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Improving dose delivery by adding interstitial catheters to fixed geometry applicators in high-dose-rate brachytherapy for cervical cancer

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ABSTRACT

PURPOSE: Image-guided brachytherapy (IGBT) is an essential component of the treatment of locally advanced cervical cancer. Interstitial (IS) catheters are being increasingly used for bulkier tumors. We have retrospectively assessed the dosimetric impact of IS catheters.

METHODS AND MATERIALS: All patients who received IGBT for cervical cancer between August 2014 and February 2017 were identified. Clinical and dosimetric data were collected. Patients were grouped into the intracavitary (IC) cohort or the IC and IS implant (IC/IS) cohort. Ten patients who had been treated with IS catheters (IC/IS plan) had their brachytherapy replanned without IS catheters (IC plan). The total D_{90}% received by the high-risk clinical target volume (CTV_{HR}) and the D_2cm^3 (minimum dose received by the most irradiated 2 cm^3) to the bladder, bowel, sigmoid, and rectum were compared.

RESULTS: Forty-two patients received IGBT in this period. Seventy-four percent of patients were treated with IS catheters. Sixty-one percent of patients in the IC/IS cohort had CTV_{HR} volumes $\geq$30 cm^3 at Fraction 1 compared to 18% in the IC cohort ($p = 0.014$). There was no difference in cumulative D_{90}% to CTV_{HR} between the IC/IS cohort and the IC cohort. The replanned brachytherapy showed that the cumulative CTV_{HR} D_{90}% was on average 5.8 Gy higher when IS catheters were used (mean CTV_{HR} D_{90}% 86.1 compared to 80.3 Gy, $p < 0.001$). The D_2cm^3 to the organs at risk was not significantly increased.

CONCLUSIONS: IS catheters allow the dose to the CTV_{HR} to be escalated significantly without increasing the dose to the bladder, bowel, sigmoid, and rectum in patients with bulky tumors.

Keywords: Cervical cancer; Brachytherapy; Image guidance; Interstitial catheters

Introduction

Cervical cancer is the fourth most common cancer worldwide in women (1). Locally advanced cervical cancer is treated with chemoradiotherapy and brachytherapy as a standard of care (2, 3). Brachytherapy is an essential component of treatment and is independently associated with improved cancer-specific and overall survival (OS) (4).

Groupe Européen de Curiethérapie−European Society for Radiotherapy and Oncology (5, 6) and the Royal College of Radiologists (7) have published guidelines on the implementation of image-guided brachytherapy (IGBT) to delineate the high-risk clinical target volume (CTV_{HR}). The dose can therefore be prescribed to the high-risk volume rather than to a point. IGBT allows dose escalation while keeping within the tolerances of the organs at risk (OAR), which improves local control and survival (8−10). A D_{90}% to CTV_{HR} > 86 Gy leads to local control rates >90% (11). There are indications that MRI-based IGBT may improve OS compared to CT-based IGBT (12).

For patients with bulky disease or parametrial extension, it can be difficult to deliver an adequate dose to the CTV_{HR} with a tandem and ovoids or tandem and ring alone (13−15). Therefore, applicators that accept interstitial (IS) catheters have been developed to improve target

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coverage in these patients, which allow dose escalation while respecting the OAR constraints (16). Clinically, this leads to excellent local control and minimal late side effects (17). The benefit of IS catheters appears to be greatest in those patients with a $CTV_{HR} \geq 30$ cm^3 with an increase in 3-year local control rate of 10% for patients with IS catheters (intracavitary [IC]/IS brachytherapy) compared with those receiving IC brachytherapy only (18). The addition of IS catheters has also been shown to reduce applicator shift between imaging and dose delivery (19).

The Vienna group reported outcomes from 1998 to 2001 (learning period) before the implementation of protocol-driven MRI-guided brachytherapy and from 2001 to 2003 (protocol period) (20). The D_{90}% to CTV_{HR} was increased from 81 Gy in the first period to 90 Gy in the second period with OS at 3 years increasing from 53% to 64%. The increase in survival was only seen in patients with tumors >5 cm (28% OS in the first period compared with 58% in the second period). An update with data on patients treated between 2001 and 2008 showed a further improvement in D_{90}% to CTV_{HR} from 90 Gy in 2001−2003 to 94 Gy in 2004−2008 (8). Late gastrointestinal and genitourinary side effects also decreased from 10% in 1998−2000 to 2% in 2001−2003 (20).

We conducted a retrospective review of the use of IS catheters in locally advanced cervical cancer at our institution. Ethical approval is not required for this type of retrospective review in our institution. Patients who received IC/IS brachytherapy were identified, and each fraction of brachytherapy was replanned using source dwell positions only within the tandem and ovoids to compare the dosimetric contribution made by the IS component to the CTV_{HR} and the OAR.

Methods and materials

A retrospective review of the use of IS catheters in patients with locally advanced cervical cancer receiving IC brachytherapy at the Royal Surrey County Hospital was conducted. Patients treated between August 2014 and January 2017 were identified from the brachytherapy database. Clinical information was collected on all patients for International Federation of Gynecology and Obstetrics 2009 (21, 22) stage, histology, tumor size, lymph node involvement, chemotherapy regimen, radiotherapy dose, overall treatment time, and whether IS catheters were used. Patients were grouped into the IC cohort or the IC and IS implant (IC/IS) cohort. The dosimetric data collected on all patients were total D_{90}% to CTV_{HR}, and the proportion of patients achieving a total D_{90}% to $CTV_{HR} \geq 75$ Gy, 80 Gy, and 85 Gy was calculated.

Patients were treated with intensity-modulated radiotherapy to a dose of 45−50.4 Gy in 25−28 fractions with a pelvic side wall boost of 5.4 Gy in three fractions if imaging demonstrated the presence of cancer in the lymph nodes. Treatment was inverse-planned with two 360° coplanar RapidArc 6 MV beams. Chemotherapy consisted of weekly cisplatin chemotherapy (40 mg/m^2). Infusional 5-fluorouracil (200 $mg/m^2/d$) was added if the histology was adenocarcinoma or adenosquamous. Overall treatment time was <56 days as these are Category 1 tumors that demonstrate accelerated repopulation (23).

Image-guided high-dose-rate brachytherapy was delivered weekly from the fifth week of external beam radiotherapy (EBRT) to a dose of 14−21 Gy in two to three fractions. Magnetic resonance images were obtained using a 1.5 Tesla HDxt MRI scanner (GE Healthcare, Chicago, IL) the day before the first fraction of brachytherapy to assess tumor response and to aid brachytherapy applicator selection. Images were acquired according to our institutional protocol, which includes sagittal T2 PROPELLER images, axial T2 PROPELLER images (both at 3 mm thickness), and axial T1 pelvis fast spin-echo images (5 mm slice thickness).

If the tumor was bulky, IS catheters were used from Fraction 1 with needle position and depth of insertion chosen according to the prebrachytherapy MRI scan. For each fraction of brachytherapy, patients had a CT scan with the Utrecht applicator (Elekta, Stockholm, Sweden) *in situ* (see Fig. 1). To improve treatment pathway efficiency (24), the CTV_{HR} and OAR were contoured using Eclipse v13.7 (Varian Medical Systems, Palo Alto, CA). The applicator was reconstructed, and treatment was planned using Oncentra Brachy v4.5.2 (Elekta, Stockholm, Sweden). After Fractions 1 and 2, all patients had a second treatment plan generated (postplan) to ascertain whether addition or alteration of IS catheters would have improved CTV_{HR} D_{90}% dose or decreased dose to OAR. The site and depth of needle insertion was then specified for the next insertion.

From the larger cohort, smaller samples of patients who had received IC and IS brachytherapy were selected at random. For this retrospective planning study, a total of 10 patients were chosen to give adequate power to the study while being feasible to complete within a timely manner. Each fraction of brachytherapy was retrospectively planned using source dwell positions in the tandem and ovoids only without IS catheters. The cumulative D_{90}% (including the EBRT contribution) received by the CTV_{HR} and the cumulative D_2cm^3 to the bladder, bowel, sigmoid, and rectum were compared for each patient to assess the contribution of the IS catheters to the overall dose received. Dose reporting was based on the total (EBRT + brachytherapy) biologically equivalent dose in 2 Gy fractions using the linear−quadratic model with $\alpha/\beta = 10$ Gy for tumor and $\alpha/\beta = 3$ Gy for OAR.

Statistical analysis was performed using SPSS version 24 (IBM, New York, NY). Categorical data including patient baseline characteristics and the proportion of patients achieving a D_{90}% to $CTV_{HR} \geq 75$ Gy, 80 Gy, or 85 Gy were compared between the IC cohort and the IC/IS cohort