Radiotherapy and Oncology 125 (2017) 118–123

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Prostate cancer radiotherapy

Evaluation of high dose volumetric CT to reduce inter-observer delineation variability and PTV margins for prostate cancer radiotherapy

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ARTICLE INFO

Article history:
Received 17 January 2017
Received in revised form 20 July 2017
Accepted 7 August 2017
Available online 28 August 2017

Keywords:
Prostate radiotherapy
CT image quality enhancement
Inter-observer variability
CT and MR comparison
Planning target margin

ABSTRACT

Purpose: The aim was to determine whether the enhanced soft tissue contrast provided by high-dose volumetric CT (HDVCT) can reduce inter-observer variability in delineating prostate compared to helical conventional CT (CCT) scans and 3T MRI scans for patients undergoing radical prostate cancer radiotherapy. Secondly, to quantify the potential PTV reduction with decreased inter-observer variability.
Materials and methods: A 320 slice volumetric CT scanner was used. The wide-detector coverage of 16 cm enabled volumetric image acquisition of prostate gland in one rotation. Three imaging studies were performed on ten patients. CCT and HDVCT were performed consecutively at the same coordinate system followed by MRI. Five radiation oncologists delineated the prostate.
Results: The inter-observer variability is 2.0 ± 0.6, 1.9 ± 0.4 and 1.8 ± 0.4 mm for CCT, HDVCT and MR respectively with the maximum at the apex region. Comparing inter-observer difference variability between CCT and HDVCT with MR indicates that observers have larger variations in contouring using CCT than HDVCT especially at apex. Jaccard index of HDVCT is significantly higher than CCT with a mean difference of 0.03 ($p = 0.011$). Both MRI and HDVCT provide the opportunity for a 2 mm PTV margin reduction at the apex compared to CCT.
Conclusion: Inter-observer variability in delineation remains an important source of systematic error. HDCTV for treatment planning reduces this error without recourse to MRI and permits a PTV reduction of 2 mm at the apex. The margins required to account for residual error with any imaging modality are still greater than are used in typical current practice.
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Intensity modulated radiotherapy (IMRT) allows the dose distribution to closely match the target volume and the use of image guided radiotherapy (IGRT) [1–4] enables reproducible patient positioning at each treatment fraction. These advanced techniques improve treatment precision; however they are highly dependent on accurate delineation of the target volume in the planning images. These are most frequently computed tomography (CT) images acquired specifically for radiotherapy. In the context of prostate cancer, discriminating the prostate from the surrounding soft tissues is difficult with CT alone due to low tissue contrast at the prostate boundary [5]. Significant inter-observer variability between clinicians [6–11], resulting in systematic errors especially at the apex [12,13] and in the interface between the posterior prostate and anterior rectal wall [14], with subsequent target under-dosage and/or normal tissue over-dosage have been reported. An additional margin may be added to the target volume to limit the risk of geographic miss due to this uncertainty; however, this increases the irradiated volume and dose to rectum and surrounding normal tissues, which in turn limits the dose that can be confidently prescribed to the prostate [15]. Mounting evidence supports the role of dose-escalation to the prostate for improved oncologic outcomes [16] and therefore there is a pressing need for highly accurate identification of the prostate in order to minimize late rectal complications.

MR imaging provides unparalleled soft tissue contrast compared with other imaging modalities, and may be used for prostate radiotherapy planning. Its use is limited by availability and unfamiliarity of the oncologic community with mechanisms to account for geometric distortion of the images, electron density information, and preparation of images for daily treatment guidance, all which pose challenges for an MR-only workflow in radiotherapy [17,18].

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http://dx.doi.org/10.1016/j.radonc.2017.08.012
0167-8140/

Novel multi-slice, wide coverage detector cone beam CT systems may enhance the image quality of planning CT by enabling a higher dose volumetric CT (HDVCT) within the tube loading constraints, improve low contrast detectability (LCD) compared to conventional helical CT (CCT). Enhanced CT image quality that is sufficient to reduce the uncertainty arising from inter-observer variability may permit smaller PTV margins for the prostate and decrease the dose to normal tissue without recourse to MR for planning purposes.

The aim of the study was (1) to determine whether the enhanced soft tissue contrast to noise provided by HDVCT scans can reduce inter-observer variability in prostate gland and apex delineation compared to CCT scans and MRI; the gold standard for soft tissue contrast for patients undergoing radical prostate cancer radiotherapy, and (2) to quantify the potential PTV reduction that is associated with decreased inter-observer variability.

Methods and materials

Imaging

Toshiba Aquillion 320 slice scanner with wide detector coverage [19,20] of 16 cm enabled volumetric image acquisition of prostate gland in one rotation of gantry, eliminating the need for helical scanning. HDVCT uses this volumetric approach to acquire multiple serial acquisitions of the same anatomy in a short 6 s time interval. The rapid acquisition of the volumetric imaging results in minimal motion artifacts, no increase in partial volume effects, and maintains continuity along the superior–inferior axis.

The HDVCT method and CCT were tested and compared at several different exposure settings, ranging from 300 mAs (CCT) to 3300 mAs. The RMI phantom (Gammex, Model number 467) was used to measure the SNR at 454 (breast) contrast level corresponding to physical density of 0.99 g/cm^3 and CT number of 44 close to prostate CT number ~35 ± 10 HU. Using SNR measured values, CNR was calculated at each selected mAs for 454 contrast level. The CatPhan (Phantom Laboratory Inc., Model 504) was used to evaluate low contrast detectability (LCD) and comparison between CCT and HDVCT. The LCD was measured and compared between HDVCT and CCT by counting the maximum number of visible targets and minimum target size for each mAs at each contrast level. The number of visible targets in each image was counted by three different individuals and an average number was determined. The CTDI adult body phantom and Landauer nanoDot optically stimulated luminescence (OSL) detectors [21] were used to measure the imaging dose. The measurements were performed at central rod location of CTDI phantom for both HDVCT and CCT protocols.

Ten patients undergoing radiotherapy for localized prostate cancer provided informed consent and participated in this Research Ethics Board approved study. Three imaging studies were performed on each patient: (i) helical CCT at 120 kV, 350 mAs (voxel size of $0.88 \times 0.88 \times 2$ mm^3, 300–400 mm of z-coverage), and 10–15 s scan time. (ii) HDVCT at 120 kV, 3300 mAs (voxel size of $0.88 \times 0.88 \times 2$ mm^3, 160 mm of z-coverage) and 6 s scan time. (iii) Non-contrast enhanced T2 weighted MRI on a 3T Siemens Magnetom Verio, voxel size of $0.7 \times 0.7 \times 2$ mm^3. The CCT and HDVCT scans were performed consecutively with less than 5 s interval in the same reference frame of the CT scanner. The time interval between the CT scanning and MR scanning was less than 1 h. All scans were transferred to Pinnacle^3 version 9.8 treatment planning system (Philips Medical Systems Inc, Fitchburg, WI) for delineation and analysis.

Target delineation

Five experienced genitourinary radiation oncologists independently delineated the prostate gland on each of the 3 image sets (CCT; HDVCT; MRI) for all ten cases. For inter observer variability measurements, the delineators were blinded to the patient and to the contours of other delineators. A schedule of contouring tasks designed to minimize memory bias was employed; images from a particular case were contoured only once per session with a minimum of a week between sessions. For intra observer variability measurements, only two of the observers repeated the delineation process after 7 months on the same 3 image sets (CCT; HDVCT; MRI) for all ten cases.

Volumetric target analysis

Delineated contours on each slice of the image set were converted into a black/white mask image where the pixel value is either 0 for outside or 1 for inside of the delineated prostate contour. The mask pixel size was 0.2 mm × 0.2 mm. A 3D volume of the prostate was then reconstructed by stacking mask images. 3D surface of prostates were sampled in equally spaced sample points in polar coordinate (15 degree apart in longitudinal and 7.5 degree in latitudinal direction) at 23 × 24 sample points (longitude × latitude) with the origin at the center of mass of each prostate, totaling 552 sample points. The base of prostate is defined as the superior quarter (latitude of 45 degrees or larger) of the prostate, and the apex of the prostate is defined as the inferior quarter of the volume. Distance of each sample from the origin was used to compare prostate delineation variability.

Inter- and intra-observer variability analyses

Inter- and intra-observer variability/uncertainty was measured using the standard deviation of the 5 observations for each sample point (total of 552 for each image). The overall inter-observer variation for each sample point was calculated using $\Sigma_{\text{inter}} = \sqrt{\frac{\sum_{j=1}^{P} \sigma_j^2}{P}}$, where $P = 10$ is the number of patients. Paired t-test was used to examine the difference of uncertainty Σ_{inter} between modalities. The correlations of delineated volumes between imaging modalities were estimated using intra-cluster correlation coefficient (ICC). To compare inter- and intra-observer variability between observers and between modalities, we defined similarity index according to the methods recommended by Rasch et al. [11] in which the common volume is the smallest delineated prostate volume (intersection) by all the observers and encompassing volume is the largest volumes (union) outlined by the observers. The ratio between the common and encompassing volume is defined as the "Jaccard similarity index" and is indicative of the uncertainty in delineating the prostate in that particular scan. If the Jaccard index is small, the overlap volume is low, contour variation is high and observer-related uncertainty is large. All statistical tests were two-sided, and a p-value lesser than 0.05 was considered statistically significant. Due to the exploratory nature of this study, multiple testing was not adjusted [22].

PTV margin calculations

Daily image-guidance addresses inter-fraction motion and set up errors, leaving contouring-related variability as the major source of error to be accounted for in the PTV margin. The PTV margins arising from inter-observer variability in prostate delineation were calculated using the Van Herk's formula [23] with any error in delineation treated as an additional systematic error.

PTV margin was calculated using $2.5\boldsymbol{\Sigma} + 0.7\boldsymbol{\sigma}$, where $\sum$ is systematic error of contour that includes 95% of the inter-observer variability ($\sum_{\text{inter}}$) at all sample points in each region (Base, Mid, Apex, Ant, Post, Lt and Rt directions). For intra-fraction motion systematic error was assumed negligible and the quadratic sum of