A COMPARATIVE ANALYSIS OF THE 3-FIELD RADIATION TREATMENT TECHNIQUE VERSUS THE 4-FIELD RADIATION TREATMENT TECHNIQUE IN THE TREATMENT OF PATIENTS PRESENTING WITH EITHER STAGE B OR STAGE C PROSTATE CANCER

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Except for quotations specifically indicated in the text and such help as I have acknowledged, this dissertation is wholly my own work, and has not been submitted for any qualification at any other institution.

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DEDICATION

This dissertation is dedicated to my baby girl Suraishnee, who has always given me so much joy and my darling husband for giving me my little 'angel'.

This dissertation is also dedicated to the following persons:

My mom and dad for always wanting only the best for me,

Ms Ann Hesketh for dangling the 'carrot',

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ABSTRACT

PURPOSE

Radical radiotherapy is quite commonly used to treat localised prostate cancer. Acute and chronic toxicity to the bladder and rectum are dependant upon field arrangement, dose delivered to these organs and the volume of these organs that is within the target volume. A prospective study was conducted in order to determine whether the 3-field or the 4-field radiation treatment technique yields less severe bladder and rectal toxicity.

METHODS AND MATERIALS

Sixty patients with histologically confirmed stage B or C (Jewitt's staging system) prostate cancer, with or without radical prostatectomy were recruited from two private oncology institutions, 30 of whom were in group 1 (3-field technique) and 30 in group 2 (4-field technique). Pre-treatment and post-treatment prostatic specific antigen (PSA) levels were recorded in order to compare the effect of radiation on PSA. Both groups were treated in 2.00gy fractions per day to a dose of 60.00gy before the field arrangements were changed. This study therefore assessed the patients

until a dose of 60.00Gy was reached. Weekly acute toxicity to the bladder and rectum were assessed using the RTOG/EORTC grading criteria.

RESULTS

There was no significant difference in acute bladder toxicity between the two groups for weeks 1 - 6 ($p>3$ for all 6 weeks). Grade 1 acute bladder was overall highest in week 3 (48.3%), grade two in week 6 (48.3%), and grade 3 in weeks 5 and 6 (6.7%). Grade 1 acute bladder toxicity was highest in week 6 (60%) for the 3-field technique and week 3 (43.3%) for the 4 field technique. Grade 2 acute bladder toxicity was highest in week 5 (33.3%) for the 3-field technique and weeks 4,5 and 6 (30.0%) in the 4-field technique. Grade 3 acute bladder toxicity was highest in weeks 5 and 6 for the 3-field and 4-field technique (3.3% and 10% respectively). There was a statistically significant difference between the 3-field and 4-field technique in terms of acute rectal toxicity in week 2 ($p=0.022$). Grade 1 acute rectal toxicity was the highest overall in week 5 (21.7%), grade 2 toxicity in week 6 (8.3%) and grade 3 in week 4 (5.0%). Grade 1 toxicity was highest in week six (26.7%) for the 3-field technique and in week 3 (23.3%) for the 4-field technique, grade two in week 6 (16.7%) for the 3-field technique and in week 3 (6.7%) for the 4-field technique, whereas

grade 3 toxicity for the 3-field technique was constant in weeks 2-5 at 3.3% compared to the 4-field which demonstrated the highest acute rectal toxicity in week 3. No patients had grade 4 acute bladder or rectal toxicity in either of the two fields. Evaluation of pre-treatment and post-treatment PSA results demonstrated that there is a reduction in PSA levels during the course of treatment.

CONCLUSIONS

There was no statistically significant difference between the 3-field technique and the 4-field technique in terms of acute bladder toxicity. The 4-field technique, however proved more toxic than the 3-field technique in terms of acute rectal toxicity. The implementation of routine screening programs for prostate cancer is strongly advocated.

TABLE OF CONTENTS

CHAPTER THREE

3.0 METHODS AND MATERIALS

CHAPTER FOUR

4.0 RESULTS

APPENDICES

LIST OF TABLES

LIST OF FIGURES

DEFINING THE TERMS

Biopsy - visual examination (usually microscopic) of tissue from a living subject (Bomford **et al.** 1993 : 578).

Conformal radiotherapy - tailoring of high-dose volume to the target volume in a patient simultaneously delivering a low dose to non-target tissue (Webb 1993 : 3).

Gray - the unit for absorbed dose (Bomford **et al.** 1993 : 72).

Histology - microscopic study of tissues and organs, and of cells arranged in tissue (Bomford **et al.** 1993 : 589).

Hormonal manipulation - therapy involving the removal of the body's own hormones or the addition of synthetic hormones to either stimulate, control or eradicate tumour growth (Bomford **et al.** 1993 : 545).

Oncology - science of tumours in all their aspects (Bomford **et al.** 1993 : 583).

Prostatectomy - surgery to remove part of the prostate gland. Radical prostatectomy is surgery to remove the entire prostate. (Loveday, 1993 : 168).

Radical - treatment initiated with intention to cure (Griffiths 1994 : 1-2).

Radiotherapy - the treatment of disease, primarily malignancies, using electromagnetic and particle radiations (Griffiths 1994 : 1).

Target volume - refers to that volume regarded by the clinician as being the tumour or lesion surrounded by any margin he or she chooses to include in the treatment (Bomford **et al.** 1993 : 97).

Transurethral resection (of the prostate) - the use of instruments inserted into the penis to remove tissue from the prostate. Also called TUR and TURP- (Loveday 1993 : 168).

Treatment volume - refers to that volume actually covered by the radiation beams and raised to a greater than the minimum dose in the target volume (Bomford **et al.** 1993 : 97).

LIST OF ABBREVIATIONS

CRT	-	Conformal Radiation Therapy
CT	-	Computerised Tomography
DVH	-	Dose Volume Histogram
EORTC	-	European Oncology and Radiation Therapy Committee
Gy	-	Gray
JCRT	-	Joint Center for Radiation Therapy
PSA	-	Prostatic Specific Antigen
RTOG	-	Radiation Therapy Oncology Group
SRT	-	Standard Radiation Therapy
TDF	-	Time, Dose, Fractionation
3D-CRT	-	3-dimensional Conformal Radiation Therapy

CHAPTER ONE : INTRODUCTION

Prostate cancer is currently causing a substantial public health burden. This disease is unique amongst other human cancers, in that it demonstrates late clinical signs and symptoms, which has subsequently led to the search for earlier histological and biochemical methods of detection. It is therefore important to appreciate the broad biological potential and behaviour pattern of prostate cancer, since it is definitely a heterogeneous disease, with some tumours being very small; well to moderately differentiated and confined to the prostate gland (stage A and B - Refer to Appendix C). Some are only found at autopsy and seem unlikely to ever cause clinical disease or death, unless left without intervention for decades. The larger, more poorly differentiated cancers of the prostate are the ones that are the cause of greatest concern in males generally above the age of 50 years (Abbas and Scardino 1997).

The disease tends to affect males mostly above the age of 50 years with a peak incidence at 72 years of age. As many as 30% of men older than 50 years of age have histological evidence of prostate cancer upon autopsy. It is believed that most males die with prostate cancer rather

than of the disease although no studies have as yet been executed in order to confirm this belief (Newman, 1996; *Zeneca Medical Publications*, 1997:1). In South Africa alone, an average of 2621 new cases of prostate cancer were reported to the National Cancer Registry (NCR) between 1993 to 1995 (Sitas **et al.** 1998).

It is the most common form of cancer in males except for skin and lung cancer and is the second highest cause of cancer deaths, after lung cancer (Neal and Hoskin, 1994; *Zeneca Medical Publications* 1997:1). According to Sitas **et al.** (1998), the incidence of prostate cancer is constantly on the increase in South Africa with the possibility of 1 in 31 males in South Africa having a lifetime risk of developing the disease. Sitas **et al.** (1998) further argues that there is a lower incidence in South African Black males (13:100 000) as compared to South African White males (57.8:100 000) with a seemingly increasing familial incidence. With seemingly increasing incidence in the South African population, the available methods of treatment must be considered.

"The goal of treatment of local and locally advanced prostate cancer is to cure without causing unacceptable complications..."(Chuba **et al.**

1997:1449-1454), or morbidity including acute and chronic toxicities that may or may not require further or surgical intervention. The realisation that prostate cancer treated with 'traditional' methods including standard radiation therapy, offers lower cure rates than previously anticipated, has led to the search for improved techniques in terms of less severe toxicities and better cure rates. 3-D conformal radiotherapy and hormonal therapy appear to be amongst the promising techniques. Advances in 3-D conformal radiotherapy, hormonal therapy, biotherapy and immunotherapy have already begun although their efficacy has not as yet been fully established (Chuba **et al.** 1997).

"No currently available treatment for prostate cancer has been proven capable of doing more good than harm" (Feeney 1988: 1). Because of this state of art, questions arise on how patients with prostate cancer can be managed in order firstly to cure the disease or even prolong life and secondly how to attempt to minimise the acute toxicities experienced by the patients as a result of the radiotherapy treatment. Radiotherapy for patients with prostate cancer is generally advocated for stage B and C (Refer to Appendix C). Table 1-1 summarises the recommended

treatment for Prostate Cancer according to Stage. Table 1-2 provides the 5-year survival rates with radiation therapy according to stage.

Table 1-1 : Treatment Recommendation of Prostatic Cancer (Osterling 1995).

STAGE	RECOMMENDED TREATMENT
A1	OBSERVATION
A2, B	SURGERY / RADIOTHERAPY
B2	RADIOTHERAPY / SURGERY
C	RADIOTHERAPY
D	HORMONES, ± RADIOTHERAPY

Table 1-2 : Survival according to Stage for Prostate Cancer (De Vita **et al.** 1997)

STAGE	5-YEAR SURVIVAL (%)
B	71 - 90
C	39 - 58

The radiation technique used to treat prostate cancer depends upon the size and shape of the target volume with the smaller field sizes being used for stages A and B (Refer to Appendix C) and the larger field sizes for the more advanced and larger tumours that occur in stages C and D in order to include the relevant pelvic nodes in the treatment port. (Cosgrove **et al.** 1973; De Vita **et al.** 1997 : 1353).

Dobbs **et al.** (1999 : 277) describe two techniques that are currently used. The 4-field technique (Refer to Appendix Ai) that comprises one anteroposterior (AP), one posteroanterior (PA) and two lateral fields (i.e. the four-field 'box' technique) results in a very high dose to the prostate with a low dose to the rectal wall. The 3-field technique (Refer to Appendix Aii) that comprises one anterior and two lateral fields results in good tumour coverage and sparing of the rectum but a high dose to the femoral heads.

According to Perez and Brady (1998 : 1616) using high megavoltage energy in the region of 18MeV or more can reduce this high dose to the femoral heads. With photon energies lower than 18 MeV, lateral portals are always necessary to deliver part of the dose, in addition to the AP and PA portals. With photon energies higher than 8MeV, lateral portals are not strictly necessary except if the patient has an AP diameter of 20.0cm because the increase in dose distribution is marginal. The main advantage of using the 'box' technique is a decrease in the erythema and skin desquamation in the intergluteal fold which generally occurs with the AP/PA portals. The toxicities experienced affect the patient's quality of life throughout and even after their disease-free survival.

The acute toxicities associated with radiotherapy for prostate cancer is well documented (Ang and Van der Scheuren, 1982; Bagshaw, 1973; Soffen **et al.** 1991) and are most often graded using the Radiation Therapy Oncology Group (RTOG) and European Oncology Radiation Therapy Committee (EORTC) grading systems (Tables 1-3 and 1-4). The acute toxicities include diarrhoea, abdominal cramping, rectal discomfort and associated rectal bleeding. Diarrhoea is defined as frequent loose bowel movements with or without associated rectal irritation (tenesmus). Persistent proctitis or proctosigmoiditis does occur and may necessitate colostomy. Genitourinary symptoms experienced are cystourethritis and are characterised by dysuria, frequency and nocturia. The urine may be clear, or with microscopic, or gross haematuria. The most frequent urinary sequellae are generally urethral stricture and cystitis with intermittent haematuria. Cystitis is usually associated with bladder symptoms such as frequency and dysuria. Haematuria generally occurs in grades 2 to 4 (Dearnaley **et al.** 1999; DeVita **et al.** 1997 : 1355; Perez and Brady, 1998 : 1662-1664).

Grade 2 rectal and urinary symptoms (Tables 1-3 and 1-4) generally appear in the third week of treatment and may resolve days or weeks after

treatment has been completed (DeVita **et al.** 1997 : 1355; Perez and Brady 1998 : 1662-1664). In an analysis of approximately 1000 patients in two major Radiation Therapy Oncology Group (RTOG) prostate protocols (7506 and 7706) presented by Lawton **et al.** 1991, severe intestinal (grade 3 -Tables 1-3 and 1-4) occurred in 3.3% of patients and life-threatening morbidity (grade 4 - Tables 1-3 and 1-4), such as bowel perforation or obstruction occurred in less than 0,6% of patients. Urinary toxicity was moderate in 7.7% of patients and major in less than 0.5% of patients who required surgical intervention.

TABLE 1-3 : RTOG/EORTC GRADING CRITERIA FOR ACUTE RECTAL TOXICITY (Diarrhoea) (Muller **et al.** 1981)

GRADE	
0	NO DIARRHOEA
1	TRANSIENT DIARRHOEA (< 2 DAYS)
2	TOLERABLE DIARRHOEA (> 2 DAYS)
3	INTOLERABLE DIARRHOEA - REQUIRE TREATMENT
4	HAEMORRHAGIC DEHYDRATION

TABLE 1-4 : RTOG/EORTC GRADING CRITERIA FOR ACUTE BLADDER TOXICITY (Dysuria, Nocturia, Frequency) (Vijaykumar **et al.** 1993)

GRADE	
0	No change in urination habits.
1	Frequency of urination or nocturia twice pre-treatment habit. Dysuria, urgency not requiring medication.
2	Frequency of urination or nocturia, which is less frequent than every hour. Dysuria, urgency, bladder spasm requiring local anaesthetic.
3	Frequency with urgency and nocturia hourly or more frequently. Dysuria, pelvis pain or bladder spasm requiring regular, frequent narcotic. Gross haematuria with/without clot passage.
4	Haematuria requiring transfusion. Acute bladder obstruction not secondary to clot passage, ulceration, necrosis.

Vijaykumar **et al.** (1993), in a retrospective study, conducted at two institutions (Michael Reese Hospital and La Grange Memorial Hospital) in Chicago, compared the week-by-week acute toxicities associated with a conventional group of 16 patients (group A), computerised tomography based group of 57 patients (group B), and a beam's eye view based group of 43 patients (group C) during 7 weeks of radiotherapy. All patients, except for 3, were treated with the 4-field technique. The 3 patients were treated with the 4-field technique plus bilateral arcs because they had

prosthetic hip replacements. The study demonstrated that the acute toxicities increased from week 1 through to week 4 and thereafter either generally decreased or plateaued. Group C patients showed a significantly decreased severity of acute toxicities as compared to groups A and B. Vijaykumar **et al.** (1993) in their concluding discussion, recommended that prospective studies be executed in order to confirm the findings of their study. The study conducted by Vijaykumar **et al.** (1993) evaluated different planning techniques but all patients were treated with the 4 fields. To date no prospective studies involving the comparison of the 3-field technique to the 4-field technique in terms of acute toxicities have as yet been reported hence the undertaking of the current study.

It is possible that better control of local disease can be attained by using higher doses than are currently employed. To facilitate such dose escalation, however, conformation of the target volume must be precisely established. Equally important, the acute toxicities associated with these techniques must be investigated.

The significance of the current study lies in determining which radiation treatment technique (the 3-field or 4-field treatment technique) will result in the patient experiencing less severe acute rectal and bladder toxicities. Chapter two focuses on an overview of the literature related to prostate cancer whereas Chapter three provides a detailed account of the methods and materials that were used for the study. Chapter four presents the results as well as an analysis of the results that were obtained from the study. In Chapter five, a detailed discussion on the study including the pitfalls, suggestions and recommendations is provided, which is then followed by Chapter six which concludes the dissertation.

CHAPTER TWO : REVIEW OF LITERATURE

2.1 INTRODUCTION

In this chapter, a review of the literature related to prostate cancer is provided. The review encompasses important aspects including anatomy and physiology prostate, bladder and rectum, aetiological and epidemiological factors, diagnosing the disease, the preferred methods of treatment and the possible treatment-related complications that may arise by presenting views from various different authors, including Perez and Brady (1998), Perez **et al.** (2000), Vijaykumar **et al.** (1993), Storey **et al.** (2000), Beard **et al.** (1998), Michalski **et al.** (2000), De Vita **et al.** (1997) and Neal and Hoskin (1994).

2.2 ANATOMY AND PHYSIOLOGY OF THE PELVIC ORGANS (PROSTATE, BLADDER AND RECTUM)

Knowledge of the anatomy and physiology of the prostate, bladder and rectum are essential to the current study since although the prostate is the organ that requires treatment with radiation, these other two pelvic organs, (bladder, which lies anterior to the prostate, and rectum which lies posterior to the prostate) also receive a substantial percentage of the total

dose delivered to the prostate, irrespective of the field arrangements used, resulting in both acute and late bladder and rectal toxicity.

The pelvis is the region where the trunk and the lower limbs meet. The pelvic cavity is the basin-shaped inferior part of the abdominopelvic cavity. The bony pelvis is formed anteriorly by the two hip bones (cossa coxae), posteriorly by the sacrum and coccyx and anteriorly by the meeting of the two pubic bones at the pubic symphysis. It is divided into the pelvis major (false pelvis) and the pelvis minor (true pelvis). The pelvis major lies superior to the superior pelvic aperture (pelvic inlet) and is actually considered part of the abdominal cavity. The pelvis minor (pelvic outlet) lies inferior to the superior pelvic aperture and contains the pelvic organs including the prostate, bladder and rectum (Moore 1992 : 279-281).

The prostate gland is a male sex organ that is partly glandular and partly muscular. It is a walnut-shaped organ weighing approximately 20 grams, which surrounds the beginning of the male urethra (Moore, 1992 : 279-281; Newman, 1996). It has an apex, which is directed downwards, and a base superiorly, a posterior surface, an anterior surface and two

inferolateral surfaces. It is related inferiorly to the bladder and is anterior to the rectum (Moore 1992 : 279-281).

To facilitate easier description of the location of disease in the prostate gland, it is divided into 5 different histologically distinct zones. These include an anterior zone, peripheral zone (accounts for 75% of prostatic volume and is the area where most cancers are located), central zone, preprostatic urethra and a transitional zone. The gland comprises 30 to 50 incompletely defined lobules in a radial arrangement with a stroma of fibromuscular connective tissue, blood vessels, lymphatics and nerves (Moore, 1992 : 297-281; Newman, 1996).

The arteries supplying the prostate include the internal vesicle, middle rectal and branches of the internal iliac artery. The venous drainage is derived from the prostatic venous plexus (situated around the sides and the base of the prostate) that drains into the internal iliac veins and communicates with the vesicle and vertebral venous plexuses. The lymph vessels terminate mainly into the internal iliac and sacral lymph nodes. Some vessels that arise in the posterior aspect of the prostate pass with lymph vessels of the bladder to the external iliac lymph nodes.

Parasympathetic innervation arises from the pelvic splanchnic nerves (2nd, 3rd and 4th sacral vertebra) whilst the sympathetic innervation is derived from the inferior hypogastric plexuses (Moore 1992 : 279-281).

According to Newman (1996), the functions of the prostate gland are still not well understood and needs to be further elucidated by researchers. The gland produces an alkaline fluid (pH 6.5) that constitutes approximately 30% of seminal fluid ejaculate. This ejaculate contains calcium, zinc, acid phosphatase, a clotting enzyme, profibrolysin and fructose (Newman 1996).

The rectum is the fixed, terminal part of the large intestine. It is continuous superiorly with the sigmoid colon. The rectum begins anterior to the level of the third sacral vertebra. It follows the sacral curve and terminates 3 to 4 cm anterior to the tip of the coccyx. Inferiorly, the rectum lies posterior to the prostate in the male and vagina in the female. The termination of the rectum lies posterior to the apex of the prostate in the male. The function of the rectum is for the purpose of elimination of fecal matter from the body (Moore 1992 : 279-281).

The urinary bladder is a hollow, muscular vesicle for storing urine. In the adult, the empty bladder lies in the pelvis minor and posterior and slightly superior to the pubic bones. It is generally superior to the pelvic floor and posterior to the pubic symphysis. As it fills, it ascends into the pelvis major. The function of the bladder is a temporary storage area for urine until the urine can be passed out (Moore 1992 : 279-281).

2.4 AETIOLOGY, INCIDENCE AND PREDISPOSING FACTORS

The aetiology of prostate cancer is still not well understood, with several risk factors having been identified including race, age, hereditary factors, hormones, benign prostatic hyperplasia, diet, socio-economic factors, occupation, smoking, sexual behaviour, vasectomy and religion (Cohen, 1992; Giovannucci, 1995; Neal and Hoskin, 1994; Newman, 1996; *Zeneca Medical Publications*, 1997). Race, Age, and Heredity are discussed below since these factors will be discussed later in the current study.

In developed countries (e.g United States of America), prostate cancer is the third most common malignancy following lung and colorectal cancers (Giovannucci, 1995; Neal and Hoskin, 1994 : 119). There are

approximately 10 800 cases in the United Kingdom each year, with an incidence of 19 in 100 000 having been established (Neal and Hoskin 1994 : 119). The highest mortality rate appears to be in Switzerland followed by Scandinavia (*Zeneca Medical Publications* 1997 : 1). The incidence of prostate cancer has increased dramatically worldwide over the past 20 years. In 1995 alone 224,000 new cases were diagnosed compared to 180,000 in 1994 (Newman, 1996; *Zeneca Medical Publications*, 1997 : 1).

Cancer of the prostate develops in approximately 300,000 men each year worldwide (Giovannucci 1995). According to Sitas **et al.** (1998) of the NCR, 1 in 31 males in South Africa have a lifetime risk of developing prostate cancer. The incidence for South African Blacks (13:100 000) are lower than those for South African Whites (57.8:100 000). In the United States the incidence in Black males is 91 in 100 000 compared to 51 in 100 000 in White males and 6 in 100 000 in Japan (Neal and Hoskin 1994). Table 2-1 provides the incidence of prostate cancer in South Africans according to race.

Table 2-1 : Rates of Incidence In South African Males (Sitas **et al.** 1998).

Race	Incidence	%
Whites	1273	62.5
Blacks	646	31.7
Coloureds	86	4.22
Asians	32	1.57

The disease is rare under 45 years but increases with age and is almost universal at post-mortem in men aged over 80 years (Neal and Hoskin 2994 : 119; De Vita **et al.** 1997 : 1331). The risk of having asymptomatic prostatic cancer is 22% for men in their 60's and 39% for men in their 70's (Newman 1996).

There is also an increased incidence of prostate cancer in males who have other affected family members suggesting that it may actually be a hereditary type of cancer. Familial associations are important especially in younger patients who have affected first-degree relatives. An overall 9% of cases may be directly attributed to family history of prostate cancer (Giovannucci, 1995; Neal and Hoskin, 1994 : 119). This trend seems to emphasise the need for the implementation of screening programs (Newman 1996).

Prostate growth and function are regulated by testosterone which is produced largely by the testes with a supplementary supply from the adrenal glands (which produces approximately 10%), and dihydrotestosterone. Although high circulating levels of testosterone have not been commonly or consistently found in males with prostate cancer, there does seem to be an increased conversion rate to testosterone in males with prostate cancer (Newman 1996).

2.4 COMMON SIGNS AND SYMPTOMS

According to Bomford **et al.** (1993 : 433); Burns (1997 : 586-588); Neal and Hoskin (1994 : 120) and prostatism, frequency, urgency and difficulty of micturition, is the commonest presenting symptom. Some patients have also presented with poor stream and terminal dribble. Nearly 50% present with urinary outflow obstruction, 25% in acute urinary retention, 5% with haematuria and 7% with bone pain (Bomford **et al.** 1993 : 433). The symptoms seem to appear suddenly and worsen rapidly. Acute or chronic retention of urine is a common presenting symptom. Hypercalcaemia may also occur if there are skeletal metastases (Neal and Hoskin 1996 : 121).

Spreading of the cancer to the floor of the pelvis may cause pain in the lower abdomen and the perineum. Generalised debility and loss of weight is very common because the tumour often spreads throughout the body causing local symptoms. Metastases to the bones of the pelvis and lumbosacral spine often cause bone pain, pathological fractures and sometimes spinal cord compression. When sciatica develops in elderly males, it may be caused by bony metastases from a malignant prostate gland (Bomford **et al.** 1993 : 433; Burns, 1997 : 586-588; Neal and Hoskin, 1994 : 121).

On clinical examination, the bladder will be palpable if there is urine retention. 90% of prostate cancers are diagnosed by rectal examination. On rectal examination, the prostate gland is generally asymmetrically enlarged or distorted, irregular in contour and heterogeneous in texture. Some areas may be hard and knobbly and others soft. The median sulcus may be absent and the rectal mucosa may be tethered to the gland. The tumour may infiltrate the tissues of the pelvis lateral to the gland and around the rectum. This is commonly referred to as 'winging' of the prostate (Bomford **et al.** 1993 : 431; Burns, 1997 : 586-588; Neal and

Hoskin, 1994 : 120; Newman 1996; Perez and Brady 1998 : 1594; Rubin 1993 : 433).

The only other physical signs will be those caused by metastases. Cancer of the prostate may sometimes give rise to metastases in the skin. If the spread around the rectum is extensive, the tumour may spread along the lymphatics of the anal canal to the inguinal lymph nodes (Bomford **et al.** 1993 : 431; Burns, 1997 : 586-588; Neal and Hoskin 1994 : 120).

2.5 WORK-UP PROCEDURES

According to Bomford **et al.** (1993) : 431; De Vita **et al.** (1997) : 1335-1342; Neal and Hoskin (1994) :120-121; Perez and Brady (1998) : 1594-1598 and Rubin 1993 : 433-444, the work-up procedures executed include physical and rectal examinations which assess both the patient's condition as well as the status of the prostate gland. An intravenous urogram will demonstrate the enlarged prostate gland indenting the bladder as well as any hydronephrosis if present. Computed tomography (CT) scan yields greater detail of the surrounding of the soft tissue, in particular lymph node enlargement and seminal vesicle involvement if any

present. Transrectal ultrasound of the prostate is the most sensitive means of assessing the prostate gland and may be used when directing needle biopsy toward any suspicious areas in the gland. A serum acid phosphatase test is generally raised in metastatic disease.

PSA is measured in the blood and is more specific than serum acid phosphatase and is useful, especially when used in combination with other investigations, in order to aid in diagnosis of the disease, assessing prognosis and as a screening tool. A chest radiograph is done to establish the presence of lung metastases. Radioisotope bone scan is essential to rule out bone metastases and has largely replaced the previously used radiographic bone survey. A full blood count may demonstrate reduction of hemoglobin whereas biochemistry tests may show evidence of hypercalcaemia and/or uraemia (Neal and Hoskin 1994 :120-121).

Diagnosis is made either at transurethral resection of the prostate (TURP) or on needle biopsy per rectum. TURP seems to be associated with a higher incidence of dissemination of disease therefore simple needle

biopsy is preferred in most cases in the absence of other indications for transurethral resection (TUR) (Neal and Hoskin 1994 : 121).

For the current study all patients had to have a full blood count, urea and electrolytes count, pre-treatment PSA tests, histologic confirmation of the presence of a tumour in the prostate, digital rectal examination a CT scan for diagnostic and planning purposes as the work up procedures.

2.6 PROSTATIC SPECIFIC ANTIGEN (PSA)

PSA is currently the most sensitive marker in diagnosing, staging and monitoring progression and response to therapy in patients with prostate cancer (Osterling 1995). The current study also evaluates the effect of radiation on PSA levels during the course of treatment.

The PSA gene was cloned in the 1980's. It is a serine protease homologous to the kallikreins. It is produced by both normal and neoplastic cells and its levels may be elevated (>4ng/ml) in conditions including nodular hyperplasia, prostatitis and carcinomas. Because of this, the value of PSA in screening is limited and needs to be used in conjunction with other procedures including transrectal ultrasound, digital

rectal examination (DRE) and needle biopsy (Brawer **et al.** 1992; Burns, 1997 : 586-588; Osterling 1995; Peehl, 1995).

The major site of PSA expression is the prostate where it is secreted by the luminal cells of the epithelium. The most likely sites of action of PSA seem to be in the seminal fluid, prostate and metastatic sites. In seminal fluid, it seems to change the consistency and structure of the fluid rendering it more liquid. In the prostate and metastatic sites it may directly affect growth and differentiation of the PSA-producing cells themselves or of surrounding cells (Brawer **et al.** 1992; Burns, 1997 : 586-588; Peehl, 1995).

Serum PSA can detect twice as many prostate cancers compared to digital rectal examination. Nearly two thirds of those detected by PSA are organ-confined and potentially curable. There are varying ranges of serum PSA for different age groups. Table 2-2 provides a summary of these reference values (Brawer **et al.** 1992; Osterling, 1995; Perez and Brady 1997 : 1590).

Table 2-2 : Serum PSA and Age (Brawer **et al.** 1992; Osterling, 1995; Perez and Brady 1997 : 1590).

Age Range (Year)	Median Value (ng/ml)	Reference range (ng/ml)
40 – 49	0.7	0.0 - 2.5
50 – 59	1.0	0.0 - 3.5
60 – 69	1.4	0.0 - 4.5
70 – 79	2.0	0.0 - 6.5

PSA is a sensitive marker of the response of prostate cancer to definitive treatment with either radical prostatectomy or radical radiation therapy Table 2-3 indicates the specificity, sensitivity, and detection rate of PSA tests as compared to DRE and transrectal ultrasound (TRUS) (De Vita **et al.** 1997 : 1335).

Table 2-3 : PSA versus DRE and TRUS (De Vita **et al.** 1997 : 1335).

METHOD	SENSITIVITY %	SPECIFICITY %	DETECTION RATE
DRE	69-89	84-98	1.3-1.7
PSA	57-79	59-68	2.2-2.6
TRUS	36-85	41-79	2.6

Although clinically, PSA is the most important, accurate and clinically useful tumour marker in prostate cancer, the most complete prostate

evaluation without surgical intervention is achieved through PSA determination and DRE together (Newman, 1996; Osterling, 1994).

2.7 STAGING SYSTEMS

Two of the most commonly used staging systems include the Jewitt system (A-D) and the tumour, node, metastases (TNM) staging both widely adopted in the United States of America (De Vita **et al.** 1997 : 1335; Neal and Hoskin, 1994 : 1335; Perez and Brady, 1998 : 1599). (Refer to Appendix C) The current study used the Jewitt's staging system to obtain the stage of the patient.

2.8 GLEASON SCORE

For the purpose of histological grading, the Gleason grading system seems to be the most widely accepted grading system. This is a five part scheme that assigns a score between 1-5 for the primary and secondary growth patterns. Pattern 1 tumours are the most differentiated with discrete glandular formation whereas pattern 5 are the most undifferentiated cells with virtually complete loss of glandular architecture (Refer to Appendix B). The two scores are combined to form a score of between 2-10. A Gleason grade score of less than 4 is suggestive of a

well differentiated tumour, whereas a score of between 5-7 represents a moderately differentiated tumour and a score of between 8-10 a poorly differentiated tumour. The higher the score, the greater the chance of extracapsular spread, nodal involvement and subsequent metastases (De Vita **et al.** 1997 1326-1327; Perez and Brady, 1998 : 1603-1605; Rubin, 1993 : 435).

2.9 EXTERNAL BEAM RADIATION THERAPY

The technique selected generally depends upon the size and shape of the target volume. With the advent of the megavoltage equipment, irradiation has been increasingly advocated for stage B and stage C prostate cancer (Cosgrove et al. 1973 and Delregato, 1979). Some institutions utilise the anteroposterior ports with perineal appositional fields, and lateral ports ('box' technique) as well as rotational fields to supplement the dose to the prostate gland itself (De Vita **et al.** 1997).

At least four weeks should elapse before the initiation of external beam radiation therapy, on patients who are experiencing obstructive lower urinary tract symptoms after having undergone transurethral resection.

This is done in an attempt to decrease the sequellae including urinary incontinence and urethral strictures (De Vita **et al.** 1997 : 1666).

There seems to be conflicting evidence in the literature as to the value of radiotherapy to the lymph node drainage areas. For example according to Ashell **et al.** (1998) there is an increased toxicity associated with irradiation of the entire pelvis is with a small potential benefit. Moosa **et al.** (1986) however found no evidence of efficacy by irradiating the whole pelvis. Further, they found that irradiating the whole pelvis, which includes the pelvic lymphatics, resulted in 40% of the patients in their study experiencing acute toxicities. Their work is discussed in greater detail further on in this chapter.

With early stage prostate cancer, (stages A and B) it would seem more beneficial to actually treat a small volume, rather than the larger volume. Margins of the small target volume are determined by the tumour extent as palpated rectally and visualised on CT scans. Lateral borders should extend to the pelvic sidewalls. Anterior border usually passes through the mid symphysis pubis. The posterior border usually includes the anterior

third of the rectum. The volume is usually $8cm^3$ but may be extended to $9cm^3$ where there is seminal vesicle involvement (De Vita **et al.** 1997 : 1353).

At the Washington University Medical Center the treatment port includes treating the pelvic lymph nodes for stages A and B using a surface field size of 15 x l5cm which corresponds to a 16.5cm equivalent at the isocenter. For stages C and D, a slightly larger surface field size of 15 x l8cm is used which corresponds to a 20.5cm field size at the isocenter. The slightly larger field size has to be employed in order to cover the relevant pelvic nodes. The field size is then reduced to treat the prostatic volume. Commonly employed reduced field sizes are 7 x 9cm and 10 x l2cm. This field size depends largely on the size of the prostate gland and well as the apparent periprostatic extensions (Perez and Brady 1998 : 1611).

The use of megavoltage photon beams (>10MeV), generally obtained from Linear Accelerators, often results in a successful technique with low morbidity. The technique used by Washington University Medical Center delivers 50.00gy through the anteroposterior and posteroanterior ports.

The additional dose is delivered through the lateral ports bringing the dose up to as high as 70.00gy for stage C and 68-00gy for stage A2 and B. Most institutions worldwide employ either 1.80Gy or 2.00Gy per fraction once daily using 5 fractions per week (Perez and Brady 1998 : 1616; Dobbs **et al.** 1998 :278).

The Sandton Oncology Center in Johannesburg, South Africa, reported on 34 patients referred to the Center with apparent localised disease. These patients were treated using external beam radiation with limited fields. The technique included two anterior oblique fields at 45 degrees and 135 degrees and two posterior oblique fields at 225 degrees and 315 degrees using field sizes of either 8x8cm, 9x9cm or IOxIOcm. The patient was supine for the anterior-oblique fields and then turned prone to facilitate the posterior oblique fields. Patients were treated using a split course regime where 2.85gy was delivered daily for 2 weeks followed by a $2^1/_2$ week break after which the dose prescription was repeated. The split course resulted in a time-dose-fractionation (TDF) of 114 (Muelenaene, 1992). In the current study carried out by the researcher, the patients were not treated using the split course of radiotherapy but a continuous course, which continued for approximately 6 weeks.

Perez **et al.** (2000) presented preliminary results of a non-randomised comparison of three-dimensional conformal radiotherapy (3D CRT) and standard radiotherapy (SRT) in localized cancer of the prostate in two groups of patients at the Washington University Medical Center. One hundred and forty six (146) patients were treated with 3D CRT and 131 patients with SRT for clinical stage T1c or T2 histologically confirmed cancer of the prostate. None of these patients received hormonal therapy. 3D CRT comprised seven intersecting fields to deliver 68.00 - 73.80Gy to the prostate whereas SRT consisted of bilateral 120-degree rotational arcs to deliver 68.00 - 70.00Gy to the prostate. Dose-volume histograms (DVHs) of the bladder, rectum and planning target volume were obtained for the 3D CRT. Chemical disease-free survival was a post-irradiation PSA value following the American Society for Therapeutic Radiation and Oncology guidelines. Weekly quantitated symptoms were documented and late effects were assessed every 4 to 6 months. The DVHs showed one-third reduction in normal bladder or rectum receiving 70.00Gy or more with 3D CRT. Higher 5-year chemical disease-free survival was observed with 3D CRT (91% for T1c and 96% for T2 tumours), compared with SRT (52% and 58% respectively). Comparative reported values for

moderate dysuria and difficulty in urinating, urinary frequency and nocturia, moderate loose stools/diarrhoea (usually after the fourth week of treatment) and late intestinal morbidity (proctitis, rectal bleeding) are summarized in Table 2-4

Table 2-4 : Comparative toxicities between 3D CRT and SRT (Perez **et al.** 2000)

TOXICITY	3D CRT (%)	SRT (%)
Moderate dysuria and difficulty in urinating	2-5	6-9
Urinary frequency and nocturia	18-24	18-27
Moderate loose stools and diarrhoea	3-5	8-19
Late intestinal morbidity	1.7	8

Longer follow up is required to confirm the findings, but preliminary findings seem to suggest that 3D CRT offers more normal tissue sparing, yields higher disease-free survival, and less treatment morbidity than SRT in treatment of stage T1c-T2 prostate cancer.

2.10 DOSIMETRY

The two main considerations in pelvic irradiation are firstly how to achieve a homogenous dose distribution in the target volume and secondly, how to minimise the dose to the rectum and the bladder. An anterior and two posterior oblique or two opposing lateral fields give a high dose to the prostate with a low dose to the posterior rectal wall. The posterior fields

may be wedged in order to compensate for patient contour and are usually angled at 110 degrees to 120 degrees. A decrease in the gantry angle decreases the dose to the rectum but increases the dose to the femoral heads. Two lateral arcs of 120 degrees or two opposing lateral wedged fields may obtain sparing of the rectum (Dobbs **et al.** 1999 : 305-308).

2.11 ACUTE TOXICITY

The acute toxicity associated with conventional radiation therapy techniques for prostate cancer is well documented (Ang **et al.** 1982; Bagshaw, 1973, Soffen **et al.** 1991). These acute toxicities include diarrhoea, abdominal cramping, rectal discomfort, and occasional rectal bleeding which may be associated with transient enteroproctitis. Patients with haemorrhoids may experience discomfort earlier than other patients. These patients may require immediate aggressive symptomatic treatment. The symptoms may be controlled with diphenoxylane hydrochloride with atropine sulphate (lomotil), opium solutions (immodium), and emolients (pectin). Local symptoms of proctitis and rectal discomfort can be relieved with small enemas of cod liver oil and suppositories. An adequate diet with low residue and no grease or spices helps to decrease the

gastrointestinal symptoms (De Vita **et al.** 1997 : 1355; Perez and Brady, 1998 : 1662-1666).

Genitourinary symptoms are secondary to cystourethritis and are characterised by dysuria, frequency and nocturia. The urine is usually clear with microscopic/gross haematuria. Manelamine and antispasmodics, such as urispas, cistospas, are useful in relieving these symptoms (De Vita **et al.** 1997 : 1355; Perez and Brady, 1998 : 1662-1666).

Erythema or dry to moist desquamation in the perineum or interstitial fold may develop. Good skin hygiene and topical application of vaseline, aquaphor or lanolin are useful. For the more serious or severe reactions zinc oxide ointment with intensive skin care is recommended (De Vita **et al.** 1997 : 1355; Perez and Brady, 1998 : 1662-1666).

Persistent proctitis or proctosigmoiditis with the occasional need for colostomy does occur. Chronic cystitis is observed in less than 5% of patients with doses of more than 75.00gy to the bladder. Haemorrhagic cystitis may develop requiring a cystectomy but this occurrence is

prevalent in less than 1% of patients. Urethral strictures have been reported in approximately 5% of patients most frequently in patients who underwent transurethral prostatic resection before or during radiation therapy (De Vita **et al.** 1997 : 1355; Perez and Brady, 1998 : 1662-1666).

Beard **et al.** (1998) reported on 441 patients with non-metastatic adenocarcinoma of the prostate who were treated at hospitals affiliated with the Joint Center for Radiation Therapy (JCRT) between 1985 – 1989 and retrospectively analysed to assess gastrointestinal, genitourinary and sexual function by using a patient scoring 5-grade toxicity scale. The association between clinical and technical variables and rectal, bladder and sexual toxicities were examined. Seventy-four (20%) patients received small field (<12.5 x 12.5 cm) external beam irradiation (EBI) via a four-field 'box' technique on a 6MeV linear accelerator. One hundred and forty patients (37%) were treated on an 8MeV linear accelerator and 161 (43%) of the patients were treated on a 15MeV linear accelerator.

One hundred and thirty seven (39%) reported of rectal complications after treatment of which 20 (6%) had haem-positive stools as their only symptom and 66 (19%) had mild symptoms not requiring treatment. Only

14% of the entire group required intervention. Of the 117 patients, 33% were evaluated for bladder complications, of which 14 (4%) had asymptomatic haematuria, 71 (20%) had mild symptoms not requiring treatment and 32 (9%) required treatment. No statistically significant associations were identified between machine energy and complications (Beard **et al.** 1998).

The study carried out by Moosa **et al.** (1986) reported complications of proctitis, which cleared up within a few weeks after the radiation treatment was completed. One percent of patients complained of rectal bleeding, 50% of which was mild and occasional without any discomfort. Only one patient required a colostomy to control the bleeding. Two patients had bladder complications requiring diversion. The vast majority however had no nocturia or frequency at all. The study by Moosa **et al.** (1986) evaluated patients whose entire pelvis was irradiated whereas the current study evaluated patients being treated with fields confined to the prostatic volume. The limitation of the technique as described by Moosa **et al.** (1986) would seem to be the change in patient position that would be required in order to facilitate treating both oblique fields adequately. At Addington Hospital in Durban, in order to facilitate treating both oblique

fields adequately the design of the table is such that the beams can usually be directed from both posterior oblique directions without requiring a change in the patient position from supine to prone.

Storey **et al.** (2000) compared early and late side effects in 189 patients with stage T1b - T3 disease, randomised to receive either 70.00gy or 78.00gy at the M.D. Anderson cancer Center in Houston, Texas. All patients were initially treated with a 4-field 'box' technique to an isocenter dose of 46.00Gy in 2.00Gy fractions. The 70.00Gy arm was then taken to 70,00Gy using a 4-field reduced volume technique. The 78.00Gy arm was continued to a reduced volume using a 6-field arrangement. Acute rectal and bladder toxicities were then graded on a 1 to 4 scale using the RTOG grading criteria (Tables 1-3 and 1-4). No significant difference in acute rectal or bladder toxicity was seen between the two treatment techniques. There did however seem to be a significant correlation between the percentage of rectum irradiated and the likelihood of late rectal complications occurring when the DVHs of the 78.00Gy arm was analysed. Late rectal complications were evident when more than 25% of the rectum received 70.00Gy or more.

In an analysis of approximately 1000 patients in two major radiation therapy oncology group (RTOG) prostate protocols (7506 and 7706), presented by Lawton **et al.** (1991) severe intestinal complications (grade 3) occurred in 3.3% of patients and life-threatening morbidity (grade 4), such as bowel perforation or obstruction in less than 0.6%. Urinary toxicity was moderate in 7.7% of patients and major in less than 0.5% of patients who required surgery. As with the study carried out by Moosa **et al.** (1986), in the analysis by Lawton et al. (1991), the entire pelvis was irradiated, whereas the current study required irradiation of only the prostatic volume.

The majority of the studies documenting acute toxicities associated with radiation therapy required that the entire pelvis be irradiated to a dose of 40.00 to 50.00Gy to the entire pelvis followed by a boost to the prostatic volume taking the dose received by the prostate gland to 65.00 to 70.00Gy. The RTOG trial however (Ashell **et al.** 1988), showed almost similar results with limited fields *versus* whole pelvis irradiation and since this report, there has been an increasing number of radiation oncologists in the United States of America who have started treating patients with localised-stage prostate cancer with limited fields rather than whole pelvic

irradiation. In addition, many institutions worldwide are also beginning to use conformal techniques (Lincter 1991).

In a prospective phase 1 dose escalation study involving 288 cases, conducted by Michalski **et al.** (2000) to determine the maximally-tolerated radiation dose in men treated with 3D CRT for localised prostate cancer, it was found that there was a better than expected tolerance to high-dose 3D CRT for stage T1 and T2 prostate cancer as compared to low-dose RTOG experience. It was further noted that it appears to be a dose-volume relationship with respect to the development of both acute and late bladder toxicities. Fifty-three to fifty-four percent of group I patients and 62% of group II patients had either none or grade I acute toxicity. Three percent of all patients experienced grade III bowel or bladder toxicity whilst no grade IV or V toxicities were seen.

2.12 SUMMARY

Prostate cancer is currently taking a heavy toll on the lives of men in many countries of the world, including South Africa. According to Abbas and Scardino (1997) early detection and treatment appears to be promising, but no prospective clinical trial or comparative population-based study can as yet confirm this hypothesis.

Radiation therapy has played an increasingly important role in the treatment of prostate cancer. Initially, it was used for patients considered medically inoperable or when the disease was considered to be outside the capsule (stage C), or locally restricted to the pelvis (stage D). More recently, it has begun to play a role in the treatment of patients with stage A and B disease with 5 and 10-year survival rates comparable to that of radical prostatectomy (Abbas and Scardino 1997).

The incidence of intestinal and urinary complications due to external beam radiotherapy is a function of dose and volume factors. Based on the major study carried out by the RTOG, it has been suggested that external beam radiotherapy is an excellent alternative to radical prostatectomy because

of the relatively low incidence of complications that is associated with external beam irradiation (Rubin 1993 : 438).

Deciding upon exactly which external beam radiation therapy technique to employ now causes further concern. Logically, the treatment regime that results in the lowest morbidity and least severe toxicities should be employed.

Based on personal communications with Dr Callaghan (1999), a Durban based Radiation Oncologist at Parklands Hospital, the radiation therapy technique currently being employed at Parklands Hospital in Durban South Africa is conformal radiation therapy using the 3-field technique. Based on personal communications with to Dr Hacking (1999) and Dr Heslop (1999), both consulting Radiation Oncologists providing a service at Durban Oncology Center in Durban South Africa, the 4-field technique is used at this center to treat their patients.

To date no studies have been carried out comparing the 3-field and the 4-field technique in terms of acute radiation toxicity involving the rectum and the bladder. The current study therefore evaluates these two techniques

in order to determine which of the two yields the lower acute bladder and rectal toxicity.

CHAPTER THREE : METHODS AND MATERIALS

3.1 INTRODUCTION

This chapter provides a detailed account of the research methodology that was employed in the study. It highlights the data used, the method of patient selection, details of the planning process and the treatment techniques that was employed. In addition this chapter also describes the methods of acute toxicity assessment criteria, methods of data analysis and statistics that were used. It concludes with a summary of the statistics procedures that were utilized to analyse the results obtained.

3.2 THE DATA

The data that were used for the purpose of this research included both primary and secondary data. The primary data are the recorded acute rectal and bladder toxicities that the patients experienced during the course of radiation therapy, that were obtained from the questionnaires (Refer to Appendices Di and Dii).

The secondary data includes the journal articles in which the two techniques under investigation were evaluated. Journal articles on other studies that were conducted, where different radiation techniques are compared in patients with histologically confirmed stage B or C prostate cancer, were helpful to show their accuracy. Information from books regarding the evolution of management of patients with prostate cancer was also necessary for a thorough understanding of the techniques under evaluation. The Internet was accessed in order to obtain the most current information available.

Information regarding the protocol for oncological management of patients with prostate cancer was obtained from the oncology departments of Parklands Hospital and Durban Oncology Center respectively by means of personal communications. The records of each patient were read to ensure that the patient fitted into the inclusion criteria. Personal communications were also necessary in order to obtain unrecorded data from professionals.

Only data required by the researcher from each patient's files were used. Data obtained from the questionnaires that were handed out, on a weekly

basis, to all patients in the study, at each weekly follow-up, were collected from the patient's files.

3.3 THE RESEARCH METHODOLOGY

3.3.1 REQUESTING PERMISSION

Letters requesting permission to execute the study were sent out to the relevant persons at the two institutions used in the current study, namely Parklands Hospital and Durban Oncology Center (Refer to Appendices Ei-Eiv).

3.3.2 PILOT STUDY

A pilot study was carried out by handing the questionnaires, (Refer to Appendices Di and Dii), to three males of different race groups and ages in order to ensure that there was no ambiguity in the wording as well as to ensure that the question were easy to understand and answer.

3.3.3 PATIENT SELECTION

The convenient sampling technique (Mann 1999) was used to select 60 patients for the purpose of this study. 30 patients were recruited from Durban Oncology Center and 30 patients from Parklands Hospital.

3.3.3.1 INCLUSION CRITERIA

The patients were either histologically confirmed stage B or C according to the Jewitt staging system (Refer to Appendix C). Patients who had undergone hormonal manipulation and/or surgery were considered for the study. The patients had either transurethral resection, transrectal or transurethral biopsy of the prostate gland. Only patients who had a full blood count and a urea and electrolytes test before the treatment commenced were included in the study. Only patients who had a CT scan for planning and positioning purposes were selected. The patients had to have a pre-treatment PSA test in order to be entered into the study. Patients without chest radiographs and bone scans were also considered for this study.

3.3.3.2 EXCLUSION CRITERIA

Patients who did not present to either one of the two institutions used for this study were not included in the study. Patients who had stage A or D prostate cancer were excluded from the study. Patients with hip replacements and prostheses were not selected for the study. Patients who were not planned using either the 3-field or the 4-field technique were also excluded from the study.

3.3.3.3 ETHICAL CONSIDERATIONS

When the patient was informed about the study, the researcher also informed each patient that their identity and results would be kept confidential, that their participation in the study was voluntary and that they could withdraw from the study without needing to provide any reason as well as that their withdrawal would not affect the treatment that they were receiving in any way. This was also reiterated in the patient information sheet (Refer to Appendix F) and the consent form (Refer to Appendix G).

3.3.4 PATIENT CONSULTATION WITH THE ONCOLOGIST

The patients presented to the oncologist, who assessed them, with the proviso that all the relevant tests and work-up procedures had been completed and the results of these tests were available. A decision was taken by the researcher as to whether the patient fitted the specified inclusion criteria stated in 3.3.2.1. If the criteria were met, then the patient was informed of the study by the oncologist and the researcher and were assured of confidentiality of their identity and the results. A patient information sheet (Refer to Appendix F) was handed to the patient who read and kept it. Any questions that the patient had thereafter were addressed by the researcher and oncologist. Once the patient agreed to participate in the study, he was given an informed consent form (Refer to Appendix G) that he filled in and signed. The researcher filled in a patient details sheet (Refer to Appendix H) in order to record relevant patient details. An appointment was then made for the patient to return for simulation and mark-up of the fields.

3.3.5 PLANNING PROCESS

Prior to the initiation of planning, the patient was assessed by the oncologist. This was achieved by rectal examination, systems review, and

general physical examination. A CT scan was done in order to define the extent of the primary tumour and spread to the seminal vesicles, anterior rectal wall or bladder (if any spread was evident).

Work on the actual treatment plan only commenced once the patient had a planning CT scan and the target volume was defined. The patients were planned using either the 3-field technique (Refer to Appendix Aii), which included an anterior and two opposing lateral wedged fields or the 4-field technique (Refer to Appendix Ai), which included two anterior and posterior opposing fields and two opposing lateral wedged fields. For the planning CT scan, the patient was positioned in the same supine position that was used for the treatment.

The plan was based on the central axis slice. The oncologist determined the target area. The planning technique was 3-D conformal radiotherapy. During the planning process, three reference points were defined from the CT scan of each patient. The first point (point A – Refer to Appendix A) was located at the isocenter (isocentric dose). The second point (point B – Refer to Appendix A) for the bladder was located in the most posterior aspect of the bladder in midline. The third point, (point C – Refer to

Appendix A) for the rectum, was located in the most anterior aspect of the rectum in midline. If both or either one of these two points did not appear on the central axis planning slice, then the nearest slice to the central axis planning slice on which these two points appeared, was selected. The dose that was received by these two points was recorded at each weekly evaluation of the patient, in order to correlate the acute toxicity being experienced by the patient with the dose that the point on the rectum and bladder had received.

3.3.6 TREATMENT TECHNIQUE

After the simulation and mark-up were complete, the patient presented to the treatment unit for the verification films and the first fraction of the prescribed treatment.

Group A consisted of 30 patients who were treated using the 4-field 'box' technique (i.e. one anterior and one posterior parallel opposed fields and two lateral parallel opposed fields). Group B consisted of 30 patients who were treated using the 3- field technique (One anterior field and two opposing lateral wedged fields). All patients were treated everyday, 5 days a week with external beam radiation, unless technical machine

defaults or public holidays intervened. The patients that were treated with the 4-field technique were treated using a photon energy beam of 6 MeV on megavoltage treatment unit whereas the patients that were treated with the 3-field technique were treated using a photon energy beam of 18 MeV. The total dose received by the prostate was between 66.00 to 70.00gy, treating 5 days per week, in 2.00Gy fractions.

3.3.7 ASSESSMENT OF ACUTE TOXICITY

Acute toxicity was graded using the RTOG criteria (Vijaykumar **et al.** 1993 - Table 1-3; **Muller et al.** 1981 - Table 1-4). All patients were evaluated by the oncologist, on a weekly basis (generally after every 5 fractions of treatment) during the course of treatment and 1 month following the completion of treatment. At the first weekly evaluation, each patient was asked questions from a questionnaire (Refer to Appendices Di and Dii). The patients had to answer the questionnaires based on the degree of acute rectal and bladder toxicity that they were experiencing.

At each of the subsequent weekly follow-ups, the patient was again asked to answer the exact same questions in the questionnaire. The researcher asked the patients the questions and interviewed them. Based on the

patient's responses from the questionnaires, an appropriate grade of acute toxicity was assigned and recorded in the summary sheet (Refer to Appendix I).

Patients who complained of burning during micturition that was intolerable, were asked to take citrosoda 3-4 times per day and they were also advised to drink large amounts of fluid, especially water. If there was an indication of leukocytes in the urine, a urine microscopy test was carried out. If the test was positive for infection, the appropriate antibiotic for that infection was prescribed.

Patients who had intolerable diarrhoea and required medication were given loperamide (immodium) or lomotil (as advocated by Perez and Brady 1998 : 1662-1666) until the diarrhoea subsided.

A urine dipstix test was done at each weekly evaluation in order to assess whether there was any microscopic evidence of blood in the urine. The presence or absence of leukocytes in the urine was also established using the urine dipstix. If the patient tested positive for either microscopic haematuria or leukocytes in the urine, they were immediately referred to

the Oncologist who then ordered a urine microscopy for that patient. The responses were statistically analysed and interpreted. Table 1-3 (Vijaykumar **et al.** 1993) and Table 1-4 (Muller **et al.** 1981) summaries the grading systems that were used.

3.3.8 STATISTICAL METHODS

3.3.8.1. PATIENT SELECTION AND SAMPLE SIZE

Two institutions were selected for the purpose of this study. The 3-field technique was employed at Parklands Hospital and the 4-field technique at Durban Oncology Center. All eligible patients at these two institutions were considered for the purpose of this study.

Between February 2000 and February 2001, 60 patients were selected using the convenient sampling method which is advantageous since it does not consume time but the disadvantage is that the results obtained are not as authentic as the results yielded by the random sampling technique (Mann, 1999; Drapper,1988). This technique however is the only technique that can be used in a study such as the current one.

Group 1 consisted of patients being treated using the clinical method one (3-field technique). The patients were treated with this method until a dose of 60.00Gy in 2.00Gy fractions was reached. The field arrangement was then changed to a six field arrangement with smaller field sizes.

Group 2 consisted of patients being treated using clinical method two (4-field technique). The patients were treated with this method until a dose of 60.00Gy in 2.00Gy fractions was reached. The field arrangement was thereafter retained but the size of the fields were reduced.

The current study assessed both groups in terms of the acute bladder and rectal toxicities that the patients experienced until they reached 60.00Gy since too many other variables were introduced when the reduced fields commenced. The sample size per group was 30.

3.3.8.2. METHOD OF DATA ANALYSIS

Procedure 1 : Frequency distributions

The frequency distributions and contingency tables were required for the construction of bar charts which provide a visual representation of the results that were obtained during the analysis of the data.

The frequency distributions for the doses received by points B (bladder) and C (rectum) were obtained in order to assess if there were any correlation between the doses that these points received to the acute toxicity that was experienced.

Frequency distributions were conducted for age, race, stage, Gleason score, differentiation and surgical procedure in order to illustrate the patient characteristics.

Procedure 2 : Chi-Square test for age and stage and stage and differentiation

Contingency tables were drawn and Chi-Square tests performed for age and stage as well as for differentiation and stage to assess if there was any relationship between the two attributes.

THE SAMPLE : $n \geq 60$.

THE HYPOTHESIS :

Ho : There is no relationship between the attributes.

H_1 : There is a relationship between the attributes.

THE DECISION RULE :

If $\rho \leq \alpha$ reject Ho.

If $\rho > \alpha$ accept Ho.

where the level of significance for α = 5% (0.05).

Procedure 3 : Comparison between groups 1 and 2

Since the sample size per group was large, a parametric test was used to compare groups 1 and 2 in terms of the weekly acute toxicities. The test used was the two-sample unpaired t-test. All assumptions needed for the test were satisfied.

For the two-tailed tests the statistical methods were as follows:

THE SAMPLE : $n_1 \geq 30$ and $n_2 \geq 30$.

THE HYPOTHESIS :

The null hypothesis (Ho) stated that: $\mu_1 = \mu_2$.

The alternative hypothesis (H_1) stated that $\mu_1 \neq \mu_2$. (Two-tailed test)

THE DECISION RULE :

1. Reject Ho if $p \leq \frac{\alpha}{2}$.
2. Accept Ho if $p > \frac{\alpha}{2}$.

where the level of significance for α = 5% (0.05).

Procedure 4 : Comparison between the 3-field and the 4-field group in terms of presence or absence of blood and / or leukocytes in the urine

The Independent Samples t-test was done in order to assess whether there was any significant difference in the presence of blood and leukocytes between the two groups for the duration of the treatment.

For the two-tailed tests the statistical methods were as follows:

THE SAMPLE : $n_1 \geq 30$ and $n_2 \geq 30$.

THE HYPOTHESIS :

The null hypothesis (Ho) stated that: $\mu_1 = \mu_2$.

The alternative hypothesis (H_1) stated that $\mu_1 \neq \mu_2$. (Two-tailed test)

THE DECISION RULE :

1. Reject Ho if $p \leq \frac{\alpha}{2}$.
2. Accept Ho if $p > \frac{\alpha}{2}$

where the level of significance for α = 5% (0.05).

Procedure 5 : Comparison within the groups 1 and 2

In order to compare the pre and post PSA levels for all the patients, the paired t-test was used.

For the one-tailed test the statistical methods were as follows:

THE SAMPLE : $n \geq 60$.

THE HYPOTHESIS :

The null hypothesis (Ho) stated that: $\mu_1 = \mu_2$.

The alternative hypothesis (H_1) stated that $\mu_1 > \mu_2$,

where : μ_1 = pretreatment PSA and μ_2 = post-treatment PSA.

THE DECISION RULE :

1. Reject Ho if $p \leq \alpha$.

2. Accept Ho if $p > \alpha$.

where the level of significance for α = 5% (0.05).

Procedure 6: Means, standard deviations and averages

The means and averages were needed for the construction of bar charts.

The means and standard deviation were calculated for the 3-field and 4-Points A, B and C as well as for the volume of rectum and bladder that received doses of more than 50.00Gy in order to calculate the co-efficient of variation which was then used to determine which method yielded fewer variations.

The calculation was done using the following formula :

Co-efficient of variation (field type) = (std. deviation ÷ mean) x 100%

The field type for which the coefficient of variation is minimum is more consistent (i.e there is less variation).

Statistical Package

All the data entry and analysis procedures were accomplished using the SPSS package with the help of a statistician who certified that each procedure was correctly done (Refer to Appendix M)

CHAPTER FOUR : RESULTS

4.1 INTRODUCTION

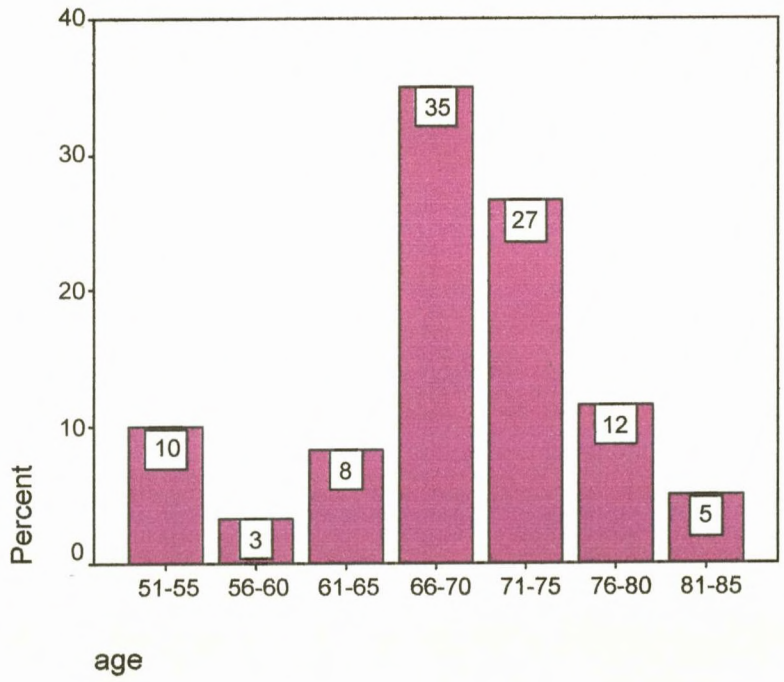
This chapter encompasses the results obtained from the statistical analysis of the quantitative and the qualitative data for both groups 1 and 2. It includes intra and inter-group as well as inter-variable analysis. The aims of this chapter includes trying to obtain a measure of association between each of the given variables, to see if there is any statistical difference between the two groups in terms of acute bladder and rectal toxicity, to determine whether there is any improvement between the pre and post-treatment PSA results and to test the hypotheses stated in chapter 3.0.

4.2 PATIENT CHARACTERISTICS

Patient characteristics for all 60 patients included in the study as per radiation treatment fields is shown in Table 4-1. The characteristics that appear in Table 4-1 and Figure 4-1 - 4-6 are highlighted below. The frequency distribution for each individual characteristic is included in Appendix J.

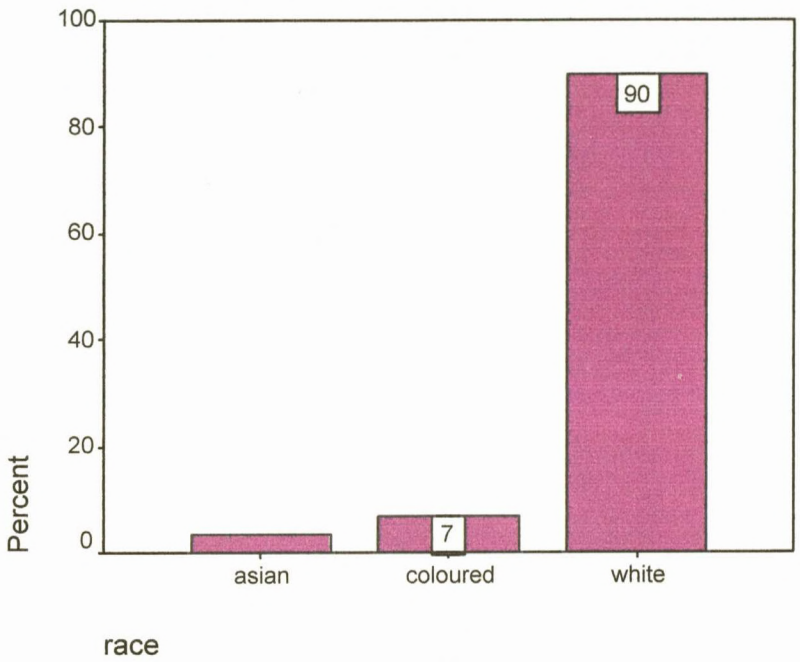
Twenty one (35%) patients were in the 66-70 year old group (Table 4-1) of which 15 (71.4%) were in the 4-field group and 6 (28.6%) in the 3-field group. The minimum age group was 51-55 years in which there was a total of 6 (10%) patients. The maximum age group was 81-85 years which comprised 3 (5%) of the patient population (Figure 4-1). The mean age at diagnosis was 67 years (Table 4-2).

Figure 4-1 : Frequency Distribution of Age



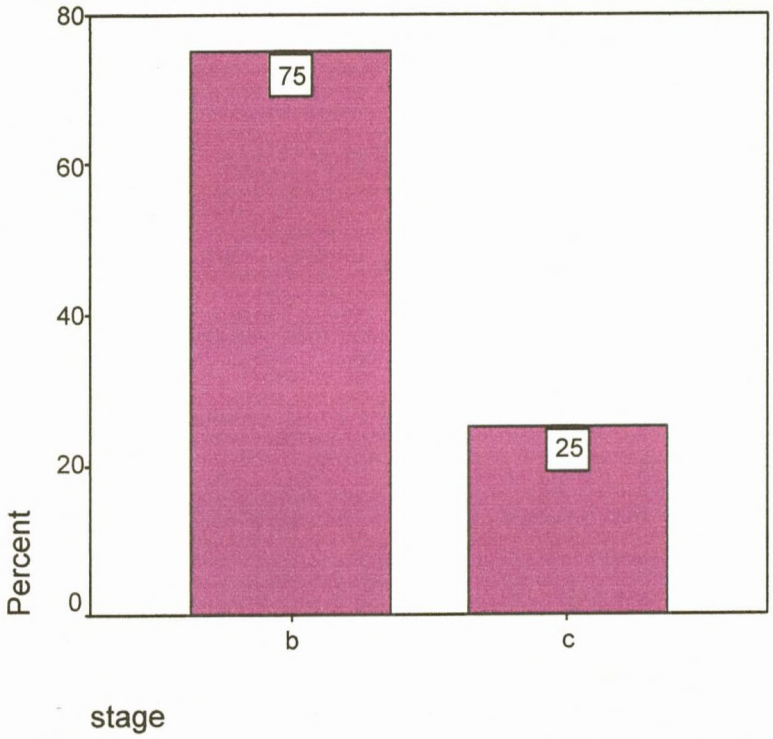
Fifty four (90%) patients were White males (Table 4-1) whereas the Coloured and Asian race groups comprised 6 (10%) of the population (Figure 4-2). There were no Black males in the study.

Figure 4-2 : Frequency Distribution of Race



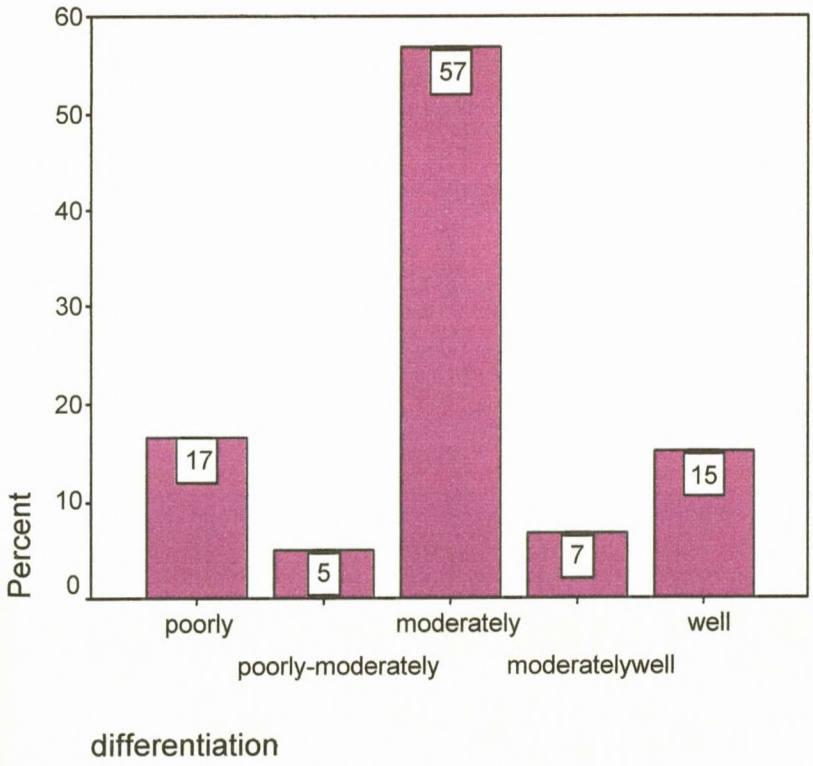
Forty four (75%) patients were histologically confirmed stage B (Table 4-1) (Jewitt's staging system - Refer to Appendix C) and 15 (25%) were histologically confirmed stage C (Figure 4-3) (Jewitt's staging system - Refer to appendix A).

Figure 4-3 : Frequency Distribution of Stage



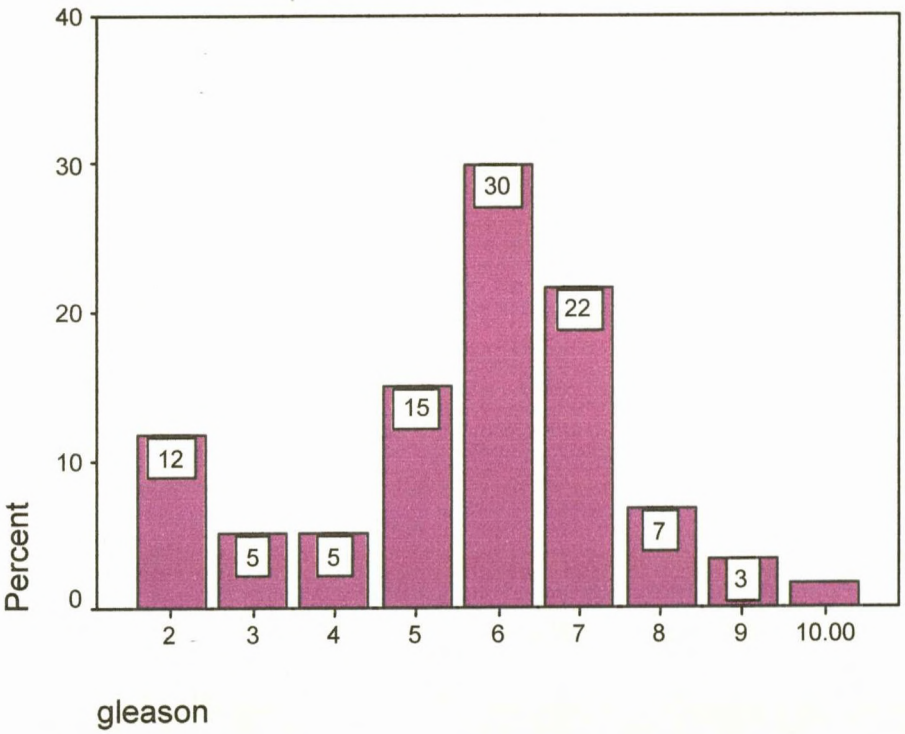
Thirty four (56.7%) patients presented with tumours that were histologically graded as moderately differentiated. Ten (16.76%) patients presented with histologically graded poorly differentiated tumours whereas 9 (15%) were graded as well differentiated tumours. The remaining 7 (11.7%) patients had either poorly-moderately differentiated or moderatley-well differentiated tumours (Table 4-1 and Figure 4-4).

Figure 4-4 : Frequency Distribution of Differentiation



Eighteen (30%) patients had histologically confirmed Gleason scoring of 6/10, followed by 13 (21.7%) patients who had a Gleason score of 7/10. The minimum Gleason score 2/10 which 7 (11.7%) of the patients had whereas the maximum Gleason score was 10/10 which only 1 (1.7%) of the patients had (Table 4-1 and Figure 4-5).

Figure 4-5 : Frequency Distribution of Gleason Score



Of the 60 patients in this study, 34 (56.7%) had biopsies done whereas the remaining 26 (43.3%) patients had surgery (transurethral resection of the prostate - TURP) (Table 4-1 and Figure 4-6).

Figure 4-6 : Frequency Distribution of Surgery/Biopsy

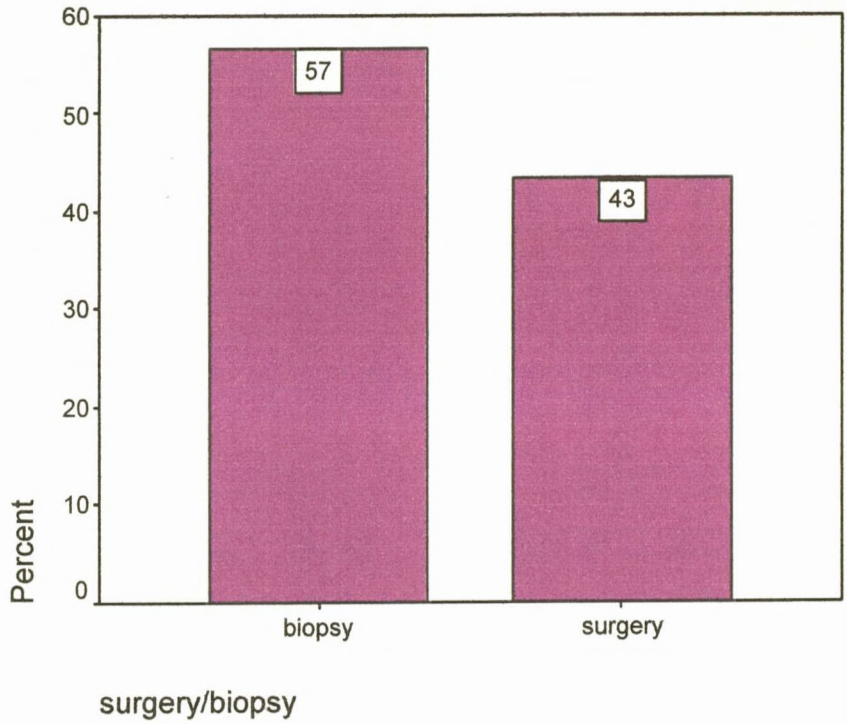


Table 4-1 : Frequencies of Age, Race, Stage, Differentiation, Gleason Score and Surgery/Biopsy

		FIELD TYPE	
		3-fIELD	4-fIELD
AGE	51-55	2	4
	56-60	1	1
	61-65	2	3
	66-70	6	15
	71-75	11	5
	76-80	6	1
	81-85	2	1
RACE	asian	1	1
	coloured	1	3
	white	28	26
STAGE	b	21	24
	c	9	6
DIFFERENTIATION	poorly	5	5
	poorly-moderately	2	1
	moderately	14	20
	moderatelywell	4	0
	well	5	4
GLEASON	2	4	3
	3	1	2
	4	1	2
	5	2	7
	6	11	7
	7	8	5
	8	2	2
	9	1	1
	10.00	0	1
SURGERY/BIOPSY	biopsy	14	20
	surgery	16	10

Table 4-2 Mean Age at Diagnosis

N	Valid	60
	Missing	0
Mean		67.9500

4.3 CHI-SQUARE ANALYSIS OF AGE AND STAGE AND STAGE AND TUMOUR DIFFERENTIATION

The Chi-Square analysis (Table 4-4) of the age and stage demonstrated that there was a significant relationship between these two variables with the ρ value $\leq \alpha$ (0.05). Of the 60 patients evaluated, 21 (35%) patients were in the 66-70 year age group of which 13 (61.9%) patients were stage B and 8 (38.1%) were stage C. This age group was followed by the 71-75 age group which comprised of 16 (26.7%) of the total number of patients evaluated. Of these 16 patients, 11 (68.8%) were in stage B and the remaining 5 (31.2%) patients were in stage C. Tables 4-3 and Figure 4-7 outlines the distribution of patients according to age and stage. Since ρ value $\leq \alpha$ (0.05), the Ho is rejected (i.e there is a relationship between the attributes).

Table 4-3 : Patient Distribution as per Age versus Stage

		STAGE	
		B	C
AGE	51-55	5	1
	56-60	2	0
	61-65	4	1
	66-70	13	8
	71-75	11	5
	76-80	7	0
	81-85	3	0

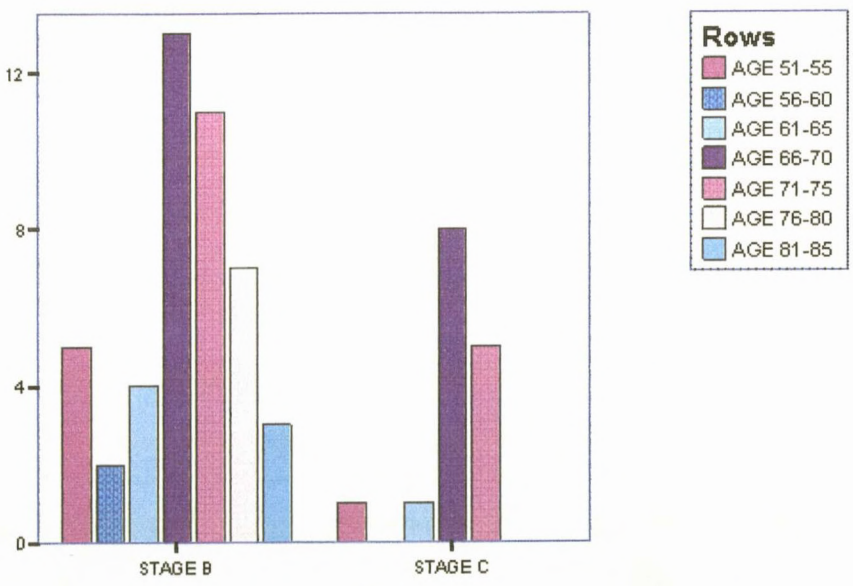
Table 4-4 : Chi-Square test for Age and Stage

	AGE	STAGE
Chi-Square[a,b]	35.667	15.000
df	6	1
Asymp. Sig.	.000	.000

a. 0 cells (.0%) have expected frequencies less than 5. The minimum expected cell frequency is 8.6.

b. 0 cells (.0%) have expected frequencies less than 5. The minimum expected cell frequency is 30.0.

Figure 4-7 : Frequency Distribution for Age versus Stage



Chi-Square analysis (Tables 4-6) of stage *versus* differentiation also demonstrated a significant relationship between these two variables with the ρ value $\leq \alpha$ (0.05). Of the 60 patients evaluated, 34 (56.7%) patients had moderately differentiated tumours, 28 (82.4%) of whom were stage B and 6 (17.7%) stage C. Table 4-5 and Figure 4-8 outline the distribution of patients according to stage and differentiation.

Since ρ value $\leq \alpha$ (0.05), the Ho is rejected (i.e there is a relationship between the attributes).

Table 4-5 : Frequency of Stage versus Differentiation

		STAGE	
		B	C
DIFFERENTIATION	poorly	5	5
	poorly-moderately	2	1
	moderately	28	6
	moderatelywell	2	2
	well	8	1

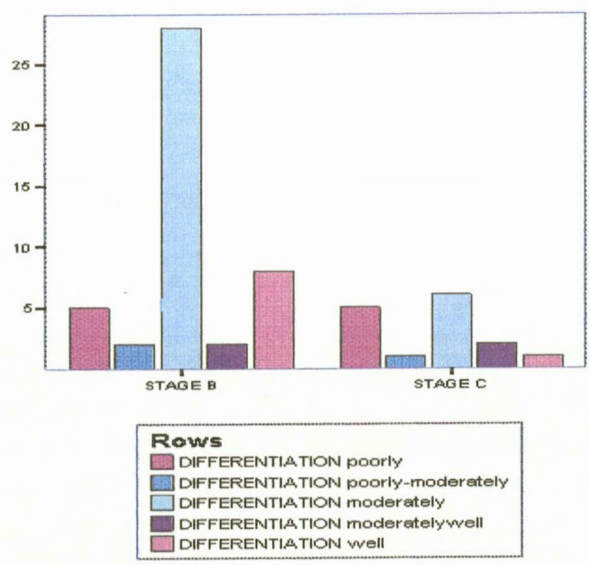
Table 4-6 : Chi-Square Test of Stage and Differentiation

	STAGE	DIFFERENTIATION
Chi-Square[a,b]	15.000	53.500
df	1	4
Asymp. Sig.	.000	.000

a. 0 cells (.0%) have expected frequencies less thar
5. The minimum expected cell frequency is 30.0.

b. 0 cells (.0%) have expected frequencies less thai
5. The minimum expected cell frequency is 12.0.

Figure 4-8 : Frequency Distribution for stage Versus Differentiation



4.4 ANALYSIS OF THE PRESENCE / ABSENCE OF BLOOD AND/OR LEUKOCYTES IN THE URINE

The Independent Samples test showed that there was no significant difference in the presence of blood or leukocytes in the urine between the two groups under evaluation for all 6 weeks. There were no patients who had leukocytes in the urine for week six (Table 4-7). The t and ρ values for weeks one to five are demonstrated in Table 4-8.

Since all ρ values are greater than 0.025, it is concluded that there are no differences between the two groups.

Table 4-7 Leukocytes in urine - week 6

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no	60	100.0	100.0	100.0

Table 4-8 : Independent samples t-Test for Prescence/Absence of blood/leukocytes in urine

		t-test for Equality of Mean		
		t	df	Sig. (2-tailed)
blood in urine - week 1	Equal variances assumed	-2.112	58	.039
	Equal variances not assumed	-2.112	29.000	.043
blood in urine - week 2	Equal variances assumed	-1.795	58	.078
	Equal variances not assumed	-1.795	29.000	.083
blood in urine - week 3	Equal variances assumed	-1.439	58	.155
	Equal variances not assumed	-1.439	29.000	.161
blood in urine - week 4	Equal variances assumed	-1.439	58	.155
	Equal variances not assumed	-1.439	29.000	.161
blood in urine - week 5	Equal variances assumed	-1.795	58	.078
	Equal variances not assumed	-1.795	29.000	.083
blood in urine - week 6	Equal variances assumed	-1.439	58	.155
	Equal variances not assumed	-1.439	29.000	.161
leukocytes in urine week 1	Equal variances assumed	.000	58	1.000
	Equal variances not assumed	.000	58.000	1.000
leukocytes in urine week 2	Equal variances assumed	.000	58	1.000
	Equal variances not assumed	.000	58.000	1.000
leuckocytes in urine - week 3	Equal variances assumed	-.584	58	.561
	Equal variances not assumed	-.584	52.684	.562
leukocytes in urine week 4	Equal variances assumed	.584	58	.561
	Equal variances not assumed	.584	52.684	.562
leukocytes in urine week 5	Equal variances assumed	.000	58	1.000
	Equal variances not assumed	.000	58.000	1.000

4.5 ANALYSIS OF THE PRE-TREATMENT AND POST-TREATMENT PSA LEVELS

There was a high statistical significance and relationship demonstrated between the pre-treatment PSA levels and the post-treatment PSA levels (Table 4-9) with the t value at 8.753 and the ρ value at 0.000 ($\rho \leq \alpha$). This implies that there was a definite improvement (reduction) in the PSA values denoting an improvement in the patients' conditions. The actual pre-treatment and post-treatment values are demonstrated in Appendix K.

Since $\rho \leq \alpha$ (0.05), the Ho was rejected (i.e there was an improvement in the PSA levels).

Table 4-9 : Paired Samples t-Test for Pre and Post- Treatment PSA

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	pretreatment PSA	9.9650	60	6.8009	.8780
	posttreatment PSA	1.5688	60	3.1589	.4078

Table 4-9 : Paired Samples t-Test for Pre and Post- Treatment PSA (cont.)

		N	Correlation	Sig.
Pair 1	pretreatment PSA & posttreatment PSA	60	.024	.857

Table 4-9 : Paired Samples t-Test for Pre and Post- Treatment PSA (cont.)

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	pretreatment PSA - posttreatment PSA	3962	7.4303	.9592	6.4767	10.32	8.75	59	.000

4.6 ANALYSIS OF THE 3-FIELD VERSUS THE 4-FIELD TECHNIQUE BLADDER TOXICITY

The Independent Sample Test demonstrated no statistical significance between the two groups under evaluation in terms of weekly acute bladder toxicity. The t and ρ values are demonstrated in Table 4-10. Figure 4-9 gives a graphical representation of the frequency distribution for weekly bladder toxicity for all 60 patients for both the 3-field technique and the 4-field technique. Since $\rho > \alpha/2$ for all weeks, the Ho is accepted (i.e there is no difference between the two groups).

Table 4-10 : Independent Samples Test for weekly Bladder Toxicity

		t-test for Equality of Means		
		t	df	Sig. (2-tailed)
bladder toxicity - week 1	Equal variances assumed	-.637	58	.527
	Equal variances not assumed	-.637	57.095	.527
bladder toxicity - week 2	Equal variances assumed	.574	58	.568
	Equal variances not assumed	.574	57.979	.568
bladder toxicity week 3	Equal variances assumed	1.022	58	.311
	Equal variances not assumed	1.022	56.408	.311
bladder toxicity - week 4	Equal variances assumed	.000	58	1.000
	Equal variances not assumed	.000	52.296	1.000
bladder toxicity - week 5	Equal variances assumed	.150	58	.882
	Equal variances not assumed	.150	54.167	.882
bladder toxicity - week 6	Equal variances assumed	-.157	58	.876
	Equal variances not assumed	-.157	52.655	.876

In week one, 48 (80%) (Table 4-11) patients did not experience any acute bladder toxicity at all. Of the 12 (20%) patients who did experience grade 1 acute bladder toxicity, 5 (41.7%) were from the 3-field group and 7 (58.3%) patients were from the 4-field group. No patients experienced grade 2,3 or 4 acute bladder toxicity (Table 4-12).

In week two, 31 (51.7%) (Table 4-11) patients did not experience any acute bladder toxicity at all. Twenty three (38.3%) patients experienced grade 1 toxicity, of which 13 (56.5%) were in the 3-field group and 10 (43.5%) were in the 4-field (50%) from each of the groups. No patients experienced grade 3 or 4 acute bladder toxicity (Table 4-12).

In week three, 17 (28.3%) (Table 4-11) patients did not experience any bladder toxicity. Twenty nine (48.3%) patients experienced grade 1 acute bladder toxicity, 16 (55.2%) from the 3-field group and 13 (44.8%) from the 4-field group. Thirteen (21.7%) patients experienced grade 2 acute bladder toxicity, 8 (61.5%) from the 3-field group and 5 (38.5%) from the 4-field group. Only one patient experienced grade 3 acute bladder toxicity and he was from the 4-field group. No patients experienced grade 4 acute bladder toxicity. (Table 4-12)

In week four, 12 (20%) (Table 4-11) patients did not experience any acute bladder toxicity. Twenty eight (46.7%) patients experienced grade 1 acute bladder toxicity of which 17 (60.7%) were from the 3-field group and 11 (39.3%) from the 4-field group. Eighteen (30%) patients experienced grade 2 acute bladder reactions of which there were 9 (50%) patients from each of the groups. Two (3.3%) of the patients had grade 3 acute bladder reactions, both of whom were in the 4-field group. No patients experienced grade 4 acute bladder toxicity (Table 4-12).

In week five, 12 (20%) (Table 4-11) patients did not experience any acute bladder toxicity. Twenty five (41.7%) patients experienced grade 1 acute bladder toxicity of which 15 (60%) patients were from the 3-field group and 10 (40%) were from the 4-field group. Nineteen (31.7%) patients had grade 2 acute bladder toxicity, of which 10 (52.6%) were from the 3-field group and 9 (47.4%) were from the 4-field group. Four (6.7%) patients experienced grade 3 acute bladder toxicity, of which 1(25%) was from the 3-field group and 3 (75%) were from the 4-field group. No patients experienced grade 4 acute bladder toxicity (Table 4-12).

In week six, 10 (16.7%) (Table 4-11) patients did not experience any acute bladder toxicity. Of the 29 (48.3%) patients who experienced grade 1 acute bladder toxicity, 18 (62.1%) were from the 3-field group and 9 (37.9%) were from the 4-field group. Seventeen (28.3%) patients experienced grade 2 acute bladder toxicity, of which 8 (47.1%) were from the 3-field group and 9 (52.9%) were from the 4-field group. Of the 4 (6.7) patients who experienced grade 3 acute bladder toxicity, 1 (25%) was from the 3-field group and 3 (75%) were from the 4-field group. No patients experienced grade 4 acute bladder toxicity (Table 4-12).

In the 3-field technique, grade 1 bladder toxicity increased from week 1 through to week 4 than decreased in week 5 and rose again slightly in week 6. In the 4-field technique, the bladder toxicity increased from week one through to week 3, then plateaued from there on grade 2 bladder toxicity also increased from week 1 until week 5 then decreased for both the 3-field and the 4-field. The 3-field peaked in week 5 whereas the 4-field peaked in week 4. Grade 3 acute bladder toxicity was consistent in week 5 and 6 for the 3-field whereas it increased from week 3 in the 4-field (Figure 4-9).

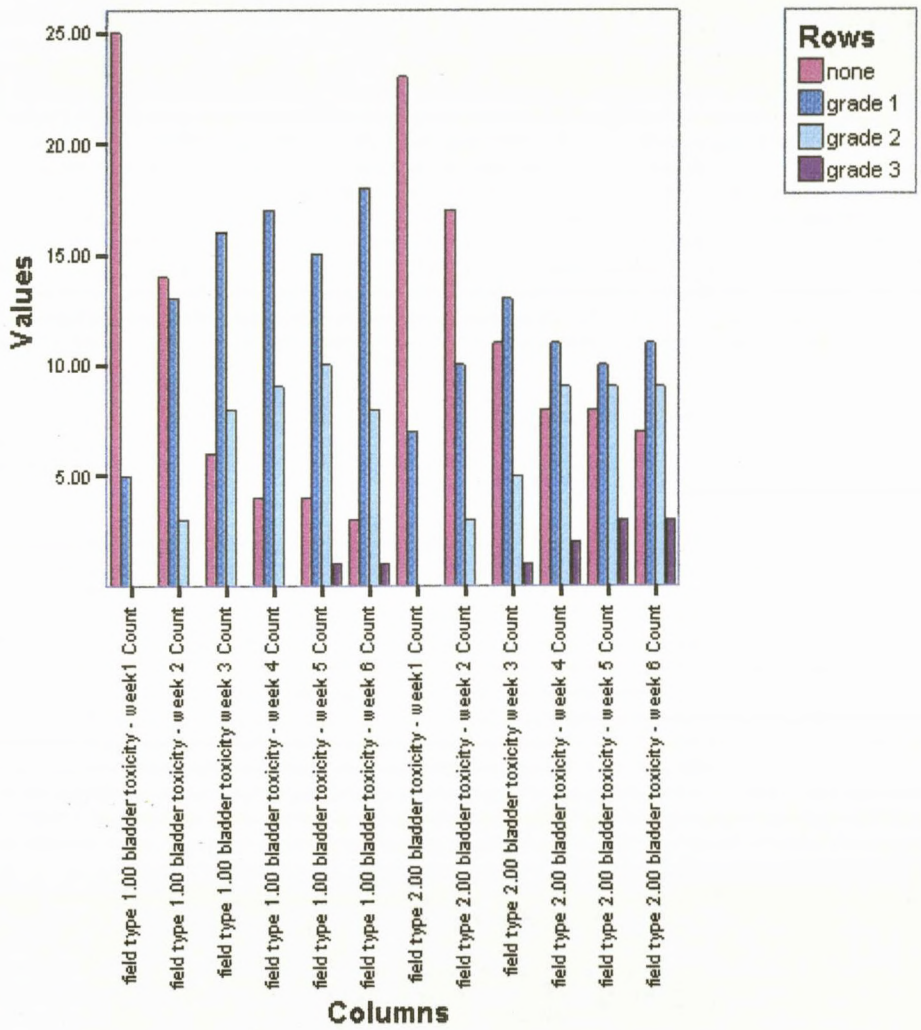
Table 4-11 : Frequency Distribution for Weekly Bladder Toxicity for ALL Patients

		bladder toxicity - week1	bladder toxicity - week 2	bladder toxicity week 3	bladder toxicity - week 4	bladder toxicity - week 5	bladder toxicity - week 6
none	Count	48	31	17	12	12	10
	%	(80.0%)	(51.7%)	(28.3%)	(20.0%)	(20.0%)	(16.7%)
grade 1	Count	12	23	29	28	25	29
	%	(20.0%)	(38.3%)	(48.3%)	(46.7%)	(41.7%)	(48.3%)
grade 2	Count		6	13	18	19	17
	%		(10.0%)	(21.7%)	(30.0%)	(31.7%)	(28.3%)
grade 3	Count			1	2	4	4
	%			(1.7%)	(3.3%)	(6.7%)	(6.7%)
Total	Count	60	60	60	60	60	60
	%	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)

Table 4-12 :: Frequency Distributions for the Weekly Bladder Toxicity for the 3-Filed and 4-Field Techniques

		FIELD TYPE											
		3-FIELD						4-FIELD					
		bladder toxicity - week1	bladder toxicity - week 2	bladder toxicity week 3	bladder toxicity - week 4	bladder toxicity - week 5	bladder toxicity - week 6	bladder toxicity - week1	bladder toxicity - week 2	bladder toxicity week 3	bladder toxicity - week 4	bladder toxicity - week 5	bladder toxicity - week 6
none	Count	25	14	6	4	4	3	23	17	11	8	8	7
	%	(83.3%)	(46.7%)	(20.0%)	(13.3%)	(13.3%)	(10.0%)	(76.7%)	(56.7%)	(36.7%)	(26.7%)	(26.7%)	(23.3%)
grade 1	Count	5	13	16	17	15	18	7	10	13	11	10	11
	%	(16.7%)	(43.3%)	(53.3%)	(56.7%)	(50.0%)	(60.0%)	(23.3%)	(33.3%)	(43.3%)	(36.7%)	(33.3%)	(36.7%)
grade 2	Count	0	3	8	9	10	8	0	3	5	9	9	9
	%	(.0%)	(10.0%)	(26.7%)	(30.0%)	(33.3%)	(26.7%)	(.0%)	(10.0%)	(16.7%)	(30.0%)	(30.0%)	(30.0%)
grade 3	Count	0	0	0	0	1	1	0	0	1	2	3	3
	%	(.0%)	(.0%)	(.0%)	(.0%)	(3.3%)	(3.3%)	(.0%)	(.0%)	(3.3%)	(6.7%)	(10.0%)	(10.0%)
Total	Count	30	30	30	30	30	30	30	30	30	30	30	30
	%	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)

Figure 4-9 : Frequency Distribution for Weekly Bladder Toxicity For ALL Patients for 3-Field and 4-Field



4.7 ANALYSIS OF THE 3-FIELD VERSUS THE 4-FIELD TECHNIQUE RECTAL TOXICITY

There was a statistical significance between the two groups under evaluation in terms of weekly acute rectal toxicity (Table 4-13). The 4-field group demonstrated a greater acute toxicity that the 3-field group. This was seen in week two which demonstrated a t value of 2.374 and a ρ value of 0.022 when equal variances were assumed and 0.025 when equal variances were not assumed.

Since $\rho \leq \alpha/2$ (0.025), Ho is rejected (i.e there is a difference between the two fields).

In week one, 56 (93.3%) (Table 4-14) patients did not experience any acute rectal toxicity. Of the 4 (6.7%) patients who did have acute rectal complications, there were 2 (50%) in each of the groups. No patients experienced grades 2,3 or 4 acute rectal toxicity (Table 4-15).

In week two, 50 (83.3%) (Table 4-14) patients did not experience any acute rectal toxicity. Of the 6 (10%) patients who experienced grade 1 acute

Table 4-13 : Independent Samples Test for Weekly Rectal Toxicity

		t-test for Equality of Means		
		t	df	Sig. (2-tailed)
rectal toxicity - week1	Equal variances assumed	.000	58	1.000
	Equal variances not assumed	.000	58.000	1.000
rectal toxicity week 2	Equal variances assumed	2.347	58	.022
	Equal variances not assumed	2.347	34.539	.025
rectal toxicity - week 3	Equal variances assumed	.185	58	.854
	Equal variances not assumed	.185	55.292	.854
rectal toxicity - week 4	Equal variances assumed	-.506	58	.615
	Equal variances not assumed	-.506	54.442	.615
rectal toxicity - week 5	Equal variances assumed	.518	58	.606
	Equal variances not assumed	.518	57.657	.606
rectal toxicity - week 6	Equal variances assumed	2.023	58	.048
	Equal variances not assumed	2.023	55.678	.048

rectal toxicity, 4 (66.7%) were from the 3-field group and 2 (33.3%) from the 4-field group. Three (5%) patients experienced grade 2 acute rectal toxicity, all of whom were from the 3-field group. Only one patient who was from the 3-field group experienced grade 3 acute rectal toxicity. No patients experienced grade 4 acute rectal toxicity (Table 4-15).

In week three, 43 (71.7%) (Table 4-14) patients did not experience any acute rectal complications. Of the 12 (20%) patients who did experience grade 1 acute rectal complications, 5 (41.7%) patients were from the 3-field group and 7 (58.3%) from the 4-field group. four (6.7%) patients experienced grade 2 acute rectal toxicity, 2 (50%) patients from each group. Only one (1.7%) patient who was in the 3-field group experienced grade 3 acute rectal toxicity. No patients experienced grade 4 acute rectal toxicity (Table 4-15).

In week four, 44 (73.3%) (Table 4-14) patients did not experience any acute rectal complications. Of the 12 (20%) patients who did experience grade 1 acute rectal toxicity, 7 (58.3%) were from the 3-field group and 5 (41.7%) were from the 4-field group. The one (1.7%) who experienced grade 2 acute rectal toxicity was from the 3-field group. Of the 3 (5%) patients who

experienced grade 3 acute rectal toxicity, one (33.3%) was from the 3-field group and 2 (66.7%) were from the 4-field group. No patients experienced grade 4 acute rectal toxicity (Table 4-15).

In week five, 42 (70%) (Table 14-14) patients did not experience any acute rectal complications. Of the 13 (21.7%) who experienced grade 1 acute rectal toxicity, 7 (53.8%) were from the 3-field group and 5 (46.9%) were from the 4-field group. Three (5%) experienced grade 2 acute rectal complications, of which 2 (66.7%) were from the 3-field group and the remaining 1 (33.3%) was from the 4-field group. Of the 2 (3.3%) patients who experienced grade 3 acute rectal toxicity, there was 1 (50%) patient from each of the groups. None of the patients experienced grade 4 acute rectal toxicity (Table 4-15).

In week six, 42 (70%) (Table 4-14) patients did not experience any acute rectal complications. Of the 12 (20%) patients who did experience grade 1 acute rectal toxicity, 8 (66.7%) were from the 3-field group and 4 (33.3%) were from the 4-field group. All of the 5 (8.3%) patients who experienced grade 2 acute rectal toxicity were from the 3-field group. The one (1.7%)

patient who experienced 3 acute rectal toxicity was also from the 3-field group. No patients experienced grade 4 acute rectal toxicity (Table 4-15).

Grade 1 acute toxicity for the rectum in the 3-field technique increased from week 1 to week 4, plateaued in week 5 and increased slightly again in week 6 whereas in the 4-field technique it peaked in week 3 then plateaued. Grade 2 rectal toxicity for the 3-field technique peaked in week 6 whereas in the 4-field technique it peaked in week 3 then plateaued in week 4 and 5. Grade 3 toxicity was fairly consistent in field 3 whereas in the 4-field there was a slight peak in week 4 before it plateaued in weeks 5 and 6 (Figure 4.10).

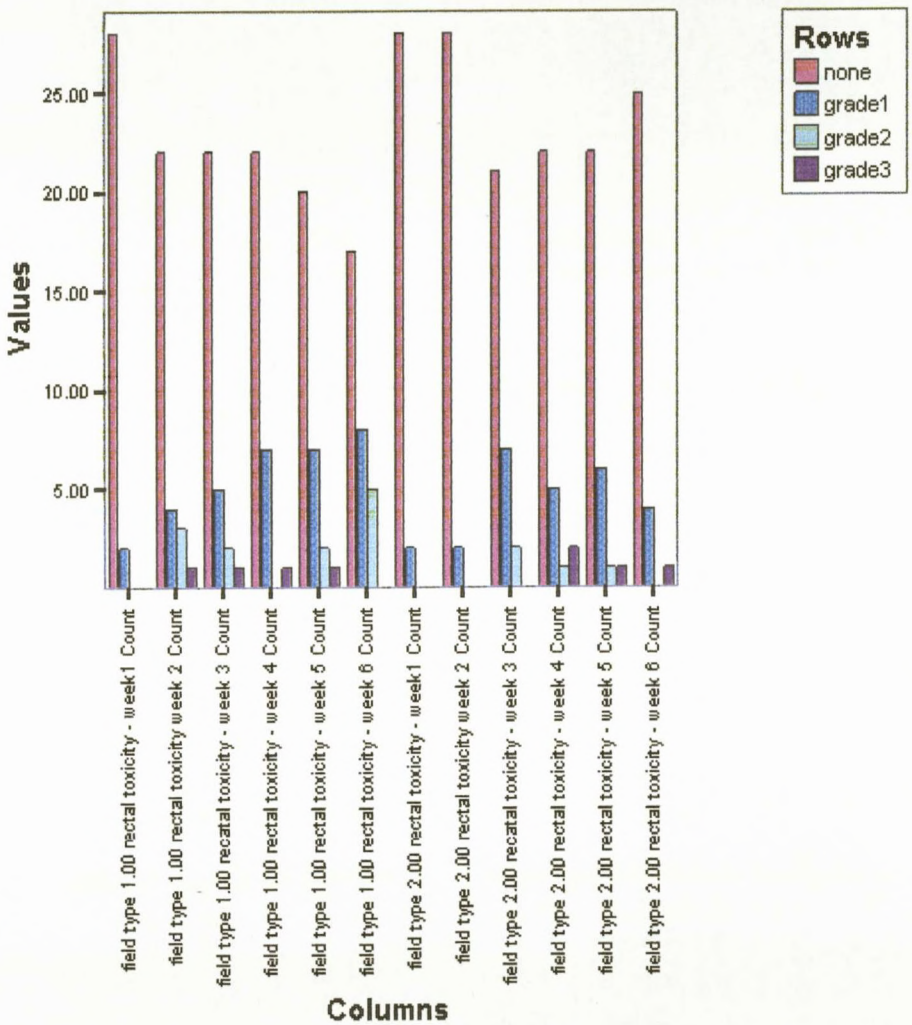
Table 4-14 : Frequency Distribution for the Weekly Rectal Toxicity ALL Patients

		rectal toxicity - week1	rectal toxicity - week 2	rectal toxicity - week 3	rectal toxicity - week 4	rectal toxicity - week 5	rectal toxicity - week 6
none	Count	56	50	43	44	42	42
	%	(93.3%)	(83.3%)	(71.7%)	(73.3%)	(70.0%)	(70.0%)
grade1	Count	4	6	12	12	13	12
	%	(6.7%)	(10.0%)	(20.0%)	(20.0%)	(21.7%)	(20.0%)
grade2	Count	0	3	4	1	3	5
	%	(.0%)	(5.0%)	(6.7%)	(1.7%)	(5.0%)	(8.3%)
grade3	Count	0	1	1	3	2	1
	%	(.0%)	(1.7%)	(1.7%)	(5.0%)	(3.3%)	(1.7%)
Total	Count	60	60	60	60	60	60
	%	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)

Table 4-15 : Frequency Distribution of Weekly Rectal Toxicity for the 3-Filed and 4-Field Technique

		FIELD TYPE											
		3-FIELD						4-FIELD					
		rectal toxicity - week1	rectal toxicity week 2	rectal toxicity - week 3	rectal toxicity - week 4	rectal toxicity - week 5	rectal toxicity - week 6	rectal toxicity - week1	rectal toxicity week 2	rectal toxicity - week 3	rectal toxicity - week 4	rectal toxicity - week 5	rectal toxicity - week 6
none	Count	28	22	22	22	20	17	28	28	21	22	22	25
	%	(93.3%)	(73.3%)	(73.3%)	(73.3%)	(66.7%)	(56.7%)	(93.3%)	(93.3%)	(70.0%)	(73.3%)	(73.3%)	(83.3%)
grade1	Count	2	4	5	7	7	8	2	2	7	5	6	4
	%	(6.7%)	(13.3%)	(16.7%)	(23.3%)	(23.3%)	(26.7%)	(6.7%)	(6.7%)	(23.3%)	(16.7%)	(20.0%)	(13.3%)
grade2	Count	0	3	2	0	2	5	0	0	2	1	1	0
	%	(.0%)	(10.0%)	(6.7%)	(.0%)	(6.7%)	(16.7%)	(.0%)	(.0%)	(6.7%)	(3.3%)	(3.3%)	(.0%)
grade3	Count	0	1	1	1	1	0	0	0	0	2	1	1
	%	(.0%)	(3.3%)	(3.3%)	(3.3%)	(3.3%)	(.0%)	(.0%)	(.0%)	(.0%)	(6.7%)	(3.3%)	(3.3%)
Total	Count	30	30	30	30	30	30	30	30	30	30	30	30
	%	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)

Figure 4-10 : Frequency Distribution for Weekly Rectal Toxicity for ALL Patients for 3-Field and 4-Field



4.8 MEANS AND STANDARD DEVIATIONS FOR DOSE TO POINTS A, B, AND C

The means and the standard deviations for the doses to Points A, B, and C were obtained from executing descriptive statistics for these variables. Table 4-16 contains the means and standard deviations for the 3-field technique and Table 4-17 contains the means and standard deviations for the 4-field technique. The calculations for the co-efficient of variation are shown below.

Co-efficient of Variation = (Standard Deviation ÷ Mean) x 100%

3-Field Technique - Point A	4-Field Technique - Point A
(0.4302 ÷ 2.2333) x 100	(0.3051 ÷ 2.1000) x 100
=19.26 %	=14.52 %

These results indicate that the 4-field technique is more consistent than the 3-field technique with regards to isocentric doses (i.e there is less variation).

3-Field Technique - Point B

(0.4302 ÷ 2.2333) x 100%

=19.26 %

4-Field Technique - Point B

(0.4068 ÷ 2.2000) x 100%

=18.49 %

These results indicate that the 4-field technique is more consistent than the 3-field technique with regards to dose to Point B in the bladder (i.e there is less variation).

3-Field Technique - Point C

(0.4611 ÷ 2.1667) x 100

=21.28 %

4-Field Technique - Point C

(0.2573 ÷ 2.0667) x 100

=12.28 %

These results indicate that the 4-field technique is more consistent than the 3-field technique with regards to dose to Point C in the rectum (i.e there is less variation).

Table 4-16 : Standard Deviation and means of Daily Doses (%) to Points A, B, C for the 3-Field Technique

		% daily isocentric dose	total isocentric dose	% daily bladder dose	total bladder dose	% daily rectal dose	total rectal dose
N	Valid	30	30	30	30	30	30
	Missing	0	0	0	0	0	0
Mean		2.1000	2.1000	2.2000	2.2333	2.0667	2.0667
Std. Deviation		.3051	.3051	.4068	.4302	.2537	.2537
Minimum		2.00	2.00	2.00	2.00	2.00	2.00
Maximum		3.00	3.00	3.00	3.00	3.00	3.00

Table 4-17 : Standard Deviation and Means of Daily Doses to Points A, B, C for the 4-Field Technique

		% daily isocentric dose	total isocentric dose	% daily bladder dose	total bladder dose	% daily rectal dose	total rectal dose
N	Valid	30	30	30	30	30	30
	Missing	0	0	0	0	0	0
Mean		2.2333	2.2333	2.2333	2.2333	2.1667	2.1667
Std. Deviation		.4302	.4302	.4302	.4302	.4611	.4611
Minimum		2.00	2.00	2.00	2.00	1.00	1.00
Maximum		3.00	3.00	3.00	3.00	3.00	3.00

4.9 MEANS AND STANDARD DEVIATIONS FOR VOLUME OF BLADDER AND RECTUM RECEIVING MORE THAN 50.00Gy

The means and the standard deviations for the volume of bladder and rectum receiving more than 50.00Gy were obtained from executing descriptive statistics for these variables. Table 4-18 contains the means and standard deviations for the 3-field technique and Table 4-19 contains the means and standard deviations for the 4-field technique. The calculations for the co-efficient of variation are shown below.

Co-efficient of Variant = (Standard Deviation ÷ Mean) x 100%

3-Field Bladder	4-Field Bladder
(0.9965 ÷ 2.2000) x 100%	(0.8867 ÷ 1.8000) x 100%
=45.30 %	=49.26 %

These results indicate that the 3-field technique is more consistent than the 4-field technique in terms of volume of bladder receiving more than 50.00Gy (i.e there is less variation).

3-Field Rectum	4-Field Rectum
(1.0483 ÷ 2.9333) x 100%	(0.8899 ÷ 2.3667) x 100%
=35.74 %	=37.60 %

These results indicate that the 3-field technique is more consistent than the 4-field technique in terms of volume of rectum receiving more than 50.00Gy (i.e there is less variation).

Of 60 patients, there were 4 (6.7%) patients whose bladders received more than 50.00Gy. Three (75%) of these patients were from the 4-field group and the 1 (25%) was from the 3-field group. There were 13 (21.7%) patients whose rectums received more than 50.00Gy. Of these 13 patients, 9 (69.2%) were from the 4-field technique and 4 (30.8%) were from the 3-field group (Refer to Appendix L).

Table 4-18 : Standard Deviation and Mean for % Bladder and Rectum receiving more than 50.00 Gy - 3Field

		% bladder receiving more than 50 Gy	% rectum receiving more than 50 Gy
N	Valid	30	30
	Missing	0	0
Mean		2.2000	2.9333
Std. Deviation		.9965	1.0483
Minimum		1.00	1.00
Maximum		5.00	5.00

Table 4-19 : Standard Deviation and Mean of % Bladder and Rectum receiving more than 50.00 Gy - 4-Field

		% bladder receiving more than 50 Gy	% rectum receiving more than 50 Gy
N	Valid	30	30
	Missing	0	0
Mean		1.8000	2.3667
Std. Deviation		.8867	.8899
Minimum		1.00	1.00
Maximum		4.00	4.00

CHAPTER 5.0 : DISCUSSION

5.1 INTRODUCTION

The results that were obtained from the data and presented in the form of tables, figures, graphs and statements in Chapter 4.0 are discussed in the current chapter.

5.2 REDEFINITION OF AIMS OF THE STUDY

The aim of this study was to analyse the 3-field radiation treatment technique and the 4-field radiation treatment technique in order to determine which technique is more toxic in terms of acute bladder and rectal toxicity in patients presenting with histologically confirmed stage B or C prostate cancer.

5.3 CLASSIFICATION OF THE DISCUSSION

The discussion will be classified under 3 major sections:

5.1.1 Intragroup Comparisons,

5.1.2 Inter-variable Comparisons, and

5.1.3 Intergroup Comparisons

Intra-group comparisons include discussions on the frequency distributions for the patient demographics which were presented as per Table 4-1, Appendix J, and Figures 4-1 - 4-6.

Inter-variable comparisons focus on whether there are any relationships between various different variables.

Inter-group comparisons encompass determining whether there was any statistical significance between the 3-field and the 4-field treatment techniques.

5.3.1 INTRAGROUP COMPARISONS

Prostate cancer is primarily a disease of older men and age is an important factor in its development (De Vita **et al.** 1997 : 1331; Neal and Hoskin, 1996 : 119; Newman, 1996; Perez and Brady, 1998 : 1600). Newman (1996) stated that the median age for diagnosis in Black American males was 70 years compared to 72 years in white American males. The median age at diagnosis for the current study was 68 years (Figure 4-2). For the 3-field group, the median age was between 71-75 years compared to 66-70 years in the 4-field group.

The decrease in the median age at which the patients presented could be due to one of or a combination of two factors discussed below. It could be attributed to an increased awareness of the disease as a whole or to the implementation of informal routine screening programs. This statement holds true in the light of the fact that 6 (10%) patients of the 60 patients entered into this study were actually differentially diagnosed during routine physical examinations for insurance purposes.

It must also be noted that a degree of bias may have been introduced into this study, since all the patients were recruited from two private sector oncology practices. The consequences of this are discussed in 5.3.1.2 of this chapter.

Of the 6 patients who were incidentally diagnosed with the disease, 5 (83.3%) were between 52-55 years of age (Table 5-1).

Table 5-1 : Median Age of Patients with Incidental Diagnosis

Patient	1	2	3	4	5	6	Median
Age	55	61	53	54	53	52	55

Perez and Brady (1998 : 1589-1594) advocates the decrease in the median age at diagnosis to the increase in the use of PSA tests which are currently being used. The value of PSA are discussed in 5.3.2.2 of this Chapter.

The results of this study as well as comments made by various other authors (De Vita et al. 1997 : 1335-1340; Neal and Hoskin : 118; Newman, 1996; Perez and Brady, 1998 : 1589-1594) advocate the need for routine screening for prostate cancer. The manner in which this screening should be undertaken will be discussed in Chapter 6.0.

Fifty four patients were White males (Table 4-1) comprising 90% (Figure 4-2) of the total sample size, whereas the 10% of the patient population consisted of Coloured and Asian males. There were no Black males in the current study. There are a few factors that could be the cause of this state as discussed below.

Perez and Brady (1997) state that racial incidence may be related to one of several factors including immune competence, biological aggressiveness of tumours, testosterone levels, environmental and socioeconomic factors.

The rates of incidence (Table 2-1) in South African White males is the highest amongst all four race groups at 62.5%, compared to South African Black males (31.7%). South African Coloured fall third in this category with 4.22% and the South African Asian male have the lowest incidence at 1.57% (Sitas 1999).

There could have been an element of patient selection bias introduced into the study as mentioned in 5.3.1, since all patients in the study were recruited form two private sector institutions. The higher socioeconomic population (generally predominantly white) have easier access to these facilities especially in terms of finance whereas the patients in the lower socioeconomic groups generally end up going to the provincial hospitals for their medical care. These patients often present at the provincial hospitals with late stage disease but this needs to be confirmed by conducting studies.

The reasons for late stage presentation could be three-fold. It may be due to lack of education in general or especially the disease (uninformed about the early signs and symptoms that may occur). Secondly the patients from the lower socioeconomic groups are generally from the more rural areas in

the country and there is not only difficulty financially but also difficulty in obtaining transportation as also advocated by Perez and Brady (1997). Thirdly, questions arise as to whether there is a cultural aspect to the late presentations. All three factors mentioned above need to be verified by conducting studies.

Seeing that 45 (75%) patients (Figure 4-3) presented with stage B cancer and bearing in mind the possible patient selection bias mentioned in 5.3.1 and 5.3.2, it is expected that the majority of the patients would have earlier stage disease. This could however, also be due to possibility of the patients being informed about the disease because they are from a higher socioeconomic group.

Differentiation and Gleason score are closely related, since in order to obtain a Gleason score, the differentiation of the prostatic cells have to be determined. Appendix B provides a brief explanation of the different histological differentiations. Well-differentiated tumours (generally associated with a Gleason score of between 2- 5) usually progress slowly and are associated with a relatively low probability of dying from the

prostate cancer whereas patient's with Gleason score of between 7-10 have a high probability of dying from prostate cancer.

According to Newman (1996), the Gleason score is controversial because of lack of agreement between different researchers as well as the reproducibility of the results. Although the reproducibility of the results have been questioned states Newman (1996) there is confirmation that with a Gleasons score of less than 5, patients have a 13% chance of having nodal involvement compared to a 100% chance of nodal involvement in patients with a Gleason score of 9 or 10 (De Vita **et al.** 1997 1326-1327; Perez and Brady, 1998 : 1603-1605; Rubin, 1993 : 435).

All patients in the current study had histologically confirmed prostate cancer. The histology was generally obtained by biopsy of the prostate. If the biopsy is negative for malignancy but other factors, including PSA levels suggest the possibility of malignancy, then a resection of the prostate may be done to further investigate the gland. Transurethral resection is usually done if there is urinary outflow obstruction. Radical prostatectomy may be done in early stage disease.

5.3.2 INTER-VARIABLE COMPARISON

The current study uncovered that there is a statistically significant relationship between age and stage which may arise from similar factors as stated in 4.3 and 5.3.1 (i.e a higher socioeconomic sample of patients who are probably more informed and are therefore presenting at younger ages with earlier stages of the disease).

With regards to the pre and post-treatment PSA levels, it was noted that the levels decreased when the patients' reached 60.00Gy indicating that the PSA levels decrease during the course of treatment. According to De Vita **et al.** 1998), serum PSA levels generally decline after completion of radiation therapy, sometimes to below 1ng/ml (upper level of normal for the healthy male = 4ng/ml). If the levels decline to 1ng/ml or less there is a lesser chance of the patient developing prostatic tumour relapses than those with levels between 1-4ng/ml.

Twenty two (33.67%) patients had pre-treatment PSA levels of more than 10ng/ml and 22 patients had levels more than 1ng/ml after completion of treatment but there was no relationship between these two groups of patients (Refer to Appendix K).

The current study did however prove that PSA levels do decrease even during the course of radiation therapy which makes it ideal to use as a prognostic factor during the course of radiotherapy.

5.3.3 INTERGROUP COMPARISONS

There was no statistically significant relationship between the two groups under evaluation in terms of blood and/or leukocytes in the urine. This result is expected since both treatment techniques do deliver a dose to the bladder. The means for the percentage daily dose to Point B in the bladder for the 3-field and the 4-field technique is fairly similar at 2.20 for the 3-field and 2.23 for the 4-field (Tables 4-16 and 4-17). This means that the total doses delivered to Point B in the bladder for the two fields were almost exactly the same.

Acute bladder toxicity is usually mild with doses such as that used for the current study. It generally appears around the third week of treatment and seems to subside a few days after completion of the radiation therapy (De Vita **et al.** 1997 : 1355; Perez and Brady, 1998 : 1662-1666). It would seem that the dose (60-66Gy) that was delivered to the bladder was not high enough to cause severe acute toxicity.

Acute rectal toxicity usually begins in the third week of treatment. In the current study there were 2 (6.7%)patients who had grade 1 acute rectal toxicity from week one in both the 3-field and the 4-field groups and 6 (10%) patients who had grade 1 toxicity in week 1 of whom 4 (66.7%) from the 3-field group and 2 (33.3%) from the 4-field group (Table 4-15). The current study revealed that the doses to the rectum were not high enough to cause severe acute rectal toxicities that may have required surgical intervention as Perez and Brady (1998 : 1355) states may be used in order to treat these complications.

Some patients ate peeled apples, left out to turn brown and claimed that it had helped stop or reduce the diarrhoea. This claim needs to be investigated before its use can be advocated.

Points A, B and C were selected since they represented constant points for the plans. The patient's bladder and rectum are not always in exactly the same position for every treatment fraction. This means that these points are not an exact representation of the doses to those specified points. The isocentric dose indicates the dose to the center of the target volume

(usually center of the tumour). These values will vary for different patients since all patients do not have the same body habitus.

The volume of bladder and rectum irradiated impacts greatly on acute and late toxicities to these organs (Michalski **et al.** 2000; Vijaykumar **et al.** 1993). The greater the volume of rectum or bladder irradiated, the greater the acute toxicity and possibly the onset of late toxicities as well.

CHAPTER 6.0 : CONCLUSION

6.1 INTRODUCTION

This chapter serves to provide the conclusions obtained from the results which were presented in chapter 4.0 and discussed in chapter 5.0. Pitfalls of the study as well as recommendations are also included.

6.2 PITFALLS

Patients in the study were not randomised since the convenient sampling technique was utilised to select patients but patients in both groups were treated simultaneously. An element of patient selection bias was introduced into the study since all the patients in the sample were recruited from the two private institutions and none from the provincial hospitals in KwaZulu-Natal . This was because a different treatment technique and dose schedule are used at the provincial hospitals in KwaZulu-Natal. Some patients did not strictly receive the treatment as prescribed by the oncologist due to defaults in the treatment units. This could result in providing time for the normal tissue to recover thereby reducing the acute bladder and rectal toxicity.

6.3 CONCLUSIONS

In this prospective study the conclusions stated below can be drawn.

The median age for diagnosis of the disease is 68 years advocating the need for the implementation of routine screening programs.

The PSA levels decrease during the course of radiation therapy.

The 3-field technique delivers a more homogenous dose in terms of volume of bladder and rectum receiving more than 50.00Gy. The 4-field technique demonstrated more homogeneity in its dose delivery to Points A (isocenter), B (bladder) had C (rectum).

There was no difference between the two treatment techniques in terms of acute bladder toxicity.

The 4-field technique did however demonstrate a greater level of acute rectal toxicity than the 3-field technique did. This leads to the conclusion that the 3-field technique is a better technique than the 4-field in terms of acute toxicity to the patient.

6.4 RECOMMENDATIONS

Long term follow-up needs to be done in order to evaluate these two techniques in terms of late toxicity to the bladder and the rectum and survival rates.

Further studies need to be conducted involving both the provincial and private sector oncology departments.

The functions of the prostate gland need to be further researched in order to contribute to the current limited knowledge.

The need for the implementation of routine screening programs for prostate cancer has been highlighted. This could be in the form of PSA tests and DRE from 50 years of age onwards. This finding by the researcher corresponds with De Vita **et al.** (1997 : 1335; Osterling, 1995), who also states that routine PSA tests should be done from 45 years should there be any affected family members. The advantages of routine screening programs for prostate cancer need to be elucidated by further studies.

Future studies regarding the effect of culture and socioeconomic status on late presentations in KwaZulu-Natal, effect of socioeconomic factors on median age of diagnosis and reason for late presentation need to be established.

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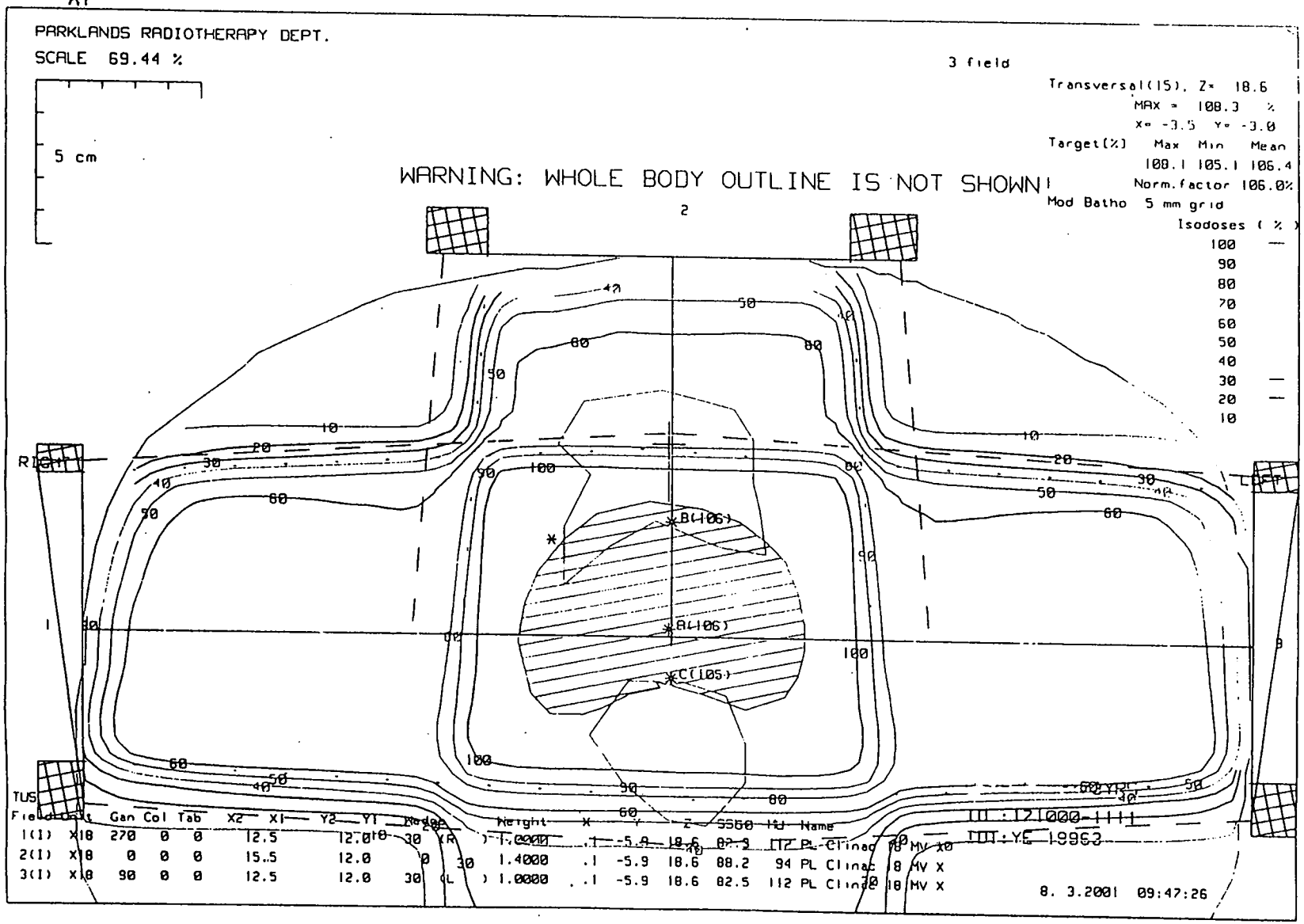
APPENDICES

APPENDIX A

Ai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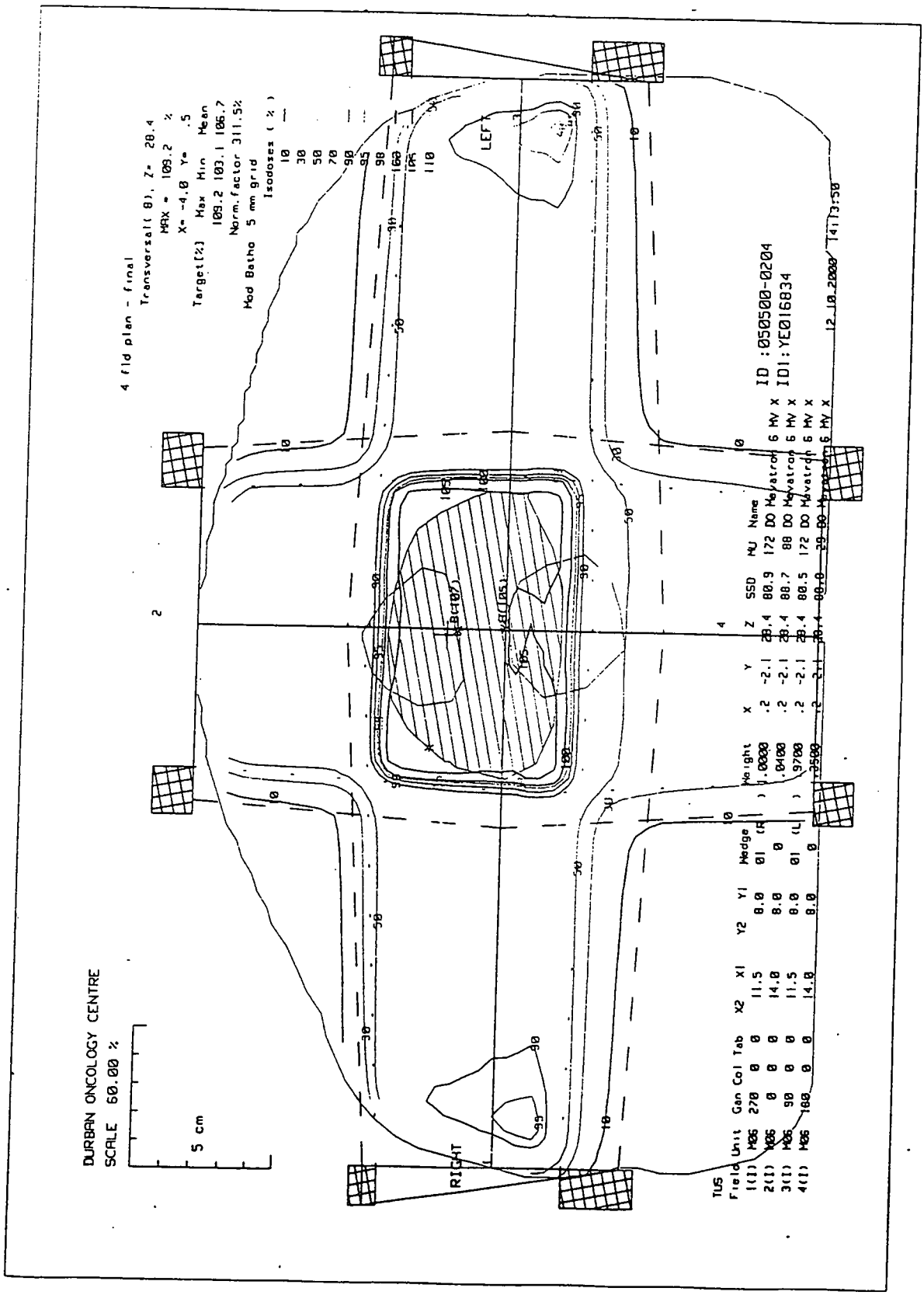
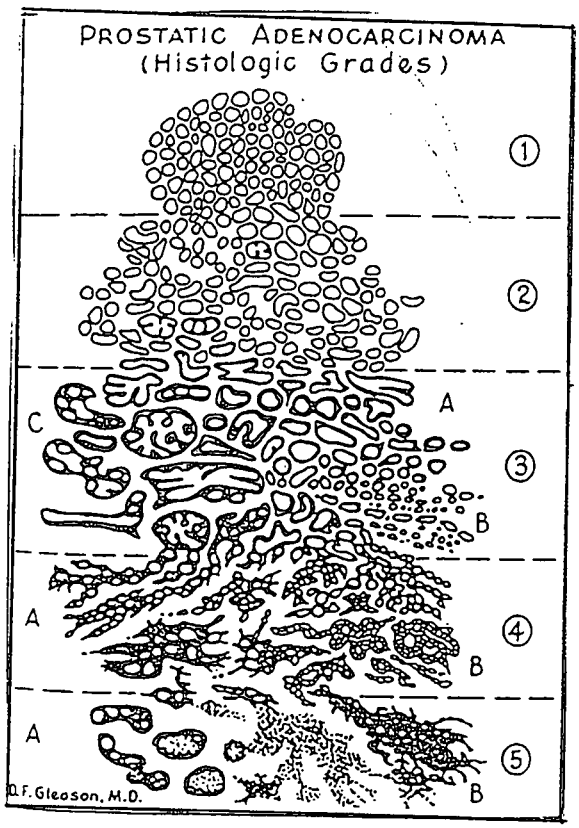
5 cm
3 field
Transversal(15), Z= 18.6
MAX = 108.3 %
X= -3.5 Y= -3.0
Target[%] Max Min Mean
108.1 105.1 106.4
Norm.factor 106.0%
Mod Batho 5 mm grid
Isodoses (%)
100
90
80
70
60
50
40
30
20
10
WARNING: WHOLE BODY OUTLINE IS NOT SHOWN!
RIGHT
LEFT
TUS
B(106)
B(106)
C(105)
Field Gan Col Tab X2 X1 Y2 Y1 Wedge Height X Y Z SSD MU Name
1(1) X18 270 0 0 12.5 12.0 30 (R) 1.0000 .1 -5.9 18.6 82.5 112 PL Clinac 18 MV X
2(1) X18 0 0 0 15.5 12.0 0 30 1.4000 .1 -5.9 18.6 88.2 94 PL Clinac 18 MV X
3(1) X18 90 0 0 12.5 12.0 30 (L) 1.0000 .1 -5.9 18.6 82.5 112 PL Clinac 18 MV X
8. 3.2001 09:47:26

Ai

Aii


4 fld plan - final
Transversal(8), Z= 28.4
MAX = 109.2 %
X= -4.0 Y= .5
Target(%) Max Min Mean
109.2 103.1 106.7
Norm.factor 311.5%
Mod Batho 5 mm grid
Isodoses (%)
10
30
50
70
90
95
98
100
105
110
LEFT
RIGHT
ID :050500-0204
ID1:YE016834
DURBAN ONCOLOGY CENTRE
SCALE 60.00 %
5 cm
12.10.2000 14:13:58

APPENDIX B



GLEASON GRADING

Grade 1	Single, separate, uniform glands in close-packed masses with definite rounded limiting edges
Grade 2	Single, separate, slightly less uniform glands, loosely packed. Definable but less sharp edge
Grade 3A	Single, separate, very variable glands, may be closely packed but usually widely separated with ragged, poorly defined tumor edge
3B	Like 3A but tiny glands or small cell clusters
3C	Sharply and smoothly circumscribed, often rounded masses of papillary or loose cribriform tumor
Grade 4A	Raggedly infiltrating "fused-glandular" tumor
4B	Like 4A but large pale cells ("hypernephroid")
Grade 5A	Sharply, smoothly circumscribed rounded masses of almost solid cribriform tumor, usually with some central necrosis ("comedocarcinoma")
5B	Ragged masses of anaplastic carcinoma with only enough gland formation or vacuoles to insure that it is an adenocarcinoma

(Rubin, P. 1993. Clinical Oncology : A multidisciplinary approach for both physicians and students. (7th ed.). Philadelphia : W.B. Saunders Company)

APPENDIX C

Comparison of the TNM and Whitmore-Jewett Staging Systems for Clinically Localized Prostate Cancer

Stage		
TNM	Whitmore-Jewett	*Description*
TX	*	Tumor cannot be assessed
T0	*	No evidence of tumor
T1a	A1	Tumor found incidentally at TURP (<5%) of resected tissue)
T1b	*	Tumor found incidentally at TURP (<5% of resected tissue)
T1c	B0	Nonpalpable tumor identified by means of an elevated serum PSA value†
T2a	B1	Tumor involves half of a lobe or less
T2b	B1	Tumor involves more than half a lobe but not both lobes
T2c	B2	Tumor involves both lobes
T3a	C1	Unilateral extracapsular extension
T3b	C1	Bilateral extracapsular extension
T4a	*	Tumor invades one or both seminal vesicles
T4b	*	Tumor invades the bladder neck, external sphincter, or rectum
		Tumor invades the levator muscles or is fixed to the pelvic side wall

* No corresponding stage.
† In the TNM staging system, the tumor should not be visible on transrectal ultrasonography.

(De Vita Jr. V.T., Hellman, J. and Rosenberg, S.A. 1997. Cancer : Principles and Practice of Oncology. (5th ed.). Philadelphia : Lippincott-Raven.)

APPENDIX D

Di

QUESTIONNAIRE - ACUTE RECTAL TOXICITY

PATIENT NAME ..... RADIOTHERAPY NUMBER .....

DATE OF PRESENTATION ..... STAGE .....

DIAGNOSIS ..... PATIENT NUMBER .....

TECHNIQUE USED : 3-FIELD ☐

4-FIELD ☐

The purpose of this questionnaire is to assess how the treatment that you are receiving is affecting you.

1. IN THE PAST WEEK, HAVE YOU HAD DIARRHOEA,

(runny tummy, loose stools)?

YES ☐

NO ☐

UNCERTAIN ☐

IF YES,

2. FOR HOW LONG HAVE YOU HAD DIARRHOEA,

(runny tummy, loose stools)?

LESS THAN 2 DAYS ☐

MORE THAN 2 DAYS ☐

OTHER (specify) ☐

3. HAS THE DIARRHOEA, (runny tummy, loose stools) BEEN :

REGULAR ☐

IRREGULAR ☐

UNCERTAIN ☐

4a. HAS THE DIARRHOEA (runny tummy, loose stools) BEEN :

BEARABLE ☐

UNBEARABLE ☐

UNCERTAIN ☐

4b. IF UNBEARABLE, EXPLAIN .....

5a. DID YOU REQUIRE ANY MEDICATION FOR IT?

YES ☐

NO ☐

UNCERTAIN ☐

IF YES,

5b. WHAT MEDICATION DID YOU TAKE? _____

5c. WHO PRESCRIBED THE MEDICATION? _____

5d. DID THE MEDICATION HELP?

YES ☐

NO ☐

UNCERTAIN ☐

6. DID YOU FEEL DEHYDRATED

(dry, a need to drink more fluids)?

YES ☐

NO ☐

UNCERTAIN ☐

Dii

QUESTIONNAIRE - ACUTE BLADDER TOXICITY

PATIENT NAME ..... RADIOTHERAPY NUMBER .....

DATE OF PRESENTATION ..... STAGE .....

DIAGNOSIS ..... PATIENT NUMBER .....

TECHNIQUE USED : 3-FIELD ☐

4-FIELD ☐

The purpose of this questionnaire is to assess how the treatment that you are receiving is affecting you.

1. HOW OFTEN DID YOU PASS URINE AT NIGHT BEFORE THE TREATMENT STARTED?

- NOT AT ALL ☐
- 1 - 3 TIMES ☐
- 4 - 6 TIMES ☐
- MORE THAN 6 TIMES (specify) ☐
- UNCERTAIN ☐

2. IN THE PAST WEEK, HOW OFTEN HAVE YOU PASSED URINE AT NIGHT?

- NOT AT ALL ☐
- 1 - 3 TIMES ☐
- 4 - 6 TIMES ☐
- MORE THAN 6 TIMES (specify) ☐
- UNCERTAIN ☐

3. IN THE PAST WEEK, HOW FREQUENTLY HAVE YOU PASSED URINE AT NIGHT?

- LESS THAN ONCE PER HOUR ☐
- AT LEAST ONCE PER HOUR ☐
- MORE THAN ONCE PER HOUR ☐

Specify .....

4a. IN THE PAST WEEK, DID YOU EXPERIENCE ANY PAIN WHEN PASSING URINE?

- YES ☐
- NO ☐
- UNCERTAIN ☐

IF YES,

4b. DID YOU NEED TO / TAKE ANY MEDICATION FOR THE PAIN?

- YES ☐
- NO ☐
- UNCERTAIN ☐

4c. WHAT MEDICATION DID YOU TAKE? _____

4d. WHO PRESCRIBED THE MEDICATION? _____

4e. DID THE MEDICATION HELP?

- YES ☐
- NO ☐
- UNCERTAIN ☐

5a. IN THE PAST WEEK, HAVE YOU FOUND IT DIFFICULT TO PUT OFF URINATING?

- YES ☐
- NO ☐
- UNCERTAIN ☐

5b. IF YES, DID YOU NEED TO / TAKE ANY MEDICATION FOR IT?

- YES ☐
- NO ☐
- UNCERTAIN ☐

5c. WHAT MEDICATION DID YOU TAKE? _____

5d. WHO PRESCRIBED THE MEDICATION? _____

5e. DID THE MEDICATION HELP?

- YES ☐
- NO ☐
- UNCERTAIN ☐

6a. IN THE PAST WEEK, DID YOU NOTICE ANY BLOOD IN YOUR URINE?

- YES ☐
- NO ☐
- UNCERTAIN ☐

6b. IF YES, DESCRIBE THE BLOOD IN THE URINE... _____

_____

_____

6c. DID YOU NEED TO / TAKE ANY MEDICATION FOR IT?

- YES ☐
- NO ☐
- UNCERTAIN ☐

6d. IF YES, WHAT MEDICATION DID YOU TAKE? _____

6e. WHO PRESCRIBED THE MEDICATION? _____

6f. DID THE MEDICATION HELP?

- YES ☐
- NO ☐
- UNCERTAIN ☐

7a. IN THE PAST WEEK, DID YOU FEEL ANY DIFFICULTY WHEN TRYING TO PASS URINE?

- YES ☐
- NO ☐
- UNCERTAIN ☐

7b. IF YES, DESCRIBE THE NATURE OF THE DIFFICULTY ... _____

_____

_____

_____

APPENDIX E

Ei

Loganee Moodley
c/o Department of Radiography
Technikon Natal
72 Ritson Road
Berea
Tel: 2042450

14 September 1999

The General Manager
c/o Parklands Hospital
Radiotherapy Department

re: REQUEST FOR PERMISSION TO EXECUTE STUDY

I am currently a Graduate Assistant in the Radiography Department at Technikon Natal, currently studying toward my Masters in Radiography (Therapy). I have already obtained a National Diploma in Radiography (Diagnostic) and a B.Tech. Radiography (Therapy).

In order to obtain my Masters Degree in Radiography (Therapy), I am required to execute a full research project and hand in a dissertation for evaluation.

Toward this end, I have decided to execute a study titled **A comparative analysis of two different radiation treatment techniques to be carried out on patients presenting with either stage B or C prostate cancer**.

The patients will be asked questions from a questionnaire and their responses used to evaluate the two techniques (ie the 3-field versus the 4-field radiation treatment technique). I would need to be present at the new patient clinic for patients with prostate cancer, be involved in the planning process, and attend the patient on treatment clinic for each patient entered into the study.

The study, I believe could be of great benefit to both future patients and doctors.
I assure you that all information about patients will be treated as confidential.

I request permission to carry out the study at Addington Hospital. I would appreciate it greatly, should permission be granted, if you would send something to me in writing.

Thanking you for you co-operation in this regard and hoping to receive a favourable reply.

Yours sincerely

_____

Loganee Moodley

Eii

Loganee Moodley
c/o Department of Radiography
Technikon Natal
72 Ritson Road
Berea
Tel: 2042450

15 September 1999

Dr. Hacking
Radiation Oncologist
Durban Oncology Centre

re: REQUEST FOR PERMISSION TO EXECUTE STUDY

I am currently a Graduate Assistant in the Radiography Department at Technikon Natal, currently studying toward my Masters in Radiography (Therapy). I have already obtained a National Diploma in Radiography (Diagnostic) and a B.Tech. Radiography (Therapy).

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Thanking you for you co-operation in this regard and hoping to receive a favourable reply.

Yours sincerely

_____
Loganee Moodley

Eiii

Parklands Hospital

75 Hopeland Road, Overport, Durban • Private Bag 37014, Overport, 4067
Tel +27 (0)31 208-8181• Fax: +27 (0)31 207-6637
Web address: www.netcare.co.za
P.R. No. 5802466

4 October 1999

Ms L. Moodley
C/o Department of Radiography
Technikon Natal
72 Ritson Road
Berea
4001

Dear Loganie

Thank you for your letter dated 14 September 1999 and my apologies for not replying sooner.

I have approached Ms Moore, the General Manager, and she is pleased to offer our Department for your research project.

It would be a privilege to be able to offer you any assistance you should require. Please do not hesitate to contact me.

Yours sincerely

JOAN MURRAY
RADIOTHERAPY MANAGER

Eiv

DR C A GOLDMAN
M.B.B.Ch., M.Med.
P.R. Number 4000250

DR D J HACKING
M.B.ChB., M.Med., F.F.Rad.T.(SA)
P.R. Number 4000420

DR L V HESLOP
M.B.ChB., F.F.Rad.T.(SA)
P.R. Number 4000897

SPECIALIST RADIATION ONCOLOGISTS

Durban Oncology Centre
99 Jan Smuts Highway
West Ridge
4091
Republic of South Africa
e-mail :doc@dbn.lia.net

Tel: (031) 261 8221 (Practice)
(031) 86 3730 (Home CAG)
(031) 208 7098 (Home DJH)
(031) 208 3563 (Home LVH)
(031) 301 3737 (After Hours)
(031) 2618156

29 September, 1999

Ms L Moodley

Dear Loganee

Thank you for your letter dated the 15th September. I and my colleagues at the Durban Oncology Centre would be only too pleased to assist you with the performance of such a study. When you are ready to proceed please make an appointment with Lyn Botha our Chief Planning Radiographer to discuss the implementation of the questionnaires and planning procedures.

Kind regards.

Yours sincerely

DR DJ HACKING

APPENDIX F

PATIENT INFORMATION SHEET

Welcome to my Research Project. Thank you for consenting to participate in this study. Your contribution to this study will be of benefit to future patients, doctors, and radiographers.

The study aims to determine the more suitable treatment technique for patients presenting with either stage B or stage C prostate cancer. You have been selected as you meet certain specific criteria of the research. You will be allocated into one of two groups.

As part of this study, you have to:

1) ensure that you have the treatment that is prescribed every day from Monday to Friday for the six weeks of the treatment.
2) be seen by the Oncologist once weekly for the duration of the treatment and once on the week following the completion of the treatment.
3) ensure that you take no other medication except for that which is prescribed by the Oncologist.

If you have any further questions or queries, please do not hesitate to ask me. Your co-operation is greatly appreciated.

Yours sincerely

_____

L. Moodley

(Research Student in Radiography)

APPENDIX G

INFORMED CONSENT FORM

(To be completed in duplicate by patient)

TITLE OF RESEARCH PROJECT :

_____

_____

_____

NAME OF SUPERVISOR : _____

NAME OF RESEARCH STUDENT : _____

_____

1.	Have you read the patient information sheet?	**YES / NO**
2.	Have you had the opportunity to ask questions?	**YES / NO**
3.	Have you received satisfactory answers to your questions?	**YES / NO**
4.	Have you had an opportunity to discuss this study?	**YES / NO**
5.	Have you received sufficient information about this study?	**YES / NO**
6.	Whom have you spoken to? _____	
7.	Do you understand the implications of your involvement in this study?	**YES / NO**
8.	Do you understand that you are free to withdraw from this study? a) at any time b) without having to give a reason for withdrawing, and c) without affecting your future health care	**YES / NO**
9.	Do you agree to voluntarily participate in this study?	**YES / NO**

PATIENT Name : _____ Signature : _____

WITNESS Name : _____ Signature : _____

RESEARCH STUDENT Name : _____ Signature : _____

APPENDIX H

Hi

PATIENT DETAILS SHEET

SURNAME..... NAME.....

AGE..... RACE..... RADIOTHERAPY NUMBER ....

ADDRESS.....
.....
.....TELEPHONE.....

STAGE..... DIFFERENTIATION..... GLEASON.....

SURGERY TYPE..... BIOPSY TYPE.....

PRE TREATMENT PSA VALUE..... OTHER CHEMICAL TESTS .....
.....
.....

BRIEF RELEVANT FAMILY, SURGICAL, MEDICAL HISTORY.....
.....
.....

ULTRASOUND COMMENTS
.....
.....

CHEST X-RAY COMMENTS
.....
.....

BONE SCAN COMMENTS
.....
.....

CT SCAN COMMENTS
.....
.....

PROPOSED TREATMENT TECHNIQUE..... .....

DOSE PRESCRIPTION
.....
.....

GENERAL EXAMINATION COMMENTS.....
.....
.....

PROSTATE EXAMINATION COMMENTS.....
.....
.....

Hii

WEEKLY DOSE TO BE RECEIVED BY ISOCENTER (POINT A) .....

WEEKLY DOSE TO BE RECEIVED BY BLADDER (POINT B) .....

WEEKLY DOSE TO BE RECEIVED BY RECTUM (POINT C) .....

URINE DIPSTIX VALUES

	BLOOD	LEUKOCYTES
WEEK 1		
WEEK 2		
WEEK 3		
WEEK 4		
WEEK 5		
WEEK 6		

PSA VALUE

	VALUE
WEEK 1	
WEEK 7	

APPENDIX I

PLEASE INDICATE WITH A CROSS THE LEVEL OF TOXICITY FOR THE PATIENT FOR THE WEEK.

WEEK 1	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
RECTUM					
BLADDER					

WEEK 2	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
RECTUM					
BLADDER					

WEEK 3	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
RECTUM					
BLADDER					

					GRADE 4
RECTUM					
BLADDER					

WEEK 5	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
RECTUM					
BLADDER					

WEEK 6	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
RECTUM					
BLADDER					

WEEK 7	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
RECTUM					
BLADDER					

APPENDIX J

Frequency of Age for 3-Field and 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	51-55	6	10.0	10.0	10.0
	56-60	2	3.3	3.3	13.3
	61-65	5	8.3	8.3	21.7
	66-70	21	35.0	35.0	56.7
	71-75	16	26.7	26.7	83.3
	76-80	7	11.7	11.7	95.0
	81-85	3	5.0	5.0	100.0
	Total	60	100.0	100.0	

Frequency of Race for 3-Field and 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	asian	2	3.3	3.3	3.3
	coloured	4	6.7	6.7	10.0
	white	54	90.0	90.0	100.0
	Total	60	100.0	100.0	

Frequency of Stage for 3-Field and 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	b	45	75.0	75.0	75.0
	c	15	25.0	25.0	100.0
	Total	60	100.0	100.0	

Frequency of Differentiation for 3-Filed and 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	poorly	10	16.7	16.7	16.7
	poorly-moderately	3	5.0	5.0	21.7
	moderately	34	56.7	56.7	78.3
	moderatelywell	4	6.7	6.7	85.0
	well	9	15.0	15.0	100.0
	Total	60	100.0	100.0	

Table 7.0 : Frequencies of Age, Race, Stage, Differentiation, Gleason Score and Surgery/Biopsy as per Treatment Field

		field type	
		3-Field	4-Field
age	51-55	2	4
	56-60	1	1
	61-65	2	3
	66-70	6	15
	71-75	11	5
	76-80	6	1
	81-85	2	1
race	asian	1	1
	coloured	1	3
	white	28	26
stage	b	21	24
	c	9	6
differentiation	poorly	5	5
	poorly-moderately	2	1
	moderately	14	20
	moderatelywell	4	0
	well	5	4
gleason	2	4	3
	3	1	2
	4	1	2
	5	2	7
	6	11	7
	7	8	5
	8	2	2
	9	1	1
	10.00	0	1
surgery/biopsy	biopsy	14	20
	surgery	16	10

Statistics of frequencies for Age, Race, Stage, Differentiation, Gleason Score and Surgery/Biopsy for 3-Field and 4-Field Technique

		age	race	stage	differentiation	gleason	surgery/biopsy
N	Valid	60	60	60	60	60	60
	Missing	0	0	0	0	0	0
Mean		5.2000	3.8333	2.2500	2.9833	4.6667	1.4333
Std. Deviation		1.5160	.5871	.4367	1.1860	1.9543	.4997
Minimum		2.00	1.00	2.00	1.00	1.00	1.00
Maximum		8.00	4.00	3.00	5.00	10.00	2.00

Frequency for Gleason Scoring for 3-Field and 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	2	7	11.7	11.7	11.7
	3	3	5.0	5.0	16.7
	4	3	5.0	5.0	21.7
	5	9	15.0	15.0	36.7
	6	18	30.0	30.0	66.7
	7	13	21.7	21.7	88.3
	8	4	6.7	6.7	95.0
	9	2	3.3	3.3	98.3
	10.00	1	1.7	1.7	100.0
	Total	60	100.0	100.0	

Frequency for Surgery/Biopsy for 3-field and 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	biopsy	34	56.7	56.7	56.7
	surgery	26	43.3	43.3	100.0
	Total	60	100.0	100.0	

Statistics of Frequencies for Age, Race, Stage, Differentiation, Gleason Score, Surgery/Biopsy for 3-Field abd 4-Field Technique

		age	race	stage	differentiation	gleason	surgery/biopsy
N	Valid	30	30	30	30	30	30
	Missing	0	0	0	0	0	0
Mean		5.6333	3.8667	2.3000	3.0667	4.7333	1.5333
Std. Deviation		1.4967	.5713	.4661	1.2576	1.8742	.5074
Minimum		2.00	1.00	2.00	1.00	1.00	1.00
Maximum		8.00	4.00	3.00	5.00	8.00	2.00

Frequency of Age for 3-field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	51-55	2	6.7	6.7	6.7
	56-60	1	3.3	3.3	10.0
	61-65	2	6.7	6.7	16.7
	66-70	6	20.0	20.0	36.7
	71-75	11	36.7	36.7	73.3
	76-80	6	20.0	20.0	93.3
	81-85	2	6.7	6.7	100.0
	Total	30	100.0	100.0	

Frequency of Race for 3-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	asian	1	3.3	3.3	3.3
	coloured	1	3.3	3.3	6.7
	white	28	93.3	93.3	100.0
	Total	30	100.0	100.0	

Frequency of Stage for 3-field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	b	21	70.0	70.0	70.0
	c	9	30.0	30.0	100.0
	Total	30	100.0	100.0	

Frequency od differentiation for 3-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	poorly	5	16.7	16.7	16.7
	poorly-moderately	2	6.7	6.7	23.3
	moderately	14	46.7	46.7	70.0
	moderatelywell	4	13.3	13.3	83.3
	well	5	16.7	16.7	100.0
	Total	30	100.0	100.0	

Frequency of Gleason for 3-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	2	4	13.3	13.3	13.3
	3	1	3.3	3.3	16.7
	4	1	3.3	3.3	20.0
	5	2	6.7	6.7	26.7
	6	11	36.7	36.7	63.3
	7	8	26.7	26.7	90.0
	8	2	6.7	6.7	96.7
	9	1	3.3	3.3	100.0
	Total	30	100.0	100.0	

Frequency for Surgery/Biopsy for 3-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	biopsy	14	46.7	46.7	46.7
	surgery	16	53.3	53.3	100.0
	Total	30	100.0	100.0	

Statistics of Frequencies of Age, Race, Stage, Differentiation, Gleason Score and Surgery/Biopsy for 4-Field Technique

		age	race	stage	differentiation	gleason	surgery/biopsy
N	Valid	30	30	30	30	30	30
	Missing	0	0	0	0	0	0
Mean		4.7667	3.8000	2.2000	2.9000	4.6000	1.3333
Std. Deviation		1.4308	.6103	.4068	1.1250	2.0611	.4795
Minimum		2.00	1.00	2.00	1.00	1.00	1.00
Maximum		8.00	4.00	3.00	5.00	10.00	2.00

Frequency for Age for 4-field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	51-55	4	13.3	13.3	13.3
	56-60	1	3.3	3.3	16.7
	61-65	3	10.0	10.0	26.7
	66-70	15	50.0	50.0	76.7
	71-75	5	16.7	16.7	93.3
	76-80	1	3.3	3.3	96.7
	81-85	1	3.3	3.3	100.0
	Total	30	100.0	100.0	

Frequency for Race for 4- Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	asian	1	3.3	3.3	3.3
	coloured	3	10.0	10.0	13.3
	white	26	86.7	86.7	100.0
	Total	30	100.0	100.0	

Frequency for Stage for 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	b	24	80.0	80.0	80.0
	c	6	20.0	20.0	100.0
	Total	30	100.0	100.0	

Frequency for Differentiation for 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	poorly	5	16.7	16.7	16.7
	poorly-moderately	1	3.3	3.3	20.0
	moderately	20	66.7	66.7	86.7
	well	4	13.3	13.3	100.0
	Total	30	100.0	100.0	

Frequency for Gleason Score for 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	2	3	10.0	10.0	10.0
	3	2	6.7	6.7	16.7
	4	2	6.7	6.7	23.3
	5	7	23.3	23.3	46.7
	6	7	23.3	23.3	70.0
	7	5	16.7	16.7	86.7
	8	2	6.7	6.7	93.3
	9	1	3.3	3.3	96.7
	10.00	1	3.3	3.3	100.0
	Total	30	100.0	100.0	

Frequency for Surgery/Biopsy for 4-Field Technique

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	biopsy	20	66.7	66.7	66.7
	surgery	10	33.3	33.3	100.0
	Total	30	100.0	100.0	

APPENDIX K

pretreatment PSA

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.19	1	1.7	1.7	1.7
	2.00	1	1.7	1.7	3.3
	2.03	1	1.7	1.7	5.0
	2.21	1	1.7	1.7	6.7
	2.25	1	1.7	1.7	8.3
	2.45	1	1.7	1.7	10.0
	3.70	1	1.7	1.7	11.7
	4.24	1	1.7	1.7	13.3
	4.30	2	3.3	3.3	16.7
	4.56	1	1.7	1.7	18.3
	4.90	1	1.7	1.7	20.0
	5.00	1	1.7	1.7	21.7
	5.30	2	3.3	3.3	25.0
	5.50	1	1.7	1.7	26.7
	5.60	1	1.7	1.7	28.3
	6.20	1	1.7	1.7	30.0
	6.70	2	3.3	3.3	33.3
	6.80	1	1.7	1.7	35.0
	7.00	1	1.7	1.7	36.7
	7.20	1	1.7	1.7	38.3
	7.32	1	1.7	1.7	40.0
	7.39	1	1.7	1.7	41.7
	7.50	1	1.7	1.7	43.3
	7.60	1	1.7	1.7	45.0
	8.00	2	3.3	3.3	48.3
	8.30	1	1.7	1.7	50.0
	8.49	1	1.7	1.7	51.7
	8.50	1	1.7	1.7	53.3
	8.58	1	1.7	1.7	55.0
	8.70	1	1.7	1.7	56.7
	8.90	1	1.7	1.7	58.3
	9.00	2	3.3	3.3	61.7
	9.74	1	1.7	1.7	63.3
	10.00	2	3.3	3.3	66.7
	10.10	1	1.7	1.7	68.3
	10.31	1	1.7	1.7	70.0
	11.23	1	1.7	1.7	71.7
	12.00	2	3.3	3.3	75.0
	12.90	1	1.7	1.7	76.7
	13.00	1	1.7	1.7	78.3
	14.00	1	1.7	1.7	80.0
	14.70	1	1.7	1.7	81.7
	15.80	1	1.7	1.7	83.3
	16.00	1	1.7	1.7	85.0
	16.60	1	1.7	1.7	86.7
	17.00	1	1.7	1.7	88.3
	18.74	1	1.7	1.7	90.0
	18.90	1	1.7	1.7	91.7
	19.70	1	1.7	1.7	93.3
	26.00	1	1.7	1.7	95.0
	29.00	1	1.7	1.7	96.7

pretreatment PSA

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	29.70	1	1.7	1.7	98.3
	30.77	1	1.7	1.7	100.0
	Total	60	100.0	100.0	

posttreatmet PSA

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.01	3	5.0	5.0	5.0
	.02	10	16.7	16.7	21.7
	.10	11	18.3	18.3	40.0
	.15	1	1.7	1.7	41.7
	.16	1	1.7	1.7	43.3
	.20	2	3.3	3.3	46.7
	.21	1	1.7	1.7	48.3
	.36	1	1.7	1.7	50.0
	.39	1	1.7	1.7	51.7
	.44	1	1.7	1.7	53.3
	.51	1	1.7	1.7	55.0
	.55	2	3.3	3.3	58.3
	.58	1	1.7	1.7	60.0
	.76	1	1.7	1.7	61.7
	.98	1	1.7	1.7	63.3
	1.00	1	1.7	1.7	65.0
	1.29	1	1.7	1.7	66.7
	1.36	1	1.7	1.7	68.3
	1.41	1	1.7	1.7	70.0
	1.50	2	3.3	3.3	73.3
	1.57	1	1.7	1.7	75.0
	1.78	1	1.7	1.7	76.7
	1.81	2	3.3	3.3	80.0
	1.97	1	1.7	1.7	81.7
	2.00	1	1.7	1.7	83.3
	2.34	1	1.7	1.7	85.0
	2.79	1	1.7	1.7	86.7
	3.13	1	1.7	1.7	88.3
	3.18	1	1.7	1.7	90.0
	3.25	1	1.7	1.7	91.7
	3.79	1	1.7	1.7	93.3
	7.50	1	1.7	1.7	95.0
	12.21	1	1.7	1.7	96.7
	14.00	1	1.7	1.7	98.3
	15.57	1	1.7	1.7	100.0
	Total	60	100.0	100.0	

Case Summaries[a]

	Case Number	pretreatment PSA	posttreatment PSA
1	1	18.90	.21
2	2	6.20	.10
3	3	2.25	1.36
4	4	5.30	.16
5	5	.19	.39
6	6	12.00	.02
7	7	4.90	1.50
8	8	14.00	.10
9	9	7.60	2.00
10	10	18.74	1.41
11	11	5.50	.02
12	12	3.70	3.79
13	13	4.24	.02
14	14	5.00	.02
15	15	9.00	12.21
16	16	5.60	1.78
17	17	17.00	7.50
18	18	8.58	3.25
19	19	12.00	3.13
20	20	10.00	1.29
21	21	7.39	.02
22	22	4.56	2.79
23	23	8.30	.02
24	24	29.00	.51
25	25	4.30	.02
26	26	8.50	.15
27	27	13.00	15.57
28	28	6.70	.01
29	29	19.70	.01
30	30	2.45	.20
31	31	9.00	1.57
32	32	7.50	.55
33	33	26.00	.10
34	34	2.00	.10
35	35	2.03	.10
36	36	8.90	.10
37	37	16.60	.10
38	38	7.00	2.34
39	39	8.49	1.97
40	40	10.10	3.18
41	41	8.00	.76
42	42	8.00	.10
43	43	5.30	1.81
44	44	7.32	.58
45	45	6.80	1.50
46	46	2.21	.36
47	47	10.31	.98
48	48	12.90	.10
49	49	11.23	14.00
50	50	4.30	.02
51	51	15.80	.55

Case Summaries[a]

	Case Number	pretreatment PSA	posttreatmet PSA
52	52	8.70	.44
53	53	10.00	.10
54	54	6.70	1.81
55	55	16.00	1.00
56	56	7.20	.20
57	57	29.70	.02
58	58	9.74	.01
59	59	30.77	.10
60	60	14.70	.02
Total N		60	60

a. Limited to first 100 cases.

APPENDIX L

% bladder receiving more than 50 gy - 4-field

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0-20%	7	23.3	23.3	23.3
	21-40%	14	46.7	46.7	70.0
	41-60%	6	20.0	20.0	90.0
	61-80%	2	6.7	6.7	96.7
	above 80%	1	3.3	3.3	100.0
	Total	30	100.0	100.0	

% rectum receiving more 50 - 4-field

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0-20%	2	6.7	6.7	6.7
	21-40%	9	30.0	30.0	36.7
	41-60%	10	33.3	33.3	70.0
	61-80%	7	23.3	23.3	93.3
	above 80%	2	6.7	6.7	100.0
	Total	30	100.0	100.0	

% bladder receiving more than 50 gy - 3-field

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0-20%	14	46.7	46.7	46.7
	21-40%	9	30.0	30.0	76.7
	41-60%	6	20.0	20.0	96.7
	61-80%	1	3.3	3.3	100.0
	Total	30	100.0	100.0	

% rectum receiving more 50 - 3-field

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0-20%	4	13.3	13.3	13.3
	21-40%	15	50.0	50.0	63.3
	41-60%	7	23.3	23.3	86.7
	61-80%	4	13.3	13.3	100.0
	Total	30	100.0	100.0	

APPENDIX M

TECHNIKON NATAL

Department of Mathematics & Statistics

Office of the Research Statistician

Assessment of Statistical Methods

Name of Student..Mrs. Loganee Moodley..**Student Number**....9350527.....

Department..Radiography.....**Faculty**....Health.....**Proposed Degree**..M Tech

Title of Thesis....Comparative Analysis of the 3-field technique

Versus 4-field technique in patients with stage B or C

prostate cancer.

Remarks:

1, Sample Size.....Large sample (n=60).....

2.Data Collection Technique.....Random sampling technique.....

3. Consistency between G186 and Methods used.....yes.....

4. Justifications for Methods/Test procedures applied.....Justified.....

5 Data Analysis.....SPSS.....

6. Accuracy of work.....accurate.....

7. Explanation of Decision Rules.....well done.....

8. Conclusions.....well concluded.....

9. References.....-.....

Recommendation:

Thesis recommended / ~~not recommended~~ for Examination

Signature.....Date....14 March 2001.

Name of Statistician....Kavanal Thomas