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Analysis of nodal coverage utilizing image guided radiation therapy for primary gynecologic tumor volumes

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ABSTRACT

Purpose: To evaluate radiation dose delivered to pelvic lymph nodes, if daily Image Guided Radiation Therapy (IGRT) was implemented with treatment shifts based on the primary site (primary clinical target volume [CTV]). Our secondary goal was to compare dosimetric coverage with patient outcomes.
Materials and methods: A total of 10 female patients with gynecologic malignancies were evaluated retrospectively after completion of definitive intensity-modulated radiation therapy (IMRT) to their pelvic lymph nodes and primary tumor site. IGRT consisted of daily kilovoltage computed tomography (CT)-on-rails imaging fused with initial planning scans for position verification. The initial plan was created using Varian's Eclipse treatment planning software. Patients were treated with a median radiation dose of 45 Gy (range: 37.5 to 50 Gy) to the primary volume and 45 Gy (range: 45 to 64.8 Gy) to nodal structures. One IGRT scan per week was randomly selected from each patient's treatment course and re-planned on the Eclipse treatment planning station. CTVs were recreated by fusion on the IGRT image series, and the patient's treatment plan was applied to the new image set to calculate delivered dose. We evaluated the minimum, maximum, and 95% dose coverage for primary and nodal structures. Reconstructed primary tumor volumes were recreated within 4.7% of initial planning volume (0.9% to 8.6%), and reconstructed nodal volumes were recreated to within 2.9% of initial planning volume (0.01% to 5.5%).
Results: Dosimetric parameters averaged less than 10% (range: 1% to 9%) of the original planned dose (45 Gy) for primary and nodal volumes on all patients ($n = 10$). For all patients, ≥99.3% of the primary tumor volume received ≥ 95% the prescribed dose (V95%) and the average minimum dose was 96.1% of the prescribed dose. In evaluating nodal CTV coverage, ≥ 99.8% of the volume received ≥ 95% the prescribed dose and the average minimum dose was 93%. In evaluating individual IGRT sessions, we found that 6 patients had an estimated minimal nodal CTV dose less than 90% (range: 78 to 99%) of that planned. With a median follow-up of 42.5 months, 2 patients experienced systemic disease progression at an average of 19.6 months. One patient was found to have a local or regional failure with an average follow-up of 42 months.
Conclusion: Using only 3 dimensional IGRT corrections in gynecological radiation allows excellent coverage of the primary target volume and good average nodal CTV coverage. If IGRT corrections are based on alignment to the primary tumor volume, and is only able to be corrected in 3 degrees, this can create situations in which nodal volumes may be under dosed. Utilizing multiple IGRT sessions appears to average out dose discrepancies over the course of treatment. The implication of underdosing in a single IGRT session needs further evaluation in future studies. Based on the concern of minimum dose to a nodal target volume, these findings may signal caution when using IGRT and IMRT in gynecological radiation patients. Possible techniques to overcome this situation may include averaging shifts between tumor and nodal volume, use of a treatment couch with 6° of freedom, deformable registration, or adaptive planning.

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Introduction

Radiation therapy planning continues to evolve as developments in imaging and tumor volume registration techniques improve. Specifically, intensity-modulated radiation therapy (IMRT) treatments have gained increased attention for allowing smaller planning margins, dose escalation, and lower toxicity.[1-3] The benefits of IMRT, however, are only possible through accurate patient positioning. Reproducible positioning of the patient can be improved with image guidance radiation therapy (IGRT). The capability to accurately determine the targets and the organs at risk (OAR) is made more effective with the ability to account for organ motion, inter-fractional changes, and setup variability. For primary gynecologic targets, inter-fraction motion has been reported to change dose distribution when using IMRT, suggesting that image guidance be utilized to account for such changes.[4] With the utilization of IMRT and IGRT, there is potential for a greater precision in delivery of radiotherapy by accounting for and correcting these variables. This may permit a smaller planning target volume (PTV) expansion, than would otherwise have to be used. By allowing for the creation of smaller PTV expansion, there may be a reduction of dose to the OAR. With better planning, tumor control improves by allowing a larger fraction size or total dose to be delivered to the desired target volume.[5]

Correcting for positional change can be accomplished with image guidance. Random target shifts, occurring day to day, or systematic shifts, taking place as a result of persistent target change, may vary based on target site. Imaging of bony anatomy, as a surrogate for soft tissue positions, allows modest setup verification, but data has shown that shifts based on bony pelvic anatomy can be significantly inaccurate when related to body mass changes.[6,7] Pelvic bony alignment can be inaccurate to account for target motion regardless of body mass index changes as well.[8] The RTOG GOG 1203 randomized phase III study of standard *vs* IMRT pelvic radiation for postoperative treatment of endometrial and cervical cancer (TIME-C) has recently completed accrual and sheds further light on reproducibility of pelvic nodal volumes. This study was not active when patients were treated. The use of IGRT has seen an increasing trend. Surveys from the American Society of Radiation Oncology reported greater than 90% of radiation oncology centers, academic and private, are now using IGRT in routine treatment of patients and in 58% of patients with GYN malignancies.[9] Treatment of gynecologic tumors utilizing IGRT has been sparsely evaluated in comparison to prostate, lung, and head and neck. Tumors of the endometrium, cervix, and vulva are particularly at risk for inter-fractional movement because of their close association of the bladder and rectum.[10,11]

When accounting for primary target change, it is imperative to evaluate and correlate nodal dosimetry to prevent treatment failures. To account for shifts, it has been suggested to enlarge the planning margins not only for the primary gynecologic volume, but also for the at risk lymph node treatment volumes.[12] IMRT with IGRT has shown less potential for dose toxicity to the small bowel, rectum, and bone marrow.[13-15] However, gynecologic nodal dosimetry with IGRT based on primary volumes has yet to be evaluated. With retrospective studies describing a greater chance of failure for gynecologic cancer patients with nodal involvement, it is important to ensure adequate nodal coverage when employing image guidance.[16,17]

Furthermore, it is unclear for gynecological patients whether the inter-fractional shifts of the primary target and those of the nodal volumes are the same or even comparable. If the 2 volumes move in an independent manner, then the coverage of one or both targets may be compromised depending on the shifting strategy used for repositioning the patient under IGRT treatment. The aim of this project is to evaluate how nodal volume coverage is affected when inter-fractional shifts of the primary target are corrected with IGRT in 3 dimensions.

Table 1
Tumor control and characteristics

Patient	FIGO stage	Primary site	Follow-up (months)	Local recurrence (months)	Distant recurrence (months)
1	IC	Endometrial	39	0	15.7
2	IIA, N1	Cervix	57	0	0
3	IIA	Endometrial	29	0	0
4	IC	Endometrial	29	0	0
5	IIIA	Endometrial	35	0	23.4
6	IIB	Cervix	46	0	0
7	IB	Endometrial	51	0	0
8	IIB	Endometrial	61	0	0
9	IVA	Vulva	47	29	0
10	IB	Cervix	27	0	0
Average:			**42**	**29**	**19.6**

There were 2 patients with distant recurrences, and 1 local recurrence in the cohort. The average time for distant recurrences was 19.6 months. Both recurrence patients failed in the lung. Our average clinical follow-up time from diagnosis was 42 months. All patients are surviving.

Methods and Materials

A total of 10 patients who received radiation treatment between 2008 and 2011 for gynecological tumors at the University of Utah were retrospectively analyzed to estimate nodal dose delivered based on daily IGRT corrections from primary target volume shifts (Table 1). All patients were treated with IMRT to include the primary tumor site (intact or postoperative bed) and at risk lymph nodes. Treatment was performed using intensity-modulated radiation, based on CT volumes. For all cases, the treatment plans were created using the Eclipse treatment planning system (Version 10, Varian Medical Systems, Palo Alto, CA). The primary sites were prescribed 1.8 to 2.6 Gy per fraction, whereas the nodal volumes were prescribed a fractional dose of 1.8 Gy. Nodes were covered using a 7-mm CTV expansion around vessels and a 5-mm PTV expansion from CTV.

Patients were treated on a Siemens Artiste linear accelerator (Oncology Care Systems, Concord, CA) in a vault that contains a CT-on-rails (CTOR) system (SOMATOM Sensation 40, Siemens Healthcare, Erlangen, Germany) used for IGRT. Overall, 49 weekly IGRT sessions, with the 10 original planning CT image sets, were used for assessment.

For each CT dataset, CTOR images were fused to the planning CT and 3D translations were calculated for the purposes of virtually repositioning the patient. Clinical shifts were done daily based on CTOR information to best align the primary site and the lymph nodes. When there was a discrepancy, coverage of the primary site was the first priority. To recalculate the dose, each CTOR dataset was imported back into Eclipse and the primary and nodal volumes were re-contoured by one physician and independently confirmed by a second physician. Once the target volumes were re-contoured, the originally planned beams, with their respective fluencies, were used to recalculate the dose that was actually delivered to the patient for that particular fraction. We aimed to have 99% of the nodal volume receive 95% of the dose. One dataset per week was used for analysis. The dosimetric effect of the weekly IGRT was then analyzed using specific parameters including the maximum dose to the primary tumor volume, the minimum dose to the primary volume, the percentage of the primary volume receiving 95% of the prescribed dose, and the percentage of the primary volume receiving 105% of the prescribed dose (Table 2).

Results

Patient and tumor characteristics are shown in Table 1. The primary clinical target volume (CTV) from weekly fractions and the initial treatment plan on average was 105.88 cc (103.53 to 111.65 cc) for the cohort. Nodal volumes on average were 301.34 cc (294.6 to 311.6 cc) for the cohort (Table 2). The recreated volumes of the primary targets were found to be within an average of 4.67% of the initial planning volume (0.87% to 8.58%), whereas the volumes of the re-contoured nodal volumes were within an average of 2.98% of initial nodal volumes on average (0.01% to 5.52%).