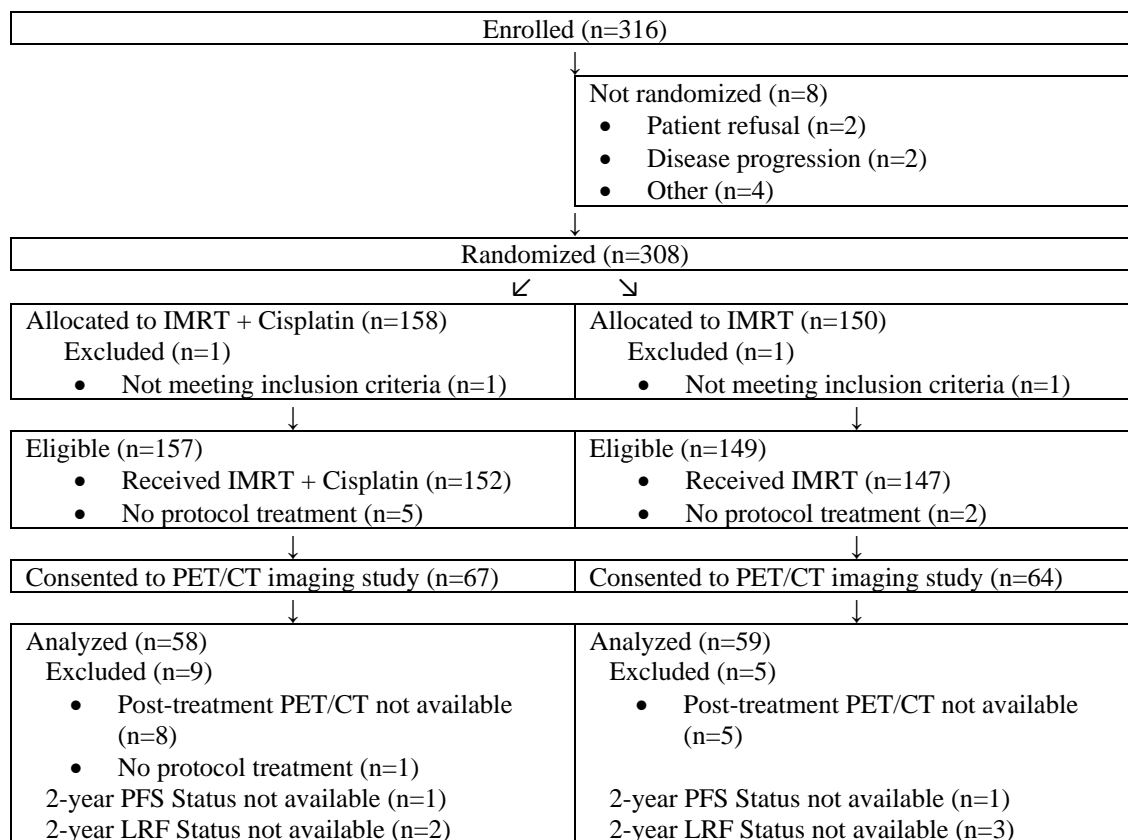


Supplemental Figure 1. CONSORT Flow Diagram



Supplemental Table 1
Patient and Tumor Characteristics by PET/CT Consent

	Did Not Consent to PET/CT		Consented to PET/CT		Total		p-value
	n	%	n	%	n	%	
Age (years)							
≤ 49	23	13.1	19	14.5	42	13.7	0.2911 [1]
50 - 59	74	42.3	42	32.1	116	37.9	
60 - 69	54	30.9	47	35.9	101	33.0	
≥ 70	24	13.7	23	17.6	47	15.4	
Gender							
Male	142	81.1	115	87.8	257	84.0	0.1558 [2]
Female	33	18.9	16	12.2	49	16.0	
Race							0.1772 [2]

	Did Not Consent to PET/CT		Consented to PET/CT		Total		p-value
	n	%	n	%	n	%	
American Indian/Alaska Native	1	0.6	1	0.8	2	0.7	
Asian	4	2.3	0	0.0	4	1.3	
Black or African American	2	1.1	1	0.8	3	1.0	
White	162	92.6	119	90.8	281	91.8	
Unknown or not reported	6	3.4	10	7.6	16	5.2	
Ethnicity							0.7358 [2]
Hispanic or Latino	6	3.4	4	3.1	10	3.3	
Not Hispanic or Latino	154	88.0	119	90.8	273	89.2	
Unknown	15	8.6	8	6.1	23	7.5	
Zubrod performance status							0.7743 [2]
0	139	79.4	106	80.9	245	80.1	
1	36	20.6	25	19.1	61	19.9	
Smoking history: pack-years							0.9399 [1]
0	120	68.6	93	71.0	213	69.6	
>0 - <5	36	20.6	22	16.8	58	19.0	
5 - 10	19	10.9	16	12.2	35	11.4	
Primary site							0.8785 [2]
Oropharynx NOS	10	5.7	7	5.3	17	5.6	
Tonsillar fossa, tonsil	88	50.3	73	55.7	161	52.6	
Base of tongue	75	42.9	51	38.9	126	41.2	
Pharyngeal oropharynx	1	0.6	0	0.0	1	0.3	
Posterior pharyngeal wall	1	0.6	0	0.0	1	0.3	
T stage, clinical							0.5475 [2]
T1	67	38.3	48	36.6	115	37.6	
T2	80	45.7	67	51.1	147	48.0	
T3	28	16.0	16	12.2	44	14.4	
N stage, clinical							0.8581 [2]
N0	9	5.1	4	3.1	13	4.2	
N1	36	20.6	26	19.8	62	20.3	
N2a	24	13.7	19	14.5	43	14.1	
N2b	106	60.6	82	62.6	188	61.4	
RT planning (as stratified)							0.2683 [2]
Unilateral	52	29.7	47	35.9	99	32.4	
Bilateral	123	70.3	84	64.1	207	67.6	
RT planning (per central review)							0.9618 [2]

	Did Not Consent to PET/CT		Consented to PET/CT		Total		p-value
	n	%	n	%	n	%	
Unilateral	22	12.6	15	11.5	37	12.1	
Bilateral	148	84.6	113	86.3	261	85.3	
Unknown	5	2.9	3	2.3	8	2.6	
Assigned Treatment Arm							
IMRT + Cisplatin	90	51.4	67	51.1	157	51.3	1.000 [2]
IMRT	85	48.6	64	48.9	149	48.7	
Total	175	100.0	131	100.0	306	100.0	

[1] Two-sided p-value for Wilcoxon rank-sum test between consent groups

[2] Two-sided p-value for Fisher's exact test between consent groups

Supplemental Table 2. Patient and Tumor Characteristics for Patients Eligible for PET/CT Analysis

Patient or Tumor Characteristic	IMRT + Cisplatin		IMRT		Total		p-value
	n	%	n	%	n	%	
Age (years)							0.5484 [1]
≤ 49	14	24.1	4	6.8	18	15.4	
50 - 59	12	20.7	23	39.0	35	29.9	
60 - 69	20	34.5	24	40.7	44	37.6	
≥ 70	12	20.7	8	13.6	20	17.1	
Gender							
Male	51	87.9	51	86.4	102	87.2	1.000 [2]
Female	7	12.1	8	13.6	15	12.8	
Race							
American Indian/Alaska Native	0	0.0	1	1.7	1	0.9	0.1444 [2]
Black or African American	1	1.7	0	0.0	1	0.9	
White	55	94.8	51	86.4	106	90.6	
Unknown or not reported	2	3.4	7	11.9	9	7.7	
Ethnicity							0.1627 [2]
Hispanic or Latino	0	0.0	4	6.8	4	3.4	
Not Hispanic or Latino	55	94.8	51	86.4	106	90.6	
Unknown	3	5.2	4	6.8	7	6.0	
Zubrod performance status							0.2369 [2]
0	50	86.2	45	76.3	95	81.2	
1	8	13.8	14	23.7	22	18.8	

Patient or Tumor Characteristic	IMRT + Cisplatin		IMRT		Total		p-value
	n	%	n	%	n	%	
Smoking history: pack-years							
0	37	63.8	43	72.9	80	68.4	0.3199 [1]
>0 - <5	12	20.7	10	16.9	22	18.8	
5 - 10	9	15.5	6	10.2	15	12.8	
Primary site							0.5765 [2]
Oropharynx NOS	2	3.4	5	8.5	7	6.0	
Tonsillar fossa, tonsil	32	55.2	32	54.2	64	54.7	
Base of tongue	24	41.4	22	37.3	46	39.3	
T stage, clinical							0.3925 [2]
T1	24	41.4	18	30.5	42	35.9	
T2	26	44.8	34	57.6	60	51.3	
T3	8	13.8	7	11.9	15	12.8	
N stage, clinical							0.9122 [2]
N0	1	1.7	2	3.4	3	2.6	
N1	12	20.7	12	20.3	24	20.5	
N2a	8	13.8	6	10.2	14	12.0	
N2b	37	63.8	39	66.1	76	65.0	
RT planning (as stratified)							0.3454 [2]
Unilateral	25	43.1	20	33.9	45	38.5	
Bilateral	33	56.9	39	66.1	72	61.5	
RT planning (per central review)							0.7769 [2]
Unilateral	6	10.3	8	13.6	14	12.0	
Bilateral	52	89.7	51	86.4	103	88.0	
Total	58	100.0	59	100.0	117	100.0	

[1] Two-sided p-value for Wilcoxon rank-sum test between arms

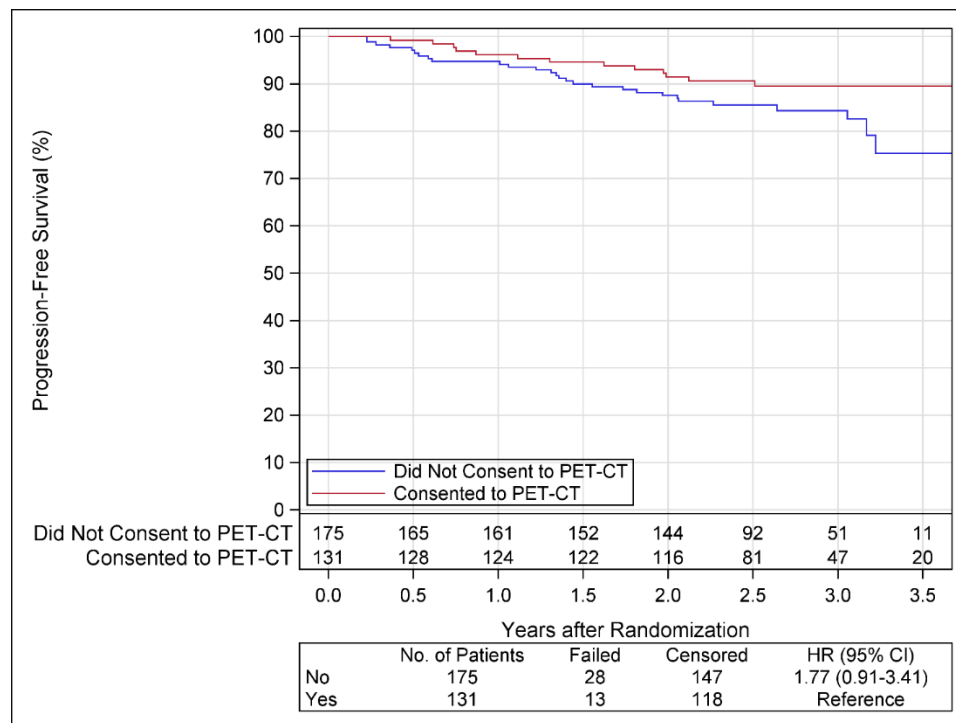
[2] Two-sided p-value for Fisher's exact test between arms

Supplemental Table 3. PET/CT Scan Evaluations per Central Review

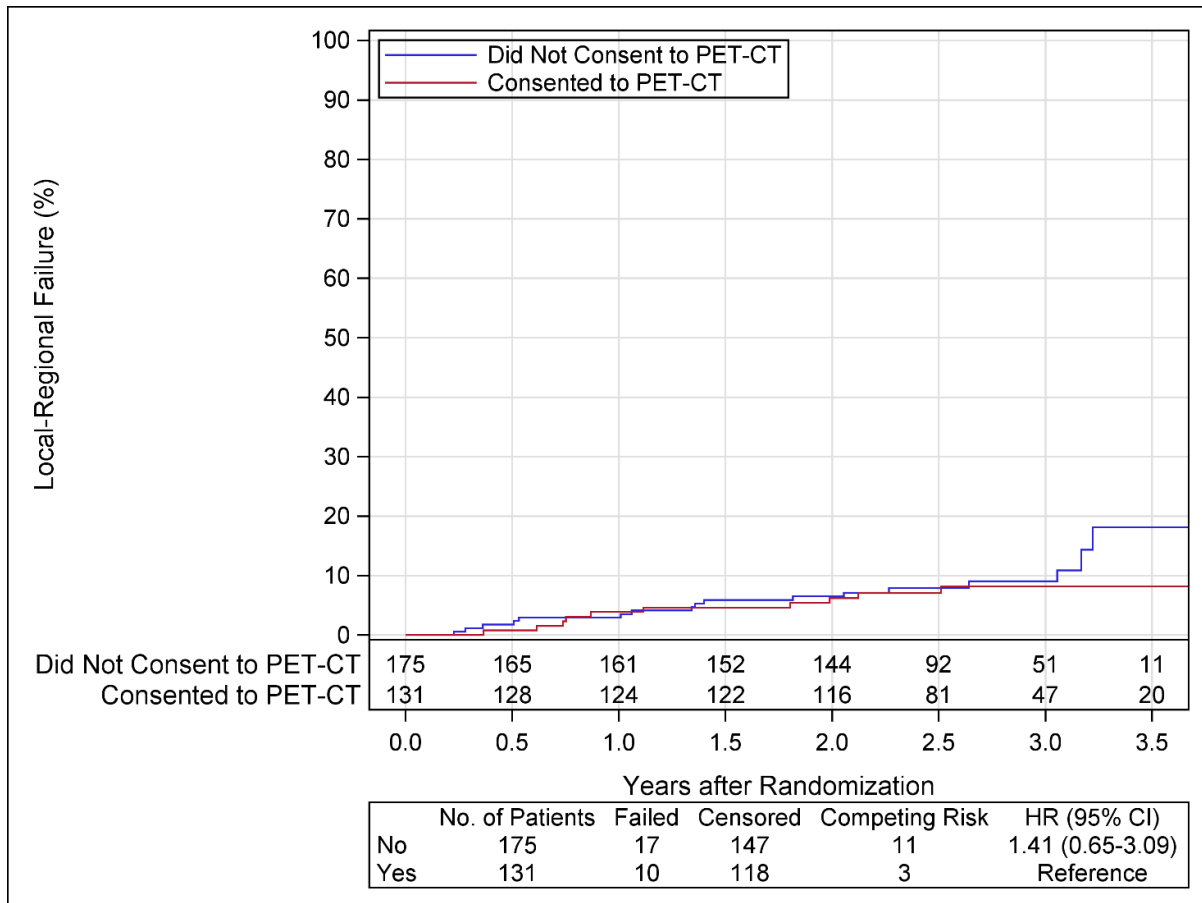
	IMRT + Cisplatin	IMRT	Total
PET primary tumor assessment			
Definite complete metabolic response	57 (98.3%)	56 (94.9%)	113 (96.6%)

	IMRT + Cisplatin	IMRT	Total
Likely complete metabolic response	1 (1.7%)	0 (0.0%)	1 (0.9%)
Likely inflammatory	0 (0.0%)	2 (3.4%)	2 (1.7%)
Definite residual metabolic disease	0 (0.0%)	1 (1.7%)	1 (0.9%)
PET right neck assessment			
Definite complete metabolic response	55 (94.8%)	57 (96.6%)	112 (95.7%)
Likely complete metabolic response	3 (5.2%)	2 (3.4%)	5 (4.3%)
PET left neck assessment			
Definite complete metabolic response	56 (96.6%)	54 (91.5%)	110 (94.0%)
Likely complete metabolic response	2 (3.4%)	2 (3.4%)	4 (3.4%)
Likely inflammatory	0 (0.0%)	1 (1.7%)	1 (0.9%)
Likely residual metabolic disease	0 (0.0%)	2 (3.4%)	2 (1.7%)
PET overall interpretation			
Negative for residual tumor	58 (100.0%)	57 (96.6%)	115 (98.3%)
Positive for residual tumor	0 (0.0%)	2 (3.4%)	2 (1.7%)

Supplemental Figure 2
Progression-Free Survival by PET/CT Consent



Supplemental Figure 3
Local-Regional Failure by PET/CT Consent



Supplemental Table 4. Sensitivity Analysis: Negative Predictive Value per Central Review for Two-Year Progression-Free Survival

	IMRT + Cisplatin	IMRT	Total
PET overall interpretation			
Positive for residual tumor	0 (0.0%)	2 (3.8%)	2 (1.9%)
Negative for residual tumor	51 (100.0%)	51 (96.2%)	102 (98.1%)
2-year progression-free survival status			
Failure	3 (5.9%)	5 (9.8%)	8 (7.8%)
Non-failure	48 (94.1%)	46 (90.2%)	94 (92.2%)

	IMRT + Cisplatin	IMRT	Total
NPV of 2-yr PFS	94.1%	90.2%	92.2%
(95% exact CI)	(83.8-98.8%)	(78.6-96.7%)	(85.1-96.6%)
(One-sided 90% exact LCB)	(87.4%)	(82.6%)	(87.6%)
H0: NPV \leq 90% vs HA: NPV >90%			
p-value (exact)			0.2982

CI, confidence interval; LCB, lower confidence bound

Note: Sensitivity analysis only includes scans within 10-16 weeks post end of RT

Supplemental Table 5. Sensitivity Analysis: Negative Predictive Value per Central Review for Two-Year Locoregional Control

	IMRT + Cisplatin	IMRT	Total
PET overall interpretation			
Positive for residual tumor	0 (0.0%)	2 (3.9%)	2 (2.0%)
Negative for residual tumor	50 (100.0%)	49 (96.1%)	99 (98.0%)
2-year local-regional control status			
Failure	2 (4.0%)	3 (6.1%)	5 (5.1%)
Non-failure	48 (96.0%)	46 (93.9%)	94 (94.9%)
NPV of 2-yr LRC	96.0%	93.9%	94.9%
(95% exact CI)	(86.3-99.5%)	(83.1-98.7%)	(88.6-98.3%)
(One-sided 90% exact LCB)	(89.7%)	(86.9%)	(90.8%)
H0: NPV \leq 90% vs HA: NPV >90%			
p-value (exact)			0.0612

CI, confidence interval; LCB, lower confidence bound

Note: Sensitivity analysis only includes scans within 10-16 weeks post end of RT

Supplemental Table 6. Negative Predictive Value per Local Review for Two-Year Progression-Free Survival

	IMRT + Cisplatin	IMRT	Total
Primary Analysis			
PET overall interpretation			
Positive for residual tumor	3 (6.3%)	3 (5.9%)	6 (6.1%)

	IMRT + Cisplatin	IMRT	Total
Indeterminate	3 (6.3%)	5 (9.8%)	8 (8.1%)
Negative for residual tumor	42 (87.5%)	43 (84.3%)	85 (85.9%)
2-year progression-free survival status			
Failure	3 (7.1%)	4 (9.3%)	7 (8.2%)
Non-failure	39 (92.9%)	39 (90.7%)	78 (91.8%)
NPV of 2-yr PFS	92.9%	90.7%	91.8%
(95% exact CI)	(80.5-98.5%)	(77.9-97.4%)	(83.8-96.6%)
(One-sided 90% exact LCB)	(84.8%)	(82.3%)	(86.5%)
H0: NPV ≤90% vs HA: NPV >90%			
p-value (exact)			0.3753
Sensitivity Analysis			
PET overall interpretation			
Positive for residual tumor	3 (7.0%)	3 (6.5%)	6 (6.7%)
Indeterminate	2 (4.7%)	5 (10.9%)	7 (7.9%)
Negative for residual tumor	38 (88.4%)	38 (82.6%)	76 (85.4%)
2-year progression-free survival status			
Failure	2 (5.3%)	4 (10.5%)	6 (7.9%)
Non-failure	36 (94.7%)	34 (89.5%)	70 (92.1%)
NPV of 2-yr PFS	94.7%	89.5%	92.1%
(95% exact CI)	(82.3-99.4%)	(75.2-97.1%)	(83.6-97.0%)
(One-sided 90% exact LCB)	(86.6%)	(80.1%)	(86.6%)
H0: NPV ≤90% vs HA: NPV >90%			
p-value (exact)			0.3533

CI, confidence interval; LCB, lower confidence bound

Note: Sensitivity analysis only includes scans within 10-16 weeks post end of RT

Supplemental Table 7.
Negative Predictive Value per Local Review for Two-Year Locoregional Control

		IMRT + Cisplatin	IMRT	Total
Primary Analysis	PET overall interpretation			
	Positive for residual tumor	3 (6.4%)	3 (6.1%)	6 (6.3%)
	Indeterminate	3 (6.4%)	5 (10.2%)	8 (8.3%)
	Negative for residual tumor	41 (87.2%)	41 (83.7%)	82 (85.4%)
	2-year local-regional control status			
	Failure	2 (4.9%)	2 (4.9%)	4 (4.9%)
	Non-failure	39 (95.1%)	39 (95.1%)	78 (95.1%)
	NPV of 2-yr LRC (95% exact CI)	95.1% (83.5-99.4%)	95.1% (83.5-99.4%)	95.1% (88.0-98.7%)
	(One-sided 90% exact LCB)	(87.5%)	(87.5%)	(90.5%)
	H0: NPV \leq 90% vs HA: NPV >90% p-value (exact)			0.0777
Sensitivity Analysis	PET overall interpretation			
	Positive for residual tumor	3 (7.1%)	3 (6.8%)	6 (7.0%)
	Indeterminate	2 (4.8%)	5 (11.4%)	7 (8.1%)
	Negative for residual tumor	37 (88.1%)	36 (81.8%)	73 (84.9%)
	2-year local-regional control status			
	Failure	1 (2.7%)	2 (5.6%)	3 (4.1%)
	Non-failure	36 (97.3%)	34 (94.4%)	70 (95.9%)
	NPV of 2-yr LRC (95% exact CI)	97.3% (85.8-99.9%)	94.4% (81.3-99.3%)	95.9% (88.5-99.1%)
	(One-sided 90% exact LCB)	(89.9%)	(85.9%)	(91.1%)
	H0: NPV \leq 90% vs HA: NPV >90% p-value (exact)			0.0580

CI, confidence interval; LCB, lower confidence bound

Note: Sensitivity analysis only includes scans within 10-16 weeks post end of RT

Supplemental Table 8.1
Neck Site PET/CT Score Agreement Between Local and Central Reviews

Local Review		Central Review				
		Definite complete metabolic response	Likely complete metabolic response	Likely inflammatory	Likely residual metabolic disease	Definite residual metabolic disease
Primary Site (N=100)	Definite complete metabolic response	70 (72.9%)	1 (100.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)
	Likely complete metabolic response	13 (13.5%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)
	Likely inflammatory	10 (10.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	Likely residual metabolic disease	2 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Definite residual metabolic disease	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Right Neck (N=91)	Definite complete metabolic response	75 (85.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Likely complete metabolic response	6 (6.8%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Likely inflammatory	3 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Likely residual metabolic disease	3 (3.4%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Definite residual metabolic disease	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Left Neck (N=89)	Definite complete metabolic response	70 (83.3%)	3 (100.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)
	Likely complete metabolic response	10 (11.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Likely inflammatory	4 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Likely residual metabolic disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Definite residual metabolic disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)

Supplemental Table 8.2
Overall PET/CT Score Agreement Between Local and Central Reviews

		Central Review		
		Negative for residual tumor	Positive for residual tumor	Indeterminate
Local Review				
Overall (N=100)	Negative for residual tumor	86 (87.8%)	0 (0.0%)	0 (0.0%)
	Positive for residual tumor	5 (5.1%)	1 (50.0%)	0 (0.0%)
	Indeterminate	7 (7.1%)	1 (50.0%)	0 (0.0%)

Supplemental Table 8.3
Measure of Agreement (95% CI) Between Local and Central Reviews

	Overall	Primary Site*	Right Neck*	Left Neck*
Gwet's AC1/AC2 (95% CI)	0.86 (0.78, 0.94)	0.84 (0.78, 0.91)	0.91 (0.86, 0.97)	0.92 (0.87, 0.96)
Brennan-Prediger (95% CI)	0.80 (0.70, 0.91)	0.69 (0.59, 0.8)	0.81 (0.71, 0.92)	0.82 (0.75, 0.90)
Percent Agreement (95% CI)	0.87 (0.80, 0.94)	0.88 (0.84, 0.92)	0.93 (0.88, 0.97)	0.93 (0.90, 0.96)

*Weighted Coefficients (linear weights)