



PHYSICS

Validation of the impact of heart base dose on survival in NSCLC patients from the PET-plan trial

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What was your motivation for initiating this study?

The RTOG0617 trial compared standard-dose (60Gy) with high-dose (74Gy) radiotherapy with concurrent chemotherapy and unexpectedly reported poorer survival on the high dose arm. Subsequent multivariable analysis identified two heart dose metrics as predictive of overall survival. This ignited a new area of research focusing on the impact of cardiac dose in lung cancer patients. Dozens of retrospective studies have probed the link between cardiac dose and overall survival, and almost all have reported a significant association, albeit with highly inconsistent dose metrics [1]. The field is now moving from the use of whole heart dose metrics to the superior anatomical specificity that is offered by the analysis of cardiac substructure doses. From a small number of such studies, the base of the heart has been identified as a potential region of enhanced dose sensitivity [2,3]. This study aims to develop the evidence base regarding the importance of heart dose in lung-cancer patients by performing a voxel-wise dosimetric analysis in the patient cohort of the PET†-Plan trial (NCT00697333) and, for the first time, will account for baseline cardiac function. († Positron Emission Tomography)

What is the most important finding of your study?

We identified a dose-sensitive region within the base of the heart that is centred on the origin of the left coronary artery and the region of the atrioventricular node. This result is broadly consistent with the findings of previous studies. Few patients fell into the poor (<50%) ejection fraction group, so definitive conclusions on the impact of baseline cardiac function were not possible. However, the results suggest that heart-base dose remains a modifiable risk factor when accounting for baseline cardiac function.

What are the implications of this research?

Sparing of the base of the heart could lead to an improvement in the short-term survival of NSCLC patients of the order of five months [2]. Planning studies indicate sparing of the heart base is achievable in most patients without exceeding established dose constraints for other organs at risk. Clinical evaluation of cardiac sparing radiotherapy for lung-cancer patients is now required.



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References

1. T. W. Zhang et al., "Is the Importance of Heart Dose Overstated in the Treatment of Non-Small Cell Lung Cancer? A Systematic Review of the Literature," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 104, no. 3, pp. 582–589, 2019, doi: 10.1016/j.ijrobp.2018.12.044.
2. A. McWilliam, J. Kennedy, C. Hodgson, E. Vasquez Osorio, C. Faivre-Finn, and M. van Herk, "Radiation dose to heart base linked with poorer survival in lung cancer patients," *Eur. J. Cancer*, vol. 85, pp. 106–113, 2017, doi: 10.1016/j.ejca.2017.07.053.
3. B. Stam et al., "Dose to heart substructures is associated with non-cancer death after SBRT in stage I-II NSCLC patients," *Radiother. Oncol.*, vol. 123, no. 3, pp. 370–375, 2017, doi: 10.1016/j.radonc.2017.04.017.

