

Propensity score-matched evaluation of the incidence of radiation pneumonitis and secondary cancer risk for breast cancer patients treated with IMRT/VMAT

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Supplementary

Tables

Table S1. Initial candidate predictive factors for RP NTCP modeling.

No.	Description	Range or Classification	Median or frequency	<i>p</i> -value
1	MD	8.75-26.34	14.99	0.009
2	IV ₅	33.48-91.75	53.67	0.095
3	IV ₁₀	21.99-82.80	38.99	0.039
4	IV ₁₃	18.70-74.53	34.48	0.027
5	IV ₁₅	17.14-68.30	32.12	0.022
6	IV ₂₀	14.23-48.09	27.44	0.013
7	IV ₂₅	11.56-40.45	23.84	0.008
8	IV ₃₀	9.15-37.50	20.73	0.005
9	IV ₄₀	4.90-31.58	14.73	0.003
10	IV ₅₀	0.87-16.46	7.19	0.004

Abbreviations: MD, mean dose to the ipsilateral lung; IV₅ (the volume of the ipsilateral lung receiving at least 5 Gy; the following parameters are similar), IV₁₀~IV₅₀; *p*-value, univariate logistic test.

Table S2. Parameters used for Schneider's parameterization models

Organs	α	R	β	γ_e	γ_a
BS and SC	0.018	0.23	0.7	-0.024	2.38
Breast	0.044	0.15	8.2	-0.037	1.70
Lung (total)	0.042	0.83	8.0	0.002	4.23
Liver	0.323	0.29	2.4	-0.021	3.60
Stomach	0.460	0.46	5.2	-0.002	1.90

Abbreviation: Note this β is used for EAR calculation only. β within the α/β ratio is calculated from α based on $\alpha/\beta = 3$ Gy for all tissues. The EAR has units of excess cases per 10,000 person-years (PY)/Gy.

Table S3. Absorbed dose results for 6 OARs in patients treated with IMRT/VMAT

No.	IMRT							VMAT						
	Mean dose (Gy)						IV ₄₀ (%)	Mean dose						IV ₄₀ (%)
	SC	Liver	C-Breast	Stomach	C-Lung	I-Lung	I-Lung	SC	Liver	C-Breast	Stomach	C-Lung	I-Lung	I-Lung
1	0.18	0.44	0.90	5.31	0.64	12.22	12.54	0.46	1.45	1.41	0.72	2.52	9.82	16.48
2	0.19	0.65	0.59	4.30	0.29	13.21	14.79	0.46	1.45	1.41	0.72	0.92	9.82	9.47
3	0.25	3.69	2.29	0.38	0.51	14.06	15.33	0.52	0.53	2.29	0.51	0.74	9.41	8.19
4	0.25	1.22	3.79	0.88	2.64	14.75	15.51	0.86	2.13	2.68	2.77	2.74	8.75	4.90
5	1.09	0.96	0.78	3.36	0.53	15.92	18.42	1.31	1.71	2.96	2.79	1.87	9.48	7.22
6	0.23	3.05	1.11	0.19	0.36	16.16	18.07	0.97	0.84	2.97	0.76	1.06	10.19	7.21
7	2.40	5.06	0.78	0.22	0.52	14.88	14.45	0.44	0.56	1.93	1.44	1.95	10.58	21.00
8	1.54	3.15	2.17	15.67	1.63	15.44	17.43	0.92	1.13	1.45	2.80	1.21	10.98	9.08
9	1.59	7.36	2.46	0.83	0.83	13.91	20.65	0.63	1.23	1.79	0.22	2.07	12.56	14.32
10	1.02	3.59	2.31	0.76	0.73	17.05	18.77	0.87	1.35	2.74	0.88	1.12	12.19	12.01
11	1.81	3.80	9.23	2.39	3.01	14.67	13.98	1.31	2.97	2.07	0.72	1.18	10.85	8.80
12	1.21	3.08	1.41	14.72	0.86	18.00	13.55	1.28	4.10	2.13	1.16	1.27	11.53	10.63
13	1.16	4.91	2.17	4.19	0.56	17.06	17.89	0.95	1.94	2.14	0.66	1.75	11.97	10.68
14	0.41	2.03	1.54	0.25	0.44	17.62	20.74	0.88	0.44	3.20	0.84	1.33	10.92	7.63
15	0.35	2.30	1.39	4.90	0.59	17.35	20.07	1.00	1.25	5.20	0.70	1.40	12.08	9.93
16	0.45	1.96	1.52	2.00	2.82	18.32	22.68	1.86	2.24	2.34	2.18	1.69	12.56	11.79
17	1.46	13.61	2.20	2.38	1.06	17.18	19.37	2.14	0.78	0.86	1.07	1.90	10.71	5.34
18	1.61	9.24	5.93	2.68	1.36	16.17	16.04	0.49	0.96	1.26	3.71	1.13	15.41	8.33
19	0.90	6.90	3.24	0.78	1.80	16.58	17.36	7.79	3.15	2.84	0.55	2.88	13.95	13.13
0	0.31	9.20	1.26	0.26	0.30	18.81	19.97	3.66	1.58	5.16	0.46	2.38	13.93	13.75
21	2.82	0.68	0.59	2.13	0.79	17.30	12.74	1.26	3.95	6.92	2.06	3.87	12.56	8.63
22	1.85	2.77	2.06	7.63	1.07	17.78	18.42	0.99	0.92	2.18	4.65	1.31	12.13	11.64
23	1.60	10.28	1.97	0.77	0.56	18.58	20.49	0.99	0.92	2.18	4.65	1.11	12.13	8.24
24	1.71	0.78	2.73	2.35	1.08	18.33	19.20	0.85	3.18	1.25	0.76	1.01	12.50	8.91
25	4.19	0.50	1.76	3.33	0.93	20.97	24.28	5.22	1.11	3.21	0.62	2.78	13.69	13.17
26	1.91	11.48	5.03	1.09	1.40	16.55	11.30	0.92	1.94	1.61	11.79	1.01	11.98	7.16
27	1.68	3.85	4.11	13.13	2.05	19.46	20.33	1.65	9.96	2.21	1.43	1.50	13.50	9.08
28	2.12	2.50	1.70	9.61	1.04	20.20	23.13	2.94	5.81	2.13	0.40	1.08	17.24	17.13
29	2.24	1.94	2.03	11.18	1.96	26.34	31.58	4.21	1.60	2.15	1.53	2.65	16.43	15.43
30	0.92	6.14	2.66	0.61	0.97	24.81	22.31	2.51	2.18	4.30	4.06	2.00	16.77	15.63

Abbreviations: OED, organ equivalent doses; IMRT, intensity-modulated radiotherapy; VMAT, volumetric-modulated arc therapy; C-Breast, contralateral breast; I-Lung, ipsilateral lung; C-Lung, contralateral lung.

Table S4. OED results for patients treated with IMRT/VMAT

No.	IMRT - OED (Gy)						VMAT - OED (Gy)					
	SC	Liver	C-Breast	Stomach	I-Lung	C-Lung	SC	Liver	C-Breast	Stomach	I-Lung	C-Lung
1	0.18	0.28	0.77	0.49	4.85	0.64	0.60	0.63	1.64	0.53	4.03	2.52
2	0.19	0.29	0.54	0.56	5.03	0.29	0.45	0.60	1.27	0.48	4.11	0.92
3	0.25	0.75	1.18	0.31	5.49	0.51	0.51	0.38	1.74	0.38	4.21	0.74
4	0.25	0.44	2.12	0.49	5.85	2.64	0.85	0.84	2.16	0.83	4.54	2.74
5	1.05	0.35	0.68	0.79	5.92	0.53	1.27	0.52	2.08	0.63	4.76	1.87
6	0.23	0.62	0.81	0.17	5.96	0.36	0.95	0.51	2.31	0.41	4.83	1.06
7	2.11	0.72	0.66	0.19	6.01	0.52	0.43	0.39	1.56	0.57	4.86	1.95
8	1.48	0.99	1.87	0.87	6.20	1.63	0.89	0.57	1.30	0.66	4.98	1.21
9	1.52	0.94	2.01	0.47	6.24	0.83	0.62	0.40	1.51	0.19	5.01	2.07
10	0.98	0.73	1.94	0.45	6.26	0.73	0.85	0.57	2.23	0.34	5.02	1.12
11	1.72	0.81	1.62	0.77	6.35	3.01	1.27	0.76	1.73	0.47	5.06	1.18
12	1.14	0.47	1.14	0.79	6.41	0.86	1.25	0.89	1.83	0.62	5.08	1.27
13	1.15	0.67	1.44	0.62	6.47	0.56	0.93	0.55	1.73	0.40	5.31	1.75
14	0.41	0.61	0.85	0.22	6.49	0.44	0.86	0.35	2.44	0.52	5.39	1.33
15	0.35	0.41	1.03	0.64	6.51	0.59	0.98	0.62	2.87	0.46	5.44	1.40
16	0.44	0.60	1.29	0.72	6.57	2.82	1.62	0.66	1.77	0.58	5.48	1.69
17	1.39	0.93	1.86	0.87	6.60	1.06	2.00	0.53	2.82	0.58	5.73	1.90
18	1.53	0.93	1.89	0.82	6.66	1.36	0.49	0.60	1.12	0.64	5.73	1.13
19	0.88	0.84	2.24	0.53	6.67	1.80	6.39	0.81	2.40	0.40	5.74	2.88
20	0.31	0.80	1.00	0.22	6.69	0.30	3.25	0.61	3.33	0.35	5.80	2.38
21	2.37	0.34	0.51	0.78	6.96	0.79	1.22	0.71	4.57	0.70	5.87	3.87
22	1.74	0.53	1.19	0.85	7.08	1.07	0.97	0.55	1.84	0.72	5.89	1.31
23	1.50	0.92	1.57	0.46	7.18	0.56	0.97	0.55	1.84	0.72	5.89	1.11
24	1.61	0.47	2.20	0.76	7.19	1.08	0.83	0.95	1.16	0.53	5.89	1.01
25	3.44	0.30	1.28	0.80	7.20	0.93	4.41	0.62	2.45	0.43	5.92	2.78
26	1.82	0.92	2.96	0.50	7.22	1.40	0.90	0.74	1.44	0.89	5.94	1.01
27	1.61	0.93	2.79	0.76	7.55	2.05	1.60	0.98	1.91	0.77	6.49	1.50
28	2.03	0.52	1.30	0.86	7.81	1.04	2.65	0.86	1.41	0.33	6.77	1.08
29	2.03	0.58	1.67	0.82	9.21	1.96	3.79	0.79	1.79	0.67	6.81	2.65
30	0.90	0.76	2.14	0.40	9.73	0.97	2.36	0.79	2.61	0.81	7.01	2.00

Abbreviation: OED, organ equivalent doses; IMRT, intensity modulated radiotherapy; VMAT, volumetric modulated arc therapy; C-Breast, contralateral breast; I-Lung, ipsilateral lung; C-Lung, contralateral lung.

Table S5. EAR results for patients treated with IMRT/VMAT

No.	IMRT (EAR/10000 PY)						VMAT (EAR/10000 PY)					
	SC	Liver	C-Breast	Stomach	I-Lung	C-Lung	SC	Liver	C-Breast	Stomach	I-Lung	C-Lung
1	0.09	0.49	3.47	2.49	40.03	4.63	0.25	1.17	7.19	2.46	33.55	20.57
2	0.06	0.36	1.40	2.72	42.85	2.47	0.19	0.91	4.61	2.41	34.36	7.69
3	0.09	0.95	3.18	1.53	46.65	4.33	0.23	0.62	7.07	1.89	34.96	6.15
4	0.09	0.59	6.17	2.42	49.45	22.34	0.35	1.27	7.83	4.14	37.94	22.59
5	0.37	0.46	1.97	3.90	50.09	4.99	0.56	0.84	8.43	3.14	39.60	15.54
6	0.11	1.03	3.56	0.86	49.29	2.98	0.38	0.75	8.09	2.05	40.46	8.88
7	0.85	1.06	2.32	0.96	50.36	4.36	0.15	0.49	4.20	2.78	41.27	16.56
8	0.74	1.78	9.14	4.42	51.00	13.41	0.58	1.29	9.54	3.44	40.08	9.74
9	0.58	1.33	6.55	2.32	52.47	7.09	0.26	0.61	5.67	0.95	41.83	17.27
10	0.72	1.82	17.16	2.37	49.85	5.82	0.35	0.86	8.10	1.71	41.93	9.36
11	0.70	1.20	12.66	3.84	53.23	25.21	0.58	1.25	7.29	2.36	42.00	9.79
12	0.36	0.57	2.76	3.87	54.82	7.12	0.67	1.70	9.98	3.16	41.51	10.39
13	0.46	1.02	3.27	2.85	55.41	8.32	0.37	0.79	5.85	1.99	44.53	14.69
14	0.17	0.93	3.09	1.09	54.28	3.68	0.43	0.63	11.90	2.63	44.30	10.94
15	0.17	0.71	4.85	3.23	53.63	4.86	0.51	1.16	15.10	2.34	44.58	11.47
16	0.14	0.72	3.12	3.49	56.16	24.10	0.69	1.05	7.01	2.81	45.74	14.13
17	0.56	1.38	6.52	4.30	55.32	8.88	0.98	0.92	3.88	2.95	47.20	15.66
18	0.59	1.31	12.64	4.07	55.98	11.44	0.20	0.91	4.08	3.19	47.91	9.45
19	0.41	1.42	9.79	2.68	55.17	14.99	2.18	1.03	6.47	1.94	48.77	24.46
20	0.17	1.52	5.45	1.12	54.70	2.45	1.06	0.75	8.37	1.71	49.50	20.30
21	0.89	0.48	1.61	3.87	58.69	6.64	0.67	1.38	25.89	3.55	47.87	31.59
22	0.67	0.76	3.89	4.18	59.56	9.00	0.31	0.67	4.62	3.52	50.24	11.17
23	0.59	1.34	5.30	2.26	60.25	4.70	0.47	0.95	8.66	3.64	48.56	9.15
24	0.72	0.75	8.95	3.79	59.76	8.97	0.52	2.06	7.90	2.71	47.62	8.16
25	1.89	0.59	7.24	4.06	58.74	7.59	1.78	0.92	8.57	2.14	49.61	23.29
26	0.64	1.20	8.29	2.43	61.18	11.87	0.53	1.52	9.09	4.57	48.16	8.19
27	0.59	1.26	8.42	3.75	63.78	17.31	0.95	2.03	12.07	3.92	52.62	12.17
28	1.17	1.05	7.92	4.41	63.53	8.45	0.92	1.12	3.95	1.62	57.37	9.10
29	0.76	0.81	5.22	4.05	77.60	16.52	1.32	1.03	5.02	3.29	57.70	22.47
30	0.30	0.95	5.56	1.95	82.82	8.26	0.87	1.08	7.87	3.98	59.16	16.89

Abbreviation: EAR, excess absolute risks; IMRT, intensity modulated radiotherapy; VMAT, volumetric modulated arc therapy; C-Breast, contralateral breast; I-Lung, ipsilateral lung; C-Lung, contralateral lung. The EAR has units of excess cases per 10,000 person-years (PY)/Gy.

Table S6. Difference comparison between IMRT and VMAT with OED and EAR

Techniques Organs	averaged OED (Gy) (30: 30)			averaged EAR (/10000 PY) (30: 30)		
	IMRT	VMAT	<i>p</i>	IMRT	VMAT	<i>P</i>
Spinal cord	1.22	1.54	0.27	0.52	0.64	0.28
C-Breast	1.48	2.03	<0.01	6.05	8.14	0.05
I-Lung	6.68	5.45	<0.01	55.89	45.36	<0.01
C-Lung	1.11	1.71	<0.01	9.43	14.26	<0.01
Liver	0.65	0.64	0.94	0.99	1.06	0.53
Stomach	0.60	0.55	0.38	2.98	2.77	0.42

Abbreviations: IMRT, intensity-modulated radiotherapy; VMAT, volumetric-modulated arc therapy; OED, organ equivalent doses; EAR, excess absolute risks; C-Breast, contralateral breast; I-Lung, ipsilateral lung; C-Lung, contralateral lung. The EAR has units of excess cases per 10,000 person-years (PY)/Gy.

Supplementary

Figures

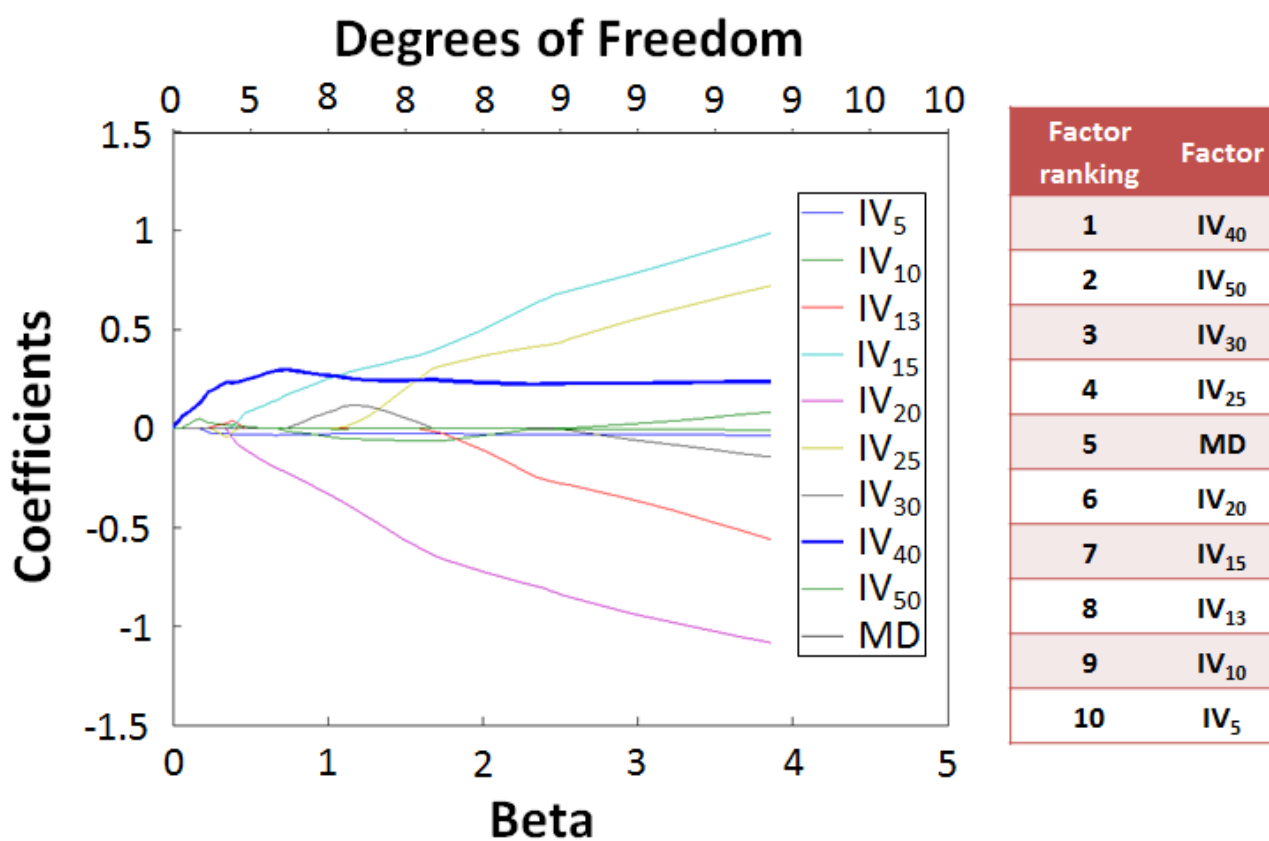


Figure S1: The LASSO trace plot of dosimetric candidate predictive factors and the factors ranking list.

Abbreviations: IV₄₀: the volume of the ipsilateral lung receiving at least 40 Gy; the following parameters are similar; IV₅~IV₅₀; LASSO: least absolute shrinkage and selection operator.

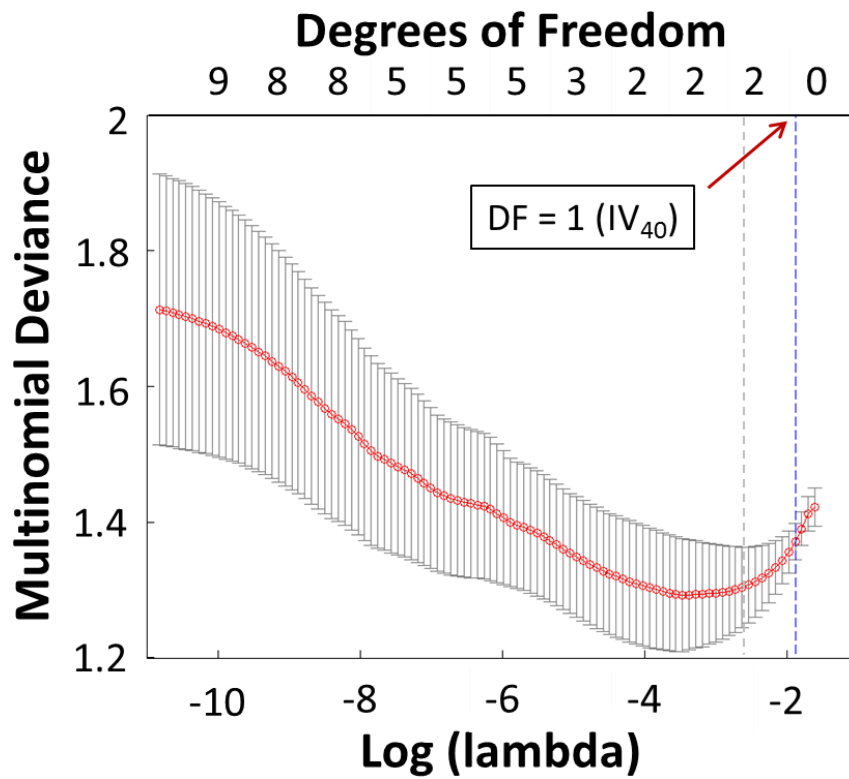


Figure S2: The cross-validated mean squared error (MSE) of the LASSOGLM fit. IV_{40} was selected as the dominant risk factor for the RP NTCP model by LASSO using cross-validation.

Abbreviations: LASSO, least absolute shrinkage and selection operator; RP, radiation-induced pneumonitis; NTCP, normal tissue complication probability; IV_{40} : the volume of the ipsilateral lung receiving at least 40 Gy;