Original paper

A comparison of dose distribution from Manchester-style and Fletcher-style intracavitary brachytherapy applicator systems in cervical cancer

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Abstract

Purpose: During intracavitary brachytherapy (ICBT) for cervical cancer, the choice of applicator system remains rather arbitrary. However, as the applicator geometry may play an important role in dose distribution, thereby improving the therapeutic ratio, this study was conducted to compare the Manchester-style and Fletcher-style applicator systems.

Material and methods: After completion of EBRT, 22 patients with cervical cancer (stage IIA-IIIB) underwent intracavitary brachytherapy. Two different types of applicators: Manchester-style and Fletcher-style were used for each patient for alternate insertions. The purpose was to compare the dose distribution obtained when two different applicators were applied to the same patient. CT based computerized treatment planning was done and dose was prescribed to point A. After optimization, height, width and thickness of the 100% isodose curve, as well as the 100% isodose volume were noted. Dose received by the urinary bladder and rectum were noted.

Results: The 100% isodose volume and its maximum width were significantly greater (P value < 0.0001 in both occasions) when Manchester-style applicator was used. However, the dose received by 0.1 cc, 1.0 cc and 2.0 cc of the urinary bladder were all significantly greater (P value < 0.0001) with the Manchester-style applicator. No significant difference was found in rectal doses.

Conclusions: The larger 100% isodose volume, as well as the greater width achieved with the use of Manchester-style applicator can be helpful in circumstances where the tumour is large in size. However, this must be balanced against the increased dose received by the urinary bladder.

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Key words: brachytherapy, cervical cancer, Fletcher-suit applicator, Manchester-style applicator.

Purpose

Cervical cancer, particularly squamous cell carcinoma, is one of the most common cancers among Indian women, especially in the rural areas of India [1]. Except for the very early cases, radiation therapy is the major curative treatment option for this disease. Brachytherapy is an integral component in any radiation therapy protocol for cervical cancer. Intracavitary brachytherapy (ICBT) is the most frequently performed procedure, while interstitial brachytherapy is reserved for selected indications e.g. narrow vagina, poor geometry etc.

While various recommendations are available for intracavitary insertion techniques, dosage schedule, dose prescriptions as well as for reporting of the full ICBT treatment procedure, nothing is said regarding the selection of the applicator [2-5]. Selection of the applicator is rather arbitrary and also dependent upon the availability of the applicator type. However, since the dose distribution in brachytherapy is mainly dependant on the inverse square law, different kind of dose distribution may be achieved with two different applicator systems, which may help to achieve higher therapeutic ratio (by sparing the OARs while at the same time covering the target in a more satisfactory manner). Also, there may be a kind of optimum applicator system for a patient, so that the applicator system may be individualized for a specific patient depending both upon her pelvic geometry as well as extension of the disease.

The aim of this study was to compare two different intracavitary applicator systems – the Manchester-style and the Fletcher-style. We intentionally did not consider the ring applicator, which is also available at our institute, for the comparison purpose at that time since the dose distribution obtained with the ring applicator is rather different from the conventional tandem and ovoid applicators.

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Material and methods

At our institute, Medical College, Kolkata, every year we treat around four hundred newly-diagnosed cases of cervical cancer. Among them 22 patients were selected for this study. Patients suffering from locally advanced cervical cancer (stage IIA-IIIB), squamous cell carcinoma in histology, with good performance status (ECOG 0-2) without any other significant co-morbidities which might alter treatment outcomes were selected for the study. Patients with very narrow vagina or whose poor geometry precluded satisfactory intracavitary application were excluded from the study, as in those cases at our institution we prefer interstitial brachytherapy. All patients received a dose of 50 Gy to the whole pelvis in conventional fractionation with four field box technique prior to brachytherapy along with concurrent chemotherapy with cisplatin 40 mg/m^2 given weekly. In patients with extensive parametrial disease involvement, a further 10 Gy parametrial boost (conventional fractionation) was delivered by AP-PA technique. However, in these patients, if required, brachytherapy insertions were interdigitated between the parametrial boost fractions to keep the total duration of treatment within eight weeks.

During intracavitary brachytherapy, two types of applicators, the Manchester-style and the Fletcher-style applicator (Varian Medical System Inc., Palo Alto, CA®), were used in the same patient in two different fractions. For each patient included in this study, the type of applicator and sequence of insertion was randomly assigned using a blind envelope method. The patient was randomly assigned to receive her first insertion using one of the two applicators (i.e. Manchester-style or Fletcher-style applicator), the other type being used for the second insertion. This statistical design allowed for the use of each patient as her own control removing confounding factors related to the patient's individual anatomy. The random assignment of the insertion sequence ensured that changes in geometry in local anatomy due to progressive tumour shrinkage between the two insertions, as well as general patient condition at the time of insertion would be balanced between two study arms. The basic parameters for insertion, e.g. the intra-uterine tandem length and angulation, separation between two ovoids etc., were kept as similar as feasible in the same patient for both applicators.

The applicators, the Manchester-style applicator based on the classical Manchester technique of cervical brachytherapy, consist of the uterine tandem and two vaginal ovoids; all three of them lay more or less in the same plane, the positions of these in respect to each other are fixed by a clamp. Three different angulations of the tandem were available, namely zero, fifteen and thirty degrees. On the other hand, the Fletcher applicator was first designed by Gilbert Fletcher as a replacement for the live loaded Manchester applicators of Tod and Meredith. It was later adapted by Suit for use with afterloading devices and Declos for remote afterloading. The available Fletcher-style applicator consists of an intrauterine tube and tilted cylindrical vaginal ovoids, so that the ovoids lie at a plane almost perpendicular to the plane of the uterine tandem. The tilt is designed to take advantage of the anisotropic properties of the source in the direction of the two main organs at risk, i.e. the bladder and rectum. As with the Manchester-style applicator, the tandem was available in three different angulations. Ovoid caps of various diameters were available. The largest size of a cap that fits comfortably into the vaginal fornices was chosen in order to minimize the dose to the vaginal mucosa.

After intracavitary insertion under spinal anesthesia, all patients underwent a CT scan with the applicators in place. Urinary bladder and the rectum were contoured on the CT image as the OARs. Varian's BrachyVision (Varian Medical Systems Inc., Palo Alto, CA®) was used for all three-dimensional (3D) treatment planning. The reference points identified on the CT scan based digitally reconstructed radiographs (DRRs) were the bladder and rectal points (as defined by ICRU) [6] and Point A (right and left). The dose was prescribed to Point A (normalized to left Point A).

Although the American Brachytherapy Society (ABS) [2] had recommended the use of < 7.5 Gy per fraction dose for HDR brachytherapy and in most institutions 7 Gy per fraction (total four fractions) is used, we usually use 9 Gy per fraction (total two fractions), according to the protocol developed at the Postgraduate Institute of Medical Education and Research, Chandigarh, India [7]. However, in this study, in order to maintain comparability, a dose of 8 Gy was prescribed to the left-sided Point A in all insertions and all relevant dosage data were noted. Initial loading patterns were kept as similar between two insertions as feasible and then optimization was done, so that the dose to the OARs could be kept as low as practicable without compromising the dose to the disease. As Point A based dose prescription method was used, the dose to the GTV, HR CTV etc. was not noted separately.

Statistical methods

For comparing the dose distribution provided by the two applicators, the 100% isodose curve characteristics (i.e. the treated volume) as well as the OAR dose data, as recommended by the GEC-ESTRO Working Group, were noted [3,4]. Volume covered by the 100% isodose curve, maximum height, width and thickness (as described on the ICRU Report no. 38) [6] of the 100% isodose curve, width and thickness of the 100% isodose curve at the level of Point A and the volume of the isodose curve. To assess the dose volume parameters of the OARs, following criteria were used: maximum and minimum dose received by the organs-at-risk (urinary bladder and rectum), dose at ICRU point (i.e. ICRU bladder and rectal points), dose received by the OARs at specific volumes; specifically the dose received by 0.1 cc, 1 cc and 2 cc of urinary bladder and rectum. As mentioned before, this was CT scan-based planning and Point A-based dose prescription. Therefore, dose to the GTV, HR CTV etc. were not noted. For analysis of the collected data of the 22 patients, paired t test was applied.

Results

Twenty-two patients were analyzed in our study and most presented with stage IIB (Table 1). In order to maintain comparability, the dose (8 Gy) was prescribed to the left-sided Point A on all insertions. The resulting mean point A dose

Table 1. Patient characteristics according to stage

Stage of the disease	Number of patients	Percent
IIA	3	13.64
IIB	12	54.54
IIIB	7	31.82

Table 2. Mean dose at point A with two different applicators

Mean dose at point A (Gy)			
Manchester applicator		Fletcher applicator	
Mean	Standard deviation	Mean	Standard deviation
8.02	0.122	7.95	0.159

Table 3. Dose distribution (of 100% isodose curve) characteristics when two different applicators are used in a single patient for two separate insertions for intracavitary brachytherapy

Dose distribution	Manchester-style applicator			Fletcher-style applicator			Paired *t* test *P* value
	Mean	Median	SD	Mean	Median	SD	
Volume of 100% isodose (cc)	127.5	125.5	10.3	108.5	108.1	7.44	< 0.0001
Max height of 100% isodose (cm)	7.73	7.83	0.58	7.56	7.62	0.46	0.1789
Max width of 100% isodose (cm)	7.74	7.81	0.37	6.93	7.16	0.66	< 0.0001
Max thickness of 100% isodose (cm)	4.2	4.2	0.16	4.2	4.2	0.24	0.6652
Width of 100% isodose at point A (cm)	4.1	4.1	0.1	4.0	4.0	0.1	0.062
Thickness of 100% isodose at Pt A (cm)	4.0	4.1	0.13	4.0	4.1	0.13	0.289

Table 4. Comparison of dose volume data regarding urinary bladder and ICRU bladder point dose for two different applicators

Dose received by bladder (Gy)	Manchester-style applicator			Fletcher-style applicator			Paired *t* test *P* value
	Mean	Median	SD	Mean	Median	SD	
Maximum dose	12.7	14.1	3.46	12.1	11.8	2.72	0.003
Minimum dose	1.2	1.3	0.30	1.2	1.2	0.33	0.748
Dose at ICRU point	8.4	8.6	1.67	7.9	7.9	1.90	0.08
0.1 cc dose	11.6	12.0	2.25	10.5	10.1	2.08	< 0.0001
1.0 cc dose	9.8	9.8	1.81	8.6	8.3	1.60	< 0.0001
2.0 cc dose	8.2	8.5	1.78	7.3	7.1	1.82	< 0.0001

was not significantly different for the two applicators (Table 2). Regarding the 100% isodose curve (treated volume) characteristics, there was some very interesting difference between the two applicator types (Table 3). The 100% isodose volume was significantly greater when the Manchester-style applicator was used as was the maximum width of the 100% isodose curve. Even the maximum height was greater for the Manchester-style one, though not statistically significant. The dose received by the OARs e.g. the urinary bladder as well as the rectum was different too. The ICRU Bladder and Rectum point dose and the dose received by 0.1 cc, 1.0 cc and 2.0 cc of bladder and rectum were compared using the aforementioned two applicators. The dose received by the urinary bladder (at the ICRU Bladder Point as well as 0.1 cc, 1.0 cc and 2.0 cc of bladder) was significantly greater when Manchester-style applicator was used and these differences were statistically significant (Table 4). However, the dose received by another major OAR i.e. rectum was comparable between the two applicator types (Table 5).

Discussion

In brachytherapy, the dose delivered to the tissues is mainly determined by the inverse square law and not by the attenuation caused by the intervening tissue layers. Therefore, applicator geometry may play an important role in dose distribution in brachytherapy. Although both the Fletcher-style and the Manchester-style applicator systems are based on the Manchester system, their geometry is quite different. So, it was reasonable to assume that even when applied to the same patient, the two applicators might give rise to two different types of dose distributions. Keeping this assumption in mind, we proceeded with this study. When we

Table 5. Comparison of dose volume data regarding rectum and ICRU rectal point dose for two different applicators

Dose received by rectum (Gy)	Manchester-style applicator			Fletcher-style applicator			Paired *t* test *P* value
	Mean	Median	SD	Mean	Median	SD	
Maximum dose	9.3	10.1	2.89	9.0	10.1	2.07	0.979
Minimum dose	1.0	1.1	0.32	1.1	1.1	0.29	0.153
Dose at ICRU point	7.2	7.3	1.22	7.3	7.4	1.20	0.830
0.1 cc dose	8.9	9.2	2.17	8.6	9.0	1.57	0.583
1.0 cc dose	7.8	7.8	1.52	7.4	7.6	1.17	0.447
2.0 cc dose	6.7	6.8	1.20	6.6	6.7	0.91	0.359

searched literature, we could find only one similar study comparing two different applicators in the same patient. That study was conducted to compare two different LDR applicator devices using ICRU point based dose recordings. In that study, Thirion *et al*. [8] compared the dose distribution produced by two different LDR brachytherapy applicators when they were applied to the same patient. The applicators tested were the Henschke applicator and the Fletcher-Suit-Declos applicator. Two dimensional planning was done and data were recorded according to the ICRU 38 recommendations. One of the applicators, the Henschke applicator was shielded on the anterior and posterior aspects with a tungsten alloy to reduce the dose to the bladder and rectum, respectively, while the other applicator was not shielded. During treatment planning, an in-house correction, based on transmission measurements was applied to account for the presence of tungsten shielding elements in the vaginal ovoids. The hypothesis on which the study was based was that the choice of intracavitary brachytherapy applicator could affect the therapeutic ratio. Their primary objective was to compare the dose at OARs as a percentage of the Point A dose and also to compare the ICRU reference volume. A secondary objective was to assess the effect of ovoid shielding and the applicator geometry on critical organ sparing. They showed that a significant reduction of the dose delivered to the bladder was possible with the use of the Henschke applicator and also the rectal dose was less with this applicator, though not statistically significant. A significant reduction in the reference volume was observed with the Henschke applicator. On further analysis they concluded that the advantage for this applicator could be attributed to the shielding only and not to its specific geometry.

Although the study concluded that the applicator geometry is not an important determinant in the specific dose distribution produced after a brachytherapy insertion, it had comprehensively been shown that choice of applicator can alter the therapeutic ratio in intracavitary brachytherapy. However, one of the major deficiencies in this study was that the study was based on two-dimensional planning. Another one was that the study was done with LDR brachytherapy, although completed with remote afterloading using Cs^{137} pellets, the optimization with dwell-time and dwell-positions was not as adequately feasible as with HDR brachytherapy. One can think that perhaps, in a three-dimensional treatment planning with cross-sectional images, it is possible to compensate the deficiencies of one applicator with appropriate optimization. And thirdly, the study compared one shielded applicator with another unshielded applicator. Thus, a definite comment about the effect of applicator geometry on dose distribution cannot be made based on these observations only.

Even previous to that study, Nath *et al*. [9] performed dosimetric analysis of three different applicator systems: Morris, Henschke and Fletcher systems. They also started with the assumption that due to the marked differences in the geometric configuration of radioactive sources in different systems, the dose rate distributions were expected to be different. However, they included another factor in this study, i.e. the different treatment protocols used historically and the protocols which were in use at that time. They had used equivalent geometric configuration for each system from their clinical experience, which we think, was a major drawback of that study, as that did not take in account the complexity of using each applicator in a real patient. Also, by comparing six different treatment protocols and by integrating the different EBRT protocols, any advantage or disadvantage of one applicator could not be elicited clearly.

According to our knowledge, ours is the first study comparing two HDR applicator devices using dose volume data for the OARs for comparison. Since we wanted to test the effect of applicator geometry on the dose distribution and on the dose to the OARs, we avoided the use of shielded applicator, as the shielding can mask the difference in dose distribution due to different applicator geometry. Also, we preferred to compare the absolute dose to the OARs and not the dose to the OARs as a percentage of the prescribed dose, since we believed that it was the absolute dose delivered to an organ that caused the adverse outcomes and thus the absolute dose was important.

During post-insertion CT image based 3D planning, we prescribed the dose to applicator based Point A, as described on the ABS recommendations [2]. The dose to the left-sided Point A was kept at 8 Gy for all insertions to maintain comparability. This was necessary to compare the dose volume data produced by two different applicators in the same patient. We noted the maximum height, maximum width and the maximum thickness of the 100% isodose curve, along with the 100% isodose volume (i.e. volume covered by the 100% isodose curve) (Fig. 1A, B). The first three parameters were recorded according to the ICRU 38 guidelines (as directed to measure the maximum height, width and thickness of the reference volume e.g. the 60 Gy isodose) [10]. We noted the maximum height, width and thickness of the 100% isodose curve, as they are clinically meaningful to tumour control in endocervical canal and extension to the endometrium, tumour control in parametrium and bladder

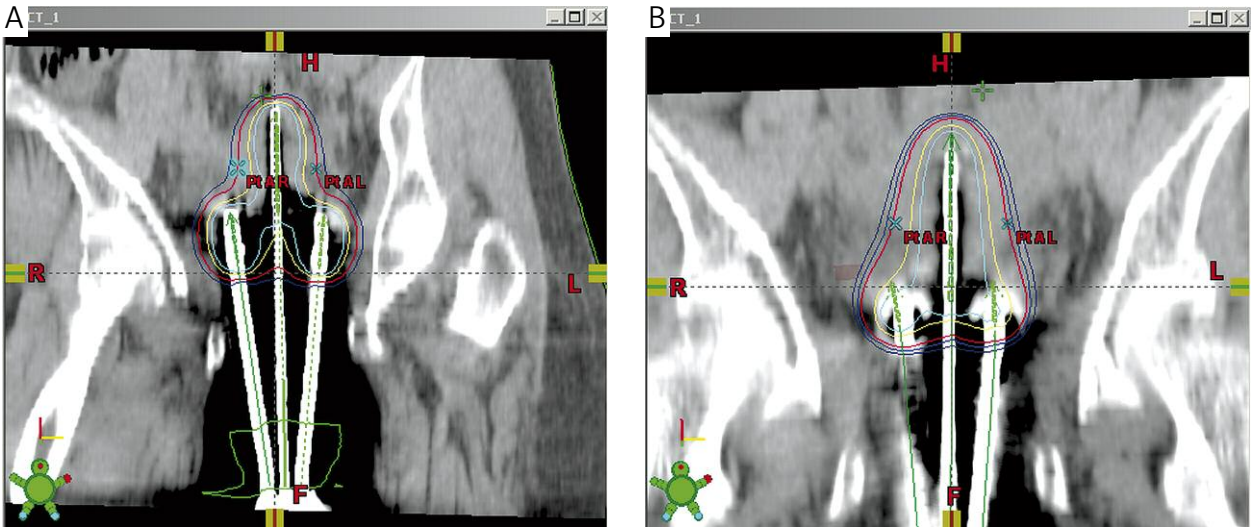

Fig. 1. A) Dose distribution for Manchester applicator. B) Dose distribution for Fletcher applicator

and rectal complications, respectively [9]. Also, the width and the thickness of the 100% isodose were noted at the level of Point A, since these dimensions are closely related to the clinical target volume [10].

The dose to the bladder and rectum were recorded according to the GEC-ESTRO recommendations [5]. Dose received by 0.1 cc, 1.0 cc and 2.0 cc of bladder and rectum (i.e. D0.1cc, D1.0cc and D2.0cc of the OARs) were noted. All these dose volume data were based on cumulative DVH (Fig. 2A, B). In this study, dose received by 1.0 cc or 2.0 cc of OAR (i.e. D1.0cc or D2.0cc) signifies the minimum dose to the most irradiated contiguous 1 cc, 2 cc volume, derived from the cumulative DVH. However, in case of bladder, the high-dose areas may not be contiguous e.g.in lateral recesses, thus it is assumed that these volumes are contiguous [5]. Dose to the ICRU reference points (i.e. ICRU bladder and rectum points) was noted as well as the maximum and minimum dose received by these structures [6].

In our study, we found that the volume of the 100% isodose curve (the Point A volume or the treated volume) was significantly greater when the Manchester-style applicator was used. Whether this difference is clinically useful or is related to increased incidence of adverse effects is to be determined by further clinical trials. Also, compared to the Fletcher style applicator, the maximum width of the 100% isodose was significantly greater when Manchester applicator was used. The difference in maximum height and thickness of the 100% isodose in two different applicators, though greater with the Manchester-style applicator, did not reach the level of statistical significance. Theoretically, the increased width of the 100% isodose may be useful in delivering higher dose to the parametrial tissues and may be useful in patients with more extensive parametrial involvement. However, the maximum width and maximum thickness of the 100% isodose at the level of point A were not significantly superior when the Manchester type applicator was used over the Fletcher applicator. Therefore, how much of this increased width of dose distribution reaches the proper parametrial tissues is yet to be clear. The clinical relevance of these data are to be verified by proper randomized controlled trial with a fairly large number of subjects.

Regarding dose volume data from urinary bladder, the maximum dose received by the urinary bladder as well as the dose received by 0.1 cc, 1.0 cc and 2.0 cc of bladder were

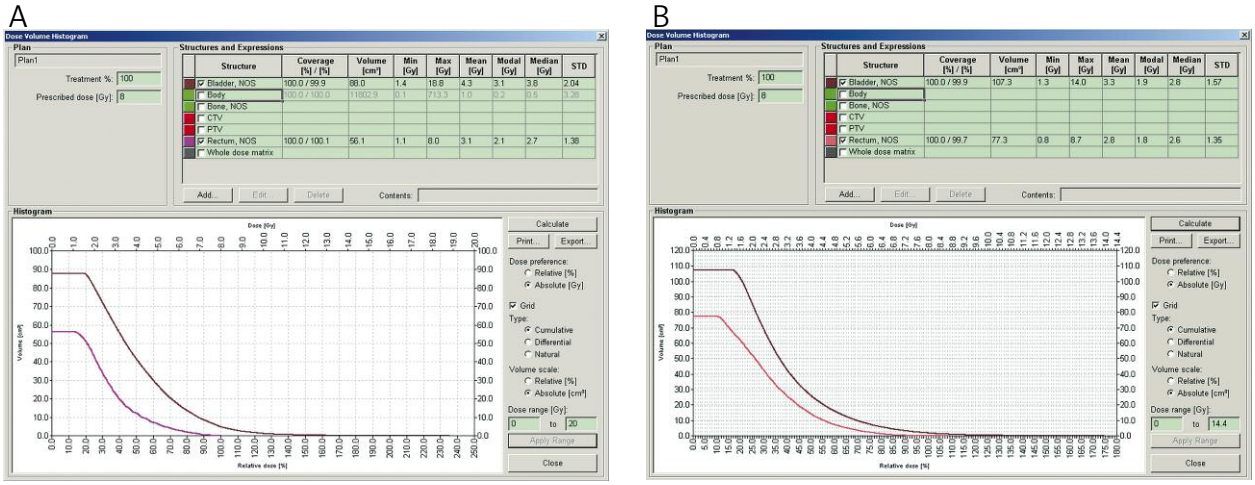

Fig. 2. A) Cumulative dose volume histograms (DVH) for OAR (Organ at Risk) bladder and rectum for Manchester applicator. B) Cumulative dose volume histograms (DVH) for OAR (Organ at Risk) bladder and rectum for Fletcher applicator

all significantly greater when the Manchester-style applicator was used compared to the Fletcher applicator. The dose at ICRU bladder point, although greater with the Manchester type applicator, was not significantly different. And finally, regarding the dose volume data from the rectum, the DVHs were not significantly different when one applicator was used over another. Therefore, as this trial shows, the dose received by the bladder was substantially greater when the Manchester-style applicator was used. As we know that excessive dose received by a small volume of organ can give rise to complications like fistula etc., this extra dose received by bladder due to use of Manchester applicator should always be kept in mind. On the other hand, in a narrow vagina, Fletcher-style applicator is comparatively difficult to place due to its angulated vaginal colpostat design, whereas the Manchester-style applicator is always remarkably easy to insert and posterior packing is much easier when the Manchester type applicator is used. Also, the greater Point A dose volume and maximum width of the 100% isodose observed with the Manchester type applicator can be of help in locally more advanced diseases.

This study can only indicate at the increased possibility of bladder toxicity when the Manchester type applicator is used (in comparison to the Fletcher type applicator), since there is increase in dose received by small volumes of the urinary bladder. Certainly, with calculation of BED and EQD2, this increased dose is risky. If we consider that the same 2 cc of bladder is going to receive this extra dose on each days of brachytherapy and calculate the BED or EQD2 accordingly, then this increased dose is very likely to give rise to bladder complications. However, in real life, the scenario is different. There is a day-to-day variation in applicator positioning and also variation in organ size and shape. Multiple studies have shown that there are significant day to day positional variations in applicator positions in the same patient, even when the insertions are done under the same settings and by the same physician [11-13]. This variation is neither dependent upon the age of the patient and stage of the disease, nor upon the gap between EBRT and brachytherapy. Therefore, there are inherent problems in assessing the DVH for intracavitary brachytherapy for carcinoma of uterine cervix. These problems include the set-up variability of the brachytherapy applicator from session to session and the interfractional variations in the bladder and rectum resulting from differences in emptying and filling. These variations could significantly affect the actual dose distributions around the area of steep dose gradients, thus influencing the reliability of the effect of the dose – volume parameters derived from the initial CT scan [14]. Also, as tumours shrink during the course of radiation, there is a change in tumour volume and configuration over time and consequently a change in normal tissue topography over time. Thus, in all probabilities, the specific 2 cc of bladder receiving the highest dose one day may not receive the highest dose on the next day; next day it is most likely that an altogether different 2 cc of bladder would be receiving the highest dose, although in calculation of total BED (or EQD2) it is assumed that same 1.0 cc or 2.0 cc of OAR receives the highest dose on every insertion.

So, this study hints at the possibility of gaining wider target coverage with the use of Manchester-style applicator - in comparison to the Fletcher-style applicator – at the cost of an increased dose to the urinary bladder. The clinical significance of this difference – i.e. whether we can get better clinical outcome at the cost of more bladder toxicity with Manchester-style applicator – can only be verified by a large prospective study.

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