Technical Note

Evaluation of Healthy Tissue Dose at Different Regions between Volumetric-Modulated Arc Therapy and Intensity-Modulated Radiation Therapy Plans in the Treatment of Various Cancers

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Abstract

Background: Radiotherapy plays an important role in the management of cancer. Although the improved technologies increase therapeutic index, different delivery techniques deliver different dose pattern to the healthy tissue within and outside treatment volume. **Objective:** The objective of this study was to evaluate the low, intermediate, and high dose to healthy tissue within and outside the treatment volume and to find the relation between tumor volume and various doses received healthy tissue volume. **Materials and Methods:** A total of 150 patients were included. For all patients, planning computed tomography images were acquired. Tumors, critical structures, and healthy tissue volumes at different regions were delineated. Two sets of plans, one with volumetric-modulated arc therapy and another with intensity-modulated radiation therapy (IMRT) were created, optimized for 6 MV photons and dose was calculated. Dosimetry results for tumor, organs at risks (OARs), and healthy tissue from both the techniques were evaluated and compared. **Results:** Tumor coverage and dose to OARs was significantly better with volumetric-modulated arc therapy (VMAT). Volume of healthy tissue received high-dose within the treatment volume as well as volume of healthy tissue received low and intermediate-dose out of treatment volume were significantly ($P < 0.002$) lesser with VMAT. Besides, the results showed that as the tumor volume increased, the various dose received healthy tissue volume also increased. **Conclusions:** VMAT plan can reduce the risk of secondary malignancy while treating different sites of cancer. VMAT is the most appropriate technique than IMRT, especially in the treatment of large tumor volume. Special attention has to be given, especially while treating women and children.

Keywords: Healthy tissue, intensity-modulated radiation therapy, secondary cancer, target volume, volumetric-modulated arc therapy

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Introduction

Cancer is a significant cause of mortality in India, and globally as well.[1] Although other treatment modalities such as radiotherapy, chemotherapy, and surgery have been used, radiotherapy has played an important role in the treatment of cancer.[1] The capabilities of the principal radiotherapy modality have steadily progressed over the past two decades, i.e., image-based treatment planning with various delivery techniques such as three-dimensional conformal radiation therapy, intensity-modulated radiation therapy (IMRT), and volumetric-modulated arc therapy (VMAT) (RapidArc)[2] for the treatment of cancers.

IMRT is a sophisticated technique that uses multiple radiation beams to modulate dose intensity and permits the delivery of a highly sculpted dose to the tumor region. This technique helps to deliver the dose to tumor with high conformity as well as sparing of the adjacent organs to a higher level, thereby minimizing toxicities and widening the therapeutic index.[3]

Otto[4] proposed VMAT, a new form of intensity-modulated arc therapy optimization where treatment is delivered in a single intensity-modulated arc. With VMAT, three dynamic parameters – dose rate, beam aperture shape (multileaf collimator), and the speed of gantry rotation can be continuously varied to deliver the prescribed dose to planning

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target volume (PTV) while sparing the organs at risk (OARs) and healthy tissue.

In external radiotherapy, even though the technologies have improved for conformal delivery of prescribed dose to the tumor, the healthy tissues are unavoidably irradiated. Few studies reported that radiation is one of the clear risk factors for secondary cancers.[5,6] Risk of secondary malignancy changed based on age, sex, and dose distribution. Risk of secondary malignancy is increased in younger age patients, predominantly among radiation-associated secondary cancers.[7,8]

Secondary malignancy risk changes (1) according to irradiation of different locations' healthy tissues and (2) according to different dose distributions such as low, intermediate, and high dose.[9,10] The different locations of healthy tissues are classified into two categories: (i) healthy tissues within the treatment volume (primary treatment volume) and (ii) the healthy tissues outside of the treatment volume (field edge and peripheral volume).[9] The different dose distributions are classified into three categories based on the approximate dose level: (i) high dose (>30 Gy or 50% of the prescribed dose), (ii) intermediate dose (3–30 Gy or 5%–50% of the prescribed dose), and (iii) low dose (<3 Gy or 5% of the prescribed dose).[9]

Diallo *et al*. found that 66% of secondary cancers occurred at the periphery of the treatment volume (from the field edge to 5 cm), 22% occurred beyond 5 cm from the treatment field, and 12% occurred within the treatment volume.[11]

Dose distribution with different delivery techniques differs due to their degrees of freedom. The requirement of each technique is different. For example, method of delivery, required number of monitor units (MUs), number of fields, and treatment time are different.[12,13] Even if IMRT technique has made it possible to achieve higher dose conformity to the tumor and to reduce the dose to healthy tissue structures, the degree of delivery freedom for dose delivery between IMRT and VMAT are entirely different.[14] Consequently, the increased degrees of freedom with VMAT technique, whether it helps to reduce dose to healthy tissues without compromising on target coverage and sparing of OARs has to be evaluated.

The quantification of secondary malignancy risk is not trivial due to the missing information on dose distribution.[5] Therefore, the objective of this study is to categorize the dose in different regions of the irradiated volume for various sites and to evaluate the relationship between the target volume and the dose to healthy tissues. Eventually, the results with VMAT technique are to be compared with the IMRT technique for the evaluation of relative merits.

Materials and Methods

Source of data

The data were obtained from the Department of Radiation Oncology at Mangalore Institute of Oncology, Mangalore, Karnataka. Informed consent was obtained from the patients or his/her representatives at the beginning of the study after explaining about the treatment technique.

Procedure

Patient positioning, immobilization, and computed tomography simulation

A total of 150 patients comprising of 64 (42.70%) head-and-neck cancers, 30 (20.0%) lower third esophagus cancer, 21 (14.0%) cervical cancer with para-aortic nodes involvement, 20 (13.33%) cervical cancer, and 15 (10.00%) prostate cancer were studied. All patients were immobilized with thermoplastic mask and/or Vac-Lok and simulated. Planning computed tomography (CT) images were acquired with a slice thickness of 3 mm.

Delineation of tumor and critical organs

According to the International Commission on Radiation Units and Measurements (ICRU) 62, all tumors and critical structures were delineated on CT. Based on the treatment sites, different margins were given to clinical target volume to account for daily patient setup error during treatment delivery. To find the scatter dose at different regions, three nontargeted healthy tissues were delineated: (a) healthy tissues within the treatment volume, (b) healthy tissues from field edge to 5 cm on both side of the treatment volume, and (c) healthy tissues beyond 5 cm of the field edge on both sides of the treatment volume [Figure 1].

Dose prescription

The details of the dose prescription case-wise are as follows:

i. Head and neck: 70 and 54 Gy simultaneously prescribed in 35 fractions to the PTV_{70Gy} and to PTV_{54Gy}, respectively
ii. Lower-third esophagus: 60 and 45 Gy simultaneously prescribed in 30 fractions to the PTV_{60Gy} and to PTV_{45Gy}, respectively
iii. Cervix with PA involvement: 54 Gy in 27 fractions to the PTV_{54Gy} and 45 Gy in 25 fractions to the PTV_{45Gy} was prescribed
iv. Cervix: 54 Gy in 27 fractions was prescribed to the PTV_{54Gy}
v. Prostate: 80 Gy and 54 Gy simultaneously prescribed in 40 fractions to the PTV_{80Gy} and to seminal vesicles, respectively.

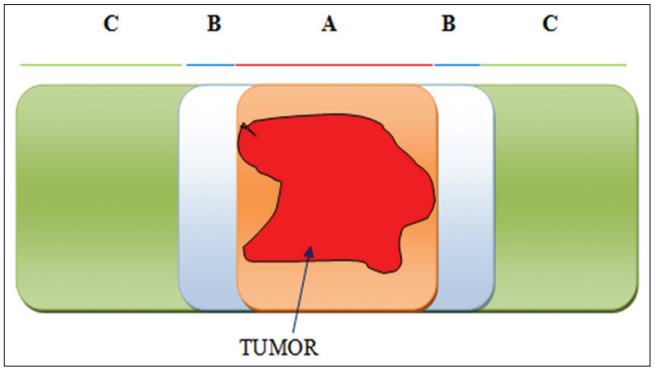

Figure 1: The schematic diagram of the classification of healthy tissues

Treatment planning

For all the patients, two sets of treatment plans, one with IMRT and another with VMAT were generated in Varian Eclipse treatment planning system (10.0.39). According to the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) and ICRU 62, the planning objectives were defined.

Volumetric-modulated arc therapy (RapidArc) plan

VMAT plans were generated for all the patients with 1–2 RapidArc fields with arc lengths of 656°–716°, and the collimator angle ± 20° was given for all the arc fields. The generated treatment plans were optimized with progressive resolution optimizer-III algorithm to meet the given planning objectives. Dose to tumor and critical structures by the optimized plan was calculated in AAA algorithm with 2.5-mm grid resolution and inhomogeneity correction "ON" for 6 MV energy. The plan was evaluated with the planning objectives. A verification plan of the evaluated plan was calculated and analyzed against the measurement values using portal dosimetry.

Intensity-modulated radiation therapy plan

Similarly, IMRT plan for each patient was generated with 7–9 fields with equal intervals of gantry angle, and the collimator angle of all the fields was ± 20°. The created treatment plans were optimized using dose-volume optimizer to meet the same given planning objectives. Dose to the tumor and critical structures by the optimized plan was calculated in AAA algorithm with 2.5-mm grid resolution and inhomogeneity correction ON for 6 MV energy. The plan was evaluated with the planning objectives in mind. A verification plan of the evaluated plan was calculated and analyzed against the measurement values using portal dosimetry.

Plan evaluation

Confirmation number (CN), ICRU recommended conformity index (CI), coverage index (COVI), homogeneity index (HI), and dose gradient index (GI) were used for the evaluation of tumor dose coverage with both plans. In the evaluation of OARs sparing level, QUANTEC recommendations were followed. While selecting a relatively better plan for treatment, the high dose (50%) receiving percentage of healthy tissue volume within treatment volume as well as the volume from field edge to 5 cm outside the treatment volume receiving low dose (5%) and intermediate dose (10%) were also analyzed with VMAT and IMRT techniques. All the above-mentioned doses and healthy tissue volume of all the treatment sites were noted down in percentage for comparison between VMAT and IMRT as well as to find the relationship between tumor volume and dose to healthy tissue volume.

These values were analyzed and compared between VMAT and IMRT in each site separately. A graph was plotted using all sites' values to assess the relationship between tumor volumes and percentage of healthy tissue volume at each dose level separately. The required number of MU for VMAT and IMRT plans was also recorded and compared.

The healthy tissue volume beyond 5 cm from the field edges was not reported due to inadequately acquired CT images.

Statistics

The descriptive and inferential statistics of between-group comparison of both dosimetric and technical parameters was performed using the IBM SPSS version "16" (IBM, Chicago, IL, USA).

The statistical inferences were made for alpha (α) at 5% ($P < 0.05$), 80% power (1-β), and 95% of confidence interval. $P < 0.05$ was considered as statistically significant. Paired *t*-tests and Wilcoxon signed-rank test were used to compare the mean of the plans between the techniques.

Results

Table 1 shows the descriptive statistics of the tumor volumes in the various treatment sites. In this, prostate cancer tumor volume was the smallest one and cervix with para-aortic nodes involvement was the largest one. The tumor volume of head-and-neck and esophagus cancers is closer to each other. The tumor volume of cervix cancer is the second largest volume.

Tables 2 and 3 show that both VMAT and IMRT plans achieved acceptable tumor coverage and spared the critical structures below the tolerance. However, VMAT shows significantly better CN and CI along with higher sparing of critical structures in all the treatment sites.

Table 4 describes the comparison results of low-dose, intermediate-dose, and high-dose received by healthy tissue volume within the treatment volume. Volume of healthy tissue received the low and intermediate-dose was significantly lesser ($P < 0.05$) in IMRT in the treatment of prostate and lower-third esophagus cancer, whereas in the treatment of head-and-neck cancers, cervix, and cervix with para-aortic nodes involvement, the healthy volume did not differ significantly between VMAT and IMRT. However, the healthy tissue volume with high-dose was significantly lesser ($P < 0.05$) in VMAT in all the treatment sites, than IMRT.

Table 5 describes the comparison results of volume of healthy tissue received low and intermediate-dose from field

Table 1: Descriptive statistics of the various treatment site tumor volumes

Treatment sites, *n* (%)	All targets' volume (cubic centimeter)			
	Mean±SD	Minimum	Maximum	Median
Head and neck - 64 (42.7)	609.29±194.39	154	1286	598.11
Esophagus - 30 (20)	820.84±292.18	385	2007	750.5
Cervix-PA - 21 (14)	2128.30±695.95	1272	3405.4	1976
Cervix - 20 (13.3)	1273.12±340.02	769	2028	1258.5
Prostate - 15 (10)	256.75±213.57	93.1	727	179.22

Cervix-PA: Cervical cancer with para-aortic nodes involvement, SD: Standard deviation

Table 2: Site-wise comparison results of various indices for target dose coverage

Site (*n*)	Indices	Mean±SD		*P**
		VMAT	IMRT	
Head and neck (64)	CN	0.822±0.07	0.739±0.09	<0.001
	DGI	0.113±0.05	0.110±0.052	0.015
	COVI	0.980±0.02	0.977±0.03	0.102
	CI	1.184±0.12	1.313±0.18	<0.001
	HI	0.087±0.02	0.096±0.03	0.013
Lower-third esophagus (30)	CN	0.899±0.04	0.811±0.07	<0.001
	DGI	0.182±0.06	0.150±0.06	<0.001
	COVI	0.960±0.02	0.926±0.05	0.001
	CI	1.033±0.03	1.061±0.09	0.078
	HI	0.125±0.06	0.106±0.03	0.110
Cervix -PA (21)	CN	0.804±0.07	0.713±0.08	<0.001
	DGI	0.262±0.05	0.249±0.05	0.024
	COVI	0.971±0.03	0.973±0.03	0.571
	CI	1.178±0.12	1.346±0.17	<0.001
	HI	0.126±0.03	0.140±0.07	0.374
Cervix (20)	CN	0.819±0.05	0.747±0.07	<0.001
	DGI	0.239±0.03	0.219±0.03	<0.001
	COVI	0.980±0.01	0.983±0.01	0.926
	CI	1.185±0.08	1.306±0.13	<0.001
	HI	0.096±0.02	0.112±0.04	0.074
Prostate (15)	CN	0.876±0.05	0.792±0.08	<0.001
	DGI	0.196±0.07	0.161±0.06	<0.001
	COVI	0.970±0.02	0.960±0.05	0.117
	CI	1.085±0.08	1.167±0.16	0.013
	HI	0.074±0.02	0.099±0.04	0.046

*Paired *t*-test. VMAT: Volumetric-modulated arc therapy, IMRT: Intensity-modulated radiation therapy, Cervix-PA: Cervical cancer with para-aortic nodes involvement, CN: Confirmation number, DGI: Dose Gradient Index, COVI: Coverage Index, CI: Conformity Index, HI: Homogeneity Index, SD: Standard deviation

edge to 5 cm. Both volume of healthy tissue received low-dose and volume of healthy tissue received intermediate-dose were significantly lesser ($P < 0.05$) in VMAT in all the treatment sites than IMRT. The table shows that as the target volume increased, the volume of healthy tissue with low and intermediate-dose also increased.

The required MU in VMAT technique was significantly lesser than IMRT technique ($P < 0.001$). Similar results were observed in all the treatment sites. Especially in the case of cervical cancer with para-aortic nodes involvement, the average required MU in VMAT technique was 30% of the average MU of IMRT technique [Table 6].

Figure 2a-c show the relationship between tumor volume (cm^3) and volume of healthy tissue received low,intermediate and high-dose (%) within the treatment field in VMAT (red dots) and IMRT plans (blue dots).

Figure 2a shows the low dose delivered to the healthy tissue in IMRT plans was relatively lesser in the case of lesser tumor volume. In the case of larger tumor volume, the volume of healthy tissue with low-dose was similar to each other between VMAT and IMRT plans, and this volume slightly increased as the tumor volume increased in both VMAT and IMRT plans.

Similarly, the intermediate-dose delivered to the healthy tissue in IMRT plans was also relatively lesser in the case of lesser tumor volume. In most of the cases, the healthy tissue volume with intermediate-dose increased as the tumor volume increased in VMAT as well as IMRT plans [Figure 2b].

In the case of high dose, VMAT plans reduced the healthy tissue volume with high dose better than IMRT in all the ranges of tumor volume. The healthy tissue volume with high-dose increased slightly as the tumor volume increased in VMAT and IMRT plans [Figure 2c].

However, the linear regression coefficients (R^2) of both VMAT and IMRT plans in all the cases indicate that no linear relation existed between the tumor volume and low dose, tumor volume and intermediate dose, as well as tumor volume and high dose to healthy tissues within treatment field [Figure 2a-c].

Figure 3a and b show the relation between tumor volume (cm^3) and dose received by healthy tissue volume (%) out of treatment field in VMAT (red dots) and IMRT plans (blue dots).

Figure 3a shows that the volume of healthy tissue with low-dose (out of the field) was larger in IMRT plans than VMAT plans. The healthy tissue volume with low-dose did not linearly increase as the target volume increased. Moreover, irradiation of larger healthy tissue volume was observed while treating the target volume between 600 cc to 1100 cc in VMAT as well as IMRT plans.

Similarly, the volume of healthy tissue with intermediate-dose (out of treatment volume) also was larger in IMRT plans than VMAT plans. In this case, we also observed that the healthy tissue volume with intermediate-dose did not linearly increase as the target volume increased. Moreover, irradiation of larger healthy tissue volume was observed while treating the target volume between 600 cc to 1200 cc in VMAT as well as IMRT plans [Figure 3b].

The linear regression coefficients (R^2) of both VMAT and IMRT plans indicate that no linear relation existed between tumor volume and volume of healthy tissue with low and intermediate-dose (out of treatment volume) [Figure 3a and b].

Figure 4 shows how many MU were required to deliver the prescribed dose to various target volumes in VMAT (red dots) and IMRT plans (blue dots). The required MU of all the VMAT plans was <1000 but with IMRT most of the plans required >1000 MU. The linear regression coefficient ($R^2 = 0.3011$) and gradient (0.6461) of IMRT plans were relatively higher than of VMAT plans ($R^2 = 0.2289$ and gradient = 0.1097). These values indicate that the required MU increases with IMRT plans as tumor volume increases. However, the lesser R^2 value ensures that no strong linear relation exists.

Table 3: Site-wise comparison of doses to various organs at risk

Treatment site	OARs	Planning objectives	Mean±SD		*P**
			VMAT	IMRT	
Head and neck (64)	Spinal cord	D_{max}<45 Gy	39.685±3.72	40.918±5.10	0.013
	Left parotid	Mean<26 Gy	21.795±10.40	22.600±10.74	0.012
	Right parotid	Mean<26 Gy	20.857±8.97	22.04±8.87	0.001
	Larynx	Mean<35 Gy	38.635±7.90	40.758±8.24	0.011
	Oral cavity	Mean<45 Gy	33.874±9.19	36.381±8.77	<0.001
Esophagus (30)	Spinal cord	D_{max}<45 Gy	37.52±3.83	39.822±5.10	0.002
	Total lung	Mean<17 Gy	15.758±2.72	16.461±2.83	0.022
		V_{20Gy}<25%	24.127±9.02	29.034±11.80	0.004
	Heart	Mean<26 Gy	31.456±5.98	32.382±6.91	0.171
		V_{30Gy}<46%	43.682±17.71	48.129±23.71	0.089
	Liver	Mean<20 Gy	14.33±6.73	15.058±6.95	0.017
	Left kidney	Mean<15 Gy	5.288±3.15	6.167±4.16	0.174
	Right kidney	Mean<15 Gy	3.202±2.26	3.447±2.42	0.468
Cervix - PA (21)	Bladder	$D_{2\%}$<58.5 Gy	56.617±2.16	59.750±8.91	0.135
	Rectum	$D_{2\%}$<58.5 Gy	55.182±2.02	54.735±3.13	0.346
	Left-FH	Mean=Minimize	29.766±3.70	30.706±5.64	0.503
	Right-FH	Mean=Minimize	30.191±3.55	29.327±6.36	0.558
	Small bowel	$D_{40\%}$=Minimize	29.480±3.86	31.812±3.25	0.006
		$D_{2\%}$<58.5 Gy	48.743±3.88	51.287±3.91	0.027
	Spinal cord	D_{max}<45 Gy	35.230±10.96	35.755±7.80	0.660
	Liver	Mean<20 Gy	5.371±3.92	5.531±3.92	0.892
	Left kidney	Mean<15 Gy	8.125±3.70	9.665±4.30	0.025
	Right kidney	Mean<15 Gy	8.561±3.39	9.977±3.81	0.036
	Bone marrow	Mean=Minimize	31.026±4.68	33.850±6.09	0.002
		V_{40Gy}=Minimize	32.647±6.01	36.547±7.71	<0.001
Cervix (20)	Bladder	$D_{2\%}$<53.5 Gy	51.845±0.82	52.223±2.16	0.407
	Rectum	$D_{2\%}$<53.5 Gy	49.147±5.00	49.381±3.81	0.616
	Bone marrow	Mean=Minimize	31.308±2.57	34.884±2.67	<0.001
		V_{40gy}=Minimize	18.891±8.56	32.516±14.44	<0.001
	Small bowel	$D_{40\%}$=Minimize	27.580±5.86	29.830±3.12	0.062
		$D_{2\%}$<53.5 Gy	45.418±2.97	45.586±2.81	0.646
	Left-FH	Mean=Minimize	25.831±4.54	24.356±4.52	0.207
	Right-FH	Mean=Minimize	26.258±4.40	24.890±5.31	0.129
Prostate (15)	Bladder	V_{60Gy}<50%	19.460±11.15	19.258±10.49	0.868
		V_{70Gy}<35%	13.447±8.39	14.074±9.19	0.420
		V_{75Gy}<25%	11.260±7.81	11.737±8.53	0.520
	Rectum	V_{50Gy}<50%	24.854±9.57	26.311±15.40	0.666
		V_{60Gy}<35%	14.763±7.17	15.768±9.52	0.627
		V_{70Gy}<20%	8.538±5.04	8.792±5.49	0.830
	Left-FH	$D_{2\%}$<45 Gy	27.362±3.60	32.157±6.60	0.002
	Right-FH	$D_{2\%}$<45 Gy	27.922±3.53	32.547±6.65	0.027

*Paired *t*-test. VMAT: Volumetric-modulated arc therapy, IMRT: Intensity-modulated radiation therapy, OARs: Organs at risk, D_{max}: Maximum dose (Gy), V_{xGy}: X_{Gy} dose received volume (%), $D_{2\%}$: 2% volume received dose (Gy), FH: Femoral head, SD: Standard deviation

Discussion

In the management of cancer, radiotherapy plays an important role.[1] The different techniques developed are used to achieve conformal dose to tumor as well as reduce the dose to critical structures below the tolerance by modulating the beam intensity.[2] Although these techniques are achieving the planning goal, irradiation of the nontargeted tissues (healthy tissues) is still unavoidable.[9]

Based on the three-dose classifications that is low dose, intermediate dose, and high dose, the high-dose irradiation of the healthy tissues within treatment volume as well as low and intermediate doses to healthy tissues outside of the field can cause severe risk of secondary malignancy.[11]

Irradiated healthy tissue volume and dose distributions are two main factors which might increase the risk of secondary cancers. Especially close to the primary cancer treatment

Table 4: Percentage of healthy tissues volume of different doses in the treatment volume in volumetric-modulated arc therapy and intensity-modulated radiation therapy techniques

Different dose to healthy tissues site wise (%)	Dose received volume of healthy tissues within treatment region, mean±SD		*P*
	VMAT	IMRT	
Head and neck			
Low dose (5)	94.397±4.28	93.757±4.19	0.038*
Intermediate dose (10)	83.316±9.19	85.410±7.69	<0.001*
High dose (50)	15.501±12.93	20.241±15.59	<0.001$
Esophagus			
Low dose (5)	94.457±2.74	92.041±4.10	<0.001*
Intermediate dose (10)	74.481±10.97	74.264±9.75	0.846*
High dose (50)	9.469±5.54	12.831±6.39	<0.001$
Cervix-PA			
Low dose (5)	97.516±1.80	97.098±6.62	0.780*
Intermediate dose (10)	87.392±7.81	89.727±11.44	0.381*
High dose (50)	13.351±16.26	22.511±18.10	<0.001$
Cervix			
Low dose (5)	96.027±4.41	96.994±2.17	0.225*
Intermediate dose (10)	86.764±8.14	87.772±6.02	0.262*
High dose (50)	19.835±8.89	24.925±11.37	<0.001$
Prostate			
Low dose (5)	95.661±1.53	92.055±6.13	0.025*
Intermediate dose (10)	82.555±5.22	75.772±9.74	0.008*
High dose (50)	6.163±3.13	8.355±3.43	<0.001$

All the values are in percentage. *Paired *t*-test, $Wilcoxon signed-rank test. VMAT: Volumetric-modulated arc therapy, IMRT: Intensity-modulated radiation therapy, Cervix-PA: Cervix with para-aortic nodes involvement, SD: Standard deviation

Table 5: Percentage of healthy tissues volume of different doses at the volume of field edge to 5cm in volumetric-modulated arc therapy and intensity-modulated radiation therapy techniques

Different dose to healthy tissues site wise (%)	Dose received volume of healthy tissues from field edge to 5 cm, smean±SD		*P*$
	VMAT	IMRT	
Head and neck			
Low dose (5)	19.064±11.94	27.342±15.89	<0.001
Intermediate dose (10)	5.817±9.16	11.204±11.38	<0.001
Esophagus			
Low dose (5)	12.837±12.16	14.380±11.78	0.001
Intermediate dose (10)	3.807±8.37	4.731±8.93	<0.001
Cervix-PA			
Low dose (5)	27.708±17.63	37.221±18.67	<0.001
Intermediate dose (10)	8.737±7.57	14.137±9.45	<0.001
Cervix			
Low dose (5)	22.417±12.20	28.845±12.40	<0.001
Intermediate dose (10)	5.761±4.80	9.616±6.80	<0.001
Prostate			
Low dose (5)	8.965±3.70	12.081±5.69	0.002
Intermediate dose (10)	1.525±0.84	3.181±1.86	0.001

All the values are in percentage. $Wilcoxon signed-rank test. VMAT: Volumetric-modulated arc therapy, IMRT: Intensity-modulated radiation therapy, Cervix-PA: Cervix with para-aortic nodes involvement, SD: Standard deviation

field, bone and soft-tissue sarcoma solid cancers are mostly found.[11,15] However, the evaluation of dose distribution to these healthy tissues by different modulation techniques may address the relative benefit to reduce the risk of secondary malignancy. Many studies have reported that VMAT achieves better coverage and sparing of OARs than IMRT.[16-18] However, the dose to healthy tissues was not evaluated adequately and there is no current guidance to follow in terms of dosimetry and limitation of the planning systems.[9] Thus, this comparison study evaluated the dose to healthy tissues within the treatment volume and outside of the treatment volume (field edge to 5 cm) between VMAT and IMRT techniques along with tumor coverage and dose to OARs. Both target coverage and OARs sparing in VMAT technique were significantly better than IMRT.

Table 6: Required monitor units to deliver the prescribed dose by volumetric-modulated arc therapy and intensity-modulated radiation therapy plan

Treatment site (*n*)	Mean±SD		Mean difference	*P**
	VMAT	IMRT		
Head and neck (64)	512.9±103.7	2193.1±527.9	1680.2	<0.001
Esophagus (30)	423.90±72.15	1461.5±392.49	1037.6	<0.001
Cervix-PA (21)	720.0±217.6	2872.0±828.2	2152.0	<0.001
Cervix (20)	603.85±96.27	2832.45±531.3	2228.6	<0.001
Prostate (15)	566.67±108.84	1318.93±388.15	752.2	<0.001

*Paired *t*-test. VMAT: Volumetric-modulated arc therapy, IMRT: Intensity-modulated radiation therapy, Cervix-PA: Cervix with para-aortic nodes involvement, SD: Standard deviation

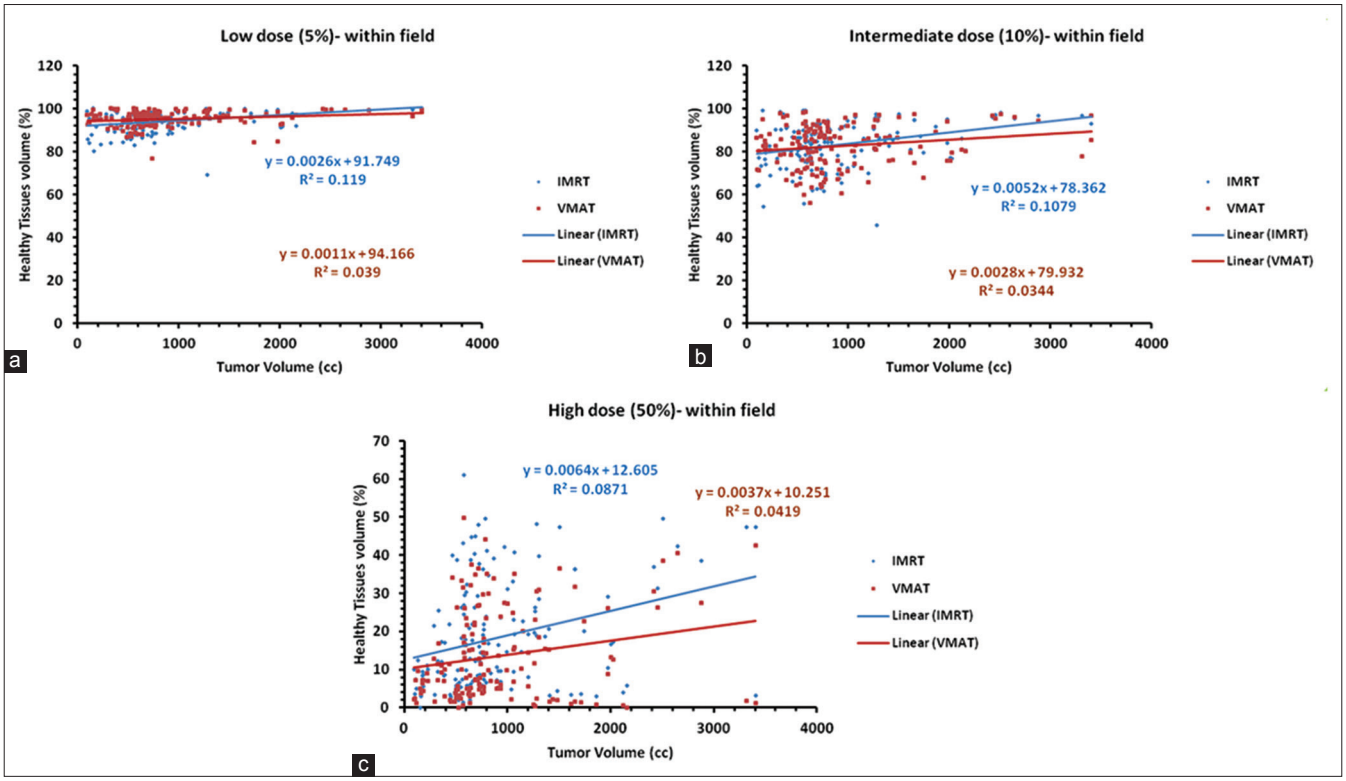

Figure 2: (a-c) Relation between tumor volume (cm^3) and dose received by healthy tissue volume (%) within treatment volume. VMAT: Volumetric-modulated arc therapy, IMRT: Intensity-modulated radiation therapy, cc: Cubic centimeter

Brenner *et al*.[19] and Chaturvedi *et al*.[20] reported that the majority of cancers occurred in intermediate-to-high-dose regions than the low-dose regions (<1 Gy). The results of healthy tissue volume with high-dose in VMAT and IMRT plans between 450 cc and 1100 cc (head-and-neck cancer patients) was similar to the highest target volume range. It implies that the complexity of the plan would increase the high dose to healthy tissues even with smaller tumor volumes. Moreover, the volume of healthy tissue with high-dose within treatment volume is significantly lesser in VMAT technique in all the treatment sites (irrespective of tumor volumes). Therefore, most of the secondary cancer occur in high-dose[11] can be reduced with VMAT.

Ron *et al*.[21] reported that dose delivered far outside the primary field is even lesser, and it has also been associated with the risk of second malignancy. Low radiation outside the treatment volume can cause deleterious effects to the patient.[21] Especially from field edge to 5 cm, the secondary malignancy risk is relatively higher.[11] Our study shows that the volume of healthy tissues from field edge to 5 cm (out of the field) receiving low dose (5%) and intermediate dose (10%) were significantly reduced with VMAT technique. The substantial control of low doses as well as intermediate doses to the nontargeted tissues outside of the treatment volume can reduce the risk of secondary malignancy.

Several studies have reported that the measured dose at peripheral location is directly proportional to the number of MU used and shielding of the machine.[22,23] The number of MU used in dynamic IMRT delivery can increase the leakage and scatter dose around the patient body which can cause

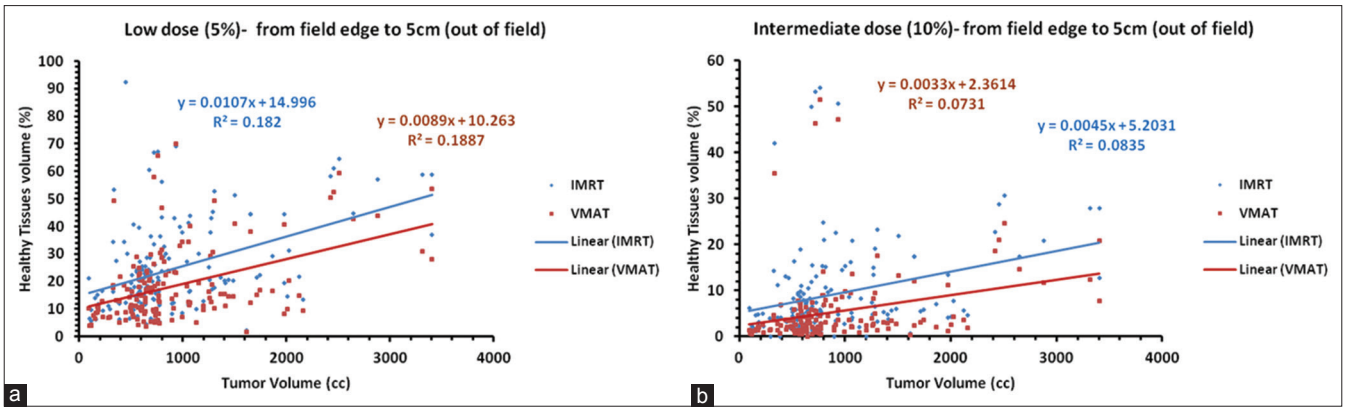

Figure 3: (a and b) Relation between tumor volume (cm^3) and dose received by the healthy tissue volume (%) from field edge to 5cm. VMAT: Volumetric-modulated arc therapy, IMRT: Intensity-modulated radiation therapy, cc: Cubic centimeter

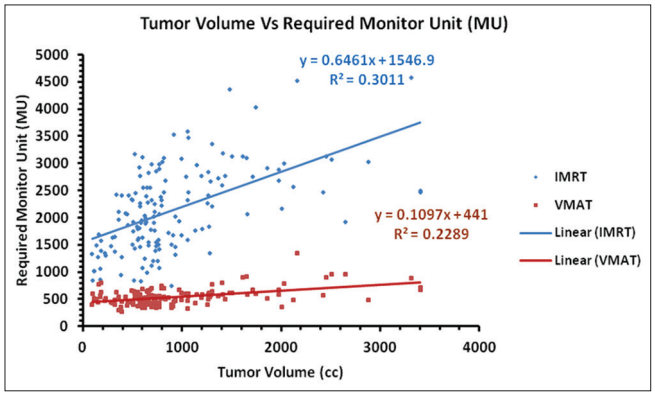

Figure 4: Relation between tumor volume (cm^3) and required monitor unit with volumetric-modulated arc therapy and intensity-modulated radiation therapy

potential risk of secondary malignancy.[24] The significantly lesser MU of VMAT plan in all the treatment sites will produce lesser leakage and scatter dose as compared to IMRT. Therefore, the healthy tissues in the peripheral region (beyond 5 cm) would receive low doses in larger volumes with IMRT than VMAT.

The calculation of the dose volume beyond 5 cm (peripheral region) requires special attention in beam configuration, and at the same time, the dose contribution from head leakage is predominant.[9] Therefore, accurate dose measurements have to be carried out for a meaningful comparison of healthy tissue doses in the peripheral region.

Conclusions

Improved delivery technologies help to get a better conformal delivery plan. However, to select a better plan from two different kinds of techniques, the dose to healthy tissues within treatment volume and outside of the treatment volume has to be considered along with the proposed indices such as CI, GI, COVI, and HI.

VMAT plan can achieve better dose control outside of the treatment volume and reduce the volume of healthy tissue receives high-dose within treatment volume than IMRT. VMAT is the most appropriate technique for achieving the given planning objectives than IMRT, especially in the treatment of large tumor volume. Special attention has to be given to the out of field dose to reduce the secondary malignancy risk, especially while treating women and children.

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Conflicts of interest

There are no conflicts of interest.

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