



# An update on NTCP data

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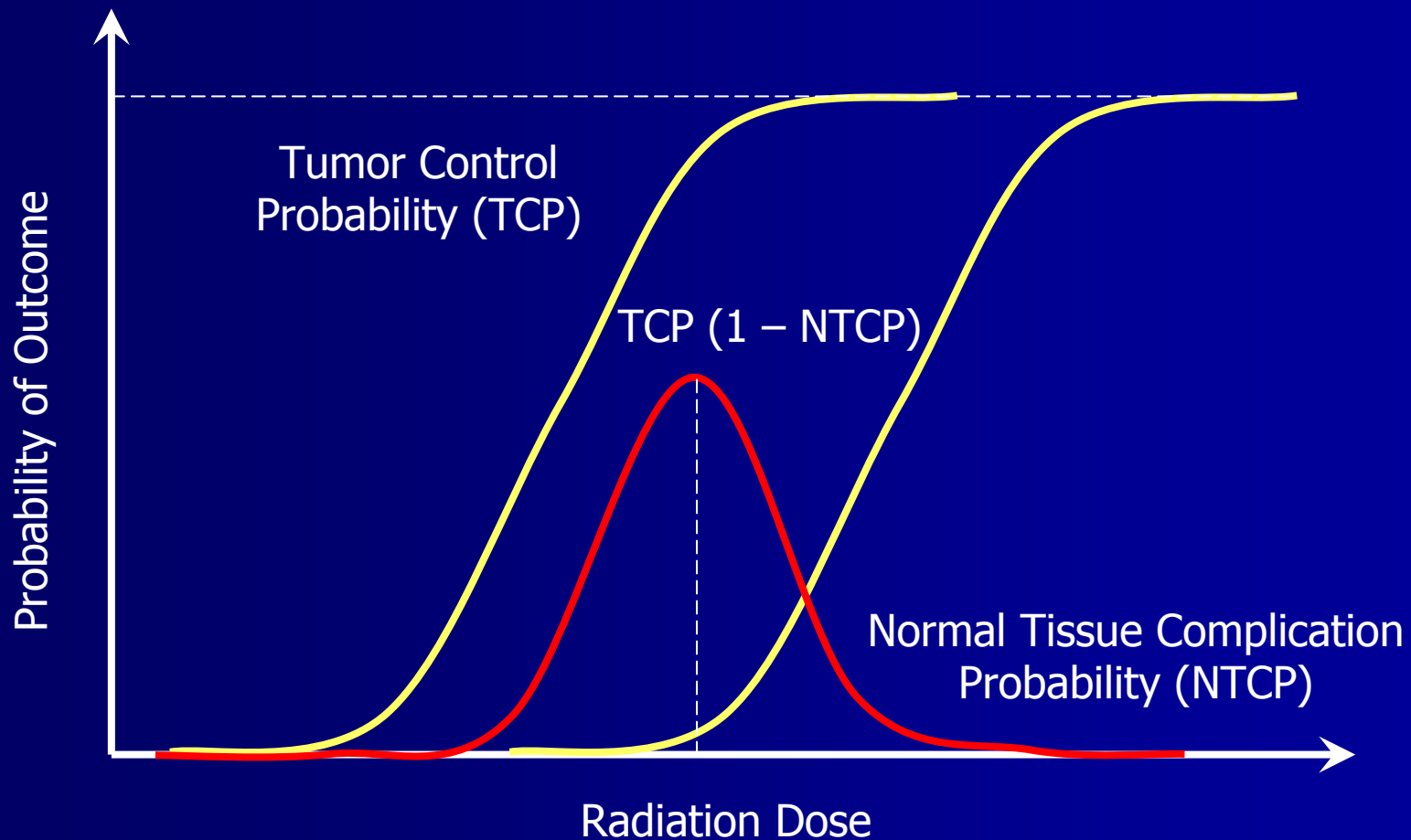
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# Goal of Radiation Therapy

- Maximize probability of tumor eradication
- Minimize probability of injury to surrounding normal tissues

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- Maximize probability of tumor eradication → Deliver sufficient dose to tumor cells
- Minimize probability of injury to surrounding normal tissues → Reduce normal tissue doses to acceptable levels

# Tissue Tolerance Data

- Emami *et al.* IJROBP 21, 109-22, 1991
- Review of literature and personal experience of the authors
- 28 critical sites, TD 5/5 and TD 50/5 for one-third, two-thirds and the whole organ
- Data fit to the Lyman model by Burman *et al.* (IJROBP 21, 123-35, 1991)  $\rightarrow n, m, TD_{50}$

# Lyman-Kutcher-Burman (LKB) Model

- Lyman Radiat. Res. 104, S13-9, 1985; Kutcher and Burman IJROBP 16, 1623-30, 1989

- $$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^t e^{-\frac{x^2}{2}} dx \quad t = \frac{D_{eff} - TD_{50}}{mTD_{50}} \quad D_{eff} = \left( \sum_i v_i D_i^{1/n} \right)^n$$

- 3 parameters:  $n, m, TD_{50}$

- $n = 1 \rightarrow D_{eff} = D_{mean} = \sum_i v_i D_i$

# Lyman Model in Clinical Practice

- Dose-escalation study for intrahepatic cancers; NTCP = 10% (McGinn *et al.* JCO 16, 2246-52, 1998)
- 3D-CRT dose-escalation studies for NSCLC; NTCP  $\leq$  25% (Rozenzweig *et al.* Cancer 103, 2118-27, 2005)
- SBRT (3  $\times$  9-15 Gy/fr); NTCP  $\leq$  20%  $\rightarrow$  4 out of 17 patients had grade 1-2 RP (Song *et al.* AJCO 28, 591-6, 2005)

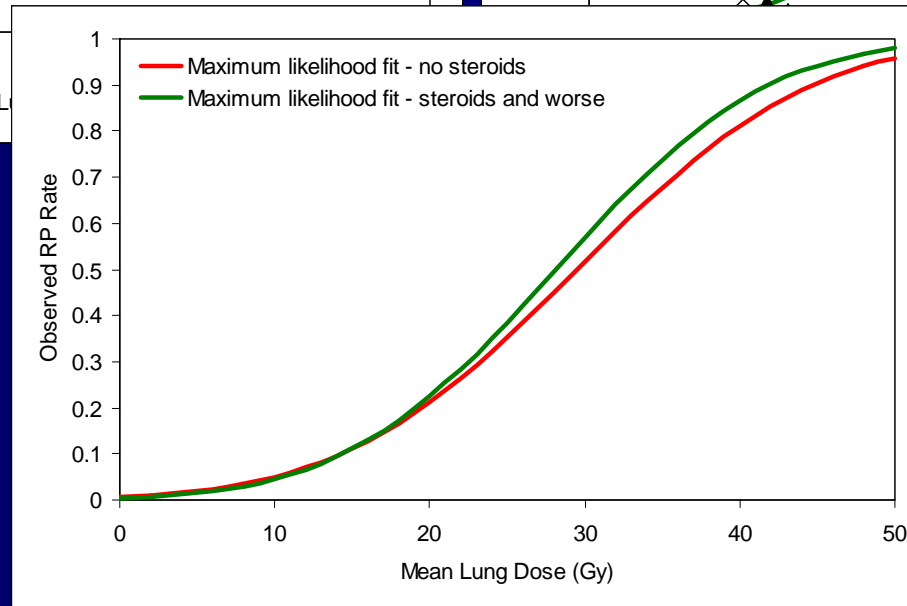
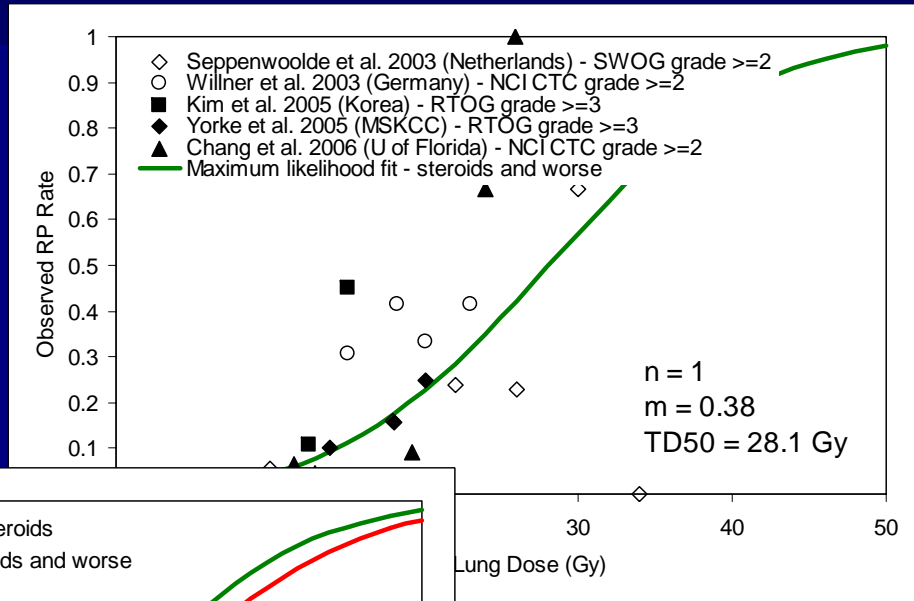
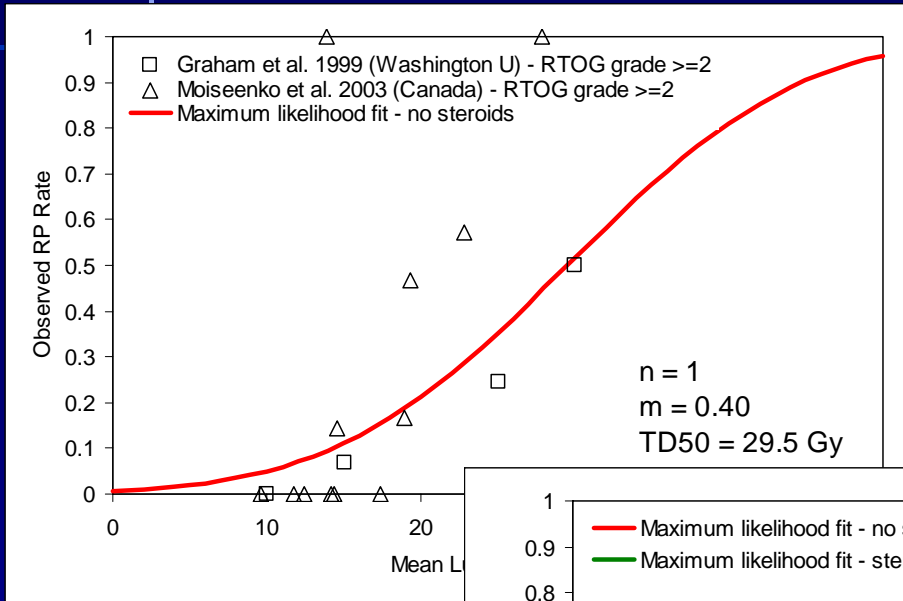
# Project Goal

- To identify reliable estimates of Lyman model parameters for the purposes of biologically-based treatment planning

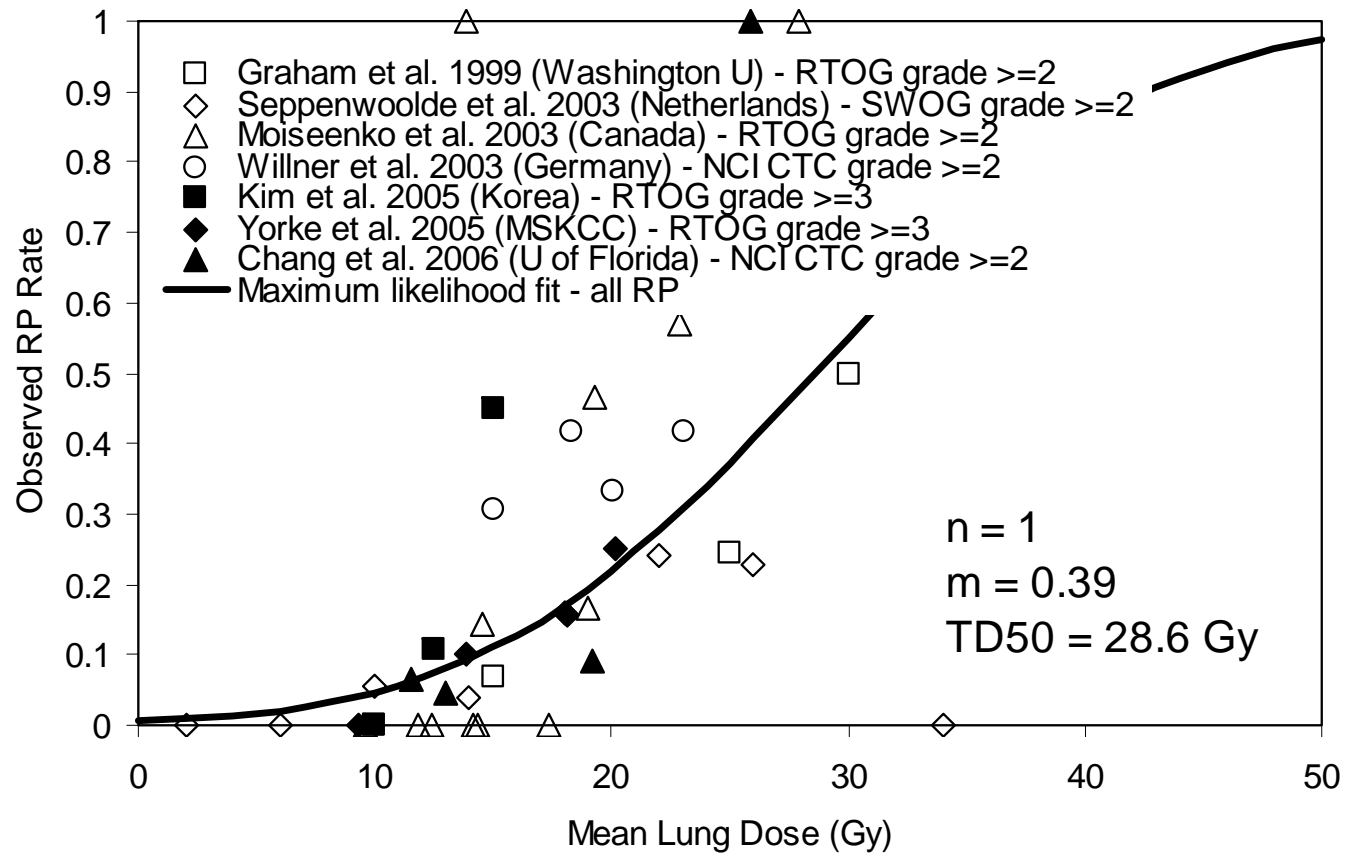
# Lung

Reference	n	m	TD <sub>50</sub> (Gy)	Endpoint	Fractionation Scheme
<i>Lung</i>					
Burman <i>et al.</i> 1991	0.87	0.18	24.5	Pneumonitis	1.8-2 Gy q.d.
Martel <i>et al.</i> 1994	0.87	0.18	28	SWOG grade $\geq 1$ RP	1.8-2 Gy q.d.
Kwa <i>et al.</i> 1998	1	0.30	30.5	SWOG grade $\geq 2$ RP	1-2.7 Gy q.d.; normalized to 2 Gy/fr using $\alpha/\beta$ of 2.5 or 3 Gy
Seppenwoolde <i>et al.</i> 2003	0.99	0.37	30.8	SWOG grade $\geq 2$ RP	1-2.7 Gy q.d.; normalized to 2 Gy/fr using $\alpha/\beta$ of 2.5 or 3 Gy
	1	0.28	43	SWOG grade 3 RP	
Moiseenko <i>et al.</i> 2003	1.02	0.26	21.0	Symptomatic pneumonitis	1-2 Gy q.d.; normalized to 2 Gy/fr using $\alpha/\beta$ of 3 Gy
	0.80	0.37	21.9	Radiographic and symptomatic pneumonitis	

# Lung



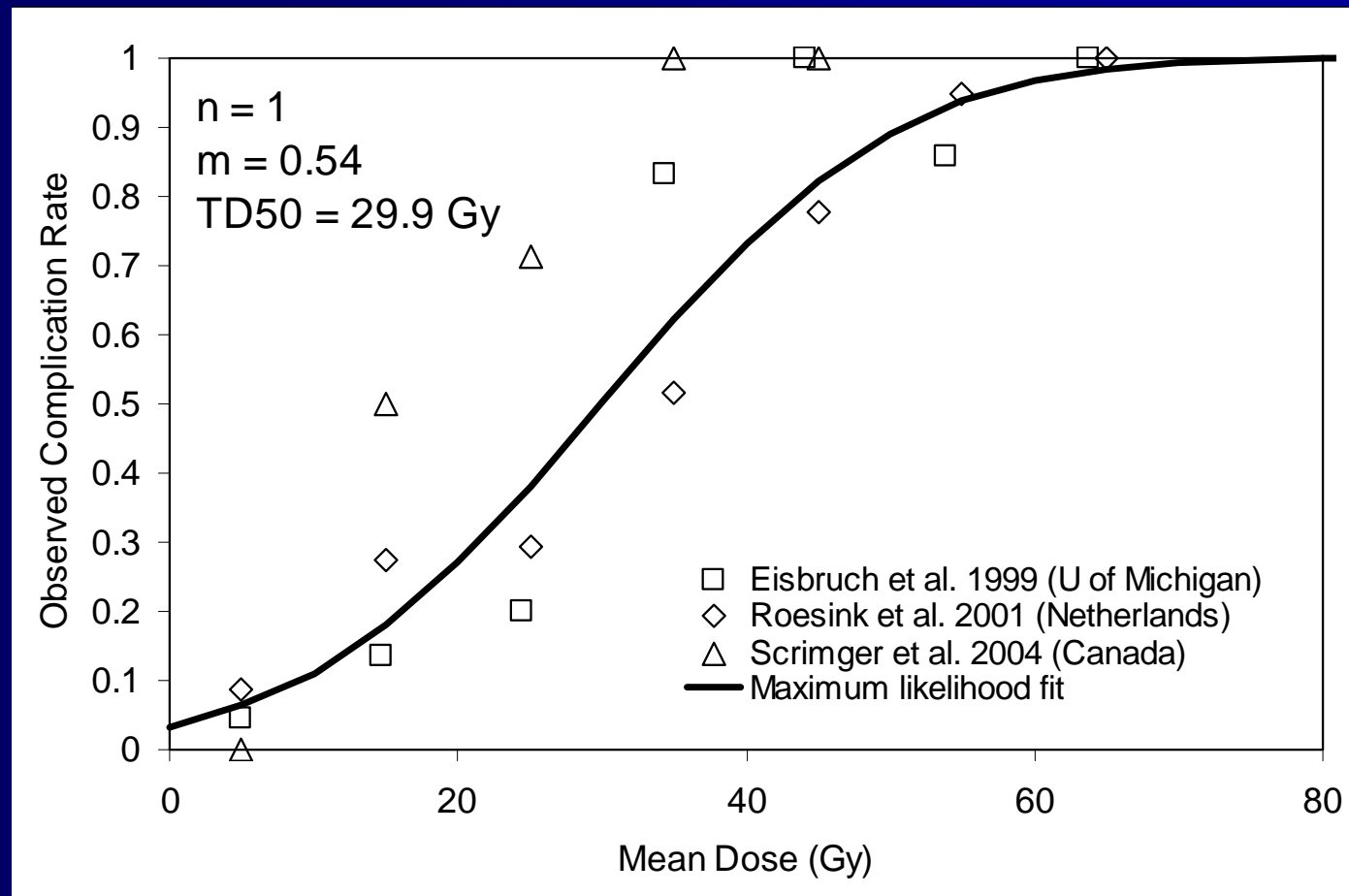
# Lung



# Parotid Gland

Reference	n	m	TD <sub>50</sub> (Gy)	Endpoint	Fractionation Scheme
<i>Parotid gland</i>					
Burman <i>et al.</i> 1991	0.70	0.18	46	Xerostomia	1.8-2 Gy q.d.
Eisbruch <i>et al.</i> 1999	1	0.18	28.4	RTOG grade 4 toxicity (stimulated salivary flow rate reduced to $\leq 25\%$ pre-RT flow at 12 months)	1.8-2 Gy q.d.
Schilstra and Meertens 2001	1.3	0.26	38	SSF $\leq 25\%$ at 13 weeks	2 Gy q.d.
Roesink <i>et al.</i> 2001	1	0.54	31	SSF $\leq 25\%$ at 6 weeks	2 Gy q.d.
	1	0.46	35	SSF $\leq 25\%$ at 6 months	
	1	0.45	39	SSF $\leq 25\%$ at 12 months	
Braam <i>et al.</i> 2005	1	0.37	34	SSF $\leq 25\%$ at 6 weeks	2 Gy q.d.
	1	0.33	40	SSF $\leq 25\%$ at 6 months	
	1	0.37	42	SSF $\leq 25\%$ at 12 months	
	1	0.53	46	SSF $\leq 25\%$ at 5 years	

# Parotid Gland



# Esophagus

Reference	n	m	TD <sub>50</sub> (Gy)	Endpoint	Fractionation Scheme
<i>Esophagus</i>					
Burman <i>et al.</i> 1991	0.06	0.11	68	Clinical stricture/perforation	1.8-2 Gy q.d.
Belderbos <i>et al.</i> 2005	0.69	0.36	47	RTOG grade $\geq$ 2 AE	2.25-2.75 Gy q.d.; normalized to 2 Gy/fr using $\alpha/\beta$ of 10 Gy
Chapet <i>et al.</i> 2005	0.44	0.32	51	RTOG grade $\geq$ 2 AE	2.1 Gy q.d.; normalized to 2 Gy/fr using $\alpha/\beta$ of 10 Gy
<b>This work</b>	<b>0.57</b>	<b>0.34</b>	<b>49</b>	<b>RTOG grade <math>\geq</math> 2 AE</b>	<b>2 Gy q.d.</b>

# Liver

Reference	n	m	TD <sub>50</sub> (Gy)	Endpoint	Fractionation Scheme
<i>Liver</i>					
Burman <i>et al.</i> 1991	0.32	0.15	40	Liver failure	1.8-2 Gy q.d.
Lawrence <i>et al.</i> 1992/ <b>This work</b>	<b>0.69</b>	<b>0.15</b>	<b>45</b>	RTOG grade $\geq$ 3 RILD at $\leq$ 4 months	1.5-1.65 Gy b.i.d.
Ten Haken <i>et al.</i> 2000	0.994	0.165	42.9	RTOG grade $\geq$ 3 RILD at $\leq$ 4 months	1.5-1.65 Gy b.i.d.; normalized to 1.5 Gy/fr using $\alpha/\beta$ of 2 Gy
Dawson <i>et al.</i> 2001	0.94	0.16	42.0	RTOG grade $\geq$ 3 RILD at $\leq$ 4 months	1.5-1.65 Gy b.i.d.; normalized to 1.5 Gy/fr using $\alpha/\beta$ of 2 Gy
Dawson <i>et al.</i> 2002	0.97	0.12	45.8	RTOG grade $\geq$ 3 RILD at $\leq$ 4 months patients with liver metastases	1.5-1.65 Gy b.i.d.; normalized to 1.5 Gy/fr using $\alpha/\beta$ of 2 Gy
	0.97	0.12	39.8	primary hepatobiliary cancer patients	
Cheng <i>et al.</i> 2002	0.4	0.26	43	NCI CTC grade $\geq$ 3 RILD at $\leq$ 4 months	1.8-2 Gy q.d.
Cheng <i>et al.</i> 2004	0.35	0.39	49.4	NCI CTC grade $\geq$ 3 RILD at $\leq$ 4 months	1.8-3 Gy q.d.; normalized to 2 Gy/fr using $\alpha/\beta$ of 2 Gy
Xu <i>et al.</i> 2006	1.1	0.28	40.5	NCI CTC grade $\geq$ 3 RILD at $\leq$ 4 months Child-Pugh grade A liver cirrhosis	4-6 Gy q.d.
	0.7	0.43	23	Child-Pugh grade B liver cirrhosis	

# New LKB Model Parameters

Organ	n	m	TD <sub>50</sub> (Gy)	Endpoint	Fractionation Scheme
Lung	1	0.39 (0.34, 0.45)	28.6 (26.2, 31.4)	RTOG grade $\geq$ 2 RP	2 Gy q.d.
Parotid gland	1	0.54 (0.42, 0.75)	29.9 (26.4, 34.2)	SSF $\leq$ 25% at $\leq$ 3 months	2 Gy q.d.
Esophagus	0.57	0.34	49	RTOG grade $\geq$ 2 AE	2 Gy q.d.
Liver	0.69	0.15	45	RTOG grade $\geq$ 3 RILD at $\leq$ 4 months	1.5-1.65 Gy b.i.d.
Optic nerve	0.25	0.14	72	Visual field defects and/or unilateral blindness	1.8 Gy q.d.
Heart	0.636	0.13	50.6	Pericarditis of any grade	2 Gy q.d.
Brain stem	0.04	0.15	15.3	Any new or aggravated cranial nerve deficit	10-20 Gy single fraction (radiosurgery)
Rectum	0.12	0.15	80	Severe proctitis/necrosis/stenosis/fistula	1.8-2 Gy q.d.
Bladder	0.13	0.11	62	RTOG grade $\geq$ 3 bladder complications	2 Gy q.d.

# Conclusions

- Lyman model parameter estimates for nine critical organs identified
- These estimates are based on post-Emami experience and represent the next iteration in identifying reliable normal tissue complication data for biologically-based treatment planning