

16-21 months) for left-sided and 15 months (95%CI 13-17 months) for right-sided patients.

Including lung mean doses in the multi-variable analysis resulted in HR 1.02 (95%CI 1.01-1.03, $p=0.03$) for the right lung and for HR 1.00 (95%CI 0.99-1.1, $p=0.65$) the left lung. In this model laterality was no longer significant, indicating it is a surrogate for individual lung mean doses. In both analysis, tumour volume (continuous, $p<0.001$), age (continuous, $p<0.01$), gender ($p<0.04$), performance status (categorical, $p<0.05$) and nodal stage (categorical, $p<0.01$) were also significant.

	Multi-variable		Multi-variable	
	HR (95% CI)	P	HR (95% CI)	P
Tumour volume (continuous)	1.01 (1.00–1.01)	<0.001	1.01 (1.00–1.01)	<0.001
Laterality (right vs. left)	1.25 (1.08–1.48)	<0.01	1.11 (0.84–1.48)	0.45
Left lung mean dose (continuous)			1.00 (0.99–1.01)	0.65
Right lung mean dose (continuous)			1.02 (1.01–1.03)	0.03
Age (continuous)	1.02 (1.01–1.03)	<0.01	1.02 (1.01–1.03)	<0.01
Gender (Male vs. female)	1.18 (1.01–1.38)	0.04	1.19 (1.15–1.39)	0.03
T-stage (T1 reference)				
T2	1.18 (0.92–1.52)	0.19	1.14 (0.87–1.46)	0.33
T3	1.24 (0.95–1.65)	0.11	1.22 (0.93–1.62)	0.16
T4	1.36 (1.01–1.82)	0.04	1.30 (0.97–1.76)	0.08
N-stage (N0 reference)				
N1	0.91 (0.72–1.17)	0.48	0.89 (0.69–1.13)	0.32
N2	1.52 (1.26–1.84)	<0.01	1.41 (1.15–1.74)	<0.01
N3	1.80 (1.32–2.44)	<0.01	1.68 (1.22–2.30)	<0.01
Performance status (PS 0 reference)				
1	1.19 (0.92–1.52)	0.17	1.22 (0.95–1.56)	0.12
2	1.39 (1.08–1.80)	0.01	1.44 (1.11–1.86)	0.01
3	1.43 (1.00–1.52)	0.05	1.49 (1.03–2.16)	0.03

Table 1. Multi-variable cox-regression analysis performed with laterality and common patient and tumour characteristics, without and with left and right mean lung doses. The results show that right-sided lung tumours have significantly worse survival, likely due to dose to the right lung having a more detrimental effect on patient survival.

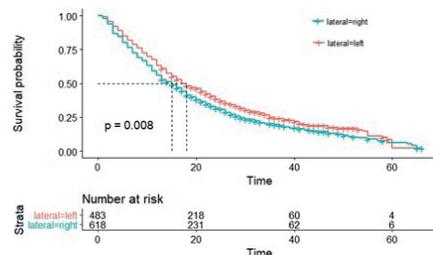


Figure 1. Kaplan-Meier survival curve showing patient survival for patients with left-sided and right-sided lung tumours. Patients with right-sided lung tumours have significantly worse survival than those with left-sided (log-rank $p=0.008$). Median survival times were 18 and 15 months for left-sided and right-sided patients, respectively, while patient and tumour characteristics are well balanced.

Conclusion

To our knowledge, our study is the first to show that laterality has a significant impact on survival of lung cancer patients post curative-intent radiotherapy, with right sided lung tumours showing worse survival. Our analysis indicates the effect of laterality is through a difference in dose-response for individual lungs. The right lung is larger, and the same amount of excess dose, compared to the left lung, has a greater impact on patient survival. These results suggest toxicity of the normal lung tissue may display a serial component, where dose can affect lung function throughout the organ's structure.

PV-0037 Correlation between coronary artery doses and survival in locally advanced lung cancer patients
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Purpose or Objective

It has been demonstrated that irradiating the base of the heart is linked to poorer overall survival (OS) in both early stage and locally advanced non-small cell lung cancer (NSCLC) patients^{1,2}. In this study, we hypothesised that the origin of both coronary arteries are the dose sensitive structure driving this increased mortality. We therefore investigated the correlation between OS and the dose to the origin of the left and right coronary arteries (LCA and RCA) in a large, single-institution cohort.

Material and Methods

Two observers identified the origin of the LCA and RCA on contrast enhanced CT scans from a total of 804 patients treated between 2010 and 2013 with curative-intent radiotherapy (55Gy in 20 fractions). For 167 of 804 patients, LCA and RCA were identified by both observers, allowing intra-observer variation to be calculated. The mean lung dose (MLD) and dose to the origin of RCA and LCA (D_{RCA} , D_{LCA}) were extracted from the radiotherapy plan. These were used in a multivariate survival analysis including patient and tumour characteristics (age, sex, tumour size, TNM stage, induction chemotherapy and performance status). Smoking status was available for less than one third of the cohort and was not included in the analysis. Data on co-morbidities and cause of deaths were not available, so only overall survival was analysed.

Results

Median follow up was 18 months and 623 deaths were recorded. Observers deviated in their identification of the LCA and RCA (average vector length 8 mm). Tumour size, sex, MLD, TNM stage, performance status as well as D_{RCA} and D_{LCA} were significant ($p < 0.05$) on univariate Cox-regression. However, D_{RCA} and D_{LCA} did not remain significant when included in a multivariate analysis (Table 1).

	Univariate analysis	Multivariate analysis		
		HR (95% CI)	p	
Tumour volume (median 27 cm ³)	1.005 (1.004-1.006)	***	1.004 (1.002-1.005)	***
Age (median 74 years)	1.007 (0.999-1.014)	NS		
Sex (421 M, 383 F)	1.22 (1.07-1.40)	**	1.46 (1.20-1.78)	***
Chemo (145 Yes, 659 No)	1.08 (0.92-1.25)	NS		
T stage (140 T1)				
T2 (342)	1.36 (1.10-1.69)	**	1.27 (0.96-1.68)	NS
T3 (155)	1.72 (1.37-2.18)	***	1.41 (1.03-1.95)	*
T4 (92)	1.93 (1.50-2.47)	***	1.53 (1.07-2.18)	*
N stage (N0 493)				
N1 (100)	0.98 (0.79-1.23)	NS	0.75 (0.56-1.01)	NS
N2 (124)	1.63 (1.38-1.91)	***	1.27 (0.99-1.64)	NS
N3 (23)	1.57 (1.19-2.07)	**	1.27 (0.76-2.12)	NS
M stage (750 M0, 31 M1)	1.90 (1.41-2.56)	***	1.92 (1.24-2.30)	**
Performance status (106 PS 0)				
1 (302)	1.29 (1.03-1.60)	*	1.20 (0.15-1.18)	NS
2 (254)	1.32 (1.05-1.66)	*	1.34 (0.15-1.90)	NS
3 (38)	1.69 (1.21-2.35)	**	1.18 (0.25-1.66)	NS
Mean lung dose (median 10.9 Gy)	1.07 (1.05-1.08)	***	1.037 (1.004-1.071)	*
LCA dose (median 11.6 Gy)	1.008 (1.001-1.014)	*	0.993 (0.982-1.004)	NS
RCA dose (median 4.4 Gy)	1.019 (1.009-1.028)	***	1.009 (0.994-1.023)	NS

Table 1: results from the Cox regression analysis. HR: hazard ratio, CI: confidence interval. *** <0.001 , ** <0.01 , * <0.05 , NS: not significant.

Conclusion

Even though the dose to the base of the heart has been linked with survival, in this cohort, the dose to the origin of the coronary arteries was not an independent predictor of OS. However, the inter-observer variation in localising the origin of the LCA and RCA was substantial, suggesting that manual identification of cardiac substructures on planning CT scans is challenging. Future work in our institution will include automatic voxel-based methods to identify the sensitive cardiac substructures in NSCLC patients to explain previous observations.

1. McWilliam et al EJC 2017
2. Stam et al R&O 2017