

Figure Supplement 1: Late Toxicity and Failure or Death by Fraction Size

Late Toxicity by Fraction Size

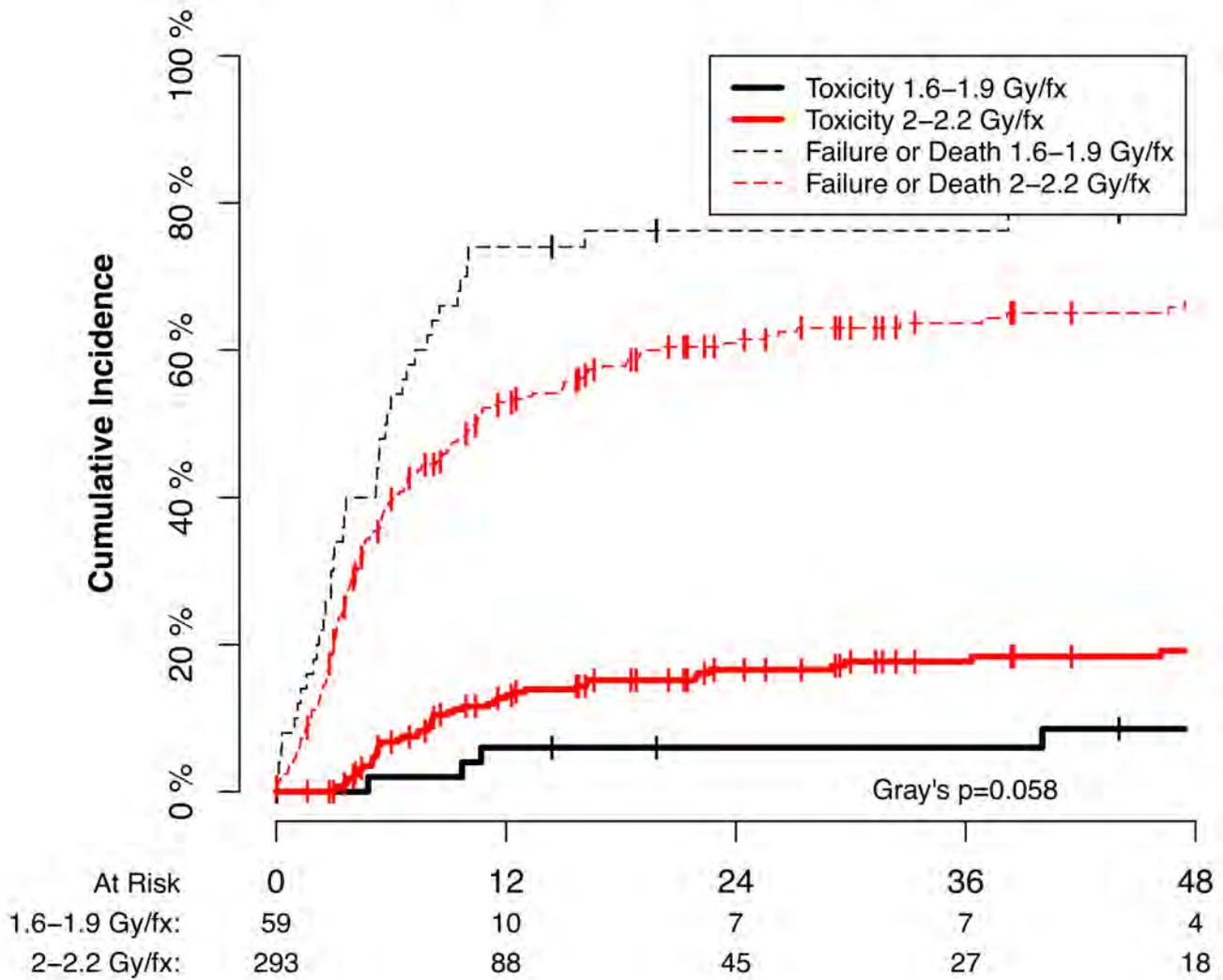
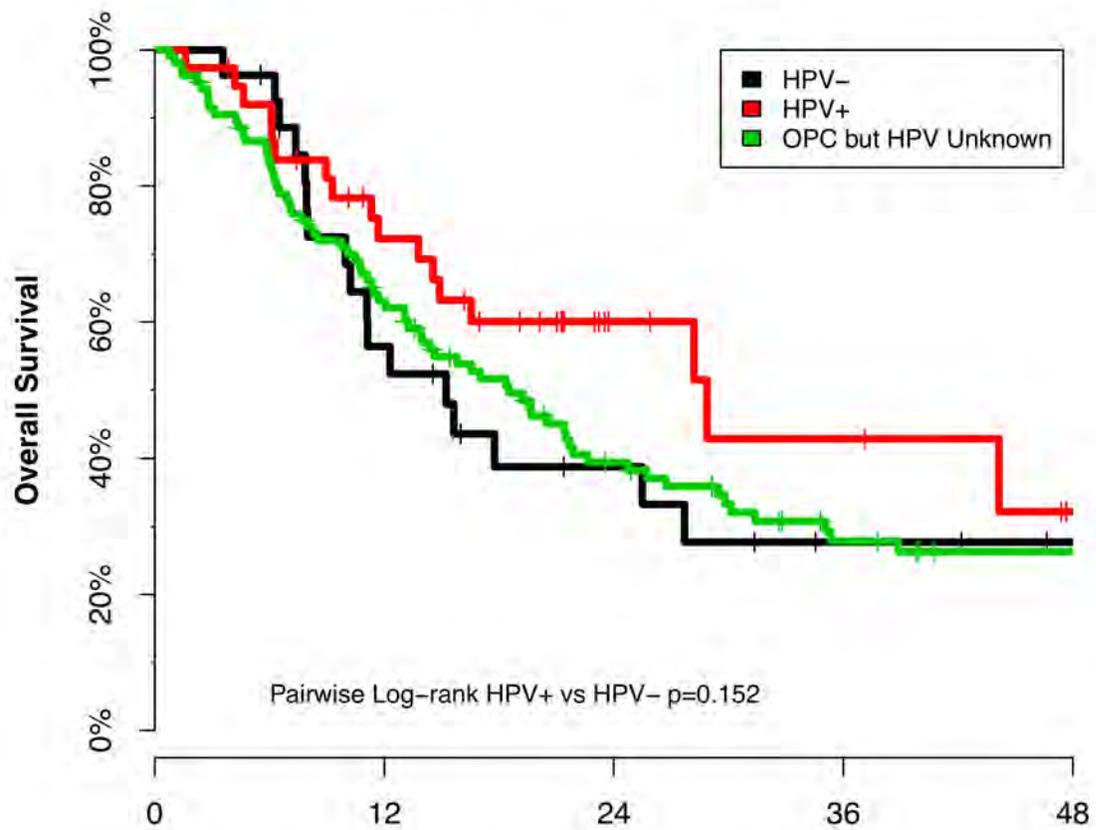


Figure Supplement 2: HPV Status in Recurrent or Second Primary Oropharynx Cancer

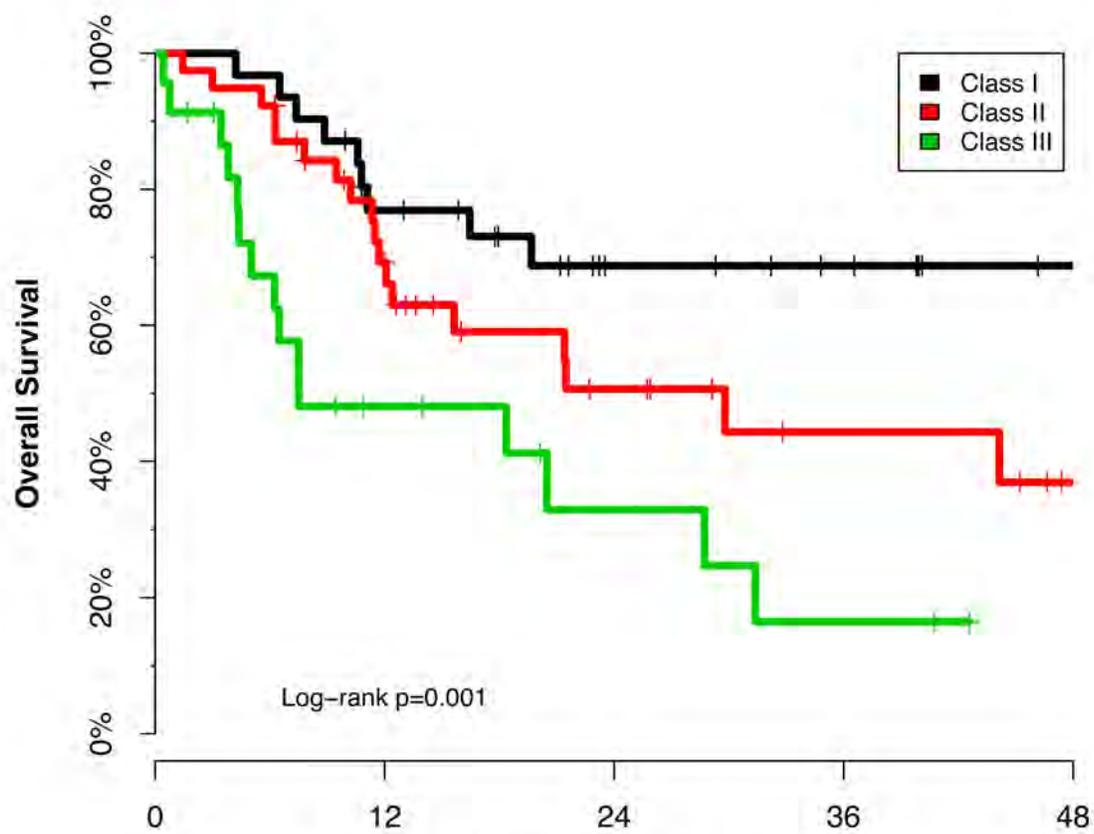
Overall Survival by HPV Status



At Risk	Time (Months)				
	0	12	24	36	48
HPV-:	27	14	7	3	1
HPV+:	38	24	8	5	1
HPV Unk:	106	63	34	19	14

Figure Supplement 3: External Validation of the RPA

Overall Survival by RPA Class (New Patients)



At Risk	Time (Months)				
	0	12	24	36	48
Class I:	31	22	11	7	1
Class II:	39	23	11	6	2
Class III:	23	8	4	2	0

Supplementary Table 1: Logistic Regression for Acute Grade ≥ 3 Toxicity		Univariable		
		OR	95% CI	p
Age	Cont.	1.006	0.986-1.027	0.544
Gender	M vs. F	1.370	0.835-2.2137	0.204
Charlson	1 vs. 0	1.296	0.738-2.231	0.356
	≥ 2 vs. 0	1.245	0.710-2.139	0.434
Tumor Site	OPC/Larynx/Hypopharynx vs All Others	1.137	0.732-1.767	0.568
Recurrence or 2nd Primary	Recurrent vs. 2nd Primary	1.231	0.741-2.107	0.433
KPS	≤ 70 vs. >70	1.234	0.635-2.286	0.518
rT Classification	rT4 vs. Others	2.021	1.286-3.170	0.002
rN Classification	N+ vs. N0	1.239	0.780-1.975	0.365
Organ Dysfunction	Yes vs. No	0.966	0.620-1.500	0.877
Elective Neck Irradiation	Yes vs. No	1.102	0.703-1.722	0.671
Time Between RT	Cont.	1.010	0.972-1.047	0.610
	≤ 2 years vs. >2 years	1.010	0.648-1.569	0.965
Systemic Therapy	Yes vs. No	1.745	0.995-3.229	0.061
Re-IMRT Dose	≥ 66 Gy vs. <66 Gy	0.813	0.498-1.301	0.396
Fractionation	BID vs. QD	1.002	0.571-1.702	0.994
Re-IMRT Timing (Surgery)	Postoperative vs. Definitive	0.984	0.633-1.529	0.942
Multivariable				
Treatment intent and Elective Neck Irradiation <i>(Interaction)</i>	Definitive without Elective Neck Irradiation	Ref	Ref	Ref
	Definitive with Elective Neck Irradiation	0.640	0.292-1.332	0.238
	Postoperative without Elective Neck Irradiation	0.498	0.241-0.986	0.046
	Postoperative with Elective Neck Irradiation	3.454	1.266-9.889	0.015
rT Classification	rT4 vs. Others	2.320	1.451- 3.717	<0.001
Systemic Therapy	Yes vs. No	1.442	0.795-2.745	0.234
Re-IMRT Dose	≥ 66 Gy vs. <66 Gy	0.840	0.499-1.390	0.501

Supplemental Table 2: Acute and Late Toxicity Events

Acute Events*				First Late Event	
	N	% Yes			N
Feeding Tube**	38	8%		Esophageal Stricture Dilatation	21
Wound/Soft Tissue Necrosis	21	5%		FT Dependence >1 year	17
Grade 2 Aspiration	20	4%		Osteoradionecrosis	14
Other Grade ≥3	18	4%		Aspiration Pneumonia	12
Grade 3 Aspiration	16	3%		New Feeding Tube Placement	4
Bleeding	7	2%		Other Late Toxicity	3
Neutropenic Fever	6	1%		Fistula/Soft Tissue Complication	3
Stricture	5	1%		Carotid Blowout	1
Mucositis	4	1%			
Tracheostomy Use***	3	1%		TOTAL WITH LATE TOXICITY	85
				Cumulative Incidence Late Toxicity at 2-Years****	16.7%
Overall Grade ≥3 Acute	102	19.1%		Multiple Late Events	12 of 56 (21%)

*Acute rates calculated as a crude proportion of patients with complete toxicity data available on all endpoints (N=462, 91%)

**Omitting pre-existing feeding tube dependence

***In patients who did not undergo laryngectomy & tracheostomy was not pre-existing re-irradiation

****Cumulative incidence of late toxicity calculated using Gray's method accounting for competing risks of recurrence or death (see text for details)