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ORIGINAL ARTICLE **OPEN ACCESS**

Dosimetric study of volumetric-modulated arc radiotherapy optimization in patients with cervical cancer: a comparison with intensity-modulated radiotherapy optimization technique

Neha Yadav[1], Manisha Singh[1], S.P. Mishra[2], Shanawaz Ansari[3]
[1]Department of Applied Physics, Amity School of Engineering & Technology, Amity University Madhya Pradesh, Gwalior, 474005 India
[2]Department of Radiation Oncology, Dr. RMLIMS, Lucknow, 226010 India
[3]Department of Radiotherapy, Apollo Hospitals, Bilaspur Chhattisgarh, 495006 India
Corresponding Email: nehadav51990@gmail.com

ABSTRACT
Volumetric modulated arc therapy (VMAT) or Rapid Arc therapy, a complex form of intensity modulated radiation therapy (IMRT) optimization, is now widely used to treat the cancer patients. The aim of this study was to compare volumetric-modulated arc therapy (RapidArc) plans with conventional intensity-modulated radiation therapy (IMRT) plans in cervical cancer. Twenty patients with cervical cancer previously treated with IMRT in our institution were selected for the analysis and original plans were subsequently re-optimized using the VMAT technique. Plans were generated with dose prescription 5040 cGy in 28 fractions. Inverse planning was done by Eclipse (Varian Medical Systems) treatment planning system for 6MV photon beams from computed tomography data. Dual arcs were used for VMAT plans. The quality of treatment plans was evaluated by calculating standard mean deviations, conformity index (CI), homogeneity index (HI), coverage and monitor units (MU) for each plan. The VMAT and IMRT techniques achieved highly conformal treatment plans in the case of cervical cancer patients. VMAT has the advantage of re-optimizing and small arcs of variable parameters in dose delivery, taking into account the maximum speed of gantry and MLCs. It provided a better OARs sparing and significant reductions of MU and treatment time per fraction.
Keywords: Intensity-modulated radiation therapy; Volumetric-modulated arc therapy; Cervical cancer; Dosimetry

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INTRODUCTION

Cervical cancer is the second most common type of cancer in female worldwide, after breast cancer. Radiotherapy plays a vital role in the treatment of cervical cancer [1-3].In modern radiotherapy, many advance technology have been introduced like three dimensional conformal radiotherapy (3DCRT), and intensity modulated radiation therapy (IMRT) in the cancer treatment. According to several studies, IMRT appears of producing conformal dose distribution and reduce the radiation dose to surrounding normal tissues and vital organs as compared with 3DCRT technique for the treatment of various cancers [4-8]. IMRT is a treatment delivery technique based on inverse planning optimization to modulate intensity beams by using multileaf collimator (MLC). During radiation delivery, the leaves are adjusted while the beam is on. IMRT allows the possibility of producing concave dose distributions and providing specific sparing of normal tissue [9]. Although there are significant benefits of using IMRT, disadvantage also exist. This technique has usually requires multiple fixed gantry angle beams, and it may cost of increased treatment time and also greater discomfort in patients. Moreover, a large volume of normal tissue receiving low radiation dose, this rises a greater concern of secondary radiation induced malignancies [10],which is of particular relevance to young patients or those with long future life expectancies.
VMAT is the extension of the principle of intensity modulated arc therapy proposed by Yu in 1995 [11].It is radiation delivery technique which involves simultaneous rotational movement of the gantry of linear accelerator along with movement of the multi-leaf collimator (MLC) leaves to produce fluence modulation while beam is on [12]. The ability of the VMAT technique to synchronize dose rate, gantry speed, and MLC motion during radiation beam-on. With this capability of delivering a highly conformal dose distribution within a short time interval, VMAT has been widely accepted by the radiotherapy community[13].Details of the VMAT process and quality assurance are detailed in several publications [17-18].Many authors have conducted a study on IMRT but Otto *et al*[17] and Palma *et al*.[18] reported that VMAT technique

generates superior target coverage and provides superior organs at risk (OARs) sparing in comparison to IMRT. VMAT is more efficient in treatment delivery as it reduces number of monitor units (MUs) and requires less beam on time [19-21]. Rao *et al*. [22] compared volumetric modulated arc therapy (VMAT) with fixed field IMRT. They reported that VMAT time varied from 2.1 to 4.6 min, IMRT treatment varied from 7.9 to 11.1 min, and tomotherapy time varied from 4 to 7 min. Zhai *et al* [23] found that there were no significant differences in the volume of irradiated OARs (small bowel, rectum, and bladder) between IMRT and VMAT plans, whereas Cozzi *et al* [24] found that irradiated volumes of the rectum, bladder, and small bowel were decreased statistically significantly in VMAT plans. Due to differential design methods and small sample sizes, results from these studies are inconsistent.
Intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) are two of the main treatment techniques for cervical cancer. Whether either technique significantly reduces irradiated volumes of organs at risk (OARs) remains controversial. The aim of this study was to explore which of these treatment technique is the superior technique in cervical treatment, taking clinical outcomes and treatment efficiency from published findings into consideration.

MATERIAL AND METHODS

Patient selection

We selected twenty patients with postoperative cervical cancer with ages 37-70 (Average 53.5) years. The patients had already received radical treatment using IMRT technique in our institution. Patients treated between 2017 and 2019 were included, specially ten patients had a clinical stage of T2 stage, and ten had a T3 stage.

CT Simulation

All twenty patients were immobilized in supine position with the help of thermoplastic cast and knee rest. Patients had undergone computed tomography (CT) simulation using a Toshiba Alexion 16 multi- slice CT scanner. CT scans were acquired with 3 mm slice thickness covering from L2 to the proximal half of the femur's diaphysis and scanning voltage of 140KV. Patients were scanned with full bladder as per the departmental protocol. After the simulation, the CT images were transferred into the Eclipse treatment planning system (V 11.0.31).

Target and organs at risk delineation

The clinical target volume (CTV) was delineated on CT images according to the Radiation Therapy Oncology Group (RTOG) guidelines. The planning target volume (PTV) was created by using a uniform 5mm margin of the CTV. OARs such as bladder, rectum, bowel beg, bilateral femoral head, bone marrow and other normal tissues were also contoured.

Planning Technique

9-fields IMRT planning for cervical cancer patients

Nine equally spaced coplanar fields were used for IMRT plans. Planning was carried out using the departmental IMRT protocol in the eclipse (version 11.0.31) treatment planning system (TPS). All patients were treated on Clinac iX (Varian Medical Systems, Palo Alto, USA) linear accelerators, which is capable of delivering IMRT and VMAT. The progressive resolution optimizer (V 11.0.30) algorithm was used for optimization and anisotropic analytical algorithm (V 11.0.31) with grid size0.25 cm was used for photon dose calculation for all plans. All plans were generated with single energy 6MV with dose rate 600MU/min. The gantry angles of each field were 0°, 40°, 80°, 120°, 160°, 200°, 240°, 280° and 320°, (***Figure 1***). The prescription dose was 50.4 Gy in 28 fractions (daily dose of 1.8 Gy). All 9F-IMRT plans were normalized to cover 95% of the planning target volume (PTV) with 98% of the prescription dose(PD) and not to exceed 110% as maximum dose.

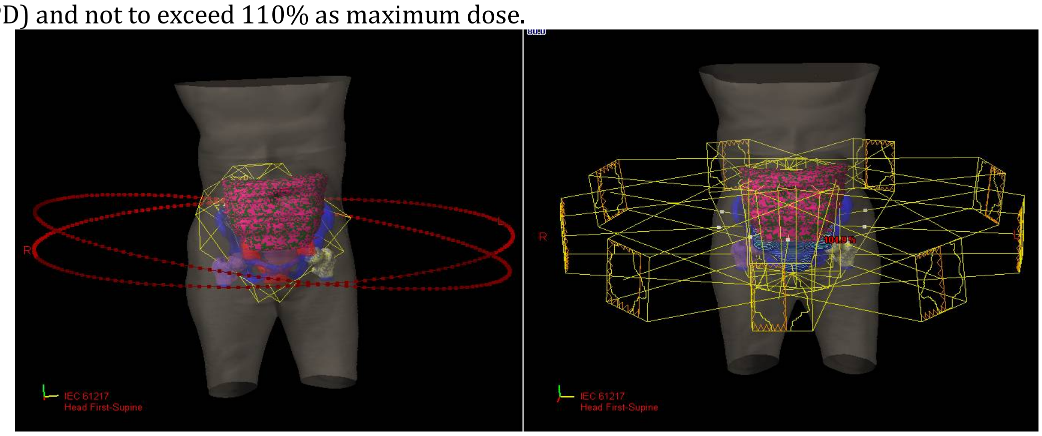

Figure 1. Beam Angles representation of dual arcs VMAT and 9 *fields* IMRT Technique

VMAT planning for cervical cancer patients

Twenty patients reported with cervical cancer previously treated with IMRT in our institution were selected for this study. The original plans were subsequently re-optimized using the VMAT technique. The prescription dose for the VMAT plans was the same as the 9F-IMRT plans (50.4 Gy in 28 fractions). Dual arcs were used for all the VMAT plans. The first arc was clockwise rotation with gantry angle 181° to 179° and collimation angle 30°. The second arc was counter clockwise rotation with gantry angle 179° to 181°and collimation angle 330° (Figure 1). All VMAT plans were normalized to cover 95% of the planning target volume (PTV) with 98% of the prescription dose (PD) and not to exceed 110% as maximum dose same as IMRT protocol.

Dosimetric comparison and plan evaluation

The quality of treatment plans was evaluated by calculating standard deviations (SD), conformity index (CI), homogeneity index (HI), coverage and monitor units (MU) for each plan. Cumulative dose volume histogram generated by TPS was used to evaluate dosimetric parameters. The PTV coverage were evaluated by calculating $V_{95\%}$ (PTV volume receiving 95% of PD), mean dose, CI, HI and standard mean deviation. Bladder, rectum, bowel beg, bone marrow and femoral heads were evaluated for mean dose, maximum dose and minimum dose.

The conformity index (CI) and homogeneity index (HI) were calculated by using following formulae

CI (for 98% of PD) = Volume receiving 98% of PD/PTV

$HI = D_{5\%}/D_{95\%}$

Where $D_{5\%}$ and $D_{95\%}$are the dose to 5% and 95% PTV volumes respectively.

Results

Quality of IMRT and VMAT plans interms of PTV coverage, HI, CI, GM and SD is analyzed and compared in this study. The results of dosimetric comparison between 9F-IMRT and dual arcs VMAT plans are shown in Table 1 and in Figures 3, 4, 5, 6, 7, 8. It was found that, there was no significant difference in HI values for PTV between the VMAT and 9F-IMRT plan (p=0.124699) however the CI was significantly higher for VMAT plans (p=0.000059).

Table 1. Minimum, Mean and Maximum Doses of IMRT and VMAT Plans

Dosimetric parameters	**IMRT Plans (in cGy) Average of 20 plans**	**VMAT Plans (in cGy) Average of 20 plans**	**t-value**	***p*- value**
PTV				
Dmax	5350.45	5540.50		
Dmean	5037.04	5096.15	-3.17625	0.001479
Dmin	4349.20	4427.18		
Bladder				
Dmax	4974.99	4964.01	0.60643	0.273919 NS
Dmean	3668.09	342	2.45416	0.009408
Dmin	2166	2078.5	0.58568	0.280778 NS
Rectum				
Dmax	4832.23	4871.04	-0.64973	0.259889 NS
Dmean	3540.02	3302.60	1.76734	0.042601
Dmin	1455.4	974.01	1.60303	0.058605 NS
Right Femur				
Dmax	47.41	49.20	-3.14501	0.00161
Dmean	19.24	15.48	2.95056	0.002703
Left Femur				
Dmax	47.41	48.48	-1.82038	0.038292
Dmean	18.96	15.54	2.95796	0.002651
Bowel Beg				
Dmean	1837.00	1848.03	-0.10546	0.458284 *P<0.5 NS*
Bone Marrow				
Dmean	3178.03	3064.76	2.52985	0.007839

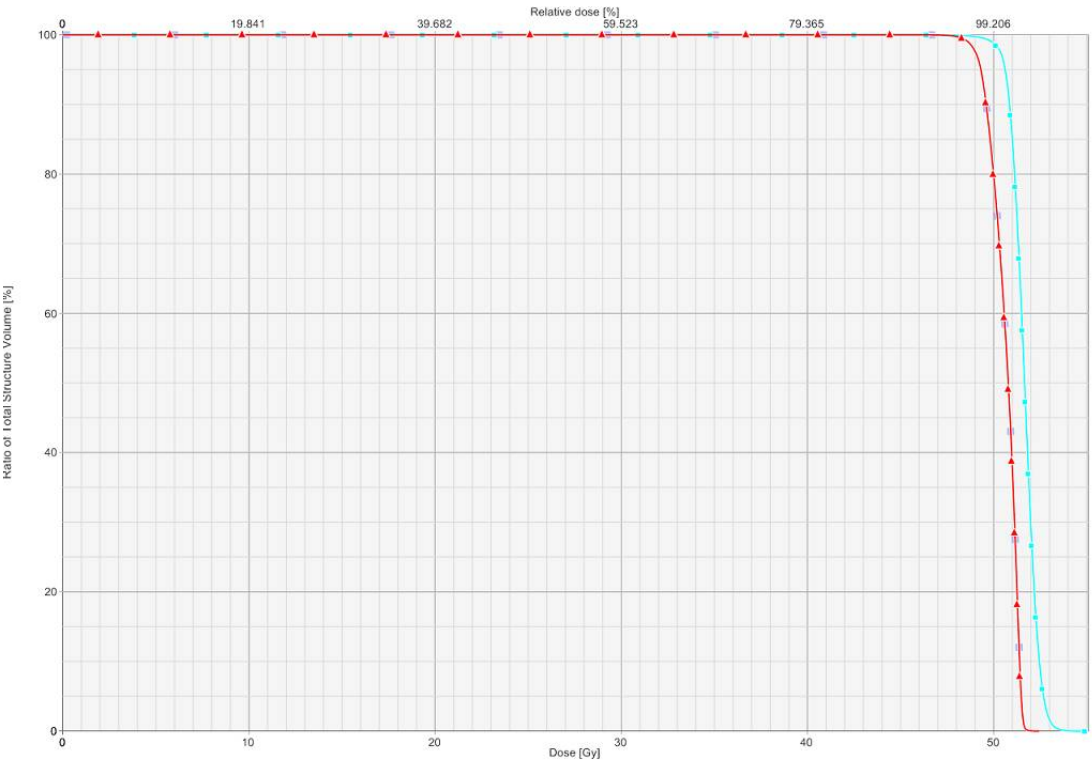

Figure3. Displaying the differences of PTV- DVH between 9F-IMRT and VMAT

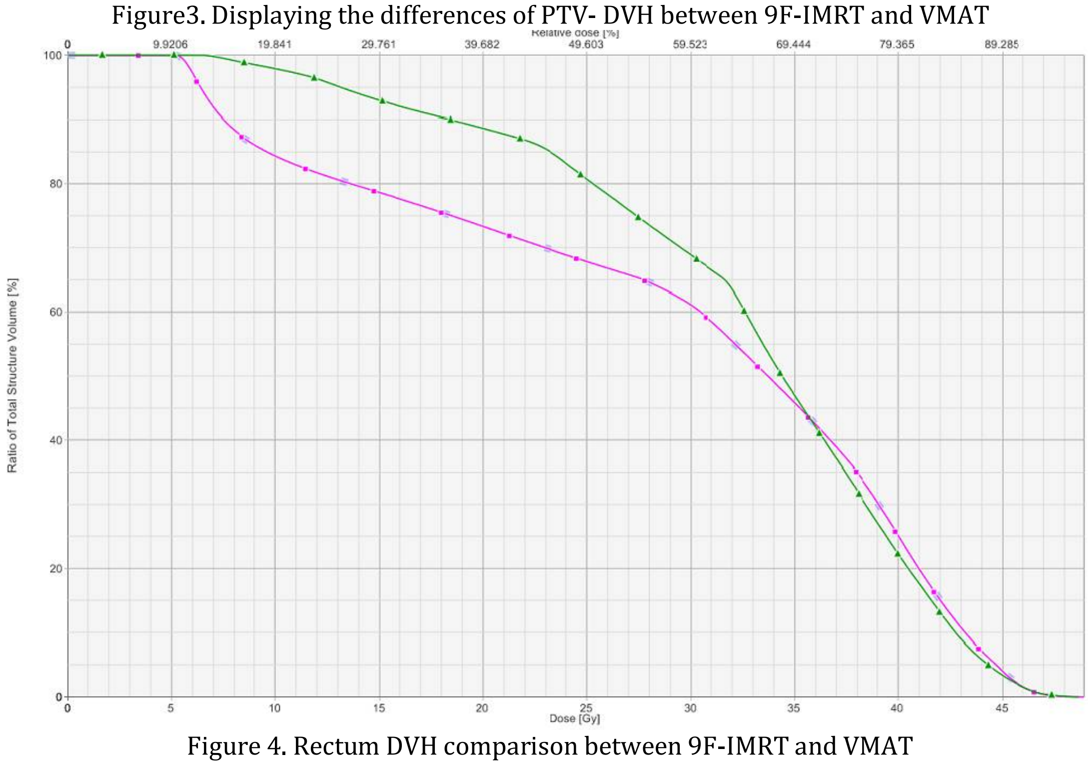

Figure 4. Rectum DVH comparison between 9F-IMRT and VMAT

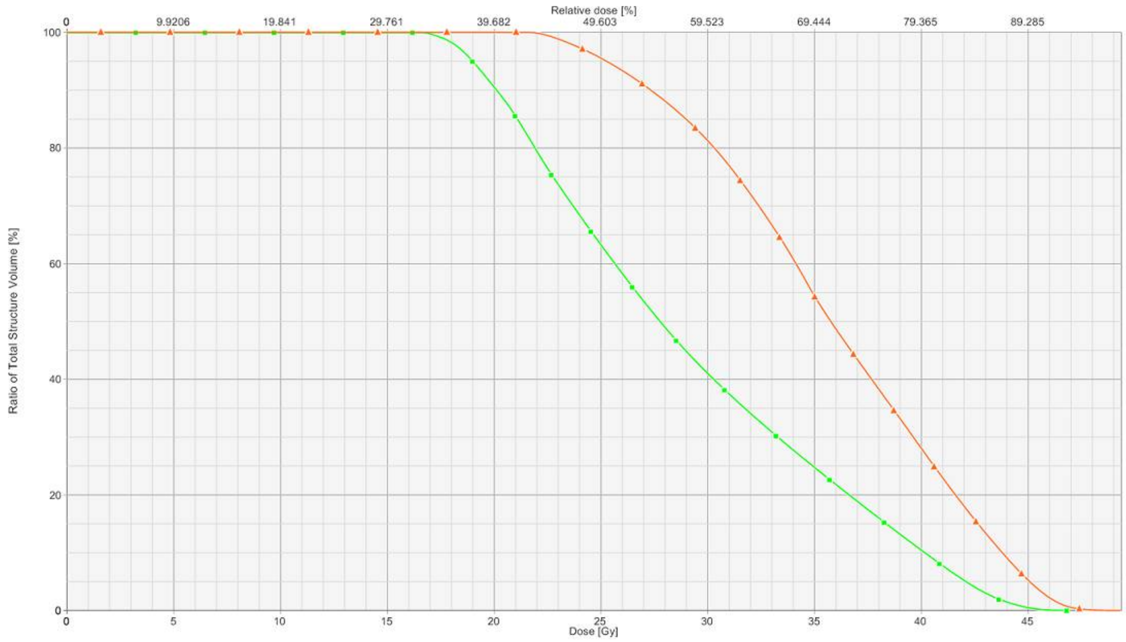

Figure5. Bladder DVH comparison between 9F IMRT and VMAT

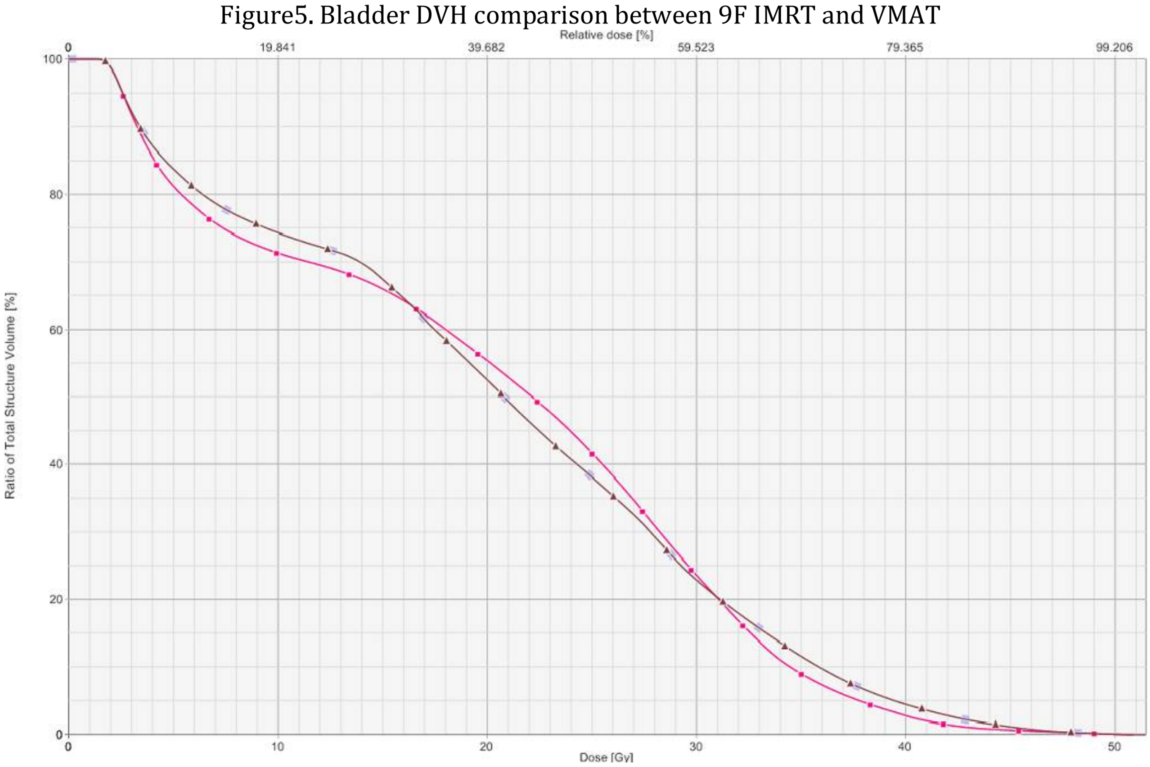

Figure6. Bowel DVH comparison between 9F IMRT and VMAT

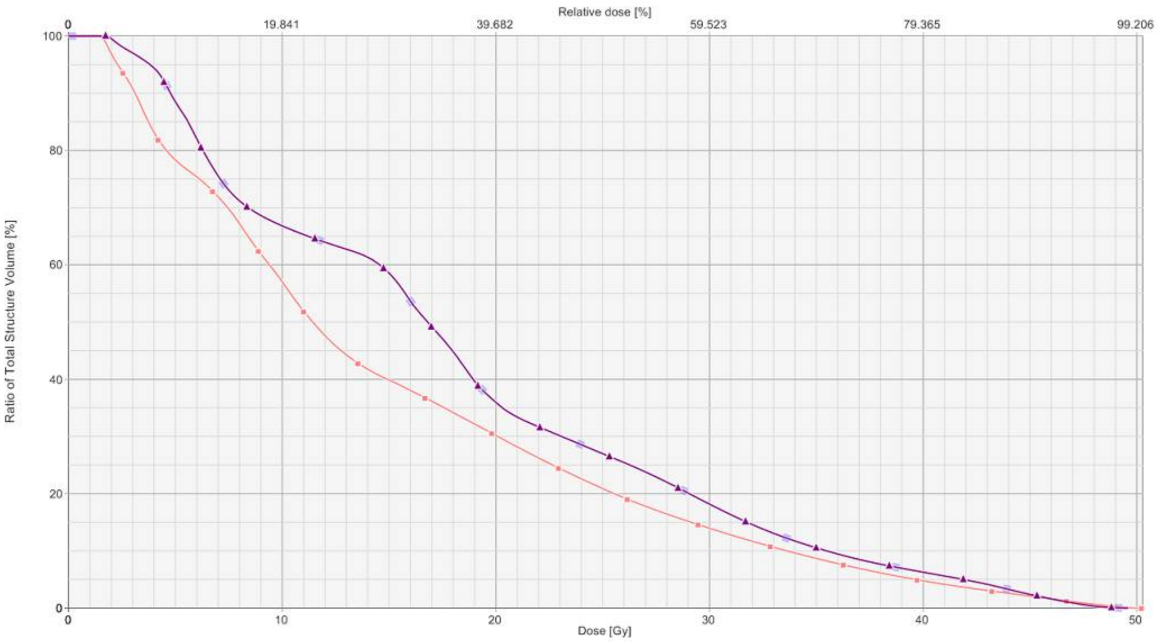

Figure7. Right Femur DVH comparison between 9F IMRT and VMAT

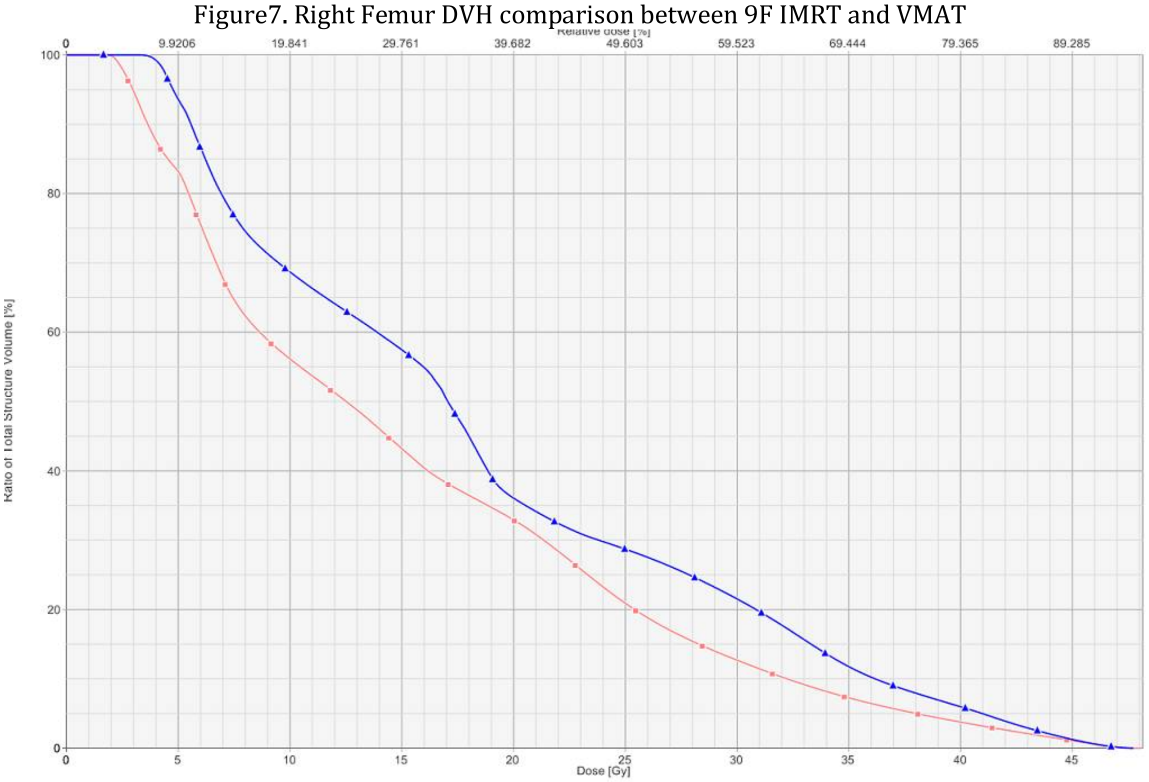

Figure8. Left Femur DVH comparison between 9F IMRT and VMAT

Table2. Average, t-value and *p*-value of dosimetric indices of 9F-IMRT and VMAT plans for cervical cancer patients

	IMRT	VMAT	t-value	*p*-value
CI	0.55	0.737	-4.2918	0.000059
HI	0.9719	0.978	-1.16972	0.124699
GM	5.1175	4.183	4.48284	0.000033
SD	1.53	1.98	-4.43398	0.000038
Coverage ($V_{95\%}$)	98.12	98.59	-2.38837	0.0109
MUs	1430	424	14.53987	0.00001

DISCUSSION

Earlier in radiotherapy, cervical cancer patients were treated with 2-dimensional whole pelvic radiation therapy (WPRT), which is associated with severe side effects. In recent years, with the continued improvement of radiotherapy technology, 3-dimensional conformal radiotherapy (3D-CRT) and fixed-field intensity-modulated radiotherapy (IMRT) have been extensively applied in the treatment of cervical cancer [25-26]. IMRT has been demonstrated to provide the superiorities over 3DCRT technology because the dose distribution is more justifiable and also IMRT has the ability to reduce the radiation dose to the normal tissues at risk, including the kidneys, femoral heads, rectum, bladder, and small intestine. After that, IMRT uses a large number of MU per treatment, which leads to greater scatter dose to normal tissues and this rises great concern about an increased risk of induction of secondary malignancy. Consequently, it can alleviate adverse reactions, thus improving the radiotherapy efficacy for cervical cancer. Huang ***et al***. [28] evaluated the dose distribution between VMAT and 7F-IMRT in 13 cervical cancer patients and found that VMAT regimen showed marked advantages over 7-IMRT in terms of target region dose homogeneity and protection of endangered organs. Meanwhile, Nguyen ***et al***. [29] also found that, compared with a conventional IMRT regimen, VMAT could achieve a highly conformal target region dose distribution and greater protection of normal tissues. Osborne ***et al***. [30] reported that using extended-field radiation therapy for patients with cervical cancer with PALN metastasis improved patient's condition in concurrence with advances in treatment. Portelance ***et al***. [31] reported that, compared with 3D-CRT, IMRT reduces small bowel, rectum, and bladder doses in patients with cervical cancer receiving pelvic and para-aortic irradiation. However, there is no research or report that compares IMRT and VMAT treatment plans for cervical cancer patients with PALN metastasis.

This study compared the dosimetric difference and the dosimetric parameters in 20 cervical cancer patients between 9F-IMRT and VMAT plans. The results in the current study indicate that the target region doses in both regimens can satisfy the dosimetric requirement. In terms of the target homogeneity and CI, the VMAT plan was superior to the 9F-IMRT plan, and the calculated treatment time of the 9F-IMRT was longer than that of the VMAT plan. VMAT can reduce the patient's discomfort caused by maintaining the same posture for a long time, reduce the errors caused by the body position during the treatment, and improve the accuracy of the treatment. The 9F-IMRT plans are delivered with the static IMRT technique, which needs more time to rotate the gantry and to move the MLCs between each beam-on [32]. The 9F-IMRT plan has a disadvantage of relatively longer treatment times compared to VMAT.

CONCLUSION

The VMAT plan is more accurate and safely be delivered radiation dose to planning target volume (PTV) as compared to9F-IMRT plan. VMAT can better protect OARs like rectum, bladder, and femoral heads. VMAT plans, reducing normal tissues irradiated volume and reducing toxicity as one of IMRT disadvantages is the presence of secondary malignancies due to large irradiated volume with low doses during treatment.Also VMAT has advantage of re-optimizing and small arcs of variable parameters in dose delivery, taking into account the maximum gantry speed and MLCs. In addition, VMAT contributes to reducing the exposure time and lowering the number of errors induced by position and organ movement during radiation treatment of the patients.. Therefore, the VMAT plans are dosimetrically superior radiotherapy technique to 9F-IMRT plans in the radiotherapy treatment for cervical cancer patients.

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