Clinical Investigation: Genitourinary Cancer

Adaptive Image-Guided Radiotherapy (IGRT) Eliminates the Risk of Biochemical Failure Caused by the Bias of Rectal Distension in Prostate Cancer Treatment Planning: Clinical Evidence

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Summary

CT-based offline adaptive IGRT allows for the correction of patient-specific, inter-fractional, prostate position secondary to internal organ motion and deformation. The incorporation of adaptive IGRT into prostate cancer treatment appears to reduce the risk of geometric miss and results in good biochemical control that is independent of rectal volume at the time of simulation while maintaining low rates of toxicity.

Purpose: Rectal distension has been shown to decrease the probability of biochemical control. Adaptive image-guided radiotherapy (IGRT) corrects for target position and volume variations, reducing the risk of biochemical failure while yielding acceptable rates of gastrointestinal (GI)/ genitourinary (GU) toxicities.

Methods and Materials: Between 1998 and 2006, 962 patients were treated with computed tomography (CT)-based offline adaptive IGRT. Patients were stratified into low ($n = 400$) vs. intermediate/high ($n = 562$) National Comprehensive Cancer Network (NCCN) risk groups. Target motion was assessed with daily CT during the first week. Electronic portal imaging device (EPID) was used to measure daily setup error. Patient-specific confidence-limited planning target volumes (cl-PTV) were then constructed, reducing the standard PTV and compensating for geometric variation of the target and setup errors. Rectal volume (RV), cross-sectional area (CSA), and rectal volume from the seminal vesicles to the inferior prostate (SVP) were assessed on the planning CT. The impact of these volumetric parameters on 5-year biochemical control (BC) and chronic Grades ≥ 2 and 3 GU and GI toxicity were examined.

Results: Median follow-up was 5.5 years. Median minimum dose covering cl-PTV was 75.6 Gy. Median values for RV, CSA, and SVP were 82.8 cm^3, 5.6 cm^2, and 53.3 cm^3, respectively. The 5-year BC was 89% for the entire group: 96% for low risk and 83% for intermediate/high risk ($p < 0.001$). No statistically significant differences in BC were seen with stratification by RV, CSA, and SVP in quartiles. Maximum chronic Grades ≥ 2 and 3 GI toxicities were 21.2% and 2.9%, respectively. Respective values for GU toxicities were 15.5% and 4.3%. No differences in GI or GU toxicities were noted when patients were stratified by RV.

Conclusions: Incorporation of adaptive IGRT reduces the risk of geometric miss and results in excellent biochemical control that is independent of rectal volume/distension while maintaining very low rates of chronic GI toxicity. © 2012 Elsevier Inc.

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Conflict of interest: none.

Introduction

The advent of three-dimensional conformal (3D-CRT) and intensity-modulated radiotherapy (IMRT) for prostate cancer has allowed for improved target conformality and isodose coverage. This has translated into improved biochemical control (BC) by means of permitting dose escalation. The premise of dose escalation, however, is limited by the radiation dose delivered to the organs at risk (OAR): the bladder and the rectum. This emphasizes the importance of minimizing the margins added to the clinical target volume (CTV) when accounting for patient position and internal organ motion variations. A caveat in deriving a planning target volume (PTV) with a limited CTV expansion is the increased possibility of geometric miss and inferior clinical outcomes, especially when rectal distension is noted at the time of computed tomography (CT) simulation (1–3).

Prior reports have demonstrated an association between rectal distension and increased risk of biochemical failure (BF) (1–3). These reports have also documented a decreased incidence of rectal toxicity in patients with distended rectum (1, 3). One of the major limitations has been the lack of image guidance during treatment (1), despite the use of CT simulation and 3D-CRT planning. Kupelian *et al.* have demonstrated the value of IGRT in that they have reported similar BC between patients with distended and nondistended rectum at the time of the planning CT when ultrasound-based prostate position was verified daily (4). The incorporation of image guidance exploits the goal of conformal therapy—that is, to provide a "tight" isodose distribution to adequately cover the PTV and to minimize the dose to the OAR.

CT-based offline adaptive image-guided radiotherapy (IGRT) has been incorporated into prostate cancer treatment since 1997 at William Beaumont Hospital. As a part of the adaptive radiotherapy (ART) process, four serial helical CT scans are obtained during the first week of treatment, which allows for the correction of patient-specific interfractional prostate position secondary to internal organ motion/deformation. The patient-specific confidence-limited PTV (cl-PTV) is generated, which usually has a smaller CTV-to-PTV expansion to allow for safe dose escalation and a maximally minimizing dose to the OAR. The aim of this retrospective analysis is to study the effect of rectal volume/distension on BC and gastrointestinal (GI)/genitourinary (GU) toxicity in patients treated with the ART technique.

Methods and Materials

Patient population

Between 1998 and 2006, 962 patients with clinically localized (T1-3N0M0), biopsy-proven prostate adenocarcinoma were treated with CT-based offline adaptive IGRT at William Beaumont Hospital. Patients were stratified into either low (group I; $n = 400$) or intermediate/high (group II; $n = 562$) National Comprehensive Cancer Network (NCCN) risk groups. Patients were assigned to group I if they met all of the following criteria: Gleason score ≤ 6, prostate-specific antigen (PSA) <10, and clinical stage $\leq$T2a. Group II included the remaining patients. A total of 228 patients (23.7%) received neoadjuvant androgen deprivation. This study was approved by the Human Investigation Committee (Protocol #2006-038).

All patients were evaluated with history and physical examination, including a digital rectal examination, chest roentgenogram, complete blood count, basic metabolic panel, and a pretreatment PSA. Pelvic CT and bone scans were performed at the treating physician's discretion. After treatment, patients were clinically evaluated with digital rectal examination and PSAs every 3–6 months.

CT-based offline adaptive IGRT technique

Our offline adaptive IGRT has been previously described (5). Briefly, patients underwent a virtual CT simulation with urethrogram. No bladder catheterizations, diet modification, laxatives, or rectal enemas were used. GTV and normal structures including the bladder, rectum, and small bowel were defined on the initial planning CT. Four additional CT images were obtained after each fraction during the first week to account for patient-specific organ motion and deformation. For group I, the CTV encompassed the prostate only, whereas the proximal 2 cm of the seminal vesicles were included for group II, which is based on our prior pathologic analysis (6). The PTV for the initial five fractions (9 Gy) was derived by CTV+1 cm uniform expansion. A standard four-field 3D conformal plan was designed to cover the PTV with at least 95% of the prescribing dose. The first four daily CT images were registered based on bony anatomy to the planning CT, the CTV was manually delineated on each daily CT image, and an internal target volume (ITV) was generated by a union of all five CTVs on the planning CT and four daily CTs. Patient bony setup variation was accounted for using electronic portal images. These imaging data were then entered into a prediction model to generate a cl-PTV, which compensates for geometric variation of the target motion and patient setup (5). A new 3D-CRT or IMRT treatment plan was then generated to cover the cl-PTV with a minimum dose of 70.2–79.2 Gy at 1.8 Gy per fraction. The total dose selected for each patient was based on predefined dose-volume constraints to the rectal wall and the bladder defined on the planning CT image: rectal wall dose constraints of $V_{82Gy} \leq 5\%$ and $V_{75.6Gy} \leq 30\%$ and bladder constraints of $V_{75.6Gy} \leq 50\%$ with a maximum of <85 Gy. No more than 10% dose inhomogeneity was allowed within cl-PTV.

Assessment of rectal distension

The rectal distension was assessed on the planning CT by measuring three volumetric parameters: rectal volume (RV, from rectosigmoid junction to anal verge), cross-sectional area (CSA, rectal volume/length), and the rectal volume from the top of the seminal vesicles to the most inferior portion of the prostate (SVP). Each parameter was subdivided into four groups based on quartiles: RV (<63.3, 63.3–82.8, 82.9–115.4, and >115.4 mL), CSA (<4.4, 4.4–5.6, 5.7–7.9, and >7.9 cm^2), and SVP (<39.5, 39.5–53.3, 53.4–75.2, and >75.2 mL).