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

| | | | | <u> </u> | | |
|-------------------------|---|---|---|---|--------------------|--|
| Organ | Volume segmented | Irradiation type (partial organ unless otherwise stated) [†] | Endpoint | Dose (Gy), or dose/volume parameters [†] | Rate (%) | Notes on dose/volume parameters |
| Brain | Whole organ Whole organ Whole organ | 3D-CRT 3D-CRT 3D-CRT | Symptomatic necrosis Symptomatic necrosis Symptomatic necrosis | Dmax <60 Dmax = 72 Dmax = 90 | <3 5 10 | Data at 72 and 90 Gy, extrapolated from BED models |
| | 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 | Dmax <54 | <5 | |
| | Whole organ | 3D-CRT | neuropathy or necrosis Permanent cranial neuropathy or necrosis | D1-10 $cc^{\parallel} \le 59$ | <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 Whole organ Whole organ | 3D-CRT 3D-CRT 3D-CRT | Optic neuropathy Optic neuropathy Optic neuropathy | Dmax <55 Dmax 55–60 Dmax >60 | <3 3–7 >7-20 | Given the small size, 3D CRT is often whole organ ^{‡‡} |
| | Whole organ | SRS (single fraction) | Optic neuropathy | Dmax <12 | <10 | |
| Spinal cord | Partial organ Partial organ Partial organ | 3D-CRT 3D-CRT 3D-CRT | Myelopathy Myelopathy Myelopathy | Dmax = 50 Dmax = 60 Dmax = 69 | 0.2 6 50 | Including full cord cross-section |
| | Partial organ Partial organ | SRS (single fraction) SRS (hypofraction) | Myelopathy Myelopathy | Dmax = 13 Dmax = 20 | 1 1 | Partial cord cross-section irradiated 3 fractions, partial cord cross-section irradiated |
| 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 ¶ |
| | 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 |
| | | | | | | (Continued) |

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

| Organ | Volume segmented | Irradiation type (partial organ unless otherwise stated) [†] | Endpoint | Dose (Gy), or dose/volume parameters [†] | Rate (%) | Notes on dose/volume parameters |
|-----------|--------------------------------|---|---|---|----------|--|
| | 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) \P |
| 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 |
| | Whole organ | 3D-CRT | Edema | V50 <27% | <20 | larynx cancer** |
| 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 |
| | Whole organ | 3D-CRT 3D-CRT | Symptomatic pneumonitis | Mean dose = 13 Mean dose = 20 | 10 20 | irradiation |
| | Whole organ Whole organ | 3D-CRT 3D-CRT | Symptomatic pneumonitis Symptomatic pneumonitis | Mean dose = 20 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 |
| | Whole organ | 3D-CRT | Grade ≥2 acute esophagitis | V50 <40% | <30 | have been implicated. Appears to be a dose/volume response |
| | 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 |
| | | · | | | | (Continued) |

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

| Organ | Volume segmented | Irradiation type (partial organ unless otherwise stated) [†] | Endpoint | Dose (Gy), or dose/volume parameters [†] | Rate (%) | Notes on dose/volume parameters |
|-------------|---|---|--|---|----------|--|
| Liver | Whole liver – GTV | 3D-CRT or Whole organ | Classic RILD ^{††} | 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 | are lower in these patients |
| | 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 |
| | Whole liver – GTV | 3D-CRT | Classic RILD | Mean dose <36 | <50 | as an endpoint |
| | 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 | $^{\mathrm{D}_{\mathrm{max}} < 15}$ use <10 $^{<5}$ | | Critical volume based, in 3–5 fractions |
| Kidney | Bilateral whole kidney [‡] | Bilateral whole organ or 3D-CRT | Clinically relevant renal dysfunction | Mean dose <15–18 | <5 | |
| | Bilateral whole kidney [‡] | Bilateral whole organ | Clinically relevant renal dysfunction | Mean dose <28 | <50 | |
| | Bilateral whole kidney [‡] | 3D-CRT | Clinically relevant renal dysfuntction | V12 <55% V20 <32% V23 <30% V28 <20% | <5 | For combined kidney |
| Stomach | Whole organ | Whole organ | Ulceration | D100 <45 | <7 | |
| Small bowel | Individual small bowel loops | 3D-CRT | Grade ≥ 3 acute toxicity [§] | 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§ | V45 <195 cc | <10 | Volume based on the entire potential space within the peritoneal cavity |
| | | | | | | (Continued) |

| Organ | Volume segmented | Irradiation type (partial organ unless otherwise stated) [†] | Endpoint | Dose (Gy), or dose/volume parameters [†] | Rate (%) | Notes on dose/volume parameters |
|-------------|----------------------------|---|---|---|------------|---|
| Rectum | Whole organ | 3D-CRT | Grade ≥ 2 late rectal toxicity, Grade ≥ 3 late rectal toxicity | V50 <50% | <15 <10 | Prostate cancer treatment |
| | Whole organ | 3D-CRT | Grade ≥ 3 late rectal toxicity Grade ≥ 2 late rectal toxicity Grade ≥ 3 late rectal toxicity | V60 <35% | <15 <10 | |
| | Whole organ | 3D-CRT | Grade ≥ 3 late rectal toxicity, Grade ≥ 3 late rectal toxicity | V65 <25% | <15 <10 | |
| | Whole organ | 3D-CRT | Grade ≥ 2 late rectal toxicity, Grade ≥ 3 late rectal toxicity | V70 <20% | <15 <10 | |
| | Whole organ | 3D-CRT | Grade ≥ 2 late rectal toxicity, Grade ≥ 3 late rectal toxicity | V75 <15% | <15 <10 | |
| Bladder | Whole organ | 3D-CRT | Grade ≥ 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 ≥3 late RTOG | V65 ≤50 % V70 ≤35 % V75 ≤25 % V80 ≤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 Whole organ | 3D-CRT 3D-CRT | Severe erectile dysfunction Severe erectile dysfunction | D90 <50 D60-70 <70 | <35 <55 | |

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

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.

[†] 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 ≥ x Gy. Dmax = Maximum radiation dose.

[‡] Non-TBI.

[§] With combined chemotherapy.

Dx = minimum dose received by the "hottest" x% (or x cc's) of the organ.

[¶] Severe xerostomia is related to additional factors including the doses to the submandibular glands.

^{**} Estimated by Dr. Eisbruch.

^{††} 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).

 $^{^{\}ddagger \ddagger}$ For optic nerve, the cases of neuropathy in the 55 to 60 Gy range received ≈ 59 Gy (see optic nerve paper for details). Excludes patients with pituitary tumors where the tolerance may be reduced.