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ORIGINAL ARTICLE

Long-term clinical outcome and dosimetric comparison of tandem and ring versus tandem and ovoids intracavitary application in cervical cancer

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Summary

Purpose: *The two most common applicators used in the treatment of high dose rate (HDR) intracavitary brachytherapy (ICBT) are tandem and ovoid (TO) and tandem and ring (TR). We aimed to evaluate the relationship between these treatment plans with short and long-term clinical outcomes.*

Methods: *This retrospective study included 50 patients who received a partial or complete response to external beam radiotherapy treatment (EBRT) and who were diagnosed with cervical cancer in our clinic between November 2015 and October 2019, including 25 TO patients and 25 TR patients. Left and right point A, high-risk clinical target volume (HR-CTV) EQD2, $D_{0.1cc,\ 1cc,\ 2cc}$ for the bladder, rectum, sigmoid, upper, middle, and lower vagina doses were recorded and compared according to the applicator type using the dose–volume histogram (DVH) parameter calculated from 200 computed tomography (CT) databases.*

Results: *Right point A dose EQD2, HR-$CTVD_{90,95,98}$, D_{2cc} rectum EQD2, upper vagina $V_{7Gy,\ 10Gy}$, middle and lower vagina $_{0.1,\ 1,\ 2cc}$, upper vagina 5-mm lateral point dose and upper, middle, lower vagina average doses were all found to be significantly lower for TR than for TO ($p<0.005$).*

Conclusions: *Although right point A dose EQD2, HR-$CTVD_{90,95,98}$ values were higher in TO than in TR, the rectum and vaginal doses also seemed more advantageous in TR. GUS and GIS toxicities, local control, distant metastasis, treatment responses and survival rates were similar in both the applicators, although vaginal toxicity was observed more in TO. Studies with a higher number of patients are warranted in the future.*

Key words: *brachytherapy, cervical cancer, dosimetry, clinical results, radiotherapy*

Introduction

Cervical cancer remains the most devastating disease affecting women's health worldwide. Five hundred thousand new cases are diagnosed globally each year, and most of them are in developing countries [1]. The standard primary treatment for locally advanced cervical cancer consists of a concomitant combination of cisplatin-based chemoradiotherapy and brachytherapy. Different chemotherapeutic combinations have also been investigated accordingly with other patient biological characteristics and the sensitivity of the tumour [2].

Intracavitary brachytherapy is an important part of the definitive treatment of locally advanced cervical cancer [3]. The two most widespread applicators used in the treatment of high-dose rate (HDR) intracavitary brachytherapy are tandem and ovoid (TO) and tandem and ring (TR) [4]. Levin et al performed dosimetric comparisons of TO and TR using computed tomography (CT)-guided volume determination after the applicator was placed in patients with stage II–IV cervical cancer. The authors found that, although the optimisation point

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doses were similar between the two applicators, the TO applicator clearly showed a larger isodose volume than the TR applicator, albeit no correlation was noted between the dosimetric profiles and the clinical outcomes [5].

The selection of the applicator is quite arbitrary and depends on its availability, the patients' pelvic anatomy and the extent of disease. However, since the dose distribution in brachytherapy follows the inverse square law, different dose distribution patterns are manufactured with different applicator systems, some of which should protect the organs at risk (OARs) and provide more satisfactory targeting than others [6]. In TR, when compared to that in TO, a narrower dose distribution is achieved in the vagina, which is ideal for straight vaginas, where the lateral fornices are wiped. The TO is suitable for barrel-shaped cervices. Larger ovoids cause deterioration of the dose distribution and spread the dose to the lower vagina. With the TO applicator, a wide dose distribution can be achieved at the level of the cervix [7].

In this study, we compared the dose distribution of target therapy and critical organs, which were performed in patients with cervical cancer by using TR and TO applicators in our clinic, and the relationship between the treatment plans with short and long-term clinical outcomes were determined.

Methods

Patients

The study was approved by the Institutional Ethics committee, and patient's consent was waived off since this was a retrospective study (decision number: 2020-01/507, date: 08/01/2020).

This retrospective study involved 50 patients who were treated for cervical cancer and who visited our clinic between November 2015 and October 2019. The included patients received external beam radiotherapy (EBRT) from 45 Gy in 25 fractions prior to intracavitary brachytherapy (ICBT). The median pelvic external radiotherapy dose was 45 Gy (range: 45–50.4). Lymph node boost doses (range: 5.4-12 Gy) and midline blocked doses (45-Gy pelvic, then 5.4-9 Gy) were applied. The patients received EBRT with intensity-modulated radiotherapy (IMRT) or volumetric modulated arc therapy technique, with 40 mg/m^2 cisplatin chemotherapy conducted weekly in patients with the appropriate renal functions. The patients were checked weekly with the cone beam CT (CBCT).

Patients who showed a partial or complete response to EBRT treatment, and, in accordance with the International Federation of Gynaecology and Obstetrics (FIGO, 2018) staging IA-IIIC2, patients aged 18-70 years who did not interrupt their treatment for >2 weeks were included in the study [8].

The patients were administered the HDR ICBT treatment with the Ir 192 source. The ICBT dose was administered twice weekly at 7 Gy/fraction, in a total of 4 fractions.

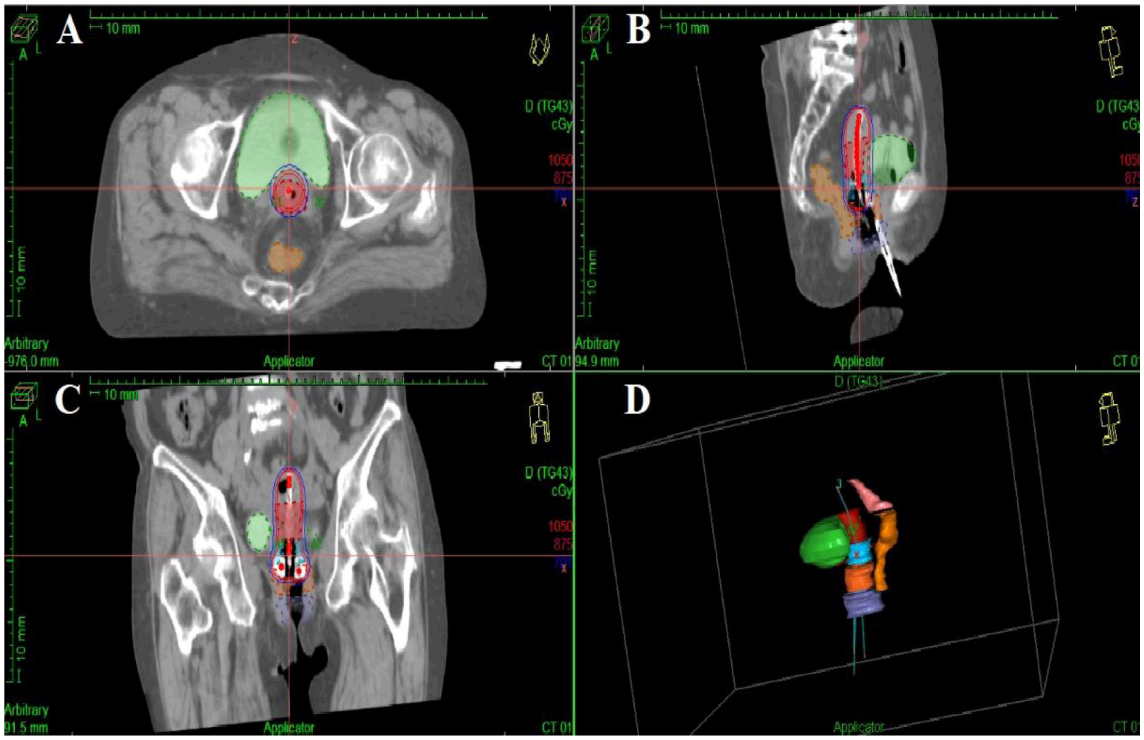

Figure 1. Figure showing axial, sagittal and coronal isodose distributions applicators: **A:** in the axial plane for TO; **B:** in the sagittal plane for TO; **C:** in the coronal plane for TO; **D:** Target and cricital organ conturing for TO (CT guided volume determination and application).

Brachytherapy application procedure

Gynaecological examination and a lower abdomen MRI were performed to determine the tumour remaining before the first brachytherapy application, anatomical examination and selection of the most suitable applicator for the patient.

The procedure was performed under general anaesthesia for patient comfort and safety. A Foley catheter was placed in the bladder, which was filled with 30-60 cc of diluted contrast material in accordance with the International Commission on Radiation Units and Measurements (ICRU)-38 recommendations [9]. Depending on the patient, after placing the TO or TR applicator (Nucletron, Elekta Company, Stockholm, Sweden), a rectal retractor was placed. The applicators were immobilised with external fixation tools.

For TR applications, 4-cm and 6-cm tandem lengths were commonly used. The most common ovoid size for TO applications was 2.5 cm. The most common tandem angle used for TO applicator was 30 degrees. A 45-degree tandem angle was most commonly used for TR applicators.

After each insertion and the subsequent recovery from sedation, the patient underwent CT simulation (3-mm slice) using a 4-dimensional CT (4DCT) simulator (Philips Healthcare, Inc., Andover, MA). All patients were scanned in supine position.

Brachytherapy contouring, target delineation and treatment planning

The Oncentra® Brachy (version 4.5.3) treatment planning system (Nucletron, Elekta Company, Stockholm, Sweden) was used for 3D treatment planning.

CT simulator images were shot, and T2-weighted MRI images were acquired prior to brachytherapy in order to identify the extent of residual disease as well as to guide the delineation of HR-CTV. This study included 50 patients whose residual tumours did not exceed one-third of the parametrium following external chemoradiotherapy, obtained from T2-weighted MRI images. Patients with greater residual tumour extension were excluded from the current study, but they were directed to interstitial therapy.

Contouring was performed in accordance with the Groupe European Curietherapy-European Society for Therapeutic Radiation Oncology (GEC-ESTRO)'s 3-dimensional contouring guides [10]. In contouring HR-CTV, with reference to the MRI findings, the critical organs i.e. the bladder, rectum and sigmoid were drawn. Vaginal contouring used a 0.4-cm fixed brush at the times of EBRT and brachytherapy on CT imaging. The upper, middle and lower portions of the vaginal mucosa were contoured separately.

The posterior-inferior border of the symphysis (PIBS) vaginal dose point acted as a reference for defining the anatomical dose points along the vagina as well as the vaginal reference length (VRL). The PIBS vaginal dose point was defined at a point 2 cm behind the PIBS in the sagittal direction for EBRT and at 2 cm behind the line where it crossed the applicator tandem for ICRT. Additional vaginal dose points for EBRT were selected per centimetre (PIBS + 3 cm PIBS-up to 2 cm) and the middle VRL in the craniocaudal trunk axis. For

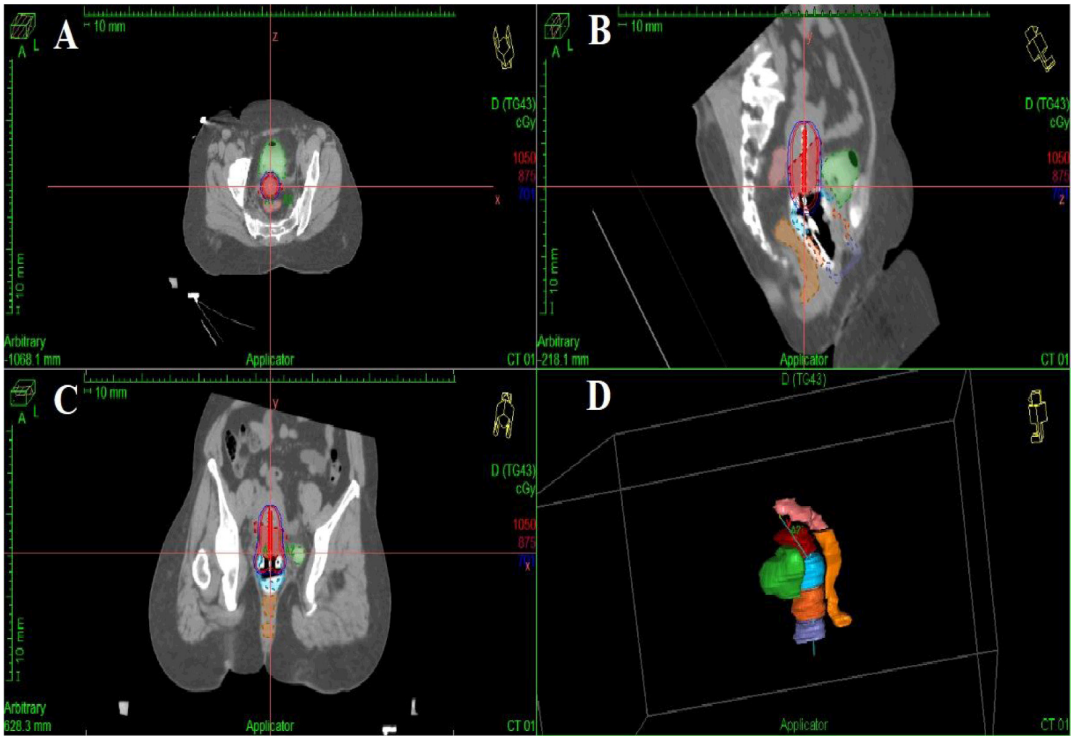

Figure 2. Figure showing axial, sagittal and coronal isodose distributions applicators: **A:** in the axial plane for TR; **B:** in the sagittal plane for TR; **C:** in the coronal plane for TR; **D:** Target and cricital organ conturing for TR (CT guided volume determination and application).

Table 1. Demographic characteristics of the patients and the disease states

Variables	*TO* *n (%)*	*TR* *n (%)*
Age (median, years)	49 (30-70)	51 (28-77)
Histopathology		
SCC	24 (96)	25 (100)
Adeno Ca	1 (4)	-
Stage		
1B3	-	1 (4)
2A2	2 (8)	1 (4)
2B	7 (28)	8 (32)
3B	1 (4)	1 (4)
3C1	10 (40)	11 (44)
3C2	5 (20)	3 (12)
ECOG performance status		
ECOG 0	16 (64)	14 (56)
ECOG 1	8 (32)	11 (44)
ECOG 2	1 (4)	-
Diagnosis PETmax SUV_{Median}	13.1 (6-24.1)	15 (5.4-29.1)
Menopausal status		
Premenopausal	11 (44)	15 (60)
Postmenopousal	14 (56)	10 (40)
Comorbidity		
DM	3 (12)	-
HT	2 (8)	2 (8)
CRF	6 (24)	1 (4)
COPD	-	1 (4)
Concurrent chemotherapy		
Cisplatin	22 (88)	21 (84)
Carboplatin	1 (4)	-
Fraction dose, median (cGy)	180 (180-200)	180 (180-205)
EBRT total dose median (cGy)	5040 (4500-6000)	4680 (4500-5400)
EBRT fields		
Pelvic lymphatics+uterine+vagina	20 (80)	22 (88)
Pelvic paraaortic lymphatics +uterine+vagina	5 (20)	3 (12)
Tumour diameter EBRT onset median (cm)	5.4 (2.3-9.7)	5 (2-9)
Residual pathological tissue after EBRT median (cm)	2 (0-5.8)	2 (0-6)
Residual pathological tissue after EBRT median (cm)		
≤ 4	20 (80)	21 (84)
>4	5 (20)	4 (16)
VLR	5.38 (3-7.7)	5.78 (3.8-7.5)
Vaginal involvement at the time of diagnosis		
No	9 (36)	6 (24)
Vaginal 1/3	14 (56)	18 (72)
Vaginal 2/3	2 (8)	1 (4)
Diagnosis, hemoglobin level	11.3 (7.5-15)	11.2 (9.5-14.6)
Weight median (kg)	64 (45-74)	70.5 (55-128)
Follow-up time median (months)	51.6 (2.6-86.4months)	30.7 (6.4-62.1 months)

TO: tandem and ovoid, TR: tandem and ring, SCC: squamous cell carcinoma, ECOG: Eastern Cooperative Oncology Group, PET: Positron emission tomography, EBRT: External Beam Radiotherapy, VLR: Vaginal reference length, DM: diabetes mellitus, HT: Hypertension, CRF: Chronic renal failure, COPD: Chronic obstructive pulmonary disease

the ICRT, the same vaginal dose points were selected on the tandem axis that was supposed to represent the centre of the vagina. The PIBS-2 cm point was accepted as the indicator of vaginal introitus, and the PIBS +2 point was selected as the indicator of the anatomical middle of the vagina [11].

HR-CTV included a residual tumour following external radiotherapy, the entire cervix and the presumed extra-cervical tumour extension at the time of brachytherapy.

According to these guidelines, the treatment plan should include the doses taken by the reference points, as determined by the Dose and Volume Specification for Reporting Intracavitary Therapy in Gynaecology, ICRU-38, and the D_{90} dose of HR-CTV in reference to the GEC-ESTRO manual [9,10].

HDR brachytherapy (dose ratio>12 Gy/h) was planned in full response or in patients with residual tumours of size<4 cm. EQD2 (HDR brachytherapy dose converted to 2 Gy equivalent dose), D_{90} ≥80 Gy, and D_{90} (dose taken by 90% of the volume) with a residue >4 cm were planned to be 85-90 Gy.

The linear-quadratic (LQ) model provides calculation estimates of the biologically equivalent dose, with due consideration of the dose rate per fraction. The LQ model doses for HDR were normalised to an equivalent dose at 2 Gy (EQD2). A critical component of the LQ model was used for cervical cancer tumour, where the α/β ratio is 10 Gy and the normal tissues of the α/β ratio is 3 Gy [12].

EQD2 calculations were performed using the LQ spreadsheet available at the American Brachytherapy Society's website [13].

The D_{2cc} definition was used for OAR dose limits. The EQD2 limits for D_{2cc} for the rectum-sigmoid was ≤70-75 Gy and for the bladder was ≤90 Gy [14].

After each application, the treatment plan and dose-volume histograms (DVH) were calculated to achieve the target and OAR doses. Optimisation was conducted, which did not exceed the GEC-ESTRO guidelines for the organs at risk. All dwell positions were at first activated. Next, by using an isodose shaper tool and based on the dwell time changes, the isodose was modified and manual modifications were made to maintain the pear-shaped dose distribution while excluding the rectum, sigmoid and bladder from the final optimised plan.

Isodose lines are demonstrated in the axial, sagittal, coronal plane, target and critical organ contouring for TO (Figures 1A, B, C, D) and TR (Figures 2A, B, C, D) applicators.

In our study, DVHs were generated over a total of 200 CT databases. Left and right point A, high-risk clinical target volume (HR-CTV D_{90}) EQD2, HR-CTV $D_{90,95,98}$, $D_{0.1cc,\ 1cc,\ 2cc}$ for the bladder, rectum, sigmoid, upper, middle, lower vagina doses, upper vagina V_{7Gy},10 Gy cc, upper, middle, lower vagina 5-mm lateral point doses and upper, middle, lower vagina average doses were recorded and compared according to the applicator type, and the clinical outcomes and survival analyses of the patients' follow-up appointments were accordingly evaluated.

Statistics

Statistical analyses were conducted using the SPSS statistical package version 23 (IBM Corp., Armonk, New York, USA). Descriptive statistics, such as the mean and standard deviation, were calculated. Statistical analyses were conducted using an independent samples T-test and Mann–Whitney U test to assess the relationship between the dosimetric volume and other parameters of TO and TR applicators. Kaplan-Meier method and log-rank test were performed for survival analyses. Significance was set at $p<0.05$.

Results

Demographic and treatments features of the patients are shown in Table 1 according to the TO and TR applicators.

Right point A dose EQD2, HR-CTV$D_{90,95,98}$, D_{2cc} rectum EQD2, upper vagina $V_{7Gy,\ 10\ Gy}$, middle and lower vagina $_{0,1,\ 1,\ 2cc}$, upper vagina 5-mm lateral point dose and upper, middle and lower vagina average doses were all found to be significantly lower for TR than for TO ($p<0.005$). Statistical significance was not determined for other parameters (Tables 2, 3).

Locoregional recurrence (LRR) developed in 3 (12%) TO patients. Of the patients who developed distant metastases, 2 (8%) developed lung metastasis and 4 (16%) developed bone metastasis.

Table 2. Comparative assessment of dose Left and Right Point A, D_{2cc} rectum, bladder, sigmoid, HRCTVD90, Upper vaginal lateral point dose EQD2 values of all patients

	TO (mean±SD)	*TR (mean±SD)*	*p value*
Left Point A dose (EQD_2 α/β=10Gy)	88.40±20.09	77.28±19.27	0.16
Right Point A dose (EQD_2 α/β=10Gy)	89.23±16.09	76.10±18.30	0.03
D_{2cc} Rectum (EQD_2 α/β=3Gy)	73.93±7.66	65.38±7.21	0.01
D_{2cc} Bladder (EQD_2 α/β=3Gy)	81.94±10.69	84.48±6.28	0.3
D_{2cc} Sigmoid (EQD_2 α/β=3Gy)	60.56±13.51	62.04±7.87	0.63
HR-$CTVD_{90}$ (EQD_2 α/β=10Gy)	85.58±7.32	82.73±6.73	0.15
Upper vaginal lateral point dose EQD_2 (EQD_2 α/β=3Gy)	105.45±32.77	86.68±33.55	0.09

TO: tandem and ovoid, TR: tandem and ring, EQD_2: LQ model doses for HDR are normalized to an equivalent dose at 2 Gy

Table 3. Fraction doses comparison of high-risk clinical target volumes and organs at risk between the TO and TR applicators

Organ at risk/HR-CTV	*TO (mean±SD)*	*TR (mean±SD)*	*p value*
HR-CTV D_{90}	780.57±247.25	669.94±138.85	**0.03**
HR-CTV D_{95}	696.19±234.91	558.97±130.72	**0.03**
HR-CTV D_{98}	621.43±224.36	506.85±118.15	**0.01**
HR-CTV volume cm^3	46.81±32.66	41.02±14.23	0.42
Bladder volume	102.52±21.78	127.23±16.58	**0.001**
Rectum volume	55.64±21.55	55.43±18.92	0.86
Sigmoid volume	23.82±20.80	23.99±14.55	0.39
Rectum $_{0.1cc}$ (cGy)	600.71±160.73	518.66±191.58	0.10
Rectum $_{1cc}$ (cGy)	491.44±120.78	419.72±143.46	0.06
Bladder $_{0.1cc}$ (cGy)	675.19±212.43	720.86±166.02	0.40
Bladder $_{1cc}$ (cGy)	572.88±161.70	594.00±98.89	0.58
Sigmoid $_{0.1cc}$ (cGy)	431.17±182.19	410.10±182.28	0.68
Sigmoid $_{1cc}$ (cGy)	345.51±146.86	325.02±149.77	0.62
Upper vagina $_{0.1cc}$ (cGy)	2595.21±1818.05	3121.85±2013.40	0.42
Upper vagina $_{1cc}$ (cGy)	1530.77±997.40	2363.56±1466.58	0.08
Upper vagina $_{2cc}$ (cGy)	1253.77±795.76	1665.73±1007.16	0.11
Upper vagina 7Gy cc	35.12±64.08	8.53±3.82	**0.001**
Upper vagina 10Gy cc	10.01±5.25	4.22±2.70	**0.001**
Middle vagina $_{0.1cc}$ (cGy)	1390.77±1325.67	366.46±215.66	**0.006**
Middle vagina $_{1cc}$ (cGy)	839.24±676.02	315.78±191.51	**0.012**
Middle vagina $_{2cc}$ (cGy)	685.26±525.54	268.46±156.27	**0.014**
Lower vagina $_{0.1cc}$ (cGy)	255.44±153.84	135.05±62.81	**0.002**
Lower vagina $_{1cc}$ (cGy)	190.41±129.33	109.19±56.06	**0.001**
Lower vagina $_{2cc}$ (cGy)	174.35±115.19	98.93±51.85	**0.001**
Upper vagina 5mm lateral point dose	743.87±400.32	535.08±308.47	**0.04**
Middle vagina 5mm lateral point dose	223.23±209.31	159.76±82.70	0.39
Lower vagina 5mm lateral point dose	108.96±79.04	76.70±30.42	0.17
Upper vagina average	1023.53±244.63	806.52±408.75	**0.02**
Middle vagina average	372.97±203.51	197.14±114.50	**0.003**
Lower vagina average	118.96±88.01	74.50±46.06	**0.03**

HR-CTV: High risk critical target volume. Bold numbers denote statistical significance

Of the TR patients, 3 (12%) patients developed locoregional recurrence (LRR). Patients with distant metastases developed lung metastasis (4%), liver metastasis (4%), and bone metastasis (4%) in one patient each.

RT acute side effects were: lower GIS grade 1-2 side effects 10 (40%) in TO, 8 (32%) patients in TR, GUS grade 1-2 side effects 12 (48%) in TO, 12 (48%) in TR, which was observed in the patient. Among the chronic side effects in TO patients, only GUS grade 1 in 1 (4%), only nephrotoxicity in 1 (4%), vaginal stricture in 2 (8%), vaginal dryness in 8 (32%), vaginal fibrosis in 2 (8%), GUS grade 2 side effects with vaginal dryness in 1 (4%), vaginal dryness and nephrotoxicity in 1 (4%), and vesicovaginal fistula in 1 (4%) were observed. Among the TR patients, nephrotoxicity was observed in 3 (12%) patients, stricture in the small intestine in 1 (4%), vaginal dryness in 4 (16%), and GUS grade 1 side effects with vaginal stricture in 1 (4%) patient.

Of the TO patients, 18 (72%) showed a complete response, 6 (24%) progressed, and 1 (4%) showed a partial response. Of the TR patients, 20 (80%) showed a complete response, 4 (16%) progressed, and 1 (4%) showed a partial response.

The overall survival rates were 88% and 77% for TR 1-year and 5-year, respectively, and 88% and 58% for TO. No statistically significant difference was found between the 2 applicators for overall survival (p=0.296).

Discussion

In the study conducted by Rehman et al, dose distributions for TO and TR applicators were evaluated at the ICRU A point, bladder and rectal points

using the Abacus software. They observed that the dose at point A was significantly higher and that the doses to the bladder and rectal points were statistically insignificantly lower for TO. The authors concluded that the TO applicator reached a better dose distribution and thus predicted a better treatment result [15]. Levin et al investigated dosimetric comparisons of these 2 applicators. The authors showed that although the optimisation point doses, were similar between the 2 applicators, the TO applicator clearly exhibited a larger isodose volume relative to TR [5].

Tuncell et al in his dosimetric study found that when TR applicators are used according to the recommended dwell positions, the maximum rectum reference dose decreased compared to TO applicators; On the other hand, it has been reported that the size of the reference volume has also reduced significantly [16].

Ma et al compared the short-term toxicity and dosimeter of these applicators. Although rectal D_{2cc} was statistically similar between TO and TR, they observed that the mean rectal dose in TR was lower. V95, V85, V50, and V20 were all significantly higher for TO than for TR ($p<0.018$). Despite the larger isodose volume recorded for TO, the percent of CTV that received 100% of the prescribed dose (CTV 100%) and the percent of the prescription dose that covered 90% of CTV (D_{90}) were not statistically different [17].

Chakrabarti et al. reported that the A point, $HRCTVD_{90}$ EQD2, D_{2cc} rectum, sigmoid colon, and bladder EQD2 doses in TO were significantly higher than that in TR [18].

In a study by Erickson et al, the TO applicator demonstrated a significantly higher rectal and sigmoid dose and treatment volume. The TO and TR applicators and bladder doses were not significantly different in this study, which was attributable to the angle of the tandem used. While the most common tandem angle used for the TR applicator was 45 degrees, it was stated to be 30 degrees for the TO applicator [19].

In our study, when we compared the right point A dose EQD2 between TO and TR, we noted a statistically significantly higher dose in TO. The D_{2cc} rectum EQD2, $HR\text{-}CTVD_{90,95,98}$ doses were found to be statistically higher in TO than in TR. No statistically significant difference was noted between TO and TR in $HRCTVD_{90}$ EQD2, D_{2cc} bladder EQD2 and D_{2cc} sigmoid EQD2 values. Our findings were compatible with those reported in the literature.

Serban et al reported that the mean vaginal 5-mm lateral point dose was larger by 19.6 Gy for TR ICRT application than for TO [20]. In our study, this dose was found to be 18.7 Gy more for TO than for TR. Biltekin et al reported that the upper vaginal mucosa (V_{7Gy}) and the middle and lower vaginal mucosa $D_{0.1, 2cc}$ doses were statistically significantly lower in TR than in TO [21]. In our study, upper vagina $V_{7Gy, 10\ Gy}$, middle and lower vagina $_{0,1, 1, 2cc}$, upper vagina 5 mm lateral point dose and upper, middle and lower vagina average doses were all found to be significantly lower for TR than for TO. In late vaginal toxicity rates, less vaginal toxicity in TR patients may explain this situation. Rectovaginal reference doses were not given in our study. Studies that do not give rectovaginal reference doses, such as our study, are available in the literature.

We calculated both volume and average doses of the critical organ, (vagina), by drawing it directly instead of calculating it from indirect doses. In the literature there are very little clinical comparisons by applicator type by giving such detailed vaginal doses. In our study, $D_{0.1cc, 1cc, 2cc}$ for the bladder, rectum, sigmoid, upper, middle, lower vagina doses, upper vagina v_{7Gy},10 Gy cc, upper, middle, lower vagina 5-mm lateral point doses and upper, middle, lower vagina average doses are given [22,23]. However, there are insufficient studies in the literature that associate the dose distribution of the 2 applicators with their long-term clinical outcomes. with this study, we attempted to investigate this relationship, although the small number of patients in our study restricts our study.

In their study, Ma et al states no statistically significant difference in the RTOG acute ≥ grade 2 gastrointestinal (GI) or ≥ grade 2 genitourinary (GU) toxicities clinically reported between TO and TR. Acute grade 2 GI toxicity was observed in two patients in the TO group, while acute grade 2 GI toxicity was observed in one patient in the TR group. During a short-term follow-up, no vaginal fibrosis or stenosis was detected in either of the groups. No group of patients had ≥ grade 2 GU toxicity [17].

In our study, no statistically significant difference was noted between TO and TR in terms of acute side effects of lower GI grade 1-2 and GU grade 1-2 toxicity. In the present study, although the D_{2cc} rectum EQD2 dose was found to be statistically higher in TO than in TR, it was not statistically significantly reflected in acute lower GI toxicity. Similar results were reported in the literature.

The limitation of our study is the small sample size. Future studies including a greater number of patients are expected to help identify

patients who exhibited dosimetry profiles and long-term outcomes.

Although right point A dose EQD2, HR-CTV$D_{90,95,98}$ values were higher in TO than in TR, the rectum and vaginal doses also seemed more advantageous in TR. GUS and GIS toxicities, local control, distant metastasis, treatment responses and survival rates were similar in both the applicators, although vaginal toxicity was observed more in TO than in TR. Studies with a larger sample size are needed.

Conflict of interests

The authors declare no conflict of interests.

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