

Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)\*

Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated) <sup>†</sup>	Endpoint	Dose (Gy), or dose/volume parameters <sup>‡</sup>	Rate (%)	Notes on dose/volume parameters
Brain	Whole organ	3D-CRT	Symptomatic necrosis	Dmax <60	<3	Data at 72 and 90 Gy, extrapolated from BED models
	Whole organ	3D-CRT	Symptomatic necrosis	Dmax = 72	5	
	Whole organ	3D-CRT	Symptomatic necrosis	Dmax = 90	10	
	Whole organ	SRS (single fraction)	Symptomatic necrosis	V12 <5–10 cc	<20	Rapid rise when V12 > 5–10 cc
Brain stem	Whole organ	Whole organ	Permanent cranial neuropathy or necrosis	Dmax <54	<5	
	Whole organ	3D-CRT	Permanent cranial neuropathy or necrosis	D1–10 cc <sup>  </sup> ≤59	<5	
	Whole organ	3D-CRT	Permanent cranial neuropathy or necrosis	Dmax <64	<5	Point dose <<1 cc
	Whole organ	SRS (single fraction)	Permanent cranial neuropathy or necrosis	Dmax <12.5	<5	For patients with acoustic tumors
Optic nerve / chiasm	Whole organ	3D-CRT	Optic neuropathy	Dmax <55	<3	Given the small size, 3D CRT is often whole organ <sup>‡‡</sup>
	Whole organ	3D-CRT	Optic neuropathy	Dmax 55–60	3–7	
	Whole organ	3D-CRT	Optic neuropathy	Dmax >60	>7–20	
	Whole organ	SRS (single fraction)	Optic neuropathy	Dmax <12 use <8	<10	
Spinal cord	Partial organ	3D-CRT	Myelopathy	Dmax = 50	0.2	Including full cord cross-section
	Partial organ	3D-CRT	Myelopathy	Dmax = 60	6	
	Partial organ	3D-CRT	Myelopathy	Dmax = 69	50	
	Partial organ	SRS (single fraction)	Myelopathy	Dmax = 13	1	Partial cord cross-section irradiated
	Partial organ	SRS (hypofraction)	Myelopathy	Dmax = 20	1	
Cochlea	Whole organ	3D-CRT	Sensory neural hearing loss	Mean dose ≤45	<30	Mean dose to cochlear, hearing at 4 kHz
	Whole organ	SRS (single fraction)	Sensory neural hearing loss	Prescription dose ≤14	<25	Serviceable hearing
Parotid	Bilateral whole parotid glands	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <25	<20	For combined parotid glands <sup>¶</sup>
	Unilateral whole parotid gland	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <20	<20	For single parotid gland. At least one parotid gland spared to <20 Gy <sup>¶</sup>

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	Bilateral whole parotid glands	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <39	<50	For combined parotid glands (per Fig. 3 in paper) <sup>¶</sup>
Pharynx	Pharyngeal constrictors	Whole organ	Symptomatic dysphagia and aspiration	Mean dose <50	<20	Based on Section B4 in paper
Larynx	Whole organ	3D-CRT	Vocal dysfunction	Dmax <66	<20	With chemotherapy, based on single study (see Section A4.2 in paper)
	Whole organ	3D-CRT	Aspiration	Mean dose <50	<30	With chemotherapy, based on single study (see Fig. 1 in paper)
	Whole organ	3D-CRT	Edema	Mean dose <44	<20	Without chemotherapy, based on single study in patients without larynx cancer**
	Whole organ	3D-CRT	Edema	V50 <27%	<20	
Lung	Whole organ	3D-CRT	Symptomatic pneumonitis	V20 ≤ 30%	<20	For combined lung. Gradual dose response
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 7	5	Excludes purposeful whole lung irradiation
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 13	10	
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 20	20	
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 24	30	
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 27	40	
Esophagus	Whole organ	3D-CRT	Grade ≥3 acute esophagitis	Mean dose <34	5–20	Based on RTOG and several studies
	Whole organ	3D-CRT	Grade ≥2 acute esophagitis	V35 <50%	<30	A variety of alternate threshold doses have been implicated.
	Whole organ	3D-CRT	Grade ≥2 acute esophagitis	V50 <40%	<30	
	Whole organ	3D-CRT	Grade ≥2 acute esophagitis	V70 <20%	<30	Appears to be a dose/volume response
Heart	Pericardium	3D-CRT	Pericarditis	Mean dose <26	<15	Based on single study
	Pericardium	3D-CRT	Pericarditis	V30 <46%	<15	
	Whole organ	3D-CRT	Long-term cardiac mortality	V25 <10%	<1	Overly safe risk estimate based on model predictions

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Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated) <sup>†</sup>	Endpoint	Dose (Gy), or dose/volume parameters <sup>†</sup>	Rate (%)	Notes on dose/volume parameters
Liver	Whole liver – GTV	3D-CRT or Whole organ	Classic RILD <sup>††</sup>	Mean dose <30-32	<5	Excluding patients with pre-existing liver disease or hepatocellular carcinoma, as tolerance doses are lower in these patients
	Whole liver – GTV	3D-CRT	Classic RILD	Mean dose <42	<50	
	Whole liver – GTV	3D-CRT or Whole organ	Classic RILD	Mean dose <28	<5	In patients with Child-Pugh A preexisting liver disease or hepatocellular carcinoma, excluding hepatitis B reactivation as an endpoint
	Whole liver – GTV	3D-CRT	Classic RILD	Mean dose <36	<50	
	Whole liver –GTV	SBRT (hypofraction)	Classic RILD	Mean dose <13 <18	<5 <5	3 fractions, for primary liver cancer 6 fractions, for primary liver cancer
	Whole liver – GTV	SBRT (hypofraction)	Classic RILD	Mean dose <15 <20	<5 <5	3 fractions, for liver metastases 6 fractions, for liver metastases
	>700 cc of normal liver	SBRT (hypofraction)	Classic RILD	D <sub>max</sub> <15 <b>use &lt;10</b>	<5	Critical volume based, in 3–5 fractions
Kidney	Bilateral whole kidney <sup>‡</sup>	Bilateral whole organ or 3D-CRT	Clinically relevant renal dysfunction	Mean dose <15–18	<5	
	Bilateral whole kidney <sup>‡</sup>	Bilateral whole organ	Clinically relevant renal dysfunction	Mean dose <28	<50	
	Bilateral whole kidney <sup>‡</sup>	3D-CRT	Clinically relevant renal dysfunction	V12 <55% V20 <32% V23 <30% V28 <20%	<5	For combined kidney
Stomach	Whole organ	Whole organ	Ulceration	D100 <sup>  </sup> <45	<7	
Small bowel	Individual small bowel loops	3D-CRT	Grade ≥ 3 acute toxicity <sup>§</sup>	V15 <120 cc	<10	Volume based on segmentation of the individual loops of bowel, not the entire potential peritoneal space
	Entire potential space within peritoneal cavity	3D-CRT	Grade ≥ 3 acute toxicity <sup>§</sup>	V45 <195 cc	<10	Volume based on the entire potential space within the peritoneal cavity

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Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated) <sup>†</sup>	Endpoint	Dose (Gy), or dose/volume parameters <sup>†</sup>	Rate (%)	Notes on dose/volume parameters
Rectum	Whole organ	3D-CRT	Grade $\geq$ 2 late rectal toxicity, Grade $\geq$ 3 late rectal toxicity	V50 <50%	<15 <10	Prostate cancer treatment
	Whole organ	3D-CRT	Grade $\geq$ 2 late rectal toxicity, Grade $\geq$ 3 late rectal toxicity	V60 <35%	<15 <10	
	Whole organ	3D-CRT	Grade $\geq$ 2 late rectal toxicity, Grade $\geq$ 3 late rectal toxicity	V65 <25%	<15 <10	
	Whole organ	3D-CRT	Grade $\geq$ 2 late rectal toxicity, Grade $\geq$ 3 late rectal toxicity	V70 <20%	<15 <10	
	Whole organ	3D-CRT	Grade $\geq$ 2 late rectal toxicity, Grade $\geq$ 3 late rectal toxicity	V75 <15%	<15 <10	
Bladder	Whole organ	3D-CRT	Grade $\geq$ 3 late RTOG	Dmax <65	<6	Bladder cancer treatment. Variations in bladder size/shape/ location during RT hamper ability to generate accurate data
	Whole organ	3D-CRT	Grade $\geq$ 3 late RTOG	V65 $\leq$ 50 % V70 $\leq$ 35 % V75 $\leq$ 25 % V80 $\leq$ 15 %		Prostate cancer treatment Based on current RTOG 0415 recommendation
Penile bulb	Whole organ	3D-CRT	Severe erectile dysfunction	Mean dose to 95% of gland <50	<35	
	Whole organ	3D-CRT	Severe erectile dysfunction	D90 <sup>  </sup> <50	<35	
	Whole organ	3D-CRT	Severe erectile dysfunction	D60-70 <70	<55	

*Abbreviations:* 3D-CRT = 3-dimensional conformal radiotherapy, SRS = stereotactic radiosurgery, BED = Biologically effective dose, SBRT = stereotactic body radiotherapy, RILD = radiation-induced liver disease, RTOG = Radiation Therapy Oncology Group.

\* All data are estimated from the literature summarized in the QUANTEC reviews unless otherwise noted. Clinically, these data should be applied with caution. Clinicians are strongly advised to use the individual QUANTEC articles to check the applicability of these limits to the clinical situation at hand. They largely do not reflect modern IMRT.

<sup>†</sup> All at standard fractionation (*i.e.*, 1.8–2.0 Gy per daily fraction) unless otherwise noted. Vx is the volume of the organ receiving  $\geq$  x Gy. Dmax = Maximum radiation dose.

<sup>‡</sup> Non-TBI.

<sup>§</sup> With combined chemotherapy.

<sup>||</sup> Dx = minimum dose received by the “hottest” x% (or x cc’s) of the organ.

<sup>¶</sup> Severe xerostomia is related to additional factors including the doses to the submandibular glands.

\*\* Estimated by Dr. Eisbruch.

<sup>††</sup> Classic Radiation induced liver disease (RILD) involves anicteric hepatomegaly and ascites, typically occurring between 2 weeks and 3 months after therapy. Classic RILD also involves elevated alkaline phosphatase (more than twice the upper limit of normal or baseline value).

<sup>‡‡</sup> For optic nerve, the cases of neuropathy in the 55 to 60 Gy range received  $\approx$  59 Gy (see optic nerve paper for details). Excludes patients with pituitary tumors where the tolerance may be reduced.