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Dosimetric Study of Coplanar and Non-Coplanar Intensity-Modulated Radiation Therapy Planning for Esophageal Carcinoma*

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ABSTRACT

Purpose: To compare the dosimetric impact of coplanar intensity modulated radiation therapy (IMRT) and non-coplanar IMRT for the esophageal carcinoma. **Methods:** There are forty-five esophageal carcinoma patients, fifteen of whom were cervical and upper thoracic (Group 1) and thirty were middle and lower thoracic (Group 2). Gross tumor volume (GTV), clinical target volume (CTV), and organs at risk (OAR) were contoured by the chief physician in the CMS-XiO treatment planning system. For each patient, one coplanar plan and two non-coplanar plans have been created using the same physical objective function. A detailed dose-volume histogram (DVH) comparison among three plans was then carried out in a tabulated format. **Results:** 1) In Group 1 patients with PTV volume less than 100cc, the mean dose and dose gradient of non-coplanar plan were much better than those in coplanar plan. 2) In Group 2 patients, the conformity index (CI) for coplanar and two non-coplanar plans were 0.69 ± 0.13, 0.41 ± 0.13, and 0.68 ± 0.15, respectively. The V5, V10, V20, and the mean dose to the lung were lower in the non-coplanar plans compared to ones in coplanar plan. However, the non-coplanar plans resulted in an increase in a dose to the heart, but the dose was still within heart toxicity tolerance. **Conclusion:** For Group 1 patients, the non-coplanar IMRT plan had less dose gradient and better mean dose than the coplanar IMRT plan. For Group 2 patients, the non-coplanar IMRT could the decrease dose to the lung tissue, thus lowering the probability of radiation pneumonia to esophageal cancer patients. The drawback of non-coplanar IMRT is that, even within toxicity tolerance, it could deliver a higher dose to the heart and spinal cord compared to the coplanar plan. Therefore, for patients with cardiology and neurology concern, non-coplanar IMRT should be used with caution.

Keywords: Esophageal Carcinoma; Coplanar IMRT; Non-Coplanar IMRT

1. Introduction

Radiotherapy is the primary treatment modality for the inoperable or unresectable esophageal carcinoma. The goal of radiotherapy for esophageal cancer is to kill the cancer cell inside the target volume while sparing the normal tissues. In the recent years, intensity-modulated radiation therapy (IMRT) has been broadly used in treating esophageal carcinoma [1]. IMRT has been proven to be superior to Three Dimensional Conformal Radiotherapy (3DCRT) with respect to dose conformity in Planning Treatment Volume (PTV) and the normal tissue preservation [2,3]. However, depending on the volume and location of the esophageal cancer tumor, the normal lung tissue may be exposed to high doses of radiation. Several studies have shown that the incidence and severity of radiation pneumonia were related to the irradiation to normal lung tissue in esophageal carcinoma radiotherapy. For instance, Wang *et al.* [4] found that, among 100 patients, 49% of them have developed various severity pneumonia, in whom 27% have grade 1, 16% have grade 2, 6% have grade 3 pneumonia. From a clinical aspect, decreasing the side effect of radiotherapy is another way to improve the survival rate.

Since non-coplanar IMRT plan usually takes longer treatment planning time and it requires complex patient setup and treatment, the majority of the esophageal carcinoma cases are treated by coplanar IMRT, and clinicians have yet to explore the feasibility of non-coplanar IMRT in treating esophageal cancer. The main purposes

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of this study were to optimize the treatment approach for the esophageal cancer and improve the treatment quality by investigating the dosimetric impact of non-coplanar IMRT in our hospital. Additionally, this study aims to establish radiotherapy treatment strategies for future clinical trials, especially for esophageal carcinoma.

2. Methods and Materials

2.1. Patient Selection

Forty-five patients with esophageal carcinoma were enrolled in this study. Fifteen of them had cervical and upper thoracic tumors (Group 1), and the remaining thirty patients had middle and lower thoracic section tumors (Group 2). Median age of patients was 61 years (range, 48 - 72 years), and the median PTV was 114.98cc (range, 30.7cc - 235.12cc). All patients in this study had tumors located away from the distal esophagus and gastro-esophageal junction.

2.2. Simulation

Both the Groups 1 and 2 patients were simulated in a supine position under the thermoplastic mask immobilization of the head, neck and shoulders. Patients were simulated on a computed tomography (CT) scanner (Somotom-sensation Plus-16) using slice thickness of 5-mm from mandible to the costophrenic angle. This extended CT scan volume was used to fully visualize the non-coplanar beams in treatment planning system (TPS). The acquired CT images covered the entire thorax and upper abdomen. The CT images were then transferred to the TPS via a local area network.

2.3. Contouring

The gross tumor volume (GTV) was contoured by a radiation oncologist. The clinical target volume (CTV) was expanded with a 0.5 cm in radial direction and a 3 to 5 cm superior-inferior direction, which followed our clinical guidelines. The PTV was defined as an additional 0.5 cm expansion around the CTV. The organ at risk (OAR) included the spinal cord, lung, and heart.

2.4. Treatment Planning

For each patient, one coplanar IMRT plan (referred as *Plan A*) and two non-coplanar IMRT plans (referred as *Plan B and C*) were created in the XiO TPS, version 4.40 (ELEKTA, CMS St Louis, USA). Specifically, the coplanar plan (*Plan A*) was considered as the reference plan with three to five beams arrangement. For Group 1 patients, if the plan A has three beams, we used the beam setup of one posterior-anterior (PA) and two anterior-oblique (AO) beams (gantry angle at 180˚ ± 10˚, 50˚ ± 10˚, and 310˚ ± 10˚). If it is a four-beam *Plan A*, we used one PA, one anterior-posterior (AP), and two AO (gantry angle at 0˚, 50˚ ± 10˚, 230˚ ± 10˚, and 310˚ ± 10˚). Similarly, five-beam *Plan A* consisted of one AP, two AO, and two PO beams (gantry angle at 0˚, 50˚ ± 10˚, 130˚ ± 10˚, 230˚ ± 10˚, and 310˚ ± 10˚).

For Group 2 patients, if it is a three-beam *Plan A*, one AP and two PO (gantry angle at 0˚, 130˚ ± 10˚, and 230˚ ± 10˚) were used; if it is four-beam *Plan A*, one PA, one AP, and two AO or one parallel-opposed oblique beams (gantry angle at 0˚ and/or 180˚, 50˚ ± 10˚ and/or 310˚ ± 10˚, 130˚ ± 10˚ and/or 230˚ ± 10˚) were used; if it is five-beam *Plan A*, one AP, one PA, two AO, and one PO beams (gantry angle at 0˚, 50˚ ± 10˚, 130˚ ± 10˚, 180˚ ± 10˚, and 310˚ ± 10˚) were used. The couch angle was always set to 0˚.

For each patient case, the non-coplanar *Plan B* was morphed from the reference *Plan A* by converting one or two of the coplanar beams in *Plan A* into the non-coplanar beam/s. For *Plan B*, the total beams of 3 to 5 were used, and the gantry angle of the non-coplanar beam was set to 330˚ or 30˚ or 150˚, and couch angle was set to 90˚. The non-coplanar *Plan C* was using the identical beam parameters as in the *Plan B*, with addition of two more non-coplanar beams with gantry angles of 330˚ and 30˚, thus, making the total of 5 to 7 beams in *Plan C*.

All the IMRT plans were generated using 6 mega-voltage (MV) X-ray beam. The intermediate dose prescribed to the PTV was 60 Gy in 30 fractions. Dose to the OARs, such as the lung, spinal cord, and heart, were minimized to the acceptable tolerances. The treatment planning was done with an objective of meeting the planning criteria: Dose to the 95% (D95%) of the PTV volume receives the prescribed dose (60 Gy); D100% of the PTV is greater than 57 Gy; D5% of PTV is less than 63 Gy. The spinal cord dose was limited to 45 Gy for 0.1cc. For the total lung, the V_5, V_{20}, and mean dose were expected to be lower than the 50%, 25%, and 13 Gy, respectively (in absolute percentage of the lung volume at 5 and 20 Gy). For the heart, the planning goals were to keep V_{40} less than 40% and mean dose less than 30 Gy (in absolute percentage of the heart volume). All the plans were calculated using superposition algorithm with a dose calculation grid size of 0.2 cm.

2.5. Plan Evaluation

Each plan was evaluated with respect to the dose distribution, dose-volume histograms (DVHs), and additional dosimetric parameters described below. Comparisons of treatment plans were based on doses delivered to the PTV and OARs. The dose distribution of PTV was assessed by evaluating the maximum dose, mean dose, and minimum dose.

To evaluate the plan quality with respect to the dose delivered to the tumor, the conformity index (CI) and heterogeneity index (HI) were computed.

$$CI=\frac{VT_{ref}}{VT}\times\frac{VT_{ref}}{V_{ref}} \quad (1)$$

where, VT is the volume of PTV; VT_{ref} is the volume of PTV enclosed by the 95% prescription isodose cloud; V_{ref} is enclosed by the 95% prescription isodose cloud. The CI is usually 0 - 1, with a larger value indicating better conformity.

$$HI=\frac{D_{5\%}}{D_{95\%}} \quad (2)$$

where, $D_{5\%}$ and $D_{95\%}$ correspond to the dose delivered to 5% and 95% volume of the PTV, respectively. Greater HI values indicate doses exceeding the prescription dose and, thus, a greater degree of dose heterogeneity in the PTV.

To evaluate the effect of IMRT on normal lung tissue, heart, and spinal cord irradiation, we computed several different dosimetric indices, including V_5, V_{10}, V_{20}, and V_{30} for the normal lung and mean dose delivered to the normal lung (MLD). The rationale behind using V_5-V_{30} for the normal lung evaluation in comparing the different plans was based on observations that lung tissue tends to have a low dose tolerance. We also calculated V_{30}, V_{40}, V_{45}, V_{50}, and V_{55} for the heart, as well as mean dose and D_{1cc} volume of spinal cord dose.

2.6. Statistical Analysis

The different plans were compared using mean statistics.

Quantile-quantile plots showed the data to be approximately normally distributed, so the differences between means were tested for significance using a two-tailed paired Student's t-test. The null hypothesis was that there was no difference between the coplanar IMRT technique and the non-coplanar IMRT treatment techniques. Statistical significance was set at $P < 0.05$.

3. Results

3.1. Group 1 Patients

Table 1 shows the doses to the PTV, CI, and HI for three different IMRT plans (*A*, *B* and *C*). The results showed that all three different plans are very similar. We further classify this group patient into two sections based on the PTV volume: First section includes the patients with PTV volume less than 100cc, and the second section consisted of patients with PTV volume greater than 100cc. In the section with PTV volume less than 100cc, the PTV mean doses (cGy) were 6528.33 ± 286.93, 6354.00 ± 270.87, 6354.00 ± 270.87 for *Plans A*, *B* and *C*, respectively. The PTV mean dose of *Plan B* was closest to the prescription dose and showed statistical difference compared with *Plan A* ($P = 0.037$). The HI of *Plan B* was closest to 1, and showed statistical difference compared with *Plan A* ($P = 0.020$). More detailed comparisons of the *Plan A*, *B*, and *C* are presented in **Table 2**.

3.2. Group 2 Patients

Table 3 shows that the CI for *Plans A*, *B*, and *C* were 0.69 ± 0.13, 0.41 ± 0.13 and 0.68 ± 0.15, respectively. The CI of plan B was the lowest and had statistical difference compared to the reference *Plan A* ($P = 0.000$). *Plan C* and *Plan A* has no statistical difference ($P = 0.807$). More detailed comparisons of the three plans are presented in **Table 3**.

The OAR analysis is presented in **Table 4**, **Figure 1**, and **Figure 2**. The results showed that the lung V_5(%), V_{10}(%), V_{20}(%), V_{30}(%), and mean lung dose (MLD) (cGy) of reference *Plan A* were 42.33 ± 8.24, 29.65 ± 8.57, 15.71 ± 4.42, 7.66 ± 4.74, and 882.70 ± 191.83, respectively. The results were consistent with the finding from the isodose distribution as lung V_5(%), V_{10}(%), V_{20}(%), V_{30}(%), and MLD (cGy) were reduced to 16.27, 10.59, 5.81, 2.35 and 248 using the *Plan B* ($P < 0.000$).

Table 5 shows the dosimetric results of the heart. The V_{30}(%),V_{40}(%), V_{45}(%), V_{50}(%), V_{55}(%), and MLD (cGy) of *Plan A* were 19.00 ± 10.23, 13.00 ± 11.98, 9.09 ± 9.35, 5.88 ± 6.46, 3.30 ± 5.02, and 1729.71 ± 1025.13, respectively. Compared to these values in *Plan A*, the *Plans B* had an increase of 11.05 for V_{30}(%), 9.79 for V_{40}(%), 7.84 for V_{45}(%), 5.86 for V_{50}(%), 4 for V_{55}(%), and 626.94 for MLD with statistical significance ($P < 0.05$). Additionally, when compared to the *Plan A*, the *Plan C* also showed an increment in V_{30}(%), V_{40}(%), V_{45}(%), but not in V_{50}(%), V_{55}(%), and MLD when a non coplanar field was used. The spinal cord D1cc（cGy）of reference *Plan A* was 3127.36 ± 740.8. Compared to *Plan A*, both the *Plan B* and *C* had slightly higher dose; however, all sets of plans had D1cc ≦ 4500 cGy for the spinal cord.

4. Discussion

In external beam radiation therapy, the choice of beam parameters plays an important role when we optimize the IMRT treatment plan. The selection of beam angle is particularly important as the beam angle directly affects the patient setup and treatment plan quality, especially in the cases where the tumor target is wrapped around multiple OARs [5].

Beam angle selection in IMRT plan optimization has been investigated by several institutions [5-8]. Allen [9] and Tucker [10] reported that non-coplanar IMRT significantly can improve the dose distribution when tumor is close to the spinal cord. Bedford *et al.* [11] reported that the use of inverse planning algorithm to generate 3 to 6 beam non-coplanar plans without intensity-modulation could provide better rectal sparing in conformal prostate plan compared to a three-field coplanar plan. Olivier *et al*. [12]

Table 1. Averaged dosimetric results of target volume in Group 1 patients.

	D_{max} (cGy)	D_{min} (cGy)	D_{mean} (cGy)	CI	HI
Plan A	6810.51 ± 777.00	5096.70 ± 930.80	6239.52 ± 623.31	0.76 ± 0.17	1.11 ± 0.08
Plan B	6616.70 ± 470.80	5144.51 ± 1021.33	6191.50 ± 569.60	0.75 ± 0.19	1.09 ± 0.06
Plan C	7012.22 ± 821.00	5222.73 ± 917.21	6339.74 ± 645.13	0.80 ± 0.10	1.14 ± 0.08
T value	1.13^{*} - $0.76^{\#}$	-0.67^{*} - $4.11^{\#}$	1.46^{*} - $0.87^{\#}$	0.65^{*} - $0.79^{\#}$	1.14^{*} - $0.80^{\#}$
P value	0.340^{*} $0.498^{\#}$	0.546^{*} $0.054^{\#}$	0.240^{*} $0.448^{\#}$	0.561^{*} $0.484^{\#}$	0.334^{*} $0.479^{\#}$

Note:* = *Plan B* compared with *Plan A*; # = *Plan C* compared with *Plan A.*

Table 2. Average dosimetric results of PTV less than 100cc in Group 1 patients.

	D_{max} (cGy)	D_{min} (cGy)	D_{mean} (cGy)	CI	HI
Plan A	7119.66 ± 576.36	5391.00 ± 883.36	6528.33 ± 286.93	0.73 ± 0.19	1.11 ± 0.06
Plan B	6797.33 ± 370.04	5424.00 ± 1046.88	6354.00 ± 270.87	0.72 ± 0.21	1.08 ± 0.04
Plan C	7385.66 ± 418.06	5535.00 ± 822.72	6661.66 ± 49.16	0.79 ± 0.12	1.13 ± 0.07
T value	2.01^{*} - $0.73^{\#}$	0.33^{*} - $4.11^{\#}$	5.05^{*} - $0.85^{\#}$	0.38^{*} - $0.98^{\#}$	3.34^{*} - $1.44^{\#}$
P value	0.182^{*} $0.537^{\#}$	0.767^{*} $0.054^{\#}$	0.037^{*} $0.483^{\#}$	0.736^{*} $0.429^{\#}$	0.020^{*} $0.209^{\#}$

Note: * = *Plan B* compared with *Plan A*; $^{\#}$ = *Plan C* compared with *Plan A.*

Table 3. Averaged dosimetric results of target volume in Group 2 patients.

	D_{max} (cGy)	D_{min} (cGy)	D_{mean} (cGy)	CI	HI
Plan A	6198.00 ± 1155.47	4413.53 ± 965.83	6230.32 ± 1171.13	0.69 ± 0.13	1.08 ± 0.04
Plan B	6156.21 ± 1021.97	4484.68 ± 1020.97	5382.15 ± 980.93	0.41 ± 0.13	1.09 ± 0.03
Plan C	6230.32 ± 1171.13	4482.15 ± 980.93	5828.52 ± 1053.96	0.68 ± 0.15	1.09 ± 0.05
T value	0.80^{*} - $1.40^{\#}$	-0.79^{*} - $1.50^{\#}$	2.00^{*} $1.01^{\#}$	7.98^{*} $0.24^{\#}$	-0.80^{*} - $0.80^{\#}$
P value	0.432^{*} $0.178^{\#}$	0.438^{*} $0.149^{\#}$	0.064^{*} $0.326^{\#}$	0.000^{*} $0.807^{\#}$	0.434^{*} $0.434^{\#}$

Note: * = *Plan B* compared with *Plan A*; $^{\#}$ = *Plan C* compared with *Plan A.*

Table 4. Averaged dosimetric results of normal lung tissue in Group 2 patients.

	V_5 (%)	V_{10} (%)	V_{20} (%)	V_{30} (%)	MLD (cGy)
Plan A	42.33 ± 8.24	29.65 ± 8.57	15.71 ± 4.42	7.66 ± 4.74	882.71 ± 191.83
Plan B	26.06 ± 10.14	19.06 ± 8.50	9.90 ± 5.03	5.31 ± 3.32	634.00 ± 244.85
Plan C	40.04 ± 7.83	25.51 ± 7.85	12.88 ± 5.18	5.05 ± 4.02	775.94 ± 186.12
T value	7.53^{*} $3.66^{\#}$	5.82^{*} $5.07^{\#}$	6.97^{*} $4.09^{\#}$	2.37^{*} $4.39^{\#}$	6.86^{*} $6.64^{\#}$
P value	0.000^{*} $0.002^{\#}$	0.000^{*} $0.000^{\#}$	0.000^{*} $0.001^{\#}$	0.020^{*} $0.000^{\#}$	0.000^{*} $0.000^{\#}$

Note: * = *Plan B* compared with *Plan A*; $^{\#}$ = *Plan C* compared with *Plan A.*

Table 5. Averaged dosimetric results heart in Group 2 patients.

	V_{30} (%)	V_{40} (%)	V_{45} (%)	V_{50} (%)	V_{55} (%)
Plan A	19.00 ± 10.23	13.00 ± 11.98	9.09 ± 9.35	5.88 ± 6.46	3.30 ± 5.02
Plan B	30.05 ± 15.35	22.79 ± 17.34	16.93 ± 13.15	11.74 ± 10.12	7.30 ± 8.95
Plan C	21.14 ± 13.83	15.85 ± 14.52	10.80 ± 10.27	6.39 ± 7.14	3.73 ± 5.56
T value	-5.32^{*} - $2.25^{\#}$	-5.36^{*} - $2.23^{\#}$	-5.99^{*} - $2.87^{\#}$	4.88^{*} - $2.05^{\#}$	-3.43^{*} - $1.25^{\#}$
P value	0.000^{*} $0.020^{\#}$	0.000^{*} $0.043^{\#}$	0.000^{*} $0.010^{\#}$	0.000^{*} $0.061^{\#}$	0.004^{*} $0.225^{\#}$

Note: * = *Plan B* compared with *Plan A*; $^{\#}$ = *Plan C* compared with *Plan A.*

found that using non-coplanar fields in three-dimensional conformal radiotherapy (3DCRT) and IMRT can dramatically reduces the dose to the heart in irradiation of middle and lower lung tumors. Liu *et al.* [13] compared and analyzed the 3DCRT plans with coplanar beam anterior field and non-coplanar beam anterior field, as well as

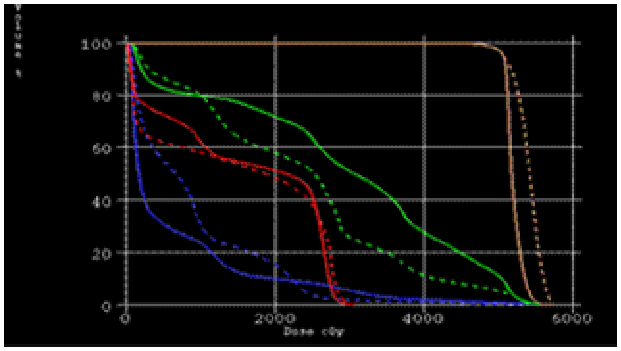

Figure 1. Discrepancy between *Plan B* and *Plan A* in Group 2 patients (Note: Dashed line = *Plan B*; Solid line = *Plan A*. Brown = PTV, Green = Heart, Red = Spinal cord, Blue = Lungs).

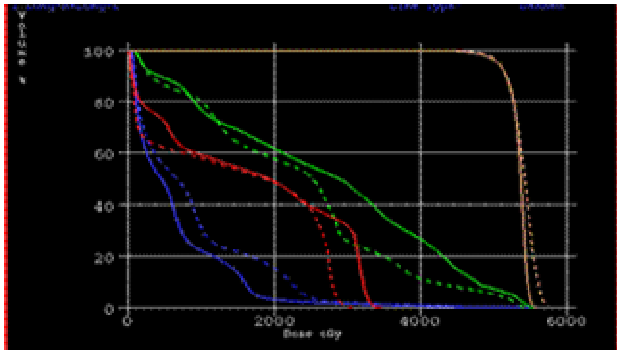

Figure 2. Discrepancy between *Plan C* and *Plan A* in Group 2 patients (Note: Dashed line = *Plan B*. Solid line = *Plan A*, Brown = PTV, Green = Heart, Red = Spinal cord, Blue = Lungs).

assess the dose distribution in the planning target volume PTV and OARs in treating thoracic esophagectomy under the conditions of the PTV length 19 cm. That study [13] found that the use of non-coplanar beam can get better dose distribution on target area and reduce the dose to spinal cord.

To date, this is the first study, which investigates the dose distribution around esophageal target and OARs in the coplanar IMRT and non-coplanar IMRT in detail for a large group of patients (n = 45). In our study, for Group 1 patients, we found that *Plan B* produced the mean PTV dose close to the prescribed dose and HI was also closer to 1. It showed some potential benefit of using non-coplanar IMRT plan as non-coplanar beam can reduce the effect of the dose distribution to the body surface to some extent, especially when the target volume is relatively small (<100cc).

Radiation pneumonitis is the main factor to limit clinical therapeutic effect and our goal was to reduce the irradiation to the lung. Graham [14] found that the incidence and degree of radiation pneumonitis are closely correlated with radiation volume and dose. There was a significant association between the degree of the radiation pneumonitis and the V_{20}, V_{30}, and mean dose of lung. Meanwhile, Allen *et al*. [15] and Tucker *et al*. [16] found that, with the increase of V_5, the mortalition of radiation pneumonitis will increase. In our study, non-coplanar IMRT plans could be an effective tool to reduce irradiation volume of lung. However, as shown for *Plan B*, reduction in the irradiation of lung may also reduce the conformality of plan. The reason we found that, compare to *Plan A*, the volume of PTV enclosed by the 95% prescription isodose cloud was similar, but the 95% prescription isodose cloud significantly increase. Using *Plan C*, it was possible to limit the irradiation of lung without reducing the conformality of plan.

We also found that non-coplanar IMRT plans increased the dose to the heart while reducing dose to the lung. In comparing our data with those from other studies on prediction of radiation injury of the heart, we found that two types of non-coplanar IMRT plans investigated in this study can meet the heart clinical constraints, which traditionally have been considered acceptable [17, 18]. Based on these results, it clearly appears that non-coplanar IMRT *Plan C* provided better benefit. It will decrease the severe acute toxicity of lung without creating the radioactivity injury of heart.

In our treatment planning study, the delivery technique was limited to the IMRT. Currently, the volumetric intensity modulated arc therapy (VMAT) technique is available for the treatment of cancer. The VMAT is gaining more popularity since VMAT requires less number of monitor units and treatment time when compared to IMRT. Recently, Rana *et al.* utilized the VMAT planning technique on esophageal cancer treatment plans to investigate the impact of dose calculation algorithms in terms of dosimetric [19] and radiobiological study [20]. The findings from those studies [19,20] of Rana *et al.* showed that the VMAT has a great potential of reducing dose to the lung tissue and heart while providing adequate target coverage for the esophageal cancer patients. Since Rana *et al.* [19,20] used the coplanar arcs in their studies, it would be interesting to further investigate the impact of non-coplanar arcs on dosimetric results of esophageal cancer treatment plans generated by the VMAT technique.

5. Conclusion

For cervical and upper thoracic (Group 1) patients, the non-coplanar IMRT plan had less dose gradient and better mean dose than the coplanar IMRT plan. For mid- dle and lower thoracic (Group 2) patients, the non-coplanar IMRT can decrease the irradiation to the lung, thus lowering the probability of radiation pneumonia to the esophageal cancer patients. The drawback of non-coplanar IMRT is that, even within toxicity tolerance, it will deliver the higher dose to the heart and spinal cord com-

pared to the coplanar IMRT plan. Therefore, for patients with cardiology and neurology concern, non-coplanar IMRT should be used with caution.

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