ELSEVIER

Brachytherapy ■ (2017) ■

BRACHYTHERAPY

Focal boost to residual gross tumor volume in brachytherapy for cervical cancer—A feasibility study

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ABSTRACT

PURPOSE: Image-guided plan optimization with MRI and CT for interstitial and intracavitary brachytherapy is an established technique in treating cervical cancer. The purpose of this study was to assess the feasibility of boosting the dose to the residual gross tumor volume (GTV-T_{res}) to 140% of the high-risk clinical target volume (HR-CTV) prescription.

METHODS AND MATERIALS: Brachytherapy plans from 50 consecutive patients were analyzed in this study. All received external beam radiotherapy followed by brachytherapy (6 Gy × 4 fraction or 7 Gy × 4 fraction to HR-CTV). The original treatment plans were reoptimized escalating the GTV-T_{res} dose 140% of the original HR-CTV prescription dose to 8.4 Gy and 9.8 Gy/ per fraction, respectively, with the aim of achieving GTV-T_{res} $V_{140} \geq 90\%$ and $D_{98} \geq 100$ Gy. The HR-CTV coverage and organ at risk (OAR) dose–volume histogram values were kept within the tolerance, which had been accepted for the original clinical plans.

RESULTS: A total of 24 patients (48%) achieved the planning goal after reoptimization. There was no significant difference between the D_{2cc} of the OARs of the clinical plan and the study boost plan. The factors having greatest impact on the delivered dose to the GTV-T_{res} are proximity of the OAR, intrauterine positioned outside the GTV-T_{res}, and suboptimal interstitial placement for boosting GTV-T_{res}.

CONCLUSIONS: It is possible to boost the prescription dose to the GTV-T_{res} achieving 140% increase, which equates to an $EQD_{2\alpha/\beta=10} > 100$ Gy. Plans without both interstitial catheters and/or intrauterine within the GTV-T_{res} are most likely to be suboptimal. This planning study demonstrates that dose escalation to the GTV-T_{res} is feasible and further work into clinical application should be considered.

Keywords: Cervical cancer; Dose escalation; Image-guided adaptive brachytherapy; Target volumes

Introduction

The established standard of practice for locally advanced cervical cancer is definitive concurrent cisplatin-based chemoradiotherapy and brachytherapy (BT) (1, 2). BT is an integral component of the multimodality approach in managing cervical cancer with multiple published series demonstrating inferior local control and overall survival outcome when omitted (3, 4). In recent years, there has been significant improvement in imaging, which has seen the practice of BT planning move from 2D-based orthogonal images with dose prescribed to point A to highly conformal MRI volume–based adaptive plans (5–7). The advantage of MRI-based planning is better differentiation of soft-tissue structures, enabling improved definition of target volume and organs at risk (OARs). In practice, often a fusion of CT and MRI imaging is used to aid applicator tracking. Image-guided adaptive brachytherapy not only has the advantage of tailored treatment but also recent publications demonstrate improved overall survival compared to historical controls (8).

The use of interstitial (IS)-combined and intracavitary (IC)-combined insertions for plan optimization and improved dose–volume histogram (DVH) parameters have been reported (9). The greatest advantage of such a method is mainly seen with large residual disease after external beam radiation therapy (EBRT) where IC applicators alone

Received 7 March 2017; received in revised form 4 September 2017; accepted 18 September 2017.

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1538-4721/$ - see front matter
https://doi.org/10.1016/j.brachy.2017.09.012

are inadequate to achieve dose of ≥85 Gy EQD_{2Gy}. IC-IS applicators also allow for greater flexibility in dose escalation of target volume and deescalation of surrounding organs ensuring OAR dose constraints are adhered to. Planning studies addressing feasibility of dose escalation to the HR-CTV are able to achieve an increase in dose by an average of one-third without the use of IS needles (10, 11). Analysis from retroEMBRACE reports a significant increase by an average 9 Gy to the HR-CTV D_{90} in their IC-IS versus IC cohort (12). This is reflected in an improved local control rate increase of 5%.

Contemporary data from the EMBRACE collaboration show the emerging importance of delivered dose to target volume with improved tumor control rates when the HR-CTV D_{90} increases from 85 Gy to 90−95 Gy (13−15). This is reflected in single-institution series using a variety of different applicators and treatment with either high-dose-rate brachytherapy (HDR-BT) or pulsed dose rate brachytherapy (16−18). Further evidence for the role of dose escalation to the primary tumor comes from animal data demonstrating a clear tumor response when dose is increased to intratumoral hypoxic subvolumes. Thus, dose escalation to residual macroscopic tumor after external beam chemoradiation using MRI-guided focal brachytherapy boost may prove to be important in overcoming radiobiological resistance and achieving better local tumor control (19, 20).

To date, there are limited published data in cervical cancer addressing the role of a focal boost to residual tumor at the time of BT. The purpose of this study was to assess the feasibility of a 40% dose escalation to the gross tumor volume at the time of BT (GTV-T_{res}) while maintaining current clinically acceptable dose to OARs. This dose escalation was chosen to achieve GTV-T_{res} D_{98} ≥ 100 Gy EQD_2.

Methods

A retrospective cohort of 50 consecutive patients with histologically confirmed locally advanced cervical cancer (Fédération Internationale de Gynécologie et d'Obstétrique 1B1−IVA) treated with definitive chemoradiation therapy followed by HDR-BT between July 2014 and December 2015 was included in this planning study. All patients were treated with EBRT to the pelvis to a dose of 45−50.2 Gy in 1.8−2 Gy fractions using megavoltage photons followed by HDR-BT (6 Gy × 4 or 7 Gy × 4). BT using either intrauterine tube and Vienna-style ring or Fletcher-style ovoid IC applicator with or without IS needles was performed under anesthetic using ultrasound guidance for implantation. Prior to insertion, an examination under anesthetic was conducted, and that along with the Week-5 T2-weighted MRI (Siemens Magnetom C! 0.35 T, Munich, Germany) was used to determine optimal IC/IC-IS configuration for HR-CTV coverage. Patients without residual disease (i.e., complete response on Week-5 MRI) or where MRI at the time of BT was contraindicated were excluded from this planning study.

BT planning

After implantation of the IC applicators under general anesthetic, patients with just IC applicators underwent a planning MRI scan only. Patients implanted with IC and IS applicators had an MRI and CT scan (3-mm slice thickness with an additional reconstruction, from the same projection data, at 1-mm slice thickness). The addition of the CT scan in these cases allows for accurate tracking of the IS needles which are more difficult to visualize on MRI alone. The CT images were fused with the MRI for ease of OARs and disease contouring. Contouring of target volumes (HR-CTV, GTV-T_{res}) and OARs were done in accordance with The Groupe Europeen de Curietherapie-European Society for radiotherapy and oncology recommendations (Fig. 1) (21). The nonfocal boost HR-CTV region was defined as HR-CTV_2 = HR-CTV − GTV-$T_{res.}$ The dose was prescribed to the HR-CTV D_{90}.

For the purpose of this dosimetric study, the first-fraction planning images were used with the cumulative total dose extrapolated for fractions 2 −4 by simple multiplication assuming the same dosimetry for each fraction.

The treatment plans were generated using Brachyvision (Version 11, Varian Medical Systems, Palo Alto, CA). The original HR-CTV planning aim of OAR constraints was to achieve an HR-CTV D_{90} ≥ 84 Gy, D_{2cc} to bladder of 81.1 Gy, and 73.2 Gy for both rectum and sigmoid.

Boost planning study

For this boost planning study, the clinical plans that had been used to deliver treatment according to a dose prescribed to the HR-CTV were reoptimized to fit the criteria GTV-T_{res} V_{140} ≥ 90% and D_{98} ≥ 100 Gy. The planning goal for HR-CTV_2 was V_{100} ≥ 90%.

The dose prescribed to the GTV-T_{res} was 9.8 Gy for the 7 Gy per fraction plans and 8.4 Gy for the 6 Gy per fraction plans. This is a 40% increase of the current prescribed dose that equates to an increase of 60% in EQD_2 of the BT component, giving a total EDQ_2 including the external beam component of at least 100 Gy $_{\alpha/\beta 10}$. The OAR parameters were kept to less than or equal to those that were accepted for the original clinical plans.

The quality of the reoptimized plans was quantified using DVH parameters. Treatment plans were classed as either "pass" or "fail" based on the constraint objectives. All plans were reoptimized by a single experienced planner including predetermined factors affecting "pass" or "fail" rate.

Results are presented using descriptive statistics with DVH parameters. Student's two-tailed *t* test was performed using IBM SPSS v.24 (New York, NY) for OAR parameters and IC versus IC and IS with a significant *p*-value of <0.05. The linear quadratric model was used for radiobiological conversions with an α/β = 10 Gy for tumor and 3.5 Gy (22, 23) for OARs using the formula $EQD_{2Gy} = D_{xGy}\ [(x + \alpha/\beta)/(2 + \alpha/\beta)]$.