

Table S1: Radiobiological parameters for EUD, TCP and NTCP calculations

Organ	α/β	γ	m	n	a	TD_{50}	Endpoint	Reference
PTV_Eval	4	1.3	/	/	-7.2	30.89	Tumor Control	[23, 25]
Breast	3	/	0.35	0.012	/	132	grade ≥ 2 breast fibrosis	[30]
Skin	10	/	0.14	0.38	/	39	RTOG grade ≥ 3 acute radiation dermatitis	[31, 32]
Lungs	3	/	0.18	0.87	/	24.5	Radiation pneumonitis	[34]
Heart	3	/	0.1	0.35	/	48	Pericarditis	[34]
Thyroid	3	/	0.26	0.22	/	80	Hypothyroidism	[35]

Table S2: Parameters for secondary cancer risk (EAR) calculation

Site	β_{EAR}	γ_e	γ_a	α (Gy $^{-1}$)	α/β	R
breast	9.2	-0.037	1.7	0.044	3	0.15
lung	7.5	0.002	4.23	0.042	3	0.83

Table S3: Other OAR equivalent uniform doses (EUDs) across the eight fractionation regimens

Regimen	Heart	Thyroid	Lungs	Contralateral breast
24 Gy/4f	0.77 $\pm$ 0.77	0.039 $\pm$ 0.016	2.02 $\pm$ 0.35	0.40 $\pm$ 0.09
25 Gy/4f	0.81 $\pm$ 0.82	0.040 $\pm$ 0.017	2.14 $\pm$ 0.37	0.42 $\pm$ 0.09
28 Gy/4f	0.93 $\pm$ 0.98	0.044 $\pm$ 0.019	2.53 $\pm$ 0.45	0.47 $\pm$ 0.11
32 Gy/4f	1.11 $\pm$ 1.21	0.050 $\pm$ 0.022	3.10 $\pm$ 0.56	0.54 $\pm$ 0.12
26 Gy/5f	0.80 $\pm$ 0.77	0.041 $\pm$ 0.018	2.06 $\pm$ 0.34	0.43 $\pm$ 0.10
30 Gy/5f	0.96 $\pm$ 0.96	0.047 $\pm$ 0.021	2.52 $\pm$ 0.43	0.50 $\pm$ 0.11
35 Gy/5f	1.17 $\pm$ 1.22	0.055 $\pm$ 0.024	3.17 $\pm$ 0.56	0.59 $\pm$ 0.13
40 Gy/5f	1.39 $\pm$ 1.52	0.062 $\pm$ 0.028	3.87 $\pm$ 0.70	0.67 $\pm$ 0.16

Values are mean $\pm$ SD, in Gy.

Table S4: Other OAR normal tissue complication probabilities (NTCPs) across the eight fractionation regimens

Regimen	Heart	Thyroid	Lungs	Contralateral breast
24 Gy/4f	$\sim 10^{-23}$	$\sim 6 \times 10^{-5}$	$\sim 1.5 \times 10^{-7}$	0.00219 ± 0.00002
25 Gy/4f	$\sim 10^{-23}$	$\sim 6 \times 10^{-5}$	$\sim 1.8 \times 10^{-7}$	0.00219 ± 0.00002
28 Gy/4f	$\sim 10^{-23}$	$\sim 6 \times 10^{-5}$	$\sim 2.7 \times 10^{-7}$	0.00220 ± 0.00002
32 Gy/4f	$\sim 10^{-23}$	$\sim 6 \times 10^{-5}$	$\sim 5.0 \times 10^{-7}$	0.00221 ± 0.00002
26 Gy/5f	$\sim 10^{-23}$	$\sim 6 \times 10^{-5}$	$\sim 1.6 \times 10^{-7}$	0.00219 ± 0.00002
30 Gy/5f	$\sim 10^{-23}$	$\sim 6 \times 10^{-5}$	$\sim 2.5 \times 10^{-7}$	0.00220 ± 0.00002
35 Gy/5f	$\sim 10^{-23}$	$\sim 6 \times 10^{-5}$	$\sim 4.8 \times 10^{-7}$	0.00222 ± 0.00002
40 Gy/5f	$\sim 10^{-23}$	$\sim 6 \times 10^{-5}$	$\sim 9.9 \times 10^{-7}$	0.00223 ± 0.00002

Values are approximate unless shown as mean $\pm$ SD.

TCP difference (percentage points)

Table S5: Full pairwise mean-difference comparisons for TCP, NTCP and UTCP among the eight regimens

Row – column	24 Gy/4f	25 Gy/4f	28 Gy/4f	32 Gy/4f	26 Gy/5f	30 Gy/5f	35 Gy/5f	40 Gy/5f
24 Gy/4f	–	-4.4	-12.0	-15.6	+0.3	-11.2	-15.6	-16.8
25 Gy/4f	+4.4	–	-7.6	-11.2	+4.7	-6.8	-11.2	-12.4
28 Gy/4f	+12.0	+7.6	–	-3.6	+12.3	+0.8	-3.6	-4.8
32 Gy/4f	+15.6	+11.2	+3.6	–	+15.9	+4.4	+0.0	-1.2
26 Gy/5f	-0.3	-4.7	-12.3	-15.9	–	-11.5	-15.9	-17.1
30 Gy/5f	+11.2	+6.8	-0.8	-4.4	+11.5	–	-4.4	-5.6
35 Gy/5f	+15.6	+11.2	+3.6	+0.0	+15.9	+4.4	–	-1.2
40 Gy/5f	+16.8	+12.4	+4.8	+1.2	+17.1	+5.6	+1.2	–

Fibrosis NTCP difference (percentage points)

Row – column	24 Gy/4f	25 Gy/4f	28 Gy/4f	32 Gy/4f	26 Gy/5f	30 Gy/5f	35 Gy/5f	40 Gy/5f
24 Gy/4f	–	-0.50	-2.57	-7.27	+0.09	-2.06	-7.08	-16.24
25 Gy/4f	+0.50	–	-2.07	-6.77	+0.59	-1.56	-6.58	-15.74
28 Gy/4f	+2.57	+2.07	–	-4.70	+2.66	+0.51	-4.51	-13.67
32 Gy/4f	+7.27	+6.77	+4.70	–	+7.36	+5.21	+0.19	-8.97
26 Gy/5f	-0.09	-0.59	-2.66	-7.36	–	-2.15	-7.17	-16.33
30 Gy/5f	+2.06	+1.56	-0.51	-5.21	+2.15	–	-5.02	-14.18
35 Gy/5f	+7.08	+6.58	+4.51	-0.19	+7.17	+5.02	–	-9.16
40 Gy/5f	+16.24	+15.74	+13.67	+8.97	+16.33	+14.18	+9.16	–

Dermatitis NTCP difference (percentage points)

Row – column	24 Gy/4f	25 Gy/4f	28 Gy/4f	32 Gy/4f	26 Gy/5f	30 Gy/5f	35 Gy/5f	40 Gy/5f
24 Gy/4f	–	-0.002	-0.028	-0.282	-0.001	-0.032	-0.355	-3.089
25 Gy/4f	+0.002	–	-0.026	-0.280	+0.001	-0.030	-0.353	-3.087
28 Gy/4f	+0.028	+0.026	–	-0.254	+0.027	-0.004	-0.327	-3.061
32 Gy/4f	+0.282	+0.280	+0.254	–	+0.281	+0.250	-0.073	-2.807
26 Gy/5f	+0.001	-0.001	-0.027	-0.281	–	-0.031	-0.354	-3.088
30 Gy/5f	+0.032	+0.030	+0.004	-0.250	+0.031	–	-0.323	-3.057
35 Gy/5f	+0.355	+0.353	+0.327	+0.073	+0.354	+0.323	–	-2.734
40 Gy/5f	+3.089	+3.087	+3.061	+2.807	+3.088	+3.057	+2.734	–

UTCP difference (percentage points)

Row – column	24 Gy/4f	25 Gy/4f	28 Gy/4f	32 Gy/4f	26 Gy/5f	30 Gy/5f	35 Gy/5f	40 Gy/5f
24 Gy/4f	–	-3.82	-9.17	-7.77	+0.23	-8.91	-7.91	+2.28
25 Gy/4f	+3.82	–	-5.35	-3.95	+4.05	-5.09	-4.09	+6.10
28 Gy/4f	+9.17	+5.35	–	+1.40	+9.40	+0.26	+1.26	+11.45
32 Gy/4f	+7.77	+3.95	-1.40	–	+8.00	-1.14	-0.14	+10.05
26 Gy/5f	-0.23	-4.05	-9.40	-8.00	–	-9.14	-8.14	+2.05
30 Gy/5f	+8.91	+5.09	-0.26	+1.14	+9.14	–	+1.00	+11.19
35 Gy/5f	+7.91	+4.09	-1.26	+0.14	+8.14	-1.00	–	+10.19
40 Gy/5f	-2.28	-6.10	-11.45	-10.05	-2.05	-11.19	-10.19	–

Values are row mean minus column mean. Positive values indicate that the row regimen has a higher mean value than the column regimen. Statistical significance categories are shown in Figure 4.

Ipsilateral breast EAR relative difference (%)

Table S6: Full pairwise relative-difference comparisons for organ-specific EAR among the eight regimens

Row – column	24 Gy/4f	25 Gy/4f	28 Gy/4f	32 Gy/4f	26 Gy/5f	30 Gy/5f	35 Gy/5f	40 Gy/5f
24 Gy/4f	–	+2.4	+9.2	+16.5	-11.6	-3.8	+3.9	+10.5
25 Gy/4f	-2.3	–	+6.6	+13.8	-13.7	-6.0	+1.5	+8.0
28 Gy/4f	-8.4	-6.2	–	+6.7	-19.0	-11.9	-4.8	+1.3
32 Gy/4f	-14.1	-12.1	-6.3	–	-24.1	-17.4	-10.8	-5.1
26 Gy/5f	+13.2	+15.8	+23.5	+31.8	–	+8.9	+17.6	+25.1
30 Gy/5f	+3.9	+6.4	+13.5	+21.1	-8.1	–	+8.0	+14.9
35 Gy/5f	-3.8	-1.5	+5.0	+12.1	-15.0	-7.4	–	+6.4
40 Gy/5f	-9.5	-7.4	-1.3	+5.4	-20.1	-13.0	-6.0	–

Contralateral breast EAR relative difference (%)

Row – column	24 Gy/4f	25 Gy/4f	28 Gy/4f	32 Gy/4f	26 Gy/5f	30 Gy/5f	35 Gy/5f	40 Gy/5f
24 Gy/4f	–	-5.1	-14.9	-25.3	-7.5	-19.6	-31.5	-40.3
25 Gy/4f	+5.4	–	-10.3	-21.2	-2.5	-15.2	-27.8	-37.1
28 Gy/4f	+17.6	+11.5	–	-12.1	+8.7	-5.4	-19.4	-29.8
32 Gy/4f	+33.8	+26.9	+13.8	–	+23.7	+7.6	-8.3	-20.2
26 Gy/5f	+8.1	+2.6	-8.0	-19.2	–	-13.0	-25.9	-35.5
30 Gy/5f	+24.3	+17.9	+5.7	-7.1	+15.0	–	-14.8	-25.8
35 Gy/5f	+45.9	+38.5	+24.1	+9.1	+35.0	+17.4	–	-12.9
40 Gy/5f	+67.6	+59.0	+42.5	+25.3	+55.0	+34.8	+14.8	–

Ipsilateral lung EAR relative difference (%)

Row – column	24 Gy/4f	25 Gy/4f	28 Gy/4f	32 Gy/4f	26 Gy/5f	30 Gy/5f	35 Gy/5f	40 Gy/5f
24 Gy/4f	–	-2.6	-9.2	-16.3	-6.4	-14.5	-22.2	-28.1
25 Gy/4f	+2.7	–	-6.8	-14.0	-3.8	-12.2	-20.1	-26.1
28 Gy/4f	+10.2	+7.3	–	-7.8	+3.2	-5.8	-14.3	-20.8
32 Gy/4f	+19.4	+16.3	+8.4	–	+11.8	+2.1	-7.1	-14.1
26 Gy/5f	+6.8	+4.0	-3.1	-10.6	–	-8.7	-16.9	-23.2
30 Gy/5f	+17.0	+13.9	+6.2	-2.1	+9.5	–	-9.0	-15.9
35 Gy/5f	+28.5	+25.2	+16.7	+7.6	+20.4	+9.9	–	-7.5
40 Gy/5f	+39.0	+35.4	+26.2	+16.4	+30.2	+18.9	+8.2	–

Contralateral lung EAR relative difference (%)

Row – column	24 Gy/4f	25 Gy/4f	28 Gy/4f	32 Gy/4f	26 Gy/5f	30 Gy/5f	35 Gy/5f	40 Gy/5f
24 Gy/4f	–	-4.0	-14.4	-25.4	-7.0	-19.2	-31.2	-39.9
25 Gy/4f	+4.2	–	-10.8	-22.3	-3.0	-15.8	-28.3	-37.4
28 Gy/4f	+16.8	+12.1	–	-12.9	+8.7	-5.7	-19.6	-29.8
32 Gy/4f	+34.1	+28.7	+14.8	–	+24.8	+8.3	-7.7	-19.4
26 Gy/5f	+7.5	+3.1	-8.0	-19.9	–	-13.2	-26.0	-35.4
30 Gy/5f	+23.8	+18.8	+6.0	-7.7	+15.2	–	-14.8	-25.6
35 Gy/5f	+45.3	+39.5	+24.4	+8.4	+35.2	+17.4	–	-12.6
40 Gy/5f	+66.4	+59.6	+42.4	+24.0	+54.8	+34.3	+14.5	–

Values are relative differences calculated as (row mean – column mean)/column mean $\times$ 100%. Positive values indicate that the row regimen has a higher EAR than the column regimen. Statistical significance categories are shown in Figure 5.