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A Comparative Analysis of Different Prescription Points in High Dose Rate Brachytherapy of Cervical Cancer

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ABSTRACT

Introduction: The dose prescription point in high dose rate (HDR) intracavitory brachytherapy (ICBT) of cervical cancer is Manchester point A but the localization of this point has a wider variation. To minimize these variations, the American Brachytherapy Society (ABS) introduced a new definition of point A and named it as point H. In this study, these two points have been compared in terms of dosimetric parameters.

Material and Methods: Twenty HDR ICBT of cervical cancer patients were retrospectively evaluated with Manchester point A and ABS point H. Target volume covered by prescribed dose (TV), dose to 2cc (D_{2cc}) of the bladder and rectum were noted for both points. Statistical analysis using a two-tailed paired t-test was performed to compare dosimetric parameters of both the points of prescription. The maximum value, minimum value, and mean ± standard deviation along with the *p* value have been noted.

Results: On average, point H was 4.0mm ± 6.4mm shifted (superior/inferior) from point A, along the tandem direction. The average TV when the prescription was done at point H (TV_H) was 33.7cc ± 10.1cc which was higher than the average TV when the prescription was done at point A (TV_A) of 33.3cc ± 9.4 cc.D_{2cc} increased from 63% ± 23% to 68% ± 24% for the rectum and 52% ± 18% to 56% ± 20% for the bladder when the prescription point changed from A to H.

Conclusion: As observed, average TV, D_{2cc} of the bladder, and rectum were higher in the case of point H prescription plan (P_H) as compared with point A prescription plan (P_A). The dose difference between P_H and P_A was found to be statistically significant, so careful consideration is needed to implementation of new point H in clinical practice.

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Introduction

Intracavitory brachytherapy is an important component of cervical cancer treatment. Various international guidelines are available over time, so there could be heterogeneity in the overall brachytherapy system [1].According to ABS, brachytherapy should be an integral part of the treatment of cervical cancer independent of chemotherapy.

During film-based 2D treatment planning dose was prescribed to point A. Easy accessibility of 3D imaging ABS 2012 guidelines [2-4] recommended three-dimensional (3D) volumetric planning. Although the widely used imaging modality was Computed Tomography (CT), Magnetic Resonance Imaging (MRI) made it more refined with GEC ESTRO (The Groupe Europeen de Curietherapie and the European Society for Radiotherapy & Oncology) guidelines and ICRU(International Commission on Radiation Units and Measurements) 89. To have a balanced approach with limited resources and traceability a hybrid planning is often adopted in which prescription is still to point Abut dose-volume-based plan evaluation [5, 6, 7, 8]. The Manchester system is one of the oldest and the most extensively used systems in the world for dose specification [9]. It is characterized by doses to four points: point A, point B, a bladder point, and a rectum point. Point A is the point of dose prescription. Point B is defined to be 3 cm lateral to point A.

To standardize the definition of point A and also to minimize the variations in its position, ABS has recommended a new prescription point namely Point H.

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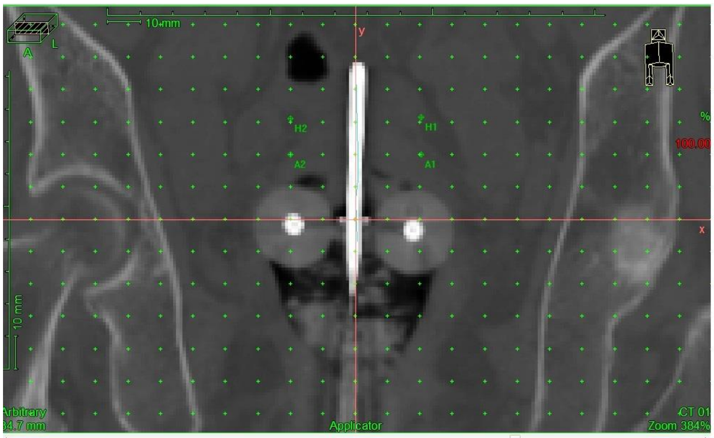

Figure 1. Manchester point A and American Brachytherapy Society (ABS) point H

Point H was determined by drawing a line through the middle of both the ovoids and from the intersection of this line with the tandem, a point was marked at a distance equal to the radius of ovoid plus 2 cm superiorly along the tandem and then point H was marked at 2cm laterally to tandem. In this study, these two points of dose prescriptions have been compared which is shown in figure 1.

In this study, retrospectively evaluation the dosimetric impact due to different points of prescription was done. Switching between two prescription point definitions in clinical practice may be problematic. Various researchers have evaluated the impact of different points of prescription. The observation of Anderson *et al*. [5], Zhang *et al.*[6] and Shraddha Srivastava *et al.*[9] matches with the present study which conclude that treatment volume enclosed by 100% isodose level is higher for plans normalized to ABS point H than the plans normalized to Manchester point A. Current study is aimed to evaluate the target volume coverage by prescribed isodose line, along with dosimetric parameters for critical normal structures and geometric shift for point A from its one definition to another.

This study may help in changing between two definitions of point A and may provide useful information for changing the clinical practice of point A based prescription to 3D target volume based prescription.

Materials and Methods

Patients Characteristics

Twenty patients diagnosed with cervical cancer were taken in the present study. These patients were given radiotherapy along with chemotherapy. The staging was done according to the International Federation of Gynecology & Obstetrics (FIGO) system. Patients with stage IIB and IIIB were enrolled in the study.

Treatment

The treatment consists of a combination of External Beam Radiotherapy (EBRT) with concurrent weekly cisplatin and HDR brachytherapy. A total dose of EBRT to pelvis was 46 Gy in 23 fractions in 4½ weeks. Brachytherapy was given using remote after loading micro-Selectron HDR V3 unit (Elekta Medical Pvt. Ltd. System) having Iridium 192 source. The ICBT procedure was initiated after the completion of EBRT. The time between completion of EBRT and first ICBT ranged from 5 to 7 days. In this study, the ICBT dose was 22.5Gy in 3 fractions (7.5Gy per fraction).

For ICBT CT-compatible Fletcher suit applicator was used, which has a pair of ovoids of different diameters (25mm, 30mm, 35mm) and a uterine tandem of 15°, 30°& 45°. To move the rectum and bladder away from the applicator and also to fix the applicator position, an appropriate vaginal packing was done. It was tried to complete the whole process within the shortest possible time so that the patient's position is stable during the CT scan.

3D CT Planning

For each HDR ICBT procedure, images were acquired using a CT Simulator (GE OPTIMA 580W) machine with a 2.5mm slice thickness. All CT slices were transferred to the Oncentra Master plan 4.3, (Elekta Medical Pvt. Ltd. System) treatment planning system (TPS).Target volume and organs at risk (OAR) on each CT slice were contoured following our institutional guidelines for cervical cancer. For target delineation, HRCTV (High Risk Clinical Target Volume) was contoured which included the whole cervix and presumed extra cervical tumor expansion area (if present) upon the brachytherapy. Safety margins were chosen according to tumor size &location; tumor spread directions, tumor regression, and treatment strategy [10]. Due to lack of MRI (Magnetic Resonance Imaging) modality and MRI compatible applicators in the institute, CT-based planning was done in which HR-CTV is the main target volume instead of gross tumour. The rectum and bladder walls were also defined and delineated on each CT slice.

3D treatment plans were created using Oncentra Master Plan system. After applicator reconstruction, the tandem flange of the applicator was determined on CT images, and Point A was created after taking the flange as the origin. Base plans were generated for all the 20 patients with a standard loading pattern (optimization was performed by changing dwell position in order to adjust the dosages to target and OARs if required) and the dose normalized at point A (P_A).Point H was created into the same axial CT image (having point A) and separate plans were generated with normalization at point H (P_H).

In this study, a hybrid planning approach was used. Dosimetric parameters like target volume (TV), and D_{2cc} of the bladder and rectum were measured for both the plan, i.e. P_A and P_H. TV was defined as the volume encompassed by the isodose line passing through the prescription point, e.g., in P_A plans and P_H plans; it was the volume encompassed by the isodose line passing through point A and point H respectively.

Statistical Analysis

All parameters of tumour and OARs were statistically evaluated. The maximum value, minimum value, and mean ± standard deviation of the shift were used to find out the actual position of point H with respect to point A. A comparison of dosimetric parameters for both target and OARs between P_A plans and P_H plans was done using two-tailed paired t-test. The p-value of <0.05 was considered statistically significant.

Results

It has been found that when the prescription point is changed from point A to point H, very careful consideration is needed. During planning it has been ensured that the average dose value to point A (left & right sides) is near the prescribed dose.

As shown in Figures2 and 3, a geometric shift for both side points H (right and left) was calculated. On average, point H was 4.0mm±6.4mm shifted (superior/inferior) from point A, along the tandem direction. Only in 4 out of 20cases, point H was inferior to point A. The superiority and inferiority of point H with respect to point A is shown in figures 4 and 5. Point H (right & left) shifting values are listed in Table 1. The target volumes covered with the prescribed dose in P_A& P_H plans are shown in figure 6. The average value of TV_H was 33.7 cc ± 10.1cc, which is higher than the average value of TV_A which was 33.3 cc ± 9.4cc. However, the difference between TV_H and TV_A is statistically insignificant with *a p*-value of 0.5.

All the dosimetric parameters are listed in Table 2.In the P_A plans the average D_{2cc} of the rectum and bladder were 63% ± 23% and 52% ± 18% respectively, compared to 68% ± 24% and 56% ± 20% with P_H plans which are shown in figures 7 and 8. The p-value for D_{2cc} of the rectum was 0.009 (for both P_A and P_H plans), which is statistically significant. The p-value for D_{2cc} of the bladder was 0.02 (for both P_A and P_H plans) which is also statistically significant.

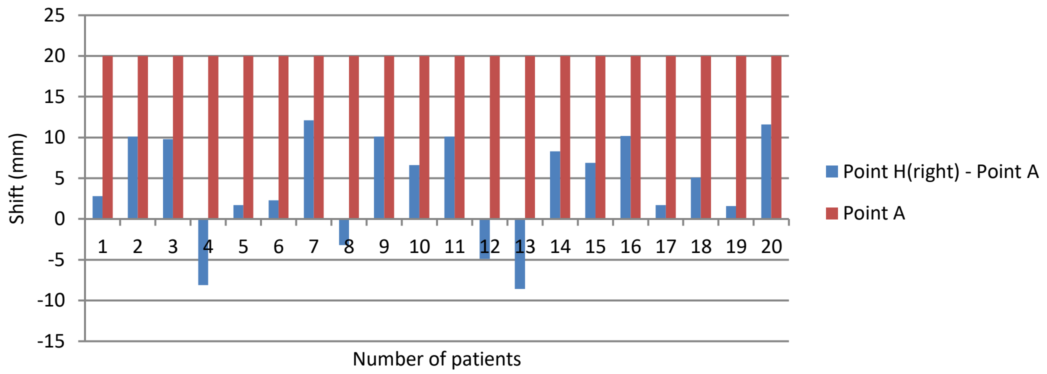

Figure 2. Shifts between point H (right) and point A

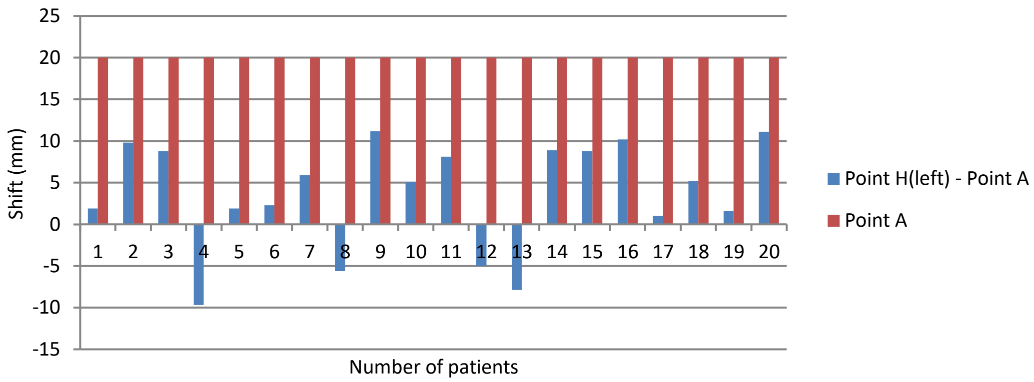

Figure. 3. Shifts between point H (left) and point A

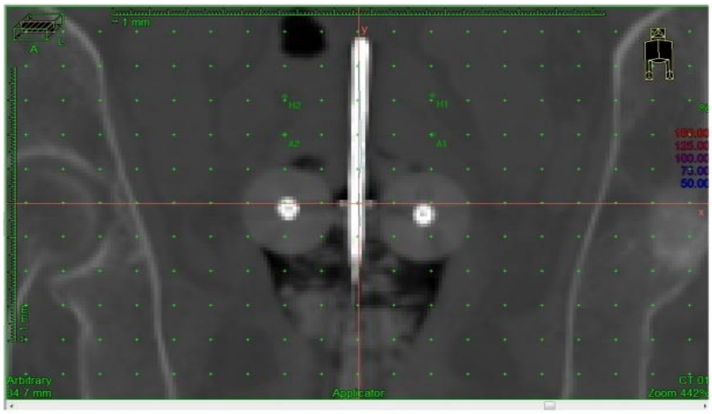

Figure 4. Point H superior to Point A

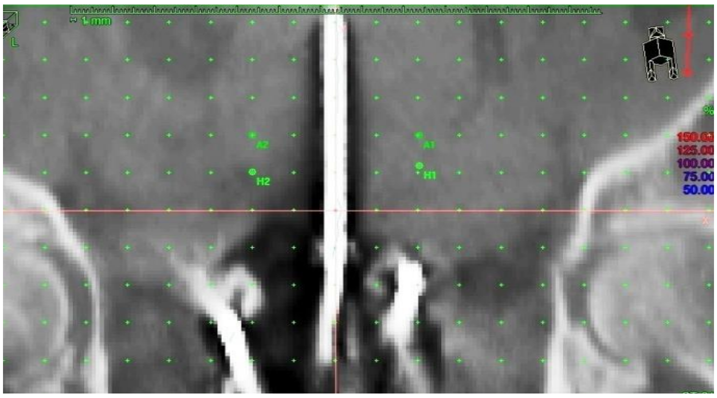

Figure 5. Point H inferior to Point A

Table 1, Actual position of point H with respect to point A.

Point H	Minimum shift(mm) from point A	Maximum shift(mm) from point A	Mean shift (mm) from point A
Point H (right)	-3.2	+12.1	4.31± 6.4
Point H (left)	-5	+11.2	3.68 ± 6.4

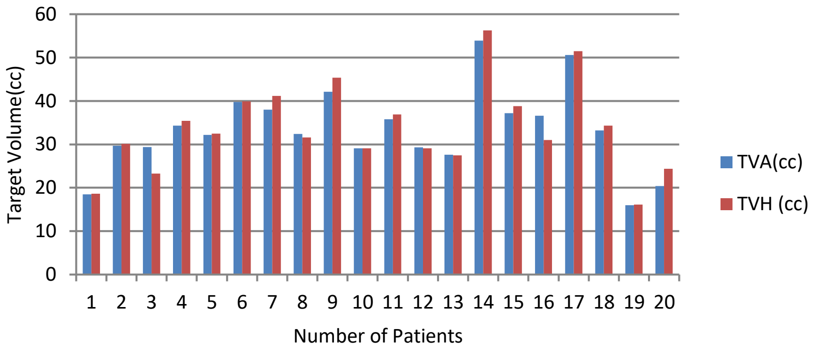

Figure. 6. Target volume covered with prescription dose in P_A& P_H plans.

Table 2. Dosimetric parameters of P_A& P_H plans.

Number of Patients	TV_A(cc)	TV_H(cc)	D_{2cc} to the Rectum (%) (P_A plan)	D_{2cc} to the Rectum (%) (P_H plan)	D_{2cc} to the Bladder (%)(P_A plan)	$D_{2cc}$to the Bladder (%)($P_H$plan)
1	18.5	18.6	63.7	64.6	52.6	53.3
2	29.7	30.1	53.4	60.7	34.9	39.7
3	29.4	23.3	49.2	42	38.1	32.5
4	34.3	35.4	59.3	61.2	44.8	46.2
5	32.2	32.5	117.2	119.3	45.5	46.3
6	39.8	39.9	36.6	37.4	65.1	66.6
7	38	41.2	36.9	43	29.8	34.8
8	32.4	31.6	84.1	77.2	47.8	43.9
9	42.1	45.4	37.9	44.6	55.1	64.9
10	29.1	29.1	116.8	125.7	62.5	67.3
11	35.8	36.9	75.7	89.9	58.1	69
12	29.3	29.1	66.7	64.7	75	72.8
13	27.6	27.5	67.1	66.7	90.9	90.3
14	53.9	56.3	65.3	74.1	46.9	53.2
15	37.2	38.8	47.1	52.1	21	23.4
16	36.6	31	68.9	77.6	46.1	52
17	50.6	51.5	41.8	43.2	69.5	71.8
18	33.2	34.3	81.4	87	25.6	27.3
19	16	16.1	48.8	49.7	65.4	66.7
20	20.4	24.4	52.8	70.8	71.3	95.6
Average	33.305	33.65	63.535	67.575	52.3	55.88
Standard Deviation	± 9.4	± 10	± 23.1	± 24.2	± 17.8	± 19.7

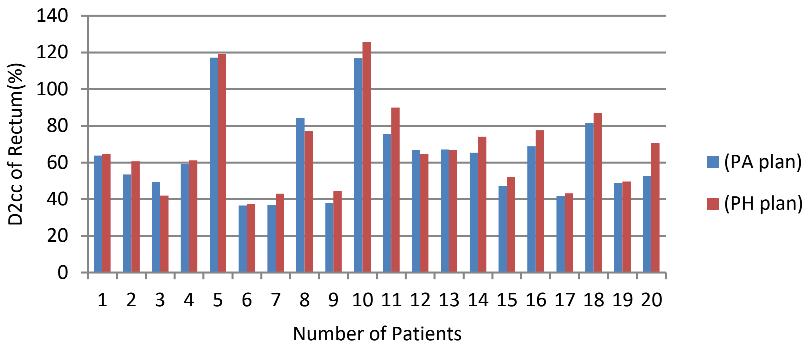

Figure 7. D_{2cc} of rectum in P_A and $P_H$plans

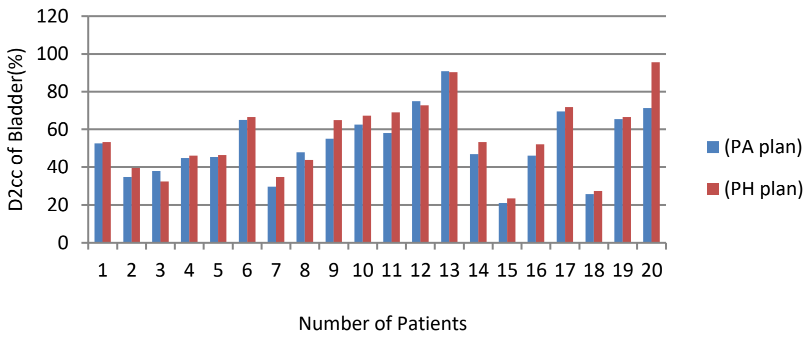

Figure 8. D_{2cc} of bladder in P_A and $P_H$plans

Discussion

In this study, information has been gathered about treatment planning on shifting prescribing points by utilizing 3D CT images. While shifting from point A to point H, there was a clear difference in dose delivered. On average, point H was 4.0 mm ± 6.4mm shifted (superior/inferior) from point A, along the tandem direction in this study. The standard deviation was 6.4mm , because the value of shift in some cases were positive for those plans in which point H was superior to point A and for those cases in which point H was inferior to point A, the value of shift was negative. This is the reason of high standard deviation in this shift. However, the shift of 6 mm, 8.9 mm ± 5.4 mm, and 9.6

mm ± 1.3 mm was observed in the studies done by Anderson *et al.*[5], Zhang *et al.*[6],and Shraddha Srivastava *et al.*[9], respectively. Differences between these observations were may be attributed to variations inter institute applicator/ovoids positioning and packing. In the current study, 4 out of 20 patients have their point H inferior to point A as in these cases ovoid positioning is below the tandem flange due to clinical limitations.

This present study also recorded, that the average D_{2cc} of the rectum and bladder in P_A plans were 63% ± 23% and 52% ± 18%, respectively when compared to 68% ± 24% and 56% ± 20% in P_H plans. In Zhang *et al.* [6] and Anderson *et al.* [5] study, they found on average higher TV in case of prescription at point A_{ovoids} (ABS point H) than prescription at point A_{os} (Manchester point A). Kim *et al.* [11] also demonstrated that using the prescription points as ABS point H increased average TV.

D_{2cc} for the bladder and rectum were increased in the case of P_H plans which resembled the result of Zhang *et al.* who found average D_{2cc} for the rectum and bladder is 51% and 89% of the prescribed dose, respectively for Manchester point A and 60% and 106% of the prescribed dose, respectively for ABS point H. Similar results were derived from the study done by Srivastava S *et al.* [9]which showed that 2cc bladder and rectum dose to ABS point H leads to be higher than Manchester point A. Higher OAR doses in ABS point H could be due to the fact that ABS point H lies superiorly above Manchester point A.

The observation of the current study is in contrast with Tod and Meredith's study [12] The patients involved in their study had massive disease, even at the time of brachytherapy and they found the change in point A from its original definition (A_{ovoid}) to modified (A_{os}) in the Manchester system because of the minimal geometric shift between these two points).

They wrote: "in the average case the lower end of the cervical canal is level with the lateral fornices, as indicated by ovoid position". The majority of the patients in that era had a disease in advanced stages, and in present days patients are well screened at an early stage because of the effective screening program and improved socio-demographic conditions. In the current study, the difference may be due to the size of the tumour at the time of treatment.

Point A based prescription and reporting have been introduced along with film-based planning. As 3D CT image-guided brachytherapy comes across, utilization of film-based planning may diminish. However, point A based prescription is still encouraged. This study also demonstrated that changes in prescribing points can lead to significant dosimetric differences. So we are still doing practice on this consideration to ensure dosimetric and clinical equivalency from the previous clinical experiences and still point H is not used for the execution of treatment.

Conclusion

While changing from point A to point H, contemplation was needed. On average, TV is more in the case of point H prescription plans, but along with that on average D_{2cc} for the bladder and rectum doses were also high, however, if OARs doses were acceptable and within limits then we can use point H as dose prescription point. Moreover, this execution still needed robust clinical data as dose differences between these plans are statistically significant, so careful consideration is needed for the implementation of new point H in clinical practice.

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