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BRACHYTHERAPY

Assessing changes to the brachytherapy target for cervical cancer using a single MRI and serial ultrasound

Sylvia van Dyk[1,*], Srinivas Kondalsamy-Chennakesavan[2], Michal Schneider[3], David Bernshaw[4], Kailash Narayan[4,5]

[1]*Radiation Therapy Services, Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia*
[2]*Rural Clinical School, University of Queensland, Toowoomba, Queensland, Australia*
[3]*Department of Medical Imaging and Radiation Science, Monash University, Clayton, Victoria, Australia*
[4]*Division of Radiation Oncology, Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia*
[5]*Department of Obstetrics and Gynaecology, Melbourne University, Melbourne, Victoria, Australia*

ABSTRACT

PURPOSE: To assess changes to the brachytherapy target over the course of treatment and the impact of these changes on planning and resources.

METHODS AND MATERIALS: Patients undergoing curative treatment with radiotherapy between January 2007 and March 2012 were included in the study. Intrauterine applicators were positioned in the uterine canal while patients were under anesthesia. Images were obtained by MRI and ultrasound at Fraction 1 and ultrasound alone at Fractions 2, 3, and 4. Cervix and uterine dimensions were measured on MRI and ultrasound and compared using Bland−Altman plots and repeated measures one-way analysis of variance.

RESULTS: Of 192 patients who underwent three fractions of brachytherapy, 141 of them received four fractions. Mean differences and standard error of differences between MRI at Fraction 1 and ultrasound at Fraction 4 for anterior cervix measurements were 2.9 (0.31), 3.5 (0.25), and 4.2 (0.27) mm and for posterior cervix 0.8 (0.3), 0.3 (0.3), and 0.9 (0.3) mm. All differences were within clinically acceptable limits. The mean differences in the cervix over the course of brachytherapy were less than 1 mm at all measurement points on the posterior surface. Replanning occurred in 11 of 192 (5.7%) patients, although changes to the cervix dimensions were not outside clinical limits.

CONCLUSIONS: There were small changes to the cervix and uterus over the course of brachytherapy that were not clinically significant. Use of intraoperative ultrasound as a verification aid accurately assesses the target at each insertion, reduces uncertainties in treatment delivery, and improves efficiency of the procedure benefiting both the patient and staff.

Keywords: Cervical cancer; Brachytherapy; Ultrasound; MRI

Introduction

There is increasing awareness of the need to incorporate soft tissue imaging into brachytherapy protocols for cervical cancer. Use of serial imaging evaluates each implant on its own merits, and early studies recommended that imaging be performed at each applicator insertion to account for variations in applicator geometry and positioning within the patient (1, 2). Similarly, imaging is now also recommended to assess the dosimetric coverage of the target and organs at risk (OAR) (3). The Groupe Europeen de Curietherapie and European Society for Radiotherapy and Oncology recommended using MRI at each brachytherapy insertion (4, 5). Significant gains in tumor control and reduced toxicity have been reported by centers using such advanced imaging (6−8). Select centers around the world have investigated the use of MRI to assess and confirm the brachytherapy target volumes but have also recognized the difficulties of obtaining an MRI for every fraction of

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* Corresponding author. Radiation Therapy Services, Peter MacCallum Cancer Centre, St Andrews Place, East Melbourne 3002, Victoria, Australia. Tel.: +61-3-96561481.

E-mail address: sylvia.vandyk@petermac.org (S. van Dyk).

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brachytherapy even in well-resourced departments (9–11). Alternative imaging modalities have to be investigated so that gains made by centers using advanced imaging can be replicated in lower resource settings. We previously investigated the use of ultrasound to identify the brachytherapy target and guide conformal planning (12). In that investigation, we validated ultrasound as a viable alternative to MRI in identifying the cervix and uterus with intracavitary applicators *in situ*. In the present study, we describe the use of a single MRI taken at Fraction 1 and use of ultrasound for verification of applicator position and target dimensions in subsequent insertions. The purpose of the study was to investigate the change in target dimensions detected with ultrasound over the course of brachytherapy and the impact on planning and departmental resources.

Methods and materials

This study was approved by the Divisional Review Panel for Retrospective studies at the Peter MacCallum Cancer Center and the Monash University Human Research Ethics Committee.

Patient selection criteria

Patients who presented to Peter MacCallum Cancer Center between January 2007 and March 2012 with previously untreated cervical cancer. Patients had to have been staged according to the clinical (International Federation of Gynecology and Obstetrics [FIGO]) staging system as Stage IB, II, III, or IVA; had an MRI at the time of brachytherapy, and been treated with curative intent.

Radiotherapy

Patients received 40 (2 Gy/fx) to 45 Gy (1.8 Gy/fx) external beam radiation therapy (EBRT) and three to four fractions of high-dose-rate brachytherapy to achieve a total combined dose to the target in the order of 80–84 Gy_{10} equivalent to doses in 2 Gy fractions. The radiation therapy, brachytherapy technique, and imaging protocols have previously been described (12, 13).

Brachytherapy

Brachytherapy was always given after the completion of EBRT. All patients in this study were treated with intracavitary applicators (Standard CT/MR and Vaginal CT/MR applicators; Nucletron, Veenendaal, The Netherlands). Applicator insertion, ultrasound imaging, planning, and treatment took place in a single session in a dedicated operating theater. All patients were anesthetized for the whole procedure. Most patients were under spinal anesthesia for Fraction 1 and general anesthesia for Fractions 2–4.

The brachytherapy target was the residual disease, whole cervix, vaginal fornices, medial myometrium, and any clinical detected disease at the time of brachytherapy. Parametrial involvement was assessed clinically (visualization with transvaginal ultrasound and palpation at the first insertion before applicator insertion and visualization with transabdominal ultrasound after applicator insertion). Parametrial coverage was then assessed on MRI after the first treatment had been delivered. Clinical assessment of parametria was performed at each subsequent insertion using palpation and visualization with transabdominal ultrasound.

Figure A1 outlines the steps in the procedure (all figures and tables designated "A" are in Appendix 1).

Study design

All data were prospectively recorded in the gynecology service database and retrieved for this analysis.

Longitudinal and axial views along the intrauterine applicator were obtained with MRI and ultrasound at Fraction 1 and ultrasound alone at subsequent fractions. Measurements and their designated nomenclature are shown in Figs. 1 and A2.

Clinical agreement criteria between MRI and ultrasound were set at 3 mm for the cervix and 5 mm for the uterus. These criteria were established in a previous study (12); see Table A1.

Cervix and uterine dimensions obtained at each measurement point with MRI and ultrasound were analyzed for each patient (MRI vs. ultrasound at Fractions 1 2, 3, and 4).

The analysis looked at agreement between MRI and the ultrasound measurements and compared ultrasound measurements obtained at each fraction.

Power and sample size

With a sample size of 141 (number of patients who received four fractions of treatment), this study achieves at least 92% power to detect a mean of paired differences of 1 mm with a known standard deviation (SD) of differences of 3.5 mm with a significance level (α) of 0.05 using a two-sided paired z test.

Statistical analyses

Data analysis was performed using Graphpad Prism, version 6.02 for Windows (Graphpad Software Inc, La Jolla, CA). The normality of the samples was tested with D'Agostino–Pearson omnibus normality test. Continuous data were expressed as mean ± SD. Agreement between MRI and ultrasound measurements was assessed using Bland–Altman analysis (14, 15). Bland–Altman plots are a graphic representation of the data with the difference between the two methods plotted against their mean. Bias is the average difference between the methods and represents systematic error. The closer the mean of differences is to