

Clinical Investigation: Gynecologic Cancer

Bladder—Rectum Spacer Balloon in High-Dose-Rate Brachytherapy in Cervix Carcinoma

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Summary

This was a randomized study to evaluate bladder and rectum doses using a bladder—rectum spacer balloon (BRSB) and standard gauze packing in the same patient receiving 2 HDR brachytherapy fractions. Significant dose reduction to the small high-dose volumes of rectum was observed with BRSB. The doses to bladder were comparable. In addition to improved dosimetry, the BRSB may offer greater reproducibility and standardized displacement of the bladder and rectum in multiple HDR brachytherapy applications.

Purpose: To compare bladder and rectum doses with the use of a bladder—rectum spacer balloon (BRSB) versus standard gauze packing in the same patient receiving 2 high-dose-rate intracavitary brachytherapy fractions.

Methods and Materials: This was a randomized study to compare the reduction in bladder and rectum doses with the use of a BRSB compared with standard gauze packing in patients with carcinoma of the cervix being treated with high-dose-rate intracavitary brachytherapy. The patients were randomized between 2 arms. In arm A, vaginal packing was done with standard gauze packing in the first application, and BRSB was used in the second application. Arm B was the reverse of arm A. The International Commission for Radiation Units and Measurement (ICRU) point doses and doses to 0.1-cm³, 1-cm³, 2-cm³, 5-cm³, and 10-cm³ volumes of bladder and rectum were compared. The patients were also subjectively assessed for the ease of application and the time taken for application. Statistical analysis was done using the paired *t* test.

Results: A total of 43 patients were enrolled; however, 3 patients had to be excluded because the BRSB could not be inserted owing to unfavorable local anatomy. Thus 40 patients (80 plans) were evaluated. The application was difficult in 3 patients with BRSB, and in 2 patients with BRSB the application time was prolonged. There was no significant difference in bladder doses to 0.1 cm³, 1 cm³, 2 cm³, 5 cm³, and 10 cm³ and ICRU bladder point. Statistically significant dose reductions to 0.1-cm³, 1-cm³, and 2-cm³ volumes for rectum were observed with the BRSB. No significant differences in 5-cm³ and 10-cm³ volumes and ICRU rectum point were observed.

Conclusion: A statistically significant dose reduction was observed for small high-dose volumes in rectum with the BRSB. The doses to bladder were comparable for BRSB and gauze packing. Transparent balloons of variable sizes are recommended for patients with a less spacious vaginal cavity. © 2013 Elsevier Inc.

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Conflict of interest: none.

Introduction

Brachytherapy forms an integral part in the management of cancer of the cervix. Although a high dose can be effectively delivered to the tumor with brachytherapy, the dose delivered to the rectum and bladder results in late toxicity to these organs (1). Adequate displacement of these organs away from the brachytherapy sources is required to minimize radiation-induced complications. Conventionally this can be done by the use of vaginal gauze packing, use of rectal retractors, posterior vaginal speculum blades, and shielded ovoids (2). Vaginal packing with gauze is preferred in many centers because it is easily available, non-traumatic, simple, and inexpensive; however, it is uncomfortable for the patient and lacks reproducibility. In high-dose-rate (HDR) brachytherapy, whereby a high dose in multiple fractions is delivered, even minute variations in applicator position may lead to significant changes in doses to the organs at risk (3, 4). Thus adequate reproducible displacement of organs at risk away from the applicator is desirable to improve the therapeutic ratio. In this context, a special latex bladder–rectum spacer balloon (BRSB) device has been designed by HLL Lifecare Limited (Karamana, Trivandrum, India; formerly Hindustan Latex Limited), a government of India enterprise, to be used instead of vaginal gauze packing during brachytherapy for carcinoma of the cervix (5). The BRSB is a disposable balloon made of latex rubber and consists of 2 parts, a bladder part and a rectal part, which are joined together by a latex adhesive. Both the balloons are independently inflatable and are individually attached to a 1-way valve at the tail end of the tubes to prevent the escape of the fluid pushed in. Each side (bladder and rectum) has a different thickness. The surface of the balloon in contact with the applicator is thicker as compared with the surface facing the vaginal walls. The balloon is also thicker in the lower part, which corresponds to the lower vagina (details of the design of the BRSB are provided in reference 5) (Fig. 1).

A randomized study was conducted at our institution using the BRSB compared with standard gauze packing in the same patient undergoing 2 fractions of brachytherapy. The aim of the study was to evaluate the difference in doses to bladder and rectum with the use of BRSB and standard gauze packing. We also sought to validate and thereby modify the design of the BRSB, if necessary as per the requirement, to improve the function of the balloon (in

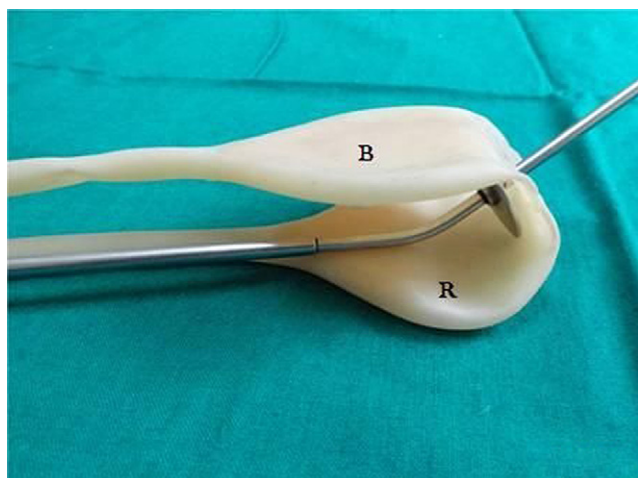


Fig. 1. Bladder–rectum spacer balloon with bladder part (B) and rectal part (R) joined together by latex adhesive.

reducing bladder and rectal toxicity) as a substitute for gauze packing in displacement of the bladder and rectum.

Methods and Materials

This was a prospective, randomized factorial trial (Registration number. CTRI/2009/091/000840) registered with the Clinical Trial Registry of India. Forty-three patients with cancer of the cervix undergoing HDR brachytherapy from November 2009 to December 2011 were included in the study. All patients underwent CT-based computerized 3-dimensional conformal radiation therapy or external intensity-modulated radiation therapy planning. A dose of 46 Gy in 2 Gy per fraction was delivered over 4 1/2 weeks with concurrent weekly cisplatin (40 mg/m²). The patients were assessed for brachytherapy toward the 4th week of radiation, and brachytherapy was performed after completion of external radiation. The patients were planned for 9 Gy per fraction in 2 fractions delivered 1 week apart. The overall treatment time was kept to <50 days.

Brachytherapy procedure

The patients were randomized to group A and group B before the procedure. In group A, in the first brachytherapy fraction gauze packing was done, followed by BRSB packing in the second fraction. In group B, the opposite was done (ie, in the first fraction vaginal packing was done using the BRSB, followed by gauze packing in the second fraction).

The intracavitary brachytherapy application was done under general anesthesia, with the patient in the lithotomy position. In all patients, a rectal enema was done before the procedure to ensure complete evacuation of the rectum. The patients were asked to empty the bladder just before the procedure, and the bladder was catheterized. An examination under anesthesia was performed to note the extent of residual disease and the local anatomy before application. Uterine sounding was done to ascertain the length of the uterine cavity and confirm the orientation of the uterus. The application was done using the Nucletron HDR tandem ovoid applicator (Nucletron, Veenendaal, Netherlands). Dry gauze packing was done anterior and posterior to the ovoids to ensure maximum displacement of the rectum and bladder and in the upper vagina to stabilize the applicator. Alternately, the BRSB was applied. Before placing the balloon it was checked visually and after inflation with air, to check for any leaks. Then the selected intrauterine tandem was passed through the hole in the balloon and inserted in the cervix under visual guidance, such that the thick portion of the balloon faces the applicator. The bladder portion of the balloon was placed anteriorly and the rectal part posteriorly. The ovoids were then inserted one after the other, keeping the tails of the balloon apart to allow easy and accurate placement. After ensuring that the applicator had not rotated or displaced, 20–30 mL of normal saline mixed with 4–5 mL of ionized contrast media was injected in the bladder and rectal balloons with a syringe, depending on the vaginal capacity (Fig. 2). During this phase the applicator was held steady to minimize any displacement. Minimal packing was done distal to the implant to immobilize the applicator and prevent its slippage. Labial sutures and a T-bandage were used for immobilization of the applicator. To avoid interobserver variability, as far as possible, both the applications were done by the same clinician, and the same applicator was used in both brachytherapy fractions. After the procedure the patient was taken for a CT scan. Computed

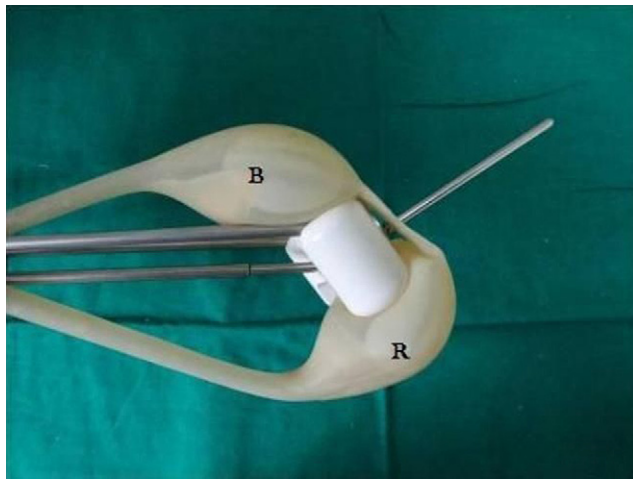


Fig. 2. Bladder–rectum spacer balloon inserted through the tandem and the balloon filled with 20–30 mL saline with diluted contrast.

tomography slices were taken at 2.5-cm intervals from the level of 3–4 cm above the fundus superiorly to the level of the ischial tuberosities inferiorly. The CT scans were transferred to the Plato treatment planning system (Plato BPS, Veenendaal, The Netherlands). A dose of 9 Gy was prescribed to point A. International Commission on Radiation Units and Measurements (ICRU) point doses and doses to 0.1-cm³, 1-cm³, 2-cm³, 5-cm³, and 10-cm³ volumes of bladder and rectum were measured for both fractions and compared. Assessment for ease of application and time taken for application were compared.

Statistical analysis

The values for ICRU point doses and doses to 0.1-cm³, 1-cm³, 2-cm³, 5-cm³, and 10-cm³ volumes of bladder and rectum were generated for each application done with gauze and the BRSB and were analyzed. For comparison between the 2 modalities (ie, gauze packing and the BRSB) a 2-sided paired *t* test was performed (6). *P* values along with SD and confidence intervals were assessed. *P* values of <.05 were considered significant. Statistical analysis was done using SPSS software version 19 (SPSS, Chicago, IL).

Results

A total of 43 patients were enrolled in the study; however, in 3 patients BRSB could not be inserted owing to unfavorable

anatomy. The narrow vaginal apex in these patients precluded the proper placement of the applicator. In these patients standard vaginal packing was done with gauze. Thus 40 patients were evaluable, and a total of 80 plans were studied. A subjective assessment for the ease of application was done. The applications were assessed as easy, fair, and difficult, depending on the clinician’s evaluation. In 3 of the 40 patients, insertion of the BRSB was found to be difficult. When time for application was evaluated, it was observed that in 2 patients with BRSB the time for application exceeded 30 minutes, whereas in all patients with vaginal gauze packing the application was done within <30 minutes. This was because all 3 patients in whom the application was difficult had a relatively narrow vagina. Because only a standard size of the balloon was available, the “oversized” balloon crowded up inside the vagina. In addition, because the balloon was not transparent, it completely obscured the visualization of the external os once the balloon was mounted on the tandem, thus making the application both difficult and time consuming.

Both ICRU point doses and doses to 0.1-cm³, 1-cm³, 2-cm³, 5-cm³, and 10-cm³ volumes of the bladder and rectum were compared. On comparing the mean doses to the bladder there was no statistical difference observed in the ICRU point doses and volume doses between vaginal gauze packing and BRSB (*P* = .89, .62, .69, .68, .42, and .078 for 0.1 cm³, 1 cm³, 2 cm³, 5 cm³, 10 cm³, and ICRU point, respectively) (Table 1). On evaluating the CT slices it was observed that in some patients although the BRSB led to a greater anterior displacement of the bladder, bladder doses were not much different from those with gauze packing. In these patients it was observed that the over-displacement with the balloon led to displacement of urine into the lateral recesses (Figs. 1 and 2) as compared with gauze packing. On comparing the doses to rectum, the mean rectum doses for 0.1 cm³ (balloon: 633.72 cGy; gauze: 732.16 cGy; *P* = .018), 1 cm³ (balloon: 505.08 cGy; gauze: 558.16; *P* = .005), and 2 cm³ (balloon: 463.55 cGy; gauze: 506.22 cGy; *P* = .010) were significantly lower for BRSB as compared with gauze (Table 2). The largest displacement (in terms of absolute dose reduction) was observed for 0.1 cm³, followed by 1 cm³ and 2 cm³. The doses to 10-cm³ volumes and ICRU rectal points did not significantly vary between BRSB and vaginal gauze packing. Thus a significant dose reduction was observed for most irradiated tissue volumes (ie, the high-dose regions close to the applicator).

No major complications occurred during and after the procedure. Because the balloon filling was done according to the vaginal capacity of the patient, we did not need to take out the fluid from the balloon. However, in 1 patient a minor vaginal tear occurred as a result of overinflation of the BRSB.

Table 1 Doses to bladder (mean ± SD), with confidence intervals (CI)

Parameter	Dose (cGy)		95% CI	<i>P</i>
	Gauze packing	BRSB		
ICRU point	711.30 ± 256.12	785.75 ± 289.9	−8.72, 157.61	.078
0.1 cm ³	1083.44 ± 279.87	1088.44 ± 266.4	−78.18, 68.18	.890
1 cm ³	893.67 ± 201.16	912.17 ± 266.79	−57.07, 94.07	.622
2 cm ³	807.53 ± 182.28	820.19 ± 227.7	−53.13, 78.46	.698
5 cm ³	705.05 ± 705.05	785.75 ± 193.36	−75.08, 49.97	.686
10 cm ³	608.97 ± 150.23	589.67 ± 141.9	−67.93, 29.32	.426

Abbreviations: BRSB = bladder–rectum spacer balloon; ICRU = International Commission on Radiation Units and Measurement.

Table 2 Doses to rectum (mean \pm SD), with confidence intervals (CI)

Parameter	Dose (cGy)		95% CI difference	P
	Gauze packing	BRSB		
ICRU point	505.64 \pm 137.10	482.97 \pm 102.65	-56.82, 11.49	.187
0.1 cm ³	732.17 \pm 250.68	633.28 \pm 196.35	-179.48, -18.29	.018*
1 cm ³	558.16 \pm 148.88	505.08 \pm 113.09	-89.0, -17.17	.005*
2 cm ³	506.22 \pm 132.98	463.56 \pm 107.31	-74.34, -10.99	.010*
5 cm ³	421.92 \pm 102.20	407.47 \pm 99.41	-41.67, 12.78	.289
10 cm ³	350.94 \pm 84.04	341.14 \pm 83.17	-31.33, 11.72	.361

Abbreviations as in Table 1.

* Statistically significant.

This healed spontaneously within 1 week and did not require any intervention.

Discussion

In HDR brachytherapy, whereby multiple high-dose brachytherapy fractions are delivered, uniform and adequate displacement of the organs at risk, namely the bladder and rectum, is required to reduce late complications. The BRSB has been designed to replace gauze packing because of its anticipated benefits of greater organ displacement, along with its potential for reproducibility in subsequent brachytherapy fractions. In the literature, although various balloon-based vaginal packing systems have been used favorably over standard gauze packing, there is a lack of randomized studies comparing the two. To our knowledge, ours is the first randomized study comparing standard gauze packing with a balloon-based vaginal packing system (ie, the BRSB). In our study an inpatient comparison was done: both the balloon and gauze packing were used in the same patient. This was done to control the anatomic variation between different patients so that the actual magnitude of difference between the BRSB and gauze packing could be evaluated in the same patient. Additionally, because vaginal capacity may decrease with subsequent brachytherapy fractions, to avoid bias in the anatomic variation in the same patient, we further decided to randomize the patients before the procedure to receive either the BRSB or gauze packing in the first fraction and vice versa in the second brachytherapy fraction.

Patient comfort did not differ between the BRSB and gauze packing; however, in 3 patients with a narrow vagina the BRSB could not be inserted because the balloon awkwardly folded inside the vagina, further reducing the space in the vagina. In addition, the application time was prolonged in 2 patients in whom the BRSB was inserted owing to poor visualization of the vaginal cavity. In a study by Price et al (7), in patients undergoing intracavitary brachytherapy for each delivered fraction conventional vaginal packing was compared with a balloon-based gynecologic packing system. Balloon-based gynecologic packing was done in 11 fractions, and conventional vaginal packing was done in 14 fractions. The balloon-based system consisted of a pair of balloons, designed to be placed superior and inferior to inserted ovoids while deflated (RadiaDyne; Houston, TX). After positioning the balloons, the balloons were filled with water (20-40 mL) to displace the proximal bladder and rectal walls. A marked increase in patient comfort was reported, with a reduction in time to pack with the balloon as compared with the conventional

method (7). A similar customized inflation of the balloon was also done in our study, depending on capacity of the vagina, but we found it difficult to use the same-sized balloon for all patients. Because the BRSB lacked transparency, we found it difficult to visualize the external os once the balloon was inserted through the tandem. This precluded the proper placement of the applicator and led to an increase in application time.

On comparing the doses to the bladder, the ICRU point doses and the volume doses were comparable for the BRSB and the gauze packing. Although there was greater anterior and posterior displacement with the BRSB, it did not translate into a significant dose reduction with the BRSB as expected (Table 1). On closely examining the CT plans, we observed that the "over-displacement" actually led to the filling of urine into the lateral recesses in some patients. This lateral filling of recesses led to increased dose due to close proximation to the ovoids laterally, thus offsetting its potential advantage of dose reduction by increased anterior displacement of the bladder (Figs. 3 and 4). A statistically significant favorable dose reduction to rectum was observed with BRSB for dose: 0.1-cm³, dose: 1-cm³, and dose: 2-cm³ volumes, with a maximum dose reduction for the high-dose volume of 0.1 cm³, followed by 1-cm³ and 2-cm³ volumes. The doses were comparable for 5-cm³ and 10-cm³ volumes and the ICRU rectum point for the BRSB and gauze packing. Thus the balloon was most effective in displacing the high-dose region (represented by the D 0.1 cm³, 1 cm³, and 2 cm³) as opposed to the larger volumes.

Rockey et al (8), in a retrospective study compared the ICRU point doses for bladder and rectum and the D 2 cm³ doses for bladder, rectum and sigmoid in 29 HDR brachytherapy plans of 9 patients that were performed with gauze packing and 18 plans of 6 patients performed with the Alatus balloon packing system (RadiaDyne). In 4 patients receiving 1 to 2 fractions each with the balloon packing system and gauze packing, an inpatient comparison was also done. A comparison of 47 HDR plans did not show a significant difference in ICRU point doses and D 2 cm³ doses to the bladder, rectum, and sigmoid. However, on an inpatient comparison in 4 patients the average rectal D 2 cm³ was significantly lower for balloon packing, whereas the doses to the bladder and sigmoid were not significantly different (8).

In a similar study, Ahmed et al (9) compared Alatus vaginal balloon packing (VBP) with standard gauze packing in 4 patients undergoing fractionated HDR brachytherapy. The patients underwent alternating vaginal packing either with standard gauze packing or with Alatus VBP. Brachytherapy was performed in 5 fractions, 600 cGy per fraction. Brachytherapy planning was performed using an MRI for high risk clinical target volume. Two

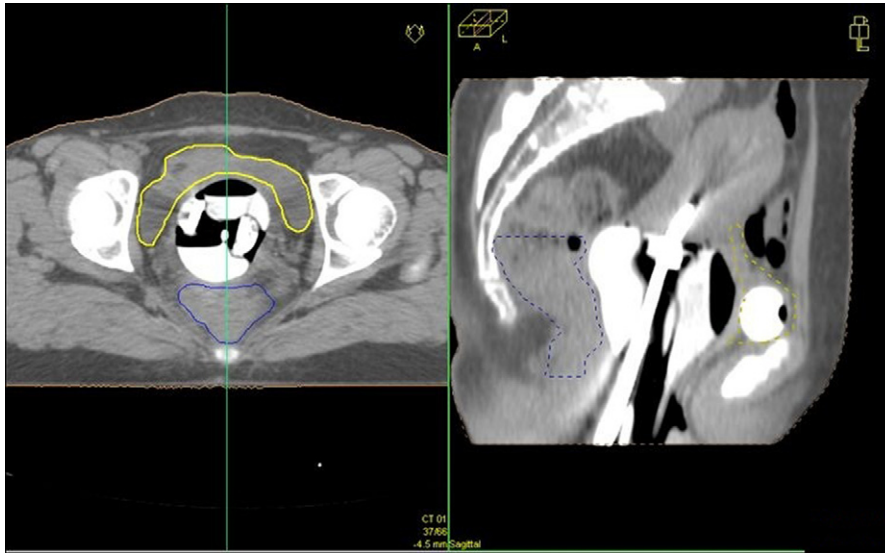


Fig. 3. Bladder–rectum spacer balloon in a patient with a narrow vagina. Note the filling of the lateral recesses of bladder due to anterior displacement by the bladder–rectum spacer balloon.

plans were generated for each fraction: one based on The Groupe Européen de Curiethérapie and the European Society for Radiotherapy & Oncology (GEC-ESTRO) working group recommendations, and the other optimized to point A. The mean average differences in doses observed for both bladder and rectum favored the use of VBP, whether planned according to GEC-ESTRO or ICRU point A. The authors concluded that rectal and vaginal dosimetry favored ALATUS VBP over standard gauze packing, whether planned according to GEC-ESTRO or ICRU point A (9). However, despite an increased average dose reduction for bladder in favor of VBP, no conclusion on the effect on doses to the bladder could be made. Both the above-cited studies failed to demonstrate an advantage of the balloon-based systems over standard gauze packing for bladder sparing. The drawbacks in both the studies were the small sample size, whereby the reason

for lack of improvement in bladder dosimetry could not be ascertained with the balloon-based systems. Because the bladder is a flabby and highly distensible organ, urine can easily get displaced into the lateral recesses if there is compression of the anterior and posterior bladder walls. The filling of the recesses may lead to the cupping of the lateral walls of the bladder close to the ovoids and the high-dose region, which may actually result in higher doses being received by the bladder. Thus, bladder filling and filling of the balloon-based packing systems may need to be optimized for effective sparing of the bladder. On the other hand, rectum can be effectively displaced owing to its tubular anatomy and musculature. The difference is, however, more pronounced for the small-volume doses representing the “high-dose regions” close to the applicator, and this has also been consistently demonstrated in the above studies.



Fig. 4. Gauze packing in a patient with a narrow vagina.

Some dosimetric studies have demonstrated a reduced dose to the posterior wall of the bladder and the anterior wall of the rectum with the use of contrast medium for filling the balloon because it causes increased attenuation of the dose as compared with the balloon filled with air or saline (10, 11). The optimal dilution of the contrast, however, needs to be taken into account both for the protective effect as well as the artifacts that appear on the CT scans, which might obscure the anatomy of the patient (11). We used 4-5 mL of ionized contrast diluted in 20-30 mL of saline for filling of the balloon, which did result in minor artifacts without much difficulty in visualizing the patient's anatomy. However, we did not attempt to assess its impact on the doses received by the bladder and rectum.

At our center, all applications are done under general anesthesia because it causes relaxation of the vagina and facilitates effective vaginal packing. However, in centers where the procedure is done under sedation or conscious anesthesia it may not always be possible to do an effective vaginal gauze packing because of inadequate relaxation of the patient. In such cases the BRSB may offer greater benefit over vaginal packing in terms of standardized displacement of the bladder and rectum along with reproducibility in multiple HDR brachytherapy applications.

Thus, in our study the BRSB was found to be as effective as gauze packing in displacing the bladder and rectum in HDR brachytherapy in cancer of the cervix. However, transparent balloons of variable sizes are recommended and would be desirable for better visualization and usage in patients with a less-capacious vagina. The major advantage of the BRSB over the gauze packing was its favorable dose reduction to 0.1-cm³, 1-cm³, and 2-cm³ rectum doses. Because these small volumes represent the high-dose regions, even minor dose reduction could translate in a clinically significant decrease in late toxicity. Because vaginal packing with gauze may vary with individual clinical experience and from fraction to fraction, the BRSB may offer greater reproducibility and standardized displacement of the bladder and rectum, especially when multiple HDR brachytherapy applications are done. A further interpatient comparison would be

required to study the reproducibility of the packing done (with BRSB and gauze) between multiple sessions and to evaluate the intersession variation in the doses to the organs at risk.

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