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Dosimetric comparison of 2D, 2D (MLC), 3DCRT and IMRT in Carcinoma of Cervix

Corresponding author: Dr. Saumen Basu MD,DNB

Department of Radiation Oncology, United Hospital, Gulshan, Dhaka - 1212, Bangladesh

Saumen Basu[1], Karthick Raj Mani[1], Fahadin Bin Hakim[2], Moumita Afrin Rakhi[2], Md Anisuzzaman Bhuiyan[1], Md Rashid Un Nabi[1], Ramaa Lingaiah[1], Sharif Ahmed[1], Kh Anamul Haque[1], Sadeka Sultana Ahmed[1], & Ashim Kumar Sengupta[1]

[1]Department of Radiation Oncology, United Hospital, Gulshan, Dhaka - 1212, Bangladesh

[2]Department of Medical Physics and Biomedical Engineering, Gono Bishwabidyalay, Savar, Dhaka, Bangladesh

Aim: To investigate the dosimetric eccentricities of 2D, 2D (MLC), 3DCRT and IMRT radiotherapy treatment techniques in carcinoma of cervix.

Materials and methods: We retrospectively included ten previously treated carcinoma of cervix in this study. All the ten patients under went CT simulation along with immobilization and positional devices. Targets and organ at risk (OAR) were delineated slice by slice for all the patients. Treatment plans were created with 15MV for 2D plans using AP/PA beams based on anatomical landmarks using the secondary jaws, whereas 2D (MLC) plans were created as same as the 2D plans, but fit the multi leaf collimator (MLC) to the planning target volume (PTV). 3D plans were created with 15MV photons using 4 field's box techniques and MLC fitted to the PTV. Intensity Modulated Radiation Therapy (IMRT) plans were created with 6MV beams with equally distributed 7 gantry angels. We intend to deliver 50 Gy in 25 fractions for all the patients. Doses to the critical structures and targets were recorded from the dose volume histogram for evaluation.

Results: Target homogeneity for all the 2D, 2D (MLC), 3DCRT and IMRT plans were comparable. Conformity index shows that 2D plans over treat by 660% more than PTV volume, 2D (MLC) plans by 363%, 3DCRT by 152% and IMRT by 22%. Low dose volumes (V5, V10 & V15) were high in IMRT, but high dose regions were comparatively less in IMRT. In IMRT plans, the rectal mean dose were reduced by 28% compared to 3DCRT, 2D (MLC) and 2D plans, which may result less toxicity in rectum, whereas 3DCRT reduced by 4% compare to 2D (MLC) and 2D plans. In IMRT plans bladder mean dose were reduced by 26% compared to 3DCRT, 2D (MLC) and 2D plans.

Conclusion: IMRT shows superior OAR sparing compared to 3DCRT, 2D (MLC) and 2D plans. Centers don't have IMRT / VMAT provision can use 4 field box technique using 15MV beams to reduce the high dose irradiation volume, which may results in low toxicity profile.

Introduction

Cervical cancer is the fourth most frequent cancer in women and the eighth most commonly occurring cancer overall. With an estimated 570,000 new cases in 2018 representing 6.6% of all female cancers, approximately 90% of deaths from cervical cancer occurred in low- and middle-income countries [1].

Virtually all cervical cancers are associated with human papilloma viruses (HPV). However, the majority of women with HPV do not develop cervical cancer. Women become susceptible to developing cervical cancer following HPV infection, but other environmental factors are required for the cancer to develop.Cervical cancer is one of the most common gynecologic cancers worldwide with approximately 83% of the cases happened in the developing countries [2]. According to 8th edition of the AJCC staging manual [3], 5-year survival rate for stage IA, IB, IIA, IIB, IIIA, IIB, IVA and IVB cervical cancer, is about 93%, 80%, 63%, 58%, 35%, 32%, 16% and 15% respectively.

Radiotherapy (RT) plays an important role in the adjuvant treatment of gynecologic malignancies, particularly in cervical and endometrial cancer. Radiotherapy has greatly improved local regional control of primary tumors at the cost of significant toxic effects to adjacent non-cancerous tissues. The toxicity of 2-dimensional (2D) and conventional conformal radiotherapy resulted in a large volume of normal tissues irradiation, especially intestine, rectum, bladder, bone marrow, etc. Over the last decade, interest in the use of IMRT to treat gynecologic cancer has been increasing. The IMRT technique has the potential benefit over conventional conformal radiotherapy of improving target coverage, reducing the doses to the volume of the organs at risk (OARs), and normal tissue [4]. Several studies have shown a significant reduction in the dose to small bowel, bladder, rectum, etc., with IMRT when compared to conventional conformal radiotherapy [5, 6, 7, 8, 9 & 10].

In spite of all the substantial benefits of IMRT, there are enough drawbacks in the technique. IMRT requires longer treatment time compared to the conventional static radiotherapy, which may influence the comfort of the patients, reproducibility and intra fraction motion during the radiotherapy [11]. The nature of high conformal dose distribution with IMRT may result in geographical miss due to inaccurate target delineations, inadequate planning target volume (PTV) margins, maintain the bladder and rectal filling, inter and intra observer variations in daily patient positioning, etc. Normally IMRT delivers a large monitor units (MUs) compared with traditional radiotherapy, which may result in the higher low dose volume concern the risk of secondary malignancy induced by the radiation [11, 12, 13]. The purpose of this study is to unfold the dosimetric comparison of 2D, 2D (MLC), 3DCRT and IMRT treatment techniques in the treatment of cervical cancer patients.

Materials and Methods

Patients' demographic data

Ten patients with median age of 47.4 years (range, 40 to 57 years) were retrospectively included in this study from our previously treated patient's database. The demographic data which includes age, histopathology and the staging of patients were listed in the table 1. All the staging of the patients was performed according to the International Federation of Gynecology and Obstetrics (FIGO) classification.

Table 1. Patients' demographic data

S.No	Patient	Age (Year)	Histopathological Report (HPR)	Stage
1.	Patient 1	47	Adenocarcinoma	III (Post Op.)
2.	Patient 2	45	Squamous Cell Carcinoma	IB
3.	Patient 3	50	Squamous Cell Carcinoma	IIIB
4.	Patient 4	48	Squamous Cell Carcinoma	IB
5.	Patient 5	40	Squamous Cell Carcinoma	IB
6.	Patient 6	53	Squamous Cell Carcinoma	IB2
7.	Patient 7	42	Adenocarcinoma	IIA
8.	Patient 8	46	Squamous Cell Carcinoma	IIB
9.	Patient 9	46	Adenocarcinoma	IIA
10.	Patient 10	57	Squamous Cell Carcinoma	IIIB

CT Simulation and delineation

All patients were positioned in supine position with indexed vacloc (M/SCivco) along with the ankle rest. CT simulation was performed using a GE Discovery 600 16 slice PET/CT scanner (GE Healthcare, Waukesha, WI, USA), the institution based CT protocol with full bladder was used for the data acquisition. The contrast enhanced CT data were acquired in axial mode with a slice thickness of 2.5 mm, field of view of 430 mm with a pixel resolution of 0.84 mm per pixel. Three fiducial markers were placed, one anteriorly above symphysis pubis and two lateral markers in the mid-plane and also a radio-opaque marker was placed at cervical os / vault to identify the caudal border. Once the patient CT data are acquired, the CT images were imported in DICOM format to Eclipse TPS ver. 11.0 (Varian Medical Systems). The body

structure was segmented automatically by the treatment planning system. Different anatomical structures and regions of interests were delineated. Organs-at-risk (OARs; rectum, urinary bladder, right femoral head, left femoral head, intestine and cauda equina) were delineated by the physician slice by slice on the CT images for all the patients. The CTV and nodal station were contoured according to the consensus guideline of the Radiation Therapy Oncology Group (RTOG).

The Planning Target Volume (PTV) was generated from the CTV (combining the primary and nodal CTVs) by applying an institutional margin recipe of 1 cm in cranio-caudal and 0.7 cm in other direction.

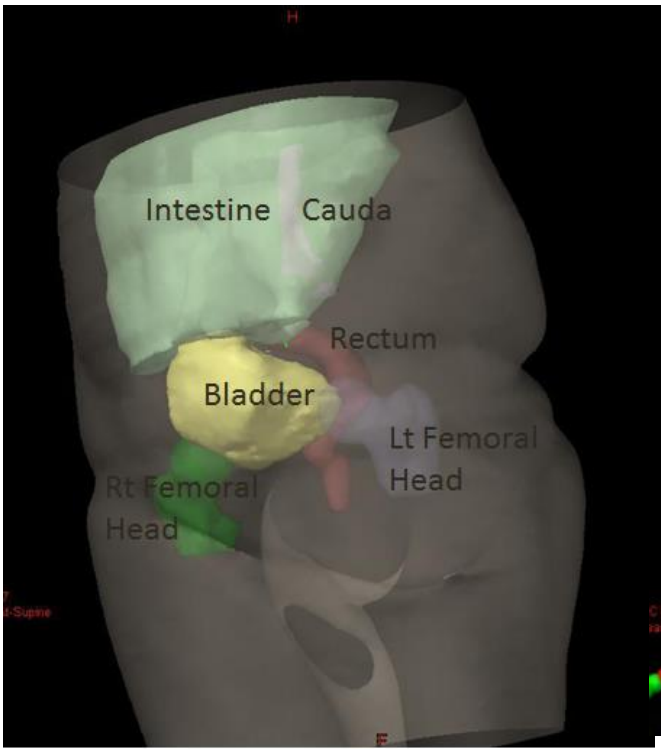


Figure 1: 3D view of Organ at Risk's

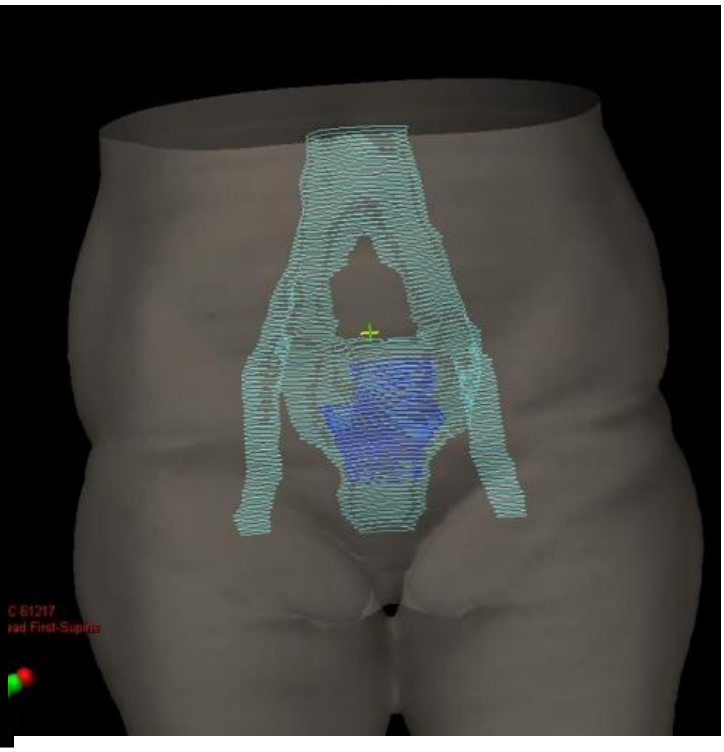


Figure 2: 3D view of PTV

Treatment Planning and Optimization

All the treatment plans for 2D, 2D(MLC), 3DCRT and IMRT were planned with TrueBeam linear accelerator (Varian Medical System, Palo Alto, USA). 2D technique was based on bony landmarks delivered by (AP-PA) parallel opposed fields defining only by the jaws using 15 MV photons. Whole pelvis was treated including clinically and radiological apparent tumor, uterine corpus, upper part of vagina, parametrium and the draining lymph nodes. The cranial border was kept at L4 - L5 interspace, caudal border was kept at lower border of obturator foramen or inferiorly extended to ensure adequate coverage of vaginal disease (radio-opaque marker placed) extension with proper margins, lateral border was kept at 2 cm from pelvic brim, the anterior border was fixed at anterior cortex of symphysis pubis and posterior border at S2-S3 junction. The 2D (MLC) plan was done with 15 MV photons using a parallel opposed (AP-PA) by fitting the MLC with a margin of 5mm to PTV where the secondary jaws were kept in the recommended positions. The conformal four field box technique also planned with 15 MV photons with MLC using a 5mm fit to PTV. The 2D, 2D MLC and 3DCRT plans were planned using SAD techniques and normalized at isocenter.

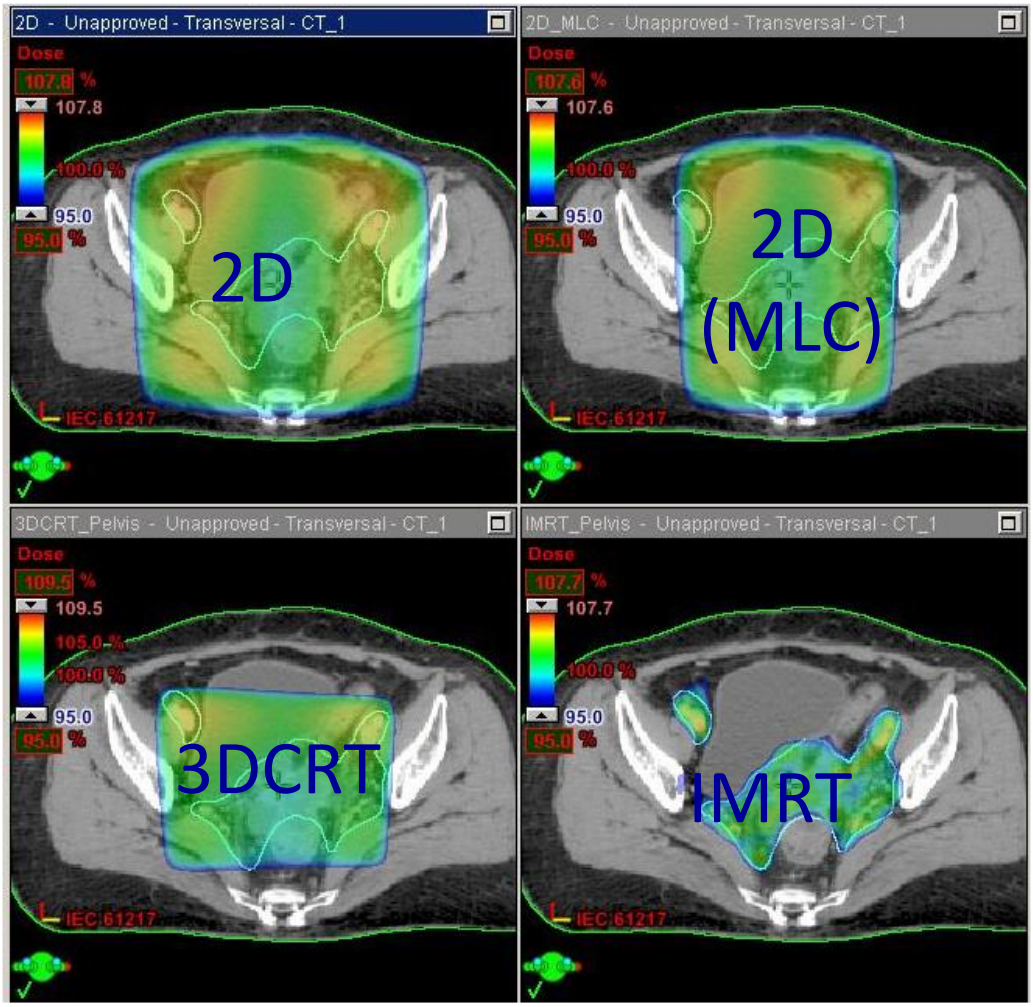


Figure 3: Typical 95% dose colour wash for all the four techniques

IMRT plans were generated for all the patients using seven equally spaced coplanar fields. The gantry angles used for the IMRT plans were 0^0, 51^0, 102^0, 153^0, 204^0, 255^0, and 306^0 with collimator rotation if necessary. The 6-MV photon flatten beam along with Millennium 120 leaf were used for the IMRT planning optimization. All IMRT plans were optimized using dose volume optimizer algorithm (DVO) ver.11.0 and the smart leaf motion calculator ver. 11.0 were used for converting the optimal fluence to actual fluence. For dose calculation, Analytical Anisotropic Algorithm (AAA) was used and normalization was done at target mean. All the treatment techniques used in this study were planned with a prescription dose of 50 Gy for PTV with 2 Gy per fraction.

Dosimetric Evaluation and Comparison

Quantitative evaluations of plans were performed by taking various dosimetric parameters from dose volume histogram (DVH). For PTV, the values of D98%, D50% and D2% (dose received by the 98%, 50% and 2% of the PTV volumes respectively) were defined as metrics for minimum, mean and maximum doses were documented for all the treatment techniques. V95% (the volume receiving at least 95% of the prescribed dose) and the PTV volumes of all the patients were documented to determine the homogeneity and the conformity indices.

To compare all these four techniques, ICRU 83 [14] definition was used to determine the dose conformity and dose homogeneity. Dose conformity and homogeneity are independent specifications of the quality of the absorbed dose distribution. Dose conformity characterizes the degree to which the high dose region conforms to the target volume whereas dose homogeneity characterizes the uniformity of the absorbed dose within the target volume.

Homogeneity index (HI):

$$HI = \frac{D2\% - D98\%}{D50\%} \quad \text{.....(1)}$$

Where, D2%, D98%, and D50% are the doses received by 2%, 98% and 50% of PTV volumes, respectively. HI = 0 (zero) is ideal value.

Conformity index (CI): In 1993, Radiation Therapy Oncology Group recommended CI as a ratio of the reference isodose (95% isodose volume) volume to the target volume.

$$CI_{RTOG} = \frac{V_{RI}}{TV} \quad \text{.....(2)}$$

where, V_{RI} is the reference isodose volume, and TV is the volume of the target (PTV).

For OAR minimum, maximum and mean doses were documented for the parallel and serial structures, respectively, for all four techniques. Additional dose parameters such as V_5, V_{10}, V_{15}, V_{20}, V_{30}, V_{40} and V_{50} (volume receiving at least 5 Gy, 10 Gy, 15 Gy, 20 Gy, 30 Gy, 40 Gy and 50 Gy respectively) for rectum, bladder, right femoral head, left femoral head, intestine and cauda were recorded. Dose conformity and dose heterogeneity were also calculated using the HI and CI using the equations (1) and (2).

Patient specific quality assurance

Patient specific quality assurance (QA) for all the 10 patients with IMRT plans were verified using 2D array I'mRT MatriXX (Scanditronix Wellhofer, Freiburg, Germany) attached to the gantry head using the gantry mount. Verification plans were created using the Eclipse TPS and irradiated using the 2D ionization chamber array and compare the measured dose profiles with the Eclipse TPS using OmniPro IMRT software.

Statistical analysis

The statistical data were presented as the average of all the patients followed by the standard deviation $\overline{X} \pm \sigma_{\overline{X}}$. All statistical analysis was conducted with paired two tailed "T-TEST" with equal variance using Microsoft Word/Excel version 2010 with $p < 0.05$ considered as significant.

Results:

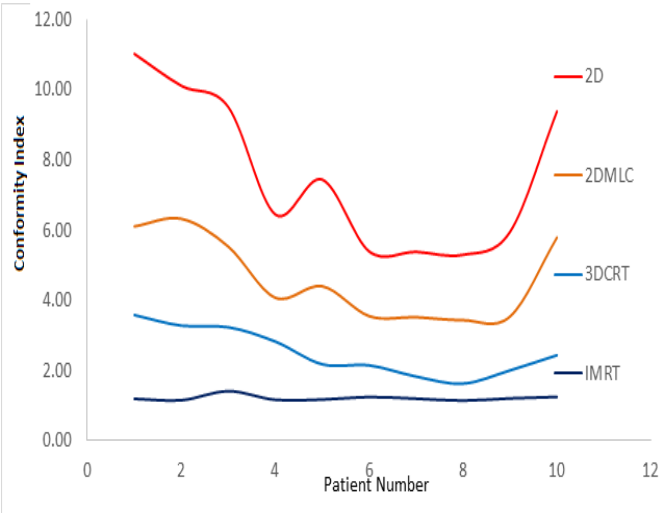
Radiation conformity index and dose homogeneity index:

The treatment plan quality has been compared using dose conformity and dose homogeneity parameters of all the four techniques. The calculated HI for all four techniques is tabulated in Table 2. The average CI values followed by standard deviation ($\overline{X} \pm \sigma_{\overline{X}}$) of all the patients were 7.60 ± 2.21 for 2D, 4.63 ± 1.18 for 2DMLC, 2.52 ± 0.68 for 3DCRT and 1.22 ± 0.08 for IMRT.

Table 2. Conformity Index

Patient No	2D	2DMLC	3DCRT	IMRT
1	11.02	6.11	3.59	1.20
2	10.12	6.33	3.29	1.16
3	9.51	5.54	3.24	1.42
4	6.45	4.08	2.83	1.17
5	7.45	4.41	2.19	1.18
6	5.40	3.56	2.15	1.25
7	5.39	3.52	1.83	1.20
8	5.30	3.44	1.63	1.15
9	5.95	3.54	2.01	1.21
10	9.39	5.79	2.44	1.25
Mean	7.60	4.63	2.52	1.22
Std. Dev	2.21	1.18	0.68	0.08

Figure 4: Conformity Index



The homogeneity index (HI) mean values followed by standard deviation ($\overline{X} \pm \sigma_{\overline{X}}$) of all the patients for 2D, 2D (MLC), 3DCRT and IMRT were 0.08 ± 0.02, 0.11 ± 0.02, 0.12 ± 0.03 and 0.07 ± 0.01 respectively. The calculated HI for all the patients with various techniques was tabulated in the **table 3**

Table 3: Homogeneity Index

Patient No	2D	2DMLC	3DCRT	IMRT
1	0.06	0.10	0.11	0.07
2	0.11	0.14	0.18	0.09
3	0.09	0.09	0.09	0.09
4	0.05	0.09	0.12	0.08
5	0.08	0.10	0.11	0.08
6	0.08	0.11	0.11	0.07
7	0.09	0.11	0.12	0.07
8	0.09	0.12	0.10	0.06
9	0.08	0.11	0.10	0.07
10	0.09	0.14	0.13	0.06
Mean	**0.08**	**0.11**	**0.12**	**0.07**
Std dev	**0.02**	**0.02**	**0.03**	**0.01**

We can conclude from the conformity index results that the 2D plans irradiate more surrounding normal structures compare to the other treatment techniques. With compared to IMRT; 3DCRT, 2D MLC and 2D plans irradiate on an average of 2.07, 3.80 and 6.23 times more normal tissue irradiation with the 95% isodose volume for all the patients. The homogeneity indexes between all the four techniques were comparable and no significant differences were observed.

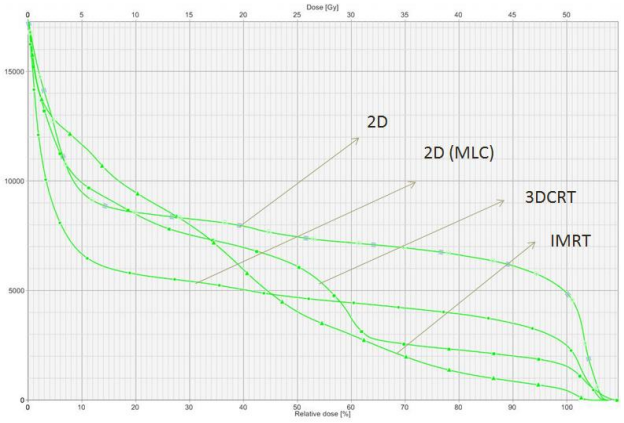
Low and high dose volumes:

The V5, V10, V15, V20, V30, V40 & V50 low dose and high dose volumes for all the patients with different treatment techniques were tabulated in the **table 4**. The mean followed by standard deviation for 2D, 2D MLC, 3DCRT and IMRT of V5 volumes were 44.86 ± 6.92, 30.87 ± 5.01, 46.53 ± 6.66 and 50.72 ± 9.11 respectively. The low dose volumes (V5 & V10) were higher in IMRT compared to the other techniques, whereas a substantial dose reduction in higher dose volumes (V50, V40 and V30) were documented. The mean V50 volumes for 2D, 2D MLC, 3DCRT for all the patients were 1262%, 647% and 343% higher compared to IMRT. Interestingly, the 2D MLC plans displayed the dose reduction in lower dose volumes (V5, V10, V15 and V20) compared to the other techniques due to conformal limited number of beams. The V5, V10, V15 and V20 were similar with 3DCRT techniques, but the V30, V40 and V50 were substantially higher in the 2D techniques.

Table 4: Low & high dose volumes:

	2D ($\bar{x} \pm \sigma_{\bar{x}}$)	2D MLC ($\bar{x} \pm \sigma_{\bar{x}}$)	3DCRT ($\bar{x} \pm \sigma_{\bar{x}}$)	IMRT ($\bar{x} \pm \sigma_{\bar{x}}$)
V5 (%)	44.86 ± 6.92	30.87 ± 5.01	46.53 ± 6.66	**50.72 ± 9.11**
V 10 (%)	39.46 ± 6.41	26.61 ± 4.35	38.83 ± 5.87	**41.95 ± 7.12**
V15 (%)	37.92 ± 6.26	25.13 ± 4.14	34.68 ± 5.14	**36.59 ± 6.40**
V20 (%)	35.50 ± 6.19	23.24 ± 3.91	32.40 ± 4.72	**28.43 ± 5.74**
V30 (%)	31.92 ± 5.67	20.84 ± 3.37	18.81 ± 3.23	**14.68 ± 3.42**
V40 (%)	29.84 ± 5.27	19.09 ± 2.99	12.42 ± 6.52	**7.57 ± 1.65**
V50 (%)	24.87 ± 9.12	12.75 ± 2.62	6.76 ± 1.93	**1.97 ± 0.43**
Mean (Gy)	**18.71 ± 3.03**	**12.41 ± 1.93**	**13.74 ± 1.98**	**12.71 ± 2.12**

Figure 5: DVH of Low and high dose volume



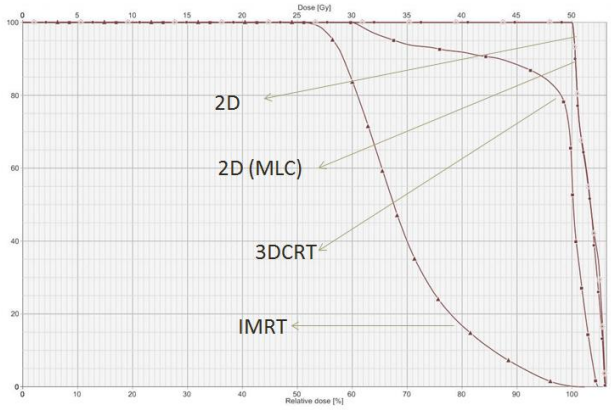
Rectum:

The mean rectal dose (Gy) followed by standard deviation ($\bar{x} \pm \sigma_{\bar{x}}$) for 2D, 2D (MLC), 3DCRT and IMRT were 52.35 ± 0.62, 51.36 ± 2.66, 48.48 ± 0.92 and 36.92 ± 5.39.

Table 5: Comparison of rectum dose for various techniques

Figure 6: DVH of Rectum for various techniques

	2D ($\bar{x} \pm \sigma_{\bar{x}}$)	2D MLC ($\bar{x} \pm \sigma_{\bar{x}}$)	3DCRT ($\bar{x} \pm \sigma_{\bar{x}}$)	IMRT ($\bar{x} \pm \sigma_{\bar{x}}$)
V5 (%)	100 ± 0.00	100 ± 0.00	100 ± 0.00	**100 ± 0.00**
V10 (%)	100 ± 0.00	100 ± 0.00	100 ± 0.00	**99.81 ± 0.60**
V15 (%)	100 ± 0.00	100 ± 0.00	99.91 ± 0.02	**99.61 ± 1.04**
V20 (%)	100 ± 0.00	100 ± 0.00	99.93 ± 0.23	**97.99 ± 2.69**
V30 (%)	99.91 ± 0.27	99.93 ± 0.14	98.98 ± 2.03	**72.40 ± 23.41**
V40 (%)	99.84 ± 0.52	98.49 ± 4.44	94.17 ± 2.71	**43.40 ± 27.58**
V50 (%)	99.53 ± 1.15	89.5 ± 31.44	57.54 ± 18.66	**2.71 ± 5.42**
Mean (Gy)	**52.35 ± 0.62**	**51.36 ± 2.66**	**48.48 ± 0.92**	**36.92 ± 5.39**



The V5, V10, V15, V20, V30, V40 and V50 for all the patients with different treatment techniques were tabulated in the **table 5.** Almost 100% of the rectal volume receives at least 15Gy and above (V15) for 2D, 2D (MLC), 3DCRT and IMRT techniques. V50 for 2D, 2D (MLC), 3DCRT and IMRT techniques were 99.53 ± 1.15, 89.5 ± 31.44, 57.54 ± 18.66 and 2.71 ± 5.42. There is substantial reduction in V50 were observed in IMRT and 3DCRT also shown a significant reduction when compared to 2D and 2D (MLC) Plans. The V5, V10, V15, V20, V30, V40 & V50 of rectal volumes for all the patients with different treatment techniques were tabulated in the **table 5**.

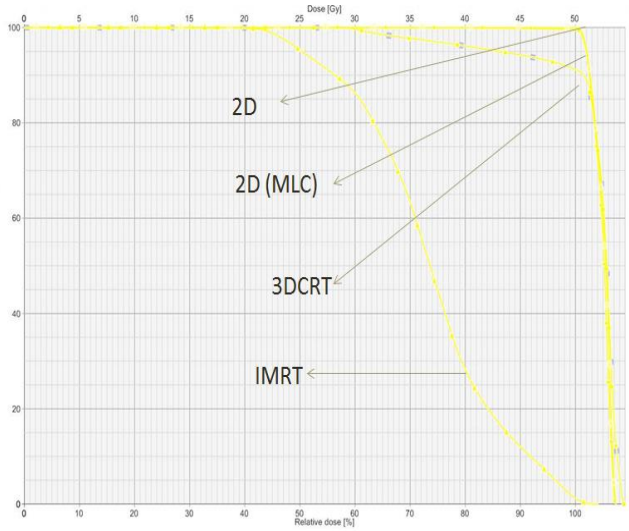
Bladder:

Table 6: Comparison of bladder dose for various techniques

The V5, V10, V15, V20, V30, V40 and V50 volumes of bladder for all the patients with different treatment techniques were tabulated in the **table 6**. The mean bladder dose (Gy) followed by standard deviation ($\bar{x} \pm \sigma_{\bar{x}}$) for 2D, 2D (MLC), 3DCRT and IMRT were 52.83 ± 0.53, 52.77 ± 0.59, 50.46 ± 1.97 and 36.96 ± 3.14. There is substantial reduction in the mean dose of bladder was observed in IMRT and there is no significant difference between 2D, 2D (MLC) and 3DCRT plans. Almost 100% of the bladder in all the four techniques was receiving at least 15Gy. In V40 and V50 volumes, there was a moderate dose reduction in 3DCRT compared to 2D and 2D (MLC) techniques. IMRT shows a significant reduction in V30, V40 and V50 compared to other treatment techniques.

Figure 7: DVH of Bladder for various techniques

	2D ($\bar{x} \pm \sigma_{\bar{x}}$)	2D MLC ($\bar{x} \pm \sigma_{\bar{x}}$)	3DCRT ($\bar{x} \pm \sigma_{\bar{x}}$)	IMRT ($\bar{x} \pm \sigma_{\bar{x}}$)
V5 (%)	100 ± 0.00	100 ± 0.00	100 ± 0.00	**100 ± 0.00**
V10 (%)	100 ± 0.00	100 ± 0.00	100 ± 0.00	**99.99 ± 0.01**
V15 (%)	100 ± 0.00	100 ± 0.00	100 ± 0.00	**99.34 ± 1.17**
V20 (%)	100 ± 0.00	100 ± 0.00	100 ± 0.00	**96.30 ± 5.49**
V30 (%)	100 ± 0.00	100 ± 0.00	99.26 ± 1.91	**75.79 ± 15.61**
V40 (%)	100 ± 0.00	99.99 ± 0.02	92.25 ± 7.35	**40.53 ± 12.15**
V50 (%)	99.99 ± 0.39	99.80 ± 0.21	84.70 ± 12.62	**4.98 ± 4.53**
Mean (Gy)	**52.83 ± 0.53**	**52.77 ± 0.59**	**50.46 ± 1.97**	**36.96 ± 3.14**



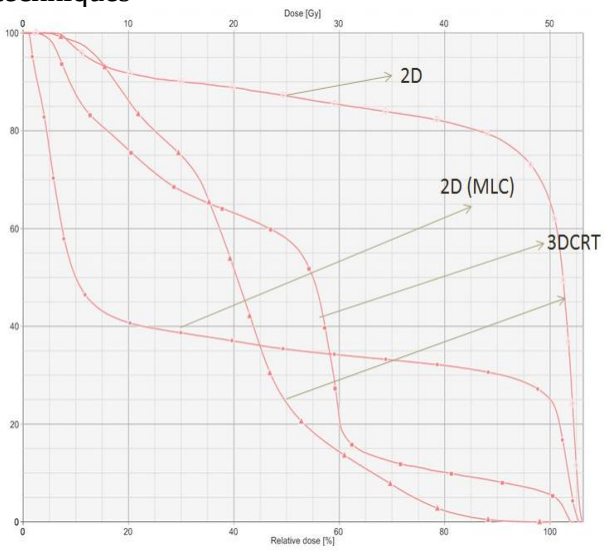
Intestine:

The mean intestine dose (Gy) followed by standard deviation ($\bar{x} \pm \sigma_{\bar{x}}$) for 2D, 2D (MLC), 3DCRT and IMRT were 43.64 ± 7.30, 26.93 ± 8.87, 25.29 ± 6.91and 23.08 ± 4.92 respectively. The V5, V10 and V15 for the intestine were comparatively less in 2D (MLC) technique due to its conformal beam geometry with parallel opposed fields. Sustainably dose reduction has been demonstrated in IMRT for V30, V40 and V50 compared to other treatment techniques. The V5, V10, V15, V20, V30, V40 and V50 volumes of intestine for all the patients with different treatment techniques were tabulated in the **table 7**. 3DCRT demonstrated a highly significant dose reduction in V40 and V50 compared to 2D and 2D (MLC) techniques due to its lateral opposing beam arrangements which avoids intestine partially.

Table 7: Comparison of intestine dose for various techniques

	2D ($\bar{x} \pm \sigma_{\bar{x}}$)	2D MLC ($\bar{x} \pm \sigma_{\bar{x}}$)	3DCRT ($\bar{x} \pm \sigma_{\bar{x}}$)	IMRT ($\bar{x} \pm \sigma_{\bar{x}}$)
V5 (%)	93.14 ± 11.14	66.76 ± 16.47	87.34 ± 12.23	**91.47 ± 13.52**
V10 (%)	89.20 ± 13.44	56.71 ± 18.33	77.98 ± 13.30	**81.96 ± 15.04**
V15 (%)	87.77 ± 14.06	54.10 ± 18.52	70.61 ± 14.29	**75.38 ± 15.69**
V20 (%)	86.50 ± 14.68	51.72 ± 18.57	66.52 ± 14.66	**61.17 ± 18.09**
V30 (%)	83.75 ± 15.34	47.89 ± 18.54	31.97 ± 20.26	**29.11 ± 15.58**
V40 (%)	81.18 ± 15.84	45.04 ± 18.58	16.42 ± 18.07	**8.62 ± 8.60**
V50 (%)	60.92 ± 22.67	32.93 ± 18.43	9.65 ± 14.89	**0.58 ± 1.61**
Mean (Gy)	**43.64 ± 7.30**	**26.93 ± 8.87**	**25.29 ± 6.91**	**23.08 ± 4.92**

Figure 8: DVH of Intestine for various techniques



Right and left femoral Head:

The V5, V10, V15, V20, V30, V40 and V50 volumes of right and left femoral head for all the patients with different treatment techniques were tabulated in the **table 8 and table 9.** The mean right femoral head dose (Gy) followed by standard deviation ($\bar{x} \pm \sigma_{\bar{x}}$) for 2D, 2D (MLC), 3DCRT and IMRT were 30.36 ± 6.5, 17.49 ± 8.31, 35.41 ± 4.49 and 23.68 ± 5.58 respectively. **.** The mean left femoral head dose (Gy) followed by standard deviation ($\bar{x} \pm \sigma_{\bar{x}}$) for 2D, 2D (MLC), 3DCRT and IMRT were 28.22 ± 7.71, 16.62 ± 7.47, 35.21 ± 3.69 and 24.79 ± 5.67 respectively. IMRT displayed a significant volume reduction in the V40 and V50 compared to other techniques. Interestingly, 2D (MLC) technique average mean dose of right and left femoral head for all the patients were much lower compared to IMRT due to corner shielding with MLC and beam geometry. The right and left femoral head displayed a similar pattern of results between all the four techniques due to its identical geometrical position with respect to the target

Table 8: Rt Femoral Head doses for various techniques

	2D ($\bar{x} \pm \sigma_{\bar{x}}$)	2D MLC ($\bar{x} \pm \sigma_{\bar{x}}$)	3DCRT ($\bar{x} \pm \sigma_{\bar{x}}$)	IMRT ($\bar{x} \pm \sigma_{\bar{x}}$)
V5 (%)	79.95 ± 14.58	53.86 ± 16.45	100 ± 0	**99.17 ± 1.99**
V10 (%)	67.40 ± 16.60	39.75 ± 18.12	98.92 ± 3.33	**92.53 ± 9.28**
V15 (%)	63.70 ± 16.44	36.05 ± 18.61	97.59 ± 3.92	**81.49 ± 15.95**
V20 (%)	61.22 ± 15.97	33.49 ± 18.72	96.11 ± 4.20	**59.11 ± 27.72**
V30 (%)	53.49 ± 14.23	27.78 ± 17.78	60.56 ± 21.84	**26.14 ± 19.09**
V40 (%)	47.32 ± 14.44	22.55 ± 16.73	30.10 ± 18.28	**8.07 ± 10.43**
V50 (%)	32.79 ± 10.07	13.10 ± 13.23	19.42 ± 16.29	**0.028 ± 0.088**
Mean	**30.36 ± 6.5**	**17.49 ± 8.31**	**35.41 ± 4.49**	**23.68 ± 5.58**

Table 9: Lt Femoral Head doses for various techniques

	2D ($\bar{x} \pm \sigma_{\bar{x}}$)	2D MLC ($\bar{x} \pm \sigma_{\bar{x}}$)	3DCRT ($\bar{x} \pm \sigma_{\bar{x}}$)	IMRT ($\bar{x} \pm \sigma_{\bar{x}}$)
V5 (%)	**76.27 ± 19.08**	**50.48 ± 17.68**	**100 ± 0**	**98.98 ± 2.45**
V10 (%)	**62.42 ± 18.07**	**37.80 ± 16.68**	**98.88 ± 3.07**	**195.60 ± 6.23**
V15 (%)	**58.85 ± 17.37**	**34.30 ± 16.54**	**97.53 ± 3.84**	**86.56 ± 13.23**
V20 (%)	**56.15 ± 16.84**	**31.91 ± 16.35**	**96.52 ± 4.25**	**64.31 ± 27.23**
V30 (%)	**48.45 ± 15.00**	**26.04 ± 15.61**	**61.94 ± 20.41**	**29.83 ± 22.03**
V40 (%)	**42.59 ± 14.13**	**21.25 ± 14.30**	**28.92 ± 15.75**	**7.69 ± 9.35**
V50 (%)	**30.25 ± 16.56**	**11.83 ± 12.20**	**17.84 ± 15.59**	**0.02 ± 0.06**
Mean (Gy)	**28.22 ± 7.71**	**16.62 ± 7.47**	**35.21 ± 3.69**	**24.79 ± 5.67**

Cauda:

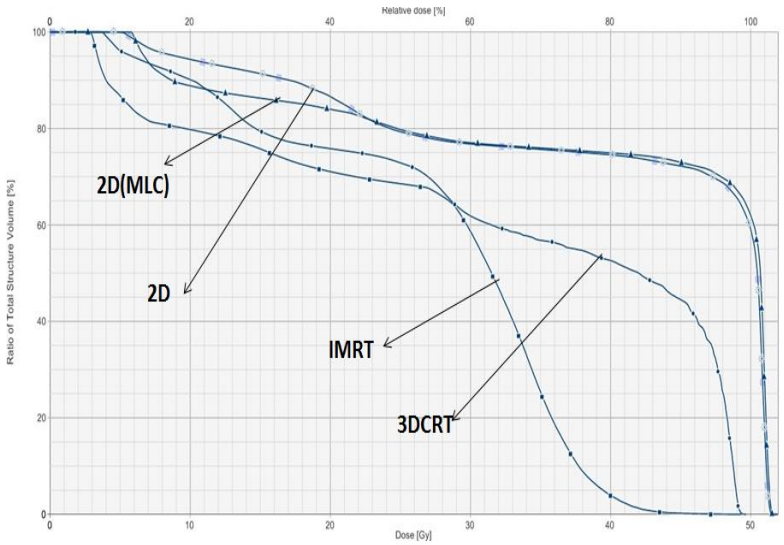
The average mean dose followed by standard deviation ($\bar{x} \pm \sigma_{\bar{x}}$) of cauda for V5, V10, V15, V20, V30, V40 ,V50 volumes, mean and maximum doses volumes for all the patients with different treatment techniques were tabulated in the **table 10.** The maximum dose (Gy) followed by standard deviation ($\bar{x} \pm \sigma_{\bar{x}}$) for 2D, 2D (MLC), 3DCRT and IMRT were 52.29 ± 0.57, 52.28 ± 0.51, 26.36 ± 5.82 and 45.08 ± 5.77 respectively.

Figure 9: DVH of Cauda for various techniques

Table 10: Cauda doses for various techniques

	2D ($\bar{x} \pm \sigma_{\bar{x}}$)	2D MLC ($\bar{x} \pm \sigma_{\bar{x}}$)	3DCRT ($\bar{x} \pm \sigma_{\bar{x}}$)	IMRT ($\bar{x} \pm \sigma_{\bar{x}}$)

V5 (%)	98.68 ± 10.75	88.03 ± 13.01	85.90 ± 13.48	85.14
V10 (%)	85.51 ± 12.07	84.51 ± 13.96	82.40 ± 14.04	79.58
V15 (%)	84.21 ± 12.51	82.88 ± 14.07	76.96 ± 14.09	75.83
V20 (%)	82.80 ± 12.84	80.87 ± 14.06	73.48 ± 13.81	72.22
V30 (%)	78.07 ± 13.80	74.76 ± 13.91	36.87 ± 24.90	53.41
V40 (%)	75.72 ± 13.97	72.22± 13.79	15.62 ± 26.71	10.21
V50 (%)	57.47 ± 21.58	50.70 ± 19.34	0.026 ± 0.08	0.069
Mean (Gy)	41.95 ± 6.17	39.85 ± 6.54	26.35 ± 7.04	**23.32**
Max (Gy)	**52.29 ± 0.57**	**52.28 ± 0.51**	**26.36 ± 5.82**	**45.08**



3DCRT displayed a significant dose reduction compared to other techniques due to its beam geometry. The mean dose of the cauda between the 3DCRT and IMRT were comparable. The 2D and 2D (MLC) resulted in higher mean and maximum dose due to its parallel opposed beam geometry, where the cauda is always inside the treatment fields.

Patient specific quality assurance:

All the ten patients with IMRT plans patient specific QA were performed using portal dosimetry. The fluence verification of IMRT plans were performed using gamma analysis with 3% dose and 3mm DTA criteria. The mean ± standard deviation of the percentage of pixels passed using gamma evaluation method for IMRT plans was 98.25 ± 1.35. The QA results reveals that the TPS predicated fluences and the delivery fluences were well within the clinical acceptance tolerance limits.

Discussion

This study provides a dosimetric comparison between the 2D, 2D (MLC), 3DCRT and IMRT in cervical cancer. Our data reveals that there were no major differences in the target homogeneity between the techniques, but the mean conformity index for 2D and 2D (MLC) were 7.60 and 4.63 respectively. Mean conformity index clearly illustrates the amount of normal tissue irradiated outside PTV were alarming. For example the mean conformity index of 7.60 and 4.63 associated to 660% and 363% more volume outside PTV were irritated with the prescribed dose. This demonstrates that at least using a corner shielding in the 2D using a block or MLC will significantly reduce your high dose volume. Further if you use a four field box 3DCRT technique, it will further reduce the mean CI substantially to 2.52 compare to 2D and 2D (MLC). IMRT resulted in the superior mean CI of 1.22, still the concern is the sharp dose fall may resulted in geographical miss due tumor shrinkage, inter/intra

fraction organ motion and volume deformation during radiotherapy.

The low dose volumes (V5 & V10) were higher in IMRT compared to the other techniques due to the large number of fields, whereas a substantial dose reduction in higher dose volumes (V50, V40 and V30) were observed. The mean V50 volumes for 2D, 2D MLC, 3DCRT for all the patients were 12.62, 6.47 and 3.43 times higher than IMRT, which is alarming. Interestingly, the 2D MLC plans displayed the dose reduction in lower dose volumes (V5, V10, V15 and V20) compared to the other techniques due to conformal limited number of beams. In IMRT the increase in the out of the field radiation doses can be neutralize by the decrease in the high dose volumes outside the PTV significantly [16]. For younger patients the probabilities of the radiation induced secondary malignancies are higher compared to the older patients after IMRT. At present, most of the clinical studies with shorter follow-up have not verified that probability of secondary malignancies increases with IMRT, only extensive follow-up studies with IMRT can provide as a real picture of radiation induced malignancies [15].

Locally advanced cervical cancers (Stage IIB – IVA) with a desired cumulative dose between 80 Gy - 90 Gy to point 'A' demonstrated a better overall survival and lower loco-regional failure [16]. A combination of concurrent chemo-radiotherapy followed by brachytherapy is still the standard treatment of care for locally advanced cervical carcinoma. To deliver a cumulative dose of 80Gy – 90Gy will be practically difficult if the rectum received a full prescribed dose as the target received. The rectal dose and bladder dose contribution from the external beam radiotherapy plays a definite role in the lower-gastrointestinal (GI) and gentinourinary (GU) toxicity compare to the brachytherapy. By reducing the rectum and bladder dose in the external beam radiotherapy will allow to escalate the point A dose to 80 Gy – 90 Gy by keeping the rectal dose within the tolerance limit. Mean rectal and bladder dose between the 2D, 2D (MLC) and 3DCRT plans in this study were relatively much higher than the IMRT plans, due to the geometrical location of the rectum and bladder with respect to the target. IMRT resulted in 23.8% and 26.8% decreased in the rectal and bladder dose compare to 3DCRT plans. Using traditionally old midline shielding technique partially during the external beam radiotherapy may be an option to reduce the rectal dose and bladder dose [17].

Isohashi et al [18] did a comparative clinical study of 3DCRT versus IMRT in carcinoma of cervix and found that the 3-year cumulative incidences of grade 2 or higher chronic gastrointestinal (GI) complications were significantly lower with IMRT compared to 3DCRT (3 % vs. 45 %, $p < 0.02$), where V40 were 65% higher in 3DCRT compared to IMRT. In this study the mean dose to the intestine between the IMRT and the 3DCRT were not significant, but the V40 (%) for 3DCRT and IMRT were 16.42 ± 18.07 and 8.62 ± 8.60 respectively. The V40 (%) which is a definite predictor of GI toxicity [18] is twice the value of IMRT compared to

the 3DCRT.

The hematological toxicity was reported in the patients undergoing chemotherapy and pelvic bone irradiation in treatment of cervix [19]. Surprisingly the lower doses were recorded for the left and right femoral head in the 2D (MLC) technique compared to the 2D, 3DCRT and IMRT techniques; this is due to the geometrical location of the femoral head and the limited conformal beam portals of 2D (MLC). Right and left femoral head resulted in approximately 31% lesser dose in IMRT compared to 3DCRT technique. Cauda maximum mean doses were much lower in 3DCRT compared to other techniques, due to conformal portal from the lateral beam portal spare the cauda. The mean dose to the cauda between the IMRT and the 3DCRT plans were comparable where else the 2D and 2D (MLC) resulted in the substantially higher doses due to the limited number of beam portals partially shielding the femoral heads.

Conclusion:

IMRT shows superior OAR sparing compared to 3DCRT, 2D (MLC) and 2D plans. Due to the very tight conformity of IMRT plans, it is recommended to use Image Guidance (CBCT or 2D/2D match) to ensure the targets are within the PTV volume. It is not recommended to use IMRT in Carcinoma of Cervix without Image guidance. Centers don't have IMRT / VMAT provision can at least use 4 field box technique using 15MV beams to reduce the high dose irradiation volume, which may results in lesser toxicity.

References:

1. Bray, F. , Ferlay, J. , Soerjomataram, I. , Siegel, R. L., Torre, L. A. and Jemal, A. (2018), Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, 68: 394-424. doi:10.3322/caac.21492
2. Jemal, A. , Bray, F. , Center, M. M., Ferlay, J. , Ward, E. and Forman, D. (2011), Global cancer statistics. CA: A Cancer Journal for Clinicians, 61: 69-90. doi:10.3322/caac.20107
3. Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, et al. (Eds.). *AJCC Cancer Staging Manual (8th edition).* Springer International Publishing: American Joint Commission on Cancer; 2017 [cited 2016 Dec 28].
4. *Georg P, Georg D, Hillbrand M, Kirisits C, Poetter R. Factors influencing bowel sparing in intensity modulated whole pelvic radiotherapy for gynaecological malignancies. RadiotherOncol. 2006;80:19–26.*
5. Gudipudi, G., Priore, G. D., & Alluri, K. (2014). Comparing intensity-modulated radiotherapy and conventional external beam radiotherapy in cervical cancer. *Gynecologic Oncology*, *133*, 13. doi: 10.1016/j.ygyno.2014.03.051
6. Lin, Y., Chen, K., Lu, Z., Zhao, L., Tao, Y., Ouyang, Y., & Cao, X. (2018). Intensity-modulated radiation therapy for definitive treatment of cervical cancer: a meta-analysis. *Radiation oncology (London, England)*, *13*(1), 177. doi:10.1186/s13014-018-1126-7
7. Naik, A., Gurjar, O., Gupta, K., Singh, K., Nag, P., & Bhandari, V. (2016). Comparison of dosimetric parameters and acute toxicity of intensity-modulated and three-dimensional radiotherapy in patients with cervix carcinoma: A

randomized prospective study. *Cancer/Radiothérapie*, *20*(5), 370–376. doi: 10.1016/j.canrad.2016.05.011

8. Ng, S. Y., Colborn, K. L., Cambridge, L., Hajj, C., Yang, T. J., Wu, A. J., & Goodman, K. A. (2016). Acute toxicity with intensity modulated radiotherapy versus 3-dimensional conformal radiotherapy during preoperative chemoradiation for locally advanced rectal cancer. *Radiotherapy and Oncology*, *121*(2), 252–257. doi: 10.1016/j.radonc.2016.09.010
9. Yang, B., Zhu, L., Cheng, H., Li, Q., Zhang, Y., & Zhao, Y. (2012). Dosimetric comparison of intensity modulated radiotherapy and three-dimensional conformal radiotherapy in patients with gynecologic malignancies: a systematic review and meta-analysis. *Radiation Oncology*, *7*(1), 197. doi: 10.1186/1748-717x-7-197
10. Lan, M.-L., Yu, X., Xiao, H., Zhou, P., Hu, N., Li, J., & Wang, G. (2016). Clinical outcomes and toxicity of postoperative intensity-modulated versus three-dimensional conformal radiation therapy in patients with cervical cancer. *Asia-Pacific Journal of Clinical Oncology*, *12*(4), 430–436. doi: 10.1111/ajco.12476
11. Jia, M. X., Zhang, X., Yin, C., Feng, G., Li, N., Gao, S., & Liu, D. W. (2014). Peripheral dose measurements in cervical cancer radiotherapy: a comparison of volumetric modulated arc therapy and step-and-shoot IMRT techniques. *Radiation Oncology*, *9*(1). doi: 10.1186/1748-717x-9-61
12. Hall EJ, Wuu CS: Radiation-induced second cancers: the impact of 3D-CRT and IMRT. Int J Radiat Oncol Biol Phys. 2003, 56: 83-88. 10.1016/S0360-3016(03)00073-7.
13. Ruben JD, Davis S, Evans C, Jones P, Gagliardi F, Harnes M, Hunter A: The effect of intensity-modulated radiotherapy on radiation-induced second malignancies. Int J Radiat Oncol Biol Phys. 2008, 70: 1530-1536. 10.1016/j.ijrobp.2007.08.046.
14. International Commission on Radiation Units and Measurements. Prescribing, recording, and reporting photonbeam intensity-modulated radiation therapy (IMRT): contents (ICRU Report 83). J ICRU 2010;10:NP.
15. Chargari, C., Goodman, K. A., Diallo, I., Guy, J.-B., Rancoule, C., Cosset, J.-M., … Magne, N. (2016). Risk of second cancers in the era of modern radiation therapy: does the risk/benefit analysis overcome theoretical models? *Cancer and Metastasis Reviews*, *35*(2), 277–288. doi: 10.1007/s10555-016-9616-2
16. Viswanathan, A. N., Beriwal, S., Santos, J. F. D. L., Demanes, D. J., Gaffney, D., Hansen, J., … Erickson, B. (2012). American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part II: High-dose-rate brachytherapy. *Brachytherapy*, *11*(1), 47–52. doi: 10.1016/j.brachy.2011.07.002
17. Tamaki, T. (2018). Midline Block (Central Shielding). *Brachytherapy*, 63–75. doi: 10.1007/978-981-13-0490-3_6
18. Isohashi, F., Mabuchi, S., Yoshioka, Y., Seo, Y., Suzuki, O., Tamari, K., … Ogawa, K. (2015). Intensity-modulated radiation therapy versus three-dimensional conformal radiation therapy with concurrent nedaplatin-based chemotherapy after radical hysterectomy for uterine cervical cancer: comparison of outcomes, complications, and dose-volume histogram parameters. *Radiation oncology (London, England)*, *10*, 180. doi:10.1186/s13014-015-0486-5
19. Hui, B., Zhang, Y., Shi, F., Wang, J., Wang, T., Wang, J., … Liu, Z. (2014). Association between bone marrow dosimetric parameters and acute hematologic toxicity in cervical cancer patients undergoing concurrent chemoradiotherapy: comparison of three-dimensional conformal

radiotherapy and intensity-modulated radiation therapy. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*, *24*(9), 1648–1652. doi:10.1097/IGC.0000000000000292