

Table 2 Mostly Unvalidated Normal Tissue Dose Constraints for SBRT

Serial Tissue	Volume (mL)	Volume Max (Gy)	Max Point Dose (Gy)	Endpoint ( $\geq$ Grade 3)
<b>SINGLE-FRACTION TREATMENT</b>				
Optic pathway	<0.2	8	10	Neuritis
Cochlea			12	Hearing loss
Brainstem	<1	10	15	Cranial neuropathy
Spinal cord	<0.25	10	14	Myelitis
	<1.2	7		
Cauda equina	<5	14	16	Neuritis
Sacral plexus	<3	14.4	16	Neuropathy
Esophagus*	<5	14.5	19	Stenosis/fistula
Ipsilateral brachial plexus	<3	14.4	16	Neuropathy
Heart/pericardium	<15	16	22	Pericarditis
Great vessels	<10	31	37	Aneurysm
Trachea and ipsilateral bronchus*	<4	8.8	22	Stenosis/fistula
Skin	<10	14.4	16	Ulceration
Stomach	<10	13	16	Ulceration/fistula
Duodenum*	<5	8.8	16	Ulceration
Jejunum/ileum*	<5	9.8	19	Enteritis/obstruction
Colon*	<20	11	22	Colitis/fistula
Rectum*	<20	11	22	Proctitis/fistula
Bladder wall	<15	8.7	22	Cystitis/fistula
Penile bulb	<3	14	34	Impotence
Femoral heads (right and left)	<10	14		Necrosis
Renal hilum/vascular trunk	<2/3 volume	10.6		Malignant hypertension
Parallel Tissue	Critical Volume (mL)	Critical Volume Dose Max (Gy)		Endpoint ( $\geq$ Grade 3)
Lung (right and left)	1,500	7		Basic lung function
Lung (right and left)	1,000	7.4		Pneumonitis
Liver	700	9.1		Basic liver function
Renal cortex (right and left)	200	8.4		Basic renal function
Serial Tissue	Volume (mL)	Volume Max (Gy)	Max Point Dose (Gy)	Endpoint ( $\geq$ Grade 3)
<b>THREE-FRACTION TREATMENT</b>				
Optic pathway	<0.2	15 (5 Gy/fx)	19.5 (6.5 Gy/fx)	Neuritis
Cochlea			20 (6.67 Gy/fx)	Hearing loss
Brainstem	<1	18 (6 Gy/fx)	23 (7.67 Gy/fx)	Cranial neuropathy
Spinal cord	<0.25	18 (6 Gy/fx)	22 (7.33 Gy/fx)	Myelitis
	<1.2	11.1 (3.7 Gy/fx)		
Cauda equina	<5	21.9 (7.3 Gy/fx)	24 (8 Gy/fx)	Neuritis
Sacral plexus	<3	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Neuropathy
Esophagus*	<5	21 (7 Gy/fx)	27 (9 Gy/fx)	Stenosis/fistula
Ipsilateral brachial plexus	<3	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Neuropathy
Heart/pericardium	<15	24 (8 Gy/fx)	30 (10 Gy/fx)	Pericarditis
Great vessels	<10	39 (13 Gy/fx)	45 (15 Gy/fx)	Aneurysm
Trachea and ipsilateral bronchus*	<4	15 (5 Gy/fx)	30 (10 Gy/fx)	Stenosis/fistula
Skin	<10	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Ulceration
Stomach	<10	21 (7 Gy/fx)	24 (8 Gy/fx)	Ulceration/fistula
Duodenum*	<5	15 (5 Gy/fx)	24 (8 Gy/fx)	Ulceration
Jejunum/ileum*	<5	16.2 (5.4 Gy/fx)	27 (9 Gy/fx)	Enteritis/obstruction
Colon*	<20	20.4 (6.8 Gy/fx)	30 (10 Gy/fx)	Colitis/fistula
Rectum*	<20	20.4 (6.8 Gy/fx)	30 (10 Gy/fx)	Proctitis/fistula
Bladder wall	<15	15 (5 Gy/fx)	30 (10 Gy/fx)	Cystitis/fistula
Penile bulb	<3	21.9 (7.3 Gy/fx)	42 (14 Gy/fx)	Impotence
Femoral heads (right and left)	<10	21.9 (7.3 Gy/fx)		Necrosis
Renal hilum/vascular trunk	<2/3 volume	18.6 (6.2 Gy/fx)		Malignant hypertension
Parallel Tissue	Critical Volume (mL)	Critical Volume Dose Max (Gy)		Endpoint ( $\geq$ Grade 3)
Lung (right and left)	1,500	10.5 (3.5 Gy/fx)		Basic lung function
Lung (right and left)	1,000	11.4 (3.8 Gy/fx)		Pneumonitis
Liver	700	17.1 (5.7 Gy/fx)		Basic liver function
Renal cortex (right and left)	200	14.4 (4.8 Gy/fx)		Basic renal function

Table 2 Continued

Serial Tissue	Volume (mL)	Volume Max (Gy)	Max Point Dose (Gy)	Endpoint ( $\geq$ Grade 3)
<b>FIVE-FRACTION TREATMENT</b>				
Optic pathway	<0.2	20 (4 Gy/fx)	25 (5 Gy/fx)	Neuritis
Cochlea			27.5 (5.5 Gy/fx)	Hearing loss
Brainstem	<1	26 (5.2 Gy/fx)	31 (6.2 Gy/fx)	Cranial neuropathy
Spinal cord	<0.25	22.5 (4.5 Gy/fx)	30 (6 Gy/fx)	Myelitis
	<1.2	13.5 (2.7 Gy/fx)		
Cauda equina	<5	30 (6 Gy/fx)	34 (6.4 Gy/fx)	Neuritis
Sacral plexus	<3	30 (6 Gy/fx)	32 (6.4 Gy/fx)	Neuropathy
Esophagus*	<5	27.5 (5.5 Gy/fx)	35 (7 Gy/fx)	Stenosis/fistula
Ipsilateral brachial plexus	<3	30 (6 Gy/fx)	32 (6.4 Gy/fx)	Neuropathy
Heart/pericardium	<15	32 (6.4 Gy/fx)	38 (7.6 Gy/fx)	Pericarditis
Great vessels	<10	47 (9.4 Gy/fx)	53 (10.6 Gy/fx)	Aneurysm
Trachea and ipsilateral bronchus*	<4	18 (3.6 Gy/fx)	38 (7.6 Gy/fx)	Stenosis/fistula
Skin	<10	30 (6 Gy/fx)	32 (6.4 Gy/fx)	Ulceration
Stomach	<10	28 (5.6 Gy/fx)	32 (6.4 Gy/fx)	Ulceration/fistula
Duodenum*	<5	18 (3.6 Gy/fx)	32 (6.4 Gy/fx)	Ulceration
Jejunum/ileum*	<5	19.5 (3.9 Gy/fx)	35 (7 Gy/fx)	enteritis/obstruction
Colon*	<20	25 (5 Gy/fx)	38 (7.6 Gy/fx)	colitis/fistula
Rectum*	<20	25 (5 Gy/fx)	38 (7.6 Gy/fx)	proctitis/fistula
Bladder wall	<15	18.3 (3.65 Gy/fx)	38 (7.6 Gy/fx)	cystitis/fistula
Penile bulb	<3	30 (6 Gy/fx)	50 (10 Gy/fx)	Impotence
Femoral heads (right and left)	<10	30 (6 Gy/fx)		Necrosis
Renal hilum/vascular trunk	<2/3 volume	23 (4.6 Gy/fx)		Malignant hypertension
Parallel Tissue	Critical Volume (mL)	Critical Volume Dose Max (Gy)		Endpoint ( $\geq$ Grade 3)
Lung (right and left)	1,500	12.5 (2.5 Gy/fx)		Basic lung function
Lung (right and left)	1000	13.5 (2.7 Gy/fx)		Pneumonitis
Liver	700	21 (4.2 Gy/fx)		Basic liver function
Renal cortex (right and left)	200	17.5 (3.5 Gy/fx)		Basic renal function

\*Avoid circumferential irradiation.

tion of a hormone from a hormone-secreting pituitary adenoma takes a much higher dose. Another example can be borrowed from the use of radioactive iodine to treat thyroid cancer. The therapy is so well targeted that massive doses reach both the thyroid cancer and residual functioning thyroid gland. These doses both disrupt clonogenicity and cellular function. Such a treatment has been termed ablative.

Not all hypofractionated radiotherapy is ablative. In general, ablation occurs at dose levels that correspond to the exponential (linear region on a logarithmic scale) portion of the cell-survival curve, which would generally involve daily dose levels of  $>8$  Gy. Below this dose range, cells have more capacity to repair. The logarithm of cell survival as a function

of dose in the lower-dose region exhibits a curviness called the shoulder. More conventional and nonablative hypofractionated radiotherapy is delivered on the shoulder. The range of 2.25 to 8 Gy per fraction, still considered hypofractionated, has mostly been used for palliation of metastatic disease. More recently, though, investigators treating common diseases like breast and prostate cancer have used nonablative hypofractionation in patients with curable tumors. This was partly championed for the cost savings associated with fewer overall fractions, but in some cases such hypofractionation has a biological rationale for improving the therapeutic ratio. A summary of the degrees of hypofractionated radiotherapy and their effects is shown in Table 3.

Table 3 Once-Daily Fractionation Options

Type of Radiotherapy	Typical Dose per Fraction (Gy)	Characteristics
Conventionally fractionated radiotherapy	1.5 to 2.0	High cumulative doses, less apt to cause "late effects"
Hypofractionated radiotherapy	$>2.0$ to 8.0	Most commonly used for palliative treatment for patients near end of life, increasingly used for curative treatment in breast and prostate cancer therapy
Ablative radiotherapy	$>8.0$	Stops both cellular division and cellular function, overwhelms tumor repair, more likely to cause "late" effects