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Rectal dose sparing and prostate immobilization using a rectal balloon in the treatment of prostate cancer with dose escalation conformal radiation therapy

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RECTAL DOSE SPARING AND PROSTATE IMMOBILIZATION USING A RECTAL BALLOON IN THE TREATMENT OF PROSTATE CANCER WITH DOSE ESCALATION CONFORMAL RADIATION THERAPY

A research report submitted to the faculty of Health Sciences, University of the Witwatersrand, in partial fulfillment of the requirements for the Degree of Master of Medicine in the branch of Radiation Oncology

BY

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June, 2008

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DECLARATION

I, Kanyike Daniel Mukasa declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in Radiation Oncology; University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

Signed……...

……..Day of…….2008

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TO

My wife Naggujja Margret Kanyike for her support throughout this period when I have been away from the family.

My children, Vvubya William, Kyabasinga Julius, Ssenje Joel and my sister in law, Nabakembo Regina for being so understanding during this period when we have been separated for a cause.

My mother Nalwoga Nawume Mukasa, She made me what I am now.

In memory of my father,

MUKASA SIMON SEMWOGERE

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PRESENTATIONS

Oral presentation of the study at

South African Society of Clinical and Radiation Oncology (SASCRO)

South African Society of Medical Oncology (SASMO)

13th National Congress 2007

27th to 30th April 2007

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ABSTRACT

Objective

The use of conformal radiation therapy in the treatment of carcinoma of the prostate has allowed for dose escalation and improved local control. The dose to the rectum is an important consideration in determining complication rates. This study aims to evaluate the effect of a Foleys rectal catheter balloon on the dose volume histograms to the rectum and to assess the effect of the balloon catheter on prostate gland immobilization during treatment of intermediate risk cancer of the prostate.

Design and methods

Ten patients with intermediate risk prostate cancer, each acting as his own control, were recruited in the study; eight patients had complete data for analysis. CT scans were done at intervals during treatment, with and without a rectal balloon filled with 30 ml of contrast. 3 pairs of CT scans for each patient were performed and were available for analysis. All patients were treated with 6-field conformal radiotherapy up to 66 Gy followed by a boost of 12 Gy in 3 fractions to the prostate using a rectal balloon and a 3-field plan. Dose volume histograms were calculated for the boost plan with and without the rectal balloon. Movements of the prostate in the superior-inferior and the anterior-posterior directions were measured with and without the balloon for each treatment.

Results

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There was a slight reduction in the dose received by 1% and 2 % of the rectal volume with the balloon (55% and 52% respectively), compared to without a balloon (57% and 54.3% respectively) ($p > 0.05$). There was a non significant increase in the dose received by 50% of the rectum ($p>0.05$) with the use of the rectal balloon due to the rectum being pushed towards the symphysis pubis by the balloon.

With the use of rectal balloon, the superior / inferior displacement of the prostate was reduced ($p=0.04$) and a displacement of more than 5 mm was observed in one out of eight patients. The anterior / posterior displacement of the prostate was decreased with the rectal balloon with a mean of 4 mm compared to 5 mm with no rectal balloon. This was not statistically significantly ($p>0.05$). However, displacement of more than 5 mm was observed in 2 patients with the rectal balloon. No grade 3 acute rectal toxicity was recorded in the 8 patients.

Conclusion

There was no significant change in the percentage dose received by the rectum with the use of the rectal balloon in this study. The study showed however that the rectal balloon significantly reduced prostate movement during treatment.

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LIST OF ABBREVIATIONS

A/P	Anterior Posterior
ASIS	Anterior Superior Iliac Spine
bNED	biochemical No Evidence of Disease
CTV	Clinical Target Volume
DFS	Disease Free Survival
DVH	Dose Volume Histograms
EBRT	External Beam Radiation Therapy
ECOG	Eastern Co-operative Oncology Group
GTV	Gross Tumour Volume
HDR	High Dose Rate
ICRU	International Commission of Radiation Units
IMRT	Intensity Modulated Radiation Therapy
MLC	Multi- Leaf Collimator
OAR	Organ at Risk
PSA	Prostate Specific Antigen
RTOG	Radiation Therapy and Oncology Group
S/I	Superior Inferior
USA	United States of America

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INTRODUCTION

1.1 Background

Prostate cancer is second to lung cancer as a cause of male cancer mortality. The incidence of the disease escalates with age with a median age at diagnosis of 68 years. The lifetime risk for prostate cancer in American men is one in six (1). In South Africa, a total of 2802 and 3715 new cases were reported in 1996 and 1997, respectively. These comprised on average 12% of all male cancer cases per year. The lifetime risk of developing cancer of the prostate in all men in South Africa was 1: 24 in 1997 (2). It is therefore one of the common causes of morbidity and mortality in men in South Africa.

With the introduction of Prostate Specific Antigen (PSA) as a screening tool for this disease in United States of America (USA), the number of patients diagnosed with prostate cancer increased, especially in the organ confined disease.

The incidence of microscopic extension beyond the capsule of the prostate gland in patients with organ confined disease ranges between 8 and 57% (1) and several alogarisms, normogrms and risk group classification schemes that are currently relevant to radiotherapy treatment of localised prostate cancer are in use (3). Nomograms that predict the probability of pathological end points have been described in literature. Partin et al. (4) developed such nomograms which are widely recognised and used to predict the extent of disease in localised prostate cancer. The tables have been since revised by

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Partin (5) as shown in appendix A. Roach et al. (6) developed 3 relatively simple formulae shown below to estimate the probability of lymph node (LN), extra capsular extension (ECE) and seminal vesicle (SV) involvement based on Partin's original nomograms.

1. ECE = (3/2) x PSA + [(GS- 3) x 10]
2. +SV = (3/3) x PSA + [(GS-6) x 10]
3. +LN = (2/3) x PSA + [(GS-6) x 10]

These have been shown to predict biochemical failure in patients under going external beam radiotherapy (7).

1.1.1 Prognosis

The most important predictors of the extent of disease in localised prostate cancer are the pre-treatment PSA, primary tumour stage and pathological tumour differentiation. The other important predictor of survival are the presence of perineural invasion and number of positive biopsies (8 9 10). The TNM staging (appendix B) fails to include all of these prognostic features and the current practice in treatment centres is to stratify the patients into risk groups using known prognostic features.

In the commonly used stratification systems, which were first used by investigators from Harvard and Memorial Sloan Kettering Cancer Center (MSKCC) (11, 12), patients are stratified into low, intermediate and high risk groups (Table 1).

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Table 1. Prostate Cancer Risk Groups

	Low risk group	Intermediate risk group	High risk group
Gleason score	2-6	7	8-10
T stage	T1c-T2a	T2b	Or T2c/T3
Pre-treat. PSA	<10 ng/l	10-20 ng/l	>20 ng/l

KEY - Pre-treat. PSA =Pre-treatment Prostate Specific Antigen

1.1.2 Treatment options

The optimal treatment of localised prostate cancer remains controversial. The natural history of the tumour is influenced by multiple prognostic factors and various treatment options that affect the quality of life of the patient.

Presently, for patients with low risk disease having similar prognostic features, there are no differences in biochemical or disease free survival (DFS) outcome when treated with radical prostatectomy (RP), high dose external beam radiotherapy (EBRT), brachytherapy (1).

For patients in the intermediate risk group and selected high risk patients, high dose EBRT has shown a gain in the 5-year no biochemical evidence of disease (bNED). External Beam Radiation Therapy (EBRT) plus brachytherapy with a permanent implant

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or High Dose Rate (HDR) brachytherapy as a boost can be used and for highly selected cases, RP may be an option.

For patients with involvement of the capsule or a Gleason Score of 8 or higher, a treatment option is high dose EBRT, with or without hormonal therapy. For patients with T4, positive lymph nodes or metastatic disease, hormonal therapy for an indefinite period is the standard. For hormonal refractory disease, chemotherapy with Taxols, Carboplatin or Mitoxanthrone is an option (1).

1.2 Treatment technique

1.2.1 Radical prostatectomy

This involves the removal of the prostate, seminal vesicles, ampullae, vas deferens and bilateral lymph node dissection. With modern surgical techniques, sexual function is preserved in 73% of patients but this is correlated with age.

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1.2.2 Radiation therapy

1.2.2.1 Conventional EBRT

This is usually limited to 6 x 6 cm or 8 x 8 cm fields around the prostate commonly using a 4-field box technique for T1/T2 disease with favourable features (1). However if the seminal vesicles or the lymph nodes are involved, then the whole pelvis is treated up to 45 Gy and this is followed with a boost to 70 Gy to the prostate. These old techniques not only used low dose but were also using small boost fields and routinely using bony land marks for the treatment borders, these problems have been over come by the 3-DCRT and more of recent the use of IMRT.

1.2.2.2 3-Dimensional Conformal Radiation Therapy (3DCRT)

This method allows delivery of higher doses of radiation to target volume while sparing surrounding normal tissues and is based on CT scanning, which images the prostate and other structures in the pelvis and generates high resolution 3-Dimensional reconstructions of the patient's anatomy. The volumetric data is used for treatment planning after the physician has outlined the Gross Tumour Volume (GTV) and the critical structures. Multi-Leaf Collimators (MLC) or blocks are used to shape the beams. The Dose Volume Histograms (DVHs) generated are used to check the dose to the tumour and critical structures. Using the critical volume tolerance method during the 3-DCRT, there is 30% reduction in dose received by 50% of the rectum, making it possible to increase minimum

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tumour dose of greater than or equal to 10% (13).With the advance in technology, the more sophisticated type of 3-DCRT called IMRT is applied in order to extend the principle of more dose to tumour while sparing the normal tissues (14).

1.2.2.3 Brachytherapy

The accuracy of this technique has improved with the use of CT and ultrasound-guided implant techniques. This treatment can be used as monotherapy in patients with T1/T2a disease, a Gleason score of 2 to 6 and a PSA <10 ng/ml, or as a boost to EBRT in T2b/T2c disease. It is not recommended for patients with a Gleason score of 7 to 10 or PSA > 10 ng/ml. The implants can be permanent or temporary, using high or low dose rates. It offers potential biological advantages over External Beam Radiotherapy but data on clinical relevance is still scarce (14).

1.3 Local control with different treatment approaches

1.3.1 Radical prostatectomy

At Johns Hopkins Hospital, Han et al. (15) reported the long term PSA relapse free survival and cancer specific survival after radical prostatectomy. For 2404 patients with a mean follow up of 6.3 years, the PSA free survival was 84%, 74%, 64% at 5, 10, 15 years, respectively. The biochemical recurrence rate was 17% and the 15-year survival

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was 66%. The biochemical recurrence rate was influenced by the clinical stage, Gleason score and the pre-treatment PSA.

The improvement in surgical results is probably due to the improvement in patient selection and the addition of postoperative radiotherapy (16).

1.3.2 EBRT

From studies before the PSA era and also during the PSA relapse free survival period, it became clear that conventional doses of EBRT do not have the capacity to control the disease and eradicate the cancer.

A study at MD Anderson by Zagar KZ et al. (17) demonstrated that even among patients with PSA<10 ng/ml, there was continuous decline in the PSA relapse free survival.

The outcome of patients with T3 stage disease treated at American College of Radiology showed 7-year local recurrence rates of 36% for 60 to 65 Gy, 32% for 65 to70 Gy and 24% for more than 70 Gy. This provided evidence that the total dose required to control prostate cancer exceeded 70 Gy (1). However efforts to give more than 70 Gy using conventional methods resulted in unacceptable complications.

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1.3.3 Brachytherapy

Local control of prostate cancer depends on the pre-treatment PSA, Gleason score, clinical stage and the radiation dose given. For patients with a pre-treatment PSA of <10 ng/ml, brachytherapy alone has produced good results comparable to RP (1).

1.3.4 EBRT with dose escalation

Both retrospective and prospective studies have demonstrated improved PSA relapse free survival with dose escalation which is possible with the use of 3-DCRT (18, 19). Single institution trials have confirmed an advantage of high dose escalation in management of localised prostate cancer (1).

This has been confirmed in the recent update of a phase III randomised trial from M D. Anderson by Pollack et al. (20) They studied 301 patients with organ confined tumours who were randomised to receive a total of 70 Gy by conventional EBRT or conventional EBRT followed by a boost using a 3-dimensional conformal radiotherapy (3DCRT) boost to total dose of 78 Gy. The freedom from clinical or biochemical failure was 64% and 70% respectively with a p-value of 0.03. For patients with PSA < 10 ng/ml, there was no advantage for the higher dose.

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Hanks et al. (21) performed a study at the Fox Chase Cancer Center with the purpose of defining the appropriate dose for individual patients with 3DCRT. Patients were divided into 3 groups by PSA <10 ng/ml, 10-19.9 ng/ml and ≥ 20 ng/ml. They were further subdivided into 6 subgroups by the presence of either favourable or unfavourable characteristics. The favourable characteristics were Tumour stage (T) 1 and 2a, Gleason Score (G/S) < 6 and no perineural invasion. The unfavourable characteristics were Tumour stage (T) 2b and 3, Gleason Score 7-10 and perineural invasion.

The five year bNED rate was estimated using the dose response function and 73 Gy was compared with 78 Gy. Patients with PSA<10 ng/ml and favourable features, as well as those with PSA ≥20 ng/ml with unfavourable features had no dose response with dose escalation, whereas the intermediate risk patient groups had a dose response ranging from 15 % to 43%.

1.4 Sequelae of treatment

1.4.1 Radical prostatectomy

Side effects vary with the surgeon and whether a unilateral or bilateral nerve-sparing surgery technique is used. The acute side effects are pain, transient incontinence, 5 to 50% blood loss of 300-4000 mls and a mortality of 1 to 2%. The incontinence recovery depends on the age. Similarly, the incidence of impotence varies with age especially in patients younger than 70 years (22).

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1.4.2 EBRT

Conventional radiotherapy doses are well tolerated and acute reactions usually occur in the 3rd week of treatment and resolve within a few weeks after treatment. Late complications are rare. The rate of complications increases as the dose exceeds 70 Gy and the dose limiting factor is rectal toxicity. Stoley et al. (23) studied the rectal toxicity of patients treated at the MD Anderson Hospital. The 5-year actuarial risk for late grade 2 rectal toxicity was 14% for 70 Gy and 21% for 78 Gy. Analysis of the DVHs of the rectum for patients treated to 78 Gy showed that there was a correlation between the percentage of rectum treated to more than 70 Gy and the likelihood of rectal toxicity.

Dearnley DP et al. (24) compared radiation side effects with conformal versus conventional radiation therapy for prostate cancer in a randomised trial. 223 patients were treated up to 64 Gy at 2 Gy per fraction. The primary end point was development of late complications measured using the Radiation Therapy and Oncology Group (RTOG) toxicity criteria (25). Fewer men developed proctitis in the conformal group than in the conventional group (37 vs. 56% respectively, with grade I $p = 0.004$ and Grade II $p = 0.01$). There was no difference in the bladder toxicity. This study demonstrated that there was a reduction in rectal toxicity with 3DCRT.

Intensity modulated radiation therapy (IMRT) has further reduced the incidence of both acute and late toxicity compared to 3DCRT (26). The 3-year actuarial incidence rates of grade 2 rectal toxicity in patients treated with 81 Gy was 2% using IMRT compared to

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14% in 3DCRT with p=0.005. DVHs have been shown to predict rectal toxicity and it is recommended that not more than 25% of the whole rectal volume should get more than 72 Gy (27). In these studies, rectal toxicity was graded using the RTOG toxicity criteria (Table 4).

1.5 Immobilisation

Large day- to- day setup errors greater than 0.5 cm can be significantly reduced by use of patient immobilisation devices and such several devices have been used (28).Although this reduces the risk of large errors, the potential for organ movement limits the use of very tight margins and Several studies have demonstrated that the prostate moves during treatment (29, 30, 31, 32). Therefore, immobilisation when using 3DCRT or IMRT includes patient immobilisation and in some instances, target organ immobilisation as well. In order to minimize the dose to an organ at risk with dose escalation and ensure coverage of the clinical target volume during treatment delivery when using 3DCRT and IMRT, the movement of the target must also be minimised.

Several methods have been described to overcome the problem by using ultrasound system or implanted prostate markers (33, 34, 35, 36). The most recent, highly technical method described by Wong JR et al. (37) used a CT-linear accelerator combination together in the treatment room sharing the same patient support system. Daily intrinsic prostate movement could be corrected before each therapy session.

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Several studies have demonstrated that a rectal balloon can be used to spare the dose to the rectum and also immobilize the prostate (38, 39). Wachter et al. (34) described a simple method of using a rectal balloon to immobilise the prostate and also reduce rectal variations during treatment.10 patients with localised disease were treated with 3DCRT. CT scans, with or without a rectal balloon, were taken at 3 different intervals during treatment. The maximum anterior/posterior displacement and rectal filling variations during treatment were significantly reduced with p-values of 0.008 and 0.04, respectively.

1.6 ICRU recommendations

In all above methods, the ICRU recommendation must be followed when contouring the target organ and the normal tissues. The International Commission of Radiation Units (ICRU) reports numbers 50 (40) and 62 (41) clearly define the volumes considered for the treatment of patients with malignant disease. GTV and CTV represent the volumes of known or suspected disease and organ at risk volumes (OARV`s) represent the normal tissues at risk.

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1.7 Hypothesis

In the intermediate risk group of prostatic cancer patients treated at Johannesburg Hospital, improved prostate immobilization and rectal dose sparing can be achieved using a Foleys rectal balloon catheter.

1.8 Study Objectives

Primary

1. To study the influence of the rectal balloon on prostate motion in patients treated with 3-dimensional conformal radiation therapy with dose escalation at Johannesburg Hospital

2. The effect of the rectal balloon on the dose volume histograms of the whole rectum during treatment with 3-dimensional conformal radiation therapy with dose escalation at Johannesburg Hospital.

Secondary

1. Investigation of acute rectal complications when using the rectal balloon with dose escalation.

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2.0 MATERIALS AND METHODS

2.1 Ethics

The study was approved by the Post Graduate Committee (appendix D)

And by the Ethics Committee of the University of the Witwatersrand for research on human subjects prior to commencing data collection (appendix C).

Written consent was obtained from the patients before enrolling them in the trial and the information leaflet and informed consent template for the University of the Witwatersrand was used.

2.2 Study population

This was a prospective study of adult male patients referred to radiation oncology department with histologically proven cancer of the prostate between January 2005 and December 2006. Patients were stratified according to Fox Chase prognostic index (table 2) and 10 patients in the intermediate group with Eastern Co-operative Oncology Group (ECOG) (42) status 0-2 (table 3) were recruited. Each patient acted as his own control in this study.

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Inclusion Criteria

Histologically proven prostate cancer patients with ECOG performance Score of 1 to 2 and intermediate risk group according to Fox Chase prognostic index were recruited.

Exclusion criteria

Patients with the history of previous pelvic irradiation, medical contraindications to radiation therapy or the inability to consent for the trial, were excluded from the trial

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Table 2. Fox Chase prognostic index for cancer of prostate. Hanks et al (21)

Risk group	Feature
Low	PSA<10 ng/ml + F F
Intermediate	**PSA<10 ng/ml + UF** **Or PSA 10-20 ng/ml + UF or FF** **Or PSA >20 ng/ml + FF**
High	PSA>20 ng/ml + UF

UF refers to: stage T2b or T3 Gleason score 7-10 pn +ve

FF refers to: Stage T1/T2a G/Score 2-6 Pn -ve

KEY:

PSA= prostate specific antigen

FF =Favorable features

UF= Unfavorable features

Pn= Perineural invasion

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Table 3. ECOG performance score. Skeel (42)

Score	ECOG performance status
0	Normal activity, asymptomatic
1	Symptomatic, but fully ambulant
2	Symptomatic, in bed less than 50% of daytime
3	Symptomatic, in bed more than 50% of daytime
4	Bedridden, almost 100% of day time in bed

Table 4. RTOG acute toxicity score of the rectum. Cox JD et al (25)

Score	Toxicity
0	Normal
1	Proctitis
2	Diarrhoea
3	Painless rectal bleeding
4	Ulceration

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3.0. METHODS

3.1 Patient preparation for radiotherapy

To achieve reproducible positioning during treatment and CT scanning, every patient had a personalized cast. The patient was immobilized in a polyurethane cast moulded from the waist to the feet. The patients were positioned supine with their knees slightly flexed and feet together.

3.2. Simulation

A reference simulation was performed for all further positioning and the patient was permanently tattooed to record the reference position. CT scans in the treatment position were then performed.

3.3. CT-scan imaging

Each patient had 6 CT scans during their treatment management. All CT scans (somatom DR3^{TM}) were done in the immobilized treatment position. Sequential scanning was used for all cases.

No rectal preparation was done for the first scan. After 10 Gy of the EBRT, two scan series were performed following overnight rectal preparation with a rectal suppository to

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empty the rectum. One scan was performed with the balloon in the rectum and the other with no rectal balloon. The scan with the rectal balloon was used to plan the 3-field boost treatment.

Similarly, the 2 scans series were repeated at the start of the booster treatment usually at 20 Gy of the large field treatment. The 6th scan was done on the day of the 2nd booster treatment, usually at 40 Gy of the large field treatment, with no rectal balloon.

Scanning of all the 6 image sets was done from the level of the anterior superior iliac spine (ASIS) to the lower border of the sacro-iliac joint in 1 cm slices, then inferiorly to 1 cm below the lower border of ischial-tuberosity using 0.5 cm slices. All scans were electronically transferred to Helax TMS^{TM} planning system for 3-dimensional treatment planning. Software Version 5. 1.1 was used for all cases.

The characteristics of each CT scan performed are shown in table 5 below.

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Table 5. Showing CT-scan characteristics for each patient

CT-scan number	Time of scan	Rectal preparation	30 cc rectal balloon used
1	Initiation of treatment planning	no	no
2	10Gy of EBRT treatment	Yes	Yes
3		Yes	No
4	1st booster treatment	Yes	Yes
5		Yes	No
6	2nd booster treatment	Yes	No

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3.4. Rectal balloon

A two-way Foleys catheter gauge 15 was used as the rectal balloon to immobilize the prostate. The patient was instructed to lie on the lateral side; the Foleys catheter was lubricated with K-Y jelly and gently introduced into the patient's rectum. 30 cc of contrast was introduced into the balloon of the catheter using a 50 cc plastic syringe. The catheter was pulled down till resistance was felt and then strapped to the patient's thigh using plaster. The patient was again positioned in the treatment position. The balloon was confirmed to be in the correct position on the CT topogram. At least 2/3 of the diameter of the balloon was required to be behind the symphysis pubis.

The position of the anal verge was marked on the catheter for future positioning of the same catheter in the rectum during treatment. After the procedure, the balloon was deflated and removed, cleaned with water and stored for all subsequent procedures for the same patient.

3.5. Organ contouring

The contours for the prostate and the organ at risk volumes were outlined by the investigator. These organs included the prostate, seminal vesicles, bladder, rectum and the femoral heads. All volumes in all cases were checked and approved by a supervisor (an experienced radiation oncologist) before treatment planning.

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For the first and last CT Scans, the GTV included the prostate and seminal vesicles. Only the prostate was outlined for the other scans. The OAR volumes were the same for all the CT scans. The external contour of the rectum was delineated from the lower border of the sacro-iliac joint to the anal–rectal junction. This was considered the total rectal volume in all cases and Dose volume histograms were generated for all the volumes.

3.6. Planning and treatment

Plans were generated for all the patient scans. A 6-field conformal technique was used for the initial treatment planning of each patient. A 3-dimensional internal margin of 1.5 cm was automatically added to the GTV, except posteriorly where a 0.8 cm margin was used. Six conformal fields with apertures shaped to fit the Beams Eyes View of each port as defined by the internal margin, were used in the initial planning. A total of 66 Gy was prescribed to the mean dose of the internal volume, based on the DVH.

The initial treatment plan was delivered according to the distribution obtained from the first CT scan. This was copied in its entirety onto the last CT scan using the same reference point. These two plans were then compared to note the effect of rectal preparation on the rectal volume.

For all the other CT scans, 3-field plans for the boost treatment were generated using 2 lateral opposing fields and 1 anterior field. In these plans, the GTV was the prostate only and no internal margin was added. In order to obtain a non-divergent beam posteriorly, an

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independent jaw was used. A total of 12 Gy was prescribed for these plans to the 100% isodose line at 4 Gy per fraction. No beam shaping devices were used in these plans. DVHs for the organs at risk were also generated for these plans. A dose constraint of 72 Gy to not more than 25% volume of the rectum was used for the rectal OAR volume. The CT scan obtained with the rectal balloon was used for the treatment of the boost.

Patients were treated daily from Monday to Friday at 2 Gy per fraction, one fraction per day to 66 Gy with a 6-field conformal plan. A concomitant boost of 4 Gy given weekly to 12 Gy was given after 20 Gy. The boost was given with the rectal balloon inserted using the same procedure as described for the CT scanning. All boosters were given after rectal preparation the previous day. Portal films to establish the isocentre placement were done at each boost fraction and were approved by the same radiation oncologist before treatment was delivered. Patients were reviewed weekly and as requested.

3.7. Data collection

The data was collected between January 2005 and December 2006 and for consistency, the CT scans were stored and analyzed at the end of the study. For the DVHs, data sheets were used to record the percentage of the prescribed dose received by percentage rectal volume. The results from the plans with the rectal balloon were compared to those with no rectal balloon. For the first and last CT scans, the effect of the preparation schedule on the volume of rectum was compared. For prostate movement, the first scan series was used as the standard to which the second series was compared to measure changes in the

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prostate position. The beams eye views of the boost plan were transferred to the rest of the image series using the anatomical landmarks in both the AP and lateral views. The position of the posterior and inferior border of the prostate in relation to the ICRU reference point was recorded in millimeters and compared to the similar borders on the reference scans to get the displacement in millimeters. Rectal toxicity scores were recorded on a weekly basis during treatment.

3.8. Data analysis

Statistical Package for Social Sciences and the Mann Whitney U test was used to compare the DVHs of the whole rectum with and without a rectal balloon. The proportions of patients with rectal movement above and below 5 mm were compared using the chi-square test.

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Descriptive statistics were used to describe the incidence of acute rectal complications (Table 4).

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4.0. RESULTS

Two patients had incomplete data at the end of trial due to technical problems. Eight patients were available for analyses. The mean age of the patients was 65 years, ranging from 52 years to 73 years of age. All had ECOG performance scores of 1 or 2 at the beginning of the study.

Table 6. The Effect of Rectal Preparation on the Prostate Volume, Rectal Volume, and the Prescribed Dose to the Prostate

	Keys to scans	Mean ranks	P value
Percentage of prescribed dose received by 90% of the prostate.	No preparation With preparation	8.69 8.31	NS
Prostate volume	No preparation With preparation	10.19 6.81	NS
Mean dose to prostate	No preparation With preparation	9.38 7.63	NS
Total volume of the rectum	No preparation With preparation	11.19 5.81	**0.024**

KEY

No Preparation: no preparation of the rectum (scan 1)

With Preparation: With preparation of the rectum (scan 6)

NS: Non significant

p value based on Mann Whitney test

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Table 7. The effect of the rectal balloon on the total volume of the rectum, mean dose to the prostate, prostate volume and percentage dose received by 90% of the prostate volume

	Keys to scans	Total Number of scans	Mean ranks	p value
% dose received by 90% of the prostate.	Rectal Balloon No Balloon	16 16	20.09 12.91	**0.030**
Prostate volume	Rectal Balloon No Balloon	16 16	15.56 17.44	NS
Mean dose to prostate	Rectal Balloon No Balloon	16 16	19.06 13.06	**0.038**
Total volume of the rectum	Rectal Balloon No Balloon	16 16	22.38 10.63	**<0.005**

KEY

Rectal Balloon: With use of rectal balloon (scan 2 and 4)

No Balloon: No rectal balloon used (scan 3 and 5)

p value based on Mann Whitney test

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4.1 Prostate volume

The prostate volumes varied in the eight patients with a median of 34 cc and maximum of 79 cc Table 8.

Table 8. Prostate volume in the 8 patients as derived from the 32 CT scans

Number of CT scans	Maximum prostate volume	Minimum prostate volume	Median	Mean
32	79 cc	18 cc	34 cc	40.31

For prostate volumes, the CT-scan 1and 6 were not considered because during planning, the 1.5 cm margin was automatically added to the prostate by the treatment planning computer and this was the volume which was used on the 2 scans.

4.2 Rectum Volume

The rectal volumes were measured using the external contour in all the CT scans. Rectal preparation (table 6), significantly reduced the volume of the rectum, p=0.024 (2-tailed) using Mann Whitney test. The insertion of the rectal balloon (Table 7) also lead to a significant increase in the total rectal volume p <0.05 (Mann Whitney test) but this increase was probably due to the 30 cc of contrast in balloon. Figure 1and 2 shows axial scans through the iso-centre with and without a rectal balloon in patient 8.

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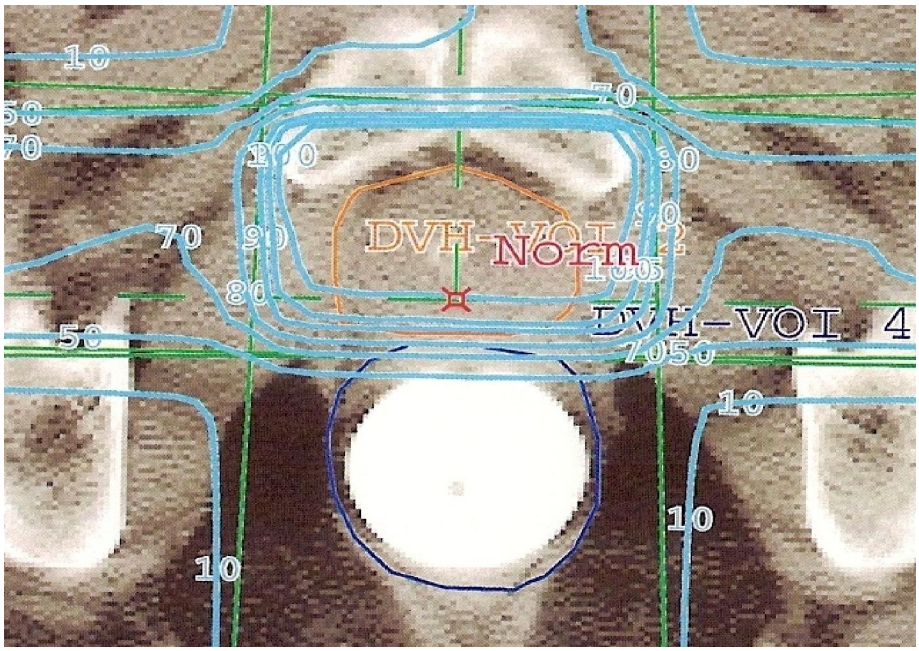

Fig. 1 With a rectal balloon

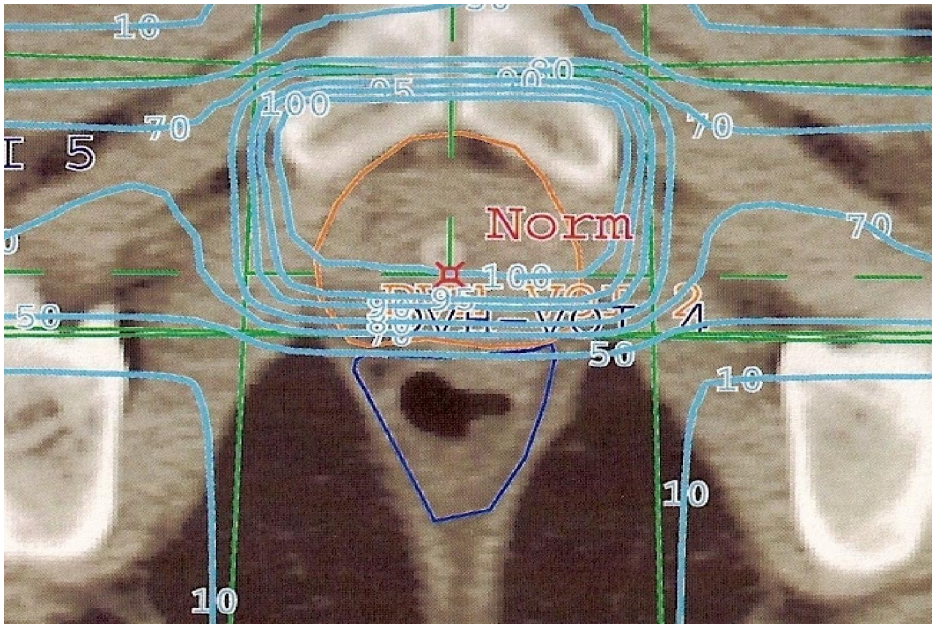

Fig. 2 Without rectal balloon

Figure 1 and 2. Axial reference CT scans at the centre of prostate for patient number 8 with and without a rectal balloon in relation to the prostate

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4.2.1 Effect of rectal balloon on DVHs of the rectum

In this study, the doses received by 1% and 2% of the volume of the rectum were slightly reduced by the use of the rectal balloon (p=>0.05). The dose received by 50% of the volume of the rectum was increased with the use of a rectal balloon (p=>0.05). There was no statistically significant difference in the DVH of the whole rectum with the use of a 30 cc rectal balloon as shown in Table 9. Figures 3 and 4 show the DVHs for a patient with a rectal balloon and without the rectal balloon.

Table 9. The effect of the rectal balloon on mean percentage dose received by the percentage volume of the whole rectum for the 8 patients

%rectal volume	1	2	20	25	30	40	50	60	70
% dose with balloon	55	52.88	37.13	33	31.38	33.88	46.36	27.94	20.38
% dose with no balloon	57.125	54.38	33.81	32.82	31.32	32.82	29.88	24.63	17.88
p value (2-tailed)	0.720	0.36	0.39	0.99	0.73	0.72	0.09	0.10	0.21

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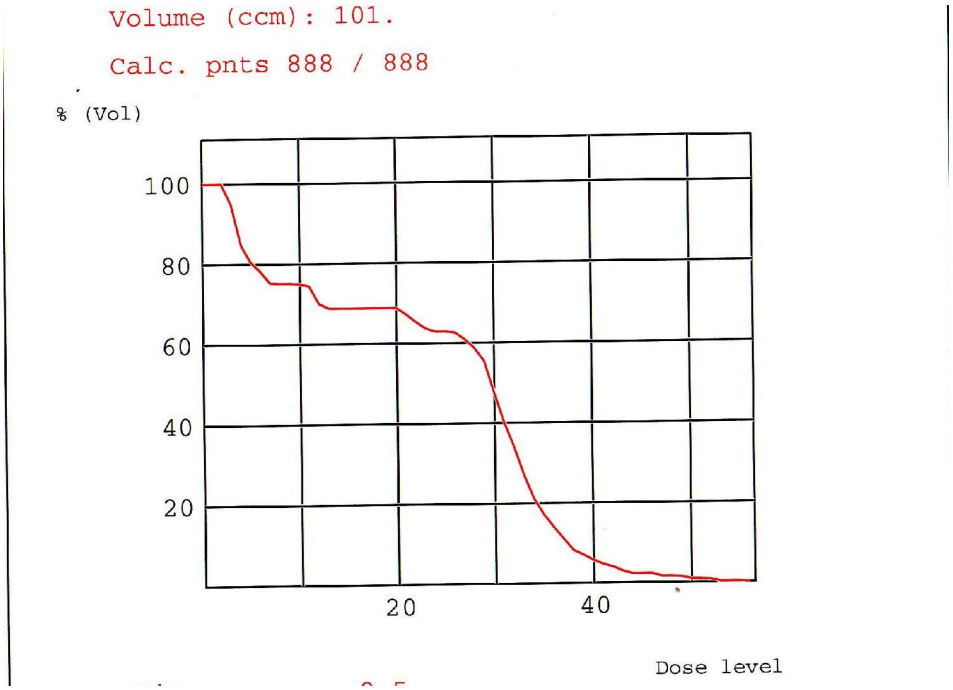

Fig. 3 DVH with a balloon

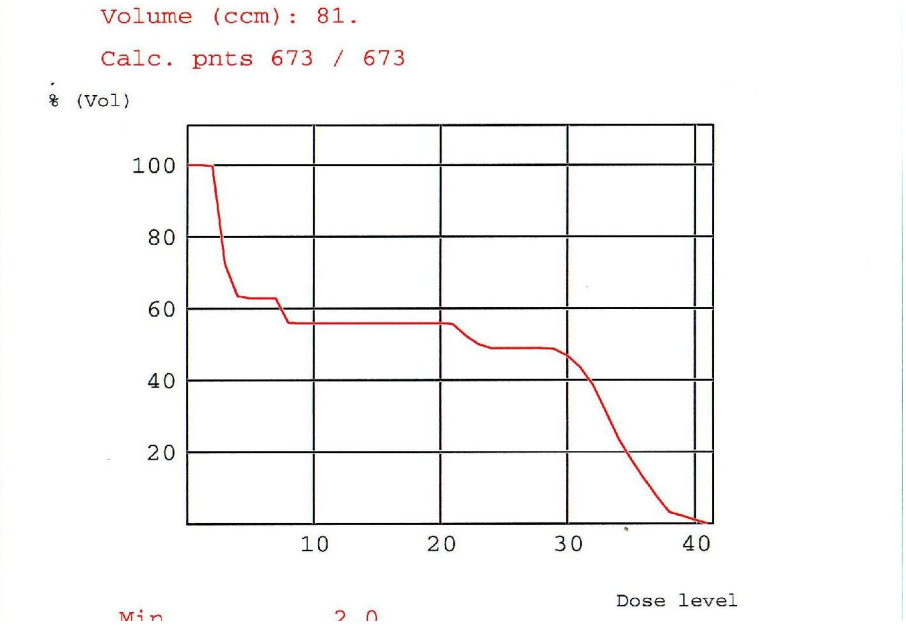

Fig. 4 DVH without a balloon

Fig 3 and 4. The DVHs of the rectum for a patient with and without a rectal balloon in position.

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4.3.0. Prostate movement

The prostate displacements were recorded as the difference between the prostate position on the lateral beam's eye view between the reference scan and the equivalent scan in the second series. The distances were measured from the ICRU reference point to the inferior and posterior border of the prostate for the superior/inferior and anterior/posterior displacements, respectively. Displacements are shown in table 10 below.

Table10. The displacement of the prostate result with and without the rectal balloon in 8 patients

Group	Patients with displacements ≤ 5 mm	Patients with displacements > 5 mm	p value (Chi-square tests)
A	7	1	
B	3	5	
C	6	2	0.049
D	4	4	

KEY

A:	Superior/inferior displacement with balloon
B:	Superior/inferior displacement without balloon
C:	Anterior/posterior displacement with balloon
D:	Anterior/posterior displacement without balloon

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4.3.1. Effect of Rectal Balloon on prostate displacement

Superior inferior

The mean superior inferior displacement with and without the balloon was 2.38 mm and 5.75 mm respectively. Only one patient had a displacement of more than 5 mm with a rectal balloon compared to 5 patients with no rectal balloon. (Table 10).

Anterior posterior

The mean anterior posterior displacement was 4 mm with the rectal balloon and 5 mm without the rectal balloon. Two patients had a displacement above 5 mm with the rectal balloon compared to 4 patients with no rectal balloon.

With the rectal balloon, there was a significant reduction in the proportion of patients with displacements above and below 5 mm in both the anterior-posterior and inferior-superior distances ($p=0.049$) using chi-square test. The percentage of the prescribed dose received by the prostate and the mean dose were significantly different with a balloon $p=0.03$ and 0.038, respectively based on the Mann Whitney test.

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4.4 Rectal toxicity

No treatment interruptions due to failure to tolerate rectal balloon or due to acute rectal toxicity were noted and all patients completed the 6-week treatment course.

Table 11 shows the rectal toxicity recorded at the end of the sixth week of treatment.

Table 11. The acute rectal toxicity score of the 8 patients

GRADE	0	1	2	3
NUMBER OF PATIENTS	1	6	1	0

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5 DISCUSSION

5.1 3-Dimensional conformal radiotherapy and IMRT treatment techniques call for extra-ordinary accuracy in directing external beam radiation (43). Previous studies have confirmed prostate motion during treatment (29, 30, 31, 32). Methods have been described and are used to overcome this problem especially during dose escalation (33, 34, 35, 36). The objectives in all these techniques are to minimize toxicity to OAR and to ensure tumour coverage all the time.

In this study, we proposed the use of a Foleys urethral catheter as a rectal balloon as an alternative to all other methods described. The advantage seen in our patient population have been several-fold. By using the rectal balloon, which is easily available in the hospital, we can achieve dose escalation while reducing the rectal toxicity and achieving immobilization of the prostate at the same time.

This paper discusses the results of a prospective study at Johannesburg Hospital using Foleys catheter filled with 30 cc of contrast as a rectal balloon to achieve similar goals.

5.2 Effect of Rectal balloon on DVH

Van Lin EN, et al (44) investigated the dosimetric consequences and endorectal wall effect of three different endorectal balloon for three Dimensional Conformal Radiotherapy and Intensity-modulated radiotherapy for prostate cancer. They looked at

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284 treatment plans from 20 patients and calculated the rectal wall mean dose, rectal wall mean tissue complication probability and the absolute rectal wall volume exposed to 50 Gy or higher and 70 Gy or higher. Partial dose distribution analysis, inner rectal wall maps and dose surface histograms were generated. In case of 3-DCRT there was a statistically significant reduction in all the parameters, however with IMRT, a statistically significant reduction on the rectal wall dose parameters could not be demonstrated for any of the endorectal balloon, however, both lead to a reduced late toxicity due to reduction of the relative inner wall surface exposed to high doses.

Wachter S (34) investigated the variations in the rectal volumes and its DVH during treatment with conformal radiotherapy. They studied the influence of a rectal balloon on the DVH of the anterior and posterior rectal wall volumes, the entire rectal wall and whole rectal volume in 10 patients. They used a commercial rectal balloon inflated with 40 ml of air. No statistically significant difference was reported with the use of their rectal balloon on the DVH of the whole rectum.

In our study there was a slight reduction in the dose received by 1 - 2% of the rectal volume which may represent the rectal wall dose but this was not statistically significant. There was also a non-significant increase in the percentage dose received by 50% of the volume of the rectum due to the balloon pushing the anterior rectal wall towards the symphysis pubis. In the Van Lin study they looked at the rectal wall dose and there was a significant reduction with the use of a balloon. A slight reduction in the dose received by 1-2% in our study may be the representative of the rectal wall dose as reported in the Van

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Lin study. The current study did not look at the rectal wall dose but the dose to the whole rectal volume. Similar findings to those reported by Wachter were found in our study regarding the effect of the rectal balloon on the DVHs of the whole rectum. Both studies did not find any statistically significant difference with the use of a rectal balloon on the DVH of the whole rectum.

5.3.0 Effect of rectal preparation on the rectal volume

Rectal preparation significantly reduced the volume of the rectum ($p=0.024$). This implies that the rectum is not always empty and that rectal position and filling can vary over the short period of time due to peristalsis and bowel gas movement. Padhni et al (45) concluded that rectal movements are related to rectal distention and results in significant prostate displacements during daily fractionations. Stasi M, et al (46) Studied rectal emptying before treatment to assess if it limits the variation of the rectum volume parameters during 3-DCRT of the prostate. Ten patients had planning CT-scans to a total of 126 scans. They were asked to empty the rectum before every CT scan and before treatment delivery. Volume analysis showed a slight systematic variation of the rectal volume between planning and treatment and the average rectal volume during therapy was larger than at the planning CT in 8/10 patients. In this study, the practice of carefully emptying the rectum during simulation and therapy for prostate cancer reduced the impact of organ motion on dose-volume parameters of the rectum. This variation in rectal

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distention was reduced in our study by using rectal preparation and is similar to that reported by the above studies.

5.3.1. Effect of rectal balloon on prostate movement

A number of studies (29, 31, 47) have shown that there is displacement of prostate with rectal filling variation and this is shown the table 12.

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Table 12 Standard deviations of prostate motion from various studies

Author	direction of motion		
	L-R (mm)	A-P (mm)	superior-inferior
Edward Melian et al (29)	1.2	4.0	3.1
John A. Antolak et al (31)	0.9	4.1	3.6
Volker Rudat et al (47)		2.8	1.4

KEY

L-R : Left- Right

A/P: Anterior-Posterior

Langen et al. (29) noted that despite different processes and study end points used, there is agreement that displacement is greatest in the anterior-posterior direction compared to the superior-inferior direction with standard deviations ranging from 1.5 mm to 4.1 mm and 1.7 mm to 4.5 mm, respectively.

Dawson et al. (48) studied 6 patients with weekly CT scans, in the supine position with empty bladders. Relative to the initial CT scan, displacement of prostate was noted to be 7.3 mm and 9.3 mm anterior posterior and superior inferior, respectively, demonstrating prostate movement.

Crooks, et al (49) studied the prostate motion, minimum motion was noted in the lateral direction with 0.1 to 0.5 cm, and in cranial caudal axis was usually 0.5 cm on average and

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43% showed more than 0.5 cm displacement and 11% more than 1 cm displacement. In the posterior direction 60% shown more than 0.5 cm and 30% shown more than 1 cm displacement.

McGrany et al. (39) studied prostate immobilization using a rectal balloon in 10 patients using CT-fusion on patients who had previously received Gold implants as internal markers. They noted a minimal displacement in the Anterior-Posterior (A/P) and lateral directions with a rectal balloon of approximately 1 mm. The superior-inferior standard deviation was 1.7 with a mean of 0.92 mm.

D'Amico et al. (33) studied immobilization of prostate using 60 cc of air in a rectal balloon designed specially to conform to the shape of prostate-rectal interface in 10 patients who underwent prostate brachytherapy using permanent radioactive seeds. Coordinates of the implant sources were compared at one minute intervals, and the mean displacement of the prostate gland when the intrarectal balloon was present was 1.3 mm versus 1.8 mm when it was not used ($p=0.03$).

Wachter et al. (34) studied the influence of a rectal balloon inflated with 40 cc of air as internal immobilization of the prostate. Six CT scans at 3 intervals were used and displacements were measured on the beams eye view with and without a rectal balloon. With the rectal balloon, the Anterior-Posterior (A/P) displacement was reduced $p=0.008$ and displacements >5 mm were noted in 2/10 patients. Superior inferior (S/I) displacements were not measured in this study.

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In the current study, more displacement was recorded in the superior inferior direction compared to the anterior posterior direction with a mean of 5.7 mm and 5.00 mm respectively with no rectal balloon. When a rectal balloon was used, there was a reduction in the displacement in the superior inferior direction of a mean of 2.38 mm. In the anterior posterior direction with the balloon, the mean was 4.00 mm. This may have been due to the fact that the rectal balloon used could not conform to the prostate.

When displacements of more than 5 mm were compared with and without the balloon, only 1/8 patients had a displacement above 5 mm with the balloon compared to 5/8 without the balloon in the superior-inferior (S/I) direction. Likewise, 2/8 compared to 4/8 in the A/P direction respectively. There was a significant increase in the dose received by 90% of prostate with the balloon ($p=0.03$) and also in the mean dose to the prostate volume ($p=0.038$). The poor coverage of the prostate with no balloon is attributed to the displacement.

When the above studies without endorectal balloon are compared with the studies with the endorectal balloon including results from our study, prostate displacements more than 5mm are greatly reduced, this makes it possible to use tight margins on the prostate during 3-DCRT or IMRT with dose escalation treatment resulting in reduced rectal toxicity.

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5.3.2. Acute toxicity during treatment

Ronson et al. (50) did a retrospective study to evaluate the rectal tolerance of conformal prostate treatment with a rectal balloon in 3561 patients. 97% tolerated a rectal balloon throughout the treatment course, and 2.7% declined balloon insertion for one or two treatments but tolerated it for up to 85% of their treatment.

Kannan, et al. (51) looked at survival and rectal toxicity for patients with adenocarcinoma of prostate treated with three Dimensional Conformal radiotherapy Out of the 51 patients in the study, the acute rectal toxicity using the RTOG criteria was grade 0 in 4 patients, grade 1 in 31 patients and grade 2 in 16 patients. No grade 3 or 4 toxicities were recorded

Bastasch MD, et al (52) reported patient tolerance and acute anorectal toxicity of an endorectal balloon used for prostate cancer immobilization during 35 daily fractions. Patients were treated with IMRT and an endorectal balloon catheter was inserted daily and inflated with 100ml of air for immobilizing the prostate gland. They received a mean dose of 77 Gy. None of the 396 patients stopped treatment because of associated toxicity. 13.9% and 18.4% had RTOG grade 1and 2 toxicity respectively and no RTOG grade 3 and 4 toxicities were recorded.

In this study, all 8 patients tolerated the balloon throughout the treatment. There were no complaints about discomfort and no treatment was discontinued because of the use of the rectal balloon. No grade 3 acute toxicity was reported in the study. Patients reporting

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grade 2 toxicity had ECOG 2 performance status at the beginning of the treatment, however all completed treatment with no deterioration in performance status. The above results compare well with the results from previous studies indicating that the rectal balloon is well tolerated.

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6.0. CONCLUSION

A simple method of using a Foleys rectal balloon catheter to achieve the immobilization of the prostate during treatment with 3-dimensional conformal radiotherapy with dose escalation has been presented.

There was no effect on the DVH of the whole rectum with the use of a 30 cc rectal balloon; however there was a non-significant reduction in the volume receiving a higher percentage dose with the use of a rectal balloon.

No Grade 3 acute rectal toxicity was recorded in the 8 patients. No comment can be made regarding chronic toxicity as the follow up period is too short.

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Appendix A

THE UPDATED PARTIN TABLES

PSA Range (ng/mL)	Pathologic Stage	Gleason Score				
		2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	Organ confined	95 (89-99)	90 (88-93)	79 (74-85)	71 (62-79)	66 (54-76)
	Extraprostatic extension	5 (1-11)	9 (7-12)	17 (13-23)	25 (18-34)	28 (20-38)
	Seminal vesicle (+)	-	0 (0-1)	2 (1-5)	2 (1-5)	4 (1-10)
	Lymph node (+)	-	-	1 (0-2)	1 (0-4)	1 (0-4)
2.6-4.0	Organ confined	92 (82-98)	84 (81-86)	68 (62-74)	58 (48-67)	52 (41-63)
	Extraprostatic extension	8 (2-18)	15 (13-18)	27 (22-33)	37 (29-46)	40 (31-50)
	Seminal vesicle (+)	-	1 (0-1)	4 (2-7)	4 (1-7)	6 (3-12)
	Lymph node (+)	-	-	1 (0-2)	1 (0-3)	1 (0-4)
4.1-6.0	Organ confined	90 (78-98)	80 (78-83)	63 (58-68)	52 (43-60)	46 (36-56)
	Extraprostatic extension	10 (2-22)	19 (16-21)	32 (27-36)	42 (35-50)	45 (36-54)
	Seminal vesicle (+)	-	1 (0-1)	3 (2-5)	3 (1-6)	5 (3-9)
	Lymph node (+)	-	0 (0-1)	2 (1-3)	3 (1-5)	3 (1-6)
6.1-10.0	Organ confined	87 (73-97)	75 (72-77)	54 (49-59)	43 (35-51)	37 (28-46)
	Extraprostatic extension	13 (3-27)	23 (21-25)	36 (32-40)	47 (40-54)	48 (39-57)
	Seminal vesicle (+)	-	2 (2-3)	8 (6-11)	8 (4-12)	13 (8-19)
	Lymph node (+)	-	0 (0-1)	2 (1-3)	2 (1-4)	3 (1-5)
>10.0	Organ confined	80 (61-95)	62 (58-64)	37 (32-42)	27 (21-34)	22 (16-30)
	Extraprostatic extension	20 (5-39)	33 (30-36)	43 (38-48)	51 (44-59)	50 (42-59)
	Seminal vesicle (+)	-	4 (3-5)	12 (9-17)	11 (6-17)	17 (10-25)
	Lymph node (+)	-	2 (1-3)	8 (5-11)	10 (5-17)	11 (5-18)

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TABLE II. Clinical Stage T2a (palpable < 1 .2 of one lobe))

PSA Range (ng/mL)	Pathologic Stage	Gleason Score				
		2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	Organ confined	91 (79-98)	81 (77-85)	64 (56-71)	53 (43-63)	47 (35-59)
	Extraprostatic extension	9 (2-21)	17 (13-21)	29 (23-36)	40 (30-49	42 (32-53)
	Seminal vesicle (+)	-	1 (0-2)	5 (1-9)	4 (1-9)	7 (2-16)
	Lymph node (+)	-	0 (0-1)	2 (0-5)	3 (0-8)	3 (0-9)
2.6-4.0	Organ confined	85 (69-96))	71 (66-75)	50 (43-57)	39 (30-48)	33 (24-44
	Extraprostatic extension	15 (4-31)	27 (23-31)	41 (35-48)	52 (43-61)	53 (44-63)
	Seminal vesicle (+)	-	2 (1-3)	7 (3-12)	6 (2-12)	10 (4-18)
	Lymph node (+)	-	0 (0-1)	2 (0-4)	2 (0-6)	3 (0-8)
4.1-6.0	Organ confined	81 (63-95)	66 (62-70)	44 (39-50)	33 (25-41)	28 (20-37)
	Extraprostatic extension	19 (5-37)	32 (28-36)	46 (40-52)	56 (48-64)	58 (49-66)
	Seminal vesicle (+)	-	1 (1-2)	5 (3-8)	5 (2-8)	8 (4-13)
	Lymph node (+)	-	1 (0-2)	4 (2-7)	6 (3-11)	6 (2-12)
6.1-10.0	Organ confined	76 (56-94)	58 (54-61)	35 (30-40)	25 (19-32)	21 (15-28)
	Extraprostatic extension	24 (6-44)	37 (34-41)	49 (43-54)	58 (51-66)	57 (48-65)
	Seminal vesicle (+)	-	4 (3-5)	13 (9-18)	11 (6-17)	17 (11-26)
	Lymph node (+)	-	1 (0-2)	3 (2-6)	5 (2-8)	5 (2-10)
>10.0	Organ confined	65 (43-89)	42 (38-46)	20 (17-24)	14 (10-18)	11 (7-15)
	Extraprostatic extension	35 (11-57)	47 (43-52)	49 (43-55)	55 (46-64)	52 (41-62)
	Seminal vesicle (+)	-	6 (4-8)	16 (11-22)	13 (7-20)	19 (12-29)
	Lymph node (+)	-	4 (3-7)	14 (9-21)	18 (10-27)	17 (9-29)

KEY: PSA = prostate-specific antigen.

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TABLE III. Clinical Stage T2b (palpable > 1 .2 of one lobe, not on both lobes)						
PSA Range (ng/mL)	Pathologic Stage	Gleason Score				
		2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	Organ confined	88 (73-97)	75 (69-81)	54 (46-63)	43 (33-54)	37 (26-49)
	Extraprostatic extension	12 (3-27)	22 (17-28)	35 (28-43)	45 (35-56)	46 (35-58)
	Seminal vesicle (+)	-	2 (0-3)	6 (2-12)	5 (1-11)	9 (2-20)
	Lymph node (+)	-	1 (0-2)	4 (0-10)	6 (0-14)	6 (0-16)
2.6-4.0	Organ confined	80 (61-95)	63 (57-69)	41 (33-48)	30 (22-39)	25 (17-34)
	Extraprostatic extension	20 (5-39)	34 (28-40)	47 (40-55)	57 (47-67)	57 (46-68)
	Seminal vesicle (+)	-	2 (1-4)	9 (4-15)	7 (3-14)	12 (5-22)
	Lymph node (+)	-	1 (0-2)	3 (0-8)	4 (0-12)	5 (0-14)
4.1-6.0	Organ confined	75 (55-93)	57 (52-63)	35 (29-40)	25 (18-32)	21 (14-29)
	Extraprostatic extension	25 (7-45)	39 (33-44)	51 (44-57)	60 (50-68)	59 (49-69)
	Seminal vesicle (+)	-	2 (1-3)	7 (4-11)	5 (3-9)	9 (4-16)
	Lymph node (+)	-	2 (1-3)	7 (4-13)	10 (5-18)	10 (4-20)
6.1-10.0	Organ confined	69 (47-91)	49 (43-54)	26 (22-31)	19 (14-25)	15 (10-21)
	Extraprostatic extension	31 (9-53)	44 (39-49)	52 (46-58)	60 (52-68)	57 (48-67)
	Seminal vesicle (+)	-	5 (3-8)	16 (10-22)	13 (7-20)	19 (11-29)
	Lymph node (+)	-	2 (1-3)	6 (4-10)	8 (5-14)	8 (4-16)
>10.0	Organ confined	57 (35-86)	33 (28-38)	14 (11-17)	9 (6-13)	7 (4-10)
	Extraprostatic extension	43 (14-65)	52 (46-56)	47 (40-53)	50 (40-60)	46 (36-59)
	Seminal vesicle (+)	-	8 (5-11)	17 (12-24)	13 (8-21)	19 (12-29)
	Lymph node (+)	-	8 (5-12)	22 (15-30)	27 (16-39)	27 (14-40)
KEY: PSA = prostate-specific antigen.						

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TABLE IV. Clinical Stage T2c (palpable on both lobes)

PSA Range (ng/mL)	Pathologic Stage	Gleason Score				
		2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	Organ confined	86 (71-97)	73 (63-81)	51 (38-63)	39 (26-54)	34 (21-48)
	Extraprostatic extension	14 (3-29)	24 (17-33)	36 (26-48)	45 (32-59)	47 (33-61)
	Seminal vesicle (+)	-	1 (0-4)	5 (1-13)	5 (1-12)	8 (2-19)
	Lymph node (+)	-	1 (0-4)	6 (0-18)	9 (0-26)	10 (0-27)
2.6-4.0	Organ confined	78 (58-94)	61 (50-70)	38 (27-50)	27 (18-40)	23 (14-34)
	Extraprostatic extension	22 (6-42)	36 (27-45)	48 (37-59)	57 (44-70)	57 (44-70)
	Seminal vesicle (+)	-	2 (1-5)	8 (2-17)	6 (2-16)	10 (3-22)
	Lymph node (+)	-	1 (0-4)	5 (0-15)	7 (0-21)	8 (0-22)
4.1-6.0	Organ confined	73 (52-93)	55 (44-64)	31 (23-41)	21 (14-31)	18 (11-28)
	Extraprostatic extension	27 (7-48)	40 (32-50)	50 (40-60)	57 (43-68)	57 (43-70)
	Seminal vesicle (+)	-	2 (1-4)	6 (2-11)	4 (1-10)	7 (2-15)
	Lymph node (+)	-	3 (1-7)	12 (5-23)	16 (6-32)	16 (6-33)
6.1-10.0	Organ confined	67 (45-91)	46 (36-56)	24 (17-32)	16 (10-24)	13 (8-20)
	Extraprostatic extension	33 (9-55)	46 (37-55)	52 (42-61)	58 (46-69)	56 (43-69)
	Seminal vesicle (+)	-	5 (2-9)	13 (6-23)	11 (4-21)	16 (6-29)
	Lymph node (+)	-	3 (1-6)	10 (5-18)	13 (6-25)	13 (5-26)
>10.0	Organ confined	54 (32-85)	30 (21-38)	11 (7-17)	7 (4-12)	6 (3-10)
	Extraprostatic extension	46 (15-68)	51 (42-60)	42 (30-55)	43 (29-59)	41 (27-57)
	Seminal vesicle (+)	-	6 (2-12)	13 (6-24)	10 (3-20)	15 (5-28)
	Lymph node (+)	-	13 (6-22)	33 (18-49)	38 (20-58)	38 (20-59)

KEY: PSA = prostate-specific antigen.

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APPENDIX B

The TNM staging of the prostate cancer

TNM definitions

Primary tumor (T)

TX: Primary tumor cannot be assessed

T0: No evidence of primary tumor

T1: Clinically unapparent tumor not palpable nor visible by imaging

T1a: Tumor incidental histologic finding in ≤5% of tissue resected

T1b: Tumor incidental histologic finding in >5% of tissue resected

T1c: Tumor identified by needle biopsy (e.g., because of elevated PSA)

T2: Tumor confined within prostate*

T2a: Tumor involves 50% of one lobe or less

T2b: Tumor involves >50% of one lobe but not both lobes

T2c: Tumor involves both lobes

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T3: Tumor extends through the prostate capsule**

T3a: Extracapsular extension (unilateral or bilateral)

T3b: Tumor invades seminal vesicle(s)

T4: Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall

* [*Note: Tumor that is found in one or both lobes by needle biopsy but is not palpable or reliably visible by imaging, is classified as T1c.*]

** [*Note: Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.*]

Regional lymph nodes (N)

Regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries. They include the following groups (laterality does not affect the N classification): pelvic (not otherwise specified [NOS]), hypogastric, obturator, iliac (i.e., internal, external, NOS), and sacral (lateral, presacral, or promontory [e.g., Gerota's], or NOS). Distant lymph nodes are outside the confines of the true pelvis. They can be imaged using ultrasound, CT, MRI, or lymphangiography, and include: aortic (para-aortic, periaortic, or lumbar), common iliac, inguinal (deep), superficial inguinal (femoral), supraclavicular, cervical, scalene, and

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retroperitoneal (NOS) nodes. Although enlarged lymph nodes can occasionally be visualized, because of a stage migration associated with PSA screening, very few patients will be found to have nodal disease, so false-positive and false-negative results are common when imaging tests are employed. In lieu of imaging, risk tables are generally used to determine individual patient risk of nodal involvement. Involvement of distant lymph nodes is classified as M1a.

NX: Regional lymph nodes were not assessed

N0: No regional lymph node metastasis

N1: Metastasis in regional lymph node(s)

Distant metastasis (M)*

MX: Distant metastasis cannot be assessed (not evaluated by any modality)

M0: No distant metastasis

M1: Distant metastasis

M1a: Nonregional lymph node(s)

M1b: Bone(s)

M1c: Other site(s) with or without bone disease

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APPENDIX C

CANDIDATE'S SURNAME: Kanyike [Please print]	FIRST NAME/S: Daniel mukasa
CURRENT QUALIFICATIONS: MbChB	STUDENT NUMBER: 0403648T

DEGREE FOR WHICH PROTOCOL IS BEING SUBMITTED: MMed Rad (T)

YEAR & TERM FIRST REGISTERED FOR THIS DEGREE: 2003 June/ July

DEPARTMENT: Radiation oncology

TITLE OF PROPOSED RESEARCH: Rectal dose sparing and prostate immobilization using a rectal balloon in the treatment of prostate cancer with dose escalation conformal radiation therapy.

CANDIDATE'S SIGNATURE: D Skanyike	DATE: 7TH/oct/2004

SUPERVISOR'S NAME: DR J Kotzen

SUPERVISOR'S QUALIFICATIONS: Bsc MBBCh, Mmed Rad (T)

SUPERVISOR'S DEPARTMENT: Radiation oncology

CO-SUPERVISOR'S NAME: PROFESSOR. B.DONDE

CO-SUPERVISOR'S QUALIFICATIONS: MBBCh MMED Rad (T)

CO-SUPERVISOR'S DEPARTMENT Head of Department for Radiation Oncology

SYNOPSIS OF RESEARCH: Eligible consecutive patients who have given informed consent will have an immobilization cast made and simulated for treatment. Two CT scans will be performed at the beginning of treatment, middle of treatment and at the end of treatment i.e. total o f 6 CT scans: 1. with bowel preparation 2. With bowel preparation and inflation of rectal catheter. Planning of the treatment will be performed on all 2 scans. The patient will receive standard conformal radiation therapy of 2 Gy per day up to66Gy following which a boost of 12Gy using a rectal balloon. Patients will be reviewed weekly till end of the treatment then every after 4 months for a period of 2 Years. All acute rectal and bowel complications will be recorded and analysed.

[Use reverse side of this page if more space is required]

ETHICS CLEARANCE No:	M04/1006
SIGNATURE OF SUPERVISOR:/S:	

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APPENDIX D

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Kanyike

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M041006**
PROJECT	Rectal Dose Sparing and Prostate Immobilisation Using a Rectal Baloon in Treatment of Prostate Cancer with Dose...
INVESTIGATORS	Dr MD Kanyike
DEPARTMENT	School of Clinical Medicine
DATE CONSIDERED	04.10.29

DECISION OF THE COMMITTEE*

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr J Kotzen

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

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APPENDIX E

Faculty of Health Sciences
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
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E-MAIL healthpg@health.wits.ac.za

DR DM KANYIKE
JOHANNESBURG HOPITAL
BLOCK D, ROOM 317
PARKTOWN
2193

APPLICATION NUMBER 0403648T
STATUS (DEG 61) (MMU00) PZZ

2005-03-15

Dear Dr Kanyike

Approval of protocol entitled Rectal dose sparing and prostate immobilization using a rectal balloon in the treatment of prostate cancer with dose escalation conformal radiation therapy

I should like to advise you that the protocol and title that you have submitted for the degree of Master Of Medicine (In Radiation Oncology) have been approved by the Postgraduate Committee at its recent meeting. Please remember that any amendment to this title has to be endorsed by your Head of Department and formally approved by the Postgraduate Committee.

Dr JA Kotzen, Prof B Donde has/have been appointed as your supervisor/s. Please maintain regular contact with your supervisor who must be kept advised of your progress.

Please note that approval by the Postgraduate Committee is always given subject to permission from the relevant Ethics Committee, and a copy of your clearance certificate should be lodged with the Faculty Office as soon as possible, if this has not already been done.

Yours sincerely

S Benn (Mrs)
Faculty Registrar
Faculty of Health Sciences

Telephone 717-2075/2076

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APPENDIX F

DATA COLLECTION SHEET FOR PATIENT NO--------

DXT no------- Hospital no--------- Age-------- Study no---------

CT scan plan. No.	%dose got by90% of prost.	%dose got by50%prost vol	Prostate Vol.	Prescribed mean dose To prostate
DXT				
DXTA				
DXTK1				
DXTk2				
DXTk3				
DXTk4				

Prostrate Displacement in Millimeters (mm)
NB .the first set of booster scans are the ref. scans.

distance of outer most prostate border from isocentre	ref.scan with balloon	2nd .scan with balloon	Ref.scan with no balloon	2nd .scan with no balloon
Superior (+)				
Inferior (-)				
Anterior (+)				
Posterior (-)				

Acute Toxicity Score of the Rectum

Week of treatment	One	Two	Three	Four	Five	Six
RTOG Score						

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CT scan plan. No.	Total vol. Of Whole Rectum	%dose got by20%vol Rect.	%dose got by25%vol Rect.	%dose got by 30% vol. Rect.	%dose got by 40% vol. Rect.	%dose got by 50% vol. Rect.	%dose got by60%vol Rect.	%dose got by 70% vol. Rect.	%dose got by 1% vol. Rect.	%dose got by 2% vol. Rect.
DXT										
DXTA										
DXTK1										
DXTk2										
DXTk3										
DXTk4										

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