

Short-term clinical outcome and dosimetric comparison of tandem and ring versus tandem and ovoids intracavitary applicators

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Abstract

Purpose: To compare the short-term toxicity and dosimetry of tandem and ring (TR), and tandem and ovoid (TO) applicators in treatment of gynecologic malignancy.

Material and methods: Following pelvic external beam radiation therapy (EBRT), a total of 52 computed tomography-based plans from 13 patients with cervical cancer (FIGO IB2-IIIb) were evaluated for HDR brachytherapy. Prescription was 7 Gy to the ICRU point A for four weekly fractions. Gastrointestinal and genitourinary toxicities were evaluated. Clinical target volume (CTV) and organs at risk were delineated on CT scans. Bladder, rectum, and sigmoid mean doses and D_{2cc} were calculated. Treatment time and irradiated tissue volume were compared. Percent of CTV receiving 100% ($CTV_{100\%}$) of the prescribed dose as well as the percent of the prescription dose covering 90% of the CTV (D_{90}) were evaluated.

Results: Gastrointestinal and genitourinary toxicities were not different between TO and TR applicators. No significant differences in the dose to the right and left point A, or the left point B were observed. TO delivered a higher dose to right point B. Organs at risk doses were similar between the two applicators, except mean rectal dose was lower for TO applicator. Overall, TO treats a larger tissue volume than TR. Mean treatment time was shorter for TR. Tumor coverage (D_{90} and $CTV_{100\%}$) was equivalent between TO and TR applicators.

Conclusion: Although TO treats a larger tissue volume than TR, short-term toxicities and tumor coverage are similar. Long-term clinical outcomes will be elucidated with longer follow up period.

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Purpose

Intracavitary brachytherapy (ICBT) is an essential part of the treatment of cervical cancer and has been shown to improve outcomes [1-3]. Secondary to sharp dose gradient, advantages in dose optimization, a lower radiation dose to personnel, and shortened hospital stay as an outpatient procedure, high-dose-rate (HDR) brachytherapy has been widely used [4]. Remote afterloading HDR brachytherapy became popular in the 1960s [5,6]. According to the American Brachytherapy Society survey in 1995, 24% of institutions use HDR brachytherapy in the treatment of cervical cancer [7]. Prevalence of HDR utilization has increased in recent years [8].

The two most common HDR ICBT applicators used in treatment of cervical cancers are the tandem and 2 ovoids (TO) and the tandem and ring (TR) [4]. TR was introduced

after TO to render additional benefits to patients such as increased patient comfort, feasibility in patients with narrow vagina, applicability in women with obliterated vaginal fornices, and improved reproducibility [9,10]. Previous studies have examined the dosimetric profiles of TO and TR via orthogonal radiographs [11] and computed tomography (CT) images [12]; however, no correlations have been made in relationship to clinical outcomes such as short-term toxicity. Erickson *et al.* compared the dose distributions of TO with those of TR applicator [11] via orthogonal radiographs. Specific point dose comparisons were made. However, no isodose volume comparisons were made secondary to a lack of post insertion computed tomography (CT) verification. In their study, the results showed a larger isodose volume in TO than TR by comparing the height and width of isodose curve in a single dimension at a time. Studies have also addressed the

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spatial reproducibility of TO and TR applicators [7,13,14]. In the study by Levin *et al.*, dosimetric comparisons of TO and TR were investigated using CT guided volume determination after applicator insertion in patients with stage II-IV cervical cancer [12]. The authors showed that even though the optimization point doses were similar between TO and TR applicators, TO applicator clearly exhibited a larger isodose volume in comparison to TR applicator. No correlation between the dosimetric profiles and clinical outcome were made.

The purpose of the present study is to correlate short term clinical outcomes with dosimetric profile comparison between TO and TR applicators using CT guided planning system in the setting of multifractionated HDR ICBT for gynecologic malignancy.

Material and methods

Patients

Between 2011 and 2013, a total of thirteen women with cervical cancer, with International Federation of Gynecology and Obstetrics (FIGO) stage IB2-IIB were treated with HDR ICBT with Ir¹⁹² sources. Patients were identified retrospectively. All patients were treated with external beam radiotherapy (EBRT) consisting of 45 Gy in 25 fractions to the pelvis prior to ICBT. Parametrial boost of 5.4 Gy in 3 fractions were given to those patient who warranted it. In the present study, eight patients were treated with TO applicator and five patients with TR applicator. HDR brachytherapy consisted of 7 Gy per fraction given one week apart for a total of four fractions.

Intraoperative procedure

The selection of applicator was based on preference and the experience of the attending physician. One physician used TO applicators exclusively, whereas the other radiation oncologist preferred TR applicators. The first insertion of ICBT applicators was performed while patients were under anesthesia in the operating room. A Foley catheter filled with saline solution was inserted into the bladder. Sounding the uterus, cervical dilation, and Smitt sleeve placement typically took place in the OR in the presence of a gynecologic oncologist. After applica-

tor placement was verified, vaginal packing was applied. The subsequent applicator insertions were performed in the outpatient clinic with the patient placed under conscious sedation. The TO and TR applicators are shown in Figure 1. Small ovoids were utilized in the 32 TO insertions. Vaginal packing was applied subsequently for TO insertions, both anterior and posterior to the tandem to minimize bladder and rectal doses. Rectal tube was inserted, after which rectal contrast was injected. For TR insertions, 60° ring and rectal retractor were utilized in all TR patients.

Computed tomography simulation

After each insertion and subsequent recovery from sedation, the patient underwent CT simulation (3 mm slice) via Philips Brilliance CT simulator (Philips Healthcare, Inc., Andover, MA) for CT based treatment planning using the software Brachyvision (Varian Medical Systems, Inc., Palo Alto, CA). All patients were scanned in the supine position.

Treatment planning and target delineation

Each patient was prescribed 7 Gy to ICRU point A for a total of four fractions. After delineation of organs at risk (OAR), a 3D treatment plan was generated. For each brachytherapy fraction, a new plan was generated for each insertion to account for inter-fraction positional or anatomical changes. The rectum, bladder, and sigmoid colon were contoured on each CT slice. Bladder, rectum, and sigmoid doses and D_{2cc} were calculated. In order to modify the isodose curve to bring OAR D_{2cc} under GEC-ESTRO recommendations, optimization was achieved by adjusting the radioactive source loading patterns, dwell positions, and dwell times. Treatment fractions were delivered with a HDR Ir¹⁹² source afterloading system.

Retrospectively, CTV was contoured using the CT based high risk CTV delineation guidelines by Viswanathan *et al.* [15]. Mean treatment time and total volume of all tissues receiving 95% (V_{95%}), 85% (V_{85%}), 50% (V_{50%}), and 20% (V_{20%}) of the brachytherapy prescription dose were compared. Percent of CTV receiving 100% (CTV_{100%}) of the prescribed dose as well as the percent of prescrip-

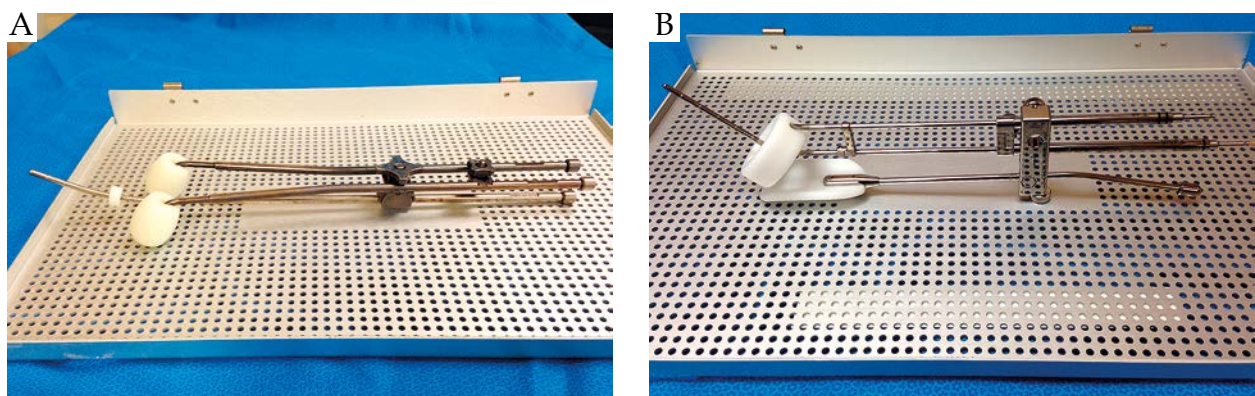


Fig. 1. A) Tandem and ovoids applicator assembled. B) Tandem and ring applicator assembled

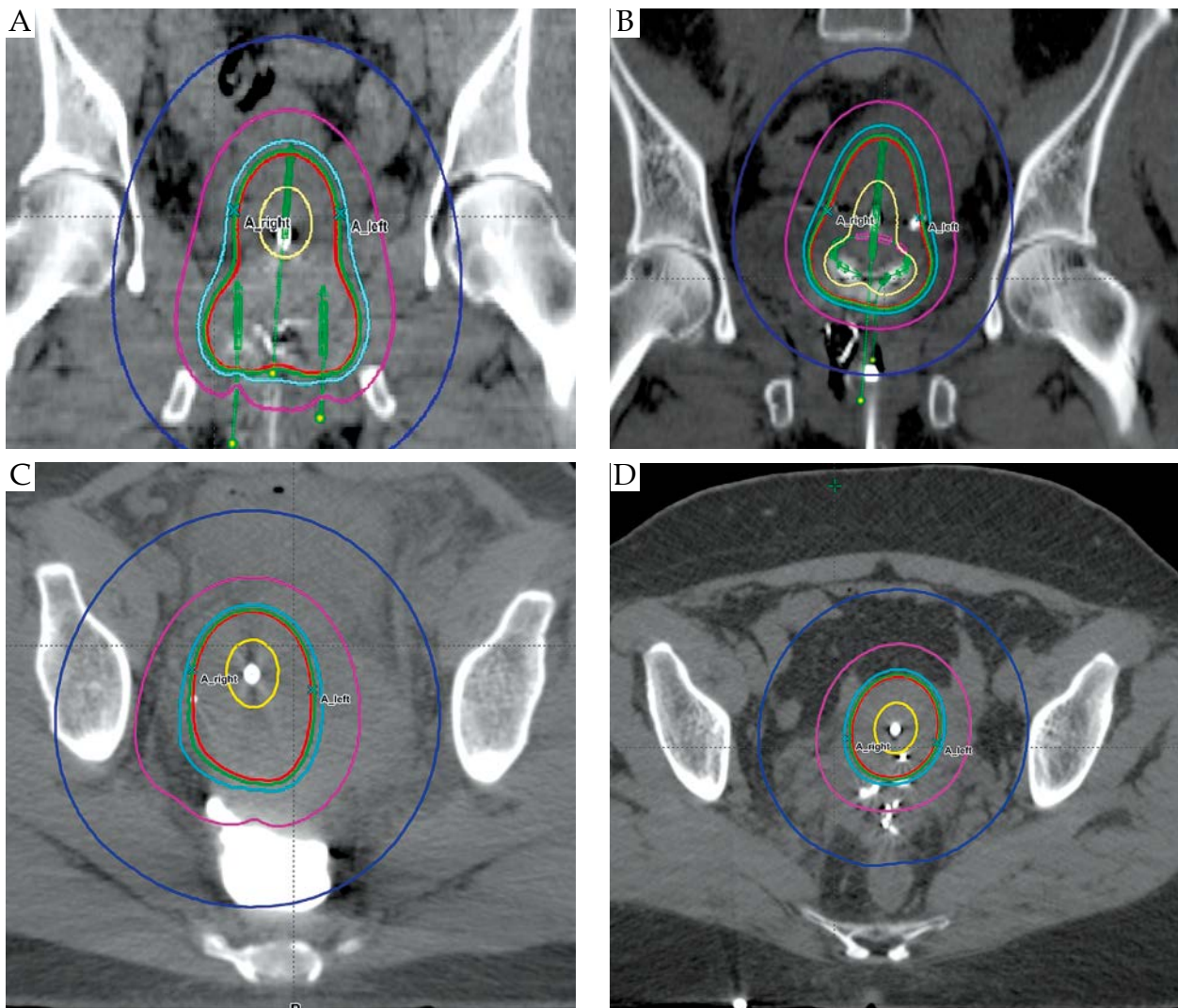


Fig. 2. Coronal and axial views of isodose distribution and prescription points A (left and right). Coronal view of tandem and ovoids isodose lines (A). Coronal view of tandem and ring isodose lines (B). Axial view of tandem and ovoids isodose lines (C). Axial view of tandem and ring isodose lines (D). Isodose lines as a percentage of the prescribed dose to point A: yellow (200%), red (100%), green (95%), cyan (85%), magenta (50%), and blue (20%). Isodose lines are shown for small ovoids in TO applicators

tion dose covering 90% of the CTV (D_{90}) were evaluated. Examples of the isodose lines are shown in the coronal plane for TO (Fig. 2A) and TR (Fig. 2B) as well as in the axial plane for TO (Fig. 2C) and TR (Fig. 2D) applicators.

Clinical outcome measurement

Gastrointestinal toxicity and genitourinary toxicity were evaluated weekly and graded according to RTOG toxicity criteria. The final evaluation for short term toxicity took place one month after the last insertion.

Statistics

Mean values, standard deviations, and standard error of mean were calculated from 32 TO and 20 TR applications. Because we could not assume whether TO or TR values would be larger or smaller, two tail *t* test was utilized to calculate *p*-value.

Results

All patients received four fractions of HDR brachytherapy for a total of 52 treatments (32 TO and 20 TR). Dosimetric results of the 52 applications and CT-based plans are presented in Table 1. Of the measured parameters, the dose to the right point B was significantly different between TO and TR. The mean dose to the right point B was higher in TO than TR. Although the rectal D_{2cc} were statistically similar between TO and TR, the mean rectal dose in TR was lower than TO. Given that the primary optimization goal was to deliver the prescription dose to points A, dosimetric results were similar for most parameters between the two applicators. Optimization goals were made to achieve GEC ESTRO dose constraints to bladder, rectum, and sigmoid colon. Hence, doses were intentionally minimized to the OAR contoured, resulting in no statistical differences seen in the dose to points A,

Table 1. Dosimetric parameters for tandem and ovoids (TO) and tandem and ring (TR) applicators

	TO (cGy)	TR (cGy)	<i>p</i> value
Right point A mean dose	693 ± 17	686 ± 39	0.55
Left point A mean dose	691 ± 21	673 ± 42	0.16
Right point B mean dose	233 ± 56	179 ± 39	0.00086
Left point B mean dose	214 ± 61	198 ± 48	0.32
Rectum mean dose	223 ± 65	162 ± 35	0.00018
Rectum D_{2cc}	408 ± 111	360 ± 105	0.148
Bladder mean dose	329 ± 112	328 ± 75	0.97
Bladder D_{2cc}	438 ± 196	397 ± 98	0.35
Sigmoid mean dose	184 ± 61	185 ± 47	0.95
Sigmoid D_{2cc}	433 ± 221	365 ± 87	0.16

Mean value and standard deviations were calculated from 32 TO and 20 TR treatments. *p* values were generated using two tail *t* test. D_{2cc} – minimum dose to the most exposed 2 cm³

the D_{2cc} rectum, the mean dose, and D_{2cc} bladder, or the mean dose and D_{2cc} sigmoid.

Treatment volumes and durations are presented in Table 2. $V_{95\%}$, $V_{85\%}$, $V_{50\%}$, and $V_{20\%}$ were all significantly higher for TO than for TR ($p < 0.018$). Qualitatively, this can be seen in Figure 2. The typical isodose line volumes (95%, 85%, 50%, and 20%) appear larger in TO than TR in both the coronal and axial dimensions. The volume enclosed by the prescription surface as well as the shape of the dose distributions were different between the two applicators. The total treatment time was significantly longer for TO vs TR applicators ($p < 0.0001$). Despite the larger isodose volume seen in TO, the percent of the CTV that received 100% of the prescription dose (CTV_{100%}) and the percent of prescription dose covering 90% of the CTV (D_{90}) were not statistically different between TO and TR applicators. For dose distributions in regards to TO applicators, the above dosimetric parameters are described for applicators using small ovoids.

Clinically, there were no statistical differences in the RTOG acute \geq grade 2 GI or \geq grade 2 GU toxicities seen between TO and TR (Table 2). Two patients in the TO group experienced acute \geq grade 2 GI toxicity, whereas one patient in the TR group experienced acute \geq grade 2 GI toxicity. No vaginal fibrosis or stenosis was detected in either group during short term follow up. No patient experienced \geq grade 2 GU toxicity in either group.

Discussion

Tandem and ring HDR brachytherapy has been gaining wider utilization secondary to increased patient comfort, ease of insertion, inter fractional consistency, and applicability in patient with narrow vagina [9]. In the current study, both applicators were able to satisfy optimization goals and OAR tolerance, but they produced very different treatment volumes and treatment times. This study kept optimization goal to 700 cGy at point A for every fraction to minimize inter-fraction differences and maintain consistency between TO and TR doses. Within the same setting, when attempting to deliver the same prescription dose to point A, TO applicator delivers

the same dose as TR to a significantly larger volume with longer treatment duration. This difference may be due to the relative changes in the anatomy, in relation to the location of the treatment volume and critical organs as the applicator is inserted. As seen qualitatively in Figure 1, the assembled TO apparatus exhibits a wider distribution at the level of the ovoids as well as thicker anterior posterior distribution. Hence, to achieve the same prescription dose to point A, the overall treated volume is higher for TO. The results are in agreement with the dosimetric findings of earlier studies using 2D radiographs [11] as well as 3D CT volumes [12]. The two applicators are not dosimetrically equivalent. Alternatively, differences in the techniques between two different radiation oncologists may account for the dosimetric differences, since each radiation oncologist clearly exhibited preference for one type of applicator over the other. Intuitively, the shape of the adjacent anatomy and hence the CTV delineation, depend on the applicator type used. It is interesting that the right point B dose is higher in TO than TR. Since the dose to point B is not an optimization goal, the results show fundamental physical differences between the two applicators. Since point A is defined in relationship to the tandem whereas point B is defined according to the anatomical midline, the differences seen in the point B dose may have resulted from fundamental differences or asymmetry in the position of the tandem to that of the ovoids. The positioning of the ovoids largely depend on the shape and symmetry of the vaginal fornix. During insertion, the tandem does not always bisect the distance between the ovoids in the midline of the coronal plane. The innate design of TO applicator allows a greater degree of motion between the tandem and the ovoids than between the tandem and the ring in the assembled TR applicator. Therefore, the differences seen in the point B dose between TO and TR applicators may be due to the differences in the design that allows more freedom of movement in TO applicator.

The more important question is addressing the clinical relevance of such dosimetric differences. Point A for both TO and TR have been optimized to 7 Gy; however, point A dose not necessarily reflect the dose to the tar-

Table 2. Volumes of all tissues that received various doses, target volume receiving prescription dose, total duration of treatment, and acute toxicities for tandem and ovoids (TO) and tandem and ring (TR) treatments

	TO	TR	p value
V _{95%} (cc)	123 ± 25	104 ± 26	0.018
V _{85%} (cc)	147 ± 30	123 ± 31	0.012
V _{50%} (cc)	329 ± 70	267 ± 68	0.0050
V _{20%} (cc)	1187 ± 253	972 ± 242	0.0064
CTV _{100%} (%)	55 ± 14	58 ± 11	0.45
D ₉₀ (%)	56 ± 16	55 ± 12	0.77
Mean treatment time (seconds)	848 ± 188	673 ± 73	0.00005
≥ grade 2 GI toxicity (%)	20	25	1.00
≥ grade 2 GU toxicity (%)	0	0	NS

Mean value and standard deviations were calculated from 32 TO and 20 TR treatments; p values were generated using two tail t test. CTV – clinical target volume, GI – gastrointestinal, GU – genitourinary, CTV_{100%} – percent of CTV receiving 100% of dose, D₉₀ – percent of the prescription dose covering 90% of the CTV; V_{95%}, V_{85%}, V_{50%}, V_{20%} – target volume receiving at least 95, 85, 50 or 20% of prescription dose

geted volume. Hence, determining the doses to the CTV, delineated via CT based contour according to guidelines by Viswanathan *et al.* [15], is essential to the comparison of future clinical outcomes such as locoregional control. In this setting, the CT based planning modality appears inferior to MRI based images in terms of distinguishing differences between the uterus, cervix, bladder, rectum, and the tumor. Though MRI based consensus guidelines are available for delineation of clinical target volumes for intensity modulated pelvic radiotherapy [13], the applicators utilized were not compatible with MRI and no MRI simulators were readily available. Therefore, the contours of CT and OAR were accomplished via CT based guidelines.

Despite the aforementioned, the total treatment volume differences seen between TO and TR, CTV_{100%}, and D₉₀ were not different between the two applicators. Under the same conditions, one would expect the same dose to the targeting volume (CTV_{100%}) and D₉₀ would result in the same LRC, an outcome that will be elucidated with longer follow up. At present, a larger treatment volume by TO applicator did not translate to differences in CTV_{100%} or D₉₀. Nor did the larger treatment volume translate to higher acute GI or GU toxicity from TO applicator. This is not surprising since the optimization goals already accounted for bladder, rectum, and sigmoid colon doses as exhibited by a lack of statistically significant differences in GEC-ESTRO recommended D_{2cc} to the bladder, rectum, or sigmoid colon between the two applicators. As such, no differences in the GI or GU toxicities were observed between patients who were treated with TO vs. TR.

Given that it is the practice at our institution to prescribe the dose to point A, we acknowledge the limitation of retrospectively outlining the target volumes after the completion of therapy. Furthermore, there are limitations to target delineation via CT simulation as compared to MRI, which is recommended by GEC-ESTRO [15]. However, due to logistic reasons, MRI is not readily available after insertion. Hence, CTV_{100%} and D₉₀ appear low when one attempts to impose 2D optimization unto a 3D volu-

metric data set. We have shown that although there were differences in the overall treatment volumes between the applicators, the same prescription dose to point A in TO and TR result in the same coverage to the clinical targeting volume with equivalent acute clinical toxicity.

Conclusions

The results show that although the two applicators deliver similar prescribed dose to point A and maintain critical organ doses below tolerance, they treat different volumes. Higher amounts of normal tissue are treated by the TO applicator, though the short-term toxicities are not increased. Even though the TR applicator covers less total tissue volume, dose distribution to the tumor volume is not compromised. Longer follow up period is required to evaluate long-term clinical outcomes such as loco-regional control, disease free survival, overall survival, long-term toxicity, quality of life, and correlation to differences seen in such parameters as V_{95%}, V_{85%}, V_{50%}, and V_{20%} between TO and TR applicators.

Disclosure

Authors report no conflict of interest.

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