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Organ motion in gynecological RT

Quantification of vaginal motion associated with daily endorectal balloon placement during whole pelvis radiotherapy for gynecologic cancers

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ABSTRACT

Background and purpose: To quantify intra-treatment vaginal motion in women treated with daily endorectal balloon (ERB) placement and external beam radiotherapy for gynecologic cancers.
Materials and methods: Eighteen post-hysterectomy women with gynecologic cancers underwent computed tomography (CT) simulation scans and daily treatment with ERB. Fiducial markers were placed at the vaginal apex prior to simulation and patients were counseled on a pre-treatment bladder filling protocol. Weekly to biweekly verification CT scans were used to calculate the intra-treatment change in bladder volumes, rectal volumes, and fiducial coordinates along all axes. The planning target volume (PTV) margins required to encompass 95% of intra-treatment fiducial movement were calculated using the van Herk margin recipe.
Results: The median bladder volume was 223 (range, 29–879) cc for verification CT scans. Mean intra-treatment fiducial displacements were 1.7 (range, 0–9.1) mm, 2.9 (range, 0–15.5) mm, and 2.5 (range, 0–11.8) mm along the left–right (L/R), superior–inferior (S/I), and anterior–posterior (A/P) axes, respectively. The van Herk PTV margins were 3 mm (L/R), 10 mm (S/I) and 7 mm (A/P).
Conclusion: When compared to existing studies, the use of daily ERB with post-hysterectomy radiotherapy reduces vaginal motion along the A/P axis. The impact of variable bladder filling on vaginal motion is most evident along the S/I axis.

Pelvic radiation therapy is commonly given in the adjuvant setting to post-hysterectomy women with either cervical or uterine cancers with high-risk features [1]. Methods have historically included conventional and 3-dimensional conformational radiation therapy. However, intensity modulated radiation therapy (IMRT) and pencil beam scanning (PBS) proton therapy are two techniques that are gaining in favor over the aforementioned therapies due to their ability to treat the tumor bed and regional lymphatics with greater precision and diminished irradiation of surrounding, normal structures [2,3]. An acknowledged difficulty in the application of IMRT and PBS proton therapy is the need to account for discrepancies in the filling of internal organs and positioning of targeted tissues, particularly when treating the vagina. Studies of IMRT to the whole pelvis in post-hysterectomy women have reported inter-fractional displacements of the vaginal apex of greater than 2 cm [4–7]. While such deviations can be anticipated by increasing the planning target volume (PTV) margins, this additional coverage of the tumor bed is achieved at the risk of increased collateral irradiation of the normal bowel, bladder, and rectum.

Variations in rectal filling have been correlated with vaginal cuff movement along the anterior/posterior axis [8]. Immobilization of the vaginal cuff through the establishment of consistent rectal filling volumes may permit more accurate localization and treatment of the tumor bed. The placement of a fluid-filled, endorectal balloon (ERB) has been found to reduce prostate displacement in the anterior/posterior and superior/inferior directions in men treated with radiation for prostate cancer [9,10]. However, its use has not been explored in the treatment of gynecologic malignancies. As our group was beginning a clinical program to treat gynecologic cancers with proton therapy and as daily cone beam computed tomography (CT) imaging was not available on our proton gantries, we were interested in evaluating the use of an ERB to reduce vaginal motion. The objective of this study was to assess the degree of intra-treatment vaginal motion in post-hysterectomy women

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receiving either IMRT or PBS proton therapy with daily ERB placement.

Materials and methods

Eighteen post-hysterectomy women diagnosed with gynecologic cancer and treated by the University of Pennsylvania Department of Radiation Oncology between January 2013 and April 2014 were enrolled in our institutional review board approved, image-guided, radiotherapy study. All patients enrolled in the study completed the prescribed course of radiation therapy treatment. The median age of participants was 59 (range, 23–75) years. Primary sites included the uterus (9), cervix (8), and vagina (1).

CT simulation

In thirteen patients, gold fiducial markers were placed at the vaginal apex prior to simulation (five patients declined fiducial placement). All patients received full bladder and empty bladder CT simulation scans in the treatment position. Patients were instructed on bowel preparation, which included an enema two hours prior to simulation and approximately 500 mL of water to drink 30 minutes prior to simulation. An ERB was placed and inflated with 50–100 mL of fluid based on patient tolerance, and the volume of fluid was recorded. Full bladder CT simulation scans were performed from T10 to the upper thigh in 3 mm slices using a knee and foot lock device for immobilization. This served as the reference CT scan. Patients were instructed to empty their bladders, and empty bladder CT simulation scans were subsequently performed in the same position.

Treatment and contours

Full and empty bladder simulation CT scans were co-registered using bony anatomy. Vaginal clinical target volumes (CTV) were contoured on each dataset using Eclipse™ Treatment Planning System (Varian Medical Systems, Palo Alto, CA) and merged to generate a vaginal internal target volume (ITV). The CTV included the vagina and paravaginal tissues as described by Radiation Therapy Oncology Group (RTOG) guidelines [11]. Asymmetric margins of 1–1.5 cm were added to the vaginal ITV and 7–8 mm to the nodal CTV to establish the PTV. All patients were prescribed simethicone and counseled to repeat the bladder filling protocol by drinking 500 mL of water 30 minutes prior to daily treatments. Daily verification of setup position was performed using orthogonal kilovoltage (kV) X-ray imaging with alignment to bony anatomy. Patients were treated with a comfortably full bladder, daily placement of an ERB inflated with the same volume of fluid as the simulation CT scan, and 45–50.4 Gy of radiation to the whole pelvis in 1.8 cobalt gray equivalent daily fractions with either IMRT or PBS proton therapy. Weekly to biweekly verification CT scans were performed following treatment. These images were registered to the full bladder simulation CT scan using bony anatomy for alignment. The vagina, rectum, bladder, and fiducial markers were contoured on all simulation and verification CT scans by one individual (NT) and reviewed by an attending radiation oncologist (LL). The volumes of contoured organs were also calculated.

Fiducial and ERB analysis

In patients in whom fiducial markers were placed, fiducial movement served as a surrogate for intra-treatment motion of the vaginal cuff during the course of radiation therapy. As intra-fractional movement cannot be documented with kV X-ray images, it was not a part of our analysis. Fiducial coordinates were determined on CT scans with respect to two bony structures – the midpoint of the femoral heads (MFH) and the pubic symphysis (PS), as seen in Supplemental Fig. 1. True intra-treatment fiducial movement was defined as the difference between the fiducial to bony anatomy distance of each verification CT scan and the same measure on the reference CT scan. Values were averaged along the left–right (L/R), superior–inferior (S/I) and anterior–posterior (A/P) axes for all patients. Absolute intra-treatment fiducial movement was defined as the absolute value of the true fiducial movement. Mean, median, minimum, and maximum values for absolute intra-treatment fiducial movement were determined for all patients. Verification CT scan bladder volumes were normalized as percentages of the bladder volume from the reference CT scan (relative bladder volume). Values for true intra-treatment fiducial movement were fitted linearly to relative bladder volumes to assess fiducial movement with respect to changes in bladder filling. Pearson's correlation coefficients and coefficients of determination were calculated for each linear fit. This process was repeated for rectal volumes.

For each patient, the coordinates of fiducial markers from the verification CT scans were plotted as points (fiducial cluster) on the reference CT scan. The fiducial margins, or confidence radii necessary to encompass 95% of the points, were identified along all axes. The van Herk margin recipe, described by the equation: PTV margin = $\alpha\sum + \beta\sigma$, was used to calculate the CTV to PTV margins [12]. The standard deviation of systematic errors related to inter-patient uncertainties ($\sum$) was determined by calculating the standard deviation of the mean of the fiducial clusters. The standard deviation of random errors related to inter-fraction uncertainties (σ) was determined by calculating the root-mean-square of the mean of the fiducial clusters. In our study, coverage of the CTV for 95% of patients (α) with the 95% isodose line (β) resulted in respective α and β values of 2.79 and 0.7.

To verify our results, we assessed inter-fractional fiducial movement using daily kV X-ray images and evaluated the ERB for placement consistency. A digitally reconstructed radiography (DRR) image was generated from the reference CT scan for each patient to serve as the reference DRR image. Applying the same process implemented for verification CT scans to the daily kV X-ray images, absolute inter-fractional fiducial movement was determined along the L/R and S/I axes with respect to the PS and along the A/P axis with respect to the MFH. The displacements of the ERB tips on verification CT scans with respect to their positions on the reference CT scans were also calculated.

Results

A total of 104 CT scans and a median of 6 (range, 4–8) CT scans per patient were available for analysis. The median empty bladder and full bladder volumes from the simulation CT scans were 109 (range, 28–772) cc and 350 (range, 57–927) cc, respectively. The median bladder volume for all patients from the verification CT scans was 223 (range, 29–879) cc. In only two patients did all of the treatment bladder volumes fall within the range established by the empty bladder and full bladder simulation scans. Compared to the bladder, less variation was observed in rectal volumes. The median rectal volumes were 139 (range, 81–177) cc during simulation and 145 (range, 74–222) cc during treatment. The greatest observed verification CT scan rectal volume was 165% of the rectal volume of the corresponding reference CT scan.

Fiducial markers were expelled from the vagina of three patients after simulation, thereby yielding fiducial information for 10 of the 13 patients in whom they were placed. On CT scan analysis, absolute intra-treatment fiducial movement distances