Impact of bladder volume on radiation dose to the rectum in the definitive treatment of prostate cancer

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Background and objective Our group created and routinely reviewed a dedicated prostate intensity-modulated radiation therapy (IMRT) delivery program. Previously, a retrospective review of our experience demonstrated that a larger bladder volume reduced radiation dose to the rectum. We conducted an observational study to confirm this relationship.

Methods Men receiving definitive radiation for prostate cancer were eligible for the study. Eligible patients received 2 computed axial tomography (CT) scans on the day of their planning CT scan: 1 with a full bladder and 1 with an empty bladder. On each CT data set, the prostate, rectum, bladder, penile bulb, and femoral heads were contoured. 2 IMRT plans were completed on each dataset: 1 by a medical dosimetrist and 1 by a medical physicist. The study plans targeted the prostate to 79.2 Gray (Gy) while respecting predefined dose tolerances to the other contoured structures. Rectal doses were compared on empty and full bladder CT data sets.

Results From June 29, 2010 to December 14, 2011, 17 full bladder data sets and 15 empty bladder data sets were available for analysis. Median change in bladder volume was 63 ml. Full vs empty bladder set-up was associated with a statistically significant reduction in the mean rectal dose of 25.41 Gy vs 27.6 Gy (P = .031).

Limitations Small sample size and small variations in bladder volumes.

Conclusions A greater bladder volume resulted in a reduced mean dose to the rectum irrespective of planning method.

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Prostate cancer is the most commonly diagnosed cancer in men in the United States[1] and is often treated definitively with radiation therapy with or without androgen deprivation therapy.[2] Modern methods of radiation delivery typically use intensity-modulated radiation therapy (IMRT) combined with some form of image guidance.[2] IMRT is a valuable delivery technique given its ability to limit dose to surrounding critical organs at risk while still delivering large doses of radiation to the prostate. This is important given the value found in dose escalation to the prostate in several phase 3 trials.[3-7] In a routine review of our prostate IMRT program, it was observed that as the volume of the bladder increased, the dose to the rectum decreased in a statistically significant manner (unpublished data). Because there is a link between mean radiation dose to the rectum and rectal injury[8] as well as to quality of life,[9] any simple measures that could be taken to reduce radiation dose to the rectum would be of potential value to community radiation oncologists and their patients. At the time of this observation, there was only 1 study that had attempted to evaluate the impact of bladder volume on rectal dose when treating prostate cancer.[10] That study, however, used a traditional four-field box and conformal planning techniques so the ability to spare the rectum was more limited than it is with modern IMRT delivery methods. Because our observation was made in a retrospective manner, we were not able to account for other variables that might have had an impact on this apparent association. We therefore conducted a prospective observational study to evaluate the impact of bladder volume on the dose received by the rectum when treating the prostate with an IMRT technique.

Methods

Men with nonmetastatic prostate cancer who elected to be treated with definitive radiation therapy targeting the prostate or prostate and seminal vesicles were eligible for enrollment on this study.

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On the day of their planning computed axial tomography (CT) scan, 2 scans were obtained back to back. At the initiation of the study, our standard practice was to obtain prostate treatment planning CT scans with IV contrast and a full bladder. After the full bladder scan was obtained, the man would be asked to void, and the second scan was immediately performed without contrast. It was noted that our standard prescan full-bladder patient instructions often resulted in very full bladders and many men were not able to empty their bladders completely in the short amount of time we requested. We therefore modified our process to allow men to arrive with empty bladders so that we could obtain the noncontrasted empty-bladder scan first. After that scan had been done, an IV would be started and contrast given. A short period of time was allowed to pass to allow some filling of the bladder (a consequence of no fluid restrictions before the CT and the effects of 100-120 ml of IV contrast) and then the full-bladder scan would be obtained. Regardless of the sequence, the goal was to have 2 CT scans obtained in relatively short order with minimal changes to internal organs other than the volume of the bladder.

Once the 2 scans were obtained, simulated treatment plans were generated from each of the paired CT data sets. The prostate as well as organs at risk (bladder, rectum, penile bulb, and femoral heads) were contoured by a physician (BF) in accordance with standards of the Radiation Therapy Oncology Group (RTOG)[11] on all CT data sets. A planning target volume (PTV) was created by expanding the prostate contour: 5 mm posterior, 6 mm superior, and 7 mm in all other directions. Standard isocenter placement and dose constraints were used for all planning. A dose of 79.2 Gy was prescribed to the PTV in which 99% of the dose was required to cover 95% of the volume. Two treatment plans were generated for each data set using a standardized five-field IMRT plan in which one of two sets of beam arrangements were permitted. One beam arrangement consisted of beams entitled G45, G105, G180, G255, and G315 while the other option consisted of G45, G95, G180, G265, and G315 in which G refers to gantry angle and the naming convention for gantry angles refers to a 360-degree arc with G0 = posterior to anterior (PA), G90 = left lateral, G180 = anterior to posterior (AP), and G270 = right lateral.

The medical dosimetrist (JF) would create a plan using the five-beam option which resulted in a plan that best maximized target coverage and minimized dose to organs at risk. The physicist (CA), would begin with whichever beam arrangement the dosimetrist used on a particular patient's data sets and would then have the dose-volume optimizer of the IMRT planning system (Eclipse 10.0.34; Varian Medical Systems) run 150 iterations using the same dose requirements and dose constraints and the final plan results recorded. Avoidance of organs at risk was achieved by using 6 dose constraints to the rectum, 3 to the bladder, 2 to the femoral heads, and 2 to the penile bulb. At all steps of planning, priority was given to achieving dose coverage to the PTV. Our purpose for testing 2 planning processes was to determine if the relationship between bladder volume and rectal dose was personnel dependent or if the observation was applicable to more than one planning process.

On each created plan (2 per CT data set), the following information was compiled from the dose volume histogram: bladder volume, mean and median rectal dose, volume of rectal tissue (percent and absolute volume measured in cubic centimeters of tissue) receiving 30 Gy, 40 Gy, 50 Gy, 60 Gy, 70 Gy, and 75Gy. Our primary analysis compared rectal dose-volume histograms (DVH) that compared each man's full bladder scan with the empty bladder scan. We evaluated the effect of bladder filling on the mean radiation dose received by the rectum, which corrected for differential bladder filling, and type of planning (dosimetrist vs unassisted planning) using a linear mixed-effect model. A P value of <.05 was considered significant. All calculations were carried out in SAS v9.2 (Cary, NC). Additional measures of dose and volume were recorded to better illustrate the impact of the planner and method of planning on a range of rectal doses.

Results

Seventeen men underwent CT-based treatment planning for clinically localized prostate cancer. Two patients were unable to void immediately after the full-bladder CT scan and were excluded from this analysis. Descriptive summary statistics are shown in Table 1. The median full and empty bladder volume differed by 63 ml in the 15 evaluable patients.

Treatment plans were generated by both a dosimetrist and a physicist for the 15 evaluable patients. There was a graduated effect of the change in the dose to the rectum, with higher dose regions experiencing less of an effect with bladder volume compared with lower dose regions. The former was true regardless of the magnitude in total bladder volume change between the empty and full state. The relationship between the dose received to the rectum and the bladder volume was evaluated in several ways: mean and median rectal dose, volume of rectal tissue (percent and absolute volume measured in cubic centimeters of tissue) receiving 30 Gy, 40 Gy, 50 Gy, 60 Gy, 70 Gy, and 75 Gy. There was no statistical significant difference at any specific dose point other than mean dose. The mode of treatment planning was not associated with the mean rectal dose (P = .083) on linear mixed-model regression analysis.

A significant amount of heterogeneity was noted across both the bladder volume and change in bladder volumes

TABLE 1 Full- and empty-bladder volumes for eligible men

	Full bladder (n = 17)	Empty bladder (n = 15)	Difference
Median volume, ml (IQR)	138.1 (97.5-245.1)	64.4 (44.1-78.0)	63 (45.1-126.6)

IQR, interquartile range

across patients. To account for the correlation between readers and varied bladder volume changes, a linear mixed-model regression analysis was used to assess the effect of full bladder compared with empty bladder on mean rectal dose. Using a linear mixed-model regression analysis, we found that a full versus empty bladder set-up was associated with a statistically significant reduction in the mean rectal dose of 25.41 Gy versus 27.6 Gy (P = .031), respectively; and that there was a statistically significant impact of using dosimetrist-based planning compared with unaided software-based planning, with a modest reduction of 1.2 Gy in mean dose to the rectum associated with dosimetrist based planning (27.0 Gy vs 25.8 Gy, P < .001, respectively). The impact of this modest reduction in mean dose to the rectum cannot completely account for the reduction in mean rectal dose seen with planning with a full bladder compared with an empty bladder scan. This would seem to further support the value of planning and treating with a full bladder as a means to limit dose to the rectum.

Discussion

The results of our study verify our retrospective review of the impact of bladder volume on mean rectal dose when IMRT is used to deliver definitive doses of radiation to the prostate. To our knowledge, this is the first study of its kind to address this association when using IMRT. One group[10] studied this association in a non-IMRT setting, but the study had several methodological issues that limited the ability to detect an effect of bladder volume on rectal dose. First, the men were instructed to empty their bladder an hour before the planning CT scan. Although this created some uniformity in the way in which men were managed, it gave ample time for bladder refilling. Furthermore, the degree of bladder refilling could not be controlled unless the men's access to fluids was controlled before and after this bladder emptying. Second, the treatment planning process included margins of 1 cm on the prostate. Although those margins were once considered standard, current treatment margins are often smaller. Thus, the larger margins may have minimized any potential impact of bladder volume on the mean rectal dose. Third, the conformal planning process consisted of a four-field box with treatment fields consisting of anterior to posterior, posterior to anterior, right lateral, and left lateral treatment fields. AP and PA treatment fields will include an increased rectal volume because of the lack of avoidance of rectal tissue from these treatment angles. With movement of the prostate predominately in a superior-inferior and anterior-posterior direction,[12] AP and PA treatment fields will limit rectal dose in only one range of prostate motion (superior-inferior). Because the anterior-posterior range of motion is not accounted for completely by the planning process, small improvements in rectal dose owing to differences in bladder volume could be negated. Our planning process allowed dose to be delivered with more flexibility for avoiding the rectum, and IMRT allowed a method for sparing the rectum in the planning process at all gantry angles. With these advancements in planning, we were able to detect a small improvement in rectal dose sparing afforded by the bladder volume.

This study was designed as a dosimetric evaluation and as such, we did not track in any way a link between our findings and acute toxicity. In fact, that would have been impossible in that each man served as his own internal control and our departmental policy was to always treat these men with a full bladder. Recently, however, Jain et al[13] reported on their experience treating high-risk prostate cancer patients using 3 different techniques to target the prostate, seminal vesicles, and pelvic nodes at risk. They found, in their acute toxicity analysis, that bladder volume had the greatest impact on acute gastrointestinal toxicity. It would be at least reasonable to theorize that a reduction in dose to the rectum as seen in our study could in part explain their findings.

Our study had limitations. First, we did not find a clear link between bladder volume and any specific dose to the rectum. This may have been a result of the small sample size. This is an important limitation in that several investigators have found rectal doses on the order of 70 Gy or greater to have prognostic value in terms of rectal toxicity.[9,14-16] It must be stressed, however, that others have found value to the mean rectal dose. In a paper by Stenmark et al,[9] the investigators observed that with an increasing mean rectal dose came an associated decrease in bowel-related quality of life. We were not able to clearly identify an explanation for this bladder volume effect on rectal dose. Although there is no clear explanation for that, the prospective evaluation of this effect did confirm our previous findings of a retrospective data analysis (data unpublished).

One value we see in these data is that this is a simple, cost-effective way of limiting dose to the rectum during

the prolonged treatment course required for the definitive treatment of prostate cancer. Other more complicated techniques are available that will affect the rectal dose delivery, such as the placement of spacer material into the body to create a space between the prostate and rectum[17-19] or the daily placement of an endorectal balloon.[20] Although spacer and endorectal balloons might result in more dramatic reductions in rectal dose, they are more invasive and not practical in many community settings. Furthermore, men treated in the community may be less willing to subject themselves to such invasive procedures. Treatment daily with a full bladder, however, is noninvasive and easily accomplished by most men.

In conclusion, treatment in men with a full bladder was associated with a statistically significant reduction in the mean rectal dose. Treating men with a full bladder is a simple cost-effective method that can be used in the community setting to reduce radiation dose to both the bladder and the rectum when targeting the prostate with radiation therapy.

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