

# A Dosimetric Study of Optimised and Non-Optimised Plans in Intracavitary Brachytherapy (ICBT) Using International Commission on Radiation Units and Measurement (ICRU) 89

Nidhi Marjara<sup>1</sup>, Anil Kumar Bansal<sup>2</sup>, Deepak Tripathi<sup>3</sup>

1. Department of Radiation Oncology, Max Superspeciality Hospital, Shalimar Bagh, Delhi
2. Department of Radiation Oncology, Max Superspeciality Hospital, Saket, Delhi
3. Amity Institute of Applied Sciences, Amity University, Noida

ARTICLE INFO	ABSTRACT
<p><b>Article type:</b> Original Paper</p> <hr/> <p><b>Article history:</b> Received: Apr 09, 2020 Accepted: Oct 12, 2020</p> <hr/> <p><b>Keywords:</b> Brachytherapy High risk CTV Carcinoma Cervix Intermediate Risk CTV ICRU Report 89</p>	<p><b>Introduction:</b> The study aimed to assess the effectiveness of the dosimetric parameters of organs-at-risks (OARs) and target coverage in optimized plans compared to non-optimized plans normalized at point A.</p> <p><b>Material and Methods:</b> This retrospective study examined 21 patients with cervical cancer in stages II and III, who had undergone a high dose rate (HDR) ICBT following external beam radiotherapy (EBRT). In this study, two treatment plans were created for each case using computed tomography (CT) images. Normalization at point A was performed in the non-optimized plans, and 90% of the high-risk clinical target volume (HR-CTV) was to receive the prescribed dose in the optimized plans. Dose-volume histograms (DVH) were used to compare <math>D_{5cc}</math>, <math>D_{2cc}</math>, <math>D_{1cc}</math>, and <math>D_{0.1cc}</math> (minimum doses received by the most irradiated volumes of 5cc, 2cc, 1cc and 0.1cc, respectively) for OARs as well as the <math>D_{90\%}</math>, <math>D_{50\%}</math>, <math>D_{98\%}</math>, <math>D_{100\%}</math>, and <math>D_{95\%}</math> coverage of HR-CTV between the non-optimized and optimized plans. Statistical analysis was performed using Wilcoxon signed rank test.</p> <p><b>Results:</b> The HR-CTV coverage improved in 80% of the patients. In the optimized plans, the rectum and bladder doses decreased by 8.75% and 9.85%, as compared to the non-optimized plans normalized at point A, respectively. In the sigmoid and bowel cases, there were dose drops by 8.95% and 9.75%, in the optimized plans, respectively.</p> <p><b>Conclusion:</b> Target coverage and OAR sparing were more satisfactory in the optimized plans than the non-optimized plans normalized at point A.</p>

► Please cite this article as:

Marjara N, Kumar Bansal A, Tripathi D. A Dosimetric Study of Optimised and Non-Optimised Plans in Intracavitary Brachytherapy (ICBT) Using International Commission on Radiation Units and Measurement (ICRU) 89. Iran J Med Phys 2021; 18: 314-320. 10.22038/ijmp.2020.47653.1764.

## Introduction

Remarkable advances in cervical cancer morbidity have been observed in the developed countries, which are mainly caused by cytological screening initiated about 50 years ago. According to the current global cancer statistics 2018, approximately 96,922 new cases were diagnosed, and 60,078 deaths were reported annually [1,2]. Radiation therapy or surgery is used for early-stage tumours. Chemo-radiation is preferred for large tumours. Commonly, radiation therapy and chemotherapy are used after surgery if there is a high risk of recurrence.

Intracavitary brachytherapy (ICBT) is considered an integral part of radiotherapy in the treatment of cervical cancer, especially in locally-advanced diseases. ICBT helps in the escalation of the dose to the primary tumour with better OARs sparing than external beam radiotherapy (EBRT) due to sharp gradient i.e. dose falls off rapidly outside the target volumes [3]. In brachytherapy, 10-15% dose fall off per mm whereas in EBRT per mm fall in dose is 1-2%

(it is an approximate percentage calculated from patient plans at 2cm with respect to target volume). Many institutions are still following two-dimensional (2D) orthogonal imaging for brachytherapy planning and treatment [4]. The dose prescription method in the 2D brachytherapy does not account for various factors, thereby leading to the overestimation or underestimation of tumour doses. It also does not account for the radiation dose of OARs, which is based on the ICRU38 recommendations [4,5].

Moreover, some studies have reported 5-30% grade 3 or grade 4 toxicity for bowel and bladder [4]. With the technology advancement, three-dimensional (3D) volumetric dose prescription and OAR dose assessment have become feasible, leading to the improved dose coverage of the cervical tumour and the application of minimal dose to the surrounding normal organs. However, the point-based prescription is still practiced at many centres worldwide since it has revealed minimal dose variation from case to case

and is believed to be an acceptable index of normal tissue tolerance.

Many studies have reported the dosimetric comparison of 2D and 3D ICBT planning. Jamalludin *et al.* [6] conducted a preliminary study and concluded that ICRU-point doses for rectum and bladder were not true dose reflectors, compared to the  $D_{2cc}$  (dose received by 2cc volume) of bladder and rectum. Rani *et al.* [7] studied 25 cervical cancer patients treated with ICBT. After comparing the  $D_{2cc}$  values of bladder and rectum, they concluded that the volumes of ICRU 38 were not a true reflection of actual doses. Tann *et al.* [8] reported a significant difference between bladder ICRU-point dose and the corresponding  $D_{2cc}$  values; however, no significant difference was noticed for rectum doses. Further, they reported that the point dose of the bladder was under-estimated compared to  $D_{2cc}$ . In another study using OARs dosimetric observations, Kim *et al.* [9] claimed that the mean ICRU bladder point dose (401cGy) was under-estimated in comparison to the bladder  $D_{2cc}$  (484cGy). However, the mean ICRU rectal point dose (412cGy) did not significantly differ from the mean rectal  $D_{2cc}$  dose (373cGy). Imanoa's *et al.* [10] study showed favourable local-/regional control and significantly the lower  $D_{2cc}$  dose of the rectum in 3D planning compared to 2D planning (mean values of 61.2Gy vs. 69.1Gy;  $p=.001$ ). Kim *et al.* [4] and Derks *et al.* [11] concluded that 3D brachytherapy should be considered for the standard management of cervical cancer as it reduced severe toxicity and improved loco regional recurrence-free survival and progression-free survival in cervical cancer patients. Wanderas *et al.* [12] document that MRI is the gold standard for ICBT planning of cervical cancer; however, computed tomography (CT) can also be used to perform planning. Accordingly, we followed the CT-based contouring guidelines for brachytherapy published by Viswanathan *et al.* [13].

In 2016, the ICRU report 89 [14] prescribed comprehensive guidelines for disease staging, contouring, dose prescription, and reporting in ICBT for cervical cancer, in which the emphasis was on volume-based dose optimisation and prescription instead of point A-based prescription. It was believed that volume-based prescription and reporting were better correlated with the expected outcomes in terms of local control and the OARs toxicities. The toxicities such as ulceration, fistula, or circumscribed telangiectasia were believed to be linked to the most irradiated small volumes described by  $D_{2cc}$  and  $D_{0.1cc}$ . The GEC-ESTRO (Groupe Européen de Curiethérapie - the European Society for Radiotherapy & Oncology) recommendations on 3D brachytherapy were published in 2005 and 2006 [1, 15], suggesting  $D_{100\%}$  and  $D_{90\%}$  (volume of HR-CTV receiving 100% and 90% of prescription dose, respectively) target volumes for reporting and prescribing. It was also

mentioned that  $D_{90\%}$  was more steady regarding random uncertainties than  $D_{100\%}$  for HR-CTV.

According to the literature, 3D planning in brachytherapy is far superior to 2D planning regarding organ sparing and survival rate. We adapted 3D planning in our setup; however, the point A-based normalization technique was also considered. After reviewing the recently published ICRU 89 report, we were to conduct this comparative dosimetric study of volume-based (plan optimised to HR-CTV) and point-based (plan normalised at point A) planning by following the ICRU 89 recommendations to detect how it would affect the target coverage and the OAR doses.

## Materials and Methods

### Patient preparation, simulation, and contouring

In a present retrospective study, 21 patients diagnosed with squamous cell carcinoma of the cervix were examined. We included those patients, who were ideal cases for the ICRT application according to clinical decisions, depending on their post-EBRT relapse, and excluded patients having already undergone ICRT application due to unavoidable complications, making them unfit for the Martinez Universal Perineal Interstitial Template MUPIT application. The stage-wise distribution was 76.2% (16 out of 21) IIB, 14.3% (3 out of 21) IIIB, and 4.8% (1 out of 21) IB. All patients received external radiation to the pelvis on a linear accelerator Unique (Varian Medical Systems, Palo Alto, CA) using 10 megavolts (MV) X-rays energy. A dose of 45Gy – 50.4Gy in 25-28 fractions was delivered during five days per week using Rapid Arc (RA) technique with two coplanar arcs (one clockwise (181°-179°) and one anti-clockwise (179°-181°)). In the last week of EBRT, the patient was assessed by a clinician for the suitability of brachytherapy. According to departmental protocol after assessing the patient vitals, bowel preparation was carried out and enema was given to the patient. Before insterting the applicator, mexaprost was given to the patients for cervix dilation as it facilitated the easy insertion of the applicator. The rectal tube was inserted during the procedure, and 10 ml diluted Omni pro contrast (1ml contrast in 9ml water) was given for rectum delineation. Following the ultrasound guidelines, the oncologist assessed the patient's anatomy and accordingly decided about the diameter of the ovoids (half ovoids, 2.5cm, 3cm, 3.5cm) and the angulations of the tandem (15°, 30°, and 45°) to be used for the application. Prior to the CT imaging, 10 ml diluted contrast was given in the bladder via Foley's catheter tube as it helped in the bladder wall delineation. The CT image with 2.5-mm slice thickness was obtained from Discovery Radiation Therapy Computed Tomography-RTCT (General Electric Healthcare, U.S.A). The images were imported to the Brachytherapy Planning System Oncentra TCS version 3.3 (Nucletron, Elekta AB, Stockholm). The bladder, rectum, sigmoid, bowel, and HR-CTV and intermediate-risk (IR)-CTV were delineated by an oncologist. We followed the following

contouring guidelines recommended by Vishwanathan *et al.*[13] for HR-CTV and IR-CTV in the CT imaging:(A) HR-CTV: The inferior extent was contoured up to the ovoid level. Superiorly it was contoured to the level where uterus indents (internal OS). Beyond this, 1cm was contoured as a cone shape. The approximate cranio-caudal extent of HR-CTV/cervix was 3cm. Laterally, the parametrial extension would be included in HR-CTV if it appeared greyish/whitish on CT/MRI. The parametrial region would not be included in the HR-CTV if it had no visible stranding on CT or if it was not marked as HR-CTV in the clinical drawing. (B) IR-CTV: It was drawn as a 5-mm margin surrounding HR-CTV in anterior-posterior directions. A 10-mm margin was taken cranio-caudally below the cervical OS in the vagina and bilaterally towards the parametria.

**Treatment planning and optimisations**

The weekly dose of 8Gy X 3 fractions was given to patients on a HDR remote after-loader machine micro

Selectron mHDR digital v3 (Nucletron, Elekta AB, Stockholm) with 30 channels.

The plans were optimised as follows:

(a) **Non-optimised plan:** Point A was defined according to the ICRU 89[14] definition: 2cm above the surface of the ovoid along the tandem and 2cm lateral to the tandem in a perpendicular direction. The dose was normalized and prescribed at the point A.

(b) **Optimised plan:** The plan was optimised to provide adequate coverage to the target (i.e. HR-CTV) as such the D<sub>90%</sub> of HR-CTV should receive 100% of the prescribed dose.

Figure 1 represents how we developed the optimised and non-optimised plans for all patients.

Table 1 represents the dosimetric parameters to be reported and recorded according to ICRU 89 for further evaluation. The D<sub>2cc</sub> of bladder, rectum, sigmoid, and bowel, and the D<sub>90%</sub> of HR-CTV are discussed below in detail since oncologists mainly focus on these parameters for plan evaluation and approval. Other parameters are recorded to evaluate the late effects of the treatment during the follow-ups.

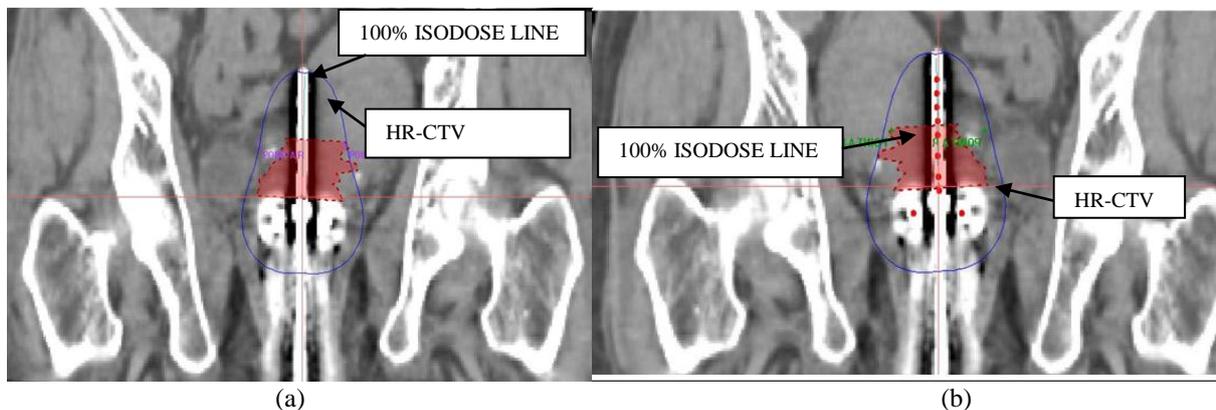


Figure 1. Schematic description of (a) non-optimised plans (normalized at point A) and (b) optimised HR-CTV plans in red, with 100% isodose line in blue

**Statistical Analysis**

The statistical analysis was performed using the Wilcoxon signed-rank test. A confidence interval of 95% was set as the significance level in testing. We compared the optimised versus non-optimised plans for each patient by calculating P-values for all dosimetric parameters.

Table 1. The dosimetric parameters used for plan evaluation in the study.

Organs	Parameters
HRCTV	D <sub>90%</sub> , D <sub>100%</sub> , D <sub>95%</sub> , D <sub>50%</sub> , D <sub>98%</sub>
IRCTV	D <sub>90%</sub> , D <sub>100%</sub> , D <sub>95%</sub> , D <sub>50%</sub> , D <sub>98%</sub>
OARs	D <sub>2cc</sub> , D <sub>0.1cc</sub> , D <sub>5cc</sub> , D <sub>1cc</sub>

\*D<sub>x%</sub>: Dose received by the X volume of the target

**Results**

In the present study, for 71.4 % (15 patients out of 21) of the patients, there was a significant decrease in the bladder, rectum, sigmoid, and bowel doses from the mean values of 5.81± 0.95Gy, 4.22 ±0.75Gy, 3.75 ± 0.98Gy, and 4.44 ± 1.33Gy in the optimised cases compared to the non-optimised cases normalized at point A with the mean values of 6.65 ± 1.01Gy, 5.1±0.88Gy, 4.49± 1.21Gy and 5.38±1.34Gy, respectively.

Table 2 presents the dosimetric comparison of the mean values of BED (α/β=3Gy) and EQD<sub>2</sub> (α/β=3Gy) for the D<sub>2cc</sub> of OARs in the optimised and non-optimised plans. A remarkable decrease was observed in the OAR doses in the optimised plans compared to the non-optimised plans.

Table 3 shows the dosimetric parameters of HR-CTV and the mean values of BED (α/β=10Gy) and EQD<sub>2</sub> (α/β=10Gy) in the optimised and non-optimised plans as well as the P-values for each parameter.

Table 2. Mean BED, and EQD<sub>2</sub> along with their P-values for OARs in optimised and non-optimised plans

Parameters	OARs	Non-optimised	Optimised	p-value
BED (Gy) for D <sub>2cc</sub> ( $\alpha/\beta=3$ Gy)	Bladder	138.6 ± 16.26	129.7 ± 16.94	0.020
	Rectum	113.4 ± 13.75	109.0 ± 12.14	0.040
	Bowel	126.3 ± 20.06	118.9 ± 16.91	0.001
	Sigmoid	109.2 ± 14.44	103.9 ± 11.71	0.003
EQD <sub>2</sub> (Gy) for D <sub>2cc</sub> ( $\alpha/\beta=3$ Gy)	Bladder	86.3 ± 14.61	77.4 ± 9.62	0.003
	Rectum	71.0 ± 11.91	65.0 ± 7.28	0.013
	Bowel	79 ± 16.29	71.4 ± 9.92	0.002
	Sigmoid	68.6 ± 13.56	62.0 ± 7.03	0.006

\*BED ± SD, EQD<sub>2</sub> ± SD

Table 3. Dosimetric parameters and p-values for HR-CTV in optimised and non-optimised plans

Target	DosimetricParameters	Optimised	Non-optimised	p-value
HR-CTV	D <sub>90%</sub> (Gy)	8.0 ± 0.06	9.0 ± 1.66	0.015
	D <sub>98%</sub> (Gy)	6.4 ± 0.34	7.2 ± 1.57	0.014
	D <sub>50%</sub> (Gy)	13.4 ± 0.84	14.9 ± 2.12	0.011
	BED( $\alpha/\beta=10$ Gy) (Gy)	97.4 ± 3.32	106.7 ± 14.14	0.002
	EQD <sub>2</sub> ( $\alpha/\beta=10$ Gy) (Gy)	87.7 ± 2.77	81.3 ± 10.08	0.006

\*D<sub>x%</sub>: Dose received by the X volume of the target

\* Dose ± SD, BED ± SD, EQD<sub>2</sub> ± SD.

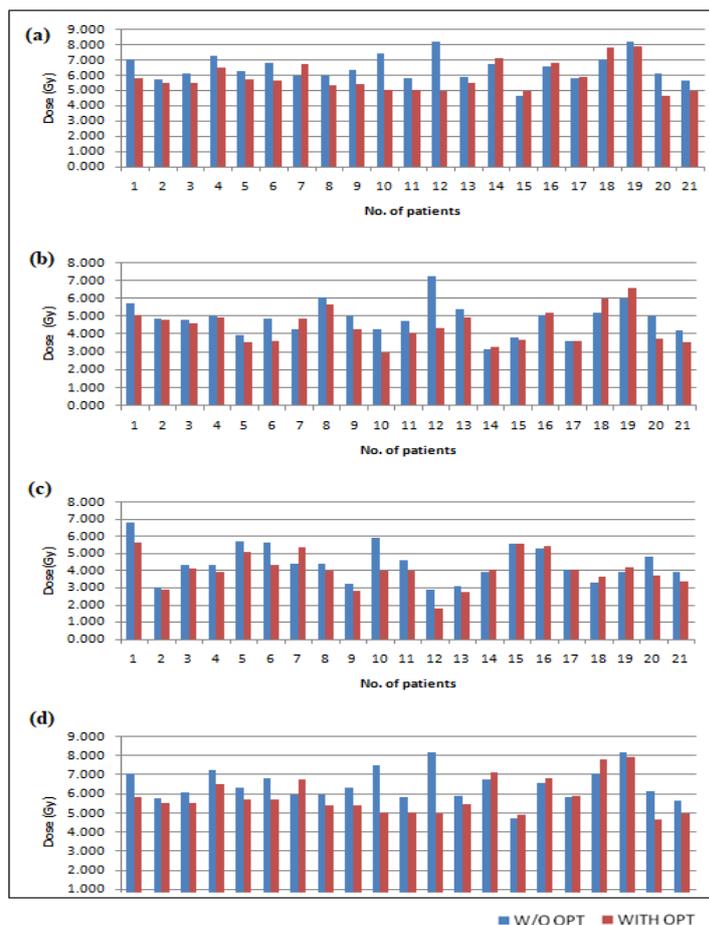


Figure 2. Data collected from 21 patients' (a) bladders, (b) rectums, (c) sigmoids, and (d) bowels in optimised and non-optimised plans

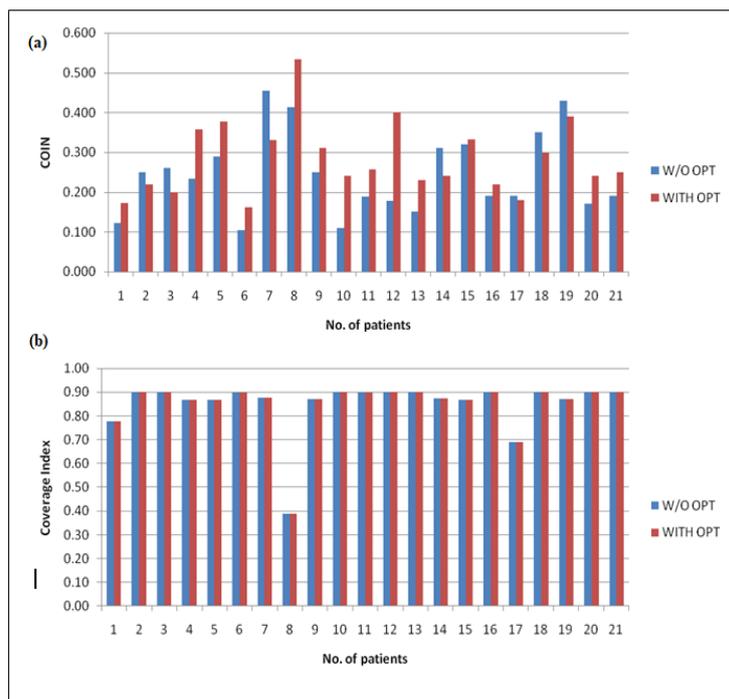


Figure 3. Collected data for (a) COIN and (b) Coverage index in optimised and non-optimised plans

We observed a significant increase in the HR-CTV coverage in the optimised plans.

In 33.4% (7 out of 21) of the patients, the  $D_{90\%}$  of HR-CTV was  $<100\%$  of the prescribed dose (7.44Gy) in the non-optimised plans, which was improved by the optimisation of the HR-CTV coverage (8.0Gy) in the optimised plans. It also led to an increase in the OAR doses in 71.4% (5 out of 7) of the patients and a decrease in the OAR doses in 28.6% (2 out of 7) of the patients. However, the BED and EQD<sub>2</sub> values of  $D_{2cc}$  for bladder, rectum, sigmoid, and bowel were well within the tolerance in both optimised and non-optimised plans. BED ( $\alpha/\beta=3\text{Gy}$ ) should be less than 140Gy for bladder and for rectum, sigmoid and bowel BED ( $\alpha/\beta=3\text{Gy}$ ) should not exceed 120Gy and EQD<sub>2</sub> ( $\alpha/\beta=3\text{Gy}$ ) for bladder should be less than 90Gy and EQD<sub>2</sub> ( $\alpha/\beta=3\text{Gy}$ ) for rectum, sigmoid and bowel should not be more than 75Gy). Figure 2 represents the comparison of doses for different OARs in each patient's optimised and non-optimised plans.

According to ICRU 89, the total EQD<sub>2</sub> ( $\alpha/\beta=10\text{Gy}$ ) of HR-CTV should be 80-90Gy for advanced cervical cancer cases. The present study decreased EQD<sub>2</sub> ( $\alpha/\beta=10\text{Gy}$ ) to the abovementioned range in 24% of patients with a mean value of 101.44Gy to 81.11Gy in the optimised plans. EQD<sub>2</sub> ( $\alpha/\beta=10\text{Gy}$ )  $> 95\text{Gy}$  resulted in an unnecessary increase in the OAR doses. In 28.6% of cases, EQD<sub>2</sub> ( $\alpha/\beta=10\text{Gy}$ ) increased from the mean value of 76.13Gy to 80Gy after optimisation. There was a significant increase in the target coverage with optimisation compared to the non-optimised plan. The mean value of conformity index (COIN) increased in 57% of the cases from 0.19 to 0.29 after optimisation at

$p= 0.025$ . Moreover, there was no compromise in the tumour coverage in the optimised plan. The mean dose to point A (mean of the points A1 and A2) in the optimised plan (mean value of 7.4Gy) was 7.5% below the mean dose to point A in the non-optimised plan (mean value of 8.0Gy). As shown in Figure 3, the conformity index improved in the optimised plans, compared to non-optimised plans, with no change in the coverage index for both optimised and non-optimised plans in all the patients.

## Discussion

We compared the non-optimised plans normalised at point A with the HR-CTV optimised plans in the present study. The literature [6, 9, 12] demonstrated that the tumour volume coverage was inadequate in the non-optimised plans, in which ICRU 38 reference points were used, compared to the HR-CTV-based optimised plans in 60% of the total cases. The non-optimised plan, which was based on ICRU bladder and rectum point doses, underestimated the corresponding  $D_{2cc}$  of rectum and bladder obtained from the CT plan. Therefore, mentioned studies and some other similar studies [6-9,12] have indicated that the ICRU reference points are not the true reflectors of organ doses. The major limitation of ICRU 38 is that it does not recommend the evaluation of doses to the small bowel and sigmoid colon in brachytherapy as they are close to the brachy sources. To resolve such issues, 3D brachytherapy planning has been used to optimise dose distribution providing volumetric information on the target volumes and the surrounding OARs [16-19]. Some researchers have reported that the dose to point 'A' in the non-

optimised plans over-estimates the tumour volume dose coverage [17-19]. Furthermore, more advanced tumour stages and larger target volumes receive less coverage with the prescribed dose at point A, thus resulting in poor local control [19-21]. This problem was sorted out by the ICRU 89 [14] recommendations, which emphasised the delineation of HR-CTV and also highlighted the parameters to be reported. According to the ICRU 89 [14] recommendation, MRI should be used for contouring target volumes in brachytherapy cases as it has better soft-tissue contrast compared to the CT images. Vishwanathan et al.[22] showed an overestimation of tumour width in the CT images in lateral direction. Their study on 10 patients generated guidelines for CT contours, indicating the mean volume of HR-CTV to be 48cc. Due to the unavailability of the MR imaging equipment such as MR compatible applicator, we followed the contouring guidelines proposed by Vishwanathan et al.[13] for HR-CTV and IR-CTV on CT images. In our study, we observed that the  $D_{90\%}$  value decreased with an increase in the target size ( $> 4\text{cm}$ ) for 33.4% of the cases (7 out of 21 patients) in the non-optimised plans. In other words, the target was not completely covered with 90% isodose. Accordingly, the coverage was improved by the optimisation of HR-CTV using the optimised plans. Similarly, it was observed that, in our cases, the average dose to point A for the optimised plan was less than the corresponding dose to point A for the non-optimised plans considering a smaller target size; however, it was more for a larger target size [12-15]. According to ICRU 89[14],  $D_{2\text{cc}}$  and  $D_{0.1\text{cc}}$  should be evaluated for OARs (bladder, rectum, sigmoid, bowel) as the volumes of the tissues are in the highest dose regions and are probably more clinically relevant.  $D_{5\text{cc}}$  was also computed since it was the minimal volume required for fistula formation [14]. In this study, we focussed on observing the dosimetric parameters mentioned in ICRU89  $D_{5\text{cc}}$ ,  $D_{2\text{cc}}$ ,  $D_{1\text{cc}}$ , and  $D_{0.1\text{cc}}$  for OARs and  $D_{90\%}$ ,  $D_{50\%}$ ,  $D_{98\%}$ ,  $D_{100\%}$ , and  $D_{95\%}$  for the HR-CTV coverage to detect whether the variations in the planning technique affect the OARs doses and HR-CTV coverage. We have used local geometric optimisation since the study mainly aimed to cover the under-dosed region of HR-CTV with 100% isodose with minimal distortion to pear shape curve and to maintain the optimal dose at point A.

In our study, the  $D_{2\text{cc}}$  parameter for OARs decreased in optimised plans where we have improved target coverage in comparison to non-optimised plans normalised at point A. We observed a reduction of 9.75%, 8.65%, 8.95%, and 9.75% in the bladder, rectum, sigmoid, and bowel doses respectively in optimised plans with respect to non-optimised plans. OARs doses were a limiting factor in the optimised plans to provide the 100% coverage of target volume. The bladder dose was the limiting factor in 71.4% of the patients. In 7% and 33.4% of the cases, the rectum and sigmoid doses were found as a hindrance respectively. Wanderas et al. [12] reported that bladder, sigmoid, and

rectal doses acted as limiting factors in 64%, 21%, and 14% of patients, respectively.

## Conclusion

The present findings showed that except 33.4% cases, in all other cases the optimised plans were better than non-optimised plans. With the same coverage index and conformity index, we could reduce the OARs doses from 8% to 10% with improved tumour coverage in 66.67% of the patients for optimised plans. We also observed that the OAR sparing was a limiting factor for large target volumes aiming at 100% coverage. Accordingly, the technique needs to be shifted to interstitial brachytherapy such as MUPIT (Martinez universal perineal interstitial template) technique for large tumour size ( $>4\text{cm}$  according to ICRU 89) [14]. The advanced technologies are expected to provide better results in terms of target coverage and OAR sparing with MRI-based planning as the HR-CTV volume would be lower in MRI compared to CT-based planning. In the future, we are to expand the present study with including three-level recommendations for reporting in ICRU 89.

## Acknowledgment

My sincere thanks to Dr. Manoj kr Semwal Dr. Lalit kumar and Mr. Pawan Kr Singh for constant support and guidance.

## References

1. Haie-Meder C, Pötter R, Van Limbergen E, Briot E, De Brabandere M, Dimopoulos J, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group☆(I): concepts and terms in 3D image-based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiotherapy and oncology*. 2005 Mar 1;74(3):235-45.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. 2018 Nov;68(6):394-424.
3. Weiner AA, Schwarz JK. Intracavitary brachytherapy for gynecologic malignancies: applications and innovations. *Missouri medicine*. 2015 Sep;112(5):366.
4. Kim YJ, Kang HC, Kim YS. Impact of intracavitary brachytherapy technique (2D versus 3D) on outcomes of cervical cancer: a systematic review and meta-analysis. *Strahlentherapie und Onkologie*. 2020 Nov;196(11):973-82.
5. Chassagne D, Dutreix A, Almond P, Burgers JMV, Busch M, Joslin CA. ICRU report 38: dose and volumespecification for reporting intracavitary therapy in gynecology. *Journal of International Commission on Radiation Units and Measurements*. 1985; 20(1).
6. Jamalludin Z, Min UN, Ishak WW, Malik RA. Preliminary experience on the implementation of computed tomography (CT)-based image guided

- brachytherapy (IGBT) of cervical cancer using high-dose-rate (HDR) Cobalt-60 source in University of Malaya Medical Centre (UMMC). In *Journal of Physics: Conference Series*. 2016; 694(1): 012016.
7. Radhika Rani, R. Srikanth. Comparative study of conventional and CT based planning of target volumes organs at risk in intracavitary brachytherapy for carcinoma of cervix. *IAIM* 2016;3(9):200-9.
  8. Tann YI, Choo BA, Lee KM. 2D to 3D evaluation of organ at risk doses in ICRT for cervical cancers. *Journal of Contemporary Brachytherapy*. 2010 Mar;2(1):37-43.
  9. Kim RY, Shen S, Duan J. Image based three-dimensional planning of intracavitary brachytherapy for cancer of the cervix: Dose-volume histograms of the bladder, rectum, sigmoid colon and small bowel. *Brachytherapy*. 2007. Jul-Sep;6(3):187-94.
  10. Imanoa N, Wadasakib K, Nishibuchia I, Nagataa Y. Comparison of clinical outcome between computed tomography-based image-guided brachytherapy and two dimensional-based brachytherapy for cervical cancer. *Gynaecology Oncology Reports*. 2019; 29:79-82.
  11. Derks K, Steenhuijsen JL, van den Berg HA, Houterman S, Cnossen J, van Haaren P, De Jaeger K. Impact of brachytherapy technique (2D versus 3D) on outcome following radiotherapy of cervical cancer. *Journal of contemporary brachytherapy*. 2018 Feb;10(1):17.
  12. Wanderas AD, Sundset M, Langdal I, Danielsen S, Frykholm G, Marthinsen AB. Adaptive brachytherapy of cervical cancer, comparison of conventional point A CT based individual treatment planning. *Acta Oncologica*. 2012 Mar;51(3):345-54.
  13. Viswanathan AN, Erickson B, Gaffney DK, Beriwal S, Bhatia SK, Burnett III OL, et al. Comparison and consensus guidelines for delineation of clinical target volume for CT-and MR-based brachytherapy in locally advanced cervical cancer. *International Journal of Radiation Oncology\* Biology\* Physics*. 2014 Oct 1;90(2):320-8.
  14. Potter R, Kirisits C, Erickson B, Haie-Meder C, Van Limbergen E, Lindegaard J. C, et al. ICRU report 89: prescribing, recording and reporting brachytherapy for cancer of the cervix. *International Commission on Radiation Units and Measurements*. 2016 July;13(1-2).
  15. Pötter R, Haie-Meder C, Van Limbergen E, Barillot I, De Brabandere M, Dimopoulos J, et al. GEC ESTRO Working Group: Recommendations from gynaecological (GYN) GEC ESTRO working group (II): concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. *Radiother Oncol*. 2006;78(1):67-77.
  16. Datta NR, Srivastava A, Das KJ, Gupta A, Rastogi N. Comparative assessment of doses to tumor, rectum, and bladder as evaluated by orthogonal radiographs vs. computer enhanced computed tomography-based intracavitary brachytherapy in cervical cancer. *Brachytherapy*. 2006 Oct 1;5(4):223-9.
  17. Wang B, Kwon A, Zhu Y, Yeo I, Henson CF. Image-guided intracavitary high-dose-rate brachytherapy for cervix cancer: A single institutional experience with three-dimensional CT-based planning. *Brachytherapy*. 2009 Apr 1;8(2):240-7.
  18. Tan LT, Coles CE, Hart C, Tait E. Clinical impact of computed tomography-based image-guided brachytherapy for cervix cancer using the tandem-ring applicator—the Addenbrooke's experience. *Clinical Oncology*. 2009 Apr 1;21(3):175-82.
  19. Shin KH, Kim TH, Cho JK, Kim JY, Park SY, Park SY, et al. CT-guided intracavitary radiotherapy for cervical cancer: comparison of conventional point A plan with clinical target volume-based three-dimensional plan using dose-volume parameters. *International Journal of Radiation Oncology\* Biology\* Physics*. 2006 Jan 1;64(1):197-204.
  20. Wachter-Gerstner N, Wachter S, Reinstadler E, Fellner C, Knocke TH, Pötter R. The impact of sectional imaging on dose escalation in endocavitary HDR-brachytherapy of cervical cancer: results of a prospective comparative trial. *Radiotherapy and oncology*. 2003 Jul 1;68(1):51-9.
  21. Pötter R, Knocke TH, Fellner C, Baldass M, Reinthaller A, Kucera H. Definitive radiotherapy based on HDR brachytherapy with iridium 192 in uterine cervix carcinoma: report on the Vienna University Hospital findings (1993-1997) compared to the preceding period in the context of ICRU 38 recommendations. *Cancer/Radiothérapie*. 2000 Mar 1;4(2):159-72.
  22. Viswanathan AN, Dimopoulos J, Kirisits C, Berger D, Pötter R. Computed tomography versus magnetic resonance imaging-based contouring in cervical cancer brachytherapy: results of a prospective trial and preliminary guidelines for standardized contours. *International Journal of Radiation Oncology\* Biology\* Physics*. 2007 Jun 1;68(2):491-8.