

Supplemental Online Content

Kim KH, Oh J, Yang G, et al. Association of sinoatrial node radiation dose with atrial fibrillation and mortality in patients with lung cancer. *JAMA Oncol*. Published online September 22, 2022. doi:10.1001/jamaoncol.2022.4202

eMethods

eFigure 1. Representative patient who developed AF after completion of definitive CRT

eFigure 2. Incidence of new onset AF and overall survival according to Heart D_{max}

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eTable 1. Time dependent area under the receiver operating characteristic curve analysis of dose variables for cardiac substructures and atrial fibrillation (AF) in total, SCLC, and NSCLC cohorts

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eTable 8. Cox proportional hazards regression analysis for overall survival in NSCLC cohort using RA D_{max}

This supplemental material has been provided by the authors to give readers additional information about their work.

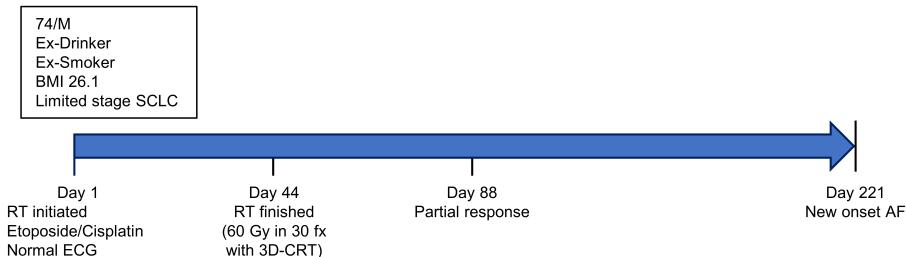
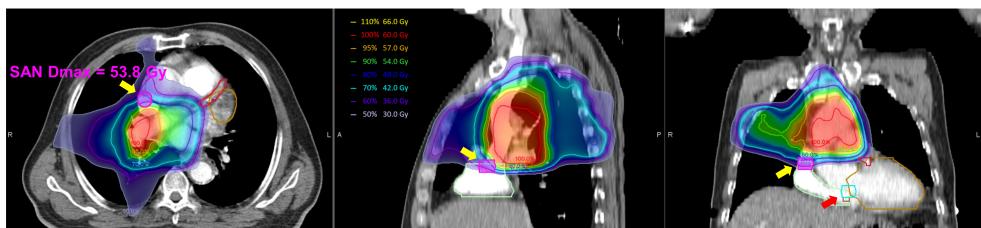
eMethods

Coronary calcium measurement

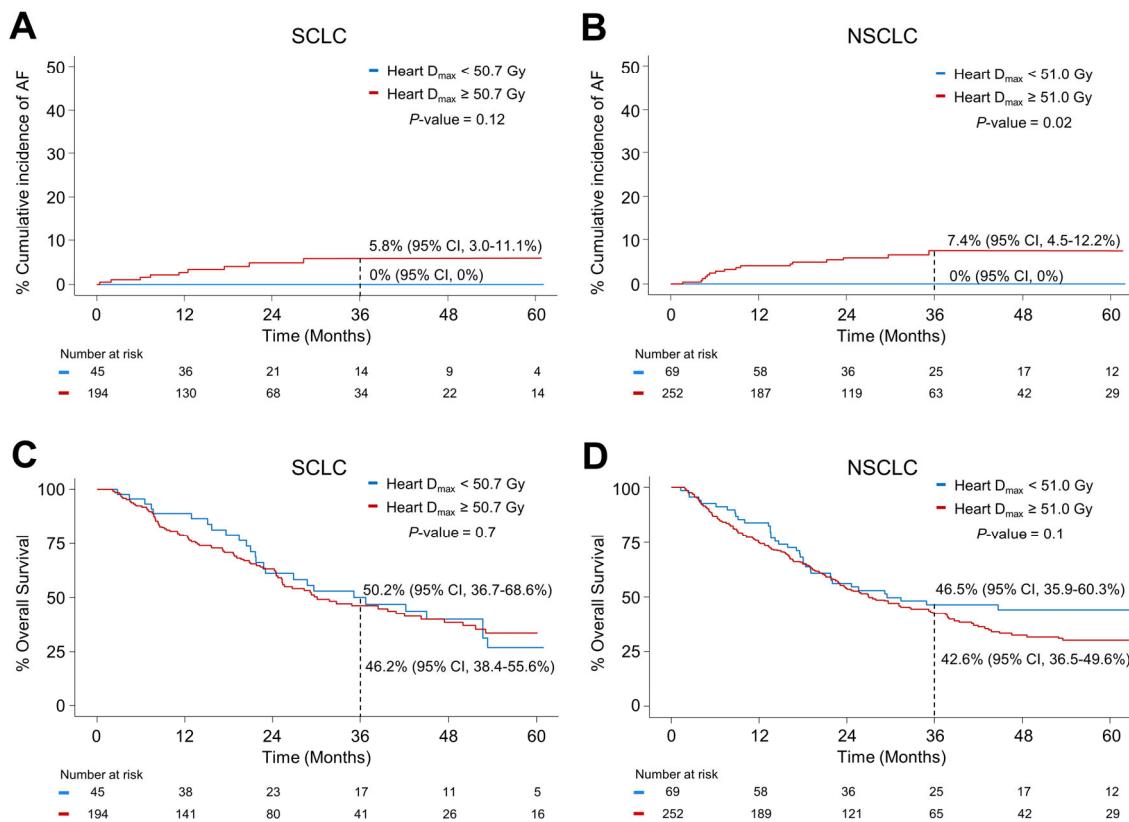
Coronary artery calcium (CAC) was assessed using planning CT scans without contrast enhancement and without electrocardiogram (ECG)-synchronization with slice distances of 3.0 mm or less. The presence of calcification in left main, left anterior descending, left circumflex, and right coronary artery was reported separately. Patients with CAC score > 0 were considered to have coronary artery calcification. In addition, calcification in the aortic valve and mitral valve was evaluated manually.

Statistical analysis

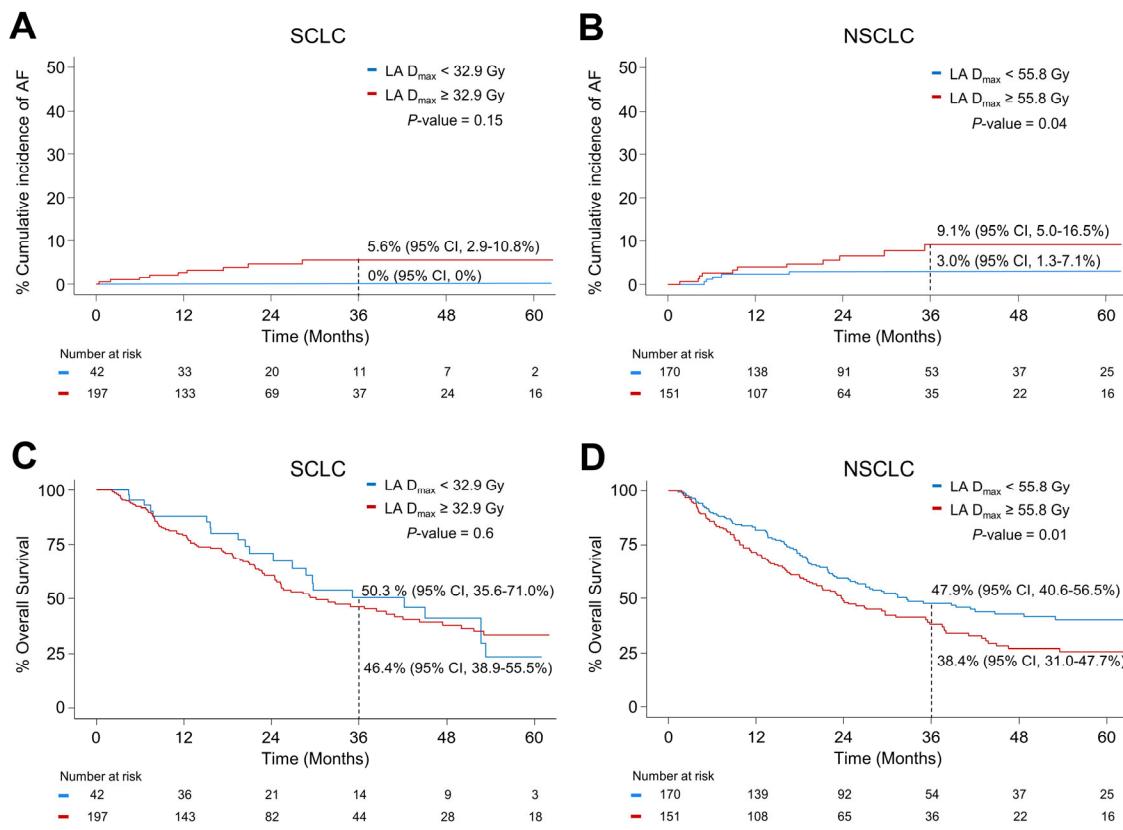
The 95% confidence interval for C-indices were estimated through bootstrapping. The cumulative incidence of the designated cardiac event was estimated using a competing risk analysis where death of any cause was considered a competing event. Comparisons were made using Gray's test. The optimal cut-off point of the selected parameter was determined where the Gray's test statistic was maximised. OS was estimated using Kaplan-Meier curves and compared with log-rank tests. For multivariable analysis, a backwards stepwise regression was performed for the multivariable analysis. The multivariable model that minimised the Akaike information criterion value was chosen.

A**B**

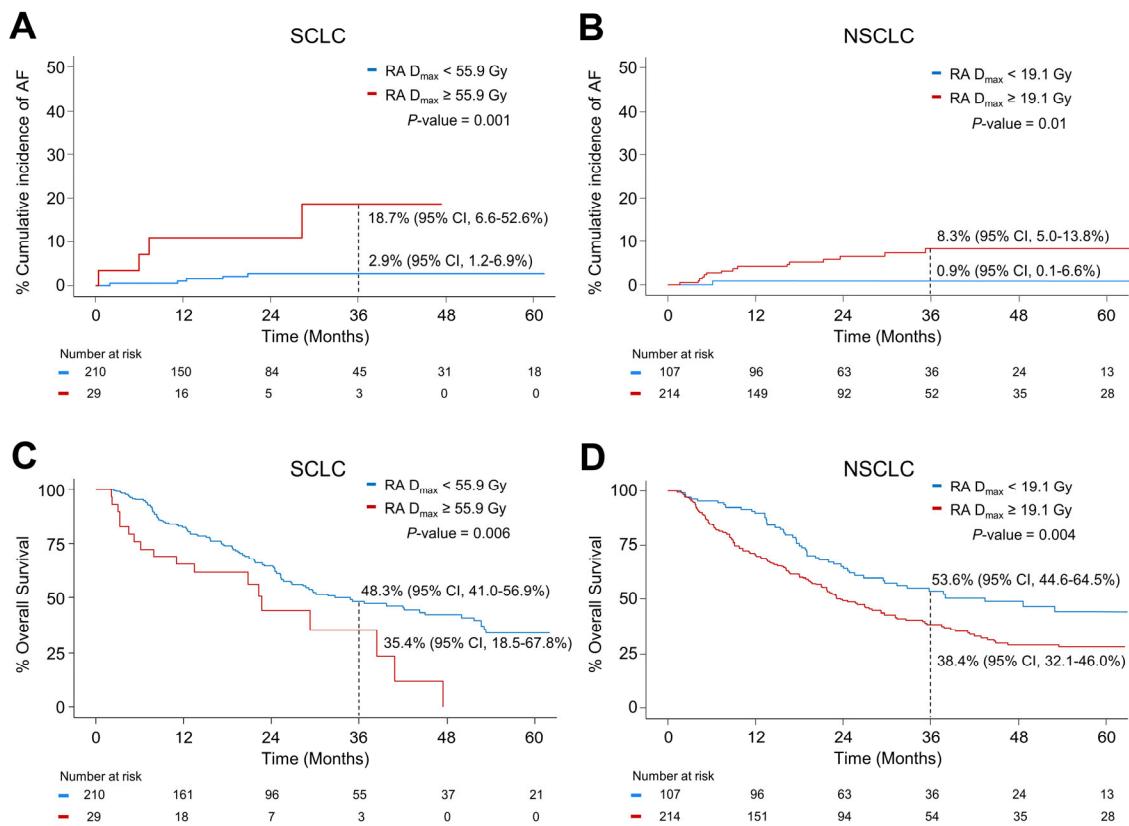
eFigure 1. Representative patient who developed AF after completion of definitive CRT. (A) A brief timeline of the treatment received, and events occurring during the follow-up period. AF developed 7 months after the initiation of CRT. (B) Isodose line is depicted on the patient's CT scan and SAN is delineated (magenta) and indicated with a yellow arrow. The AVN is delineated (sky blue) and indicated with a red arrow. SAN D_{max} is 53.8 Gy in this patient. AF = atrial fibrillation; AVN = atrioventricular node; CRT = chemoradiotherapy; SAN = sinoatrial node.



eFigure 2. Incidence of new onset AF and overall survival according to Heart D_{\max} . (A-B) Cumulative incidence of AF in the SCLC (A) and NSCLC (B) cohorts. (C-D) Overall survival in patients with SCLC (C) and NSCLC (D). Optimal cut-off values that best predicted AF were determined.



eFigure 3. Incidence of new onset AF and overall survival according to LA D_{\max} . (A-B) Cumulative incidence of AF in the SCLC (A) and NSCLC (B) cohorts. (C-D) Overall survival in patients with SCLC (C) and NSCLC (D). Optimal cut-off values that best predicted AF were determined.



eFigure 4. Incidence of new onset AF and overall survival according to RA D_{max} . (A-B) Cumulative incidence of AF in the SCLC (A) and NSCLC (B) cohorts. (C-D) Overall survival in patients with SCLC (C) and NSCLC (D). Optimal cut-off values that best predicted AF were determined.

eTable 1. Time dependent area under the receiver operating characteristic curve analysis of dose variables for cardiac substructures and atrial fibrillation (AF) in total, SCLC, and NSCLC cohorts

| | Total (n = 560) | | SCLC (n = 239) | | NSCLC (n = 321) | |
|------------|-----------------|-------------------|----------------|-------------------|-----------------|-------------------|
| Predictors | Mean (SD) | c-index (95% CI) | Mean (SD) | c-index (95% CI) | Mean (SD) | c-index (95% CI) |
| Heart_Mean | 11.80 (8.08) | 0.58 (0.51, 0.70) | 11.46 (8.08) | 0.51 (0.50, 0.65) | 12.26 (8.08) | 0.63 (0.51, 0.77) |
| Heart_Dmax | 55.94 (13.68) | 0.62 (0.56, 0.72) | 56.34 (15.14) | 0.59 (0.51, 0.75) | 55.41 (11.46) | 0.62 (0.54, 0.69) |
| Heart_V5 | 49.83 (29.94) | 0.59 (0.51, 0.67) | 48.75 (31.28) | 0.53 (0.51, 0.74) | 51.27 (28.03) | 0.63 (0.51, 0.76) |
| Heart_V10 | 36.87 (26.18) | 0.58 (0.51, 0.68) | 36.12 (27.00) | 0.51 (0.50, 0.66) | 37.87 (25.05) | 0.62 (0.51, 0.75) |
| Heart_V15 | 27.90 (22.17) | 0.57 (0.50, 0.68) | 27.34 (22.59) | 0.52 (0.50, 0.66) | 28.66 (21.61) | 0.62 (0.50, 0.77) |
| Heart_V20 | 21.86 (19.22) | 0.57 (0.50, 0.67) | 21.24 (19.19) | 0.51 (0.50, 0.67) | 22.69 (19.26) | 0.62 (0.51, 0.74) |
| Heart_V25 | 17.23 (16.49) | 0.57 (0.51, 0.67) | 16.52 (16.07) | 0.50 (0.50, 0.66) | 18.18 (17.01) | 0.61 (0.51, 0.72) |
| Heart_V30 | 13.50 (14.09) | 0.56 (0.50, 0.65) | 12.76 (13.24) | 0.51 (0.50, 0.68) | 14.50 (15.14) | 0.60 (0.51, 0.74) |
| Heart_V35 | 10.36 (11.90) | 0.55 (0.50, 0.62) | 9.61 (10.74) | 0.51 (0.50, 0.68) | 11.36 (13.26) | 0.58 (0.50, 0.68) |
| Heart_V40 | 7.66 (9.81) | 0.54 (0.50, 0.62) | 6.97 (8.63) | 0.52 (0.50, 0.69) | 8.59 (11.14) | 0.57 (0.50, 0.66) |
| Heart_V45 | 5.43 (7.99) | 0.54 (0.50, 0.61) | 4.93 (7.09) | 0.53 (0.50, 0.70) | 6.11 (9.04) | 0.56 (0.50, 0.64) |
| Heart_V50 | 3.45 (5.72) | 0.55 (0.50, 0.59) | 3.34 (5.54) | 0.53 (0.50, 0.67) | 3.59 (5.96) | 0.56 (0.50, 0.67) |
| Heart_V55 | 1.72 (3.11) | 0.54 (0.50, 0.61) | 1.98 (3.33) | 0.54 (0.50, 0.60) | 1.37 (2.75) | 0.57 (0.50, 0.68) |
| Heart_V60 | 0.75 (1.75) | 0.52 (0.50, 0.58) | 0.91 (1.75) | 0.55 (0.50, 0.66) | 0.54 (1.73) | 0.55 (0.50, 0.64) |
| RA_Mean | 11.58 (11.52) | 0.58 (0.51, 0.69) | 10.69 (10.72) | 0.53 (0.50, 0.70) | 12.78 (12.43) | 0.62 (0.51, 0.74) |
| RA_Dmax | 30.84 (20.08) | 0.62 (0.54, 0.71) | 29.98 (20.37) | 0.65 (0.51, 0.81) | 32.00 (19.68) | 0.61 (0.52, 0.71) |
| RA_V5 | 48.91 (39.81) | 0.59 (0.51, 0.67) | 46.35 (40.01) | 0.52 (0.50, 0.74) | 52.35 (39.36) | 0.63 (0.52, 0.75) |
| RA_V10 | 37.18 (37.88) | 0.58 (0.51, 0.69) | 35.16 (37.41) | 0.52 (0.50, 0.67) | 39.89 (38.42) | 0.63 (0.51, 0.76) |
| RA_V15 | 28.22 (34.18) | 0.57 (0.50, 0.67) | 26.38 (32.96) | 0.51 (0.50, 0.64) | 30.69 (35.68) | 0.61 (0.51, 0.75) |
| RA_V20 | 22.07 (30.37) | 0.57 (0.51, 0.67) | 20.20 (28.61) | 0.51 (0.50, 0.66) | 24.58 (32.48) | 0.61 (0.51, 0.73) |
| RA_V25 | 17.26 (26.90) | 0.57 (0.50, 0.66) | 15.43 (24.80) | 0.51 (0.50, 0.68) | 19.72 (29.36) | 0.61 (0.51, 0.73) |
| RA_V30 | 13.24 (23.38) | 0.57 (0.50, 0.66) | 11.47 (21.13) | 0.52 (0.50, 0.65) | 15.62 (25.95) | 0.60 (0.51, 0.71) |
| RA_V35 | 9.54 (19.29) | 0.55 (0.50, 0.64) | 7.83 (16.56) | 0.53 (0.50, 0.65) | 11.83 (22.28) | 0.57 (0.50, 0.68) |
| RA_V40 | 6.44 (15.54) | 0.54 (0.50, 0.61) | 4.85 (12.43) | 0.54 (0.50, 0.66) | 8.57 (18.74) | 0.54 (0.50, 0.65) |
| RA_V45 | 4.09 (12.25) | 0.53 (0.50, 0.59) | 3.02 (9.52) | 0.54 (0.50, 0.66) | 5.53 (15.06) | 0.52 (0.50, 0.54) |
| RA_V50 | 2.31 (9.06) | 0.52 (0.50, 0.58) | 1.79 (6.66) | 0.53 (0.50, 0.63) | 2.99 (11.51) | 0.51 (0.50, 0.58) |
| RA_V55 | 0.96 (4.61) | 0.51 (0.50, 0.53) | 0.88 (4.25) | 0.50 (0.49, 0.55) | 1.06 (5.06) | 0.50 (0.50, 0.56) |
| RA_V60 | 0.36 (2.56) | 0.51 (0.50, 0.53) | 0.35 (2.23) | 0.51 (0.50, 0.53) | 0.38 (2.95) | 0.51 (0.50, 0.54) |
| RV_Mean | 7.56 (7.41) | 0.54 (0.50, 0.64) | 7.30 (7.29) | 0.56 (0.51, 0.69) | 7.92 (7.59) | 0.60 (0.51, 0.73) |
| RV_Dmax | 27.15 (15.49) | 0.50 (0.50, 0.60) | 26.28 (15.57) | 0.55 (0.51, 0.70) | 28.32 (15.33) | 0.54 (0.50, 0.66) |
| RV_V5 | 40.40 (34.90) | 0.57 (0.51, 0.68) | 39.78 (36.10) | 0.54 (0.5, 0.69) | 41.23 (33.28) | 0.62 (0.51, 0.78) |
| RV_V10 | 27.51 (30.04) | 0.55 (0.50, 0.65) | 27.36 (30.91) | 0.57 (0.51, 0.70) | 27.71 (28.90) | 0.60 (0.50, 0.74) |
| RV_V15 | 17.97 (24.37) | 0.53 (0.50, 0.61) | 17.67 (24.51) | 0.60 (0.51, 0.74) | 18.36 (24.24) | 0.59 (0.51, 0.71) |
| RV_V20 | 11.91 (19.82) | 0.52 (0.50, 0.62) | 11.39 (19.48) | 0.58 (0.51, 0.77) | 12.60 (20.28) | 0.57 (0.50, 0.69) |
| RV_V25 | 7.57 (15.46) | 0.53 (0.50, 0.61) | 7.03 (15.34) | 0.55 (0.51, 0.75) | 8.30 (15.62) | 0.56 (0.50, 0.69) |
| RV_V30 | 4.66 (11.63) | 0.52 (0.50, 0.58) | 4.03 (10.54) | 0.52 (0.50, 0.73) | 5.51 (12.93) | 0.54 (0.50, 0.62) |
| RV_V35 | 2.82 (9.04) | 0.51 (0.50, 0.60) | 2.22 (7.58) | 0.51 (0.50, 0.64) | 3.62 (10.65) | 0.50 (0.50, 0.64) |
| RV_V40 | 1.62 (7.35) | 0.52 (0.50, 0.52) | 1.17 (5.94) | 0.51 (0.50, 0.64) | 2.22 (8.87) | 0.54 (0.50, 0.53) |
| RV_V45 | 1.04 (6.61) | 0.52 (0.50, 0.58) | 0.69 (5.15) | 0.51 (0.50, 0.60) | 1.52 (8.17) | 0.54 (0.51, 0.61) |
| RV_V50 | 0.59 (4.33) | 0.54 (0.52, 0.56) | 0.43 (3.76) | 0.55 (0.53, 0.57) | 0.81 (4.98) | 0.53 (0.51, 0.55) |
| RV_V55 | 0.17 (1.47) | 0.52 (0.51, 0.54) | 0.15 (1.27) | 0.52 (0.51, 0.54) | 0.18 (1.70) | 0.52 (0.50, 0.54) |
| RV_V60 | 0.03 (0.33) | 0.51 (0.50, 0.52) | 0.03 (0.41) | 0.50 (0.50, 0.51) | 0.02 (0.19) | 0.51 (0.50, 0.54) |

| | | | | | | |
|----------|---------------|-------------------|---------------|-------------------|---------------|-------------------|
| LA_Mean | 17.09 (11.98) | 0.59 (0.51, 0.72) | 16.49 (11.87) | 0.51 (0.50, 0.73) | 17.90 (12.09) | 0.65 (0.51, 0.79) |
| LA_Dmax | 47.47 (18.26) | 0.58 (0.50, 0.70) | 47.03 (19.76) | 0.56 (0.50, 0.73) | 48.07 (16.04) | 0.58 (0.51, 0.77) |
| LA_V5 | 65.95 (33.39) | 0.60 (0.51, 0.71) | 63.74 (34.46) | 0.55 (0.50, 0.74) | 68.93 (31.72) | 0.63 (0.51, 0.77) |
| LA_V10 | 51.71 (34.02) | 0.57 (0.51, 0.68) | 50.02 (34.30) | 0.50 (0.50, 0.76) | 53.98 (33.58) | 0.61 (0.51, 0.75) |
| LA_V15 | 40.43 (31.74) | 0.57 (0.51, 0.68) | 39.15 (31.87) | 0.51 (0.50, 0.72) | 42.16 (31.57) | 0.62 (0.51, 0.75) |
| LA_V20 | 32.56 (28.95) | 0.57 (0.51, 0.69) | 31.42 (28.86) | 0.52 (0.50, 0.72) | 34.08 (29.08) | 0.63 (0.52, 0.77) |
| LA_V25 | 26.97 (26.69) | 0.57 (0.50, 0.69) | 25.76 (26.14) | 0.54 (0.50, 0.74) | 28.61 (27.38) | 0.63 (0.51, 0.80) |
| LA_V30 | 22.41 (24.30) | 0.57 (0.50, 0.68) | 21.16 (23.29) | 0.54 (0.50, 0.74) | 24.08 (25.55) | 0.63 (0.51, 0.79) |
| LA_V35 | 18.30 (21.75) | 0.57 (0.51, 0.68) | 16.98 (20.36) | 0.54 (0.50, 0.74) | 20.07 (23.42) | 0.64 (0.52, 0.79) |
| LA_V40 | 14.46 (18.95) | 0.57 (0.51, 0.67) | 13.25 (17.50) | 0.52 (0.50, 0.73) | 16.09 (20.66) | 0.63 (0.52, 0.79) |
| LA_V45 | 10.53 (15.66) | 0.58 (0.51, 0.68) | 9.71 (14.58) | 0.51 (0.50, 0.69) | 11.64 (16.98) | 0.62 (0.53, 0.76) |
| LA_V50 | 6.83 (11.87) | 0.58 (0.51, 0.66) | 6.70 (11.50) | 0.50 (0.50, 0.68) | 7.00 (12.38) | 0.62 (0.51, 0.74) |
| LA_V55 | 3.48 (7.63) | 0.56 (0.50, 0.63) | 4.01 (8.06) | 0.56 (0.50, 0.68) | 2.78 (6.96) | 0.60 (0.51, 0.69) |
| LA_V60 | 1.40 (4.39) | 0.54 (0.51, 0.61) | 1.71 (4.74) | 0.52 (0.50, 0.63) | 0.99 (3.83) | 0.57 (0.50, 0.71) |
| LV_Mean | 7.24 (8.76) | 0.53 (0.50, 0.62) | 7.08 (8.87) | 0.50 (0.50, 0.68) | 7.45 (8.62) | 0.54 (0.50, 0.67) |
| LV_Dmax | 26.22 (19.88) | 0.55 (0.50, 0.66) | 25.15 (20.10) | 0.55 (0.50, 0.70) | 27.65 (19.53) | 0.60 (0.50, 0.71) |
| LV_V5 | 35.36 (35.90) | 0.57 (0.50, 0.68) | 35.12 (36.89) | 0.53 (0.50, 0.68) | 35.70 (34.59) | 0.59 (0.50, 0.79) |
| LV_V10 | 21.82 (30.42) | 0.53 (0.50, 0.64) | 21.70 (31.39) | 0.50 (0.50, 0.65) | 21.98 (29.14) | 0.55 (0.50, 0.68) |
| LV_V15 | 15.09 (26.40) | 0.51 (0.50, 0.60) | 15.17 (27.36) | 0.53 (0.50, 0.78) | 14.98 (25.10) | 0.54 (0.50, 0.67) |
| LV_V20 | 11.35 (22.76) | 0.50 (0.50, 0.59) | 11.28 (23.43) | 0.52 (0.50, 0.73) | 11.45 (21.87) | 0.52 (0.50, 0.62) |
| LV_V25 | 8.47 (18.74) | 0.50 (0.50, 0.58) | 8.14 (18.84) | 0.51 (0.50, 0.71) | 8.90 (18.63) | 0.51 (0.50, 0.62) |
| LV_V30 | 6.12 (15.09) | 0.50 (0.50, 0.57) | 5.67 (14.82) | 0.50 (0.50, 0.71) | 6.74 (15.46) | 0.50 (0.50, 0.60) |
| LV_V35 | 4.34 (12.14) | 0.50 (0.50, 0.57) | 3.84 (11.72) | 0.50 (0.50, 0.69) | 5.00 (12.67) | 0.50 (0.49, 0.59) |
| LV_V40 | 2.97 (9.58) | 0.50 (0.50, 0.56) | 2.55 (9.12) | 0.51 (0.50, 0.64) | 3.54 (10.15) | 0.50 (0.49, 0.58) |
| LV_V45 | 2.05 (7.89) | 0.51 (0.49, 0.55) | 1.74 (7.53) | 0.52 (0.50, 0.63) | 2.46 (8.35) | 0.50 (0.49, 0.58) |
| LV_V50 | 1.22 (6.01) | 0.51 (0.49, 0.56) | 1.11 (6.17) | 0.52 (0.50, 0.61) | 1.36 (5.80) | 0.50 (0.49, 0.57) |
| LV_V55 | 0.49 (2.88) | 0.51 (0.49, 0.55) | 0.56 (3.52) | 0.56 (0.50, 0.59) | 0.40 (1.68) | 0.50 (0.50, 0.55) |
| LV_V60 | 0.16 (0.92) | 0.52 (0.51, 0.55) | 0.17 (1.02) | 0.53 (0.51, 0.55) | 0.14 (0.77) | 0.52 (0.50, 0.55) |
| RCA_Mean | 10.42 (10.31) | 0.55 (0.50, 0.63) | 9.51 (9.50) | 0.55 (0.50, 0.69) | 11.65 (11.21) | 0.61 (0.51, 0.74) |
| RCA_Dmax | 17.38 (14.16) | 0.57 (0.51, 0.65) | 15.82 (13.58) | 0.53 (0.50, 0.73) | 19.47 (14.67) | 0.60 (0.51, 0.71) |
| RCA_V5 | 51.99 (41.74) | 0.55 (0.50, 0.65) | 48.52 (41.89) | 0.54 (0.50, 0.66) | 56.64 (41.17) | 0.60 (0.51, 0.73) |
| RCA_V10 | 38.34 (40.02) | 0.53 (0.50, 0.63) | 35.41 (39.85) | 0.55 (0.50, 0.68) | 42.27 (40.00) | 0.57 (0.50, 0.71) |
| RCA_V15 | 26.93 (35.60) | 0.53 (0.50, 0.62) | 24.76 (34.51) | 0.58 (0.50, 0.71) | 29.85 (36.89) | 0.59 (0.50, 0.72) |
| RCA_V20 | 18.86 (31.18) | 0.55 (0.50, 0.65) | 17.12 (29.66) | 0.57 (0.50, 0.67) | 21.19 (33.04) | 0.62 (0.52, 0.78) |
| RCA_V25 | 12.53 (26.20) | 0.56 (0.50, 0.64) | 11.06 (24.50) | 0.55 (0.50, 0.66) | 14.50 (28.25) | 0.63 (0.51, 0.73) |
| RCA_V30 | 8.25 (21.51) | 0.53 (0.50, 0.60) | 7.18 (19.71) | 0.52 (0.50, 0.63) | 9.70 (23.69) | 0.57 (0.50, 0.68) |
| RCA_V35 | 4.84 (16.50) | 0.52 (0.50, 0.58) | 3.65 (13.22) | 0.50 (0.50, 0.51) | 6.45 (19.99) | 0.53 (0.50, 0.59) |
| RCA_V40 | 2.77 (12.82) | 0.51 (0.50, 0.56) | 1.44 (8.38) | 0.50 (0.50, 0.57) | 4.55 (16.91) | 0.54 (0.51, 0.57) |
| RCA_V45 | 1.56 (9.34) | 0.50 (0.50, 0.53) | 0.71 (5.87) | 0.51 (0.50, 0.57) | 2.70 (12.50) | 0.52 (0.50, 0.54) |
| RCA_V50 | 0.75 (6.79) | 0.51 (0.50, 0.51) | 0.12 (1.66) | 0.51 (0.50, 0.57) | 1.60 (10.17) | 0.50 (0.49, 0.51) |
| RCA_V55 | 0.35 (4.76) | 0.50 (0.50, 0.50) | 0.04 (0.74) | 0.50 (0.50, 0.57) | 0.76 (7.23) | 0.50 (0.49, 0.51) |
| RCA_V60 | 0.07 (1.48) | 0.50 (0.50, 0.50) | 0.01 (0.26) | 0.50 (0.50, 0.50) | 0.15 (2.25) | 0.50 (0.49, 0.51) |
| LAD_Mean | 10.72 (9.65) | 0.50 (0.50, 0.60) | 10.37 (9.46) | 0.52 (0.50, 0.71) | 11.20 (9.90) | 0.51 (0.50, 0.63) |
| LAD_Dmax | 24.88 (17.12) | 0.51 (0.50, 0.60) | 23.20 (16.31) | 0.52 (0.50, 0.75) | 27.14 (17.94) | 0.51 (0.50, 0.64) |
| LAD_V5 | 53.41 (33.46) | 0.54 (0.50, 0.66) | 53.67 (34.74) | 0.51 (0.50, 0.68) | 53.07 (31.72) | 0.55 (0.50, 0.71) |
| LAD_V10 | 35.22 (33.08) | 0.51 (0.50, 0.63) | 35.40 (33.86) | 0.55 (0.51, 0.71) | 34.99 (32.07) | 0.54 (0.50, 0.69) |
| LAD_V15 | 23.76 (29.16) | 0.51 (0.50, 0.61) | 23.56 (29.99) | 0.53 (0.50, 0.73) | 24.01 (28.06) | 0.51 (0.50, 0.66) |

| | | | | | | |
|----------|---------------|-------------------|---------------|-------------------|---------------|-------------------|
| LAD_V20 | 17.48 (25.97) | 0.50 (0.50, 0.61) | 16.86 (26.51) | 0.51 (0.50, 0.73) | 18.31 (25.26) | 0.51 (0.50, 0.62) |
| LAD_V25 | 13.57 (22.88) | 0.51 (0.50, 0.59) | 12.53 (22.93) | 0.50 (0.50, 0.70) | 14.96 (22.79) | 0.51 (0.50, 0.60) |
| LAD_V30 | 10.34 (19.75) | 0.52 (0.50, 0.60) | 9.18 (19.10) | 0.51 (0.50, 0.67) | 11.90 (20.53) | 0.52 (0.50, 0.60) |
| LAD_V35 | 7.64 (17.01) | 0.53 (0.50, 0.61) | 6.41 (15.81) | 0.52 (0.50, 0.69) | 9.30 (18.40) | 0.53 (0.50, 0.60) |
| LAD_V40 | 5.32 (14.08) | 0.53 (0.50, 0.59) | 4.27 (12.79) | 0.52 (0.50, 0.66) | 6.72 (15.57) | 0.53 (0.50, 0.59) |
| LAD_V45 | 3.53 (11.82) | 0.54 (0.51, 0.53) | 2.57 (10.18) | 0.52 (0.50, 0.65) | 4.82 (13.63) | 0.56 (0.50, 0.59) |
| LAD_V50 | 2.12 (9.37) | 0.52 (0.51, 0.55) | 1.50 (8.27) | 0.51 (0.50, 0.61) | 2.96 (10.63) | 0.55 (0.53, 0.60) |
| LAD_V55 | 1.03 (5.92) | 0.54 (0.51, 0.53) | 0.71 (5.05) | 0.55 (0.52, 0.57) | 1.46 (6.92) | 0.53 (0.52, 0.59) |
| LAD_V60 | 0.37 (3.35) | 0.52 (0.51, 0.53) | 0.24 (3.10) | 0.52 (0.51, 0.55) | 0.54 (3.66) | 0.52 (0.50, 0.54) |
| LCX_Mean | 14.90 (15.97) | 0.55 (0.50, 0.60) | 14.25 (15.46) | 0.55 (0.50, 0.69) | 15.77 (16.62) | 0.53 (0.50, 0.65) |
| LCX_Dmax | 24.33 (20.38) | 0.52 (0.50, 0.64) | 23.53 (20.27) | 0.52 (0.50, 0.68) | 25.40 (20.53) | 0.52 (0.50, 0.68) |
| LCX_V5 | 58.63 (39.41) | 0.55 (0.50, 0.67) | 57.83 (40.30) | 0.55 (0.50, 0.69) | 59.72 (38.24) | 0.55 (0.50, 0.71) |
| LCX_V10 | 38.27 (39.51) | 0.52 (0.50, 0.65) | 37.76 (40.10) | 0.55 (0.50, 0.69) | 38.94 (38.78) | 0.55 (0.50, 0.69) |
| LCX_V15 | 29.76 (38.35) | 0.51 (0.50, 0.65) | 29.46 (38.38) | 0.56 (0.50, 0.70) | 30.17 (38.38) | 0.55 (0.50, 0.67) |
| LCX_V20 | 25.52 (37.13) | 0.50 (0.50, 0.60) | 24.72 (36.74) | 0.56 (0.51, 0.69) | 26.60 (37.69) | 0.52 (0.50, 0.64) |
| LCX_V25 | 22.38 (35.58) | 0.51 (0.50, 0.59) | 21.11 (34.87) | 0.56 (0.50, 0.70) | 24.09 (36.52) | 0.52 (0.50, 0.65) |
| LCX_V30 | 19.76 (34.06) | 0.52 (0.50, 0.59) | 18.34 (33.09) | 0.55 (0.51, 0.69) | 21.68 (35.31) | 0.51 (0.50, 0.66) |
| LCX_V35 | 16.96 (31.83) | 0.52 (0.50, 0.58) | 15.14 (30.11) | 0.54 (0.51, 0.67) | 19.40 (33.92) | 0.50 (0.50, 0.64) |
| LCX_V40 | 14.20 (29.25) | 0.51 (0.50, 0.58) | 12.05 (26.70) | 0.54 (0.50, 0.66) | 17.08 (32.20) | 0.51 (0.49, 0.63) |
| LCX_V45 | 11.28 (26.23) | 0.51 (0.50, 0.60) | 9.04 (23.50) | 0.55 (0.50, 0.63) | 14.29 (29.28) | 0.51 (0.50, 0.61) |
| LCX_V50 | 8.44 (22.58) | 0.51 (0.49, 0.57) | 6.82 (20.55) | 0.53 (0.51, 0.63) | 10.61 (24.92) | 0.51 (0.50, 0.61) |
| LCX_V55 | 5.01 (17.45) | 0.51 (0.50, 0.55) | 4.84 (16.86) | 0.55 (0.52, 0.56) | 5.23 (18.25) | 0.51 (0.50, 0.60) |
| LCX_V60 | 2.23 (10.77) | 0.52 (-, -) | 2.23 (11.02) | 0.53 (0.52, 0.56) | 2.24 (10.46) | 0.52 (-, -) |
| SAN_Mean | 20.87 (16.80) | 0.64 (0.53, 0.73) | 20.08 (16.44) | 0.66 (0.51, 0.85) | 21.95 (17.24) | 0.63 (0.52, 0.73) |
| SAN_Dmax | 27.35 (18.87) | 0.66 (0.56, 0.74) | 26.95 (18.81) | 0.68 (0.52, 0.84) | 27.89 (18.98) | 0.66 (0.54, 0.76) |
| SAN_V5 | 74.74 (39.29) | 0.60 (0.53, 0.66) | 73.26 (39.84) | 0.53 (0.50, 0.72) | 76.74 (38.54) | 0.64 (0.57, 0.73) |
| SAN_V10 | 61.87 (44.64) | 0.64 (0.55, 0.73) | 60.82 (44.66) | 0.61 (0.50, 0.78) | 63.28 (44.66) | 0.66 (0.55, 0.75) |
| SAN_V15 | 51.51 (45.93) | 0.66 (0.58, 0.74) | 49.81 (45.73) | 0.66 (0.51, 0.83) | 53.79 (46.20) | 0.67 (0.56, 0.77) |
| SAN_V20 | 44.64 (45.88) | 0.62 (0.53, 0.71) | 43.21 (45.30) | 0.65 (0.51, 0.81) | 46.57 (46.66) | 0.61 (0.51, 0.74) |
| SAN_V25 | 38.48 (44.85) | 0.60 (0.51, 0.70) | 36.84 (43.95) | 0.64 (0.51, 0.80) | 40.67 (46.02) | 0.58 (0.50, 0.74) |
| SAN_V30 | 31.55 (42.32) | 0.59 (0.50, 0.68) | 29.02 (40.87) | 0.63 (0.50, 0.81) | 34.94 (44.06) | 0.58 (0.51, 0.73) |
| SAN_V35 | 24.76 (38.92) | 0.61 (0.51, 0.72) | 22.64 (37.64) | 0.64 (0.51, 0.80) | 27.60 (40.48) | 0.60 (0.50, 0.74) |
| SAN_V40 | 18.26 (34.37) | 0.58 (0.51, 0.68) | 16.20 (32.26) | 0.62 (0.51, 0.77) | 21.03 (36.91) | 0.57 (0.50, 0.69) |
| SAN_V45 | 12.06 (28.28) | 0.55 (0.50, 0.64) | 10.46 (26.14) | 0.59 (0.50, 0.72) | 14.20 (30.84) | 0.53 (0.50, 0.62) |
| SAN_V50 | 6.57 (21.23) | 0.54 (0.50, 0.60) | 6.54 (21.14) | 0.57 (0.50, 0.74) | 6.61 (21.38) | 0.52 (0.50, 0.61) |
| SAN_V55 | 3.36 (14.64) | 0.51 (0.50, 0.55) | 3.22 (13.94) | 0.52 (0.49, 0.54) | 3.55 (15.55) | 0.52 (0.50, 0.59) |
| SAN_V60 | 1.06 (7.93) | 0.50 (0.50, 0.53) | 1.10 (7.75) | 0.51 (0.50, 0.52) | 1.01 (8.19) | 0.50 (0.50, 0.54) |
| AVN_Mean | 8.51 (9.96) | 0.55 (0.50, 0.64) | 7.32 (9.26) | 0.56 (0.50, 0.74) | 10.11 (10.65) | 0.61 (0.51, 0.76) |
| AVN_Dmax | 11.60 (12.51) | 0.55 (0.50, 0.65) | 9.87 (11.62) | 0.55 (0.50, 0.70) | 13.92 (13.29) | 0.62 (0.51, 0.78) |
| AVN_V5 | 43.17 (47.14) | 0.56 (0.51, 0.65) | 38.07 (46.62) | 0.51 (0.50, 0.68) | 50.02 (47.06) | 0.59 (0.51, 0.72) |
| AVN_V10 | 32.96 (43.86) | 0.52 (0.50, 0.65) | 27.95 (42.15) | 0.56 (0.50, 0.72) | 39.69 (45.27) | 0.57 (0.51, 0.69) |
| AVN_V15 | 21.79 (37.73) | 0.51 (0.50, 0.60) | 18.29 (35.37) | 0.59 (0.51, 0.70) | 26.49 (40.27) | 0.53 (0.50, 0.65) |
| AVN_V20 | 13.95 (31.15) | 0.52 (0.50, 0.63) | 11.51 (28.84) | 0.56 (0.50, 0.64) | 17.24 (33.79) | 0.56 (0.50, 0.69) |
| AVN_V25 | 8.61 (24.47) | 0.53 (0.50, 0.61) | 6.60 (21.74) | 0.54 (0.50, 0.60) | 11.30 (27.54) | 0.57 (0.50, 0.73) |
| AVN_V30 | 5.18 (18.96) | 0.53 (0.50, 0.62) | 3.77 (16.71) | 0.53 (0.50, 0.57) | 7.08 (21.52) | 0.56 (0.51, 0.69) |
| AVN_V35 | 2.92 (14.19) | 0.52 (0.50, 0.57) | 2.13 (12.54) | 0.53 (0.51, 0.56) | 3.99 (16.11) | 0.54 (0.50, 0.63) |
| AVN_V40 | 1.54 (10.22) | 0.51 (0.50, 0.53) | 1.07 (8.22) | 0.51 (0.50, 0.52) | 2.17 (12.41) | 0.51 (0.50, 0.57) |

| | | | | | | |
|---------|-------------|-------------------|-------------|-------------------|--------------|-------------------|
| AVN_V45 | 0.85 (7.48) | 0.50 (0.50, 0.51) | 0.35 (4.77) | 0.51 (0.50, 0.52) | 1.51 (10.01) | 0.50 (0.49, 0.56) |
| AVN_V50 | 0.23 (3.38) | 0.50 (0.50, 0.51) | 0.20 (3.51) | 0.50 (0.50, 0.52) | 0.28 (3.21) | 0.50 (0.49, 0.51) |
| AVN_V55 | 0.02 (0.38) | 0.50 (0.49, 0.51) | 0.03 (0.50) | - | 0.00 (0.00) | 0.50 (0.49, 0.51) |
| AVN_V60 | 0.00 (0.00) | - | 0.00 (0.00) | - | 0.00 (0.00) | - |

SCLC = small cell lung cancer; NSCLC = non-small cell lung cancer; RA = right atrium; RV = right ventricle; LA = left atrium; LV = left ventricle; RCA = right coronary artery; LAD = left anterior descending artery; LCX = left circumflex artery; SAN = sinoatrial node; AVN = atrioventricular node; SD = standard deviation.

eTable 2. C-index of the top 5 dose volume parameters for cardiac substructures predictive for atrial fibrillation in total, SCLC, and NSCLC cohorts

| Total (n = 560) | | SCLC (n = 239) | | NSCLC (n = 321) | |
|-----------------|-------------------------|----------------|-------------------------|-----------------|-------------------------|
| Predictors | c-index | Predictors | c-index | Predictors | c-index |
| SAN Dmax | 0.661 (0.563, 0.742) | SAN Dmax | 0.675 (0.516, 0.837) | SAN V15Gy | 0.665 (0.563, 0.775) |
| SAN V15Gy | 0.658 (0.577, 0.738) | SAN V15Gy | 0.659 (0.509, 0.830) | SAN Dmax | 0.660 (0.536, 0.759) |
| SAN V10Gy | 0.637 (0.552, 0.726) | SAN Dmean | 0.656 (0.509, 0.848) | SAN V10Gy | 0.659 (0.548, 0.747) |
| SAN Dmean | 0.636 (0.528, 0.735) | SAN V20Gy | 0.648 (0.512, 0.808) | LA Dmean | 0.649 (0.509, 0.787) |
| RA Dmax | 0.619 (0.537, 0.715) | RA Dmax | 0.648 (0.507, 0.809) | SAN V5Gy | 0.638 (0.568, 0.730) |

SCLC = small cell lung cancer; NSCLC = non-small cell lung cancer; RA = right atrium; LA = left atrium; SAN = sinoatrial node.

eTable 3. Cox proportional hazards regression analysis for overall survival in SCLC cohort

| Variable | HR | Univariable 95% CI | P | Multivariable aHR | 95% CI | P |
|--|------|-----------------------|-------|----------------------|-----------|--------|
| SAN D _{max} , Gy | | | | | | |
| <53.5 | 1.00 | (ref) | | 1.00 | (ref) | |
| ≥53.5 | 2.05 | 1.19-3.53 | 0.01 | 2.68 | 1.53-4.71 | <0.001 |
| Age, y | 1.03 | 1.01-1.05 | 0.002 | 1.02 | 1.00-1.05 | 0.03 |
| Sex | | | | | | |
| Male | 1.00 | (ref) | | | | |
| Female | 1.29 | 0.73-2.29 | 0.39 | | | |
| ECOG Performance | | | | | | |
| 0 | 1.00 | (ref) | | 1.00 | (ref) | |
| 1-2 | 3.17 | 1.29-7.77 | 0.01 | 2.24 | 0.89-5.61 | 0.09 |
| Tobacco use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 0.59 | 0.32-1.10 | 0.10 | | | |
| Alcohol use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 1.04 | 0.71-1.52 | 0.84 | | | |
| Hypertension | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.48 | 1.03-2.12 | 0.03 | | | |
| Diabetes | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.36 | 0.94-1.99 | 0.11 | | | |
| Cardiovascular disease | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 1.98 | 1.33-2.94 | 0.001 | 1.54 | 1.00-2.36 | 0.05 |
| Coronary artery calcium score | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 0.96 | 0.63-1.46 | 0.85 | | | |
| CAC score | 1.00 | 1.00-1.00 | 0.62 | | | |
| Number of coronary arteries with calcification | | | | | | |
| 0 | 1.00 | (ref) | | | | |
| 1-2 | 0.94 | 0.55-1.58 | 0.82 | | | |
| 3-4 | 0.97 | 0.62-1.51 | 0.88 | | | |
| Aortic valve calcification | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.35 | 0.91-2.00 | 0.13 | | | |
| Mitral valve calcification | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.43 | 0.70-2.92 | 0.33 | | | |
| Pericardial effusion | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | | | | | | |
| BMI, m ² /kg | 1.07 | 1.02-1.13 | 0.009 | 1.06 | 1.00-1.12 | 0.04 |
| AJCC Stage | | | | | | |
| I-IIIA | 1.00 | (ref) | | | | |
| IIIB-IIIC | 0.98 | 0.68-1.40 | 0.90 | | | |
| Chemotherapy | | | | | | |
| Etoposide + Cisplatin | 1.00 | (ref) | | | | |
| Etoposide + Carboplatin | 0.85 | 0.60-1.22 | 0.39 | | | |
| RT dose, Gy | 0.95 | 0.92-0.98 | 0.003 | | | |
| RT modality | | | | | | |

| | | | | | | |
|--------|------|-----------|--------|------|-----------|--------|
| 3D-CRT | 1.00 | (ref) | | 1.00 | (ref) | |
| IMRT | 0.46 | 0.31-0.68 | <0.001 | 0.50 | 0.33-0.74 | <0.001 |

AJCC = American Joint Committee on Cancer; BMI = body mass index; CVD = cardiovascular disease; ECOG = Eastern Cooperative Oncology Group; IMRT = intensity modulated radiotherapy; NA = not applicable; RT = radiotherapy; SAN D_{max} = maximum radiation dose exposed to sinoatrial node; WHO = World Health Organization; 3-DCRT = 3-dimensional conformal radiotherapy

eTable 4. Cox proportional hazards regression analysis for overall survival in NSCLC cohort

| Variable | HR | Univariable | | P | Multivariable | |
|--|------|-------------|--------|------|---------------|--------|
| | | 95% CI | P | | aHR | 95% CI |
| SAN D _{max} , Gy | | | | | | |
| <20.0 | 1.00 | (ref) | | 1.00 | (ref) | |
| ≥20.0 | 1.75 | 1.31-2.34 | <0.001 | 1.97 | 1.45-2.68 | <0.001 |
| Age, y | 1.02 | 1.01-1.04 | 0.001 | 1.03 | 1.01-1.05 | <0.001 |
| Sex | | | | | | |
| Male | 1.00 | (ref) | | 1.00 | (ref) | |
| Female | 0.63 | 0.43-0.93 | 0.02 | 0.57 | 0.38-0.85 | 0.005 |
| ECOG Performance | | | | | | |
| 0 | 1.00 | (ref) | 0.0 | 1.00 | (ref) | |
| 1-2 | 1.49 | 0.96-2.33 | 0.08 | 1.46 | 0.93-2.32 | 0.10 |
| Tobacco use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 1.55 | 1.09-2.21 | 0.02 | | | |
| Alcohol use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 0.97 | 0.73-1.30 | 0.86 | | | |
| Hypertension | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.28 | 0.97-1.69 | 0.09 | | | |
| Diabetes | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 1.49 | 1.09-2.04 | 0.01 | 1.28 | 0.92-1.77 | 0.14 |
| Cardiovascular disease | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.13 | 0.80-1.65 | 0.52 | | | |
| Coronary artery calcium score | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.38 | 0.96-1.98 | 0.08 | | | |
| CAC score | 1.00 | 1.00-1.00 | 0.02 | | | |
| Number of coronary arteries with calcification | | | | | | |
| 0 | 1.00 | (ref) | | | | |
| 1-2 | 1.21 | 0.79-1.85 | 0.38 | | | |
| 3-4 | 1.56 | 1.06-2.28 | 0.02 | | | |
| Aortic valve calcification | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 1.00 | 0.72-1.37 | 0.98 | 0.73 | 0.52-1.02 | 0.07 |
| Mitral valve calcification | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.05 | 0.64-1.72 | 0.85 | | | |
| Pericarditis | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | | | | | | |
| BMI, m ² /kg | 0.96 | 0.92-1.00 | 0.04 | 0.95 | 0.92-0.99 | 0.01 |
| AJCC Stage | | | | | | |
| II-IIIA | 1.00 | (ref) | | 1.00 | (ref) | |
| IIIB-IIIC | 1.51 | 1.11-2.05 | 0.009 | 1.53 | 1.11-2.10 | 0.009 |
| Chemotherapy | | | | | | |
| Others | 1.00 | (ref) | | | | |
| Paclitaxel + Carboplatin | 0.96 | 0.57-1.60 | 0.88 | | | |
| Maintenance ICI | | | | | | |
| No | 1.00 | (ref) | | | | |

| | | | | | | |
|-------------|------|-----------|-------|------|-----------|------|
| Yes | 0.65 | 0.43-0.98 | 0.04 | | | |
| RT dose, Gy | 0.93 | 0.90-0.97 | 0.001 | 0.95 | 0.91-0.99 | 0.03 |
| RT modality | | | | | | |
| 3D-CRT | 1.00 | (ref) | | | | |
| IMRT | 0.76 | 0.57-1.01 | 0.06 | | | |

AJCC = American Joint Committee on Cancer; BMI = body mass index; CVD = cardiovascular disease; ECOG = Eastern Cooperative Oncology Group; ICI = immune checkpoint inhibitor; IMRT = intensity modulated radiotherapy; NA = not applicable; RT = radiotherapy; SAN D_{max} = maximum radiation dose exposed to sinoatrial node; WHO = World Health Organization; 3-DCRT = 3-dimensional conformal radiotherapy

eTable 5. Competing risk regression analysis for atrial fibrillation in SCLC cohort using RA D_{max}

| Variable | HR | Univariable | | P | Multivariable | | P |
|--|-----------------|-------------|-------|-------|---------------|--------|---|
| | | 95% CI | aHR | | 95% CI | | |
| RA D _{max} , Gy | | | | | | | |
| <55.9 | 1.00 | (ref) | | 1.00 | (ref) | | |
| ≥55.9 | 6.92 | 1.89-25.4 | 0.004 | 20.54 | 5.57-75.65 | <0.001 | |
| Age, y | 1.05 | 0.99-1.11 | 0.12 | 1.09 | 1.00-1.18 | 0.05 | |
| Sex | NA ^a | | | | | | |
| Male | | | | | | | |
| Female | | | | | | | |
| ECOG Performance | NA | | | | | | |
| 0 | | | | | | | |
| 1-2 | | | | | | | |
| Tobacco use | | | | | | | |
| Never | 1.00 | (ref) | | | | | |
| Ever | 2.14 | 0.45-10.21 | 0.34 | | | | |
| Alcohol use | | | | | | | |
| Never | 1.00 | (ref) | | 1.00 | (ref) | | |
| Ever | 4.24 | 0.55-32.83 | 0.17 | 8.32 | 1.11-61.94 | 0.04 | |
| Hypertension | | | | | | | |
| No | 1.00 | (ref) | | | | | |
| Yes | 1.32 | 0.35-4.96 | 0.68 | | | | |
| Diabetes | | | | | | | |
| No | 1.00 | (ref) | | | | | |
| Yes | 0.71 | 0.15-3.44 | 0.67 | | | | |
| Cardiovascular disease | | | | | | | |
| No | 1.00 | (ref) | | | | | |
| Yes | 2.12 | 0.53-8.53 | 0.29 | | | | |
| Coronary artery calcium score | | | | | | | |
| No | 1.00 | (ref) | | | | | |
| Yes | 0.96 | 0.20-4.75 | 0.96 | | | | |
| CAC score | 1.00 | 1.00-1.00 | 0.61 | | | | |
| Number of coronary arteries with calcification | | | | | | | |
| 0 | 1.00 | (ref) | | | | | |
| 1-2 | 2.34 | 0.45-12.3 | 0.31 | 1.83 | 0.37-9.02 | 0.46 | |
| 3-4 | 0.39 | 0.05-2.83 | 0.35 | 0.18 | 0.02-1.41 | 0.10 | |
| Aortic valve calcification | | | | | | | |
| No | 1.00 | (ref) | | | | | |
| Yes | 1.40 | 0.35-5.63 | 0.64 | | | | |
| Mitral valve calcification | | | | | | | |
| No | 1.00 | (ref) | | | | | |
| Yes | 2.32 | 0.28-19.0 | 0.43 | | | | |
| Pericardial effusion | NA | | | | | | |
| No | | | | | | | |
| Yes | | | | | | | |
| Chest surgery after CRT | | | | | | | |
| No | NA | | | | | | |
| Yes | | | | | | | |
| BMI, m ² /kg | 1.18 | 1.00-1.39 | 0.05 | 1.37 | 1.04-1.82 | 0.03 | |
| AJCC Stage | | | | | | | |
| I-IIIA | 1.00 | (ref) | | | | | |
| IIIB-IIIC | 0.61 | 0.16-2.26 | 0.46 | | | | |
| Chemotherapy | | | | | | | |
| Etoposide + Cisplatin | 1.00 | (ref) | | | | | |
| Etoposide + Carboplatin | 0.92 | 0.25-3.42 | 0.91 | | | | |

| | | | | | | |
|-------------|------|-----------|------|--|--|--|
| RT dose, Gy | 0.99 | 0.89-1.10 | 0.83 | | | |
| RT modality | | | | | | |
| 3D-CRT | 1.00 | (ref) | | | | |
| IMRT | 0.32 | 0.06-1.65 | 0.18 | | | |

^aNA indicates categorical variable that had no events in one of the subgroup and not applicable for regression analysis.

AJCC = American Joint Committee on Cancer; BMI = body mass index; CVD = cardiovascular disease; DM = diabetes mellitus; ECOG = Eastern Cooperative Oncology Group; HTN = hypertension; IMRT = intensity modulated radiotherapy; NA = not applicable; RT = radiotherapy; SAN D_{max} = maximum radiation dose exposed to sinoatrial node; SCLC = small cell lung cancer; WHO = World Health Organization; 3-DCRT = 3-dimensional conformal radiotherapy

eTable 6. Competing risk regression analysis for atrial fibrillation in NSCLC cohort using RA D_{max}

| Variable | HR | Univariable | | P | Multivariable | |
|--|-----------------|-------------|-------|------|---------------|------|
| | | 95% CI | aHR | | 95% CI | P |
| RA D _{max} , Gy | | | | | | |
| <19.1 | 1.00 | (ref) | | 1.00 | (ref) | |
| ≥19.1 | 4.60 | 1.04-20.3 | 0.04 | 5.97 | 1.34-26.57 | 0.02 |
| Age, y | 1.03 | 0.97-1.09 | 0.30 | | | |
| Sex | | | | | | |
| Male | 1.00 | (ref) | | | | |
| Female | 0.53 | 0.13-2.25 | 0.39 | | | |
| ECOG Performance | | | | | | |
| 0 | 1.00 | (ref) | | | | |
| 1-2 | 2.64 | 0.35-19.96 | 0.35 | | | |
| Tobacco use | | | | | | |
| Never | 1.00 | (ref) | | 1.00 | (ref) | |
| Ever | 5.15 | 0.71-37.7 | 0.11 | 4.45 | 0.64-31.16 | 0.13 |
| Alcohol use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 0.63 | 0.25-1.63 | 0.34 | | | |
| Hypertension | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 3.38 | 1.19-9.56 | 0.02 | 3.70 | 1.26-10.85 | 0.02 |
| Diabetes | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 3.08 | 1.18-8.02 | 0.02 | | | |
| Cardiovascular disease | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 0.69 | 0.16-2.95 | 0.61 | 0.35 | 0.09-1.37 | 0.13 |
| Coronary artery calcium | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 4.16 | 0.56-31.1 | 0.16 | | | |
| CAC score | 1.00 | 1.00-1.01 | 0.03 | | | |
| Number of coronary arteries with calcification | | | | | | |
| 0 | 1.00 | (ref) | | | | |
| 1-2 | 2.97 | 0.34-26.3 | 0.33 | | | |
| 3-4 | 4.96 | 0.65-37.8 | 0.12 | | | |
| Aortic valve calcification | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 4.24 | 1.64-11 | 0.003 | 3.56 | 1.31-9.81 | 0.01 |
| Mitral valve calcification | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 2.45 | 0.69-8.64 | 0.16 | | | |
| Pericardial effusion | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 0.80 | 0.11-5.85 | 0.82 | | | |
| Chest surgery after CRT | | | | | | |
| No | NA ^a | | | | | |
| Yes | | | | | | |
| BMI, m ² /kg | 1.01 | 0.9-1.12 | 0.89 | | | |
| AJCC Stage | | | | | | |
| II-IIIA | 1.00 | (ref) | | | | |
| IIIB-IIIC | 0.94 | 0.35-2.54 | 0.90 | | | |
| Chemotherapy | | | | | | |
| Others | 1.00 | (ref) | | | | |
| Paclitaxel + Carboplatin | 0.71 | 0.16-3.11 | 0.65 | | | |

| Maintenance ICI | | | | | | |
|-----------------|------|-----------|------|--|--|--|
| No | 1.00 | (ref) | | | | |
| Yes | 0.91 | 0.26-3.15 | 0.88 | | | |
| RT dose, Gy | 1.05 | 0.94-1.17 | 0.39 | | | |
| RT modality | | | | | | |
| 3D-CRT | 1.00 | (ref) | | | | |
| IMRT | 1.50 | 0.55-4.14 | 0.43 | | | |

^aNA indicates categorical variable that had no events in one of the subgroup and not applicable for regression analysis.

AJCC = American Joint Committee on Cancer; BMI = body mass index; CVD = cardiovascular disease; DM = diabetes mellitus; ECOG = Eastern Cooperative Oncology Group; HTN = hypertension; ICI = immune checkpoint inhibitor; IMRT = intensity modulated radiotherapy; NA = not applicable; NSCLC = non-small cell lung cancer; RT = radiotherapy; SAN D_{max} = maximum radiation dose exposed to sinoatrial node; WHO = World Health Organization; 3D-CRT = 3-dimensional conformal radiotherapy

eTable 7. Cox proportional hazards regression analysis for overall survival in SCLC cohort using RA D_{max}

| Variable | HR | Univariable 95% CI | P | Multivariable aHR | 95% CI | P |
|--|------|-----------------------|-------|----------------------|-----------|-------|
| RA D _{max} , Gy | | | | | | |
| <55.9 | 1.00 | (ref) | | 1.00 | (ref) | |
| ≥55.9 | 1.88 | 1.12-3.16 | 0.02 | 2.29 | 1.34-3.91 | 0.002 |
| Age, y | 1.03 | 1.01-1.05 | 0.002 | 1.02 | 1.00-1.04 | 0.07 |
| Sex | | | | | | |
| Male | 1.00 | (ref) | | | | |
| Female | 1.29 | 0.73-2.29 | 0.39 | | | |
| ECOG Performance | | | | | | |
| 0 | 1.00 | (ref) | | 1.00 | (ref) | |
| 1-2 | 3.17 | 1.29-7.77 | 0.01 | 2.30 | 0.91-5.79 | 0.08 |
| Tobacco use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 0.59 | 0.32-1.10 | 0.10 | | | |
| Alcohol use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 1.04 | 0.71-1.52 | 0.84 | | | |
| Hypertension | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.48 | 1.03-2.12 | 0.03 | | | |
| Diabetes | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.36 | 0.94-1.99 | 0.11 | | | |
| Cardiovascular disease | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 1.98 | 1.33-2.94 | 0.001 | 1.53 | 1.00-2.35 | 0.05 |
| Coronary artery calcium score | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 0.96 | 0.63-1.46 | 0.85 | | | |
| CAC score | 1.00 | 1.00-1.00 | 0.62 | | | |
| Number of coronary arteries with calcification | | | | | | |
| 0 | 1.00 | (ref) | | | | |
| 1-2 | 0.94 | 0.55-1.58 | 0.82 | | | |
| 3-4 | 0.97 | 0.62-1.51 | 0.88 | | | |
| Aortic valve calcification | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.35 | 0.91-2.00 | 0.13 | | | |
| Mitral valve calcification | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.43 | 0.70-2.92 | 0.33 | | | |
| Pericardial effusion | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.05 | 0.51-2.14 | 0.90 | | | |
| BMI, m ² /kg | 1.07 | 1.02-1.13 | 0.009 | 1.05 | 1.00-1.11 | 0.06 |
| AJCC Stage | | | | | | |
| I-IIIA | 1.00 | (ref) | | | | |
| IIIB-IIIC | 0.98 | 0.68-1.40 | 0.90 | | | |
| Chemotherapy | | | | | | |
| Etoposide + Cisplatin | 1.00 | (ref) | | | | |
| Etoposide + Carboplatin | 0.85 | 0.60-1.22 | 0.39 | | | |
| RT dose, Gy | 0.95 | 0.92-0.98 | 0.003 | | | |
| RT modality | | | | | | |

| | | | | | | |
|--------|------|-----------|--------|------|-----------|--------|
| 3D-CRT | 1.00 | (ref) | | 1.00 | (ref) | |
| IMRT | 0.46 | 0.31-0.68 | <0.001 | 0.48 | 0.32-0.72 | <0.001 |

AJCC = American Joint Committee on Cancer; BMI = body mass index; CVD = cardiovascular disease; ECOG = Eastern Cooperative Oncology Group; IMRT = intensity modulated radiotherapy; NA = not applicable; RT = radiotherapy; SAN D_{max} = maximum radiation dose exposed to sinoatrial node; WHO = World Health Organization; 3-DCRT = 3-dimensional conformal radiotherapy

eTable 8. Cox proportional hazards regression analysis for overall survival in NSCLC cohort using RA D_{max}

| Variable | HR | Univariable | | P | Multivariable | |
|--|------|-------------|-------|------|---------------|--------|
| | | 95% CI | P | | aHR | 95% CI |
| RA D _{max} , Gy | | | | | | |
| <19.1 | 1.00 | (ref) | | 1.00 | (ref) | |
| ≥19.1 | 1.62 | 1.20-2.20 | 0.002 | 1.57 | 1.14-2.17 | 0.005 |
| Age, y | 1.02 | 1.01-1.04 | 0.001 | 1.03 | 1.01-1.04 | 0.001 |
| Sex | | | | | | |
| Male | 1.00 | (ref) | | 1.00 | (ref) | |
| Female | 0.63 | 0.43-0.93 | 0.02 | 0.62 | 0.42-0.92 | 0.02 |
| ECOG Performance | | | | | | |
| 0 | 1.00 | (ref) | | 1.00 | (ref) | |
| 1-2 | 1.49 | 0.96-2.33 | 0.08 | 1.42 | 0.89-2.24 | 0.13 |
| Tobacco use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 1.55 | 1.09-2.21 | 0.02 | | | |
| Alcohol use | | | | | | |
| Never | 1.00 | (ref) | | | | |
| Ever | 0.97 | 0.73-1.30 | 0.86 | | | |
| Hypertension | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.28 | 0.97-1.69 | 0.09 | | | |
| Diabetes | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 1.49 | 1.09-2.04 | 0.01 | 1.37 | 1.00-1.89 | 0.06 |
| Cardiovascular disease | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.13 | 0.80-1.65 | 0.52 | | | |
| Coronary artery calcium score | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.38 | 0.96-1.98 | 0.08 | | | |
| CAC score | 1.00 | 1.00-1.00 | 0.02 | | | |
| Number of coronary arteries with calcification | | | | | | |
| 0 | 1.00 | (ref) | | | | |
| 1-2 | 1.21 | 0.79-1.85 | 0.38 | | | |
| 3-4 | 1.56 | 1.06-2.28 | 0.02 | | | |
| Aortic valve calcification | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 1.00 | 0.72-1.37 | 0.98 | 0.78 | 0.56-1.10 | 0.16 |
| Mitral valve calcification | | | | | | |
| No | 1.00 | (ref) | | | | |
| Yes | 1.05 | 0.64-1.72 | 0.85 | | | |
| Pericarditis | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |
| Yes | 2.10 | 1.34-3.29 | 0.001 | 1.77 | 1.12-2.79 | 0.01 |
| BMI, m ² /kg | 0.96 | 0.92-1.00 | 0.04 | 0.97 | 0.93-1.00 | 0.08 |
| AJCC Stage | | | | | | |
| II-IIIA | 1.00 | (ref) | | 1.00 | (ref) | |
| IIIB-IIIC | 1.51 | 1.11-2.05 | 0.009 | 1.48 | 1.08-2.04 | 0.02 |
| Chemotherapy | | | | | | |
| Others | 1.00 | (ref) | | | | |
| Paclitaxel + Carboplatin | 0.96 | 0.57-1.60 | 0.88 | | | |
| Maintenance ICI | | | | | | |
| No | 1.00 | (ref) | | 1.00 | (ref) | |

| | | | | | | |
|-------------|------|-----------|-------|------|-----------|-------|
| Yes | 0.65 | 0.43-0.98 | 0.04 | 0.73 | 0.48-1.11 | 0.14 |
| RT dose, Gy | 0.93 | 0.90-0.97 | 0.001 | 0.94 | 0.90-0.98 | 0.005 |
| RT modality | | | | | | |
| 3D-CRT | 1.00 | (ref) | | | | |
| IMRT | 0.76 | 0.57-1.01 | 0.06 | | | |

AJCC = American Joint Committee on Cancer; BMI = body mass index; CVD = cardiovascular disease; ECOG = Eastern Cooperative Oncology Group; ICI = immune checkpoint inhibitor; IMRT = intensity modulated radiotherapy; NA = not applicable; RT = radiotherapy; SAN D_{max} = maximum radiation dose exposed to sinoatrial node; WHO = World Health Organization; 3-DCRT = 3-dimensional conformal radiotherapy