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The equivalent dose contribution from high-dose-rate brachytherapy to positive pelvic lymph nodes in locally advanced cervical cancer

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ABSTRACT

PURPOSE: Definitive radiation therapy for locally advanced cervical cancer involves external beam radiation therapy (EBRT) and high-dose-rate (HDR) brachytherapy. There remains controversy and practice pattern variation regarding the optimal radiation dose to metastatic pelvic lymph nodes (LNs). This study investigates the contribution of the pelvic LN dose from HDR brachytherapy.

METHODS AND MATERIALS: For 17 patients with 36 positive pelvic LNs, each LN was contoured on a computed tomography (CT) plan for EBRT and on brachytherapy planning CTs using positron emission tomographic images obtained before chemoradiation. The mean delivered dose from each plan was recorded, and an equivalent dose in 2-Gy fractions (EQD2) was calculated. A Student's *t* test was performed to determine if the mean delivered dose is significantly different from the mean prescribed dose and EQD2.

RESULTS: The average prescribed dose from the total EBRT was 54.09 Gy. The average prescribed HDR dose to International Commission on Radiation Units point A was 26.81 Gy. The average doses delivered to the involved LNs from EBRT and brachytherapy were 54.25 and 4.31 Gy, respectively, with the corresponding EQD2 of 53.45 and 4.00 Gy. There was no statistically significant difference ($p < 0.05$) between the mean delivered and the prescribed doses for EBRT and between the delivered dose and the EQD2 for EBRT and brachytherapy.

CONCLUSIONS: Our study shows that the HDR contribution is 7% (4.00 Gy) of the total EQD2 (57.45 Gy). The HDR contribution should be accounted for when prescribing the EBRT boost dose to pelvic LNs for the optimal therapeutic dose. Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: Cervical cancer; High-dose-rate brachytherapy; Pelvic lymph nodes; Equivalent dose in 2-Gy fractions

Introduction

Up to 50% of patients with locally advanced cervical cancer (LACC) present with pelvic lymph node (LN) metastases (1–5). Control of pelvic nodal disease is therefore critical for progression-free and overall survivals in LACC patients. The standard treatment for LACC is concurrent chemoradiation therapy followed by brachytherapy (1, 5–10). Although metastatic LNs have been treated with high doses (>40 Gy) of radiation (8), there is little published literature on the therapeutic dose needed for the control of involved LNs and dose–response to the LN (6). With the correct dose escalation to pelvic LN, better clinical outcomes including better local control and less toxicity could be achieved.

Surgical staging was traditionally used to identify nodal disease, but imaging has been increasingly used to assess LN involvement to decrease the delay to treatment and potential surgical morbidity of LN sampling (11). Imaging has also evolved for the diagnostic detection of metastatic involvement of LNs in LACC. Positron emission tomography (PET) or PET/computed tomography (CT) is useful for the identification of nodal diseases in LACC with a sensitivity of about 85% (9, 12–14). Although CT is known to have poor sensitivity (36%) for LN involvement (8, 15), this modality is readily accessible for radiation treatment planning and provides enhanced information on

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the electron density of the tissues, enabling the accurate dose calculation based on patient anatomy for external beam radiation therapy (EBRT) (16). The use of multimodality imaging can better detect pathologically involved LN disease for therapeutic decisions regarding dose and radiation delivery.

The aim of this study was to investigate a therapeutic dose contribution, in absolute and equivalent dose in 2-Gy fractions (EQD2), of high-dose-rate (HDR) brachytherapy to pathologically involved pelvic LN as determined by CT and PET images. The authors also examine the variation of the LN prescribed dose and actual delivered dose as determined from the CT-based EBRT and brachytherapy plans.

Methods and materials

Patients

This retrospective analysis was approved by the Institutional Review Board at University of California Davis Medical Center. Sixty-eight patients diagnosed with LACC were treated with curative intent in the Department of Radiation Oncology at University of California Davis Medical Center from September 2007 to October 2011. Seventeen patients with a total of 36 positive pelvic LNs who had PET images before and after chemoradiation were included in this study. The median age of the patients was 48 years (range, 27–76 years), and their International Federation of Gynecology and Obstetrics stages were between IB1 and IIIB. The median standardized uptake value (SUV) of the identified pelvic nodes for 16 patients was 6.5 (range, 2.4–17.5). One patient with two positive LNs did not have an SUV recorded because pretreatment PET scans were performed outside the institution. All patients received weekly cisplatin as concurrent chemotherapy. The details of the patient characteristics are shown in Table 1. Table 2 displays the anatomic distribution of the 36 positive LNs in 17 patients.

Table 1
Patient characteristics

Characteristics	*N* (%)
Age (yr)	
21–30	1 (5.88)
31–40	4 (23.54)
41–50	5 (29.41)
51–60	5 (29.41)
61–70	1 (5.88)
≥71	1 (5.88)
Median (range)	48 (27–76)
FIGO stage	
IB1	2 (11.76)
IB2	1 (5.88)
IIA	0 (0)
IIB	12 (70.60)
IIIB	2 (11.76)
Histologic type	
Squamous cell carcinoma	16 (94.12)
Adenocarcinoma	0 (0)
Other	1 (5.88)

FIGO = International Federation of Gynecology and Obstetrics.

Radiation therapy

CT scans of all patients were acquired at 3-mm intervals, and the treatment plans were generated based on these images to deliver initial radiation to the whole pelvis and supplemental boost radiation to the involved pelvic LNs. Fourteen patients were planned using Pinnacle^3 treatment planning system (Philips, Amsterdam, The Netherlands) with a 15 MV energy for three-dimensional conventional radiation therapy. Two were planned using Pinnacle^3 and one using TomoTherapy Treatment Planning System (TomoTherapy, Inc., Madison, WI) with a 6 MV energy for intensity-modulated radiation therapy. The involved pelvic LNs were identified on PET images characterized by a SUV of greater than 3 or the suspicion of the treating radiation oncologist in conjunction with the nuclear medicine physician or by approved report of the PET scan data. These LNs were then identified and contoured on the treatment planning CT scan (Fig. 1a). The median prescribed dose to 36 LNs for the total EBRT was 55.80 Gy (range, 41.40–59.80 Gy). The mean dose delivered to each contoured LN was calculated with heterogeneity corrections using a superposition/convolution algorithm and recorded. For the patient treated with TomoTherapy, a composite plan was generated by transferring the initial and boost plans to MIM software (MIM Software, Inc., Cleveland, OH) and fusing them together. Then, each pelvic LN was contoured, and the mean delivered dose was recorded on the software. All patients were treated using either an Elekta Synergy linear accelerator (Elekta AB, Stockholm, Sweden) with segmented multi-leaf collimator or a helical TomoTherapy unit.

HDR brachytherapy was delivered using a tandem and ring (15 patients), a tandem and ovoid (1 patient), or interstitial needles (1 patient). These instruments were implanted into the patient's cervix and a CT scan was acquired at 3 mm for HDR brachytherapy planning before each treatment fraction. Eight, 4, and 5 patients received five, four, and three brachytherapy insertions, respectively. Independent pelvic LNs that were contoured on the external beam radiation planning CT scans were also identified and

Table 2
Distribution of 36 positive pelvic lymph nodes

Lymph node group	*N* (%)
Common iliac	8 (22.22)
Internal iliac	9 (25.00)
External iliac	12 (33.33)
Presacral	5 (13.89)
Obturator	2 (5.56)
Total	36 (100)