Dosimetric Comparison of Two Type Brachytherapy Planning Approaches in HDR Treatment of Carcinoma Uterine Cervix: Standard Library Plan Approaches vs. 3D CT Image Based Planning

Suresh Yadav[1], S. Choudhary[2], O. P. Singh[3], Dinesh Kumar Saroj[4]
[1]Dept. of Physics, RNTU, Bhopal (M.P.) India.
[2]Dept. of Physics, RNTU, Bhopal (M.P.) India.
[3]Dept. of Radiotherapy, Gandhi Medical College, Bhopal (M.P.) India.
[4]Dept. of Radiotherapy, Chiryu Medical College, Bhopal (M.P.) India.

ABSTRACT
Due to unavailability or limited resources of imaging modality some centres in low and middle income countries (LMICs) are still unable to adopt image based treatment planning in brachytherapy practice. This study aimed to compare the volumetric dose differences between images based planning and standard library plan (SLP) approaches to find out the feasibility of using SLP approaches for HDR treatment planning in LMICs. Total ninety four plans of 47 patients image based plan were evaluated retrospectively. For each set of image based plans, one additional set of plans were generated by applying dwell positions and dwell times of SLP approach on reconstructed applicator position of CT image data of each patient. The mean dose of bladder D_{2cc}, D_{1cc} and $D_{0.1cc}$ were higher by 0.03 Gy, 0.4 Gy and 0.06 Gy respectively in SLP approach rather than image based plan (p-value > 0.05). For rectum and sigmoid colon the mean dose of D_{2cc}, D_{1cc} and $D_{0.1cc}$ were significantly increases in SLP approach rather than image based plan. Higher increase for $D_{0.1cc}$ mean dose of rectum (0.12 Gy, 2.19%) and sigmoid colon (0.12 Gy, 1.69%) were found when SLP approach was used in place of image based plan. The results of this study shows that mean doses of target and OAR (bladder, rectum and sigmoid colon) are increases with SLP approach. The increase dose to rectum, bladder and sigmoid colon in SLP approach may lead to enhance the toxicity and hence affect the quality of life. The results of this study emphasized that if limited resource settings use SLP approach the proper applicator placements, adequate packing and other accounting factors should be considered carefully.

Keywords: High dose rate, Volumetric dose, Standard library plan, Image based plan

I INTRODUCTION

Carcinoma uterine cervix (Ca Cx) is usually the most common malignancy in many low and middle income countries (LMICs), where resources are limited or unavailable for prevention, diagnosis and treatment [1]. Intracavitary high dose rate (HDR) brachytherapy either alone or in combination with external beam radiotherapy is recommended as definitive radiation therapy for Ca Cx [2]. Brachytherapy has proven as an integral component of definitive radiotherapy treatment of Ca Cx [3]. Brachytherapy follows the inverse square rule, in which physical radiation dose is inversely proportional to the square of distance from radioactive source. Intracavitary HDR brachytherapy system which allows to be delivered high localized radiation dose to uterine cervix within a short time and sparing the organ at risk (OAR) such as bladder, rectum and sigmoid colon to large extent. The characteristic rapid dose fall-off with distance from intracavitary applicator is both the major advantage and major disadvantage of brachytherapy [4]. Hence, appropriate placement of applicator is the most essential step to deliver sufficient dose to the tumor and spare OAR [4].

Various computerized planning systems are available for dose calculation and to create brachytherapy treatment plans for Ca Cx. Typically HDR intracavitary applicator mainly consists of one central tandem and two lateral ovoids generating pear-shaped isodose lines centered around the uterine cervix. This applicator system grants to delivered high dose to uterine cervix at the same time sparing OAR. In image based treatment planning the calculated doses are related to geometry of applicator, patient anatomy and dose for OAR can be made available. While, treatment planning generated with the help of computer is known as standard template plan (SLP). In SLP there is no exact idea that how much dose received by tumor and OAR. With the advent of computerized treatment planning systems it has feasible to create treatment plan in 'actual time' before treatment [5]. These treatment planning systems provides precise calculation of dose to target and OAR, well plan documentation, better estimation of implant geometry and capable to optimize the treatment plan[5].

The Radiation dose calculation and dose distribution in BrachyVision treatment planning system is based on following mathematical algorithm-

TG-43 Algorithm:- As per AAPM TG-43 algorithm [6,7,8] the dose rate $\dot{D}$ (r,θ) at a point (r, θ can be written as-

$$\dot{D}(r,\theta) = S_k . \wedge . \frac{G\ r\ \theta}{G\ r0\ \theta 0} . g(r). F(r,\theta)$$

Where,
r → the distance between centre of source to dose point, θ → Angle subtended by line joining centre of source to dose point with long axis of source, S_k → Air Kerma Strength of radioactive source, ∧ → Dose rate constant, G(r,θ) → Geometry factor, g(r) →

Radial Dose function and F (r,θ)→ Anisotropy function

With the advancement in imaging technology the use of 3 dimensional imaging MRI and CT are increasing globally and availability of CT scanners made it common 3D imaging modality for image guided brachytherapy planning. Recently, published guidelines GEC-ESTRO and ICRU-89 strongly recommended individualized 3D image based brachytherapy treatment planning in carcinoma cervix for each fraction [9, 10]. Besides advances in imagining technology some centers especially in LMICs use standard library plan instead of 2D or 3D image based plan. Image based brachytherapy treatment planning is not in approach to some centers due to unavailability or limited resources of imaging modality.

The main aims of this study was to compare the volumetric dose differences between image based plan and SLP to find out the feasibility of using SLP approaches for HDR treatment planning in LMICs.

II MATERIALS AND METHODS

Retrospectively forty seven 3D CT image based plans of 47 patients (only first fraction image based plan) who have been received intracavitary treatment for carcinoma cervix with high dose rate brachytherapy machine were selected for the study. The (mean ± s.d) age of patients was 49.11 ± 7.90 years involved in this study. The distributions of patient disease were stage ranges from IIB-IVA of FIGO staging system. All the patients had received 23-25 fractions of 2 Gy per fraction (a dose of 46-50 Gy over a period of five weeks) by external beam radiotherapy either on Linear Accelerator or on Tele-cobalt machine using either four field box technique or two parallel opposed AP-PA fields before initiation of brachytherapy treatments. Subsequently finishing the external beam radiotherapy all the patients were planned to receive 3 fractions of 7 Gy (dose of 21 Gy on weekly intervals over three weeks) by means of intracavitary brachytherapy using fixed geometry Fletcher style applicator. Patients were elucidated about image based treatment procedure before applicator insertions and informed consents were taken.

The applicator insertions were done under consideration of all aseptic precautions. For immobilization and avoid slippage of applicator assembly, adequate vaginal packing were done using Betadine soaked gauge. Foley's catheter was placed in the urinary bladder and bladder was left to drain in all patients. After insertion of applicator 3D images with 2.5 mm slice thickness were acquired on CT simulator (Discovery RT, GE Health Care) from umbilicus to mid thigh. All images were imported into Brachy Vision v. 8.9 TPS (Varian Medical Systems, Palo Alto, CA, USA) using CD/DVD. The contouring of tumour (HR-CTV) and OAR (bladder, rectum, and sigmoid colon) were performed by Radiation Oncologist following ABS/GEC-ESTRO guidelines. All applicator insertions and contouring were carried out by single Radiation Oncologist and treatment planning by single Medical Physicist to mitigate inter-personal variations.

The 3D image based brachytherapy treatment plans on CT image data of first fraction of each patient were created and dose of 7 Gy was prescribed at point 'A' as per ABS guidelines. The treatment plans were optimized in this fashion that combined EQD2 doses from external beam radiotherapy and brachytherapy were kept ≤ 90 Gy for bladder and ≤ 75 Gy for rectum and sigmoid colon. The actual brachytherapy treatment was delivered to patients with remote afterloading unit (Gamma Med Plus, Varian Medical Systems) using ^{192}Ir HDR brachytherapy source.

The standard library plan (SLP) was created for each set of applicator (tandem length and ovoid diameters) by simulating applicator assembly on CT simulator. Post simulation of applicator assembly image was imported into Brachy Vision TPS. The applicator was reconstructed and dose of 7 Gy was prescribed on point 'A' and treatment planning was performed to produce pear shape following similar image based planning procedure of actual patients.

For dosimetric comparison between standard library plan (SLP) and 3D CT image based treatment plan, re-plans were created using CT image based treatment plans of patients. One additional set of plans were generated by applying treatment parameters (dwell positions and dwell time) of SLP on reconstructed applicator position of CT image data set of each patients. In this way total two plans were generated for each patient. Thus total 94 3D CT image based plans evaluated in this study. As per established guidelines (ABS, GEC-ESTRO and ICRU 89) the dose volume parameters D90 and D100 (dose to 90% and 100% of HRCTV volume) were used for reporting target (HRCTV) doses and dose at point 'A' (right, left and mean) were also recorded and evaluated . Again dose volume parameters D_{2cc}, D_{1cc} and $D_{0.1cc}$ (minimum doses received by maximum volume of 2cc, 1cc and 0.1cc) were recorded and evaluated for OAR (bladder, rectum and sigmoid colon). These dose volume parameters for HRCTV and OAR were estimated from cumulative dose-volume histogram (DVH) as shown in Fig.1. SPSS statistics version 20 (IBM corporation, USA) software was used for statistical analysis. A paired t-test was used to assess the significance in difference between SLP approaches and 3D image based treatment planning. The p-value < 0.05 were considered for significance of statistical inferences.

III RESULTS

The comparison of volumetric doses (D90 and D100) of HR-CTV and point ‘A’ (right, left and average) doses are presented in Table.1. All the doses of HR-CTV and point ‘A’ were expressed as (mean ± s.d) in Gy. The result showed that HR-CTV D90 mean doses were 10.48 ± 1.23 and 10.68 ± 1.33 in image based plan and SLP approach respectively. There were significant differences (p-value 0.000 < 0.05) between image based plan and SLP approach. For HR-CTV D100 the mean doses were 5.52 ± 0.95 and 5.59 ± 0.99 in image based plan and SLP approach respectively. For HR-CTV D100 there were insignificant differences (p-value: 0.084 > 0.05) between image based plan and SLP approach.

The mean doses at left point ‘A’ was 6.95 ± 0.95 using image based plan, while it significantly increased to 7.05 ± 0.16 when SLP approach was used (p-value: 0.000 < 0.05). The mean dose at right point ‘A’ was 7.06 ± 0.18 using image based plan, while it significantly increased to 7.17 ± 0.16 when SLP approach was used (p-value: 0.001 < 0.05). Finally for average point ‘A’ the mean dose was 7.00 ± 0.15 using image based plan, while it significantly escalated to 7.11 ± 0.15 when SLP approach was used (p-value: 0.000 < 0.05).

Table.2 shows the various dose volume parameters (D_{2cc}, D_{1cc} and $D_{0.1cc}$) for bladder, rectum and sigmoid colon of both image based plan and SLP. All the doses of bladder, rectum and sigmoid colon were expressed as (mean ± s.d) in Gy. The bladder D_{2cc} mean dose were 4.85 ± 1.32 and 4.88 ± 1.31 in image based plan and SLP approach respectively. For bladder D_{2cc} there were statistically insignificant differences between image based and SLP approach (p-value: 0.145 > 0.05). The bladder D_{1cc} mean dose were 5.35 ± 1.51 and 5.39 ± 1.49 in image based plan and SLP approach respectively. For bladder D_{1cc} there were statistically insignificant differences between image based and SLP approach (p-value: 0.104 > 0.05). The bladder $D_{0.1cc}$ mean doses were 6.55 ± 2.04 and 6.61 ± 2.02 in image based plan and SLP approach. For bladder $D_{0.1cc}$ there were statistically insignificant differences between image based plan and SLP approach (p-value: 0.059 > 0.05).

Table 1
Comparison of HR-CTV and Point 'A' (right, left and average) doses between Image based plan and standard library plan

Parameter	Image Based Plan (mean ±s.d) in Gy	Standard Library Plan (mean ±s.d) in Gy	Mean Differences in Gy	P-value
HR-CTV D90	10.48 ± 1.23	10.68 ± 1.33	-0.20	0.000
HR-CTV D100	5.52 ± 0.95	5.59 ± 0.99	-0.09	0.084
Right A	6.95 ± 0.13	7.05 ± 0.16	-0.10	0.000
Left A	7.06 ± 0.18	7.17 ± 0.16	-0.11	0.001
Avg. A	7.00 ± 0.15	7.11 ± 0.15	-0.11	0.000

The rectum D_{2cc} mean doses were 4.19 ± 0.63 and 4.26 ± 0.67 in image based plan and SLP approach respectively. For rectum D_{2cc} there were statistically significant differences between image based and SLP approach (p-value: 0.001 < 0.05). The rectum D_{1cc} mean doses was 4.58 ± 0.95 in image based plan, while it significantly increased to 4.67 ± 0.76 when SLP approach was used (p-value: 0.000 < 0.05). The rectum $D_{0.1cc}$ mean dose was 5.48 ± 0.95 in image based plan, while it significantly increased to 5.60 ± 1.00 when SLP approach was used (p-value: 0.000 < 0.05).

Table 2
Comparing mean doses of various dose-volume parameters for organs at risk (Bladder, Rectum and Sigmoid colon) and their clinical significances

Parameter		Image Based Plan (mean ± s.d) in Gy	Stanadard Library Plan (mean ± s.d) in Gy	Mean Differences	P-value
Bladder	D_{2cc}	4.85 ± 1.32	4.88 ± 1.31	-0.03	0.145
	D_{1cc}	5.35 ± 1.51	5.39 ± 1.49	-0.04	0.104
	$D_{0.1cc}$	6.55 ± 2.04	6.61 ± 2.02	-0.06	0.059
Rectum	D_{2cc}	4.19 ± 0.63	4.26 ± 0.67	-0.07	0.001
	D_{1cc}	4.58 ± 0.72	4.67 ± 0.76	-0.09	0.000
	$D_{0.1cc}$	5.48 ± 0.95	5.60 ± 1.00	-0.12	0.000
S. Colon	D_{2cc}	5.04 ± 0.57	5.11 ± 0.62	-0.07	0.001
	D_{1cc}	5.62 ± 0.68	5.71 ± 0.72	-0.09	0.001
	$D_{0.1cc}$	7.10 ± 1.25	7.22 ± 1.26	-0.12	0.001

The sigmoid colon D_{2cc} mean dose was 5.04 ± 0.57 in image based plan, while it significantly escalated to 5.11 ± 0.62 when SLP approach was used (p-value: $0.001 < 0.05$). The sigmoid colon D_{1cc} mean dose was 5.62 ± 1.25 in image based plan, while it significantly escalated to 5.71 ± 0.72 when SLP approach was used (p-value: $0.001 < 0.05$). The sigmoid colon $D_{0.1cc}$ mean dose was 7.10 ± 1.25 in image based plan, while it significantly escalated to 7.22 ± 1.26 when SLP approach was used (p-value: $0.001 < 0.05$).

IV DISSCUSSION

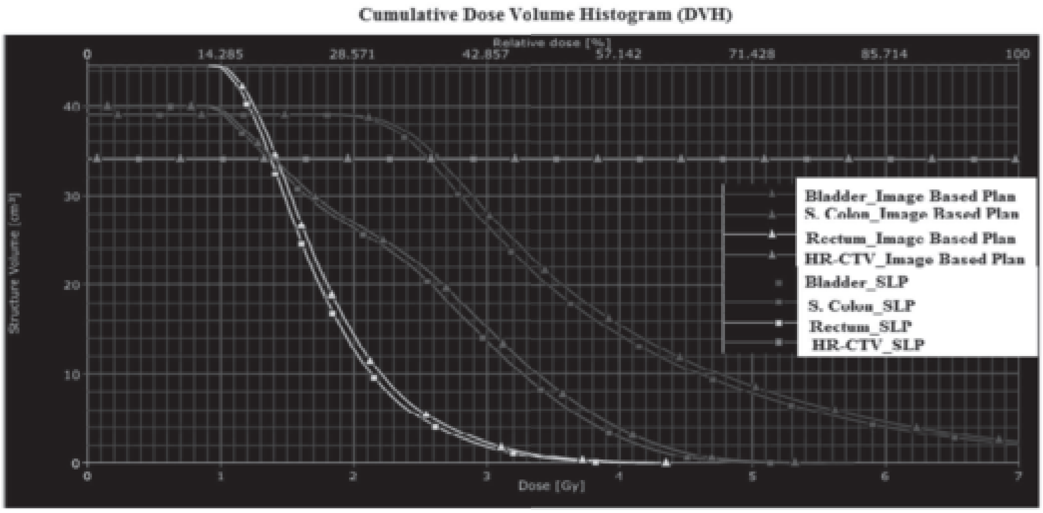
The results of our study demonstrated that HR-CTV D90 mean dose was increases 1.9% (0.20 Gy) in SLP approach than image based plan and increment was significant. A small increase of 0.07 Gy (1.2%) in HR-CTV D100 mean dose with SLP approach compared to image based plan and increment was insignificant. The Point 'A' (right, left and average) mean doses were significantly higher 1.56%, 1.44% & 1.57% respectively with SLP approach in comparison to image based plan. In image based treatment plan the calculated dose of organs (HR-CTV and OAR) are related to applicator geometry. In SLP approach doses are calculated from reconstruction of applicator assembly only, whereas in image based plan the applicators are within tumour and calculated dose reflects actual physical dose. Patone H. et al. found that there is significant dose rate dependency on applicators geometry [5].

Considerable geometrical variations occurred during multiple HDR applications and their impacts on dosimetric parameters were illustrated in literatures [4,11,12]. Since only small changes in distance between anatomical structures (bladder, rectum and s. Colon) and applicator source may produce larger deviations in dose received to these structures [12]. Hoskin et al. emphasized that it is essential to be attentive of changes in applicators positions between HDR fractions in same patient for the same treatment schedule [12].

Our study finds that bladder (D_{2cc}, D_{1cc} and $D_{0.1cc}$) mean doses are higher by 0.03 Gy, 0.4 Gy and 0.06 Gy respectively in SLP approach in comparison to image based plan. These increments are found statistically insignificant. In our study significant increase of 1.67%, 1.97% and 2.19% in rectum (D2cc, D_{1cc} and D0.1cc) mean doses are observed respectively with SLP approach in comparison to image based plan. Maximum increase of 0.12 Gy in mean dose for 0.1cc volume of rectum is noted if SLP approach used in place of image based plan. Significantly higher mean doses by 1.39% 1.60% 1.69% are recorded for sigmoid colon (D_{2cc}, D_{1cc} and $D_{0.1cc}$) when SLP approach are used in place of image based plan. In sigmoid colon also maximum increase of 0.12 Gy in mean dose are recorded for 0.1cc volume with SLP approach in comparison to image based plan.

Patone H. et al. performed a dosimetric comparison of standardized dose rate template planning and computerized treatment planning to determine the dose differences at point 'A' and ICRU 38 bladder and rectum reference points [5]. Patone H. et al. concluded that if standard template plan approach has been used, significantly higher doses would have been delivered and emphasized that standard template plan approach should have carefully considered [5]. A study by Jamema et al. was done to compare the rectal and bladder ICRU point doses between orthogonal and CT image based planning [13]. Jamema et al. concluded that ICRU rectal point doses were in correlation with maximum rectal doses, whereas ICRU bladder points dose underestimates the maximum bladder dose [13]. The higher radiation doses to OAR (bladder, rectum and sigmoid colon) will increase the complication and reduce the quality of life.

Fig.1
Dose volume Histogram (DVH)



Kirisits et al. demonstrated that there were increase in point and volume doses to OAR and target if single plan were used for all subsequent fractions of brachytherapy [14]. A study by Mobit et al. was done to assess the advantage of 3D image based planning over standard treatment planning for brachytherapy treatment of cervical cancer with tandem and ovoids [15]. Mobit et al. concluded that use of customized plans did not always cut down the OAR (bladder, rectum, sigmoid colon and small bowl) doses as compared to standardized plan [15].

Grover et al. updated the ABS survey and reported that in U.K. the use of CT, MRI and X-ray in image based brachytherapy planning were 95%, 34% and 15% respectively [16]. The results of 2014 survey by American Brachytherapy Socity revealed that use of point 'A' and HR-CTV based dose prescription were 42% and 52% in 2014 ABS survey in comparison of 76% and 14% in 2007 ABS survey [16].

V CONCLUSION

The results of this study shows that mean doses of target and OAR (bladder, rectum and sigmoid colon) are increases when SLP approach is used instead of image based planning. The increase dose to rectum, bladder and sigmoid colon in SLP approach may lead to enhance the toxicity and hence affect the quality of life. In this study the increase in dose volume parameters of target and OAR using SLP approach is firmly indicate the dependency of dose distribution on applicator geometry. The results of this study emphasized that if limited resource settings use SLP approach, the proper applicator placements, adequate packing and other accounting factors should be considered carefully. On the basis of recent research based on advanced imaging it is proposed that image based planning for each fractions will be adopted in routine brachytherapy practice if it will be feasible.

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