, fourthly : CT simulator phase for 3-D conformal radiation therapy , intensity modulated radiation therapy and image -guided radiation therapy .

3.2. Materials

CT images abdominal and pelvic regions for 55 patients in CDs collected from different diagnostic centers in Khartoum state (Almodaris, Alnileen, Royal).

TPS machine named PLNW 2000:2.5.2009.79 Produced by UJP Praha a.s contain DICOM server for PLANW 2000 is used for import of data sent by network to the system in DICOM format and for export data from individual stations of the system in DICOM format to various equipment (verification system, virtual simulation etc)

3.3 Methods

The researcher analyzed the data on all CT images for 55 men seen at the royal centre in Khartoum ,Almodaris centre in Khartoum and alnileen medical centre from January 2010 to December 2013, after collected the CT images in CDs then processing them by TPS, firstly insert the CT images , secondly made contours and select the target volumes(GTV,CTV,PTV) and the organ at risk (rectum, bladder), thirdly shaped the beam fields (3,5,7 fields)arranged one anteriorly(0) and two posterior oblique (120,240) , one anterior ,two anterior oblique (60,300),two posterior oblique (120,240), one anterior ,two anterior oblique (60,300), two posterior oblique (120,240) two laterals (90,270) respectively , fourthly distributed the dose using SAD techniques . Using field size (x*y) x according to PTV, y according to number of slices + 2cm, also using numbers field 3,5,7 and exclude 4,6,8 fields because there are high doses to rectum and head of femur . gantry angles for 3,5,7 fields (0,120,240), (0,60,300,120,240), (0,60,300,90,270,120,240) respectively . using 3,5 and 7 fields with wedge angle 15°, 30° and 45° and weighting factors for three fields (anterior field 0.4, right lateral field0.3 and left lateral field0.3), for five fields(anterior field 0.3, right posterior oblique field 0.2, left posterior oblique field 0.2, right anterior oblique field 0.15 and left anterior oblique field 0.15) and for seven fields (anterior field 0.3, right posterior oblique field 0.15, left posterior oblique field 0.15, right anterior oblique field0.1, left anterior oblique field 0.1, right lateral field 0.1 and left lateral field 0.1)

The researcher then wrote the values of doses for each CT image considered dose received by prostate, rectum, bladder and the skin.

The researcher used excels and SPSS program for analyzed and diagrams.

Chapter 4

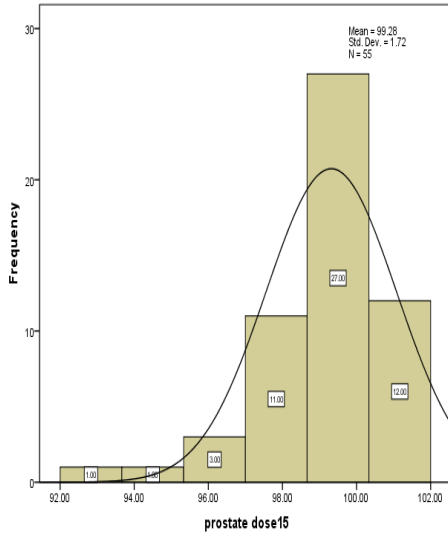
Results

Chapter 4

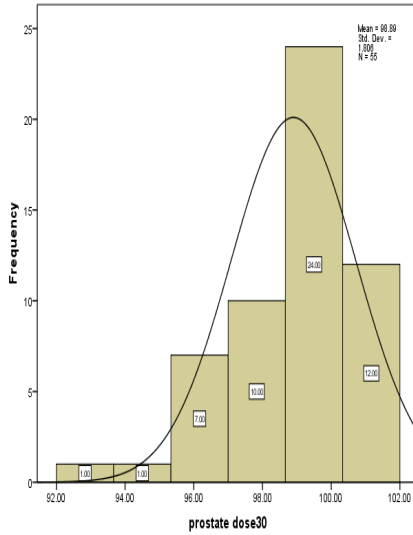
Results

4.1 CT-base imaging multi-fields comparing results

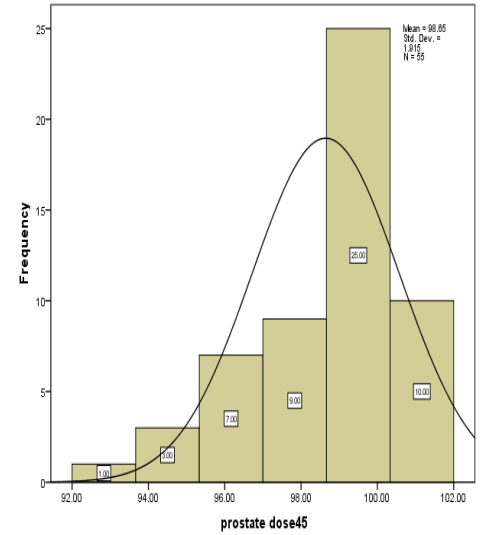
the result of this study using 3,5 and 7 fields with wedge angle 15° , 30° and 45° and weighting factors for three fields (anterior field 0.4, right lateral field 0.3 and left lateral field 0.3), for five fields (anterior field 0.3, right posterior oblique field 0.2, left posterior oblique field 0.2, right anterior oblique field 0.15 and left anterior oblique field 0.15) and for seven fields (anterior field 0.3, right posterior oblique field 0.15, left posterior oblique field 0.15, right anterior oblique field 0.1, left anterior oblique field 0.1, right lateral field 0.1 and left lateral field 0.1) for each as shown in below histogram for prostate dose figure (4-1A, Band C) for three fields, figure (4-2 A, Band C) for five fields and figure (4-3 A, B and C) for seven fields respectively.



(A)



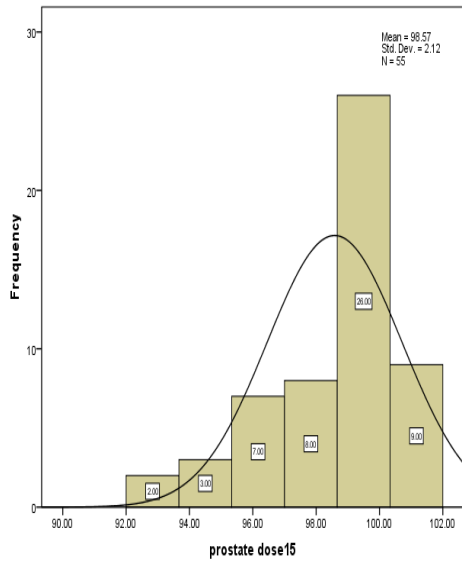
(B)



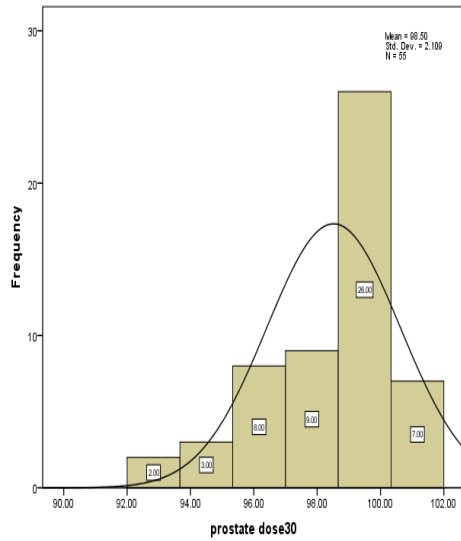
(C)

Figure (4-1) a histogram plot show the distribution of dose in prostate in (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted .

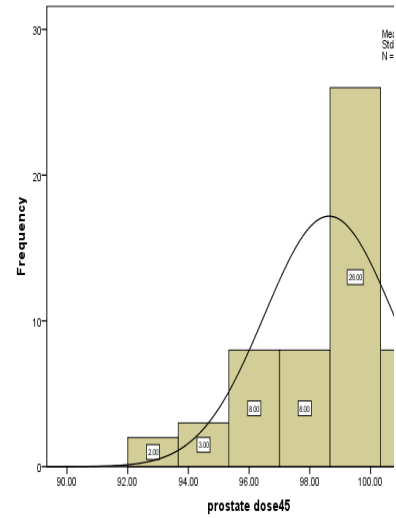
The histogram plot showed in figure (4-1) in (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° , the mean dose received by prostate was 99.28 ± 1.72 , 98.89 ± 1.80 and 98.85 ± 1.91 respectively .



(A)



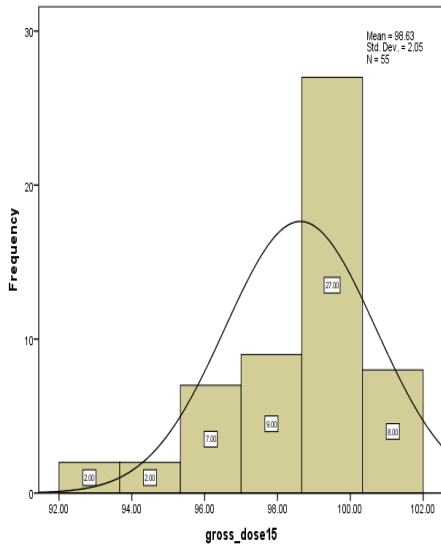
(B)



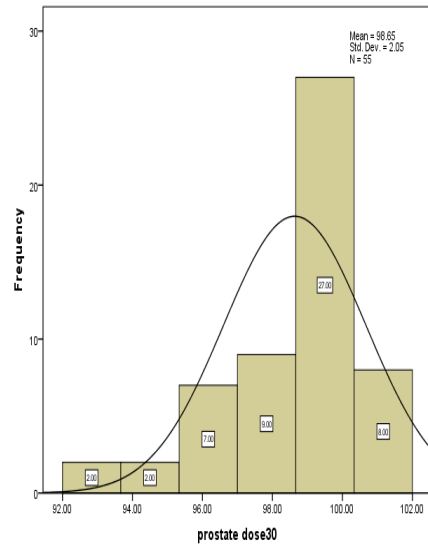
(C)

Figure (4-2) a histogram plot show the distribution of dose in prostate in (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted .

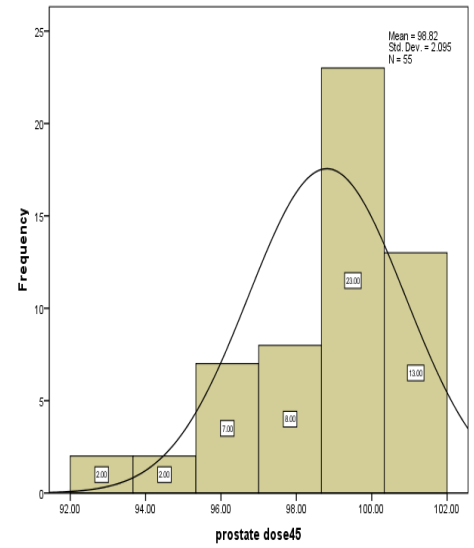
The histogram plot showed in figure (4-2) in (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° the mean dose received by prostate was 98.57 ± 2.12 , 98.50 ± 2.10 and 98.61 ± 2.11 respectively.



(A)



(B)



(C)

Figure (4-3) a histogram plot shows the distribution of dose in prostate in (A),(B) &(C) using seven fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted .

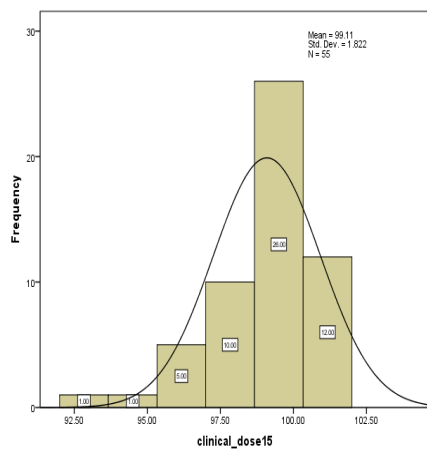
The histogram plot showed in figure (4-3) in (A),(B) &(C) using seven fields with wedge angles 15°, 30° and 45° the mean dose received by prostate was 98.63 ± 2.05 , 98.65 ± 2.05 and 98.82 ± 2.10 respectively.

As it shows in figure (4-4) scatter plot of dose received by prostate using 3, 5 and 7 fields with wedge angles the dose of the

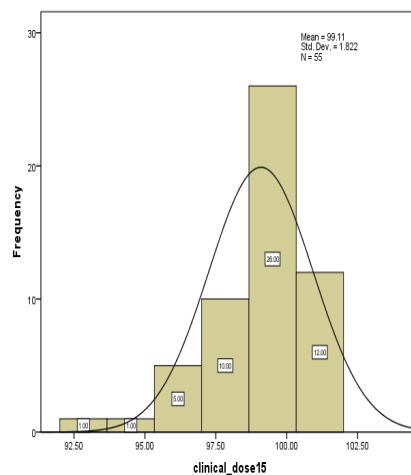
prostate decrease by 0.02 Gy /wedge angle degree for three fields and increase by 0.001Gy /wedge angle degree for five fields where the increase reach the highest value in case of using seven fields where the dose increase by 0.006 Gy/wedge angle degree.

Figure (4-4) scatter plot of dose received by prostate using 3, 5 and 7 fields with wedge angles

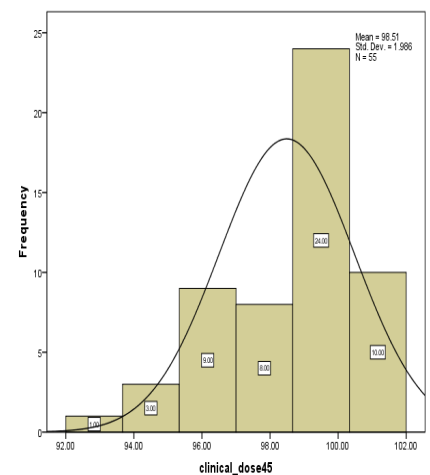
As shown in below histogram for clinical target volume dose figure (4-5A, Band C) for three fields, figure (4-6 A, B and C) for five fields and figure (4-7 A, B and C) for seven fields respectively.



(A)



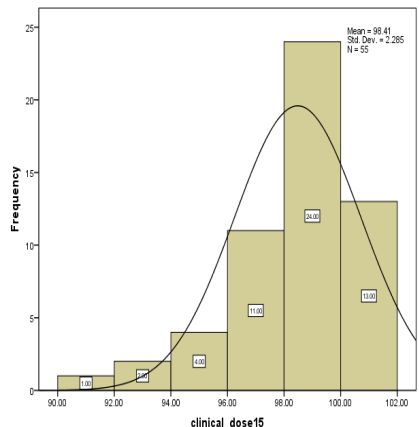
(B)



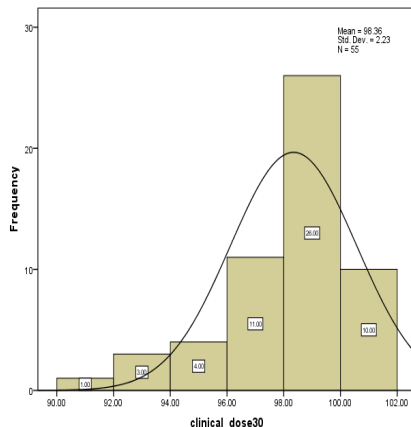
(C)

Figure (4-5) a histogram plot show the distribution of dose in clinical target volume (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted .

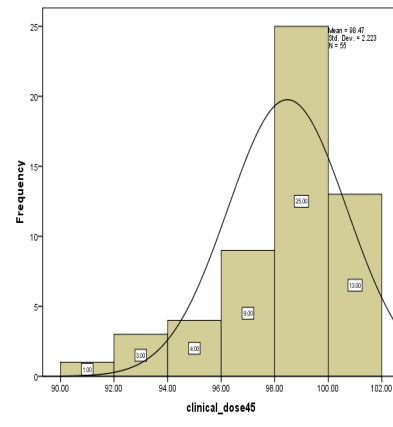
The histogram plot showed in figure (4-5) in (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° the mean dose received by clinical target volume was 99.11 ± 1.82 , 98.72 ± 1.90 and 98.51 ± 1.99 respectively.



(A)

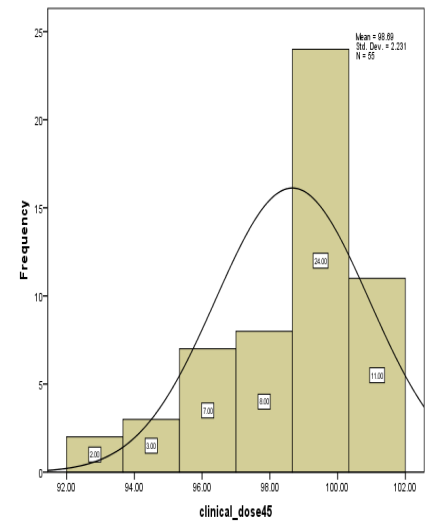
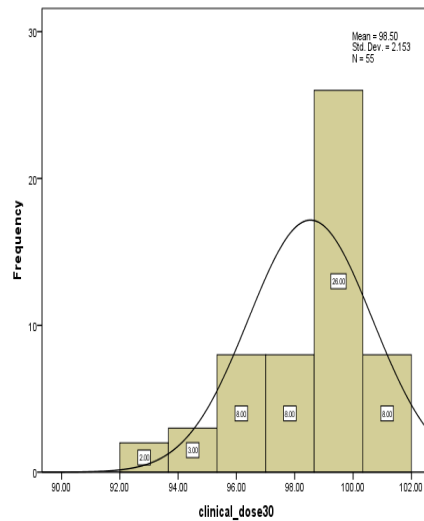
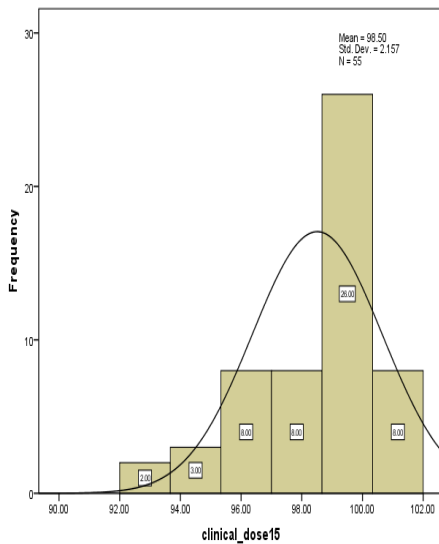


(B)



(C)

Figure (4-6) a histogram plot show the distribution of dose in clinical target volume (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted The histogram plot showed in figure (4-6) in (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° the mean dose received by clinical target volume was 98.41 ± 2.29 , 98.36 ± 2.23 and 98.47 ± 2.22 respectively.



(A)

(B)

(C)

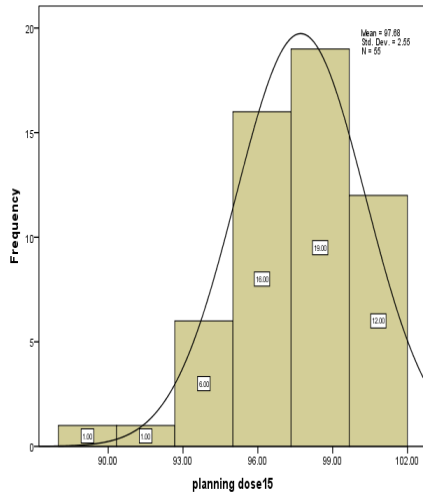
Figure (4-7) a histogram plot show the distribution of dose in clinical target volume (A),(B) &(C) using seven fields with wedge angles 15° , 30° and 45° with normal distribution curve over plotted. The histogram plot showed in figure (4-7) in (A),(B) &(C) using seven fields with wedge angles 15° , 30° and 45° the mean dose received by clinical target volume was 98.50 ± 2.16 , 98.50 ± 2.15 and 98.69 ± 2.23 respectively.

As it shows in figure (4-8) the dose of the (CTV) decrease by 0.02 Gy /wedge angle for three fields and increase by 0.002Gy /wedge angle for five fields where the increase reach the highest value in case of using seven fields where the dose increase by 0.006 Gy/wedge angle.

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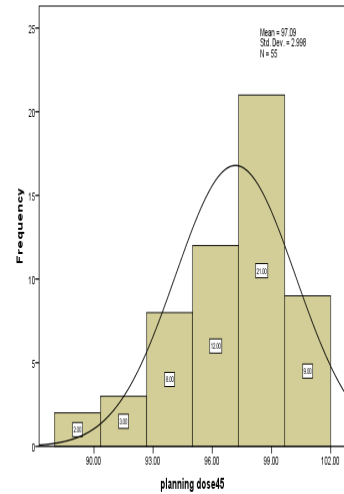
Figure (4-8) scatter plot of dose received by clinical target volume using 3, 5 and 7 fields with wedge angles.

As shown in below histogram for planning target volume(PTV) dose figure (4-9A, Band C) for three fields, figure (4-10 A, B and C) for five fields and figure (4-11 A, B and C) for seven fields respectively.



(A)

(B)



(C)

Figure (4-9) a histogram plot show the distribution of dose in planning target volume(PTV) (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-9) in (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° the mean dose received by planning target volume was 97.68 ± 2.55 , 97.30 ± 2.63 and 97.13 ± 2.71 respectively.

(A)

(B)

(C)

Figure (4-10) a histogram plot show the distribution of dose in planning target volume(PTV) (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-10) in (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° the mean dose received by planning target volume was 97.08 ± 2.96 , 96.96 ± 2.99 and 97.09 ± 2.99 respectively.

(A)

(B)

(C)

Figure (4-11) a histogram plot show the distribution of dose in planning target volume(PTV) (A),(B) &(C) using seven fields with wedge angles 15° , 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-11) in (A),(B) &(C) using seven fields with wedge angles 15° , 30° and 45° the mean dose received by planning target volume was 97.26 ± 2.99 , 97.13 ± 3.05 and 97.41 ± 3.06 respectively.

As it shows in figure (4-12) the dose of the planning target volume (PTV)decrease by $0.02 \text{ Gy /wedge angle}$ for three fields and increase by $0.0003 \text{ Gy /wedge angle}$ for five fields where the increase reach the highest value in case of using seven fields where the dose increase by $0.005 \text{ Gy/wedge angle}$.

Figure (4-12) scatter plot of dose received by planning target volume (PTV) using 3, 5 and 7 fields with wedge angles.

As shown in below histogram for rectum dose figure (4-13A, Band C) for three fields, figure (4-14 A, B and C) for five fields and figure (4-15 A, B and C) for seven fields respectively.

(A)

(B)

(C)

Figure (4-13) a histogram plot show the distribution of dose in rectum (A),(B) &(C) using three fields with wedge angles 15° , 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-13) in (A),(B) &(C) using three fields with wedge angles 15° , 30° and 45° the mean dose received by rectum was 84.63 ± 10.26 , 81.40 ± 9.73 and 79.85 ± 9.00 respectively.

(A)

(B)

(C)

Figure (4-14) a histogram plot show the distribution of dose in rectum (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-14) in (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° the mean dose received by rectum was 78.04 ± 10.34 , 77.14 ± 10.11 and 76.74 ± 9.97 respectively.

(A)

(B)

(C)

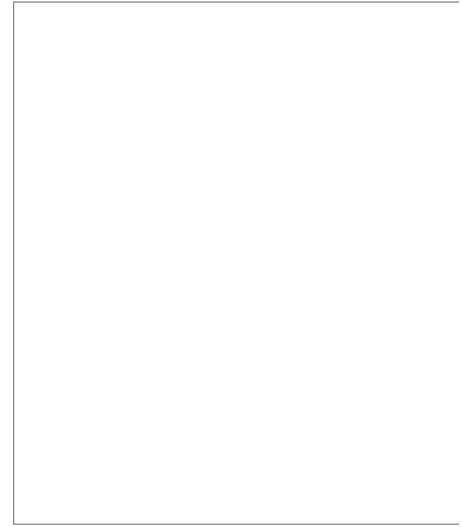


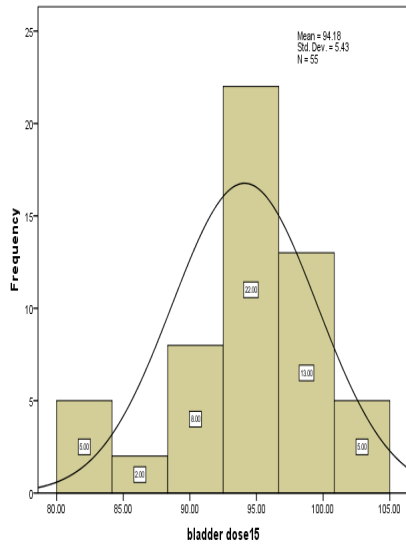
Figure (4-15) a histogram plot show the distribution of dose in rectum (A),(B) &(C) using seven fields with wedge angles 15° , 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-15) in (A),(B) &(C) using seven fields with wedge angles 15° , 30° and 45° the mean dose received by rectum was 77.41 ± 10.53 , 77.22 ± 10.49 and 76.82 ± 11.00 respectively.

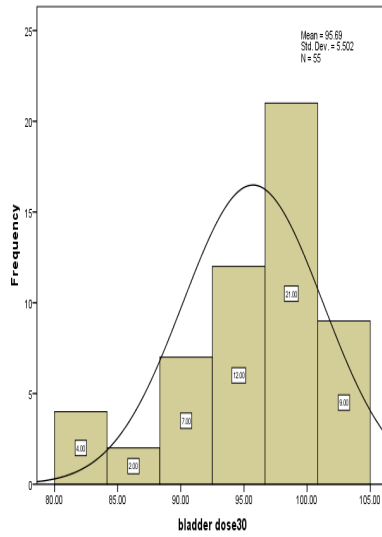
As it shows in figure (4-16), the dose of the rectum decreases by 0.2 Gy /wedge angle for three fields and decrease by 0.04Gy /wedge angle for five fields where it decreases by 0.02 Gy/wedge angle for seven fields.

Figure (4-16) scatter plot of dose received by rectum using 3, 5 and 7 fields with wedge angles.

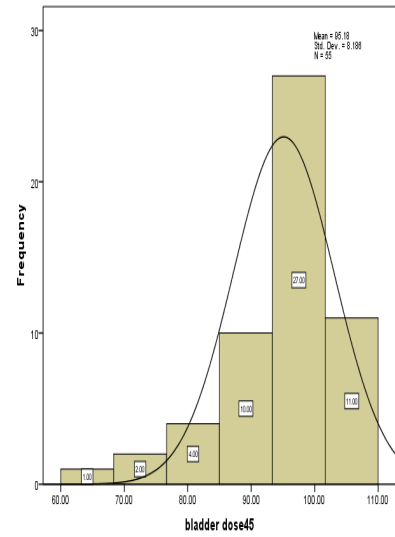
As shown in below histogram for bladder dose figure (4-17A, Band C) for three fields, figure (4-18 A, B and C) for five fields and figure (4-19 A, B and C) for seven fields respectively.



(A)



(B)



(C)

Figure (4-17) a histogram plot show the distribution of dose in bladder (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-17) in (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° the mean dose received by bladder was 94.18 ± 5.43 , 95.69 ± 5.50 and 95.18 ± 8.18 respectively.

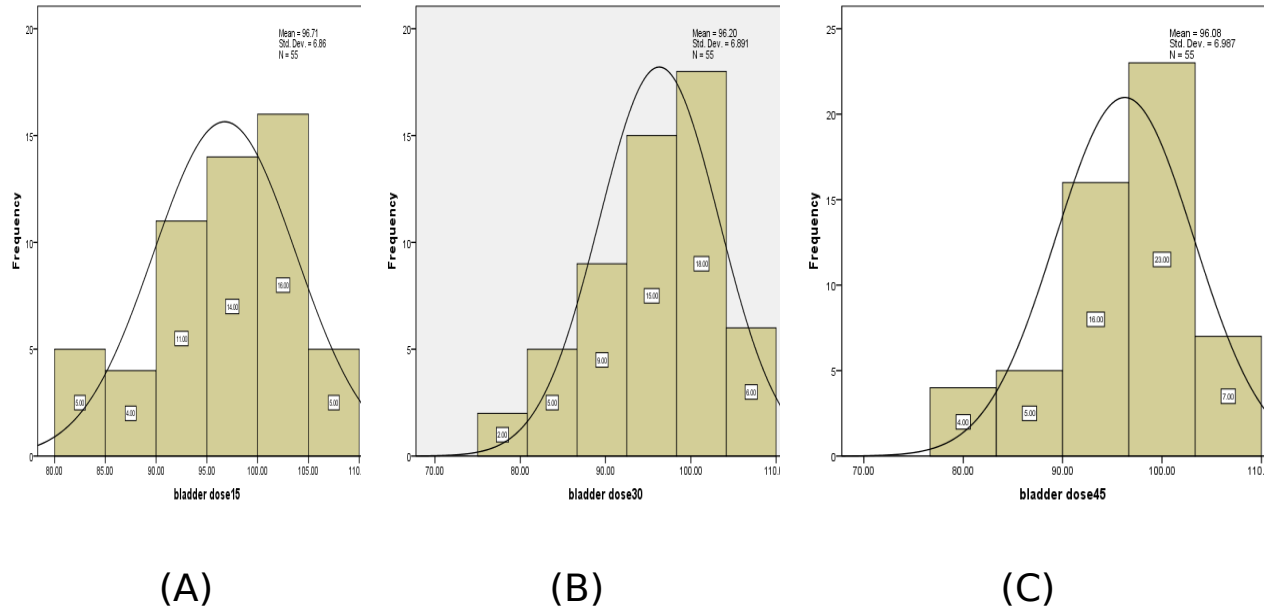
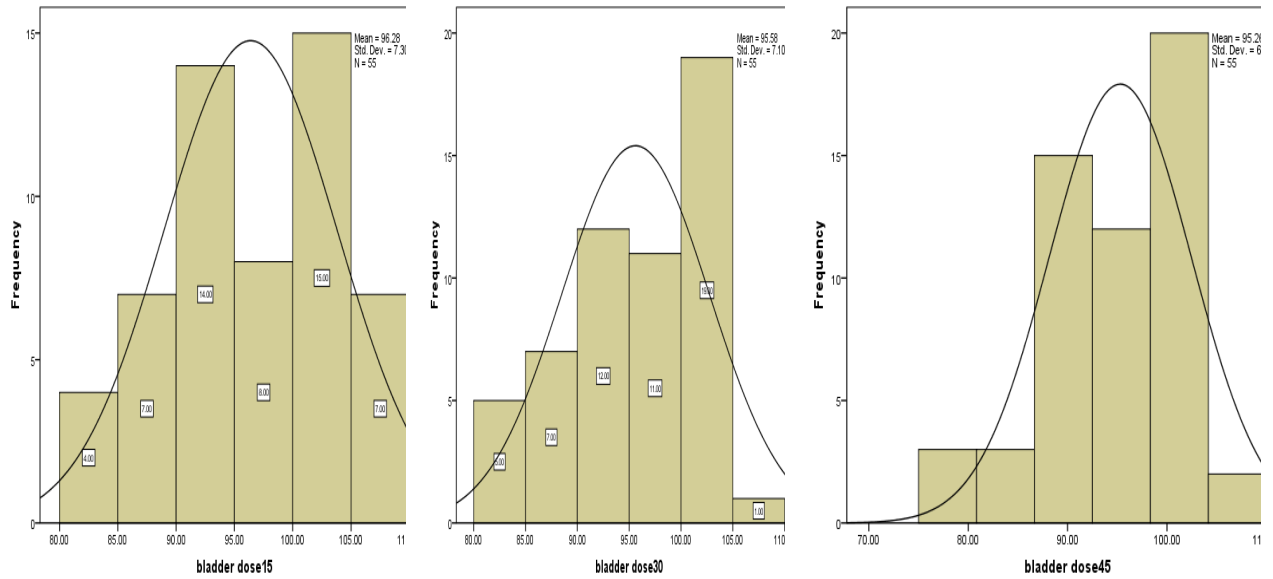


Figure (4-18) a histogram plot show the distribution of dose in bladder (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-18) in (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° the mean dose received by bladder was 96.71 ± 6.86 , 96.2 ± 6.89 and 96.08 ± 6.98 respectively.



(A)

(B)

(C)

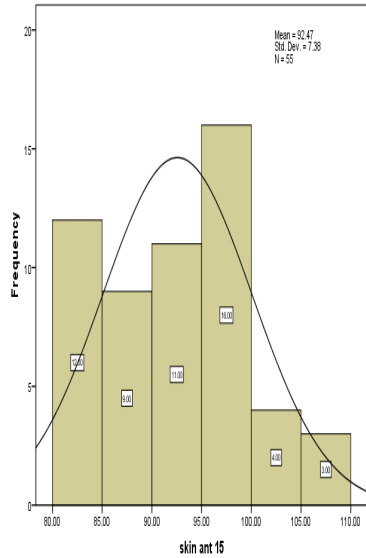
Figure (4-19) a histogram plot show the distribution of dose in bladder (A),(B) &(C) using seven fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-19) in (A),(B) &(C) using seven fields with wedge angles 15°, 30° and 45° the mean dose received by bladder was 96.28 ± 7.30 , 95.58 ± 7.10 and 95.26 ± 6.92 respectively.

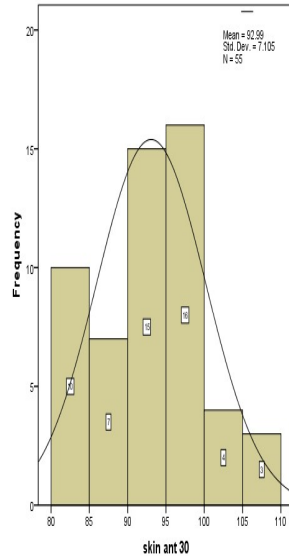
As it shows in figure (4-20) the dose of the bladder decrease by 0.03 Gy /wedge angle for three fields and decrease by 0.02Gy /wedge angle for five fields where in seven fields the dose increase by 0.03 Gy/wedge angle.

Figure (4-20) scatter plot of dose received by bladder using 3, 5 and 7 fields with wedge angles.

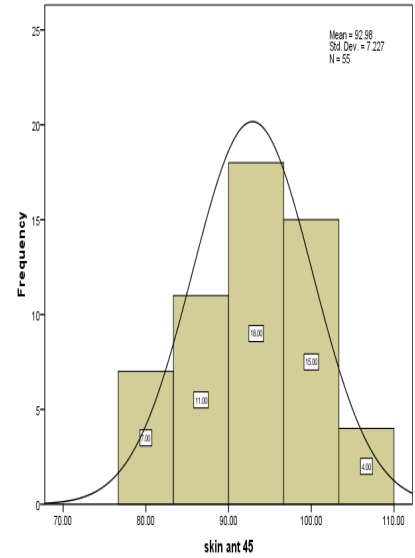
As shown in below histogram for anteriorly skin dose figure (4-21A, Band C) for three fields, figure (4-22 A, B and C) for five fields and figure (4-23 A, B and C) for seven fields respectively.



(A)



(B)



(C)

Figure (4-21) a histogram plot show the distribution of dose in skin anteriorly (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-21) in (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° the mean dose received by skin anteriorly was 92.47 ± 7.38 , 92.99 ± 7.11 and 92.98 ± 7.23 respectively

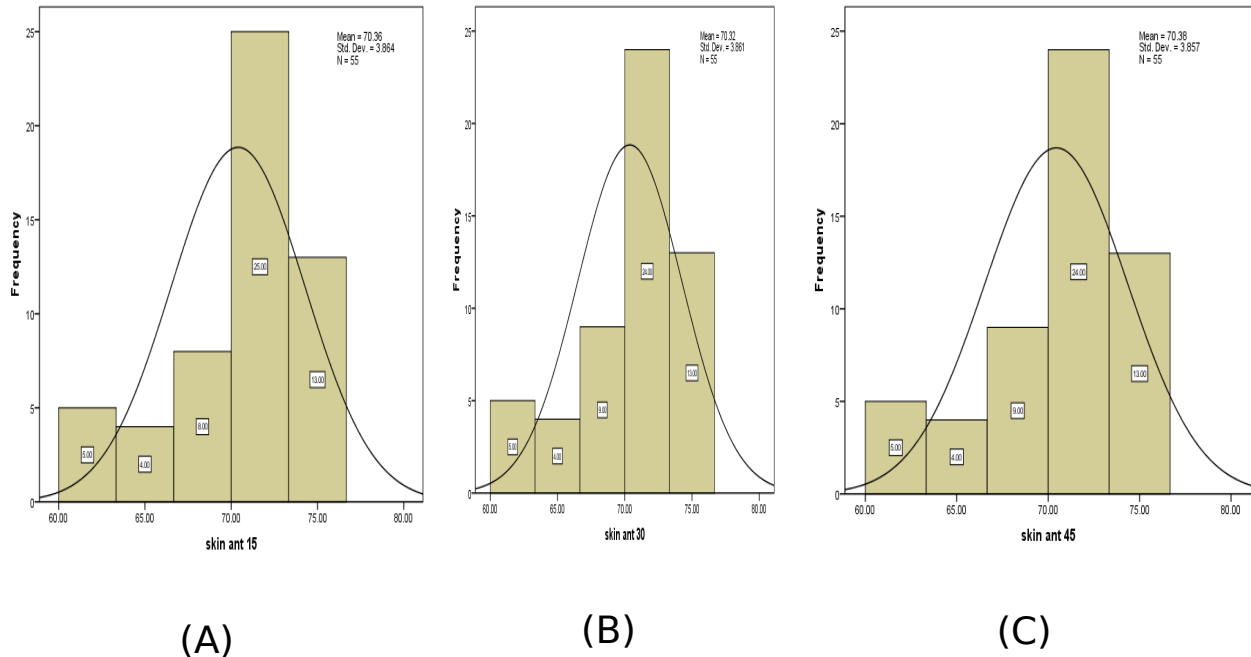


Figure (4-22) a histogram plot show the distribution of dose in skin anteriorly (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-22) in (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° the mean dose received by skin anteriorly was 70.36 ± 3.86 , 70.32 ± 3.86 and 70.38 ± 3.86 respectively.

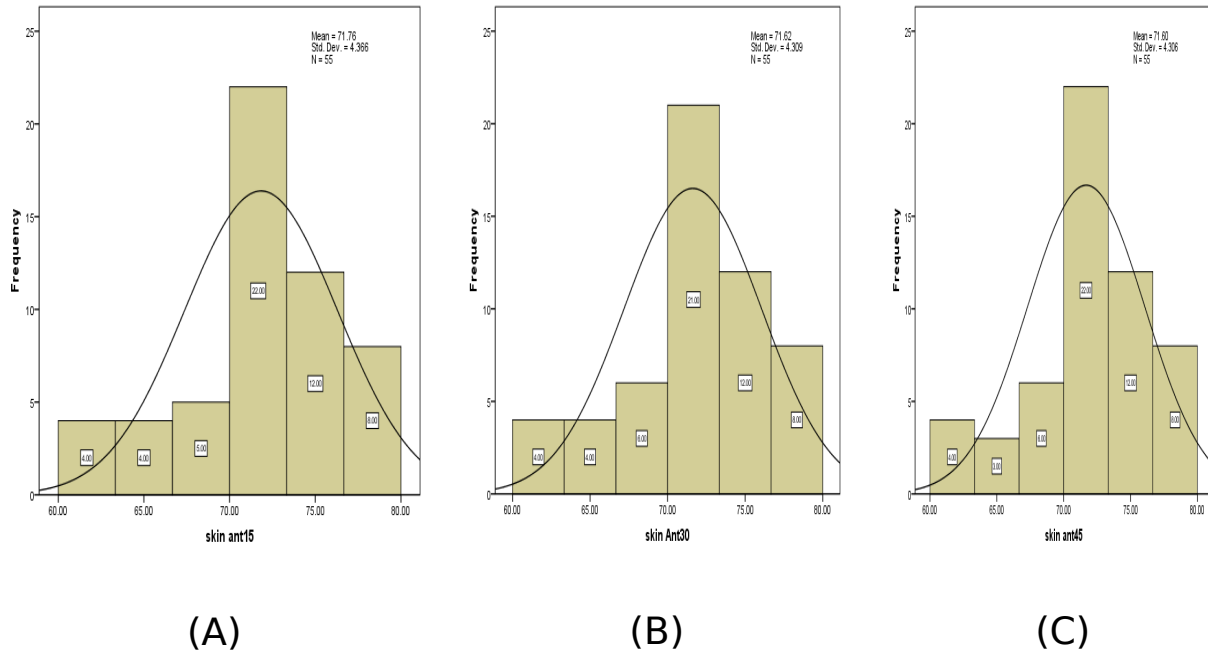


Figure (4-23) a histogram plot show the distribution of dose in skin anteriorly (A),(B) &(C) using seven fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted

The histogram plot showed in figure (4-23) in (A),(B) &(C) using seven fields with wedge angles 15°, 30° and 45° the mean dose received by skin anteriorly was 71.76 ± 4.37 , 71.62 ± 4.31 and 71.6 ± 4.31 respectively.

As it shows in figure (4-24) the dose in skin anteriorly increase by 0.02 Gy /wedge angle for three fields and increase by 0.0007Gy /wedge angle for five fields where in seven fields the dose increase by 0.005 Gy/wedge angle.

Figure (4-24) scatter plot of dose received by bladder using 3, 5 and 7 fields with wedge angles.

As shown in below histogram for right posterior oblique skin dose figure (4-25A, Band C) for three fields, figure (4-26 A, B and C) for five fields and figure (4-27 A, B and C) for seven fields respectively.

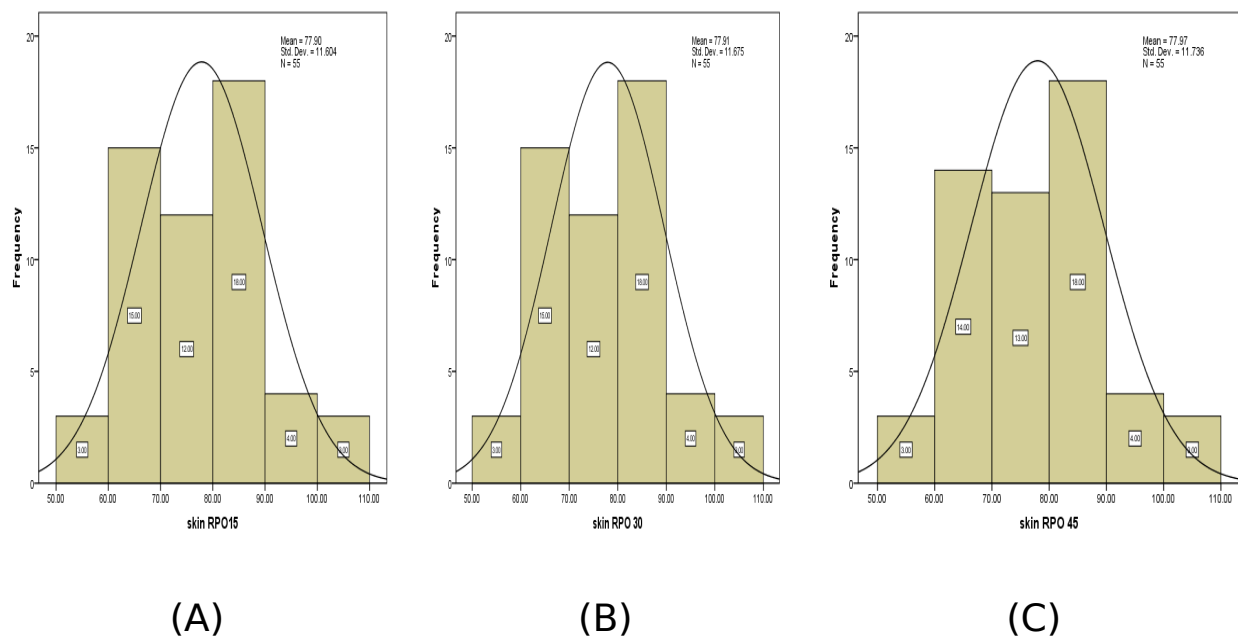


Figure (4-25) a histogram plot show the distribution of dose in skin right posterior oblique (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted. The histogram plot showed in figure (4-25) in (A),(B) &(C) using three fields with wedge angles 15°, 30° and 45° the mean dose received by skin right posterior oblique was 77.90 ± 11.61 , 77.91 ± 11.68 and 77.97 ± 11.74 respectively.

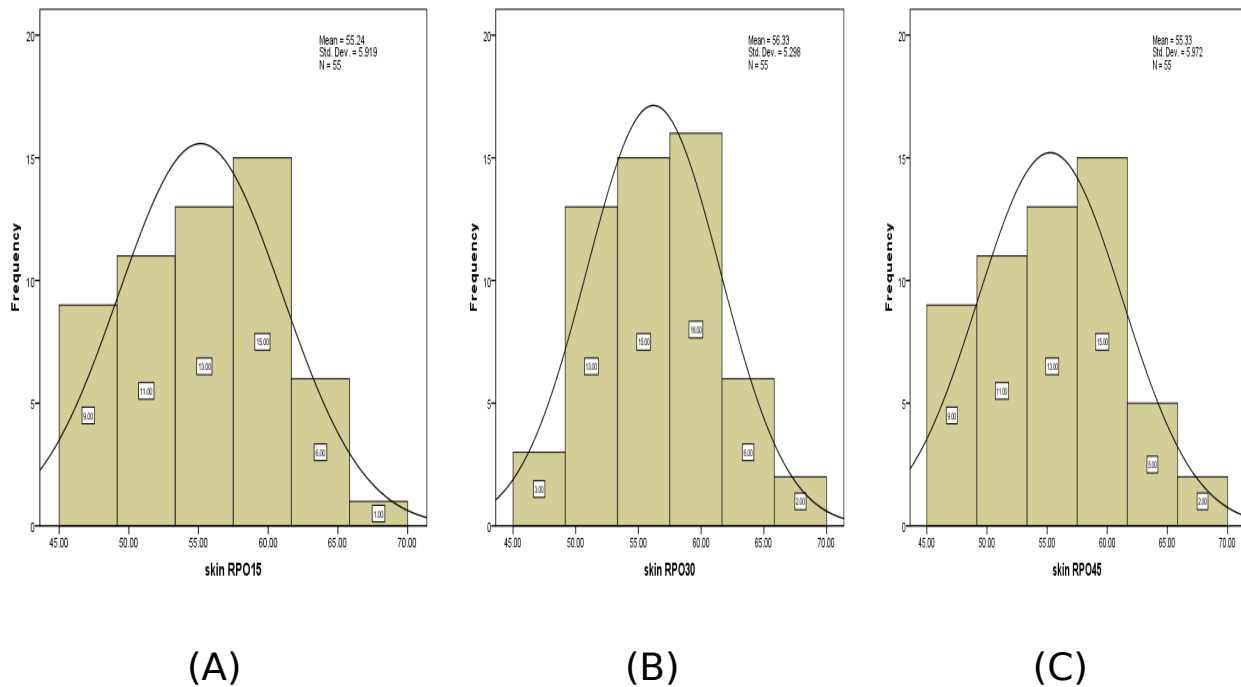


Figure (4-26) a histogram plot show the distribution of dose in skin right posterior oblique (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted.

The histogram plot showed in figure (4-26) in (A),(B) &(C) using five fields with wedge angles 15°, 30° and 45° the mean dose received by skin right posterior oblique was 55.24± 5.92, 56.33± 5.30 and 55.33± 6.00 respectively.

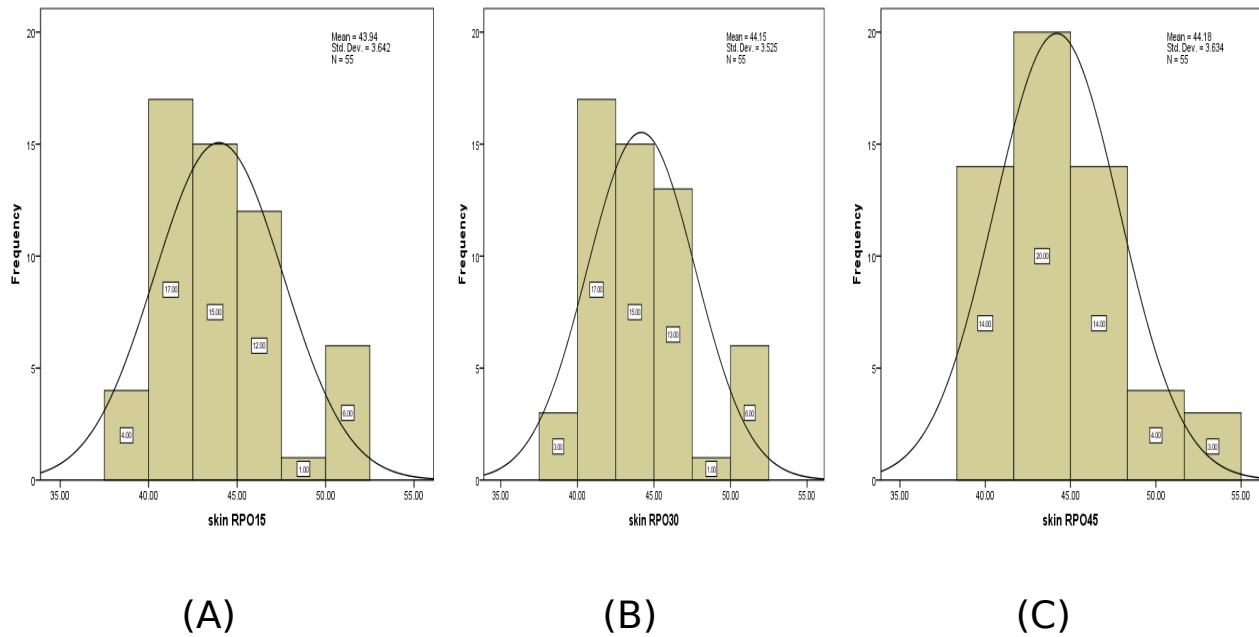


Figure (4-27) a histogram plot show the distribution of dose in skin right posterior oblique (A),(B) &(C) using seven fields with wedge angles 15°, 30° and 45° with normal distribution curve over plotted. The histogram plot showed in figure (4-27) in (A),(B) &(C) using seven fields with wedge angles 15°, 30° and 45° the mean dose

received by skin right posterior oblique was 43.49 ± 3.64 , 44.15 ± 3.53 and 44.18 ± 3.63 respectively.

4.2 Standard Model depends on standard patient CT-base results

Field name	Manual -standard <i>t</i>	Sig. (2- tailed)	Standard-CT <i>t</i>	Sig. (2-tailed)
Anterior field	2.00	0.183	1.30	0.320
			9	
Right posterior oblique field	0.458	0.691	0.18	0.867
			8	
Left posterior oblique field	0.277	0.807	0.25	0.821
			6	
Right anterior oblique field	1.732	0.225	0.86	0.477
			6	
Left anterior oblique field	0.577	0.622	0.18	0.867
			8	

Table (4.1) the mean and significant of five fields compare averages doses in case of manual contour and CT contour with the standard CT contour.

As see in table (4.1) the five fields namely anterior field, right posterior oblique, left posterior oblique, right anterior oblique and left anterior oblique respectively. The difference between standard model and CT-base was very minimum in anterior fields, right posterior oblique fields, left posterior oblique fields, right anterior oblique fields and left anterior oblique fields using t-test at $p=(0.183, 0.320), (0.691, 0.867), (0.807, 0.821), (0.225, 0.477), (0.622, 0.867)$ the result showed insignificant result with $t=(2.00, 1.309), (0.458, 0.188), (0.277, 0.256), (1.732, 0.866), (0.577,$

0.188).this result dictate that the standard and CT-base was similar or they give the same result so standard can be used instead of CT when there is difficulties in using CT.

Chapter 5
Discussion and
conclusion and
recommendations

Chapter 5

Discussion and conclusion and recommendations

5-1 Discussion

This result showed that in three fields as the wedge angle increase from 15 to 45 the dose received by the prostate decrease 0.4 % from 15° to 30° while from 30° to 45° it decreases by 0.04. In five fields from 15° to 30° it decreases by 0.07% while from 30° to 45° increases by 0.03. In seven fields from 15° to 30° increases by 0.02 while from 30° to 45° increases by 0.17. By increasing the number of fields from 3 to 7 the dose received by prostate for wedge 15° from three fields to five fields it decreases by 0.71% while from five fields to seven fields it increases by 0.06%. For wedge 30° from three fields to five fields it decreases by 0.4 while from five fields to seven fields it increases by 0.15%. For wedge 45° from three fields to five fields it decreases by 0.24% while from five fields to seven fields it increases by 0.21%. For wedge 15° from three fields to seven fields it decreases by 0.65 while for wedge 30° it decreases by 0.24 but for wedge 45° it decreases by 0.03.

This result showed that by using three fields, five fields and seven fields with wedge angle 15,30 and 45 for each the standard

deviation increase gradually from ± 1.7 to ± 2.10 by increasing both wedge angle and number of fields.

Therefore the dose received by the prostate using wedge 15° and three fields represent highest dose of the prostate relative to other combinations. This is because the wedge 15° has minimum factor dose than the other wedges. Also increase number of fields as well as the weighting factors used here and also the structures through which the field affected total dose reach to clinical target volume (CTV). The dose received by prostate increased where the number of fields increased as well as the angle of wedge. In case of three fields the dose to the prostate decrease by 0.02 Gy/wedge angle starting from 99.6 Gy. While for five fields the dose of prostate increase by 0.001 Gy/wedge angle starting from 98.5Gy. Similarly for seven fields the dose of prostate increase by 0.006 Gy/wedge angle starting from 98.5Gy.

This result showed that in three fields as the wedge angle increase from 15° to 45° the dose received by the clinical target volume decrease by 0.4 % from 15° to 30° while from 30° to 45° it decreases by 0.21%. In five fields from 15° to 30° it decreases by 0.05% while from 30° to 45° increases by 0.11%. In seven fields from 15° to 30° no change; While from 30° to 45° increases by 0.19. By increasing the number of fields from 3 to 7 the dose received by clinical target volume for wedge 15° from three fields to five

fields it decreases by 0.70% while from five fields to seven fields it increases by 0.09%. For wedge 30° from three fields to five fields it decreases by 0.36 while from five fields to seven fields it increases by 0.14%. For wedge 45° from three fields to five fields it decreases by 0.04% while from five fields to seven fields it increases by 0.22%. For wedge 15° from three fields to seven fields it decreases by 0.61 while for wedge 30° it decreases by 0.22 but for wedge 45° it increases by 0.18%.

This result showed that by using three fields, five fields and seven fields with wedge angle 15, 30 and 45 for each the standard deviation increase gradually from ± 1.82 to ± 2.23 by increasing both wedge angle and number of fields. Therefore the dose received by the clinical target volume using wedge 15° and three fields represent highest dose of the clinical target volume relative to other combination. This because as the wedge 15° has less, minimize factor dose than the other. Also increase number of fields and considering the weighting factors used here and the structures some of fields passes through affected total dose reach to clinical target volume (CTV). The dose received by (CTV) increased where the number of fields increased as well as the angle of wedge. In case of three fields the dose to the (CTV) decreases by 0.02 Gy/wedge angle starting from 99.4 Gy. While for fields the dose of (CTV) increase by 0.002 Gy/wedge angle

starting from 98.3Gy. Similarly for seven fields the dose of (CTV) increase by 0.006 Gy/wedge angle starting from 98.3Gy.

5-2 Conclusion

Comparison doses with different field's number and different wedges angles

Number of fields	Wedge angle	Prostate dose	Clinical target volume dose	Planning target volume dose	Rectum dose	Bladder dose	Anterior skin dose	Right posterior oblique dose
3	15	99.28	99.11	97.68	84.63	94.18	92.47	77.9
5	15	98.57	98.41	97.08	78.04	96.71	70.36	55.2
7	15	98.63	98.50	97.26	77.41	96.28	71.76	43.9
3	30	98.89	98.72	97.30	81.40	95.69	92.99	77.9
5	30	98.50	98.36	96.96	77.14	96.2	70.32	56.3
7	30	98.65	98.50	97.13	77.22	95.58	71.62	44.2
3	45	98.85	98.51	97.13	79.85	95.18	92.98	78
5	45	98.61	98.47	97.09	76.74	96.08	70.38	55.33
7	45	98.82	98.69	97.41	76.82	95.26	71.6	44.2

Table 5-1 Prostate, clinical & planning, rectum, bladder, anterior and right posterior oblique skin doses (in percentages).

Number of fields	Wedge angle	Prostate dose	Clinical target volume dose	Planning target volume dose	Rectum dose	Bladder dose	Anterior skin dose	Right posterior oblique dose
3	15	99.28	99.11	97.68	84.63	94.18	92.47	77.9
5	15	98.57	98.41	97.08	78.04	96.71	70.36	55.2
7	15	98.63	98.50	97.26	77.41	96.28	71.76	43.9
3	30	98.89	98.72	97.30	81.40	95.69	92.99	77.9
5	30	98.50	98.36	96.96	77.14	96.2	70.32	56.3
7	30	98.65	98.50	97.13	77.22	95.58	71.62	44.2
3	45	98.85	98.51	97.13	79.85	95.18	92.98	78
5	45	98.61	98.47	97.09	76.74	96.08	70.38	55.33
7	45	98.82	98.69	97.41	76.82	95.26	71.6	44.2

dose

3	15	9.9	9.9	9.8	3.5	2.4	2.2	4.8
5	15	9.8	9.8	9.7	4.8	2.7	4	6.5
7	15	9.8	9.8	9.7	4.7	2.6	4.1	7.4
3	30	9.8	9.8	9.7	3.1	2.5	2.3	4.8
5	30	9.8	9.8	9.6	4.7	2.6	4	6.6
7	30	9.8	9.8	9.7	4.7	2.5	4.1	7.4
3	45	9.8	9.8	9.7	3	2.5	2.3	4.8
5	45	9.8	9.8	9.7	4.6	2.6	4	5.5
7	45	9.8	9.8	9.7	4.7	2.5	4.2	6.7

Table 5-2 descending and ascending arrangement of Prostate, clinical & planning, rectum, bladder, anterior and right posterior oblique skin doses

Key 1: Prostate, clinical & planning doses, 100≡10 to 10≡1

Key 2: Rectum, bladder, anterior and right posterior oblique skin doses 100≡1 to 10≡10

Figure 5-1 compare of prostate doses using different multi-fields and different wedges angles.

Figure 5-2 compare of rectum doses using different multi-fields and different wedges angles.

Figure 5-3 compare of bladder doses using different multi-fields and different wedges angles.

Figure 5-4 compare of anterior skin doses using different multi-fields and different wedges angles.

Figure 5-5 compare of right oblique skin doses using different multi-fields and different wedges angles.

From above figures although the highest dose to prostate when using three fields with wedge angle 15 99)%) compare with others multi-fields but it find that the doses for rectum, bladder, anterior skin and right posterior oblique skin doses also are high 84 %,94%, 92% and 78% respectively .

Five and seven fields also the prostate doses are high 98.6%, 98,6% respectively. The doses for rectum, bladder, anterior skin and right posterior oblique skin (76.7%, 76.8 %),(96%,95%), (70%,71%),(55%,44%) respectively .

Find out that using five fields (one anterior (0) two anterior oblique 60)300,) two posterior oblique 120)240)) with wedge 45) is optimum than seven fields to avoid excessive dose to skin and femur bones by adding two lateral fields (90) and 270)

This protocol can be applied for wide range of population in Sudan.Using multi-fields by CO-60 machines in treatment of prostate carcinoma can replace linear accelerator machine especially in developing countries. The protocol can applied in whole African population with same conditions.

5-3 Recommendations

1. The model of CT-base radiotherapy planning can be used instead of done CT-images individually.
2. I hope further studies done for others cancers types using CT-base planning and multi-fields using Co⁶⁰ machine.

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Appendix A

Patient number	3 fields with weighing factor 04,03&03																											Separations							
	Dose cGy																								APcm	Laxcm									
	Skin						Rectum			Bladder			GTV 50%	CIV 50%	PV50%	GTV 50%	CIV 50%	PV50%	GTV 50%	CIV 50%	PV50%														
15		30		45		15	30	45	15	30	45	15	15	15	30	30	30	45	45	45	45	AmF5	RF0F5	LP0F5	prostate volume	dirical volume	planning volume	rectum volume	bladder volume						
Ant	RPO	Ant	RPO	Ant	RPO																														
1	304	57.9	81.6	57.6	82.9	57.6	104	100.2	97	98.7	100.5	102.4	101.5	101.4	100.7	100.7	100.7	100	100.2	100.2	99.5	15.2	35.2	11X11	11X11	11X11	11X11	73.3	95.3	183.4	28	92.8			
2	81.4	58.8	82.8	58.5	84.1	58.5	103.3	99.4	96.1	98.3	100.1	102.1	101.5	101.5	100.9	100.8	100.9	100.2	100.4	100.4	99.8	15.5	34.6	11X11	11X11	11X11	11X11	87.3	111.7	209.6	33.7	112.1			
3	82.4	59.6	84	59.4	85.2	59.4	102.5	98.5	95.2	97.8	99.7	101.7	101.5	101.5	101	100.9	101	100.4	100.5	100.5	100	15.7	33.9	11X11	11X11	11X11	11X11	101.3	128.1	235.7	39.3	131.3			
4	83.4	60.5	85.2	60.3	86.4	60.3	101.8	97.7	94.3	97.3	99.3	101.4	101.5	101.5	101.1	101	101.1	100.6	100.7	100.7	100.2	16	33.3	11X11	11X11	11X11	11X11	111.3	144.5	261.9	44.9	150.5			
5	84.4	61.3	86.4	61.2	87.5	61.1	101	96.8	93.4	96.8	98.9	101	101.5	101.5	101.2	101	101.1	100.7	100.8	100.8	100.4	16.2	32.6	11X11	11X11	11X11	11X11	129.2	160.9	288	50.5	169.7			
6	86.4	63	88.8	63	89.8	62.9	99.5	95.1	91.6	95.9	98.1	100.3	101.5	101.6	101.4	101.2	101.3	101	101.2	101.1	100.9	16.7	31.3	11X11	11X11	11X11	11X11	157.2	193.7	340.3	61.8	208.2			
7	87.4	63.9	90	63.9	91	63.8	98.7	94.3	90.7	95.4	97.7	100	101.5	101.6	101.5	101.3	101.4	101.2	101.3	101.3	101.1	17	30.7	11X11	11X11	11X11	11X11	171.2	210.1	366.4	67.4	227.4			
8	88.4	64.7	91.1	64.7	92	64.6	97.9	93.4	89.7	94.9	97.2	99.6	101.5	101.6	101.6	101.3	101.4	101.3	101.3	101.4	101.3	17.2	30	12X10	10X12	10X12	125.1	226.5	392.5	73	246.6				
9	88.3	66.1	91	66.1	91.1	66	93.2	89.1	85.6	94.8	97	99.3	101.1	101.2	100.9	100.9	101	100.7	100.9	101	100.7	17.3	30.5	12X10	10X12	10X12	162.9	199.7	347.2	68	211.7				
10	88.2	67.5	90	67.4	90.1	67.4	88.5	84.7	81.5	94.7	96.8	99	100.7	100.8	100.2	100.5	100.6	100	100.5	100.6	100.1	17.4	31	12X10	10X12	10X12	140.7	172.9	301.8	63	176.7				
11	87.9	70.2	88	70.1	88.2	70.2	79	75.9	73.2	84.4	86.3	88.3	89.9	100	98.8	99.7	99.8	99.7	99.6	99.8	99.8	17.5	32.1	10X7	7X10	7X10	96.3	119.3	211	52.9	106.7				
12	86	69.6	86.1	69.6	86.3	69.7	79.3	76.3	73.6	84	86.7	87.3	89.5	99.4	98	99.1	99.1	99.8	99	99	99.7	17.7	31.8	10X7	7X10	7X10	95.8	116.9	198.2	49.3	128.2				
13	84	69	84.2	69	84.4	69.1	79.6	76.6	74	83.5	85	86.3	88	98.8	97.2	98.5	98.3	96.8	98.2	98.1	96.6	17.8	31.4	10X7	7X10	7X10	95.2	114.4	185.3	45.6	149.6				
14	80.1	67.7	80.3	67.8	80.5	67.9	80.1	77.2	74.8	82.5	83.3	84.3	88.1	97.5	95.5	97.3	96.8	94.8	96.8	96.3	94.4	18.1	30.6	8X11	11X8.5	11X8.5	94.1	109.5	159.5	38.2	192.4				
15	80.6	67.6	80.8	67.7	81	67.7	76.6	73.8	71.5	81.9	82.6	83.4	88.3	97.8	95.5	97.5	97.1	94.8	97	96.6	94.4	18.3	30.9	8X11	11X8.5	11X8.5	92.4	109.8	171.5	39.8	174.5				
16	81.1	67.5	81.2	67.5	81.4	67.5	73	70.4	68.2	81.2	81.8	82.5	88.5	98	95.5	97.7	97.3	94.8	97.2	96.8	94.4	18.4	31.2	8X11	11X8.5	11X8.5	90.6	110	183.5	41.3	156.5				
17	81.6	67.4	81.7	67.3	81.8	67.3	69.5	67	64.9	80.6	81	81.6	88.7	88.2	85.5	97.9	97.5	94.8	97.4	97	94.4	18.6	31.5	8X11	11X8.5	11X8.5	88.9	110.2	156.5	42.9	138.5				
18	82	67.2	82.1	67.1	82.2	67	65.9	63.5	61.5	83.9	80.2	80.7	88.9	88.4	85.4	98.1	97.7	94.8	97.6	97.2	94.4	18.7	31.8	8X10	9X15	9X15	87.1	110.4	207.5	44.4	160.5				
19	84.4	71.5	84.6	71.5	84.8	71.4	68	65.5	78.6	81.4	81.9	82.6	88.4	97.9	94.9	97.5	97.1	94.2	96.9	96.5	93.7	19	32.3	8X10	9X15	9X15	80.7	102.9	182.2	46.7	121.2				
20	86.7	75.7	87.1	75.8	87.3	75.8	70	67.5	85.7	82.9	83.6	84.4	87.8	97.3	84.3	96.8	96.4	83.5	96.1	95.7	93	19.2	32.8	8X10	9X15	9X15	74.3	95.3	156.9	48.9	121.9				
21	89.2	80	89.6	80.1	89.9	80.2	72	69.5	82.8	84.4	85.3	86.3	87.2	96.8	83.8	86.1	85.8	82.9	85.3	85	82.3	19.4	33.3	8X10	9X15	9X15	67.9	87.7	131.6	51.1	122.6				
22	91.7	84.2	92	84.4	92.4	84.6	74	71.4	69.9	85.8	86.9	88.1	96.6	96.2	83.2	95.4	95.1	92.2	94.5	94.2	91.5	19.6	33.8	8X10	9X15	9X15	61.4	80.1	106.3	53.3	123.3				
23	92.2	88.8	92.6	88.9	93.2	90.1	97.3	92.8	89.1	96.3	98.6	101	99.5	99.6	99.1	99.3	99.4	92.8	99.3	99.4	98.8	19.7	33.2	12X10	9X12.5	9X12.5	218.4	259.9	421.6	31.5	276.3				
24	92.5	72.9	92.9	73	93.4	73.2	91.7	87.8	84.6	95.6	97.7	99.9	98	97.9	96.8	97.8	97.7	96.5	97.7	97.7	96.5	19.9	32.9	12X10	9X12.5	9X12.5	188	226.4	377.8	51	244.1				
25	92.8	76	93.1	76	93.6	76.2	86.1	82.8	80	94.9	96.7	98.7	96.4	96.2	84.4	96.2	96	94.1	96.1	96	94.1	20.1	33.5	12X10	9X12.5	9X12.5	157.6	192.8	333.9	70.4	211.9				
26	93.1	79.1	93.4	79.1	93.8	79.2	80.5	77.8	75.4	84.2	85.8	87.5	94.8	94.5	82.1	94.6	94.3	91.8	94.5	94.3	91.7	20.3	34.1	12X10	9X12.5	9X12.5	127.2	159.3	280.1	89.9	179.7				
27	93.3	82.1	93.6	82.1	93.9	82.2	74.9	72.7	70.8	83.5	84.8	86.3	93.2	92.8	83.7	93	92.6	89.4	92.8	92.5	83.3	20.4	34.7	9X7	7X9	7X9	96.7	125.7	246.2	109.3	147.4				
28	93.4	78.8	93.7	78.9	94	79	87.6	84.6	82.1	96.4	98	99.7	96.6	96.3	84.4	96.4	96.2	94.2	96.3	96.1	94.2	20.6	35.2	9X7	7X9	7X9	78.3	101.1	194.5	74.9	115.6				
29	93.5	75.5	93.8	75.6	94.1	75.7	100.2	96.5	93.3	99.3	101.1	103	99.9	99.8	99.1	99.8	99.7	99	99.8	99.7	99	20.7	35.7	11X13	13X11	13X11	59.9	76.4	142.7	40.5	83.7				
30	95.5	77.3	95.5	77.2	95.7	77.2	83	80.9	85.6	96.1	97.5	99	99.6	99.3	97.5	99	98.8	97	98.6	98.4	96.6	20.9	37.6	10X8	8X10	8X10	81.4	101.6	183.4	49.6	130.3				
31	93.4	76.4	93.4	76.4	93.5	76.4	80	85.9	82.5	85.4	86.7	88.1	98.3	98.1	86.7	97.8	97.7	96.3	97.6	97.5	96	21	36.3	10X8	8X10	8X10	122.7	150.6	263.7	53.8	144.7				
32	91.2	75.5	91.3	75.5	91.3	75.5	86.9	82.8	79.4	84.7	86.8	87.1	87	96.9	95.9	96.6	96.6	95.5	96.5	96.4	95.4	21.1	34.9	10X9	8X10	8X10	164	199.6	344	57.9	159				
33	94.2	79.8	94.4	79.7	94.7	79.8	76.1	74	72.2	81	82.4	83.9	100.8	100.7	99.2	100.6	100.5	99.1	100.5	100.4	99.2	21.3	34.4	10X9	8X10	8X10	96.7	105	177.8	141.4	213.4				
34	95.4	82.3	95.6	82.3	95.9	82.2	76.9	74.7	72.8	81.3	82.8	84.1	100.6	100.4	88.6	100.4	100.2	88.5	100.3	100.1	98.5	21.5	34.1	10X9	8X10	8X10	94.6	116.1	198.8	116.2	210.7				
35	96.6	84.7	96.8	84.6	97.1	84.6	77.6	75.3	73.4	81.5	83.2	84.2	100.3	100	97.9	100.2	99.8	97.8	100.1	99.7	97.8	21.7	33.8	10X9	8X10	8X10	102.4	127.1	219.8	90.9	207.9				
36	99	89.5	99.2	89.5	99.5	89.4	79.0	76.5	74.5	81.9	83.9	84.5	98.8	99.2	86.6	99.7	99	96.4	99.7	99	96.4	22	33.2	8X12	12X8.5	12X8.5	118	149.1	261.8	40.4	202.4				
37	99.1	87.7	99.2	87.6	99.4	87.6	80.1	77.4	75.2	84.8	86.6	87.4	99.9	99.4	86.8	99.9	99.1	96.6	99.6	99	96.5	22.3	33.9	8X12	12X8.5	12X8.5	106.5	134.9	240.4	47.3	196.6				
38	98.2	85.8	98.2	85.7	98.3	85.7	81.1	78.2	75.8	87.6	89.2	90.2	99.9	99.5	97	100	99.1	96.7	99.4	99	96.5	22.5	34.5	8X12	12X8.5	12X8.5	95	120.7	219	54.1	190.8				
39	99.3	83.9	99.2	83.8	99.2	83.8	82.1	79	76.5	90.5	91.9	93	100	99.7	97.2	99.7	99.2	96.8	99.2	99	96.6	22.7	35.2	8X12	12X8.5	12X8.5	83.5	106.5	197.6	61	185				
40	98.3	82	99.1	81.9	99.1	81.9	83.1	79.8	77.1	93.3	94.5	95.8	100	99.8	97.4	99.4</																			

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	Fbn																																									
																				Rectum					Bladder					GTV50%		GTV50%		PTV50%		GTV 50%	GTV 50%	PTV 50%	GTV 50%	GTV 50%	PTV 50%	PTV 50%
	15						30						45						15		15		15		30		30		30		45		45		45							
am	RAO	RPO	am	RAO	RPO	am	RAO	RPO	am	RAO	RPO	IS	30	45	IS	30	45	IS	30	45	IS	30	45	IS	30	45	IS	30	45	IS	30	45	IS	30	45							
1	70.1	36.2	45	69.9	36.1	45	69.8	36.1	45	69.8	36.1	45	96.8	95.5	94.7	105.4	105	105	100.1	100.2	99.7	99.9	100	99.5	99.9	100	99.5	15.2	35.2													
2	70.3	35.5	45.4	70.1	35.4	45.9	70	35.4	45.4	96	94.6	93.9	104.9	104.4	104.4	100.3	100.4	100	100.1	100.2	99.8	99.8	100.1	100.2	99.8	100	99.8	15.5	34.6													
3	70.4	34.7	45.7	70.2	34.7	54.7	70.2	34.6	45.7	95.1	93.7	93	104.3	103.8	103.8	100.5	100.6	100.2	100.3	100.4	100.3	100.3	100.3	100.4	100.3	100.3	16	33.3														
4	70.5	34	46.1	70.4	34	59.6	70.4	33.9	46.1	94.2	92.8	92.1	103.7	103.2	103.2	100.7	100.8	100.4	100.5	100.6	100.5	100.5	100.6	100.5	100.6	100.5	16	33.3														
5	70.6	33.2	46.4	70.5	33.2	64.4	70.6	33.1	46.4	93.3	91.9	91.2	103.1	102.6	102.6	100.8	100.9	100.6	100.7	100.8	100.7	100.7	100.8	100.7	100.8	100.5	16.2	32.6														
6	70.8	31.7	47.1	70.8	31.7	56.1	71	31.6	47.1	91.5	90.1	89.4	102	101.4	101.4	101.1	101.2	101	101	101.2	100.9	101.1	101.2	101	101.2	101	16.7	31.3														
7	70.9	31	47.5	70.9	31	52	71.2	30.9	47.5	90.6	89.2	88.5	101.4	100.8	100.8	101.3	101.4	101.2	101.2	101.3	101.1	101.3	101.4	101.3	101.4	101.2	17	30.7														
8	71	30.2	47.8	71	30.2	47.8	71.3	30.1	47.8	89.7	88.3	87.6	100.8	100.1	100.1	101.4	101.5	101.4	101.3	101.4	101.3	101.1	101.3	101.4	101.3	101.4	17.2	30	12x10	10x12	10x12	10x12	10x12	185.1	226.5	382.5	73	246.6				
9	70.1	32.5	48.8	70.1	32.5	48.8	70.3	32.4	48.8	85.3	84	83.3	100.2	99.5	99.5	100.9	101.1	100.8	100.8	101	100.7	101	101.1	100.8	100.8	101	17.3	30.5	12x10	10x12	10x12	10x12	10x12	162.9	199.7	347.2	68	211.7				
10	69.1	34.7	49.7	69.1	34.7	49.7	69.3	34.7	49.8	80.9	79.7	79	99.5	98.9	98.9	100.4	100.6	100.1	100.3	100.5	100	100.5	100.6	100.1	100.1	100.3	17.4	31	12x10	10x12	10x12	10x12	10x12	140.7	172.9	301.8	63	176.7				
11	67.2	39.2	51.6	67.1	39.2	51.6	67.2	39.2	51.7	72.1	71.1	70.4	98.1	97.7	97.6	99.4	99.7	98.7	99.3	99.6	98.6	99.4	99.7	98.7	98.7	17.5	32.1	10x7	7x10	7x10	7x10	7x10	96.3	119.3	211	52.9	106.7					
12	65.7	39.1	51.1	65.6	39	51.2	65.7	39	51.3	72.3	71.3	70.7	97	96.6	96.6	98.8	98.9	97.6	98.6	98.7	97.5	98.7	98.8	97.6	97.6	17.7	31.8	10x7	7x10	7x10	7x10	7x10	96.8	116.9	198.2	49.3	128.2					
13	64.1	38.9	50.6	64	38.8	50.7	64.1	38.8	50.8	72.4	71.5	70.9	95.8	95.3	95.3	98.1	98	96.5	97.9	97.8	96.4	98	97.9	96.4	96.4	17.8	31.4	10x7	7x10	7x10	7x10	7x10	95.2	114.4	185.3	45.6	149.6					
14	60.9	38.5	49.6	60.9	38.4	49.7	61	38.3	49.8	72.7	71.8	71.3	93.5	93.2	93.3	96.7	96.2	94.3	96.5	96	94.1	96.6	96	94.1	18.1	30.6	8x11	11x8.5	11x8.5	11x8.5	11x8.5	94.1	109.5	159.5	38.2	192.4						
15	61.3	38.5	49.6	61.3	38.4	49.6	61.4	38.3	49.7	69.3	68.5	68	92.6	92.4	92.5	96.8	96.3	94.2	96.6	96.1	94	96.7	96.1	94	18.3	30.9	8x11	11x8.5	11x8.5	11x8.5	11x8.5	92.4	109.8	171.5	39.8	174.5						
16	61.7	38.5	49.5	61.7	38.4	49.5	61.7	38.3	49.6	65.9	65.1	64.6	91.7	91.5	91.6	96.9	96.4	94.1	96.7	96.2	93.8	96.7	96.2	93.9	18.4	31.2	8x11	11x8.5	11x8.5	11x8.5	11x8.5	90.6	110	183.5	41.3	156.5						
17	62.1	38.5	49.5	62.1	38.4	49.4	62.1	38.3	49.5	62.5	61.7	61.3	90.8	90.6	90.7	97	96.5	94	96.8	96.3	93.7	96.8	96.3	93.8	18.6	31.5	8x11	11x8.5	11x8.5	11x8.5	11x8.5	88.9	110.2	186.5	42.9	138.5						
18	62.4	38.4	49.4	62.4	38.4	49.3	62.4	38.3	49.3	59	58.3	57.9	89.9	89.7	89.8	97	96.5	93.8	96.8	96.3	93.5	96.8	96.3	93.6	18.7	31.8	8x10	9x8.5	9x8.5	9x8.5	9x8.5	87.1	110.4	207.5	44.4	120.5						
19	64.1	38.8	51.7	64.1	38.8	51.6	64.1	38.7	51.6	60.6	59.9	59.6	92	91.7	91.8	96.1	96.7	93	96	95.5	92.7	96	95.5	92.8	19	32.3	8x10	9x8.5	9x8.5	9x8.5	9x8.5	87.1	102.9	182.2	46.7	121.2						
20	65.7	39.2	53.9	65.7	39.2	53.8	65.7	39	53.8	62.2	61.5	61.2	94	93.7	93.7	95.2	94.8	92.1	95.1	94.6	91.8	95.1	94.7	91.9	19.2	32.8	8x10	9x8.5	9x8.5	9x8.5	9x8.5	9x8.5	94.3	95.3	156.9	49.9	121.9					
21	67.3	39.6	56.1	67.3	39.6	56.1	67.3	39.4	56.1	63.8	63.1	62.8	96.1	95.7	95.6	94.3	94	91.2	94.2	93.8	91	94.2	93.9	91	19.4	33.3	8x10	9x8.5	9x8.5	9x8.5	9x8.5	9x8.5	67.9	87.7	131.6	51.1	122.6					
22	69.9	40	58.3	69.9	39.9	58.3	69.9	39.7	58.3	65.3	64.7	64.4	98.1	97.7	97.5	93.4	93.1	91.3	98.3	98.9	90.1	93.3	90	19	33.8	8x10	9x8.5	9x8.5	9x8.5	9x8.5	9x8.5	61.4	80.1	106.3	53.3	123.3						
23	73.8	43.2	53	73.9	43	53.1	74	42.9	53.2	92.4	90.8	89.8	100.6	100.1	100.1	99.5	99.6	99.3	99.5	99.6	99.2	99.6	99.8	99.4	19.7	32.2	12x10	9x12.5	9x12.5	9x12.5	9x12.5	218.4	259.9	421.6	31.5	276.3						
24	72.4	41.6	53.6	72.4	41.5	53.7	72.5	41.4	53.8	85.7	84.4	83.6	98.6	98.1	98	97.7	97.5	96.6	97.7	97.7	96.5	97.8	97.9	96.7	19.9	32.9	12x10	9x12.5	9x12.5	9x12.5	9x12.5	188	226.4	377.8	51	244.1						
25	70.9	40	54.1	70.9	39.9	54.2	71	39.8	54.3	79	77.9	77.4	96.6	96	95.8	95.8	95.3	93.9	95.8	95.7	93.8	95.9	95.9	94	20.1	33.5	12x10	9x12.5	9x12.5	9x12.5	9x12.5	157.6	192.8	333.9	70.4	211.9						
26	69.5	38.4	54.7	69.4	38.3	54.8	69.5	38.3	54.8	72.3	71.5	71.2	94.6	94	93.6	93.6	93.2	91.2	93.9	93.7	91.1	94.1	93.9	91.3	20.3	34.1	12x10	9x12.5	9x12.5	9x12.5	9x12.5	127.2	159.3	290.1	89.9	179.7						
27	68	36.8	55.2	67.9	36.7	55.3	67.9	36.7	55.3	65.5	65	64.9	92.5	91.8	91.4	92	91	88.5	92	91.7	88.4	92.2	91.9	88.6	20.4	34.7	9x7	7x9	7x9	7x9	7x9	96.7	125.7	246.2	109.3	147.4						
28	70.2	40.1	55.5	70.2	40	55.5	70.4	40	55.6	79.8	79.9	79.4	98.1	97.6	97.3	96	95.4	93.8	95.9	95.7	93.7	96	95.8	93.8	20.6	35.2	9x7	7x9	7x9	7x9	7x9	79.3	101.1	194.5	74.9	115.6						
29	72.4	43.4	55.7	72.5	43.3	55.7	72.7	43.3	55.8	94	92.7	91.8	103.7	103.3	103.2	99.9	99.8	99.1	99.8	99.7	99	99.8	99.7	99	20.7	35.7	11x13	13x11	13x11	13x11	13x11	59.9	76.4	142.7	40.5	83.7						
30	73.7	45.6	57.2	73.7	45.5	57.2	73.8	45.4	57.2	86.6	85.1	84.1	99.4	99.1	99.2	98.5	98.4	96.8	98.4	98.3	96.7	98.5	98.3	96.8	20.9	37.6	10x8	8x10	8x10	8x10	8x10	81.4	101.6	183.4	49.6	130.3						
31	71.4	44	56	71.4	43.9	56	71.5	43.9	56	83.5	82	81.1	97.9	97.6	97.7	97.9	97.8	96.5	97.7	97.7	96.3	97.8	97.7	96.4	21	36.3	10x8	8x10	8x10	8x10	8x10	122.7	150.6	263.7	53.8	144.7						
32	69	42.3	54.7	69.1	42.3	54.7	69.2	42.3	54.8	80.3	79.9	79	96.4	96.1	96.1	97.2	97.1	96.1	97	97	95.9	97.1	97	96	21.1	34.9	10x9	9x10	9x10	9x10	9x10	164	199.6	344	57.9	159						
33	69.1	37.4	54.6	69	37.3	54.6	69	37.3	54.7	71.5	71.1	71	91.1	90.5	90.2	100.1	100	98.6	100	99.9	98.9	100.1	100	98.5	21.3	34.9	10x9	9x10	9x10	9x10	9x10	96.7	105	177.8	141.4	213.4						
34	70.1	38.8	56.4	70.1	38.7	56.3	70.1	38.7	56.4	71.8	71.3	71.2	82	81.4	81.1	100.2	100	98.3	100.1	99.9	98.2	100.2	100	98.2	21.5	34.1	10x9	9x10	9x10	9x10	9x10	94.6	116.1	198.8	116.2	210.7						
35	71.1	40.2	58.1	71.1	40.1	58	71.1	40.1	58	72	71.5	71.4	82.8	82.3	82	100.3	99.9	97.9	100.2	99.8																						

Appendix B

