



Dosimetric Evaluation of Various Radiation Therapy Treatment Techniques for Carcinoma Esophagus: A Treatment Planning Study

Dinesh Kumar SAROJ,^{1,2} Gopa GHOSH,³ Shuchishree SHUKLA,³ Suresh YADAV,⁴
 Neetu PALIWAL²

¹Department of Radiotherapy, Alexis Multispecialty Hospital, Nagpur-India

²Department of Physics, Rabindranath Tagore University, Bhopal-India

³Department of Radiotherapy, Chirayu Medical College and Hospital, Bhopal-India

⁴Department of Radiotherapy, Gandhi Medical College, Bhopal-India

OBJECTIVE

The study was conducted to compare the dosimetric superiority between the three-dimensional conformal radiation therapy (3DCRT), intensity-modulated radiation therapy (IMRT) and Rapid Arc in terms of treatment plan quality.

METHODS

We have taken 15 Patients of ca-esophagus for our study from our hospital database. Patients were already treated 3DCRT plan. Retrospectively additional IMRT and RA plans were created with Planning target volume (PTV) prescription dose of 50.4Gy in 28 fractions. Prescription dose of 95% of PTV was chosen for the comparison between three treatment planning strategies. Dose volume histogram was used to analyze and compare various plan quality index and doses to the organs at risk (OARs).

RESULTS

The $D_{95\%}$ of PTV for 3DCRT plan was 47.85 ± 0.78 Gy, which significantly got improved in IMRT (48.75 ± 0.86 Gy) and RA (49.0 ± 0.64 Gy) plans. The CI value for PTV coverage in 3DCRT was 0.96 ± 0.04 ; however, the CI values in IMRT and RA plans were significant at 0.98 ± 0.01 and 0.98 ± 0.03 , respectively. The 3DCRT plan had an HI of 1.09 ± 0.03 , which was significantly raised to 1.046 ± 0.26 in the IMRT plan ($p=0.01$) and 1.06 ± 0.02 in the RA plan ($p=0.03$).

CONCLUSION

An IMRT and RA plan gives greater conformity of dose to the PTV in comparison to 3DCRT. Lesser doses to the surrounding OARs are the major importance of the IMRT and RA planning technique. Dose escalation is possible with IMRT and RA plans.

Keywords: Ca-esophagus; intensity-modulated radiation therapy; plan quality index; RA; three-dimensional conformal radiation therapy.

Copyright © 2022, Turkish Society for Radiation Oncology

INTRODUCTION

Esophageal carcinoma (EC) is one of the most aggressive types of malignant tumors worldwide. An epidemi-

ology and end data analysis on the EC report indicates that overall survival is around 18.8% after 5 years, and 15690 individuals died as a result of cancer, accounting for 2.6% of all cancer deaths.[1] EC has poor functional

Received: July 11, 2022

Accepted: August 03, 2022

Online: September 06, 2022

Accessible online at:

www.onkder.org

OPEN ACCESS This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.



Dr. Dinesh Kumar SAROJ
Department of Radiotherapy,
Alexis Multispecialty Hospital,
Nagpur-India;
Department of Physics,
Rabindranath Tagore University,
Bhopal-India
E-mail: dinesh.saraj@gmail.com

outcomes and causes problems for surgeons and radiation oncologists. Surgery is the primary treatment option for EC patients who are operable and medically fit. Concurrent chemo-radiotherapy, on the other hand, plays an essential role in the management of advanced EC patients who are medically unsuitable for surgery and generates optimum therapeutic results.[2]

However surrounding organs at risk (OARs) often limits the tumor dose. Planning target volume (PTV) is surrounded by lung, heart, and sometimes abutting to spinal cord. Studies have concluded that the use of modern radiation therapy (RT) techniques is helpful to explore the possibility of dose escalation.

Advances in RT technology have shifted for EC treatment techniques from three-dimensional conformal RT (3DCRT) to intensity-modulated RT (IMRT) and volumetric modulated arc therapy (VMAT) to allow for the sparing of normal healthy organs such as the lungs, heart, stomach, liver, kidneys, and spinal cord. IMRT treatment plan shows superiority to 3DCRT treatment plan based on dose volume analysis.[3-4] In contrast to the 3DCRT, IMRT provides more conformal dose to the target as well as higher dose gradients to surrounding tissues, which may ensure better local tumor control. [5] Nevertheless IMRT has major drawbacks of higher treatment delivery time and increased monitor units (MU), as a consequence patient will spend more time on the treatment table. Also, higher MU in IMRT will give higher irradiation to a small volume of healthy tissues and nearby OARs which increases the probability of secondary cancer risk.[6] Rapid Arc is analogous terms to VMAT, technique specified by Varian Medical system.

RA produces dose distribution similar to that of IMRT using a single or multiple arc rotation of the gantry. Recent research indicated that VMAT is superior to traditional IMRT in terms of PTV conformity and dose reduction in OARs.[7,8]

The current study's goal is to determine the potential comparative clinical benefit of the 3DCRT, IMRT, and RA treatment techniques used in the treatment of EC, to determine the dosimetrically appropriate technique in terms of dose to PTV and minimum dose to OARs, and to determine whether dose escalation is possible with higher techniques.

MATERIALS AND METHODS

In this study, 15 patients with esophageal cancer were chosen at random from our department's data bank. All of the patients were previously treated with 3DCRT on

a Varian Vital Beam Linear accelerator (LA) machine (M/S Varian Medical Systems, Palo Alto, CA, USA). All patients were immobilized in a supine position, with one arm over the head and the other in a neutral position. CT simulation was obtained using standard procedures on a Positron Emitted Tomography (PET)/Computed Tomography (CT) (Discovery IQ, GE Healthcare) scanner with 2.5 mm slices spacing.

After acquiring the CT images of the patients' gross tumor volume (GTV) and other associated target volume (TV) were contoured according to the RT Oncology Group (RTOG) 0436 protocol by the Radiation Oncologist.[3] A GTV was defined by a physician using a PET fusion imaging, and it includes the gross esophageal tumor as well as positive regional lymph nodes. In comparison to the GTV, the clinical TV (CTV) had a superior-inferior margins of 3-5 cm and lateral as well as anterior-posterior margins of 1 cm. The PTV was separated from the CTV by a 1 cm margin. PTV margins were differed from case to case and sometimes lesser posterior margins are given to avoid overlapping with spinal cord. The heart, lungs, spinal cord, stomach, and kidneys were contoured as OARs.

Dose Prescription and Treatment Objective

Each patient was scheduled to receive 1.8 Gy in 28 fractions for a total dose of 50.4 Gy. The planning goal was to deliver 95% of the prescribed dosage (PD) to 95% of the PTV volume, with no more than 2% of the PTV volume getting 107% of the PD and a maximum dose of <110% of the PD. The major aims of the OARs were defined as: Spinal cord $D_{max} < 45$ Gy; and lung $V_{20Gy} < 37\%$ and $V_{30Gy} < 25\%$. The secondary objectives were as: Mean dose of lungs <20 Gy; heart $V_{40Gy} 50\%$; and mean dose of heart <30 Gy.

Radiotherapy Planning

The LA used to deliver treatment planning was Varian Vital Beam equipped with the Millennium 120 multi-leaf collimator (MLC). Photon beam of energies 6MV, 10MV, and 15MV was used in this study for all cases treatment planning. There are total 60 pairs of leaves with 40 leaf pairs in the center and ten pairs on either side. The projection of center leaf width at isocenter was 5 mm while the outer leaves were 10 mm. The maximum travelling speed of MLC was 2.5 cm/s. The treatment planning system used for the external beam planning was Eclipse (Version 13.6.23, Varian Medical System) and final dose calculation was performed by Anisotropic Analytical Algorithm (AAA, version 13.6.23).Retrospectively new additional IMRT and RA

plan were created for each patient. Inverse optimization was performed by Photon Optimizer (PO) utilized for both IMRT and RA optimization (version 13.6.23).

Different treatment planning strategies were involved in the treatment of the esophageal cancer patient.

3D-CRT Planning

3DCRT plans were scheduled to perform into two phases of treatment, with each phase planned separately for the same PTV. Phase-I consisted of a giving 36 Gy dose to PTV with Parallel-opposed, anterior-posterior (AP), and posterior-anterior (PA) 6 MV, 10MV, and 15MV photon beam, followed by remaining dose of 14.4 Gy in Phase-II, with three photon field. Beam energy selection was based on patient thickness and PTV coverage. A beam angle for phase-II planning includes an AP field and 2 posterior oblique fields at gantry angles between 100-120° and 240-260° chosen in such a way to avoid the spinal cord. Appropriate wedge angles were used in posterior oblique beams to achieve optimum PTV dose distribution.

IMRT Planning

This treatment planning strategy involved treating the PTV with total 54 Gy in 1.8 Gy into 30 fractions. Inverse optimization was performed with PO which helps in computing optimal fluence maps from dose-volume constraints derived from the general planning objective. Varian leaf motion calculator was used to calculate actual fluence which is then delivered by MLCs to deposit the planned dose. Final dose calculation was performed by AAA algorithm.

RA Planning

The RA is unique treatment technique that allows the radiation to be delivered to the patient in a single 360° of gantry rotation that is accurately and efficiently with varying velocities and positions of the MLCs, dose rate, and gantry speed. This leads RA being an intensity-modulated dose distribution. The RA dose optimization is an aperture-based method, which incorporates MLCs leaf positions and MU weights as optimization parameters. The entire gantry rotation is described in the optimization process by a sequence of 177 control points. The optimization is based on the PO algorithm and the process is divided into five discrete multi resolution levels (MRs). The PO needed less control points to approach the convergent solution. The dose distribution is calculated during optimization with a MR dose calculation algorithm.

In this study, RA plan with two full arcs and with single isocenter was generated Arc consists of a clockwise and a counter-clockwise arc from gantry angles

181.0-179.0 and 179.0-181.0, respectively with collimator rotation of 15-20°. Collimator rotation was given to cover the entire tumor and minimize tongue and groove effect of MLCs during arc rotation.

Plan Evaluation and Statistical Methods

As per International Commission on Radiological Units and Measurements (ICRU Report 83, 2010)[9] doses to the TV, Conformity Index (CI), Homogeneity Index (HI), and OARs were recorded from their respective cumulative-dose volume histogram (cDVHs).

HI

HI was evaluated as the difference between the dose to 2% (D_2) and 98% (D_{98}) of PTV divided by dose to 50%

$$HI = (D_{2\%} - D_{98\%}) / D_{50\%} \quad (1)$$

Where $D_{2\%}$, $D_{98\%}$, and $D_{50\%}$ are the minimum dose delivered to 2%, 98%, and 50% volume of the TV, respectively. HI of zero indicated homogeneous dose distribution.

CI

A ratio evaluating the coverage of the prescription dose in treatment plans.

$$CI = \frac{\text{Target volume covered by prescription isodose volume}}{TV} \quad (2)$$

The value of CI to 1 indicates the good dose conformity. In addition, treatment parameters including the MU and beam on time (BOT) for each treatment plan were recorded for evaluation. BOT was defined as the radiation delivery time and did not incorporate gantry movement, the patient positioning and imaging procedures, which was noted while performing quality assurance.

For the evaluation of target conformation. The Conformation number (CN)[10] is defined as

$$CN = [TV_{RI} / TV] * [TV_{RI} / V_{RI}] \quad (3)$$

TV, TV_{RI}, and V_{RI} represent the treatment volume, the treatment volume at reference isodose (RI) of the prescribed dose, and the total volume at RI of the prescribed dose, respectively. The RI was defined as 95% of PTV prescribed dose. The maximum value for CN is 1, corresponding to perfect PTV coverage.

To assess overall plan quality of the treatment plans another parameter named quality factor (QF) was calculated.[11] Which consist of all measured planning index such as CI, HI, and CN. The QF for the treatment plan can be calculated in terms of combination of above set of planning indices expressed as below.

$$QF = [2.718 * \exp(-(\sum_i^N WiXi))] \quad (4)$$

Table 1 Patient characteristics tumor volume and tumor staging

Patients	Sex	Age (Years)	Tumor location	Tumor staging	PTV volume (cc)
1	M	85	Middle one Third	III	268.3
2	M	65	Middle one Third	III	315.6
3	M	57	Middle one Third	IVB	321.4
4	M	35	Middle one Third	IV	496.8
5	F	50	Middle one Third	IV	499.6
6	M	63	Middle one Third	IIIB	460.3
7	M	57	Upper one Third	IIIC	325.6
8	M	59	Middle one Third	IVB	326.3
9	M	63	Lower one Third	IIIC	728.7
10	M	74	Middle one Third	IIB	376.5
11	M	59	Middle one Third	III	357.5
12	M	71	Middle one Third	IIIA	440.8
13	F	64	Middle one Third	IIB	415.2
14	F	63	Middle one Third	IIIC	395.1
15	M	58	Middle one Third	II	410

PTV Mean Volume(cc)=408.75±116.24 (Mean±S.D) PTV Range=(268.3-728.7) cc. PTV: Planning target volume; M: Male; F: Female; cc: Cubic centimeter; SD: Standard deviation

Where the values of the weight factor (Wi) can be modified between zero and unity for all relatively weighted indices Xi for a user-defined number of indices (N) in the UPI set. Here, in our case, we have set all the weight factor to 1.

A test of significance was required to quantify the differences between observed parameters of 3DCRT, IMRT and RA plans. The one-way analysis of variance was used to compare dosimetric and volumetric indices among different plans, and when an overall significant difference among the groups was observed, the post hoc Turkey's test was used to determine which pair-wise comparisons differed. All statistical tests were done using the IBM Statistical Package for the Social Sciences (SPSS) software (release 20.0, SPSS Inc., Chicago, IL, USA). Statistical significance was defined as p<0.05.

RESULTS

Table 1 shows the patients characteristics and demographics. Out of 15 patients selected 12 were male and rest 3 were female. Patients' ages ranged from 35 to 85 years. PTV volume ranges from 268.3 to 728.7 cc with an average volume of 408.75±116.24 cc.

D_{max} dose to TV was substantially greater in the 3DCRT (54.03±0.556 Gy) plan than in the IMRT (52.46±1.031 Gy) and RA (53.2±0.41 Gy) plans, with p values of (p=0.01) and (p=0.046), respectively. There

was no significant difference in D_{max} dosage between IMRT and RA plans (p=0.069) (Table 2).

With 50.59±0.24 Gy, 50.59±0.04 Gy, and 50.06±0.24 Gy, respectively, the mean dose to PTV in 3DCRT and RA plans was higher than in IMRT plans. The D_{95%} of PTV coverage in the 3DCRT plan was 47.85±0.78 Gy, which was significantly better than the IMRT and RA plans, which were 48.75±0.86 Gy and 49.0±0.64 Gy, respectively (Fig. 1). In the 3DCRT plan, the V_{95%} of PTV volume was 384.95±121.45 cc, whereas in the IMRT and RA plans, it was 397.58±133.81 cc and 400.34±130.89 cc, respectively (Fig. 2).

The CN value for 3DCRT was reported to be 0.56±0.1, which improved significantly to 0.74±0.12 in IMRT (p=0.001) and 0.81±0.05 in RA (p=0.001), respectively. It was found that in 3DCRT, the CI value for PTV coverage was 0.96±0.04, whereas in contrast to IMRT and RA plans, the CI values were significant at 0.98±0.01 and 0.98±0.03. The HI of the TV was 1.09±0.03 in the 3DCRT plan, which was substantially enhanced to 1.046±0.26 in the IMRT plan (p=0.01) and to 1.06±0.02 in the RA plan (p=0.03).

Table 3 shows the dose volume statistics for OARs. The highest dosage to the spinal cord in the 3DCRT plan was 45.23±4.0 Gy, but in the IMRT and RA plans, the maximum dose to the spinal cord was significantly lowered to 38.84±4.34 Gy (p=0.007) and 34.80±4.02 Gy (p=0.002), respectively. The average dosage to the combined lungs was shown to be lower in 3DCRT,

Table 2 PTV dosimetric and treatment plan quality parameters

Variables	3DCRT Mean±SD	IMRT Mean±SD	RA Mean±SD	p		
				3DCRT versusIMRT	3DCRT versusRA	IMRT versusRA
D _{max} (Gy)	54.12±0.5	52.74±0.94	53.18±0.41	0.0001	0.001	0.16
D _{min} (Gy)	43.64±1.53	42.48±2.91	41.86±6.18	0.54	0.3	0.89
D _{mean} (Gy)	50.52±0.24	50.24±0.36	50.62±0.31	0.04	0.62	0.004
D _{95%} (Gy)	47.68±0.69	48.71±0.69	49.08±0.53	0.001	0.001	0.27
V _{95%} (cc)	384.75±98.67	397.70±108.56	400.56±106.24	0.89	0.89	0.89
CN	0.56±0.1	0.74±0.12	0.81±0.05	0.001	0.001	0.37
CI	0.95±0.02	0.98±0.01	0.99±0.01	0.02	0.01	0.01
HI	1.10±0.03	1.04±0.02	1.06±0.02	0.03	0.02	0.02
QF	1.52±0.18	1.27±0.15	1.18±0.06	0.001	0.001	0.001

PTV: Planning target volume; SD: Standard deviation; 3DCRT: Three-dimensional conformal radiation therapy; IMRT: Intensity-modulated radiation therapy; D_{max}: Maximum dose inside PTV; D_{min}: Minimum dose inside PTV; D_{mean}: Average dose to PTV; D_{95%}: 95percent of PTV receiving the dose; V_{95%}: 95% dose received by the PTV volume; CN: Conformation number; CI: Conformity Index; HI: Homogeneity index; QF: Quality factor; Gy: Gray

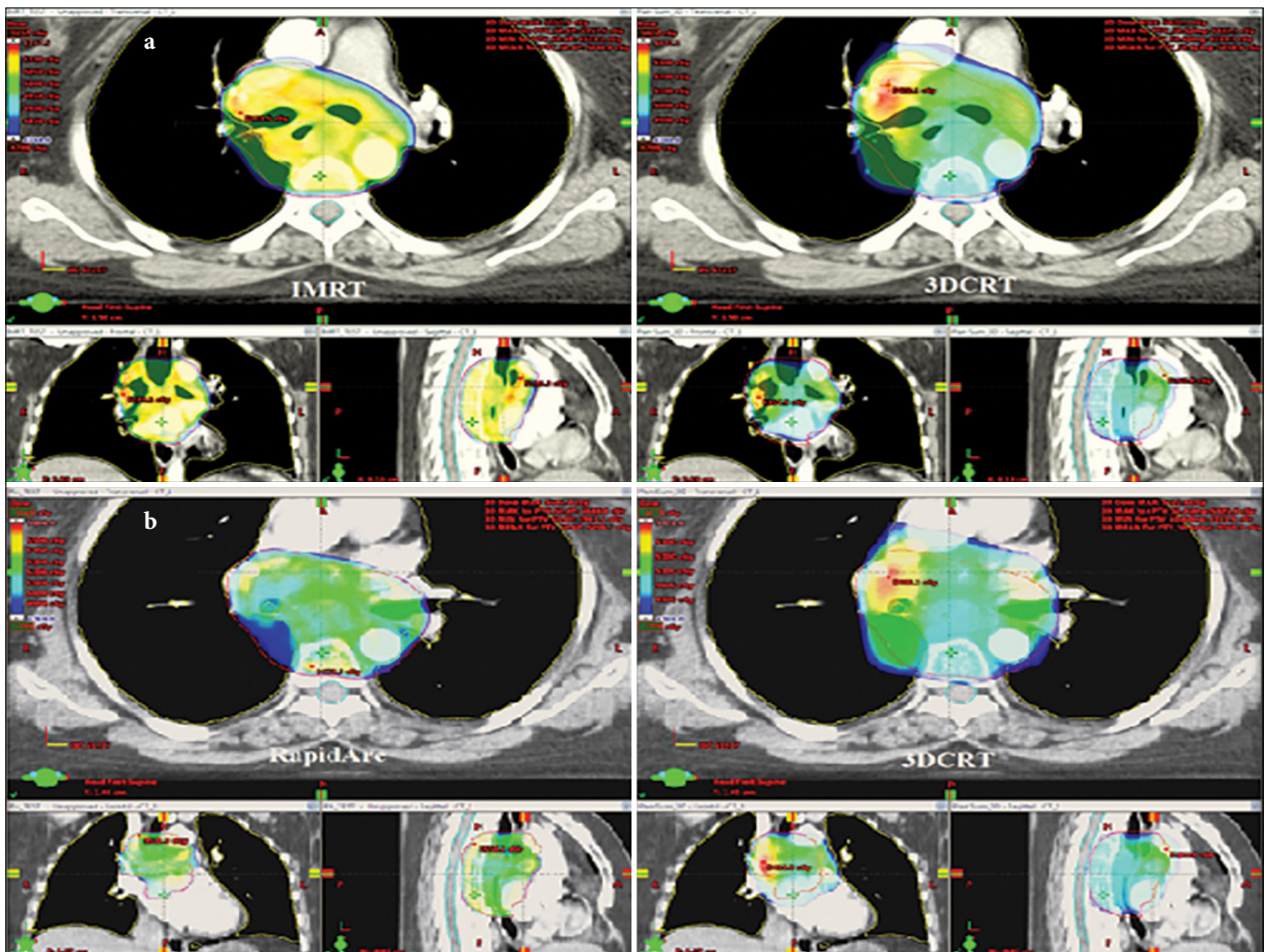


Fig. 1. The 95% color dose wash comparison between (a) 3DCRT and IMRT (b) RA and 3DCRT treatment plans for one of the patients.
IMRT: Intensity-modulated radiation therapy; 3DCRT: Three-dimensional conformal radiation therapy.

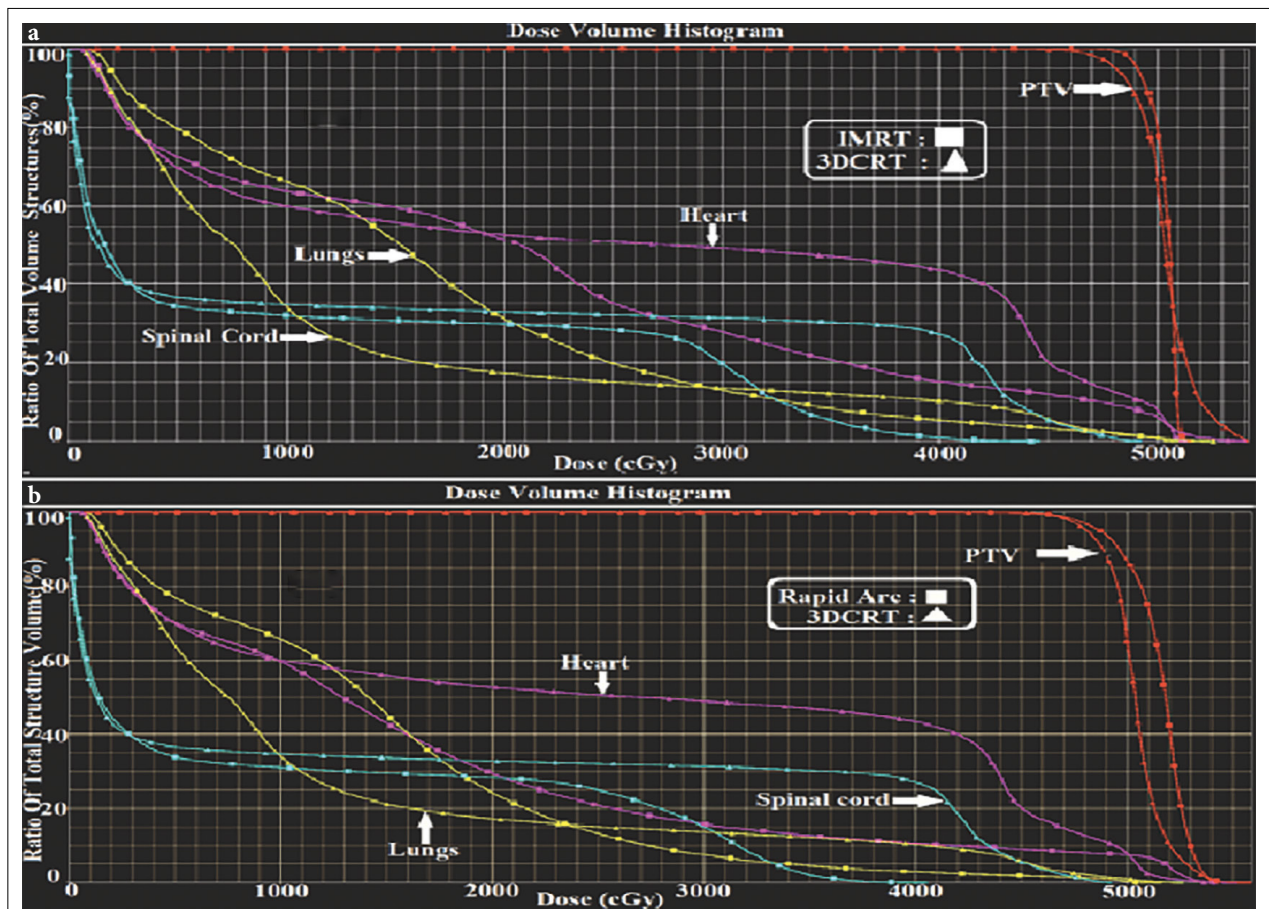


Fig. 2. The DVH comparison for PTV and various OARs between (a) IMRT and 3DCRT, (b) and 3DCRT. DVH: Dose volume histogram; PTV: Planning target volume; IMRT: Intensity-modulated radiation therapy; 3DCRT: Three-dimensional conformal radiation therapy; Gy: Gray.

with an average dose of 15.46 ± 3.36 Gy, compared to 16 ± 2.96 Gy and 17.79 ± 2.66 Gy in IMRT and RA plans, respectively. The V_{20Gy} volumetric dose parameter of the ipsilateral lung in 3DCRT was 26.69 ± 8.56 Gy, while it was 34.6 ± 7.35 Gy and 30.39 ± 9.99 Gy in the IMRT and RA plans, respectively.

The average heart dosage in 3DCRT was 32.32 ± 9.16 Gy, but the average heart dose in IMRT and the RA plan was 25.08 ± 4.8 Gy ($p=0.06$) and 22.99 ± 6.13 Gy ($p=0.015$), respectively, with significantly lower radiation dose. The heart's V_{25Gy} was 67.74 ± 23.31 Gy in 3DCRT, but this reduced to 42.83 ± 10.87 Gy ($p=0.017$) and 34.71 ± 14.97 Gy ($p=0.001$) in the IMRT and RA plans, respectively. Heart's V_{30Gy} dose in the 3DCRT plan exceeded our clinical dose requirements by a wide margin, but the dose was considerably reduced in the IMRT ($p=0.02$) and RA ($p=0$) plans. In 3DCRT, the heart's V_{30Gy} was $61.5227.06$ Gy, whereas it was only $31.697.04$ Gy ($p=0.002$) and $24.2910.43$ y ($p=0.001$) in the IMRT and RA plans, respectively.

In the 3DCRT plan, the average MU required to deliver a dose of 50.4 Gy was reported to be the lowest (218.72 ± 7.9). While the average MU required to give the same dose in IMRT and RA plans was 698.80 ± 179.0 ($p=0.001$) and 510.98 ± 86.27 ($p=0.001$), respectively. BOT was found to be less (0.43 ± 0.14 min) in 3DCRT, which increases to 1.16 ± 0.29 min and 0.85 ± 0.14 min in IMRT and RA plans, respectively (Table 4).

DISCUSSION

Squamous cell carcinomas are more common in Asian countries as compared to adenocarcinomas in western countries. RTOG94-05 demonstrated survival benefits with dose escalation but conventional 2D technique was used by the investigators and thus the study was limited by higher dose to surrounding OARs.[2] Local failures and residual disease continue to be the main therapeutic concerns in EC; therefore,

Table 3 Shows the results of average OARs DVH characteristics

Variables	3DCRT Mean±SD	IMRT Mean±SD	RA Mean±SD	p		
				3DCRT versus IMRT	3DCRT versus RA	IMRT versus RA
Spine max (Gy)	44.91±3.35	38.94±3.63	34.53±3.61	0.001	0.001	0.004
Lungs V _{5Gy} (%)	77.39±13.36	81.8±18.49	93.14±7.78	0.74	0.04	0.18
Lungs V _{10Gy} (%)	51.58±18.84	64.84±19.12	84.14±13.02	0.21	0.001	0.04
Lungs V _{20Gy} (%)	26.69±8.56	34.1±7.35	30.39±9.99	0.15	0.6	0.6
Lungs V _{30Gy} (%)	16.29±5.44	10.19±4.2	9.138±3.95	0.016	0.004	0.85
Lungs mean (Gy)	15.46±3.36	16±2.96	17.79±2.66	0.90	0.21	0.39
Heart V _{20%} (%)	71.74±19.59	58.4±16.18	47.11±18.9	0.24	0.014	0.36
Heart V _{30%} (%)	61.52±27.06	31.69±7.04	24.29±10.43	0.002	0.001	0.61
Heart V _{40%} (%)	41.09±30.87	20.19±12.97	16.24±10.09	0.07	0.027	0.9
Heart mean (Gy)	32.32±9.16	25.088±4.82	22.99±6.19	0.068	0.015	0.76

Spine max: Maximum dose received by spinal cord; V_{XGy}: XX Gy of dose received by YY% of volume. OARs: Quality index and doses to the organs at risk; DVH: Dose volume histogram; SD: Standard deviation; 3DCRT: Three-dimensional conformal radiation therapy; IMRT: Intensity-modulated radiation therapy; Gy: Gray

Table 4 The average MU and BOT in 3DCRT, IMRT, and RA treatment plans

Variables	3DCRT Mean±SD	IMRT Mean±SD	RA Mean±SD	p		
				3DCRT versus IMRT	3DCRT versus RA	IMRT versus RA
MU	218.72±7.9	698.80±179.0	510.98±86.27	0.001	0.01	0.03
BOT (Min)	0.43±0.14	1.16±0.29	0.85±0.14	0.001	0.001	0.001

MU: Number of monitor unit; BOT: Beam on time; 3DCRT: Three-dimensional conformal radiation therapy; IMRT: Intensity-modulated radiation therapy; SD: Standard deviation; Min: Minutes

this study was designed to investigate the possibility of dose escalation utilizing modern methods IMRT and RA in EC, as well as to assess dosimetric comparison between 3DCRT, IMRT, and RA planning techniques. The cDVH was used to compare and assess all treatment regimens.

In this study, the dosimetric characteristics of IMRT and RA plans in the treatment of patients with middle one-third esophageal cancers were studied by comparing them to 3DCRT plans. IMRT and RA plans showed the increased dose conformity homogeneity and PTV coverage when compared to 3DCRT (Fig. 3). Fenkell et al., Nutting et al. and Allehyani et al. [12–14] found similar results to ours in his study of comparisons of 3D-CRT versus IMRT for esophageal cancer. The normal value of QF is also unity, with values above unity referred to as overdosed and values below unity referred to as under dose of the structures contoured volume in the corresponding plan.

In RA and IMRT plans, the QF is higher than in 3DCRT. This could be due to better CI, HI, and CN values reported in IMRT and RA plans. IMRT and RA plans have the ability to cover the PTV with prescribed dose and simultaneously they deliver high dose gradient outside the PTV. This results in high conformity to the PTV. IMRT and RA plans reduced the amount of normal tissues irradiated with a high dosage while increasing the volume of normal tissues treated with a low dose. The study of Vivekanandan et al. [8] also concluded that the IMRT and RA gives superior target dose conformity compared to 3DCRT for EC. For centrally located carcinoma of the anal canal, prostate, cervical, and head and neck cancer, RA can produce dosimetry similar to that of IMRT. As a result, Zhang et al. [15] compared RA to IMRT in EC and found similar PTV coverage (p=0.26) and V₁₀ lung (p=0.1650) with the lower spinal cord D_{max} (p=0.0389), heart mean dose (p=0.0002), and V₂₀ lung (0.009) While IMRT was su-

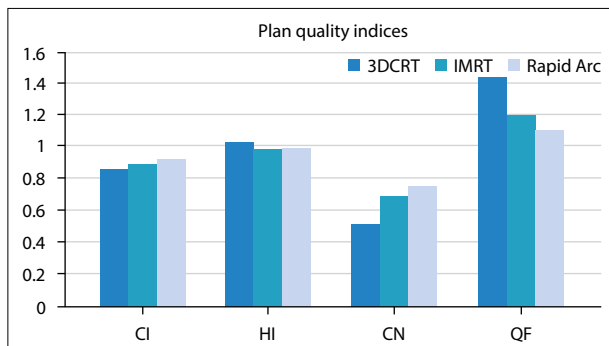


Fig. 3. The comparison of various plan quality indices between 3DCRT, IMRT and RA plans.
 3DCRT: Three-dimensional conformal radiation therapy;
 IMRT: Intensity-modulated radiation therapy.

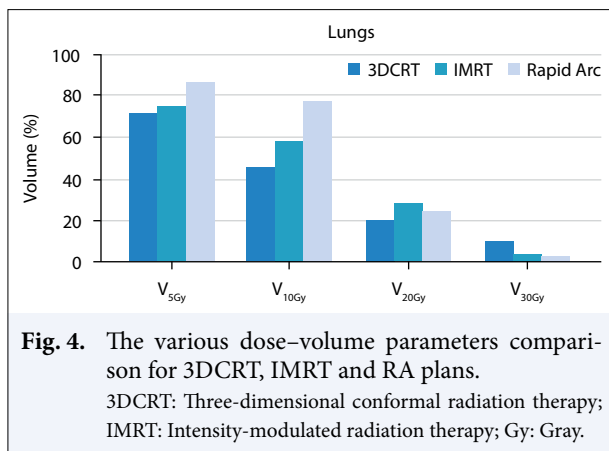


Fig. 4. The various dose-volume parameters comparison for 3DCRT, IMRT and RA plans.
 3DCRT: Three-dimensional conformal radiation therapy;
 IMRT: Intensity-modulated radiation therapy; Gy: Gray.

perior in terms of lung V_5 and mean dosage, conventional RT prevailed out. Accordingly, they found that RA has varied advantages and disadvantages in treating the mid/lower esophageal but improved PTV coverage in treating the upper EC patients as PTV is T-shaped across chest with a considerable reduction in MUs. Similar results were observed in our studies where we have seen that $V_{95\%}$ of PTV jumps to 3.36% and 4.10% in IMRT and RA plan compared to 3DCRT plan. With the effect of this our CI value also got increased in the following order 3DCRT<IMRT<RA (Fig. 4).

Pulmonary toxicity is a major potential adverse effect of treatment for esophageal cancer. As a result, the dose constraint to bilateral lung is the most important factor to consider when evaluating treatment regimens. Numerous studies had been published having contradicting parameters for predicting pulmonary toxicity,[14,15] but it was still difficult to compare them. The V_{10Gy} , V_{20Gy} , and V_{30Gy} were utilized in this investigation to assess lung toxicity. Mary et al.[16]

remarked that when the total lung V_{20Gy} reaches 25%, there is a very little chance of pneumonitis. Asakura et al.[17] reported that V_{20Gy} of >37% is a risk factor for radiation pneumonitis in RT for esophageal cancer. Moreover, D_{mean} in the lungs was reported to be correlated with pneumonitis, with D_{mean} levels of 20-23Gy recommended.[18] In our work, we are successfully able to keep the V_{20Gy} below 37% (3DCRT<RA<IMRT) and mean dose below 20Gy (3DCRT<IMRT<RA) across all three planning techniques. Regarding V_{5Gy} Jo et al.[19] suggested that V_{5Gy} of >65% is a risk factor for pneumonitis in RT for lung lesions. RA plan had highest V_{5Gy} (93.14%) followed by IMRT (81.8%) and 3DCRT (77.39%). Although RA and IMRT planning techniques offer greater target dose painting capabilities, they also irradiate a large amount of lung volume with a large number of low doses.

Numerous studies have found significant radiation-induced heart damage when the heart received more over 40Gy, and that lowering V_{40Gy} was important in reducing heart toxicities. Pao et al.[18] found that V_{30} of more than 33% and D_{mean} of more than 20Gy strongly linked with all grades of cardiac effusion in IMRT for esophageal cancer. In their investigation, V_{30Gy} of more than 65% and V_{40Gy} of more than 55% was important predictor of grade 3 or higher cardiac effusion. According to Wei et al.,[20] V_{30Gy} of 46% and D_{mean} of <26Gy were connected to the retention of cardiac effusion after chemo- RT for esophageal cancer. In our work except 3DCRT we are able to achieve the V_{30Gy} <46% in IMRT and RA plan. In comparison to 3DCRT, IMRT, and RA plans reduced V_{30Gy} by 49% and 60%, respectively. Furthermore, 3DCRT plans are unable to meet the target of heart mean dose of <26Gy. While, IMRT and RA plans were able justify the heart mean dose tolerance.

The spinal cord is a dose-restricted organ in the case of EC, and it should be kept out of the field of radiation when the neck, thorax, abdomen, and pelvis are all being treated. Kirkpatrick et al.[21] reported that a conventional fraction dose of 2Gy per day with a total spinal cord dose of 50Gy, 60Gy, and 69Gy was associated with a 0.2%, 6%, and 50% rate of myelopathy. We kept maximum dose for spinal cord as 50Gy. The highest dose to the spinal cord was well within the maximum dose of 50Gy for the 3DCRT, IMRT, and RA planning techniques. In our study, in comparison to the 3DCRT plan, the maximum spinal cord dose was reduced by 14.4% and 23.1% in the IMRT and RA plans, respectively. With IMRT and RA, the spinal cord received doses that were considerably below its toxicity limit (Fig. 5).

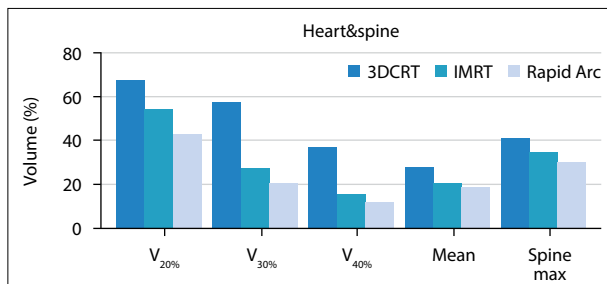


Fig. 5. The volumetric DVH comparison for Heart and spinal cord between 3DCRT, IMRT, and RA plans. 3DCRT: Three-dimensional conformal radiation therapy; IMRT: Intensity-modulated radiation therapy; DVH: Dose volume histogram.

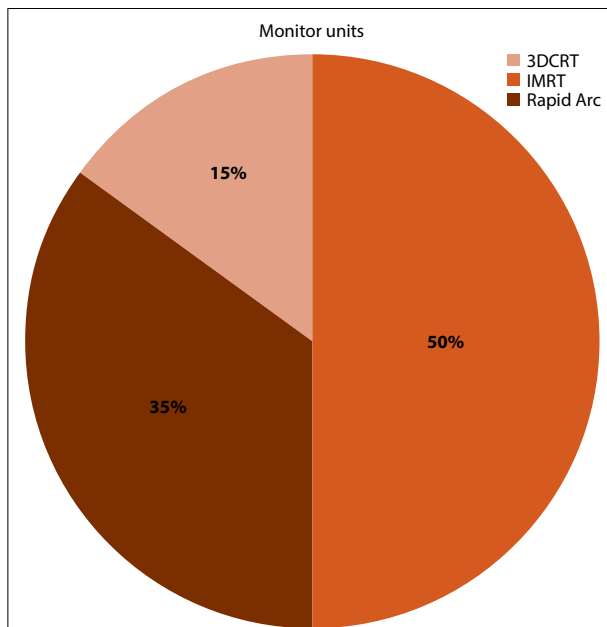


Fig. 6. The average MU distribution for 3DCRT, IMRT, and RA plans. MU: Number of monitor unit; 3DCRT: Three-dimensional conformal radiation therapy; IMRT: Intensity-modulated radiation therapy.

Scattered dose is directly related to MU number. In comparison to IMRT and RA, 3DCRT plans had the lowest MU in our study. When compared to 3DCRT, IMRT, and RA treatment plans utilize up to 3 times as many MUs (Fig. 6). The BOT is related to the amount of MU delivered in fractions. Because 3DCRT plans have a lower MU, they have a lesser BOT as compared to IMRT and RA plans. As a result, patients spend less time inside the treatment room and are more comfortable on treatment couch during treatment delivery.

CONCLUSION

According to the findings of this study, IMRT and RA provided improved PTV coverage in terms of CI, CN, HI, and lower OARs doses to the heart and spinal cord when compared to 3DCRT, but at the expense of increased average dosage and higher V_{5Gy} , V_{10Gy} dose to the lung. The normal MU ratio between the IMRT plan and the 3DCRT plan is 2-3. This adds to greater leakage radiation and, as a result, an increased dose to normal tissue and the entire body in general. As a result, IMRT and RA, in particular, can allow dose escalation in the treatment of EC as long as lung dose and low radiation to adjacent healthy tissues are successfully reduced.

Peer-review: Externally peer-reviewed.

Conflict of Interest: All authors declared no conflict of interest.

Financial Support: None declared.

Authorship contributions: Concept – D.K.S., G.G., S.S., S.Y., N.P.; Design – D.K.S., S.S., S.Y.; Supervision – S.S., D.K.S., S.Y., N.P.; Funding – None; Materials – None; Data collection and/or processing – D.K.S., S.S., S.Y.; Data analysis and/or interpretation – D.K.S., S.S., S.Y., N.P.; Literature search – D.K.S., G.G., S.S., S.Y.; Writing – D.K.S., S.Y.; Critical review – D.K.S., G.G., S.S., S.Y., N.P.

REFERENCES

1. National Cancer Institute Surveillance, Epidemiology, and End Result Program. Cancer Stat Facts: esophageal cancer (2017). Available at: <https://seer.cancer.gov/statfacts/html/esoph.html>. Accessed Aug 22, 2022.
2. Minsky BD, Pajak TF, Ginsberg RJ. INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combined-modality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy. *J Clin Oncol* 2002;20(5):1167–74
3. Ilson DH, Moughan J, Suntharalingam M, Dicker A, Kachnic LA, Konski AA. RTOG 0436: A phase III trial evaluating the addition of cetuximab to paclitaxel, cisplatin, and radiation for patients with esophageal cancer treated without surgery. *J Clin Oncol* 2014;32:15_suppl:4007.
4. Palma D, Vollans E, James K, Nakano S. 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.
5. Lin JC, Tsai JT, Chang CC. Comparing treatment plan in all locations of esophageal cancer: volumetric mod-

- ulated arc therapy versus intensity-modulated radiotherapy. *Medicine (Baltimore)* 2015;94(17):e750.
6. Choi KH, Kim J, Lee SW. Dosimetric comparison between modulated arc therapy and static intensity modulated radiotherapy in thoracic esophageal cancer: a single institutional experience. *Radiat Oncol J* 2018;36(1):63–70.
 7. Wu Z, Xie C, Hu M. Dosimetric benefits of IMRT and VMAT in the treatment of middle thoracic esophageal cancer: is the conformal radiotherapy still an alternative option? *J Appl Clin Med Phys* 2014;15(3):93–101.
 8. Vivekanandan N, Sriram P, Kumar SA. Volumetric modulated arc radiotherapy for esophageal cancer. *Med Dosim* 2012;37(1):108–13.
 9. Hodapp N. The ICRU Report 83: prescribing, recording and reporting photon-beam intensity-modulated radiation therapy (IMRT). *Strahlenther Onkol* 2012;188(1):97–9.
 10. van't Riet A, Mak AC, Moerland MA, Elders LH, van der Zee W. A conformation number to quantify the degree of conformality in brachytherapy and external beam irradiation: application to the prostate. *Int J Radiat Oncol Biol Phys* 1997;37(3):731–6.
 11. Pyakuryal A, Myint WK, Gopalakrishnan M, Jang S, Logemann JA, Mittal BB. A computational tool for the efficient analysis of dose-volume histograms from radiation therapy treatment plans. *J Appl Clin Med Phys* 2010;11(1):3013.
 12. Fenkell L, Kaminsky I, Breen S. Dosimetric comparison of IMRT vs. 3D conformal radiotherapy in the treatment of cancer of the cervical esophagus. *Radiat Oncol* 2008;89(3):287–91.
 13. Nutting C, Dearnaley DP, Webb S. Intensity modulated radiation therapy: a clinical review. *Br J Radiol* 2000;73(869):459–69.
 14. Allehyani SH, Sharyan HA, Tolba AR. 3DCRT versus RapidArc in terms of iso-dose distribution, dose volume histogram (DVH) and organs at risk for esophageal cancer (EC) dosimetric study. *AJECR* 2017;5(4):123–33.
 15. Zhang Y, Wang H, Huang X. Dosimetric comparison of TomoDirect, helical tomotherapy, VMAT, and IMRT for upper thoracic esophageal carcinoma. *Med Dosim*. 2019 Summer; 44(2):167–72.
 16. Mary VG, Purdy JA, Emami B. Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non-small cell lung cancer (NSCLC). *Int J Radiat Oncol Biol Phys* 1999;45(2):323–9.
 17. Asakura H, Hashimoto T, Zenda S. Analysis of dose-volume histogram parameters for radiation pneumonitis after definitive concurrent chemo-radiotherapy for esophageal cancer. *Radiat Oncol* 2010;95(2):240–4.
 18. Pao TH, Chang WL, Chiang NJ, Lin CY, Lai WW, Tseng YL, et al. Pericardial effusion after definitive concurrent chemotherapy and intensity modulated radiotherapy for esophageal cancer. *Radiat Oncol* 2020;15(1):48.
 19. Jo IY, Kay CS, Kim JY. Significance of low-dose radiation distribution in development of radiation pneumonitis after helical-tomotherapy-based hypofractionated radiotherapy for pulmonary metastases. *J Radiat Res* 2014;55(1):105–12.
 20. Wei X, Liu HH, Tucker SL. Risk factors for pericardial effusion in inoperable esophageal cancer patients treated with definitive chemoradiation therapy. *Int J Radiat Oncol Biol Phys* 2008;70(3):707–14.
 21. Kirkpatrick JP, van der Kogel AJ, Schultheiss TE. Radiation dose-volume effects in the spinal cord. *Int J Radiat Oncol Biol Phys* 2010;76(3 Suppl):S42–9.