Clinical Investigations

Original paper

Dosimetric evaluation of vaginal cuff brachytherapy planning in cervical and endometrial cancer patients

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Abstract

Purpose: The aim of the study was to perform a prospective analysis of dosimetric consequences of rectal enema administration before vaginal cuff brachytherapy (VCB), the dose distribution in organs at risk (OARs), and the presence of air gaps (AGs) in patients with cervical or endometrial cancer.

Material and methods: In total, 75 patients treated in 2019 were randomly divided into two groups including 38 patients with and 37 without an enema before VCB. All patients received post-operative high-dose-rate (HDR). Single-channel vaginal cylinders with active length of 2.75 cm were used. Prescription dose was 7 Gy at 5 mm depth from the applicator surface in all directions. Treatment plans were based on computed tomography (CT).

Results: Enema performed before cylinder insertion had no effect on rectosigmoid D_{max} or D_{2cm3}. Rectosigmoid median V_{100} was 0.5 cm^3 (range, 0-2.7 cm^3). $V_{100} \geq 1$ cm^3 in 22 and ≥ 2 cm^3 in 6 patients, with D_{max} up to 19.7 Gy (282%) were observed. No effect of bladder volume in the range of 27-256 cm^3 on D_{max} or D_{2cm3} was found. The median bladder V_{100} was 0.1 cm^3 (range, 0-1.4 cm^3). There were 62 (83%) patients with AGs, with 24% at the top of the vagina and 75% on the remaining length of the vagina. Most of the AGs were small (≤ 3 mm), but in 5 (8%) cases, they were bigger than 5 mm.

Conclusions: VCB planning with the use of CT is essential. CT can facilitate the selection of optimal cylinder size to reduce the occurrence of large AGs. A few percent of plans require correction of dose distribution because of hot spots in OARs and the presence of AGs. Enema before cylinder insertion does not influence rectosigmoid D_{max} and D_{2cm3}. The analysis revealed no bladder volume effect on bladder doses D_{max} and D_{2cm3}.

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Key words: HDR, CT, VCB, cervical or endometrial cancer, enema, AGs.

Purpose

The use of computed tomography (CT) in delineation of organs at risk (OARs) and target volumes is well-known. Vaginal cuff brachytherapy (VCB) is adjuvant treatment delivered after hysterectomy in cervical and endometrial cancer patients, alone or combined with external beam irradiation [1]. The primary purpose of the present study was to prospectively investigate the dosimetric consequences of administering rectal enemas prior to VCB. The secondary objective was to analyze the dose distribution in OARs, using standard planning with multiple points optimization 5 mm from the applicator surface such as 2D plans. The last goal was to record the presence of air gaps (AGs), which can potentially influence the treatment outcome.

Material and methods

In 2019, 75 consecutive patients with indications for post-operative VCB for endometrial or cervical cancer were recruited. Sixty-two patients with endometrial cancer and 13 patients with cervical cancer were treated. In 35 cases, VCB was the only adjuvant treatment. In 40 patients, post-operative treatment was composed of external beam irradiation and brachytherapy. All patients received post-operative high-dose-rate (HDR) VCB in an outpatient setting. Phosphate enema was performed in 38 patients, and 37 were not specially prepared before the applicator insertion. Patients who had an enema before the VCB were selected randomly. The patients were asked to empty their bladder before the procedure. Single-channel vaginal cylinders of the largest diameter

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(2-3.5 cm) that could fit comfortably inside the vagina vault were used. The applicators were placed while asking the patients to relax and breathe, because it is essential to use the largest possible cylinders for good coverage of vaginal mucosal tissue. The following cylinder diameters were used for the procedure: 2.0 cm (2 patients), 2.5 cm (32 patients), 3.0 cm (40 patients), and 3.5 cm (1 patient).

Pelvic CT scans were carried out in the supine position, with 3 mm slice thickness and no gap between slices. CT images were transferred to a 3D treatment planning system (Oncentra Brachy v.4.5.3, Elekta, Sweden). Organs at risk were contoured by the radiation oncologist on the consecutive CT slices according to recommendations [2]. We assessed the dose in rectum and sigmoid as the one-organ rectosigmoid. The outer bladder wall and the rectosigmoid from 1 cm over the cylinder tip to the anus were delineated. An active length of 2.75 cm (11 activated dwell source positions) was used and optimized to deliver a fraction dose of 7 Gy at 5 mm depth from the applicator surface in lateral and cranial directions. Patients were planned in accordance with the GEC-ESTRO handbook of brachytherapy, as presented in Figure 1. For a purpose of the study, we analyzed measurements for one 7 Gy fraction. Dose-volume histograms (DVHs) were generated. Brachytherapy (BT) was given to all patients using an iridium-192 (^{192}Ir) source, with an initial nominal specific activity of 10 Ci using the MicroSelectron HDR afterloading system (Elekta). The protocol and consent procedure were approved by the local medical authority.

For the purpose of this analysis, all plans were created according to the GEC-ESTRO recommendations without dose corrections – standard plan. In cases of very high doses in OARs or AGs over 5 mm in irradiated areas, we corrected the treatment plans individually for each patient. Decision was made by a physician based on the treatment history of patient. All air gaps were recorded in the whole length of vagina.

Statistical analysis

Descriptive statistics were used to describe and analyze a specific dataset, providing short summaries of the sample and measures of central tendency (mean, median, and mode), and measures of variability (standard deviation, variance, minimum and maximum values). The sets and distribution of our data were analyzed, and histograms of all variables were plotted. Distributions of all variables, except for the bladder volume, were considered as a normal distribution. The comparative analysis was performed using Student's *t*-test (enema vs. rectal dose). Then, correlation analysis (non-parametric correlation, Spearman's test) and analysis of variance (ANOVA) were used for bladder volume vs. bladder doses. The whole group (with and without enemas) was divided into three equal sets according to the variable determining the volume of bladder.

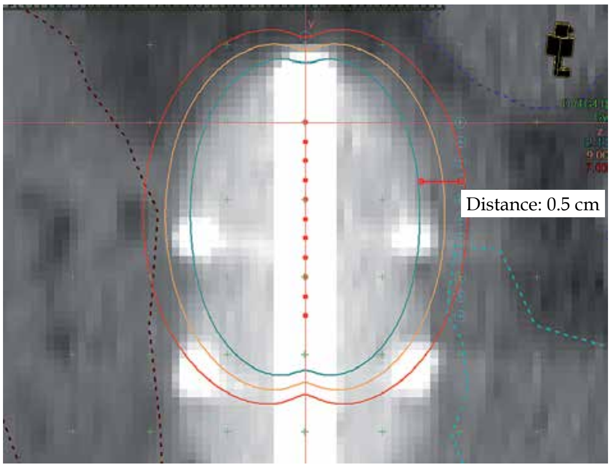

Fig. 1. Doses distribution around vaginal cylinder applicator with multiple points used for optimization

Brown – rectosigmoid, Dark blue – intestine, Light blue – bladder. Blue 259 circles are points used for optimization, Distance – 0.5 cm

Results

The median age of patients was 62 years (range, 35-85 years). Data derived from DVHs for the whole group (n = 75) are presented in Table 1.

Enema was performed in 38 patients. In 37 cases, CT was completed without any special bowel preparation for the procedure. Enema before cylinder insertion did not influence rectosigmoid D_{max} (p = 0.38) and D_{2cm3} (the minimum dose to the highest treated 2 cm^3, p = 0.056) (Figure 2). Data showing mean doses for rectosigmoid with and without enema are given in Table 2.

The bladder volume in the volume range of 27-256 cm^3 was not associated with an increase in D_{max} (p = 0.77) or D_{2cm3} (p = 0.181) in Student's *t*-test. Bladder D_{2cm3} vs. bladder volume are presented in Figure 3. In the second analysis, bladder volumes were divided into three equally numerous groups: < 46 cm^3, 46-84 cm^3, and > 84 cm^3,

Table 1. Doses given for organs at risk for the whole group of patients (n = 75)

Organ at risk		Mean	Values range	Median
Rectosigmoid D_{2cm^3}	[Gy]	5.8 (SD 0.8)	3.5-7.4	5.7
Rectosigmoid D_{max}	[Gy]	9.3 (SD 1.9)	5.8-19.7	8.8
	[%]	132.9 (SD 28.1)	82.3-282	126.2
Bladder D_{2cm^3}	[Gy]	4.9 (SD 0.9)	2.3-6.7	4.9
Bladder D_{max}	[Gy]	7.7 (SD 1.5)	3.4-11.0	7.9
	[%]	109.9 (SD 21.7)	48.5-157.9	113

SD – standard deviation, D_{2cm3} – minimum dose to the highest treated 2 cm^3 of the organ, D_{max} – maximum dose to the whole organ

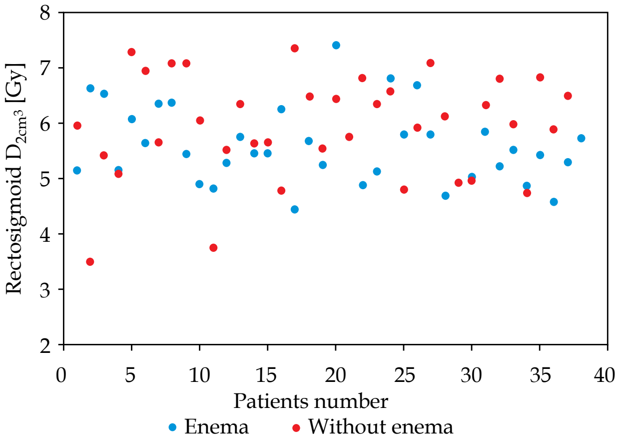

Fig. 2. Presentation of rectosigmoid dose in D_{2cm3} with and without enema

for a comparison. There were no bladder volume effect on bladder doses noted, D_{2cm^3} ($p = 0.597$) and D_{max} ($p = 0.229$).

The volume of organs at risk covered by the prescribed dose V_{100} was assessed. The median bladder V_{100} was 0.1 cm^3 (range, 0-1.4 cm^3). Rectosigmoid median V_{100} was 0.5 cm^3 (range, 0-2.7 cm^3). There were 22 patients with V_{100} bigger than 1 cm^3 and 6 patients with V_{100} bigger than 2 cm^3 in rectosigmoid. These 6 patients with $V_{100} \geq 2$ cm^3 had a D_{2cm3} doses in the range of 7.1-7.4 Gy and D_{max} in the range from 9.7 Gy (139%) to 19.7 Gy (282%).

There were 62 (83%) patients with air gaps around the cylinder in the whole group. In 15 (24%) cases, AGs were located at the apex (upper 3 cm of cylinder including the top of the vault) and in 47 (75%) patients, AGs were situated in the lower part of vagina. The AGs depth was smaller than 3 mm in 37 (59%) cases and bigger than 3 mm in 25 (40%) patients. The median thickness of AGs was 3 mm (range, 2-6.5 mm). There were 5 (8%) cases with AGs bigger than 5 mm, one in the apex of vagina, and 4 within 46-57 mm below the apex. When 7 Gy was delivered at 5 mm depth from the applicator surface, the dose on vaginal mucosa was about 12.4 Gy. In case of an AG appearance with 3 mm depth, the dose decreased to 9 Gy.

Discussion

In our study, enema performed before cylinder insertion in 38 patients did not influence rectosigmoid D_{max} and D_{2cm3}. The enema administration could potentially reduce the rectal dose by reducing the rectal volume.

In literature, results of observations are indecisive. In one study, authors reported that larger rectal volumes were associated with higher rectal dose parameters during VCB [3]. Unfortunately, we did not find a relationship between preparation for the procedure with enema and higher doses in rectosigmoid, which was also confirmed by other authors [4,5]. However, a reduction of rectal doses can be achieved by removal of gas in the rectum during VCB [6]. A significant decrease of the mean rectum volume by 29% and D_{2cm3} by 11% was observed by Sabater *et al.* [6]. In our study, we did not measure gas volume in rectosigmoid. The weak point of our study is the lack of CT planning carried out with and without enema in the same patient.

Table 2. Mean doses to rectosigmoid for patients with enema vs. without enema

	Enema (n = 38)	Without enema (n = 37)
Rectosigmoid D_{2cm^3} [Gy]	5.6 (SD 0.7)	5.9 (SD 0.9)
Rectosigmoid D_{max} [%]	130.0 (SD 30.3)	135.8 (SD 25.6)

SD – standard deviation, D_{2cm3} – minimum dose to the highest treated 2 cm^3 of the organ, D_{max} – maximum dose to the whole organ

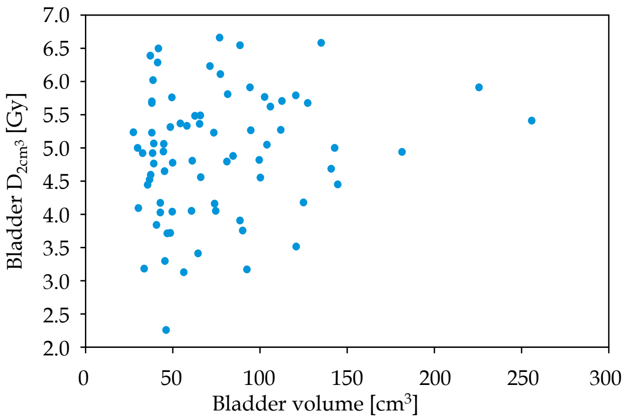

Fig. 3. Presentation of the association between bladder dose in 2 cm^3 and bladder volume

The bladder volume in the range of 27-256 cm^3 did not influence D_{max} or D_{2cm3} in our study. Literature data on the analysis of the effect of bladder volume on the dose given during VCB are also inconclusive. In a dosimetric study, Mahantshelly *et al.* compared the mean bladder volumes of 64.5 cm^3, 116.2 cm^3, and 172.9 cm^3, and a significant increase in small bowel dose in the empty bladder when compared to the full bladder was noted for intracavitary BT in cervical cancer patients. Only non-significantly higher bladder doses in 3 series were observed [7]. Like in our study, bladder filling did not increase the dose in it. The dosimetric effects of bladder filling in patients with VCB with a distended bladder preferentially reduce high-dose to the small bowel around the vaginal cuff without a significant change in dose to the bladder, rectum, or sigmoid, as reported by Hung *et al.* [8]. On the other hand, in literature, the full bladder produces a significant, 18.7% of bladder D_{2cm3} increase [9], and an empty bladder in 35 of 45 women reduced bladder doses by 0.5 Gy on average [10]. Hoskin *et al.* analyzed doses in empty and three full bladder volumes (35, 70, and 100 ml), and showed that the maximum bladder dose was lower with the empty bladder than with any of the full ones [11].

The analysis of D_{max} and V_{100} in OARs is very important. The analysis of V_{100} in the rectosigmoid revealed large differences in our study. A D_{2cm3} dose in the rectosigmoid equal to 7.4 Gy was acceptable, but D_{max} = 19.7 Gy was not. There is no recommendation concerning D_{max} and V_{100} in OARs in the literature; however, the V_{100} or D_{max} reduction in cases on overdosage is required. Our data based on standard plans, emphasized the benefit of 3D over 2D planning.

This study analyzed doses in the rectosigmoid, not only in the rectum, and it is a possible reason for the slightly higher dose in the organ. We decided not to contour these two organs (rectum and sigmoid) separately due to a short length of source position activation in the cylinder (2.75 cm), to avoid overdosage of OARs. High doses in OARs are observed in patients with thin vaginal walls and coexistent bowel loops adjacent to the apex of vagina. In such cases, it can be considered to prescribe the dose to the applicator surface, not at 0.5 cm depth. The utility of repeated OARs dose-volume histogram calculations in multifractional HDR VCB, using 3-dimensional imaging was assessed by Holloway *et al*. [12]. Variation of within-patients coefficients of $D_{0.1cm3}$ and D_{2cm3} were for the bladder: 14% and 8.1%, for the rectum: 7.9% and 5.9%, and for the sigmoid: 27.6% and 20.3%, respectively. The authors in [12] concluded that the small variation in doses to the bladder and rectum did not support reporting doses to the OARs beyond the initial fraction. In our study, CT was performed only before the first brachytherapy fraction.

Identification of AGs in our material was 83% in the whole length of the vagina, and 24% of AGs were located in the upper 3 cm of the vagina, including the top of the vault. In a meta-analysis of 9 publications, which met the requirements, 67% of patients had at least one air pocket and 59% per insertion [13]. Sapienza *et al*. in a prospective study reported that 77.2% of AGs were located within the proximal 2 cm of the cylinder, and 81.8% within the proximal 4 cm of the cylinder [13].

The depth of AGs is essential. In our study, 59% of AGs were small (≤ 3 mm), allowing the accepted dose to be given to the vaginal mucosa. In one patient, a 6 mm AG was located in the apex of vagina, adversely influencing dose distribution.

The incidence of AGs depends on the cylinder diameter, the proper fixation, and relaxation during the procedure. AGs reduce the mucosal dose in the treated area. Since the presence of AGs is often found, post-insertion CT can facilitate selection of optimal cylinder size in VCB or allow modification of dose distribution while planning the process. In our material, only some AGs were observed at the apex of the vagina (upper 3 cm).

Conclusions

Vaginal cuff brachytherapy planning with the use of CT is essential. Enema before cylinder insertion does not influence rectosigmoid D_{max} and D_{2cm3}. The analysis revealed no bladder volume effect on bladder doses D_{max} and D_{2cm3}. A few percent of plans require correction of dose distribution because of hot spots in OARs. For patients with high D_{max} and V_{100} in OARs, it should be considered to prescribe the dose to the applicator surface, or at smaller than 0.5 cm depth.

Most patients have air gaps around the cylinder, which can potentially reduce the mucosal dose. Selection of cylinder should be based on clinical findings. Post-insertion CT can facilitate a selection of optimal cylinder size. In case of major AGs, dose variation optimization of dose distribution is required. AGs less than 3 mm can be disregarded.

Disclosure

The authors report no conflict of interest.

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