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BLADDER AND RECTAL DOSES USING TWO DIFFERENT INTRACAVITARY BRACHYTHERAPY APPLICATOR SYSTEMS IN CERVICAL CANCER - A RETROSPECTIVE ANALYSIS

Oncology

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ABSTRACT

INTRODUCTION : In brachytherapy, the dose delivered to the tissues is mainly determined by the inverse square law and not by attenuation caused by intervening tissues. Applicator geometry may play an important role in such dose distribution. The study aimed to retrospectively analyze the effect of applicator geometry i.e. the choice of Manchester style or Fletcher-Suit applicators on the dose to the organs at risk (OARs) during Intracavitary Brachytherapy for Cervical Cancer.

MATERIALS AND METHODS : A single institutional retrospective study was carried out by evaluating the Dose Volume Histogram (DVH) data of 161 patients of Carcinoma Cervix Stage IB-IVA who received Intracavitary Brachytherapy (ICBT) between January 2016 and December 2017. All patients were treated with EBRT 50Gy in 25 fractions (+/- Concurrent Cisplatin 50mg/m2 weekly) followed by ICBT of 7Gy x 3 fractions using either Manchester style or Fletcher Suit applicators. D2cc, D1cc and D0.1cc were recorded for the OARs i.e. Urinary Bladder and Rectum and analyzed using IBM SPSS v23 by applying the Unpaired T-test.

RESULTS : Mean age of the study population was 50.89 years. 41.61% of patients presented with Stage IIB Carcinoma Cervix. Manchester style applicator was used in 91 patients while Fletcher Suit applicator was used in 70 patients. D2cc, D1cc and D0.1cc for Bladder were significantly higher in case of Manchester style applicator. No statistically significant difference was seen in case of the rectal dose parameters.

CONCLUSION : Fletcher Suit applicator by providing a better OAR dose distribution may improve therapeutic ratio in ICBT for Carcinoma Cervix.

KEYWORDS

Cervical Cancer, Brachytherapy, Dosimetry

INTRODUCTION

Cervical cancer is the fourth most common cancer in women worldwide and seventh overall with an estimated 528,000 new cases in 2012.The large majority of global burden occurs in the less developed regions like Africa, Asiawhere it accounts for almost 12% of all female cancers. As far as the mortality rate is concerned, almost 87% cervical cancer deaths occur in these less developed countries (Globocan, 2012). In India, It is the second most common cause of cancer accounting for approximately 1,22,644 new cases (2012).Though there has been a decreasing trend of incidence in the last forty years, still it accounts for an age standardized mortality rate of 9.8- 17.5 per 100,000 in India. [1]

In our country, majority of patients present at an advanced stage where radiotherapy forms the main treatment option. Though there are various guidelines for exact dose scheduling, the practice pattern varies widely from institution to institution as per availability of resources and workload. The standard treatment that is practised widely in our country constitutes of 50Gy of EBRT by conventional fractionation to whole pelvis with concurrent cisplatin based chemotherapy followed by intracavitary brachytherapy of 21Gy (HDR) in three Fractions of 7 Gy each, weekly. With this standard of care, the 5 year recurrence free survival is about 79% for stage IB, IIA disease and 59% for III/IVA disease with about 36.7% failing locally within the central pelvis despite this aggressive course of chemo-radiation. [2]

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 [3-6]. 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 dose distribution may be achieved with two different applicator systems.

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.

MATERIALS AND METHODS

A single institutional retrospective study was carried out by evaluating the Dose Volume Histogram (DVH) data of 161 patients of Carcinoma Cervix Stage IB-IVA who received Intracavitary Brachytherapy (ICBT) between January 2016 and December 2017. All patients were treated with EBRT 50Gy in 25 fractions (+/- Concurrent Cisplatin 50mg/m2 weekly) followed by ICBT of 7Gy x 3 fractions using either Manchester style or Fletcher Suit applicators. D_{2cc}, D_{1cc} and $D_{0.1cc}$ were recorded for the OARs i.e. Urinary Bladder and Rectum and analyzed using IBM SPSS v23 by applying

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, their positions with respect to each other being maintained 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 after-loading devices and Declos for remote after-loading. 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, 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.

Although the American Brachytherapy Society (ABS) [3] had recommended the use of < 7.5 Gy per fraction dose for HDR brachytherapy, in most institutions 7 Gy per fraction (total three fractions) is used. At our institution a dose of 7 Gy was prescribed to the left-sided Point A in all insertions.

As Point A based dose prescription method was used, the dose to the GTV, HR CTV etc. was not noted separately.

RESULTS

Mean age of the study population was 50.89 years.
77% were post-menopausal.

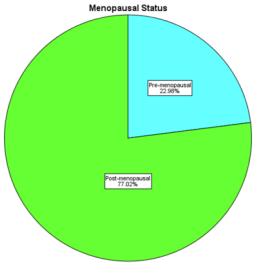

Fig. 1 – Distribution of Study Population According to Menopausal Status

Stage IIB was the most common stage of presentation accounting for 41.61%.

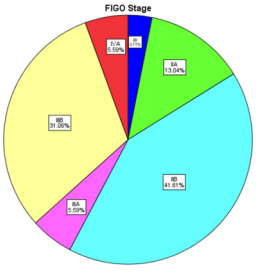

Fig. 2 - Distribution of Study Population According to Stage

Most common histology was Moderately Differentiated Squamous Cell Carcinoma accounting for 50.31%.

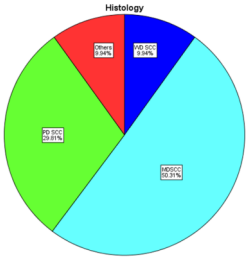

Fig. 3 - Distribution of Study Population According to Histology

Manchester style applicator was used in 91 patients and Fletcher-Suit applicator was used in 70 patients. D2cc, D1cc and D0.1cc for Urinary Bladder were higher for Manchester style applicator and the difference was statistically significant with p-values of 0.046, 0.01 and 0.001 respectively. However no statistically significant differences were seen for D2cc, D1cc and D0.1cc values for the Rectum.

Table 1 – Dosimetric Comparison Of Manchester Style and Fletcher-Suit Applicators

	MANCHESTER		FLETCHER SUIT		p-Value
	Mean (Gy)	Std. Dev. (Gy)	Mean (Gy)	Std. Dev. (Gy)	
Bladder D2cc	5.65	0.33	5.54	0.30	0.046
Bladder D1cc	6.22	0.50	6.04	0.29	0.01
Bladder D0.1cc	7.48	0.98	7.07	0.34	0.001
Rectum D2cc	4.75	1.16	4.99	0.86	0.14
Rectum D1cc	5.29	1.42	5.54	1.02	0.21
Rectum D0.1cc	6.81	1.92	6.85	1.63	0.90

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 searched literature, we could find few similar studies comparing two different applicators in the same patient. One study by Thirion *et al*. [7] 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 after-loading 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.

Basu et al in a prospective study of 22 patients indicated 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. However the study also mentioned that 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. [8]

In our study, D_{2cc}, D_{1cc} and $D_{0.1cc}$ for Bladder were significantly higher in case of Manchester style applicator. No statistically significant difference was seen in case of the rectal dose parameters.

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. 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 reality, the situation is different. There is an inter fraction variation in applicator positioning as well as organ size and shape. 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 [9-11]. 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.

The inter fraction 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 [12]. 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 may not receive the same dose on the each day of treatment, 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.

CONCLUSIONS

Fletcher-Suit applicator by providing a better dose distribution to the urinary bladder may improve the therapeutic ratio compared to Manchester style applicator in the treatment of cervical cancer by intracavitary brachytherapy.

Our study is limited by its retrospective nature and the fact that such a design does not allow us to compare the dosimetry of both applicators in a single patient. However, we believe that the large sample size can negate the limitation to a certain extent.

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