Assessment of the dosimetric consequences of prostate movement through rectal distension for patients receiving 3DCRT

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Abstract

Purpose: To investigate the dosimetric consequences of rectal distension at the time of the planning computed tomography (CT) scan and any resultant prostate movement on the planned dose delivery for patients receiving three-dimensional conformal radiotherapy (3DCRT) to the prostate.

Methods and materials: 25 prostate cancer patients whose planning CT scan demonstrated a full rectum were rescanned after following a laxative protocol. Rectal dimensions on the two scans and 3DCRT treatment plans produced on each plan were compared. The dosimetric implications of changes in rectal size on the treatment plans and the delivered dose were determined. Statistical significance was evaluated with the Wilcoxon signed ranks test.

Results: Significant differences in rectal size were found between the initial CT scan and the rescan. The corresponding median change in prostate position was 4.7 mm. The use of planning scans with a full rectum, that is unrepresentative of the rectum, during treatment causes significant reductions in planning target volume (PTV) minimum dose (median reduction 33.7%) and coverage by the 95% isodose (median reduction 3.7% of the PTV).

Conclusion: Rectal distension on the initial planning scan can lead to significant PTV underdosage. Patients presenting with large initial rectal fillings must be rescanned in order to avoid a systematic underdosing of the PTV.

Keywords
Prostate cancer; conformal radiotherapy; organ motion; rectal distension

INTRODUCTION

Prostate cancer is the most common malignancy occurring in males and can be treated with external beam radiotherapy. Advances in radiotherapy have led to the development of three-dimensional conformal radiotherapy (3DCRT) techniques and intensity-modulated radiotherapy. These methods have the ability to improve tumour control by enabling dose escalation to the target volume while sparing critical normal tissues, but are dependent upon the minimisation of margins during treatment planning. ICRU Reports 50 and 62 define target structures for use in treatment...
planning as the gross tumour volume, clinical target volume (CTV) and planning target volume (PTV). The PTV comprises the CTV with a margin to allow for setup or geometric treatment delivery uncertainties and internal organ motion. For dose escalation to be performed the PTV-CTV margin must be reduced to avoid adjacent radiosensitive structures but must be large enough to ensure target coverage.1,3,8–11

When treating prostate cancer, organ motion is very important because the prostate is a mobile organ and its position can change over the course of treatment. There are two types of organ motion: interfraction organ motion which happens between treatment fractions and intrafraction organ motion which occurs while the patient is being treated.8,9,12 Many previous studies have shown that significant interfraction movement of the prostate occurs during radiotherapy.3,4,9,11,13 The studies show a general agreement that when patients are treated in a supine position, prostate motion is greatest in the anterior–posterior direction and least in the lateral direction. This anterior–posterior organ motion has been found to be correlated more with changes in rectal volume than with changes in bladder filling.9,14,18

It is important to take into account this impact of rectum motion due to variable filling to be able to define a suitable PTV margin to reduce the risk of a geographical miss. The posterior PTV margin is the most crucial part because of the closeness of the anterior rectal wall, as late rectal toxicity is thought to be the dose-limiting factor in prostate radiotherapy. Also for 70–80% of prostate cancers, the tumour is located within the peripheral zone of the prostate. Hence, too small a margin here may result in underdosage of the tumour.3,4,19–21

Earlier research has also found that rectum volume decreases with time during the course of treatment. This decreasing rectum volume may be due to an increased frequency of bowel movements secondary to the effects of radiotherapy.3,21–23 Hence, if the rectum is less distended during treatment than it is on the original computed tomography (CT) planning scan, then the prostate may move posteriorly resulting in undertreatment of the tumour. Moreover, lower rectal toxicity rates may occur if the rectum is empty because a smaller volume of rectum will be in the treatment beam.4,24 Therefore, recent studies have demonstrated strong evidence that at the time of simulation and treatment, patients should have an empty rectum to avoid a geographical miss.3,4,19–21,24

de Crevoisier et al.4 showed that rectal distension on the planning CT scan increased the risk of biochemical and local failure for patients irradiated for prostate cancer. However, during a course of radiotherapy it is difficult to consistently control the degree of rectal filling and gas, indicating a need for daily localisation.3

Currently, in the authors’ department there is no formal, quantitative departmental protocol of when to rescan patients with regard to rectal filling. During the planning CT scan radiographers check the size of the rectum, if it looks distended then a rescan will be performed following appropriate bowel preparation. However, this is an area of uncertainty as the decision as to whether a rescan needs to be performed is highly subjective. Although criteria for making such decisions have previously been published, they are highly dependent upon setup and treatment protocols. Therefore, it is important that rescan criteria are appropriate for the techniques in use at an individual institution.

The aim of this study was to investigate the dosimetric consequences of rectal distension and any resultant prostate movement on the planned dose delivery for patients receiving 3DCRT to the prostate. First, the variation in prostate position caused by the change in rectal status was quantified. The magnitude of any changes in planned dose to the prostate and rectum resulting from these variations was then investigated. Finally, the implications for the dose delivered to the patients of a difference in rectal filling between the planning CT scan and treatment was determined.
METHOD

This retrospective planning study included patients treated with 3DCRT for prostate cancer at Weston Park Hospital, Sheffield between January 2007 and June 2008. The eligibility criterion for the study was that a patient had two CT scans for treatment planning purposes—a initial scan and a rescan on account of their rectum being considered insufficiently empty on the initial scan. Patients with a hip prosthesis were excluded from this study, due to the non-standard field arrangement used for such patients and the dosimetric uncertainties introduced by the artefacts caused by the prostheses. A total of 25 patients were eligible for this study.

The departmental protocol for bladder and bowel preparation was followed. Patients were asked to empty their bladder and drink 500 ml in the first 15 minutes of the hour prior to scanning, verification and daily treatment. Bowel preparation involves having two teaspoonfuls of milk of Magnesia daily starting 3 days before the planning CT scan and ensuring they have a bowel motion daily before treatment.

There were two main components in making the decision to rescan. A maximum diameter of 4 cm is used as a threshold above which a rescan is indicated. However, as individual measures such as the diameter at a given level have been found to be potentially misleading, given the non-uniformity of rectal filling, the size of the rectum relative to that of the prostate is also considered. This latter aspect was guided by previous experience in treatment planning for prostate cancer and was necessarily subjective in part. The decision to rescan was made by an experienced radiographer. The rescan was performed 3 days after the initial CT scan.

All the CT scans were performed with the patients in a supine position with ankle stocks used as an immobilisation device (the same setup as was subsequently used for each treatment). A GE Lightspeed CT scanner was used to acquire a helical scan, which was reconstructed with a slice spacing of 5 mm. The limits of the scans were the top of the true pelvic brim and the bottom of the ischium bones. The CT data sets were loaded into the Advantage Sim MD software, version 7.5 (GE Medical Systems, Milwaukee, IL) where contouring took place. The contouring was performed by a single radiographer experienced in prostate outlining, thereby eliminating inter-operator variability from the study. For each patient, on both the initial CT scan and the rescan, the prostate, bladder (wall and filling) and rectum (wall and filling) were contoured, the superior and inferior limits of the rectum being the rectosigmoid junction and the anus, respectively. The PTV was automatically generated by applying a 1 cm margin around the CTV, in line with current departmental protocol. Subsequently all the CT images and structure sets were transferred to the Eclipse Treatment Planning System, version 7.5.18 (Varian Oncology Systems, Palo Alto, CA) where treatment planning took place.

Six parameters were used to characterise the rectum on each CT scan. The rectal length (defined as the distance between the first and last CT slices of the contoured rectum on the sagittal view) and the anterior–posterior rectal diameter, measured at three levels, corresponding to the superior limit (base) of the prostate, the mid-prostate level and the inferior limit (apex) of the prostate, are illustrated in Figure 1. The total rectal volume was automatically calculated by the Eclipse Treatment Planning System. Six parameters were used to characterise the rectum on each CT scan. The rectal length (defined as the distance between the first and last CT slices of the contoured rectum on the sagittal view) and the anterior–posterior rectal diameter, measured at three levels, corresponding to the superior limit (base) of the prostate, the mid-prostate level and the inferior limit (apex) of the prostate, are illustrated in Figure 1. The total rectal volume was automatically calculated by the Eclipse Treatment Planning System.
System, the algorithm for which had previously been verified. A measure of the rectal distension was provided by the mean cross-sectional area of the rectum calculated by dividing the total rectal volume by the rectal length.

Isocentric treatment plans were produced for both the initial and rescan CT datasets for each patient using a conformal three-field technique consisting of an anterior beam and two lateral beams using 10 MV photons. The beams were shaped with multileaf collimators (5 mm leaf width) with a penumbra margin of 7 mm. 55 Gy was prescribed to the isocentre in 20 fractions (2.75 Gy per fraction). The aim of the planning was to achieve PTV coverage within the ICRU recommended limits of 95—107% while not exceeding organ at risk tolerances. Dose calculation was performed on a 2.5 mm grid, with inhomogeneity correction.

The magnitude of the prostate motion due to the differences in rectal filling was investigated by comparing the location of the centre of mass of the PTV in the two CT scans. For each patient, the difference in location was determined, both in each axis separately and overall. The median and range of these values were then calculated to give some measure of the movement of the prostate due to rectal filling.

A conformal three-field plan, as described above, was then produced for each of the initial and rescanned CT data sets for each patient. To investigate the impact of rectal size on how acceptable a plan is in terms of PTV and organ at risk doses, the two plans for each patient were dosimetrically compared by generating dose—volume histograms, to evaluate the following parameters. For the PTV, the minimum percentage dose \( D_{\text{min,PTV}} \) and the percentage volume receiving 95% of the prescription dose \( V_{\text{PTV95\%}} \) were compared. For the rectum the maximum percentage dose \( D_{\text{max,rec}} \), the dose received by 50% of the rectal volume \( D_{\text{rec50\%}} \) and the percentage volume of rectum which receives 90% of the prescription dose \( V_{\text{rec90\%}} \) were compared. For the bladder, the maximum dose \( D_{\text{max,blad}} \) and the dose received by 50% of the bladder volume \( D_{\text{blad50\%}} \) were compared.

Finally, the potential implications of changes in rectal volume and any resulting prostate motion on the delivered dose were investigated. For each patient the initial scan and the rescan were registered in Eclipse using the same external entry/marker points and the locations of the prostate in the two scans were compared (see Figure 2). The treatment plan produced using the initial scan was then applied without correction to the rescan and the doses delivered to the PTV and organs at risk were compared to those on the original plan.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows software release 16.0. The distributions under consideration could not be proven to be normally distributed therefore non-parametric tests were used in their comparison. The Wilcoxon matched pairs signed ranks test was used to determine the significance of the differences in the PTV and rectal doses between the two CT scans. The Spearman rank correlation coefficient was used to determine whether there was any relation between the rectal size and PTV dose.

In all comparisons, a \( p \)-value of <0.025 was considered statistically significant. A cut-off of 0.05 for statistical significance was not chosen.

![Figure 2. A representative axial slice from a patient’s initial scan showing the contoured volumes on both the initial scan and the rescan, following registration of the datasets: Bladder initial scan (pink) and rescan (light green), rectum initial scan (yellow) and rescan (dark green), PTV initial scan (blue) and rescan (red). The purple contour shows the position of the CTV on the initial scan.](https://doi.org/10.1017/S1460396910000361)
instead a Bonferroni correction was applied due to the multiple testing of the same data in this study to reduce the likelihood of it falsely giving the appearance of significance.

During treatment, the patient setup was verified by daily ultrasound imaging using the Sonar-ray system (Varian Medical Systems, Palo Alto, CA) to precisely localise the target. Shifts were performed as required in order to correct for differences in the position of the prostate from its location on the CT scan used for treatment planning. If ultrasound imaging was unavailable, for example due to machine service, offline electronic portal imaging verification of bony anatomy was used with a tolerance level of 5 mm. The magnitudes of the ultrasound shifts were used to verify the consistency of prostate location throughout the course of treatment.

**RESULTS**

Table 1 summarises the distributions of rectal length, volume, mean cross-sectional area, diameter and bladder volume for patients’ initial CT scan and rescan after emptying their rectum. The median values for all the rectal characteristics on the initial CT scan were larger than on the rescan except for the length and the anterior–posterior rectal diameter at the inferior of the prostate which were very similar. On the initial CT scan the largest anterior–posterior rectal diameter was found to be at the superior (base) of the prostate, while on the rescan there was little variation in rectal diameter along its length. On average, the differences in rectal volume and mean rectal cross-sectional area were equivalent to reductions of approximately 30% and 35%, respectively of their values on the initial scans. The median bladder volume on the initial scan was smaller than on the rescan.

Table 2 lists the differences in the dose–volume parameters between the initial CT scan and the rescan. There were no significant differences in the PTV or bladder doses between the initial CT scan and the rescan.
However, there was a statistically significant difference in both the percentage volume of the rectum receiving 90% of the prescription dose and the prescribed dose to 50% of the rectal volume between the two CT scans. The percentage volume of rectum receiving 90% of the prescription dose was significantly higher on the rescan than on the initial CT scan. The dose to 50% of the rectal volume was also significantly higher on the rescan when compared to the initial CT scan. No other significant differences were found between the initial CT scan and the rescan.

The dependence of PTV coverage on the various measures of rectal size was investigated for all plans produced on the original CT scan and the rescan (Table 3). No significant correlation was seen between the PTV dose and any of the rectal diameters or cross-sectional area. When the correlation coefficients were examined for the initial CT scan and the rescan separately, again no significant correlations were seen.

This shows that, in this study, the PTV dose was not dependent on the size of the rectum when planned on that scan.

In all patients the prostate moved in some direction due to rectal filling (see Figure 3). For the 25 patients the prostate moved, on average, by 1.1 mm in the left–right direction, 2.6 mm in the anterior–posterior axis and 3.3 mm in the superior–inferior direction, with an overall median movement of 4.7 mm with respect to the position on the original scan.

Table 4 summarises the comparison of the plans produced on the initial CT scan and the dose distribution resulting from the application of that plan onto the rescan following registration of the two scans. The maximum percentage dose to the rectum was significantly lower on the registration rescan than on the initial CT scan (median value 101.8% compared to 102.2%). A greater — and highly significant — difference was seen in the percentage volume of the PTV receiving 95% of the prescription dose. Although 100.0% of the PTV received this dose level when planning was performed on the initial scans, the application of these plans to the patient geometries on the rescan resulted in a median reduction of 3.7%. The greatest difference was seen in the minimum PTV dose, which was just 61% of the prescription dose on the registration rescans compared to nearly 95% in the original plans.

Table 5 shows the equivalent comparison between the dose distributions from the plan produced on the rescan and the distributions that resulted from applying the initial scan’s treatment plan to the rescan. In addition to significant reductions in the minimum PTV dose and the volume of the PTV receiving 95% of the prescription dose, there were significant reductions in the rectal doses (in terms of $V_{\text{rec90%}}$ and $D_{\text{rec50%}}$) on the plans produced.
on the rescans when compared with the registration rescan plans.

**DISCUSSION**

A total of 25 patients were included in this retrospective planning study which investigated the dosimetric consequences of producing treatment plans for prostate cancer patients on a planning CT scan when the patient presents with a full rectum.

Among this cohort of patients’ initial planning CT scans, the median average cross-
sectional rectal area was 13.2 cm$^2$ and the median anterior–posterior rectal diameter at the base of the prostate median value was 5.4 cm. These values exceeded other studies’ thresholds beyond which a rescan was indicated due to increased risk of biochemical failure\textsuperscript{4} or the need for increased posterior margins.\textsuperscript{21} The median rectal volume in this study was 111.1 cm$^3$ — greater than the 100 cm$^3$ limit above which Stasi et al. rescanned patients.\textsuperscript{19} The rectal characteristics of the patients included in this study suggest that the acquisition of a repeat CT scan was justified.\textsuperscript{4,20,21}

On the initial planning scan in this study the rectal diameter was found to be the largest at the superior (base) of the prostate; this corresponds with the literature. Sripadam et al.\textsuperscript{27} observed that most rectal wall displacements were at the level of the prostate base, while Fiorino et al.\textsuperscript{28} found that rectal motion was largest in the more superior part of the rectum. This indicates that the prostate moves mainly at the base because of rectal filling but prostate and rectum mobility are reduced at the apex.\textsuperscript{21,27,29}

The majority of the patients’ studied rectal characteristics on the initial planning CT scan were larger than on the rescan. Although this was to be expected as a distended rectum was the reason the rescan was performed, Pinkawa et al.\textsuperscript{21} found that repeating a planning CT scan might not be helpful, as patients with a large rectal volume initially were inclined to present again with a large, distended rectum. The reduction in all measures of distension other than rectal diameter at the level of the inferior of the prostate in all but two of our patients suggests that rectal volume can be successfully controlled with the current departmental laxative protocol given before the rescan. Therefore, the rescan values should be more representative of the state of the rectum during treatment, assuming that the laxatives work daily throughout treatment and especially when the side effects begin to occur.

A bladder filling protocol was also used, although in this study, the bladder volume was smaller on the initial CT scan than on the rescan which may have also impacted on the movement of the prostate. However, the relative change in the bladder volume between scans was much smaller than those in the rectal volume and rectal diameter at the level of the base of the prostate and many previous organ motion studies have concluded that prostate motion is correlated less strongly with changes in bladder volume than with changes in rectal volume (for example, refs.\textsuperscript{18,19,30,31,32}). (These studies along with several others form the evidence on which the practice for patients having a full bladder and an empty rectum during planning and treatment is based.\textsuperscript{13,15,16,33,34})

The median prostate displacements recorded in this study were 1 mm laterally, 2 mm in the anterior–posterior direction and 3 mm in the superior–inferior direction, with a median overall displacement of nearly 5 mm. These are comparable to data published in the previously mentioned organ motion studies. The variability in the published information on prostate displacement can be accounted for by different patient setup conditions (e.g., prone vs. supine), different rectal filling protocols and by the use of different methods to determine prostate motion.\textsuperscript{35,36} and highlights the importance of institution-specific knowledge of the effects of prostate displacement.

All the plans produced during this study met the department’s dosimetric criteria for prostate plans, with at least 99.8\% of the PTV receiving 95% of the prescription dose in every plan and all bladder and rectal doses being within tolerance. This uniformly high quality of the treatment plans produced indicated that the results were due to anatomy changes between the CT scans and not affected by inconsistent planning.

No significant differences were found in either the PTV dose parameters or the maximum bladder and rectal doses between the plans produced on the initial CT scan and the rescan. Although the maximum rectal doses were comparable, differing by less than 1\%, a statistically significant difference in the volume...
of rectum receiving lower dose levels was found between the two CT scans. The higher rectal doses on the rescan may be due to the smaller rectal volume, as a higher proportion of the rectum was included in the higher isodose regions, therefore increasing the risk of rectal toxicity.21

The changes in rectal volume and any resultant prostate motion were examined in this study to determine their implications for delivered doses. Significant differences were found between the initial planning CT scans’ PTV and rectal doses and these doses when the plan was transferred without modification to the rescan. The PTV doses on the initial planning scan were significantly higher than on the registration rescan. The homogeneity of PTV dose is known to be a significant factor in determining the probability of tumour control.37 The large increase in PTV inhomogeneity resulting from the reduction in minimum dose suggests that the outcome of the treatments in terms of tumour control would be significantly worse if the patient had not been rescanned and their treatment was planned on the initial planning scan but during treatment their rectal status resembled the rescan.

This situation is clinically realistic, as previous research has shown that during radiotherapy treatment rectal volumes decrease due to increased rectal urgency caused by the side effects of the treatment.3,20,21,38 The distended rectum on the initial planning scan introduces a systematic error as the prostate is positioned more anteriorly than during treatment, as represented by the registration rescan, when the rectum is not distended the prostate will move posteriorly resulting in underdosage of the PTV and a poorer clinical outcome.3,4,24

The results in Table 5 demonstrate that rescanning the patients resulted in higher rectal doses than would have been received, had they been planned on the initial scan. However, the median increases in the percentage of the rectum receiving 90% of the prescription dose and the dose received by half of the rectum did not take any patients outside the tolerances for the rectum in use at our institution and so would be considered clinically acceptable, given the much larger reductions in PTV coverage that accompanied them.

This planning study has demonstrated statistically significant reductions in PTV coverage if the rectum is less distended during treatment than at the time of the planning CT scan. Although planning studies cannot, by their nature, directly predict the clinical significance of these reductions, the lower tumour control probability associated with lower PTV doses is well-established and other research clinically supports these theoretical dosimetric consequences, having demonstrated that rectal distension visible on the planning CT scan results in worse biochemical failure rates and a decrease in tumour control.4,20,24

In this study, the position of the prostate was compared on only two CT scans. However, only by acquiring a CT scan at the time of each treatment fraction could the differences between the patients’ anatomy at the time of CT scanning and at treatment be fully quantified. Intra-operator variability in contouring might have influenced the comparison performed. However, this would not be expected to significantly change the results of the study, as evidence in the literature shows that intra-observer variability in contouring the rectum on radical prostate plans is sufficiently small to be unlikely to have an impact on conformal treatment planning.19,39,40

Differences in rectal volumes between the planning scan and throughout the course of treatment is an issue that is continuously being addressed in the literature. Several studies have recommended scheduling the planning session and daily treatments for a similar time of day to help with the reproducibility of rectal filling, especially after 10 AM as it is expected that the majority of people defecate in a morning.27,41,42 In addition, throughout treatment the rectum may distend due to rectal gas as well as solid contents.4 Ogino et al.43 asked patients before planning and treatment to insert their index finger and wash their rectums to remove their rectal gas. They reported that this method was effective at reducing the average rectal cross-sectional area and decreasing prostate motion. However, there
could be practical and patient compliance issues associated with this procedure. Smitsmans et al.\textsuperscript{41} also introduced the use of a dietary protocol for patients receiving prostate radiotherapy and found that it significantly decreased the incidence of faeces and moving gas in the rectum, therefore reducing prostate motion.

In this study, daily ultrasound imaging was used to verify the position of the prostate at the time of treatment. Any differences in the position from that on the CT scan were corrected for and the magnitude of the correction required recorded. The mean shifts from planned to actual positions from this ultrasound data were 0.7 mm laterally (SD 3.2 mm), 1.1 mm anteriorly (SD 3.4 mm) and 0.9 mm superiorly (SD 1.4 mm). Although larger displacements were seen on individual treatment fractions, these average values across the course of treatment represent smaller displacements than those seen between the two planning CT scans. The standard deviations on the anteroposterior and superoinferior movement are of a similar size to the movements reported by Ogino et al.\textsuperscript{43} for the patients who removed rectal gas from their rectums prior to treatment. These values suggest that the stability of rectal filling and the resultant prostate positioning in this study do not compromise the validity of the dosimetric comparisons.

The magnitudes of the prostate movements in this study were mostly less than 5 mm in any direction, so the 1 cm PTV margin seems appropriate, given current protocols. However, a systematic setup uncertainty in the same direction might result in incomplete coverage by this margin and only with image guided techniques will there be certainty that any of the issues in this study are being fully accounted for all patients. The results of this study are currently being used in the development of cone-beam CT image-guidance protocols, with which further research is to be undertaken.

**CONCLUSIONS**

This retrospective planning study has demonstrated the dosimetric consequences for prostate patients receiving 3DCRT of rectal distension at the time of the initial planning CT scan.

The results showed that the planned PTV dose was not dependent on rectum size. Rescanning showed that the use of the departmental laxative protocol resulted in significant reductions in rectal size. The reduction in rectal filling resulted in an average displacement of the prostate of almost 5 mm. If the patient was scanned with a full rectum, but treated with an empty one, the PTV would be underdosed (such that the median value of the minimum PTV dose was just 61\% and there would be a significant reduction in coverage of the 95\% isodose). Rescanning the patient removes the systematic underdosing of the PTV, although at the cost of a slightly higher, but clinically acceptable, rectal maximum dose. Therefore, patients who present for initial CT with a full rectum must be rescanned in order to avoid a systematic underdosing of the PTV.

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