Journal of Radiotherapy in Practice

cambridge.org/jrp

Dosimetric comparison of 3-dimensional conformal radiotherapy (3D-CRT) and volumetric-modulated arc therapy (VMAT) in locally advanced cancer cervix

Animesh Agrawal[1], Rahat Hadi[2], Satyajeet Rath[2], Avinav Bharati[2], Madhup Rastogi[2], Rohini Khurana[2], Kamal Sahni[2], Shantanu Sapru[2], Ajeet Kumar Gandhi[2], Anoop Kumar Srivastava[2] and Surendra Prasad Mishra[2]

[1]Department of Medical Oncology, Gujarat Cancer Research Institute, Ahmedabad, India and [2]Department of Radiation Oncology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India

Original Article

Cite this article: Agrawal A, Hadi R, Rath S, Bharati A, Rastogi M, Khurana R, Sahni K, Sapru S, Gandhi AK, Srivastava AK, and Mishra SP. (2022) Dosimetric comparison of 3-dimensional conformal radiotherapy (3D-CRT) and volumetric-modulated arc therapy (VMAT) in locally advanced cancer cervix. *Journal of Radiotherapy in Practice* **21**: 60–67. doi: 10.1017/S1460396920000849

Received: 30 June 2020
Revised: 30 August 2020
Accepted: 1 September 2020
First published online: 6 October 2020

Key words:
carcinoma cervix; dosimetry; VMAT; 3D-CRT; LACC

Author for correspondence:
Rahat Hadi, Department of Radiation Oncology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India.
Tel: 8858826619.
E-mail: drrahathadi@gmail.com

Abstract

Introduction: Dosimetric advantages of volumetric-modulated arc therapy (VMAT) over three-dimensional conformal radiotherapy (3D-CRT) are not established in a head-on comparison of a uniform group of locally advanced carcinoma of the cervix (LACC). Therefore, we conducted a dosimetric comparison of these two techniques in LACC patients.

Materials and methods: Computed tomography (CT) data of histologically proven *de novo* LACC, including Stage IIB–IIIB and earlier stages deemed inoperable, were included in this prospective observational dosimetric study. Planning was initially done by 3D-CRT technique (dose of 45–50·4 Gy @ 1·8–2 Gy/# was used in the actual treatment), followed by VMAT planning and appropriate dosimetric comparisons were done in 39 cases.

Results: For planning target volume coverage, D_{95}, D_{98} and D_{100} ($p < 0{\cdot}0001$ for all parameters) and V_{95} and V_{100} ($p = 0{\cdot}002$ and $<0{\cdot}0001$, respectively) were significantly improved with VMAT. The conformity index (CI) was significantly better with VMAT ($p = 0{\cdot}03$), while 3D-CRT had a significantly better homogeneity index (HI)($p = 0{\cdot}003$). Dose to the urinary bladder was significantly reduced with VMAT compared to 3D-CRT for V_{20}–V_{50}, except V_{10}. The doses to the rectum and abdominal cavity were significantly reduced with VMAT compared to 3D-CRT plans for all parameters (V_{10}–V_{50}). The number of organs at risks (OARs) for which constraints were met was higher with VMAT plans than with 3D-CRT plans, with at least four out of the five OARs protected in 46·1 versus 5·1% and all constraints achieved in 15·4% versus none.

Conclusion: We conclude that in dosimetric terms, VMAT is superior to 3D-CRT for LACC.

Introduction

Carcinoma of the uterine cervix is a malignancy that demonstrates stark contrast between the developing and the developed world. Worldwide it is considered to be the seventh most common cancer overall and the fourth most common in females. In India, it is the second most malignancy in females, affecting more than 20 per 100,000 females.[1] Most patients present with locally advanced diseases and for such patients, concurrent chemoradiotherapy is the management of choice.[2] Conventionally radiotherapy (RT) has been delivered through a 2-field (AP-PA) or 4-field (AP-PA and two lateral) design to cover the whole pelvis for nodal disease and parametrial spread, apart from the gross disease. After 45–50 Gy has been delivered through external beam radiotherapy (EBRT), the gross disease is given a brachytherapy boost.[3] This treatment is associated with significant morbidity, especially haematological and gastrointestinal, which increases with concurrent chemotherapy. Efforts have been made to reduce the dose delivered to normal structures through intensity-modulated conformal techniques since the turn of the century, with results from Mundt et al.[4] and Mell et al.[5] suggesting that these can reduce clinically observed toxicities. Various other studies, clinical and dosimetric, have suggested that intensity-modulated radiotherapy (IMRT) can spare the OARs while delivering the same dose to target volumes with clinically discernible benefit.[6] However, a lot of this work has included a mixed population of patients, and a significant number of patients are post-operative[7] where the uterus has been removed. The later alters clinical target volume (CTV) significantly, and one cannot extrapolate the same data to patients with an intact genital tract.

VMAT is a form of IMRT that delivers treatment in arcs by delivering dose throughout the rotation of the gantry and modulating the intensity of individual beamlets therein. VMAT is an extended form of IMRT with variable dose rate, gantry speed and dynamic multileaf collimator (MLC) movement with multiple beam entry angle options.[8] VMAT

plans with faster delivery time, fewer monitor unit (MU) and superior dose distribution than conventional step-and-shoot IMRT have been reported.[9] VMAT is rapidly becoming the treatment modality of choice when IMRT is employed, given the advantages it provides over 'conventional' IMRT—treatment time (by as much as 5 times shorter)[10,11] and lower integral dose by almost 12% as compared to IMRT.[10] It came into clinical practice less than a decade ago, but has rapidly been adopted for various sites due to its advantages of shorter treatment time and in many cases, improved OAR sparing. Its ability to deliver the same treatment as IMRT in lesser time needing fewer MUs is very favourable for gynaecological malignancies.[12] However, 3-dimensional conformal radiotherapy (3D-CRT) already provides that benefit,[13] but the dosimetric advantages specifically in these cases of VMAT over 3D-CRT are not established in a head-on comparison for a uniform group of patients. Therefore, we propose to conduct a dosimetric comparison of these two techniques in patients with LACC.

Materials and Methods

This was a single institutional, prospective, observational study on patients of LACC in a tertiary cancer centre conducted from August 2015 to August 2016. The study was approved by the Institutional Ethics Committee. Patients aged 18–80, Karnofsky performance score (KPS) ≥60 with histologically proven squamous cell carcinoma of the cervix, the International Federation of Gynecology and Obstetrics (FIGO) 2009 Stage IIB–IIIB[14] and inoperable cases belonging to earlier stages, wherein 'inoperable' shall be defined as ≥1 of inoperable disease as opined by surgical oncologist and patient unfit and/or unwilling for surgery, with normal and bone marrow reserve (Haemoglobin >10 gm%, White blood cell >4000/cc, Platelet >100,000/cc), normal renal (normal KFTs) and liver (normal LFTs). Patients having Stage IV disease, positive para-aortic node, history of any other malignancy within the last 5 years, adenocarcinoma of the cervix, patient suffering from active HIV, Hepatitis B or C and pregnant and lactating women were excluded from the study. CT data of patients who fit the inclusion criteria was used for this study.

Planning was initially done by 3D-CRT technique (which was used for actual treatment), followed by VMAT planning after EBRT completion and appropriate dosimetric comparisons were done. A minimum accrual of thirty patients was planned at the initiation of the study. After a detailed history and examination, all routine blood investigations and chest X-rays were performed. Investigations like USG/CT/MRI of the abdomen and pelvis, cystoscopy, proctoscopy, bone scan and DTPA/DMSA scans for renal status were done when indicated.

Steps of RT planning

Patients were simulated in supine position with hands above the head using a 16-slice CT simulator (Siemens Somatom Sensation open, Siemens Healthineers, Forcheim, Germany). Planning CT scans were obtained from L1 (or higher if indicated) to lesser femoral trochanter with 3 mm slice acquisition and no inter-slice gap after injection of 70–100 mL of non-iodinated contrast (Siemens Somatom Sensation Open 16 slice). A bladder protocol was followed. Patients were asked to void urine followed by drinking 500 mL water over 15 minutes. Images were taken 30 minutes thereafter. No rectal protocol was specified. Patients were asked to evacuate bowel before the scan. The lowermost extent of disease was marked by a vaginal marker placed per vaginally or by placing a radiotherapy planning (RTP) marker at the skin tag between the vulva and anal verge (this along with per vaginal findings served as a surrogate for the lowermost extent of disease). Three RTP markers were placed, two lateral and one central, before simulation. These were then tattooed after the simulation to facilitate patient positioning during treatment. Images, thus, obtained were transferred to our treatment planning system (XiO Release 5·10/Monaco v3·0, Elekta AB, Stockholm, Sweden) followed by contouring.

Treatment volumes were drawn according to ICRU 50, 62 and 83 definitions.[15–17] OARs were drawn as per the Radiotherapy Oncology Group (RTOG) guidelines for organ delineation in pelvic RT. The volumes for CTV and OARs were delineated as per the details mentioned in Table 1.[18–21] Following this, planning was performed on XiO v5·10 (for 3D-CRT) and subsequently on Monaco v3·0 (for VMAT). The total dose prescribed was 45–50·4 Gy @ 1·8–2 Gy/#, 5# a week over 4·5–5·5 weeks. Appropriate dosimetric data were recorded for both planning modalities and then compared. For the PTV, homogeneity and conformity indices were also calculated (HI and CI). All patients received radical chemoradiotherapy. Treatment was performed using 3D-CRT plans. The plan evaluation criteria for both the modalities were as follows: 95% of the PTV should receive more than or equal to 95% of the prescribed dose (Figures 1a and 1b). No part of the PTV was to receive >110% of the prescribed dose for 3D-CRT. For VMAT, no volume beyond 15 mm outside the PTV was to receive >100% of the prescribed dose. It was also ensured that no volume within PTV received <93% of the prescribed dose in VMAT (Figures 2a and 2b). The dose limit to OARs was as follows: bowel (small and large): volume of abdominal cavity receiving 45 Gy to be less than 195 cc, rectum: volume of rectum receiving 45 Gy (V_{45}) had to be less than 50%, bladder: volume of bladder receiving 45 Gy (V_{45}) had to be less than 50%, femoral heads: volume receiving 30 Gy (V_{30}) not to exceed 15%. Planning was assessed slice-by-slice and also via dose–volume histograms (DVHs). For the purpose of comparisons: the dose to 95 (V_{95}) and 100% (V_{100}) of the PTV was recorded. The dose to 95, 98 and 100% (D_{95}, D_{98}, D_{100}) of the PTV volume and the maximum isodose in the PTV (I_{max}) were obtained. Homogeneity and conformity indices were calculated (HI and CI).[22] $HI = I_{max}/RI$ (where I_{max} is the maximum isodose in the target and RI is reference isodose). $CI = V_{RI}/TV$ (where V_{RI} is volume covered by reference isodose and TV is target volume). To quantify the dose distribution of OAR, percentage volumes receiving 10, 20, 30, 40, 45 and 50 Gy (V_{10}, V_{20}, V_{30}, V_{40}, V_{45} and V_{50}) and maximum dose (D_{max}) were recorded for all OARs. Statistical analysis of data obtained from each arm was done by comparing the corresponding dose–volume parameters of the 3D-CRT and VMAT plans with the paired *t*-test (SPSS v21). The level of significance was set at 0·05.

Results

Thirty-nine patients were enrolled in this study. The median age at RT registration was 57 years (range 35–78) with most patients belonging to the 50–60 years age group. Stage IIB formed the largest group of included patients (58·97%), with their disease being mostly moderately or well-differentiated SCC (58·97%). The differentiation could not be ascertained in seven patients (17·95%).

PTV coverage

At the planning objective level of V_{95}, VMAT provided a higher coverage of the PTV (99·44% versus 98·75%, $p = 0·002$) while having a

https://doi.org/10.1017/S1460396920000849 Published online by Cambridge University Press

Table 1. Table describing contouring guidelines that were followed

CTV_Nodal	Iliac nodes were drawn from the bifurcation of the aorta to the appearance of the femoral heads; common iliac nodes could be left out based on disease stage and clinician discretion. A strip at least 10 mm wide was taken to draw the obturator nodes along the pelvic walls till the superior part of the obturator foramen. Pre-sacral region was covered by connecting the volumes on each side of the pelvis with (at least) a 10 mm strip anterior to the sacrum. A margin of 1–2 cm was given to vessels and any visible nodes.
CTV_Primary	CTV primary for carcinoma cervix included volume of the primary tumour, uterine cervix, uterine corpus, bilateral parametria and vagina. In cases with minimal or no vaginal wall involvement, the contouring was stopped 10 mm above the lower border of obturator foramen. In cases with vaginal involvement, the following procedure was adopted: for upper vaginal involvement: upper two-thirds of vagina/lower border of obturator foramen, whichever was lower, for extensive vaginal involvement: entire vagina.
CTV_Total	The volumes CTV_Nodal and CTV_Primary were added.
PTV	The PTV was created by giving a 10 mm isotropic margin around the CTV_Primary and 7 mm isotropic margin around the volume CTV_Nodal.
OARs	The OARs were delineated according to the RTOG guidelines, as follows: bladder: inferiorly from its base and superiorly to the dome, rectum: beginning from 4 to 5 cm above the anal verge, moving superiorly till the rectum loses its round shape in the axial plane and connects anteriorly with the sigmoid, femoral heads (Femur_R, Femur_L): from the lowermost level of the ischial tuberosities and superiorly to the top of the ball of the femur (including the trochanters), bowel (abdominal cavity): inferiorly from the recto-sigmoid junction, superiorly till 2 cm above the superior-most point of the PTV.

narrower range (SD 0·72 versus 1·00). The isodose line covering 98% PTV volume was also recorded: 96·04 versus 97·99% for 3D-CRT versus VMAT, respectively ($p < 0·0001$). For VMAT, 17 out of the 39 cases (43·59%) were having 98% PTV coverage for 98% isodose line. Therefore, VMAT plans consistently delivered a higher dose to the PTV (Figure 3a). For PTV coverage, VMAT significantly improved D_{95}, D_{98}, D_{100} ($p < 0·0001$ for all parameters), V_{95} ($p = 0·002$) and V_{100} ($p < 0·0001$). The CI was better with VMAT ($p = 0·03$), whereas the 3D-CRT plans had a comparatively better HI ($p = 0·003$). The mean MUs delivered for 3D-CRT and VMAT were 250 + 19·01 and 776·22 + 58·42, respectively ($p < 0·0001$).

Bladder dose

The doses to the urinary bladder were lower in VMAT as compared with 3D-CRT for V_{20}, V_{30}, V_{40}, V_{45} and V_{50} (Figure 3b). The reduction in V_{10} was not statistically significant. D_{max} tends to be higher in VMAT but was statistically insignificant. For VMAT, dose received by 40, 45 and 50% of volume was more than 1·4 times less as compared to 3D-CRT. Dose constraint ($V_{45} < 50\%$) could be met in only 1 of the 3D-CRT plans; in fact, only 4 patients had bladder doses V_{45} Gy< 60%. The remaining 35 patients all had higher volumes receiving 45 Gy. In comparison, for VMAT plans, the planning objective was met in 17 of the final plans, that is, 43·6% of all patients. To summarise, the bladder doses were lower with VMAT than with 3D-CRT for nearly all recorded parameters except the V_{10} and the D_{max}. This suggests that though it struggles somewhat at the extremes, protecting the bladder through IMAT is a reasonable objective when irradiating the pelvis.

Rectum dose

The doses to the rectum were significantly reduced with VMAT compared to 3D-CRT plans for all parameters (V_{10}, V_{20}, V_{30}, V_{40}, V_{45} and V_{50}) except D_{max} which was significantly higher (Figure 3c). VMAT plans reduced the rectal dose (by up to 1·51 times) for all but one of the recorded parameters with statistically significant reductions. The constraint set for VMAT plans ($V_{45} < 50\%$) could be met in only one of the 3D-CRT plans; two other plans had rectal doses $V_{45} < 60\%$. The remaining 36 3D-CRT plans had higher volumes receiving 45 Gy. For VMAT plans, the planning objective was met in 14 of the final plans, that is, **35·90%** of all patients. Also, with bladder relative reduction in doses was higher for the higher volumes than the lower volumes, that is, greater reductions in volume were seen for doses 40 Gy or higher than lower doses. To summarise, the rectal doses were lower with VMAT than with 3D-CRT for nearly all recorded parameters except the V_{10} and the D_{max}. Both the rectum and bladder doses followed very similar patterns, which was somewhat expected given the similar anatomic relationship of the PTV to these structures.

Abdominal cavity

V_{10} actually saw an increase of 3·8% with VMAT plans, a difference that reached statistical significance ($p = 0·038$). For all subsequent dose points, VMAT plans irradiated small volumes than 3D-CRT plans. The magnitude of this reduction progressively increased from 1·1 factorial reduction for V_{10} to 10·05 times for volume receiving the full treatment dose, that is, 50 Gy. Thus the absolute reduction in doses to the abdominal cavity saw statistically significant reductions with VMAT for all recorded parameters except for the V_{10} (Figure 3 d). The VMAT plans achieved the specified constraints in 35 out of the 39 patients (89·74%); whereas, it was met in only 12 out of the 39 3D-CRT plans (30·77%). So it can be safely said that VMAT protected the abdominal cavity in over twice the number of patients.

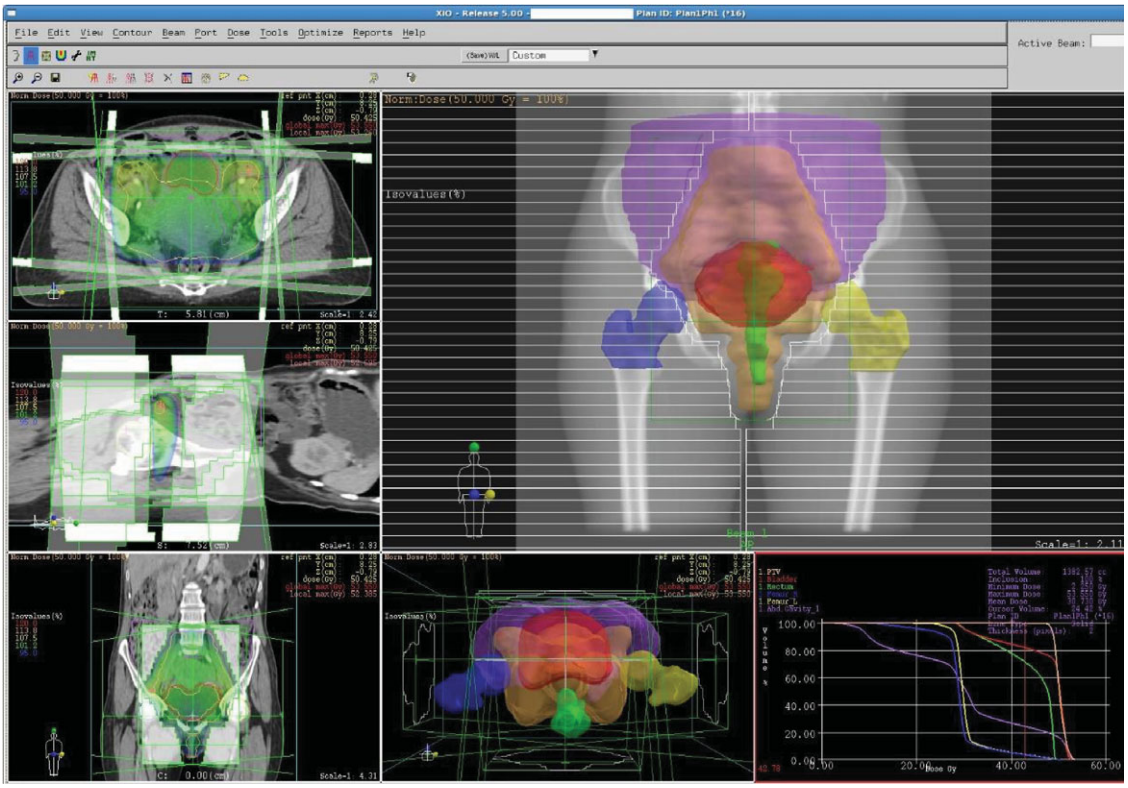
Femur dose

The volume of femoral heads was not related to the volumes irradiated to these doses. The curves for the mean doses with both femurs (Figures 3e and 3f) separated out early to be wide apart at the femoral dose constraint of 30 Gy with VMAT producing sharp falls in volumes irradiated to 20 Gy or more. With 3D-CRT the fall came with volumes irradiated to 30 Gy, but despite this fall the dose constraint was met in only 6/39 patients (15·38%) for both femora separately, they were met for bilateral femur in four of these six patients (10·26%). The femoral doses showed that they can be protected with VMAT (by over 2 times, statistically significant dose reduction for bilateral heads of the femur).

The number of OARs for which constraints were met was higher with VMAT plans than with 3D-CRT plans, with at least four out of the five OARs protected in 46·1 versus 5·1% and all constraints were achieved in 15·4% versus none, respectively. The low dose (2 and 5 Gy) volume outside the PTV was significantly higher with VMAT plans than with 3D-CRT plans. Consequently, the integral dose was on the higher side for VMAT planning as

https://doi.org/10.1017/S1460396920000849 Published online by Cambridge University Press

(a)



(b)

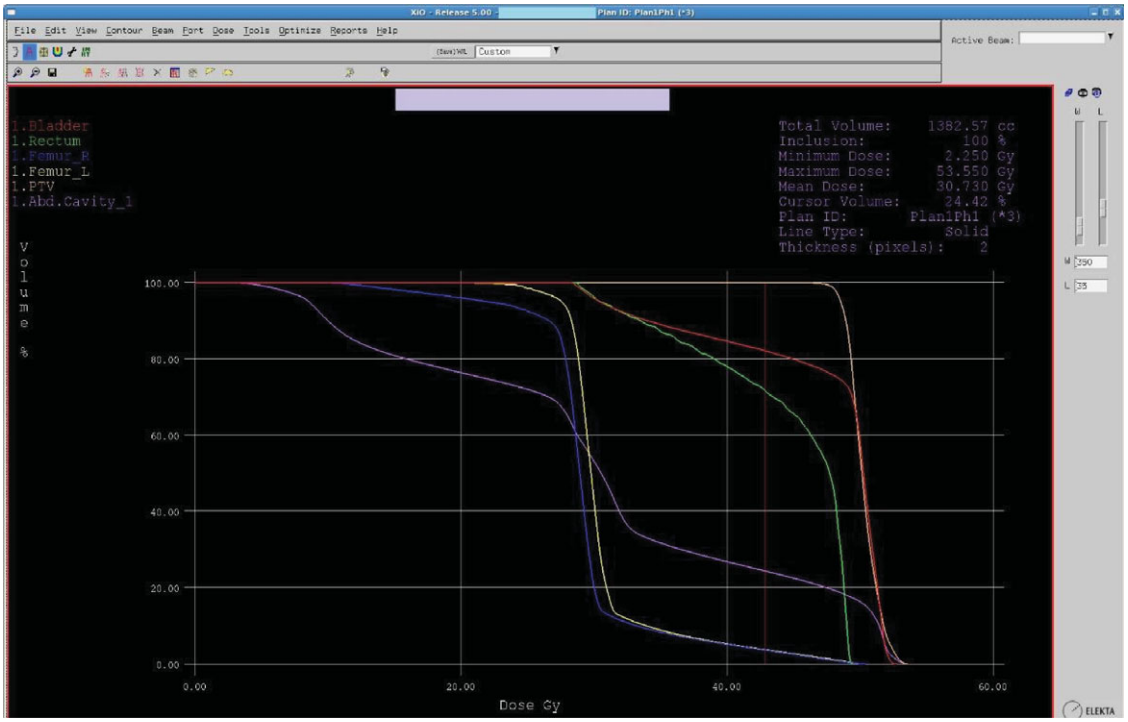
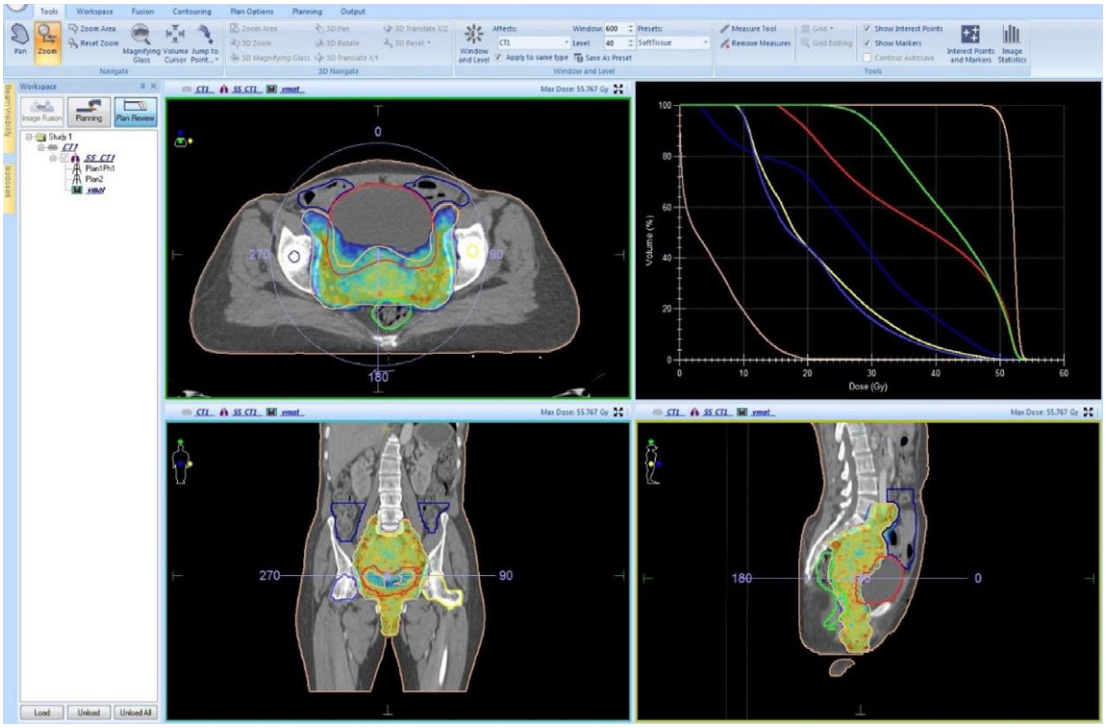


Figure 1. (a) Image above shows a typical 3D-CRT plan. A 4-field box was employed with shielding of normal structures by MLCs. The 4-field arrangement and dose distribution (95%) can be seen. (b) The DVH of the above plan. Dose was 50 Gy/25#, with 95% volume covered by 97% isodose.

compared to 3D-CRT plan. With VMAT, none of the constraints were met in 1 patient while the corresponding number for 3D-CRT plans were 19 (2·56 versus 48·72%) (Tables 2 and 3). With 3D-CRT, none of the plans were able to meet the dose constraints for all OARs versus 6 for VMAT. At least one constraint was met in just over half of all patients (51·3%) versus 38 (97·4%) for VMAT, with the median number of OARs receiving doses as per constraints being 3 for VMAT and 1 for 3D-CRT. Overall VMAT plans were better at

https://doi.org/10.1017/S1460396920000849 Published online by Cambridge University Press

(a)



(b)

DVH Statistics (Total Volume) @Elekta-PC - CT1, vmat]

Statistics | Display

Structure	Volume (cm³)	Min. Dose (Gy)	Max. Dose (Gy)	Mean Dose (Gy)	Cold Ref. (Gy)	Volume < (%)	Hot Ref. (Gy)	Volume > (%)
PTV	1199.607	30.218	55.767	52.040			**47.500**	99.84
Abd.Cavity_1	1233.927	2.423	53.210	26.328			**45.000**	7.81
Bladder	303.528	13.818	54.718	37.396			**45.000**	39.96
Femur_L	98.271	8.230	51.816	21.092			**30.000**	19.28
Femur_R	99.780	8.548	50.245	20.210			**30.000**	15.97
Rectum	59.841	20.503	54.428	42.302			**45.000**	45.30

(c)

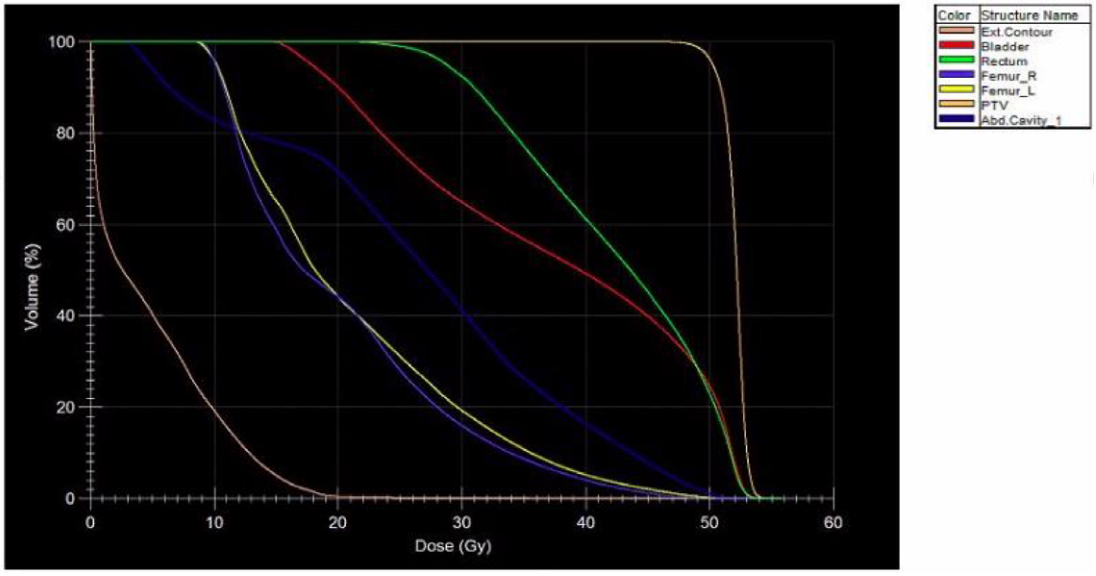


Figure 2. (a) The VMAT dose distribution for the same patient as above. The 95% isodose line can be seen as hugging to the PTV boundaries far more closely than the 3D-CRT plan. (b) The VMAT dose parameters for this patient. Constraints were met for the bladder and abdominal cavity but neither femur nor rectal constraints could be achieved. (c) DVH of the VMAT plan: OAR curves have shifted to the left compared to the 3D-CRT plan.

https://doi.org/10.1017/S1460396920000849 Published online by Cambridge University Press

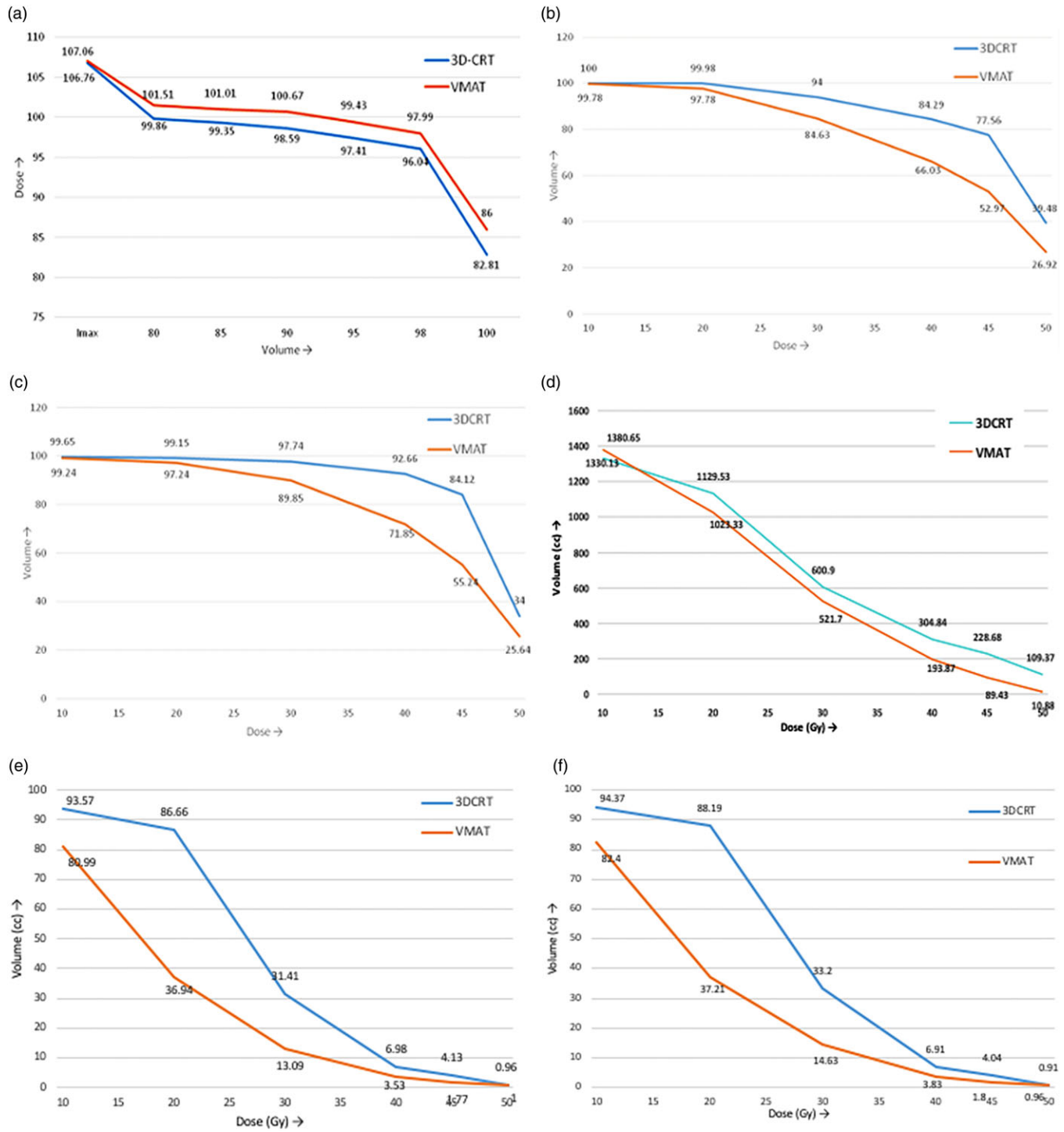


Figure 3. (a) PTV coverage, (b) dose–volume metrics for bladder: as recorded in terms of volume covering V_{10}–V_{50}, (c) dose–volume metrics for bladder: as recorded in terms of volume covering V_{10}–V_{50}, (d) dose–volume metrics for abdominal cavity: as recorded in terms of volume receiving 10–50 Gy, (e) dose–volume metrics for right femur: as recorded in terms of volume receiving 10–50 Gy, (f) dose–volume metrics for left femur: recorded in terms of volume receiving 10–50 Gy.

sparing normal structures. Compared to 3D-CRT, they improved upon most dose–volume metrics and met the specified dose constraints often.

Discussion

One of the major reasons why IMRT for gynaecological malignancies hasn't been taken up as enthusiastically as in other sites is the wide range of organ motion. The uterus and cervix aren't fixed organs within the pelvis. Lee et al.[23] working with orthogonal X-rays and fiducial markers reported inter-fraction of the cervix to a maximum of 36 mm. They used gold seeds or a uterine sleeve as fiducials. Beadle et al.[24] in 16 patients performed CT-based weekly assessment of cervical points of interest and found 2·3 and 1·3 cm superior and inferior; 1·7 and 1·8 cm anterior–posterior and 0·76 and 0·94 cm in the right and left lateral

https://doi.org/10.1017/S1460396920000849 Published online by Cambridge University Press

Table 2. Dose constraints achieved in VMAT and 3D-CRT plans

	VMAT		3D-CRT	
N–39	No. of patients	%	No. of patients	%
Abdominal cavity	35	89·74	12	30·77
Bladder	17	43·59	1	2·56
Rectum	14	35·90	1	2·56
Femur				
Right	25	64·10	6	15·38
Left	22	56·41	6	15·38
Both	22	56·41	4	10·26

Table 3. Percentages of patients for whom dose constraints were achieved

	VMAT		3D-CRT	
Number of constraints met	Number of patients (%)	Cumulative frequency (%)	Number of patients (%)	Cumulative frequency (%)
5 (All)	6 (15·38%)	6 (15·38%)	0	0
4	12 (30·77%)	18 (46·15%)	2 (5·13%)	2 (5·13%)
3	7 (17·95%)	25 (64·10%)	2 (5·13%)	4 (10·26%)
2	6 (15·38%)	31 (79·49%)	1 (2·56%)	5 (12·82%)
1	7 (17·95%)	38 (97·44%)	15 (36·42%)	20 (51·28%)
None	1 (2·56%)	39 (100%)	19 (48·72%)	39 (100%)

directions. Buchali et al.[25] in 29 cervix cancer patients took 2 CT scans, with empty and full bladder rectum, and found the median superior movement of cervix and uterus to be 4 and 7 mm, respectively. Lee et al.[26] on comparing weekly CTs with planning CT, found uterus motion to range up to 45 mm in supero-inferior direction and 28 mm in antero–posterior direction. Chan et al.[27] using the weekly cine MRIs found uterine inter-fraction motion up to 40 mm. Taylor and Powell et al.[28] performed MRI scans on 33 gynaecological cancer patients for 2 consecutive days and found mean displacement of uterine body point of interests (POIs) to be 7 mm antero-posterior and supero-inferior. The tendency of IMRT plans to deliver a low dose to large volumes has been described in the literature.[6] While this was not a study objective, we assessed it by recording the volume outside the PTV irradiated to 2 and 5 Gy, and found both to be significantly increased with VMAT by 580 cc (2%) and 1055 cc (4%). This tendency of VMAT to deliver low dose to large volumes was also seen while noting the V_{10} for abdominal cavity (mean volume of which was 1717 cc) which was higher with VMAT. Additionally, the maximum dose delivered to all structures (including PTV) was higher with VMAT plans (significantly higher for PTV, rectum; trended higher without statistical significance for bladder). Thus it delivered high doses to small (point) volumes while irradiating large volumes with low doses, suggesting that VMAT struggles at the extremes.

The doses delivered to various OARs were significantly lower for nearly all recorded parameters with VMAT. The volumes receiving 10 Gy (V_{10}) were similar for the bladder, but significantly lower for the rectum and femoral heads and significantly higher for the abdominal cavity in VMAT. V_{20}, V_{30}, V_{40} and V_{45} were all significantly lower with VMAT. V_{50} was also reduced for bladder and abdominal cavity, and similarly, for rectum and femoral heads. This was possibly due to a bias being introduced by the dose constraint introduced at that level—as this was the parameter the planning system actively attempted to reduce, and hence, it was likely to be lower. OAR sparing was most consistent in the mid-doses, that is, 20–45 Gy range, with variations at the extremes, that is, 10 and 50 Gy.

Our setup comprised of Elekta Infinity LINAC (Crawley, UK) with a maximum field size 40 x 40 cm and MLC leaf width of 1 cm at isocentre. Apart from the abdominal cavity, we found it difficult to achieve OAR constraints. The abdominal cavity was the most spared OAR with both techniques: 12 (30·77%) in 3D-CRT and 35 (89·74%) in VMAT. The bladder and rectum were most difficult to spare. This was likely due to the proximity of the OARs (bladder, rectum and abdominal cavity) to the PTV, resulting in large areas of overlapping volumes. This made it difficult to achieve all constraints while maintaining coverage of the PTV. With a smaller MLC leaf width, better sparing of OARs might have been possible, especially the bladder and rectum. The results of this study show that VMAT can significantly reduce the OAR doses while adequately covering the PTV. In fact, the PTV coverage was both higher while having a a superior CI. However, the homogeneity was lower.

The strength of this work was a homogenous study group with a small range of disease stages, so that the PTV volumes was not altered due to extent of the disease. Also, the sample size of 39 patients is a large one considering the published literature which has generally reported dosimetric studies with much fewer patients. The limitations of this study include not having delineated an ITV, so that the isotropic 1 cm margin to the CTV might be inadequate to cover internal organ motion. Also, this is a dosimetric study and correlating with clinical toxicity and disease outcomes should be done only after a clinical trial on a research-based protocol.

One of the possible limitations is the algorithm being used to calculate the dose.[29,30] The two plans were generated using two different treatment planning systems—3D-CRT with XIO and VMAT with Monaco. XiO uses a superposition/convolution based algorithm while Monaco uses the Monte Carlo algorithm for dose calculation. The fundamental difference between these algorithms is in the way they incorporate the role of inhomogeneities in the path of the photon/electrons. Depending on the specific algorithm used, dose distribution differences have been demonstrated, ranging from very similar to overestimation by as much as 40%. While both these algorithms are standardised and in routine use, the inherent differences in their calculations might be responsible for some of the differences seen (or missed). The strengths of this study include a homogenous population of cervical cancer patients. While the protocol allowed for early-stage disease, all included patients belonged to the International Federation of Gynecology and Obstetrics (FIGO) Stage IIB–IIIB and those with para-aortic adenopathy were excluded. This enabled us to have uniform CTVs that did not vary significantly with the stage. We also excluded post-operative patients. The number of patients enrolled for similar previous dosimetric studies has typically ranged from about 20 to less than 10; this enabled us to detect small differences that might have otherwise been missed.

To summarise, there are limitations that preclude the widespread implementation of VMAT. Patient immobilisation is essential for daily reproducibility. Variations in daily bladder filling and bowel distention throughout the treatment are important and

https://doi.org/10.1017/S1460396920000849 Published online by Cambridge University Press

reconciling these variations with CTVs and patient setup remains a challenge. Studies investigating the effects of internal organ motion, both CTV and OAR, will be required to help generate consensus on the delineation of VMAT volumes, so that the use of this technique can be maximised while keeping the long-term effects of low doses in mind. The treatment of carcinoma cervix by RT entails significant toxicity. We conclude that compared to 3D-CRT, VMAT as an attempt to reduce this morbidity is a feasible approach. Large-scale clinical studies with a higher number of cases are needed to validate this approach both in terms of outcomes and toxicities to incorporate this approach into common clinical practice.

Conclusion

We conclude that in dosimetric terms, VMAT is superior to 3D-CRT for EBRT of locally advanced cervical cancers.

Acknowledgements. None.

Funding. None.

Disclosure. The authors declare no conflict of interest.

References

1. Ferlay J, Soerjomataram I, Dikshit R et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136 (5): E359–E386.
2. Nandakumar A, Anantha N, Venugopal TC. Incidence, mortality and survival in cancer of the cervix in Bangalore, India. Br J Cancer 1995; 71 (6): 1348–1352.
3. Peters W A 3rd, Liu P Y, Barrett RJ 2nd et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol 2000; 18 (8): 1606–1613.
4. Mundt A J, Mell L K, Roeske J C. Preliminary analysis of chronic gastrointestinal toxicity in gynecology patients treated with intensity-modulated whole pelvic radiation therapy. Int J Radiat Oncol Biol Phys 2003; 56: 1354–1360.
5. Mell L K, Tiryaki H, Ahn K H et al. Dosimetric comparison of bone marrow-sparing intensity-modulated radiotherapy versus conventional techniques for treatment of cervical cancer. Int J Radiat Oncol Biol Phys 2008; 71:1504–1510.
6. Teoh M, Clark C H, Wood K et al. Volumetric modulated arc therapy: a review of current literature and clinical use in practice. Br J Radiol 2011; 84 (1007): 967–996.
7. Lukovic J, Patil N, D'souza D et al. Intensity-modulated radiation therapy versus 3D conformal radiotherapy for postoperative gynecologic cancer: are they covering the same planning target volume? Cureus 2016; 8 (1): e467.
8. Otto K. Volumetric modulated arc therapy: IMRT in a single gantry arc. Med Phys 2008; 35:310–317.
9. Palma D, Vollans E, James K et al. Volumetric modulated arc therapy for delivery of prostate radiotherapy: comparison with intensity- modulated radiotherapy and three-dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 2008; 72 (4): 996–1001.
10. Richetti A, Fogliata A, Clivio A et al. Neoadjuvant chemoradiation of rectal cancer with volumetric modulated arc therapy: summary of technical and dosimetric features and early clinical experience. Radiat Oncol 2010; 5:14.
11. Cozzi L, Dinshaw K A, Shrivastava S K et al. A treatment planning study comparing volumetric arc modulation with RapidArc and fixed field IMRT for cervix uteri radiotherapy. Radiother Oncol 2008; 89 (2): 180–191.
12. Teoh M, Clark C H, Wood K et al. Volumetric modulated arc therapy: a review of current literature and clinical use in practice. Br J Radiol 2011; 84:967–996.
13. Yang B, Zhu L, Cheng H et al. Dosimetric comparison of intensity modulated radiotherapy and three-dimensional conformal radiotherapy in patients with gynecologic malignancies: a systematic review and meta-analysis. Radiat Oncol 2012; 7:197.
14. Pecorelli S, Zigliani L, Odicino F. Revised FIGO staging for carcinoma of the cervix. Int J Gynaecol Obstet 2009; 105 (2): 107–108.
15. International Commission on Radiation Units and Measurements. Report 50: Prescribing, Recording, and Reporting Photon Beam Therapy. Bethesda, MD: International Commission on Radiation Units and Measurements, 1993.
16. International Commission on Radiation Units and Measurements. Report 62: Prescribing, Recording, and Reporting Photon Beam Therapy (Supplement to ICRU Report 50). Bethesda, MD: International Commission on Radiation Units and Measurements, 1999.
17. ICRU. Report 83: prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy (IMRT). J ICRU 2010; 10 (1): 1–106.
18. Taylor A, Rockall A G, Reznek R H et al. Mapping pelvic lymph nodes: guidelines for delineation in intensity-modulated radiotherapy. Int J Rad Onc Biol Phys 2005; 63 (5): 1604–1612.
19. Lim K, Small W, Portelance L et al. Consensus guidelines for delineation of clinicaltarget volume for intensity-modulated pelvic radiotherapy for the definitive treatment of cervix cancer. Int J Rad Onc Biol Phys 2011; 79 (2): 348–355.
20. Bansal A, Patel F D, Rai B et al. Literature review with PGI guidelines for delineation of clinical target volume for intact carcinoma cervix. J Can Res Ther 2013; 9 (4): 574–582.
21. Small W, Mell L K, Anderson P et al. Consensus guidelines for the delineation of the clinical target volume for intensity modulated pelvic radiotherapy in the postoperative treatment of endometrial and cervical cancer. Int J Rad Oncol, Biol, Phys 2008; 71 (2): 428–434.
22. Feuvret L, Noël G, Mazeron J J et al. Conformity index: a review. Int J Radiat Oncol Biol Phys 2006; 64 (2): 333–342.
23. Lee J E, Han Y, Huh S J et al. Interfractional variation of uterine position during radical RT: weekly CT evaluation. Gynecol Oncol 2007; 104: 145–151.
24. Beadle B, Jhingran A, Salehpour M et al. Cervix regression and motion during the course of external beam chemoradiation for cervical cancer. Int J Radiat Onc Biol Phys 2009; 73 (1): 235–241.
25. Buchali A, Koswig S, Dinges S et al. Impact of the filling status of the bladder and rectum on their integral dose distribution and the movement of the uterus in the treatment planning of gynaecological cancer. Radiother Oncol 1999; 52: 29–34.
26. Lee C M, Shrieve D C, Gaffney D K. Rapid involution and mobility of carcinoma of the cervix. Int J Radiat Oncol Biol Phys 2004; 58:625–630.
27. Chan P, Dinniwell R, Haider MA et al. Inter- and intrafractional tumor and organ movement in patients with cervical cancer undergoing radiotherapy: a cinematic-MRI point-of-interest study. Int J Radiat Oncol Biol Phys 2008; 70: 1507–1515.
28. Taylor A, Powell M E. An assessment of interfractional uterine and cervical motion: implications for radiotherapy target volume definition Ingynaecological cancer. Radiother Oncol 2008; 88: 250–257.
29. Chen W-Z, Xiao Y, Li J. Impact of dose calculation algorithm on radiation therapy. World J Radiol 2014; 6 (11): 874–880.
30. Rana S. Intensity modulated radiation therapy versus volumetric intensity modulated arc therapy. J Med Rad Sci 2013; 60 (3): 81–83.

https://doi.org/10.1017/S1460396920000849 Published online by Cambridge University Press