Comparison of Plan Quality Metrics after Left Anterior Descending Coronary Artery Sparing in VMAT Esophageal Radiotherapy

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ABSTRACT

Cardiotoxicity is a significant late effect of esophageal radiotherapy (RT). Mean heart dose has been implicated with major adverse cardiac events (MACE) and emerging evidence increases MACE association with left anterior descending (LAD) coronary artery specific dose.[3] This retrospective planning study investigates the dosimetric impact of including the LAD as an OAR-sparing objective for volumetric modulated arc therapy (VMAT) based plan optimization in patients previously treated with neoadjuvant RT for esophageal cancers.

For each patient, the LAD was delineated and the treated VMAT plan was re-optimized to reduce the dose to the LAD receiving 15 Gy to less than 10%, when possible. Re-plans were performed such that 95% of the PTV received the prescription dose. A paired sample t-test was used to compare the dose between the original VMAT plan used for treatment against those re-optimized, with a significance of $p<0.05$. Aside from increased sparing of the LAD and mean heart dose, there were no statistically significant impacts on target coverage and OARs doses otherwise. Accounting for the LAD dose in treatment planning may help reduce future MACE risks. LAD dose can be reduced without compromising PTV coverage or having significant effects on other OAR dose sparing.

Keywords: *Esophageal Cancer; Major Adverse Cardiac Events; Left Anterior Descending Artery; Cardiac Substructures; Radiotherapy*

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INTRODUCTION

- Major adverse cardiac events (MACE) and toxicities are observable side effects of thoracic radiotherapy.[1]
- The risk of toxicity increases if a patient receives a high mean dose to heart or presents with pre-existing cardiac conditions.[1]
- The current dose constraint to assess the risk of cardiac toxicity in esophageal and esophagogastric junction radiotherapy involves maintaining mean heart dose of less than 30 Gy and heart V30<30 Gy.[2]
- Recent studies associate the left anterior descending coronary artery (LAD) V15 Gy>10% dose with MACE in thoracic radiotherapy.[3] This is relevant to esophageal radiotherapy since these patients typically receive a high radiation dose and the target volume can be located near the heart.
- The primary aim of this study was to investigate whether the LAD V15 Gy dose can be reduced while maintaining 95% coverage of the prescription dose to the planning target volume (PTV) in esophageal cancer patients receiving definitive radiotherapy using IMRT, and without statistically significant impact on organs at risk (OARs) dose, including the heart, spinal cord, and lungs.

METHODS AND MATERIALS

- Nineteen patients who received concurrent chemoradiotherapy with curative intent for esophageal cancer between 2017–2020 at a single institution were selected.
- All patients underwent radiotherapy with volumetric modulated arc therapy (VMAT).
- Doses were calculated using Acuros XB Algorithm or Analytical Anisotropic Algorithm with a 2–2.5mm calculation grid.
- Treatment plans were retrospectively reviewed and the PTV was evaluated for tumor volume coverage. The LAD was manually delineated.
- Treated VMAT plans were re-optimized to reduce the dose to the LAD V15 Gy to less than 10%, when possible.
- The dose calculation algorithm used in the initial plan was also selected in the replan.
- Institutional constraints were used to minimize the dose to the heart, lungs, and spinal cord.
- Re-plans were normalized to receive 95% PTV coverage.
- A paired sample t-test compared the dose between the original VMAT plan used for treatment against those re-optimized, with significance at $p<0.05$.

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	Constraint	Esophagus Original	Esophagus + LAD	*P*-value
PTV D95%	-	95	95	0.35
Maximum hotspot (%)	<110	107.9	107.95	0.36
LAD Dmax (Gy)		24.7	19.6	<0.01*
LAD V15 (%)		32.1	9.0	<0.01*
Heart Dmean (Gy)	<25	21.2	19.6	0.01*
Spinal Cord Dmax (Gy)	<45	35.1	34.7	0.11
Lungs Dmean (Gy)	<12	7.5	7.6	0.05
Lungs V5 (%)	<50	43.7	45.1	0.13
Lungs V10 (%)	<40	26.6	27.5	0.11
Lungs V20 (%)	<15	9.6	9.6	0.16

Table 1. Comparison of the plan quality metrics of the initial plan without LAD sparing (Esophagus Original) and re-plan with LAD sparing (Esophagus + LAD)

RESULTS

- Of those treated, 12 of 19 original plans (63%) exceeded the LAD constraint (V15<10%) with a mean V15 Gy of 47.1%.
- Plan re-optimization shifted the cases from 7 of 19 original plans (37%) passing the LAD V15<10% constraint to 14 of 19 re-optimized plans (74%) passing.
- LAD dmax (Gy) was significantly changed to meet constraints (*P*=<0.01) as well as the LAD V15 (%) (*P*=<0.01) (Table 1).
- The 15Gy isodose line visually pulls away from the LAD, which demonstrates low dose sparing (Figure. 1).
- There were no maximum hotspot differences (*P*=0.36) between treated plans and re-plans. (Table 1).
- Evaluated organs at risk (OARs) included the mean dose of the heart (in Gy), maximum dose of the spinal cord (in Gy), mean dose of the lungs (in Gy), as well as the percentages of lung volumes receiving doses of 5 Gy (lung V5), 10 Gy (lung V10), and 20 Gy (lung V20).
- Aside from the heart mean dose (in Gy), there were no statistically significant changes between plans (*P*>0.05) for all other OARs evaluated.
- The mean heart dose was the only OAR metric that demonstrated a statistically significant dose reduction (*P*=0.01).

DISCUSSION

- LAD V15 dose can be reduced while maintaining target coverage and OARs sparing.
- When the LAD was used as an optimization structure during treatment planning, the LAD V15 dose, LAD max dose, and heart mean dose demonstrated superior sparing compared to the original plans.
- Re-plans showed equivalent target coverage, and there was no significant increase in the maximum hotspot of the plans.
- No other evaluated OARs demonstrated significant differences in sparing.
- LAD V15 is of interest due to its correlation with MACE in other thoracic cancer sites.
- Other studies demonstrate that LAD V30 Gy≥10% is associated with increased MACE in 355 esophageal patients who received neoadjuvant or definitive radiotherapy using IMRT or PBT with a median follow-up of 67 months. The study also found that the dose received by cardiac substructures is more predictive of cardiac toxicity and MACE than the mean heart dose or V30 Gy heart dose.[4]

CONCLUSIONS

- LAD V15 Gy dose can be reduced without impacting the plan quality metrics in esophageal radiotherapy.
- Accounting for the LAD dose during treatment planning may help limit future MACE risks after radiotherapy.
- Future studies should consider additional cardiac substructures as optimization structures. The left circumflex and left ventricle may also be of interest due to their association with adverse cardiac events in other studies.[3]

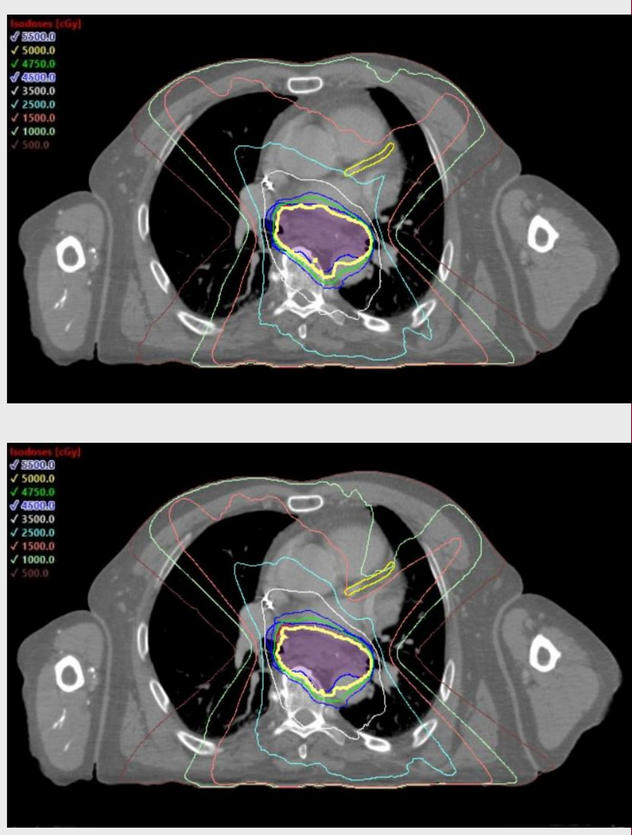

Figure 1. An axial view comparison of an example plan without LAD V15 Gy sparing (top) and with LAD V15 Gy sparing (bottom). The LAD V15Gy line is displayed in pink