

Supplementary

Table S1 The risk for second primary malignancies after radiation therapy for initial lung cancer in patients stratified by clinical and therapeutic characteristics

Characteristic	Age-adjusted competing risk regression				PSM-adjusted competing risk regression			
	N	Events	HR (95% CI)	P value	N	Events	HR (95% CI)	P value
Year of diagnosis								
1975–1984	9,753	2,274	0.72 (0.64–0.80)	<0.001	8,501	1,986	0.73 (0.65–0.81)	<0.001
1985–1994	12,295	2,854	0.79 (0.73–0.86)	<0.001	7,787	1,717	0.85 (0.77–0.94)	0.002
1995–2004	14,193	2,927	0.97 (0.89–1.05)	0.42	6,569	1,264	1.1 (0.98–1.23)	0.097
2005–2011	11,670	1,107	1.10 (0.97–1.25)	0.14	5,139	461	1.18 (0.98–1.42)	0.08
Sex								
Male	24,093	5,108	0.85 (0.80–0.90)	<0.001	15,341	3,291	0.88 (0.81–0.95)	<0.001
Female	23,818	4,054	0.88 (0.82–0.94)	<0.001	12,655	2,137	0.91 (0.83–1.00)	0.052
Race								
White	40,400	7758	0.87 (0.82–0.91)	<0.001	23,386	4,542	0.89 (0.84–0.95)	<0.001
Black	4,323	907	0.85 (0.73–0.98)	0.027	2,750	583	0.87 (0.73–1.03)	0.11
Others	3,100	497	0.86 (0.71–1.05)	<0.001	1,832	303	0.85 (0.67–1.08)	0.19
Unknown	68	0	–	–	28	0	–	–
Primary location								
Upper lobe	28,140	5,744	0.85 (0.80–0.91)	<0.001	16,358	3,388	0.88 (0.82–0.94)	<0.001
Middle lobe	2622	445	0.68 (0.52–0.89)	0.006	1,396	264	0.63 (0.46–0.87)	0.006
Lower lobe	12,216	2,235	0.81 (0.72–0.90)	<0.001	6,793	1,279	0.81 (0.71–0.93)	0.002
Main bronchus	1,154	198	1.17 (0.88–1.55)	0.28	731	127	1.04 (0.74–1.48)	0.81
Overlapping lesion	750	115	0.99 (0.66–1.49)	0.95	490	67	1.06 (0.63–1.76)	0.83
Unknown	3,029	425	1.26 (1.04–1.53)	0.02	2,228	303	1.37 (1.09–1.72)	0.007
Histologic type								
ADC	21,627	4,219	0.82 (0.76–0.89)	<0.001	10,689	2,063	0.90 (0.82–0.99)	0.03
SCC	12,125	2,583	0.78 (0.71–0.85)	<0.001	8,633	1,887	0.80 (0.72–0.89)	<0.001
SCLC	2,236	391	0.94 (0.76–1.17)	0.6	1,167	211	0.90 (0.69–1.18)	0.44
Other NSCLC	11,923	1,969	1.06 (0.97–1.17)	0.22	7,507	1,267	1.02 (0.91–1.15)	0.72
SEER stage								
Localized	17,614	3,376	0.81 (0.71–0.92)	0.001	4,593	843	0.83 (0.71–0.96)	0.013
Regional	12,157	2,093	1.09 (1.00–1.19)	0.048	8,785	1,598	1.09 (0.98–1.20)	0.10
Distant	3,483	443	1.25 (1.03–1.52)	0.026	2,375	279	1.23 (0.98–1.56)	0.079
Unknown	14,657	3,250	0.74 (0.68–0.81)	<0.001	12,243	2,708	0.76 (0.69–0.83)	<0.001
Surgery								
Yes	40,156	8,222	0.87 (0.82–0.91)	<0.001	23,146	4,931	0.87 (0.82–0.93)	<0.001
No	7,755	940	1.53 (1.33–1.76)	<0.001	4,850	497	1.32 (1.10–1.57)	0.002
Chemotherapy								
Yes	10,311	1,668	1.05 (0.95–1.16)	0.39	6,680	1,062	1.08 (0.96–1.22)	0.39
No/unknown	37,600	7,494	0.80 (0.75–0.85)	<0.001	21,316	4,366	0.83 (0.77–0.89)	<0.001

Table S2 The risk for second primary malignancies after radiation for initial lung cancer in different dose groups divided by the distance of second cancer from the lung

Second malignancy	Age-adjusted competing risk regression			PSM-adjusted competing risk regression		
	Events	HR (95% CI)	P value	Events	HR (95% CI)	P value
High-dose group	4,944	0.93 (0.87–0.99)	0.021	2,797	0.95 (0.88–1.03)	0.22
Lung and bronchus	3,908	0.95 (0.88–1.02)	0.14	2,195	1.04 (0.88–1.05)	0.41
Larynx	173	1.11 (0.80–1.55)	0.53	121	0.97 (0.66–1.42)	0.86
Esophagus	198	1.87 (1.41–2.48)	<0.001	141	1.76 (1.26–2.45)	<0.001
Female breast	607	0.67 (0.54–0.82)	<0.001	303	0.65 (0.50–0.85)	0.001
Thyroid	58	0.43 (0.20–0.90)	0.026	30	0.23 (0.07–0.77)	0.017
Medium-dose group	237	0.82 (0.61–1.11)	0.21	146	0.85 (0.59–1.22)	0.37
Oral cavity and pharynx	237	0.82 (0.61–1.11)	0.21	146	0.85 (0.59–1.22)	0.37
Low-dose group	3,123	0.78 (0.72–0.85)	<0.001	1,967	0.80 (0.73–0.89)	<0.001
Hepatobiliary system	114	0.90 (0.59–1.37)	0.62	63	0.78 (0.45–1.37)	0.39
Stomach	130	1.24 (0.86–1.80)	0.25	83	1.02 (0.64–1.61)	0.94
Colon, rectum and anus	750	0.88 (0.74–1.04)	0.12	490	0.83 (0.68–1.01)	0.058
Pancreas	200	0.63 (0.44–0.89)	0.010	119	0.71 (0.47–1.08)	0.11
Female genital system	161	0.67 (0.54–0.82)	<0.001	303	0.65 (0.50–0.85)	0.001
Prostate	909	0.60 (0.51–0.72)	<0.001	589	0.69 (0.58–0.84)	<0.001
Bladder	503	0.75 (0.61–0.93)	0.009	307	0.83 (0.65–1.07)	0.15
Melanoma of the skin	157	0.60 (0.40–0.91)	0.015	96	0.49 (0.29–0.81)	0.006
Nervous system	46	0.67 (0.32–1.40)	0.29	16	0.96 (0.33–2.77)	0.94
Kidney	153	1.15 (0.81–1.63)	0.45	93	1.40 (0.92–2.12)	0.11
Inseparable-dose group	710	0.87 (0.75–1.02)	0.092	518	0.91 (0.76–1.10)	0.33
Hematological system	498	0.87 (0.71–1.07)	0.19	302	0.94 (0.74–1.20)	0.62
Miscellaneous	155	0.91 (0.63–1.31)	0.6	95	1.03 (0.67–1.57)	0.91
Other unknown tumors	57	0.86 (0.63–1.18)	0.36	121	0.76 (0.51–1.14)	0.18