ELSEVIER

Brachytherapy ■ (2017) ■

BRACHYTHERAPY

Rectum and bladder spacing in cervical cancer brachytherapy using a novel injectable hydrogel compound

Antonio L. Damato[1], Megan Kassick[2], Akila N. Viswanathan[3,*]

[1]*Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY*
[2]*Tufts Medical School, Boston, MA*
[3]*Department of Radiation Oncology and Molecular Radiation Science, Johns Hopkins Medicine, Baltimore, MD*

ABSTRACT

PURPOSE: The aim of this study was to evaluate injection of a novel hydrogel (TraceIT; Augmenix, Waltham, MA) between the cervix, rectum, and bladder in female cadavers compared with, and in addition to, the current standard of gauze packing, for organ-at-risk sparing in cervical cancer brachytherapy planning.

METHODS AND MATERIALS: This brachytherapy cadaver study used T2-weighted MRI and CT imaging to compare three scenarios: (*1*) gauze packing alone, (*2*) hydrogel injection placed in the cervical fornices and rectovaginal septum, and (*3*) gauze packing in conjunction with hydrogel injection. Hydrogel distribution was evaluated. Doses to 2 cm^3 volumes (D_{2cc}) for the rectum, bladder, and sigmoid were collected. Statistical significance ($p < 0.05$) was evaluated using a two-tailed paired t test.

RESULTS: Hydrogel was successfully injected to space the bladder and rectum from the cervix in all five cadavers. The spacer was easily identifiable on both CT and MRI. The use of hydrogel in addition to packing resulted in a 22% decrease in rectum D_{2cc} dose ($p = 0.02$), a 10% decrease in bladder D_{2cc} ($p = 0.27$), and no change in sigmoid D_{2cc} dose. No difference was observed between hydrogel only vs. gauze packing only.

CONCLUSIONS: Our results revealed a significant clinically meaningful decrease in rectal D_{2cc} associated with the use of hydrogel in addition to gauze packing—TraceIT hydrogel holds promise as a spacer in cervical cancer therapy.

Keywords: Cervical cancer; Gynecologic cancers; Chemoradiotherapy; Brachytherapy; Radiotherapy planning; Hydrogel; Organs at risk; Rectum sparing; Bladder sparing

Introduction

The current standard of care for locally advanced cervical carcinoma is primary chemoradiation therapy (RCTX), which includes both external beam and brachytherapy components to the radiation (1). Compared with previous standards, factors including radiation therapy only, local control, progression-free survival, and overall survival are improved with brachytherapy (2). These benefits, however, are not without accompanying side effects. Both acute and late gastrointestinal toxicities, which can greatly affect quality of life, are associated with RCTX (3, 4).

The standard method for dose sparing to the rectum and bladder in cervical cancer brachytherapy is the placement of gauze packing in the vagina (5). In gynecologic cancer patients, one method that has gained recognition is the use of a polyethylene glycol hydrogel for dose reduction to organs at risk, particularly the rectum, particularly in the setting of re-irradiation (6). One absorbable spacer significantly reduces late toxicity by expanding in the perirectal space (SpaceOAR system; Augmenix, Waltham, MA). This spacer has been shown in multi-institutional clinical trials to result in increased perirectal space in prostate cancer patients, subsequently leading to rectal dose reductions and reductions in rectal toxicity severity (7, 8). Recently, TraceIT hydrogel (TH; Augmenix, Waltham, MA), a novel iodinated polyethylene glycol

Received 13 December 2016; received in revised form 19 March 2017; accepted 13 April 2017.

* Corresponding author. Department of Radiation Oncology and Molecular Radiation Science, Johns Hopkins Medicine, 401 North Broadway, Baltimore, MD 21231. Tel.: +1-410-502-1421.

E-mail address: anv@jhu.edu (A.N. Viswanathan).

1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2017.04.236

hydrogel with multimodality visibility for 3 months, was introduced. This particular hydrogel material has been assessed as a marker in cervical cancer brachytherapy but has not yet been assessed as a spacer in clinical trials in gynecologic cancers (9).

The aim of this study was to evaluate TH injection between the cervix, rectum, and bladder in female cadavers compared with, and in addition to, the current standard of gauze packing, for organ-at-risk sparing in cervical cancer radiation therapy planning. This will provide the first supporting evidence that TH may be tested in the future as a spacer in cervical cancer radiation therapy.

Methods and materials

As a part of this study, five cadavers were evaluated using CT and MRI.

The imaging, injection, and amount of material for cadavers are summarized in Table 1 and detailed in the supplemental online information. The first cadaver was evaluated without an applicator in place as a control to test the feasibility of the cadaver model. The subsequent four cadavers were implanted with a tandem and ovoids ($n = 1$) or a ring ($n = 3$) and received a series of CT/MRI with varying amount of gel inserted, with or without standard vaginal packing. More details about the gel insertion are presented in the Appendix. Distribution of the spacer was evaluated through visual inspection of CT and MRI.

A study of the effect of the use of the spacer on the organs-at-risk dose metrics was performed. Three CT series per cadaver were used: CT with applicator and packing (packing only), CT with applicator and the maximum amount of gel inserted (gel only), and CT with applicator and both gel and packing (packing and gel). Axial and sagittal T2-weighted MRIs with applicator in place after gel injection were also available. The MRIs of Cadaver 5 were not used because of an artefact noted between the rectum and the ring applicator that prohibited accurate contouring.

Contouring

The bladder, sigmoid, and rectum and gel spacer were contoured when present. A comprehensive review of the contours on the multiple image sets (CT and MRI) was performed to ensure accuracy. This review was performed for each patient to confirm consistency in contouring practice (including delineation of the rectum/sigmoid interface) among scans. Given that there was no tumor present in the cadavers, no contouring of the cervix was attempted.

Planning

All CT image sets under investigation were reconstructed with the applicator in the Oncentra Brachytherapy Planning System (Nucletron, an Elekta Company, Stockholm, Sweden). The intrauterine tandem was digitized manually in all image sets. The ovoids in the three image sets of Cadaver 2 were also digitized manually, whereas the ring in Cadaver 3, 4, and 5 were digitized using a commissioned model of the applicator. A treatment plan for a standard pear-shaped dose distribution normalized to Point A was created on each plan. Loading pattern and dwell weight were based on a previous study (10). This planning approach reflects our clinical standard for a starting plan in cervical cancer brachytherapy, before optimization.

Analysis

The three-dimensional dose distribution for each plan was calculated and exported to Eclipse treatment planning system for evaluation. Doses to 2 cm^3 volumes (D_{2cc}) for the rectum, bladder, and sigmoid were collected. To compare the differences between the three scenarios under investigation (packing only, gel only, as well as packing and gel), a comparison of the D_{2cc} as a percentage of a nominal prescription dose was performed. Increases and decreases in D_{2cc} are described as the simple difference between the percentage values of the metrics in the scenarios being evaluated. To evaluate the clinical relevance of the differences between the three scenarios, a hypothetical treatment course of 1.8 Gy × 25 fractions in external beam followed

Table 1
CT evaluation of organs-at-risk D_{2cc} as a percentage of the brachytherapy prescription dose

	Rectum D_{2cc} (% Rx)			Bladder D_{2cc} (% Rx)			Sigmoid D_{2cc} (% Rx)		
Case no.	Packing only	Gel only	Packing and gel	Packing only	Gel only	Packing and gel	Packing only	Gel only	Packing and gel
2	80	63	59	64	53	66	60	57	69
3	60	63	37	78	79	53	21	22	23
4	98	114	61	17	47	22	61	54	59
5	65	69	51	134	94	92	51	47	45
Mean	76	77 ($p = 0.84$)	52 ($p = 0.02$)	73	68 ($p = 0.74$)	58 ($p = 0.27$)	48	45 ($p = 0.10$)	49 ($p = 0.89$)
Standard deviation	17	25	11	48	22	29	18	16	20

D_{2cc} = doses to 2 cm^3 volumes; Rx = prescription dose.
The statistical significance of the difference between the mean D_{2cc} using gel (with or without packing) vs. using gauze packing is reported.