ELSEVIER

CrossMark

BRACHYTHERAPY

Brachytherapy 14 (2015) 881–888

Late rectal toxicity after image-based high-dose-rate interstitial brachytherapy for postoperative recurrent and/or residual cervical cancers: EQD2 predictors for Grade ≥II toxicity

Supriya Chopra[1,*], Tapas Dora[1], Reena Engineer[2], Siji Mechanery[1], Priyanka Agarwal[1], Sadhna Kannan[3], Yogesh Ghadi[2], Jamema Swamidas[2], Umesh Mahantshetty[2], Shyam Kishore Shrivastava[2]

[1]*Department of Radiation Oncology, Advanced Centre for Treatment Research and Education in Cancer, Tata Memorial Centre, Navi Mumbai, Maharashtra, India*

[2]*Department of Radiation Oncology, Tata Memorial Hospital, Tata Memorial Centre, Mumbai, Maharashtra, India*

[3]*Epidemiology and Clinical Trials Unit, Advanced Centre for Treatment Research and Education in Cancer, Tata Memorial Centre, Navi Mumbai, Maharashtra, India*

ABSTRACT

PURPOSE: To investigate the correlation of rectal dose volume metrics with late rectal toxicity after high-dose-rate pelvic interstitial brachytherapy.

METHODS AND MATERIALS: From October 2009 to November 2012, 50 patients with residual or recurrent cervical cancer were included. Patients received external radiation 50 Gy in 25 fractions over 5 weeks with weekly cisplatin. Rectum and rectal mucosal (RM) contours were delineated retrospectively. RM was defined as the outer surface of the flatus tube inserted at brachytherapy. The dose received by 0.1, 1, 2, 5 cc of rectum, RM, and sigmoid was recorded. Cumulative equivalent dose in 2 Gy (EQD2) for organs at risk was calculated assuming α/β of 3. Univariate analysis was performed to identify predictors of rectal toxicity.

RESULTS: At a median follow-up of 34 months (12–51 months), Grade II and III late rectal toxicity was observed in 9 (18%) and 2 (4%) patients, respectively. On univariate analysis, rectal doses were not significant predictors; however, D 0.1-cc RM dose >72 Gy ($p = 0.04$), D 1-cc RM dose >65 Gy ($p = 0.004$), D 2-cc RM dose >62.3 Gy ($p = 0.004$), and D 5-cc RM dose >60 Gy ($p = 0.007$) correlated with Grade ≥II toxicity. On probit analysis, the estimated dose in EQD2 for a 10% and 20% risk of rectal toxicity was D 2-cc rectum of 55 and 66 Gy, and RM <55 and 63 Gy, respectively.

CONCLUSIONS: Limiting 2-cc RM and rectal doses within the proposed thresholds can minimize Grade ≥II toxicity for gynecologic high-dose-rate interstitial brachytherapy.

Keywords: Cervix cancer; MUPIT; Proctitis; Interstitial brachytherapy

Introduction

Interstitial brachytherapy (ISBT) for gynecologic cancers is used wherein standard intracavitary brachytherapy (ICBT) or intravaginal brachytherapy is expected to result in inferior local control due to suboptimal dose distribution within the lateral parametrial tissues for bulky cervical cancers. Boost ISBT has also been used in patients with primary vaginal or postoperative residual and/or recurrent cervical and endometrial cancers for tumors extending beyond the medial parametrium or upper one-third of anterior or posterior vaginal wall. However, the use of

Received 30 January 2015; received in revised form 2 August 2015; accepted 20 August 2015.

Financial disclosure: The Department of Science and Technology, Tata Memorial Centre (DST SR/FT/LS:111/2012) provided funding for part of this study.

The authors report no conflicts of interest.

* Corresponding author. Department of Radiation Oncology, Advanced Centre for Treatment Research and Education in Cancer, Tata Memorial Centre, Kharghar, Navi Mumbai 410210, Maharashtra, India. Tel.: +91-22-27405113; fax: +91-22-27405085.

E-mail address: schopra@actrec.gov.in (S. Chopra).

1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2015.08.007

high-dose-rate (HDR) or low-dose-rate ISBT is associated with 4–24% incidence of severe rectal toxicity (1–10).

In comparison with ICBT, the larger clinical target volume (CTV) implanted during ISBT, proximity of the implanted needles to the rectum, and use of single or multiple daily fractionation regimen may predispose patients to higher incidence of rectal toxicity. Although the rectal dose–volume thresholds for moderate-to-severe late rectal toxicity have been investigated and defined for patients undergoing image-guided ICBT for cervical cancer (11–13), they have not been validated in patients undergoing ISBT.

The present study was designed to investigate if rectal dose–volume thresholds recommended for ICBT were accurate predictors for moderate-to-severe late rectal morbidity in patients undergoing pelvic ISBT.

Methods

From October 2009 to November 2012, patients undergoing external beam radiation therapy (EBRT), concurrent chemotherapy, and ISBT within the context of ongoing trials were included (14, 15). Patients with postoperative residual and/or recurrent cervical cancer were included. Patients with disease extension toward lateral pelvic wall or paracolpos at baseline were considered eligible for boost ISBT.

EBRT planning

All patients underwent baseline T2–weighted magnetic resonance imaging after consuming 500 mL of water. CT simulation was performed 30 min after consuming 500-mL water, and patients were injected with intravenous contrast. CT and MR data sets were transferred to Oncentra treatment planning system (version 4.1; Nucletron-Elekta, Stockholm, Sweden). MRI was used only to assist gross tumor volume (GTV) delineation, and a limited soft tissue fusion was performed in the region of interest to assist accurate delineation on CT images. GTV was expanded anteriorly by 1 cm, superiorly by 1 cm, inferiorly by 2–2.5 cm, posteriorly till the mesorectal fascia, and laterally till the pelvic muscles to generate CTV. Additional 1-cm margin (7-mm posteriorly) was used to generate planning target volume for the primary tumor. Nodal delineation was done using standard guidelines (16). Patients were treated with either three-dimensional conformal radiation therapy (3DCRT) or image-guided intensity-modulated radiation therapy using tomotherapy. All patients received 50 Gy in 25 fractions over 5 weeks with concurrent weekly cisplatin.

Interstitial brachytherapy

As part of ongoing study, all patients underwent clinicoradiological response assessment after EBRT. MRI was performed within 1–2 weeks of EBRT conclusion. In all patients, brachytherapy was performed within 3 weeks of EBRT conclusion using Martinez Universal Perineal Interstitial Template. Baseline clinical examination and MRI findings were used to decide the CTV. In all cases, GTV at diagnosis was considered as CTV. Implantation procedure followed methods previously published (17). Patient preparation for brachytherapy involved rectal soap water enema a night before and on the morning of brachytherapy procedure. All implants were performed under spinal anesthesia by radiation oncologists with ≥6 years of experience. All needles were implanted transperineally such that the needle tips are positioned 2–2.5 cm cranial to the CTV. All the needles were secured with the help of screw and plate assembly. The whole assembly was sutured to the perineal skin to prevent caudal displacement. At the end of the procedure, a rectal tube of 15-mm diameter was inserted up to rectosigmoid to facilitate passage of flatus during the course of brachytherapy. This completely decompressed the rectum such that in planning scans, the rectal mucosa (RM) closely approximated the rectal flatus tube (Figs. 1a and 1b).

Brachytherapy planning CT scans were obtained immediately after recovery from anesthesia (i.e., 1.5–3 h after the procedure). Imaged volume encompassed the entire pelvis and upper third of femur at an interslice interval of 3 mm (Somatom version 4; Siemens, Germany). These

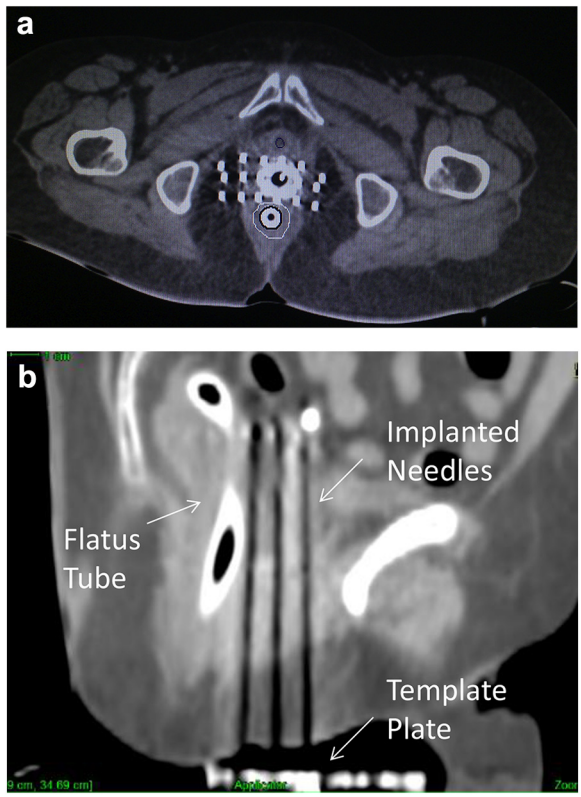

Fig. 1. (a) Figure depicting delineation methodology for rectal mucosa. The outer surface of the rectal tube was delineated as rectal mucosa (black). The white contour outside the rectal mucosa represents rectal contour. (b) Figure depicting location of needles in reference to template and flatus tube.