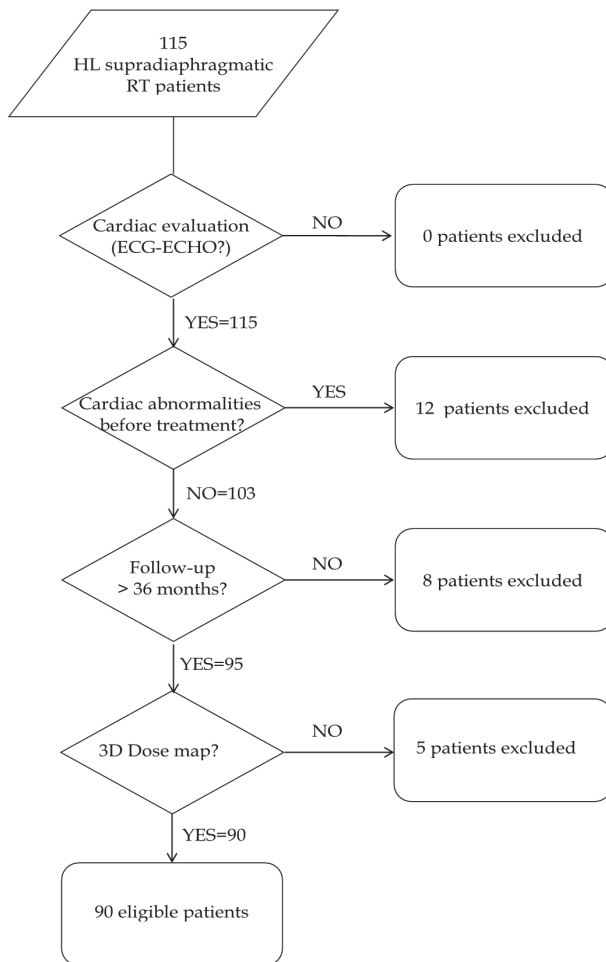
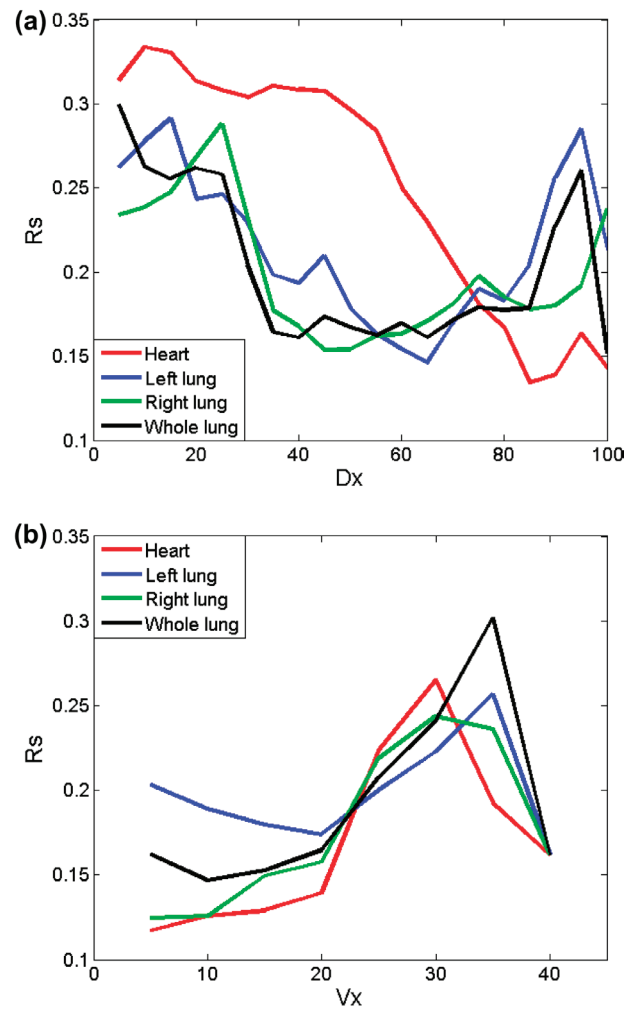


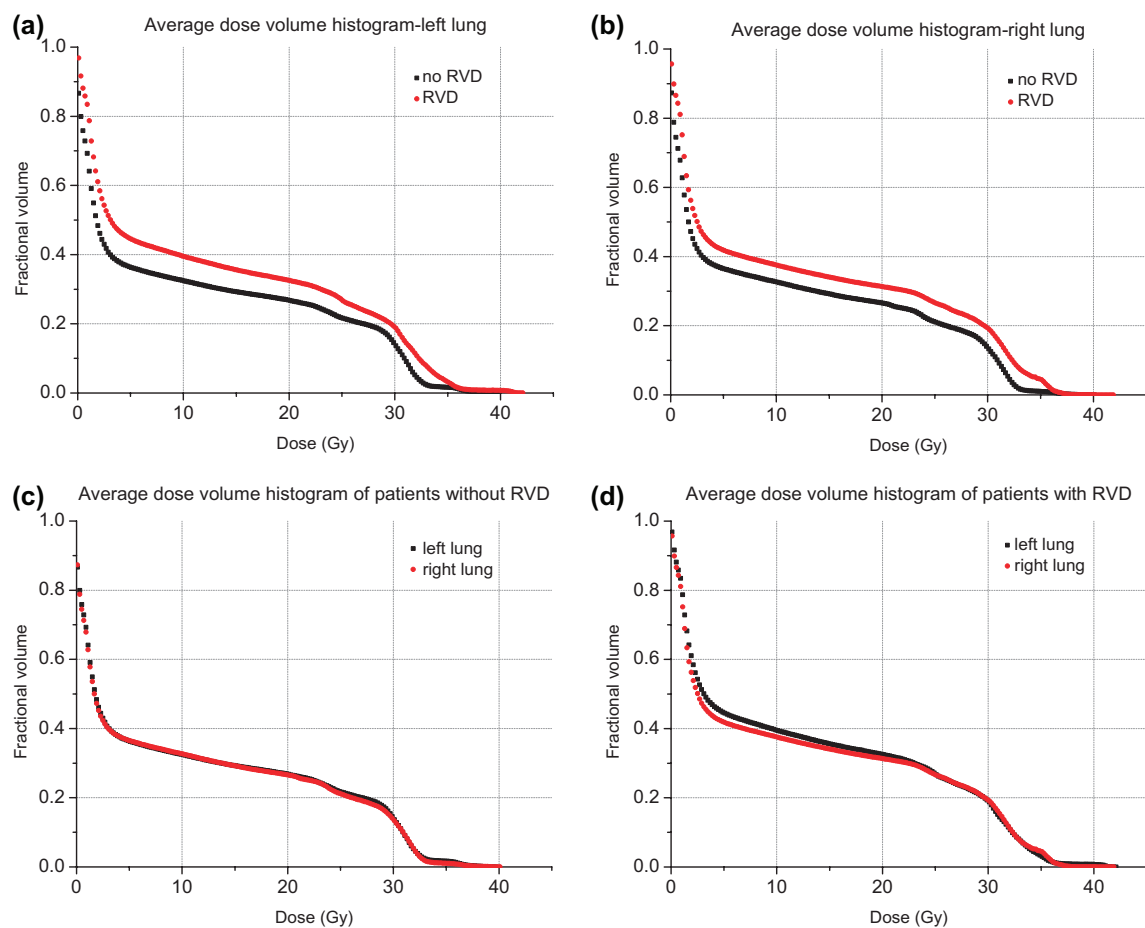
Supplementary material for Cella L. et al. Predicting radiation-induced valvular heart damage, *Acta Oncologica*, 2015, 10.3109/0284186X.2015.1016624.



Supplementary Figure 1. Patients' selection flowchart.



Supplementary Figure 2. Univariate Spearman's rank correlation coefficient of radiation-induced valvular defects with D_x (a) and V_x (b) for heart, lungs, left and right lung.



Supplementary Figure 3. Comparison of average dose volume histograms of left lung and right lung for the entire cohort of patients (a, b) and for the group of patients who developed RVD (c, d).

Supplementary Table I. Number of patients stratified by age at time of diagnosis (N) and valvular defects incidence in each age group (n).

Age (years)	N (%)	n (%)
14–25	36 (40.0)	10 (27.7)
26–35	31 (34.4)	9 (29.0)
36–45	12 (13.3)	6 (50.0)
46–55	8 (8.9)	2 (25.0)
56–65	2 (2.2)	0 (0.0)
60–70	1 (1.1)	0 (0.0)

Supplementary Table II. Summary of dosimetric statistics for heart, lungs, left and right lung and univariate analysis with RVD incidence.

			Univariate analysis		Univariate analysis				
Metric	Median (%)	Range (%)	R _s	<i>p-value</i>	Metric	Median (Gy)	Range (Gy)	R _s	<i>p-value</i>
Heart									
V5	79	0–100	0.118	0.267	D5	30.0	0.1–39.4	0.310	0.003
V10	75	0–100	0.126	0.238	D10	29.5	0.1–37.6	0.334	0.001
V15	72	0–100	0.129	0.226	D15	29.1	0.1–36.1	0.330	0.001
V20	70	0–100	0.137	0.196	D20	28.7	0.1–35.8	0.314	0.003
V25	41	0–97	0.222	0.035	D25	28.1	0.1–35.5	0.302	0.004
V30	5	0–94	0.260	0.013	D30	27.5	0.1–35.4	0.305	0.003
					D _{max}	31.4	0.1–40.9	0.312	0.003
					D _{mean}	21.0	0.1–32.9	0.234	0.027
Lungs									
V5	40	4–70	0.164	0.123	D5	31.5	2.5–40.9	0.297	0.004
V10	36	1–65	0.148	0.164	D10	30.7	0.8–38.3	0.260	0.013
V15	32	0–61	0.153	0.151	D15	30.2	0.2–37.3	0.254	0.016
V20	30	0–58	0.165	0.121	D20	28.0	0.1–36.0	0.263	0.012
V25	24	0–44	0.208	0.050	D25	24.6	0.0–35.7	0.255	0.015
V30	16	0–38	0.235	0.026	D30	19.5	0.0–35.1	0.204	0.054
					D _{max}	32.7	0.0–42.1	0.333	0.001
					D _{mean}	10.7	1.1–17.5	0.205	0.053
Right lung									
V5	43	0–66	0.124	0.246	D5	31.5	0.1–39.0	0.232	0.028
V10	38	0–61	0.126	0.238	D10	30.7	0.1–38.4	0.239	0.023
V15	33	0–55	0.148	0.163	D15	30.2	0.1–37.2	0.250	0.018
V20	30	0–51	0.159	0.135	D20	27.9	0.1–36.4	0.272	0.009
V25	24	0–45	0.218	0.039	D25	24.7	0.1–36.0	0.288	0.006
V30	16	0–39	0.232	0.028	D30	19.8	0.1–35.6	0.230	0.029
					D _{max}	32.7	0.7–41.9	0.255	0.246
					D _{mean}	11.2	0.1–17.7	0.212	0.238
Left lung									
V5	39	0–83	0.204	0.054	D5	31.2	0.5–41.3	0.259	0.014
V10	35	0–80	0.191	0.072	D10	30.6	0.3–41.1	0.279	0.008
V15	31	0–77	0.181	0.088	D15	30.1	0.2–40.8	0.290	0.006
V20	29	0–74	0.176	0.097	D20	27.3	0.1–39.9	0.243	0.021
V25	22	0–58	0.201	0.057	D25	23.6	0.1–36.4	0.245	0.020
V30	16	0–53	0.209	0.048	D30	17.0	0.1–36.2	0.232	0.028
					D _{max}	32.5	1.3–42.1	0.316	0.002
					D _{mean}	10.5	0.2–23.3	0.227	0.031

AVx, absolute volume receiving x Gy; Dmax, maximum dose; Dx, the minimum dose to x% highest dose volume; Vx, percentage volume receiving x Gy.

Supplementary Table III. Two-variable logistic regression models to investigate the cross-variable interaction between heart and lung variables (A, B and $A \times B$). AUC and Rs are calculated for each model.

Two variables and cross variable	Rs	p	AUC
Dmax left lung-left lung volume	0.4354	<0.0001	0.7743
D15 left lung-Heart volume	0.4158	<0.0001	0.7619
Dmax left lung-Heart volume	0.4111	0.0001	0.759
Dmax lungs-Heart volume	0.4111	0.0001	0.759
Dmax lungs-left lung volume	0.4102	0.0001	0.7584
AV30 heart-Heart volume	0.3981	0.0001	0.7507
D10 heart-left lung volume	0.3915	0.0001	0.7466
D25 left lung-Heart volume	0.3906	0.0001	0.746
D15 left lung-left lung volume	0.3887	0.0002	0.7449
AV30 heart-left lung volume	0.3803	0.0002	0.7396
Dmax heart-left lung volume	0.3738	0.0003	0.7354
D95 left lung-Dmax lungs	0.3696	0.0003	0.7328
D10 heart-Heart volume	0.3691	0.0003	0.7325
D95 left lung-Heart volume	0.3664	0.0004	0.7307
Dmax heart-Heart volume	0.357	0.0006	0.7249
D95 left lung-Dmax left lung	0.3542	0.0006	0.7231
D25 right lung-Heart volume	0.3514	0.0007	0.7213
D25 left lung-Dmax lungs	0.3472	0.0008	0.7187
D95 left lung-D10 heart	0.3425	0.001	0.7158
Dmax left lung-Dmax lungs	0.3421	0.001	0.7155
D25 right lung-Dmax lungs	0.3416	0.001	0.7152
D25 left lung-AV30 heart	0.3388	0.0011	0.7134
Dmax lungs-Dmax heart	0.3388	0.0011	0.7134
D15 left lung-Dmax lungs	0.3379	0.0011	0.7128
D10 heart-Dmax heart	0.337	0.0012	0.7122
Dmax right lung-Dmax lungs	0.3336	0.0013	0.7099
D15 left lung-D95 left lung	0.3323	0.0014	0.7093
D15 left lung-AV30 heart	0.3313	0.0014	0.7087
D95 left lung-Dmax heart	0.3314	0.0014	0.7087
Dmax left lung-D25 right lung	0.3309	0.0014	0.7084
D25 right lung-left lung volume	0.3271	0.0016	0.7061
Dmax lungs-D10 heart	0.3271	0.0016	0.7061
Dmax left lung-AV30 heart	0.3248	0.0018	0.7046
D95 left lung-AV30 heart	0.3247	0.0018	0.704
D25 left lung-Dmax left lung	0.3234	0.0019	0.7037
D95 left lung-left lung volume	0.3234	0.0019	0.7037
D10 heart-AV30 heart	0.3229	0.0019	0.7034
Dmax right lung-D10 heart	0.3206	0.0021	0.7019
D25 left lung-left lung volume	0.3178	0.0023	0.7002
AV30 heart-Dmax heart	0.316	0.0024	0.699
Dmax lungs-AV30 heart	0.3127	0.0027	0.6969
D15 left lung-Dmax left lung	0.3108	0.0029	0.6958
Heart volume-left lung volume	0.3066	0.0033	0.6931
D25 right lung-Dmax heart	0.3057	0.0034	0.6925
D25 right lung-D10 heart	0.3047	0.0035	0.6919
Dmax right lung-Dmax heart	0.3043	0.0035	0.6917
D95 left lung-Dmax right lung	0.3034	0.0037	0.6911
Dmax left lung-D10 heart	0.3015	0.0039	0.6899
D25 left lung-D95 left lung	0.3005	0.004	0.6893
Dmax left lung-Dmax heart	0.2987	0.0042	0.6881
D15 left lung-D25 right lung	0.2973	0.0044	0.6872
Dmax left lung-Dmax right lung	0.2931	0.0051	0.6846
D25 right lung-Dmax right lung	0.2875	0.006	0.6811
Dmax right lung-AV30 heart	0.2919	0.0052	0.6808
D15 left lung-D25 left lung	0.2805	0.0074	0.6767
D15 left lung-Dmax right lung	0.2758	0.0085	0.6737
D25 right lung-AV30 heart	0.2767	0.0083	0.6714
D25 left lung-Dmax heart	0.2707	0.0099	0.6705
D15 left lung-D10 heart	0.2702	0.01	0.6702
D25 left lung-D25 right lung	0.2693	0.0103	0.6696
D15 left lung-Dmax heart	0.2655	0.0114	0.6673
D25 left lung-Dmax right lung	0.2627	0.0124	0.6655