Dosimetric Evaluation of a Flexible Dual Balloon-Constructed Applicator in Treating Anorectal Cancer

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Abstract
Background and Purpose: To assess the dosimetric flexibility of a dual balloon brachytherapy applicator developed for the treatment of anorectal lesions. Materials and Methods: Different amounts of water were infused into the inner and outer balloon separately to study the asymmetrical distribution of the catheter, the radial distance of the active source channel to the inner surface of the global target volume, the space between the active source channels, and their dosimetric impact to target tissues and uninvolved rectum. Results: Increasing inner balloon volume directly increased both the space between the active source channels and the radial distance of the active source channel to the inner surface of the global target volume. The space between the active source channels and the percentage of global target volume received 150% or more of the prescribed dose to target had a strong inverse correlation ($r_C0.881/P = .007$, $r_C0.976/P = .001$, respectively) with the radial distance of the active source channel to the inner surface of the global target volume. The space between the active source channels and the percentage of global target volume received 150% or more of the prescribed dose was strongly correlated with the radial distance of the active source channel to the inner surface of the global target volume. Conformity index, dose to 2 cm$^3$ of rectum, and total reference air kerma were strongly correlated with the radial distance of the active source channel to the inner surface of the global target volume, with values of $0.952 (P = .001)$, $0.833 (P = .015)$, and $0.922 (P = .002)$, respectively. Percentage of global target volume received 150% or more of the prescribed dose was significantly correlated with the space between the active source channels ($0.81/P = .022$), and conformity index was strongly inversely correlated with the space between the active source channels ($-0.833/P = .015$). Conclusion: The dual balloon-constructed Anorectal Applicator offers a flexible way to adjust the distances of the active source positions to the target in relation to uninvolved rectal wall. This flexibility simplifies planning which results in a highly conformal dose distribution to the target lesion while minimizing dose to normal rectal tissue.

Keywords
rectal cancer, brachytherapy, dual balloon

Abbreviations
AR, Anorectal Applicator; BT, brachytherapy; COIN, conformity index; CRT, chemoradiation; CT, computed tomography; $d_r$, the radial distance of the active source channel to the inner surface of the GTV; $d_s$, the space between the active source channels; D90, percentage of the prescription dose to 90% of the GTV; EBRT, external beam radiation; GTV, global target volume; LARC, locally advanced rectal cancer; PD, prescription dose; PTV, planning target volume; $r_s$, Spearman correlation coefficient; $R_{D90}$, percentage of prescription dose to 0.1 cm$^3$ rectal wall; $R_{D20}$, percentage of prescription dose to 2 cm$^3$ rectal wall; TRAK, total reference air kerma at 1 m; V150, percentage of GTV received 150% or more of the prescribed dose; $V_{in}$, inner volume; $V_{out}$, outer volume.

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Introduction

Brachytherapy (BT) has been applied to locally advanced rectal cancer (LARC) as a boost in preoperative radiotherapy or as reirradiation in recurrent disease. A randomized trial conducted in Canada and Denmark suggested no significant increase in toxicity or surgical complication for patients with LARC undergoing preoperative chemoradiation (CRT) with BT as a boost after external beam radiation (EBRT) of 50.4 Gy. The group receiving BT also had a 50% increase in the rate of major response for T3 tumors compared to EBRT alone. Other nonrandomized trials with preoperative BT had higher rates of sphincter preserving resection. There is also evidence for increased pathologic response, local control, and survival in patients treated with BT when compared to surgery alone or standard CRT.

The majority of BT for LARC was performed with an intra-luminal applicator using a rigid cylinder with or without variable usage of a balloon. Many other applicators have been used in the treatment of LARC including a HAM (Mick Radio-Nuclear Instruments, Mt. Vemon, NY) applicator, which was used by Harrison et al. for intraoperative radiation therapy in cases with locally advanced primary and recurrent rectal cancer yielding a 2-year control rate of 82% and 47%, respectively. Kolotas et al. reported their techniques and results with interstitial BT and concluded that it was an effective palliation for recurrent rectal cancer.

There are fewer reports of using BT for the treatment of anal cancer. Lesions within the anal canal are easier to access using BT than lesions within the rectum. Rigid cylinders are commonly used for the treatment of anorectal cancer. Balloon-type applicators were initially used for treating early-stage breast cancer as well as the vaginal cuff in gynecologic malignancies. The usage of balloon alone in treating early-stage breast cancer as well as the vaginal cuff in gynecologic malignancies. The majority of BT for LARC was performed with an intra-luminal applicator using a rigid cylinder with or without variable usage of a balloon. Many other applicators have been used in the treatment of LARC including a HAM (Mick Radio-Nuclear Instruments, Mt. Vemon, NY) applicator, which was used by Harrison et al. for intraoperative radiation therapy in cases with locally advanced primary and recurrent rectal cancer yielding a 2-year control rate of 82% and 47%, respectively. Kolotas et al. reported their techniques and results with interstitial BT and concluded that it was an effective palliation for recurrent rectal cancer.

Materials and Methods

A dual balloon-constructed Anorectal Applicator (AR™; Bio-nix, Toledo, OH; Supplemental Figure 1) is a disposable BT applicator designed specifically for the treatment of anal and rectal cancers. It has 8 to 10 cm effective treatment zone that allows treatment of the entire rectum without repositioning. It consists of 8 catheters contained within an inner balloon with an uninflated diameter of 2.3 cm. The outer balloon creates an adaptable shape that conforms to the rectal wall and distends the rectum which ensures fixation during treatment. The flexible inflatable inner balloon (which can be inflated up to a diameter of 3.5-4 cm) creates a variable distance between the source channel and rectum as well as a variable spacing between catheters. This study investigates the feasibility of using AR in treating localized rectal lesions. Phantom experiments were designed and conducted to test the asymmetry of dual balloon in air (Supplemental Figure 2) and associated dosimetric outcomes in phantom.

Dosimetric Study of Dual Balloon in Phantom

A prostate phantom (CIRS, Tissue Simulation and Phantom Technology, Norfolk, Virginia) was used for the insertion of the AR applicator. A 0.5 cm bolus measuring 2 x 2 cm was placed on top of the AR applicator before the insertion. Different combinations of water volume were infused into the inner and outer balloons. The outer balloon was contoured on planning computed tomography (CT) images. The global target volume (GTV) was defined as the delineated bolus area. The rectal wall was defined as the outer balloon with a 3-mm margin minus GTV. The planning target volume (PTV) was defined as GTV plus a 2-mm margin minus the outer balloon. Plans were created using Oncentra TPS version 4.3 (Nucletron; Elekta, Stockholm, Sweden). Dose points were placed on the outer surface of the GTV. After point dose optimization, a graphic optimization was followed by manual adjustment of the isodose lines. Plan criteria included D90 = 100% (percentage of the prescription dose (PD) to 90% of the GTV), minimization of V150 (percentage of GTV received 150% or more of the prescribed dose), and dose to 0.1 cm³ and 2 cm³ rectal wall (R₀,1cc and R₂,2cc).

Dosimetric Comparison Between Dual Balloon, Solid Multichannel Applicator, and Combination of Solid Applicator With Balloon

1. Two multichannel cylindrical applicators (Miami applicator; Varian, Palo Alto, California; Nucletron vaginal CT-MR multichannel applicator: Nucletron, an Elekta Company) of proper diameter was inserted into the prostate phantom with 0.5 cm bolus on surface described in the section “Dosimetry Study of Dual Balloon in Phantom.”
2. A single-channel cylindrical applicator having a diameter of 2 cm was inserted into the prostate phantom with 0.5 cm bolus on one side of the surface and with a deflated MammoSite balloon placed in the opposite side of the surface. Balloon was inflated against the rectal surface to immobilize the cylindrical applicator within the rectum.
3. The single-channel cylinder in (2) was replaced by the AR applicator.

Plans for (1), (2), and (3) were created using the planning procedure and criteria as described in the section “Dosimetry Study of Dual Balloon in Phantom.”

Evaluation. For each plan created using the scenarios described in the section “Dosimetric Comparison Between Dual Balloon, Solid Multichannel Applicator, and Combination of Solid Applicator With Balloon,” the radial distance of the active source channel to the inner surface of the GTV (d₁) and the space between the active source channels (d₂) was measured. D90 and V150 of GTV, P-D90 of PTV, R₀,1cc, and R₂,2cc were recorded. Moreover, a conformity index (COIN) was calculated as
insertions, and another from the cylinder combined balloon insertion. The total infused water within AR applicator was 115 cm$^3$ in each observation. Outer volume ($V_o$) was decreased from 115 to 65 cm$^3$ and inner volume ($V_i$) was increased from 0 to 50 cm$^3$. The upper case letter observations of AR insertions (A, B, C, D, and E) correspond to cases in which the AR applicator was inserted such that channel #1 was oriented at the 12 o’clock position, whereas the lower case letter observations (a, c, and e) correspond to cases in which the AR applicator was inserted such that channel #1 oriented at the 6 o’clock direction. Increasing the inner balloon volume decreased $d_r$ but increased $d_s$ at the same time. Keeping D90 the same ($100.7\% \pm 0.2\%$), a variation of $d_r$ from 1 to 10 mm and $d_s$ from 5 to 12.6 mm was observed, yielding a variation of V150, COIN, $R_{0.1cc}$, $R_{2cc}$, and TRAK ranging from 8$\%$ to 47.7$\%$, 0.75 to 0.83 cGy cm$^{-1}$ h$^{-1}$, 110$\%$ to 203.9$\%$, 33.2$\%$ to 81.7$\%$, and 0.055 to 0.147 cGy cm$^{-1}$ h$^{-1}$ at 1m, respectively, as noted in Table 1.

These results were further analyzed using Spearman correlation test to calculate the $r_s$ and its $P$ value displayed in Table 2. It was found in the AR group that $d_r$ had a strong inverse correlation ($-0.881$, $P = .007$) with $d_s$. Between all observations, only V150 was strongly and inversely correlated with $d_r$ ($-0.976/P < .001$). Conformity index, $R_{2cc}$, and TRAK were strongly correlated with $d_r$, with values of 0.952 ($P = .001$), 0.833 ($P = .015$) and 0.922 ($P = .002$), respectively. The V150 was significantly correlated with $d_s$ ($0.810/P = .022$). Conformity index was strongly and inversely correlated with $d_s$ ($-0.833/P = .015$). Both $R_{2cc}$ and TRAK had a weak correlation with $d_s$.

Comparing the AR balloon applicator with the rigid-type multichannel applicators of similar $d_r$ and $d_s$, combination (B vs I and C vs F in Table 1 and Supplemental Figure 3), B and I had similar dose distributions and dosimetric metrics, however, F had slightly worse $R_{2cc}$ and $R_{0.1cc}$ compared to C since F had larger $d_r$ and $d_s$.

**Discussion**

In this study, a constructed dual balloon AR applicator was used to deliver an increased conformal dose to a treatment target. By controlling the volume of inner and outer balloons, the distance of the source channels in relation to the target can be adjusted as compared to the rectal wall, thereby achieving an optimal dose distribution. A separate correlation test between the $V_i$ and $d_i$ in Table 2 showed that $d_i$ was strongly correlated ($-0.923$, $P < .005$) with $V_i$ when the total volume of $V_o$ and $V_i$ was constant (115 cm$^3$ in this study). In terms of the metrics V150, COIN, $R_{2cc}$, and TRAK, a smaller $d_i$ was found to be better. This seemingly implies that using larger $V_i$ could be more beneficial, however, a larger $V_i$ increases $d_o$, which resulted in a strong likelihood of increased $R_{0.1cc}$ and V150. Compared to other cylinder-type applicators, which have a fixed $d_r$ and $d_s$, the dual balloon AR applicator allows for enhanced ability to control both $d_r$ and $d_s$.

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**Results**

Figure 1 shows the dose distributions created after the AR applicator was inserted at different orientations and filled with varying amounts of water. The dose distributions of the Miami applicator (3.0 cm diameter) insertion and that of a cylinder (2.0 cm diameter) combined with a balloon insertion are shown as well. It can be seen that both the high dose (>100%) and medium dose (50%) conformed to the target better when the source channels were closer to the target. Results are summarized in Table 1, which includes the 8 observations from AR insertion, 2 observations from the multichannel applicator
Table 1. Geometry Conditions of the Implant in This Study and the Corresponding Planning Results.

| Observation | $V_o$, cm$^3$ | $V_i$, cm$^3$ | $d_r$, mm | $d_s$, mm | D90, % | V150, % | COIN | $R_{0.1\text{cc}}, \%$ | $R_{2\text{cc}}, \%$ | TRAK, U$^a$ |
|-------------|--------------|--------------|----------|----------|------|--------|-----|----------------|----------------|--------------|
| A           | 115          | 0            | 7.3      | 5        | 100.7| 14.74  | .826| 115.7          | 67.9           | .0118        |
| A           | 115          | 0            | 10.3     | 5.5      | 100.7| 8      | .832| 120.1          | 81.7           | .0147        |
| B           | 95           | 20           | 5.3      | 6.4      | 100.4| 22.8   | .819| 118.5          | 60.1           | .01         |
| C           | 85           | 30           | 1.5      | 8.4      | 100.6| 36.5   | .801| 116.5          | 37.3           | .061        |
| C           | 85           | 30           | 4.7      | 9.2      | 100.5| 35.5   | .823| 110             | 49.1           | .063        |
| D           | 75           | 40           | 1.2      | 8.9      | 100.7| 46.5   | .790| 140.4          | 37.4           | .061        |
| E           | 65           | 50           | 1        | 9.7      | 100.7| 47.7   | .754| 153.8          | 33.2           | .065        |
| E           | 65           | 50           | 1.1      | 12.6     | 100.9| 44.1   | .748| 203.9          | 52.7           | .072        |

| F            | Miami Device | 2.5          | 10       |          | 100.8| 34.5   | .719| 179.5          | 43.9           | .064        |
| G            | Cylinder + balloon | 10 |          | 100.7 | 19.8   | .792| 132.9  | .682| 116.1          | .0116         |
| H            | AR + balloon  | 2            | 4.9      |          | 100.7| 33.6   | .794| 76.3           | 28.1           | .053        |
| I            | Nucletron App$^b$ | 5            | 6.3      |          | 100.8| 27.4   | .767| 120.0          | 54.9           | .078        |

Abbreviations: AR, Anorectal Applicator; COIN, conformity index; D90, percentage of the prescription dose to 90% of the global target volume; $d_r$, the radial distance of the active source channel to the inner surface of the global target volume; $d_s$, the space between the active source channels; $R_{0.1\text{cc}}$, percentage of prescription dose to 0.1 cm$^3$ rectal wall; $R_{2\text{cc}}$, percentage of prescription dose to 2 cm$^3$ rectal wall; TRAK, total reference air kerma at 1 m; $V_o$, inner volume; $V_i$, outer volume.

$^a$CGy$^{-1}$h$^{-1}$ at 1 m.

$^b$Nucletron Multi Channel Applicator.

Table 2. Correlation Coefficient ($r_s$) and $P$ Values of the Planning Results With Implant Geometry $d_r$ or $d_s$ for Fixed 115 cm$^3$ Volume of Balloon Geometry in Table 1.

| $rs/p$ value | $d_r$ | $d_s$ | V150 | COIN | $R_{0.1\text{cc}}$ | $R_{2\text{cc}}$ | TRAK |
|--------------|-------|-------|------|------|-------------------|-------------------|------|
| $r_s$ vs $d_r$ | 1     | -0.881| -0.976| 0.952| 0.619             | 0.833             | 0.922|
| $P$ value     | <.001 | .007  | <.001| .001 | .115              | .015              | .002 |
| $r_s$ vs $d_s$ | -0.881| 0.810 | -0.833| 0.584| -0.643            | 0.707             |      |
| $P$ value     | .007  | <.001 | .022 | .015 | .171              | .096              | .058 |

Abbreviations: COIN, conformity index; D90, percentage of the prescription dose to 90% of the global target volume; $d_r$, the radial distance of the active source channel to the inner surface of the global target volume; $d_s$, the space between the active source channels; $R_{0.1\text{cc}}$, percentage of prescription dose to 0.1 cm$^3$ rectal wall; $R_{2\text{cc}}$, percentage of prescription dose to 2 cm$^3$ rectal wall; $r_s$, Spearman correlation coefficient; TRAK, total reference air kerma at 1 m.

The long, tubular shape of the anorectum that extends from the anal canal to the junction of the sigmoid colon is especially conducive to the use of an intracavitary-type cylindrical-shaped BT applicator. A single-channel cylinder with shielding insert is the easiest way to perform implant, which shields the far side uninvolved tissue, but it does not allow for dose distribution that conforms to the target, and the tungsten insert also prevents users from visualizing the target and performing dose calculation in planning system. A multichannel applicator produces nons isotropic dose distributions that can be useful in treating asymmetrical lesions. Devices that utilize an intracavitary mold applicator coupled with an endocavitary balloon are able to control the fixation of the mold applicator within the rectum using adjustable inflation. The multiring balloon (Capri) applicator is designed for intraluminal cavity insertions, which minimizes the air pocket between balloon and the luminal wall. However, the Capri applicator is likely too short to be applied effectively for rectal cancers. In the case of reirradiation in localized recurrent disease, it is essential to reduce dose to the adjacent rectal wall and nearby critical organs (eg, bladder, bowel). To produce an optimal dose distribution, a rapid dose falloff between target and normal tissue is more easily achieved by placing the source channel in close proximity to target and away from uninvolved normal tissues.

The observations A versus a, C versus c, and E versus e were created with the same amount of infused water at opposing insertion orientations using the AR applicator. A, C, and E had closer $d_r$ of the source channel to target compared to a, c, and e. It was similar to the results of the tests in air (Supplemental Figure 2) that the 8 catheters might react to the infusion of water differently such that the $d_r$ and $d_s$ between catheters were different. By using multiple inflations and deflations, the reproducibility of the channel positions was verified to be within about 1 mm. There are other existing interfraction uncertainty issues (eg, bowel preparation, migration of the markers, etc) that our daily practice still performs plan in each fraction. If using the same plan for multiple treatments, a pretreatment image verification program similar to the multilumen balloon for breast implant should be followed. Since the optimum dose distribution should be achieved with the smallest values of $d_r$ and $d_s$, a proper orientation of the channels during the implant might optimize the dose coverage and reduce the dose to the uninvolved rectal wall. In comparison with the AR implants (A-e in Table 1) to other implants (F-I in Table 1), a good AR implant had good conformity, low dose to $R_{2\text{cc}}$ and dose to $R_{0.1\text{cc}} <$120% of the PD. Using a deflated AR combined with an external balloon (H in Table 1) to decrease $d_r$ resulted the lowest $R_{0.1\text{cc}}$, however, this combination is technically more complicated and difficult as compared to AR implant alone, and the benefit of reducing $R_{0.1\text{cc}}$ to smaller than 100% PD is of likely little benefit.

Although the rectum is a tubular structure, it is narrow at the anal verge but distensible thereafter. It also has 3 or more
lateral curvatures that correspond to transverse rectal folds in the interior of the alimentary canal. Therefore, a pear-shaped balloon will conform more naturally to rectal anatomy than a rigid cylinder-type applicator. On the left in Figure 2 shows an inflated balloon in air compared to the shape change when inserted into a phantom; the right figure demonstrates the minimal shape change of the rectum after it was implanted with an AR balloon. An inflated AR balloon distends the rectum and eliminates any air pockets, which if present would likely cause significant dose uncertainties. Another great advantage of the balloon type AR is its softness that results in a substantial increase in patient comfort. Additionally, the diameter of the cylinder remains fixed during insertion, whereas the AR balloon can be inserted at a smaller diameter and inflated to proper size after insertion. It also allows patients to remain with the AR in situ during image verification, real-time planning, and treatment delivery.

In conclusion, the dual balloon-constructed AR applicator offers a flexible way to adjust the distance of the active source to the target in relation to uninvolved rectal wall. The design of the AR applicator that is comprised of an outer balloon and the multicatheters supported by an inner balloon makes it a technically user-friendly device and a dosimetrically superior BT applicator when treating recurrent rectal or anal cancers. Although this study was designed with a lesion thickness of 0.5 cm, similar conclusions can be drawn to thicker lesions where preoperative BT is desired.

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**Supplemental Material**
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**Figure 2.** Panel A, An inflated Anorectal Applicator (AR) in air and inserted to a prostate phantom. Panel B, Computed tomography (CT) images before and after AR implant.
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