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Change of SUV_{max} Slope in Dynamic Triphasic FDG-PET/CT Distinguishes Malignancy from Post-Radiation Inflammation in Head and Neck Squamous Cell Carcinoma - a Prospective Trial

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Abstract

Purpose/Objectives(s)—The positive predictive value (PPV) of post-radiation (RT) 3-month FDG-PET/CT imaging in head and neck squamous cell carcinoma (HNSCC) is limited. Dynamic data acquisition and analysis was evaluated for PPV improvement, utilizing a triphasic PET/CT technique.

Methods and Materials—We prospectively enrolled HNSCC patients who completed RT, with scheduled 3-month post-RT FDG-PET/CT. Patients underwent our standard whole-body PET/CT scan at 90 minutes, with the addition of head and neck PET/CTs at 60 and 120 minutes. Maximum standardized uptake values (SUV_{max}) of regions of interest (ROI) were measured at 60, 90, and 120 minutes. SUV_{max} slope between 60 and 120 minutes, and change of SUV_{max} slope before and after 90 minutes were calculated. Data were analyzed by primary site and nodal site disease status using the Cox regression model and Wilcoxon Rank Sum Test. Outcomes were based on pathologic and clinical follow-up.

Results—84 patients enrolled, with 79 primary and 43 nodal evaluable sites. Twenty-eight sites were interpreted positive or equivocal (18 primary, 8 nodal, 2 distant) on 3-month 90-minute FDG-PET/CT. Median follow-up was 13.3 months. All measured SUV endpoints predicted recurrence. Change of SUV_{max} slope after 90 minutes more accurately identified non-recurrence in positive or equivocal sites than our current standard of $SUV_{max} \geq 2.5$ ($p=0.02$).

Conclusions—The PPV of post-RT FDG-PET/CT may significantly improve using novel second derivative analysis of dynamic triphasic FDG-PET/CT SUV_{max} slope, accurately distinguishing tumor from inflammation on positive and equivocal scans.

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INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) accounts for 3–5% of all cancers in the United States (1). Approximately two-thirds of these patients present with locally advanced disease: either large primary site disease, or with metastases to regional lymph nodes.

Radiotherapy (RT) is a major component of treatment for locally advanced HNSCC, generally given postoperatively or as a primary modality, with or without chemotherapy to maximize organ preservation.

[¹⁸F]-fluorodeoxyglucose positron emission tomography (FDG-PET/CT) is a combined metabolic/anatomic imaging modality, which improves diagnostic accuracy and staging in HNSCC patients (2–11). However, its accuracy in assessing treatment response post-RT is poorly optimized, with scarce prospective data (12–14). Early detection of persistent and recurrent disease is important for immediate salvage treatment.

FDG-PET/CT performed approximately 3 months after RT has a high negative predictive value (>90%), but several studies demonstrate that post-RT FDG-PET/CT suffers from high false positive rates (>50%) resulting from poor differentiation between inflammation and malignancy (11, 15, 16). FDG localizes to tumor and therapy-related inflammatory tissue, with physiologic uptake in the brain and heart, and collection in the urinary system (17). Inflammation in areas treated with RT is especially problematic in HNSCC patients, as brisk RT-associated inflammation diminishes the reliability of FDG-PET/CT as a post-therapy response assessment tool (18).

Our institution uses a static measure of standardized uptake value at 90-minutes (SUV_{max} 90), 3 months post-RT for HNSCC recurrence monitoring (19). Our experience confirms a low positive predictive value (PPV) of 30–50% in these response assessment FDG-PET/CTs (7). The high FP rate of FDG-PET/CT leads to additional imaging repeat biopsies, neck dissection, and fine needle aspiration (FNA), increasing morbidity from these procedures, while incurring additional healthcare costs.

FDG uptake research suggests FDG accumulation kinetics differ between inflammatory and tumor tissues (18, 20, 21), with delayed imaging demonstrating FDG washout in areas of inflammation, but continued accumulation in areas containing residual cancer. We hypothesized the SUV_{max} slope from imaging at 60, 90, and 120 minutes after FDG injection (a dynamic triphasic FDG-PET/CT) would better predict tumor recurrences than single time point measurement of SUV_{max} . Our objective is to evaluate dynamic FDG uptake methodology as a post-therapy response assessment tool, potentially enabling accurate tumor and therapy-related inflammation differentiation, improving the post-therapy value of FDG-PET/CT.

METHODS AND MATERIALS

Patients

This prospective trial was approved by our Institutional Review Board (June 2011). Patients were eligible for inclusion if they presented with histologically proven HNSCC and received

RT as part of their overall treatment plan. There was no requirement for planned surgical resection of the malignancy or administration of chemotherapy. Patient demographic and clinical data were obtained from the patients' medical records. Each patient had clinical follow-up 1 month after completion of RT, every 6–12 weeks thereafter in the first year, and every 3–4 months in the second year. Laryngoscopy was performed at each follow-up. A triphasic FDG-PET/CT scan was obtained 3 months post-RT to assess treatment response. If recurrence was suspected, additional imaging or procedures were performed. A true head and neck recurrence was confirmed either with biopsy proven carcinoma or consensus of at least two physicians. Two years of follow-up is planned to capture additional head and neck recurrences.

Radiotherapy

All patients were treated with simultaneously integrated boost technique, intensity-modulated radiotherapy (IMRT) using the Pinnacle planning system, version 9.3 (Phillips Medical Systems, Fitchburg, WI). For definitive RT, the gross tumor volume and bulky lymph nodes received 70–74 Gy (2 Gy/fraction or 1.2 Gy/fraction BID). For postoperative RT, the tumor bed received 60–66 Gy (2 Gy/fraction). In both situations, high-risk cervical lymphatic regions were treated to 60–63 Gy (1.8–2 Gy/fraction), and low-risk cervical lymphatic regions were treated to 54–56 Gy (1.6–1.8 Gy/fraction).

FDG-PET/CT imaging

Per protocol, patients were given alprazolam and asked to rest quietly during the FDG uptake phase. In addition to our standard whole-body FDG-PET/CT scan from the vertex through mid-thighs at 90-minutes (3 minutes/bed position), enrolled patients had a PET scan of the head and neck with low-dose attenuation CT scans at 60 and 120 minutes after FDG injection. Patients remained resting quietly on the scanner table between scans. Image reconstruction used ordered subset expectation maximization with a 7mm post-reconstruction smoothing filter to minimize single pixel noise. After image reconstruction, the 90-minute whole body scan was clinically interpreted by one of 3 nuclear medicine physicians and reported in the patients' medical record. At a separate time, anonymized 60-, 90-, and 120-minute FDG-PET/CT scans were all visually inspected and interpreted by one experienced nuclear medicine physician (MG) who was blinded to patient information but used the pre-treatment FDG-PET/CT or diagnostic CT for identification of the initial pre-treatment tumor location. For images with increased focal FDG uptake remaining on the 3-month scan, areas were circled as a region of interest (ROI) and SUV_{max} was recorded for each lesion for the 3 time points. The SUV_{max} was calculated for each focus using Medview software version 12.1.3 (Medimage, Ann Arbor, MI) based on the conventional formula for SUV using body weight normalization:

$$SUV = \text{Tissue activity } (\mu\text{Ci}/\text{ml}) / [\text{injected dose } (m\text{Ci}) / \text{Body weight } (kg)].$$

The FDG dose given intravenously was 10–15 mCi based on body weight. Patients were asked to fast for at least 6 hours prior to their scan and blood glucose levels were confirmed below 200 mg/dL before FDG was administered. Patients were imaged with a CTI Biograph

duo PET/CT tomograph (Siemens Medical Systems, Hoffman Estates, IL) or CTI Biograph TruePoint 40 PET/CT (Siemens Medical Systems, Knoxville, TN). Scans were retrospectively categorized as positive, equivocal, or negative by interpretation of the 90-minute FDG-PET/CT scan in the medical record. Equivocal scans were classified as “post-RT inflammation but malignancy could not be excluded”, with recommended follow-up imaging or clinical correlation needed. Final outcome of the scans as true positive (TP), true negative (TN), false negative (FN), or false positive (FP), was based on biopsy or clinical follow-up within 1 year of the 3-month FDG-PET/CT scan. Therefore, a 3-month PET/CT interpreted as negative was “TN” if recurrence occurred beyond 12 months from the scan date.

Statistical analysis

Individual SUV_{max} slopes ($SUV_{max} 90 - SUV_{max} 60$ and $SUV_{max} 120 - SUV_{max} 90$), overall SUV_{max} slope ($SUV_{max} 120 - SUV_{max} 60$), and change of the SUV_{max} slope [$(SUV_{max} 120 - SUV_{max} 90) - (SUV_{max} 90 - SUV_{max} 60)$] were calculated, relative to the 30-minute incremental differences in measured time points. Statistical analysis focused on patients with positive or equivocal 3-month scans. The Wilcoxon rank sum test was used to compare change in SUV_{max} between those who had and had not recurred at one-year. Two patients were excluded from the Wilcoxon test due to less than one year of follow-up. All positive or equivocal patients were included in a Cox regression analysis of time-to-recurrence to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) associated with change in SUV_{max} slope. McNemar's test was used to compare performance of change in SUV_{max} slope to performance of $SUV_{max} \geq 2.5$ among recurrent patients (TP and FN) and non-recurrent patients (TN and FP). All statistical tests were two-sided and assessed for significance at the 0.05 level, using SAS 9.3 software (Cary, NC).

RESULTS

Patient characteristics

One hundred and five patients were prospectively enrolled. Fourteen patients withdrew from the study. Four patients missed at least one time point and were subsequently excluded as their SUV_{max} slope could not be calculated. Two patients were excluded from the study because their unknown primary was clinically suspected to be skin primary and a third patient was excluded who did not complete the full RT course, leaving 84 patients with complete dynamic triphasic FDG-PET/CT data for analysis at the primary and/or nodal sites. Five patients did not have an identifiable primary site on pre-therapy imaging to guide post-treatment measurements, leaving 79 evaluable primary site patients. Twenty-three patients did not have a focally positive nodal site on pre-therapy PET/CT, and an additional 18 patients did not have focal nodal uptake on the post-treatment 90-min PET/CT to guide post-treatment measurements, leaving 43 evaluable nodal site patients.

Patient characteristics are summarized in Table 1. The median age at diagnosis was 58.3 years (range, 42.5–91.4). Fifty-nine patients received definitive RT; of these, 51 patients were treated with concurrent chemotherapy and 8 were treated without chemotherapy. There were 25 patients treated with postoperative RT; of these, 12 patients were treated with

concurrent chemotherapy and 13 were treated without chemotherapy. 14.3% of patients were stage III and 76.2% of patients were stage IV. Median follow-up from conclusion of RT was 13.3 months (range, 4.0 – 32.4). Median interval from RT completion to response assessment 3-month FDG-PET/CT scan was 3.2 months (range, 2.3–4.1). For evaluation of 79 primary sites, there were 10 equivocal, 8 positive, and 61 negative scans; for the 43 nodal sites, there were 4 equivocal, 4 positive, and 35 negative scans.

Primary site recurrences within 12 months

Of the 79 patients with primary site data, 10 patients (12.7%) recurred at the primary disease site within 1 year. Nine patients received definitive chemoradiation, and 1 patient was treated with postoperative RT. Five patients had oropharyngeal cancer, 3 patients had laryngeal cancer, and 2 patients had hypopharyngeal cancer. Median follow-up from conclusion of RT was 13.9 months. Scan interpretation at 3 months was equivocal in 2, negative in 4 (4 FN) and positive in 4 (4 TP). Median time from completion of RT to biopsy or clinical confirmation of recurrence at the primary site was 5.2 months (range, 3.0–10.7).

Figure 1A shows the SUV_{max} curves for positive and equivocally interpreted FDG-PET/CT scans for the primary site, including TP, FP, and equivocal patients ($n=18$). The difference between the SUV_{max} slopes, -the second derivative- was calculated and depicted in Figure 1B. All patients with confirmed primary site recurrence had $[(SUV_{max}120 - SUV_{max}90) - (SUV_{max}90 - SUV_{max}60)]$ values that were greater or equal to -0.1 , while those without recurrence at the primary site had a 0 or negative change in SUV_{max} slope value. With Cox regression analysis, the risk of recurrence increased 2.09 times for each 0.6 unit increase (1 standard deviation) in the change of SUV_{max} slope (95% CI 1.13–3.85, $p=0.0185$). The Wilcoxon rank sum test demonstrated that the change in SUV_{max} slope is significantly associated with one-year recurrence ($p=0.004$).

McNemar's test was used to compare predictive accuracy of change in SUV_{max} slope to our current clinical standard of $SUV_{max} \geq 2.5$. Based on results in Figure 1, change in SUV_{max} slope ≥ 0 was used to represent recurrence. The 18 positive and equivocal primary site patients were classified as TP, FP, TN and FN. Change in SUV_{max} slope predictions were then compared to $SUV_{max} \geq 2.5$ predictions among recurrent (TP and FN) and non-recurrent (TN and FP) patients. Change in SUV_{max} slope more accurately identified non-recurrence due to fewer FP ($p=0.02$).

Nodal site recurrences within 12 months

Of the 43 patients with nodal site data, 3 patients (7.0%) recurred at the nodal site within 1 year. Two received definitive chemoradiation, and 1 patient was treated with postoperative RT. One patient had larynx cancer, another had oropharynx cancer, and the third had oral cavity cancer. Median follow-up from conclusion of RT was 15.2 months. Scans for these 3 confirmed recurrences were interpreted as negative in 1 (1 FN) and positive in 2 (2 TP) on the 90 minute 3-month FDG-PET/CT. Median time from completion of RT to biopsy or clinical confirmation of recurrence was 3.3 months (range, 3.0–4.2).

Figure 2A shows the nodal site SUV_{max} curves for positive and equivocally interpreted FDG-PET/CTs, including TP, FP, and equivocal scans ($n=8$). The difference of SUV_{max}

slopes, i.e. the second derivative, was calculated and depicted in Figure 2B. All patients with confirmed nodal site recurrences had $[(SUV_{max120} - SUV_{max90}) - (SUV_{max90} - SUV_{max60})]$ values that were greater or equal to -0.1 , while those without recurrence at the nodal site had a 0 or negative change in slope. Statistical analysis was not performed on this patient subset due to the small number of events.

Change of SUV_{max} slope between -0.1 and 0

For both primary and nodal ROI, sites with change of SUV_{max} slope values between -0.1 and 0 included both recurrences and non-recurrences. For those cases, the overall SUV_{max} slope ($SUV_{max120} - SUV_{max60}$) provides further differentiation between recurrence and non-recurrence cases, with the observed data indicating recurrence when overall SUV_{max} slope is greater than 1 and non-recurrence when the slope is less than 1 (Table 2). This is also shown in Figures 1A and 2A, where recurrences continued an upward trajectory and non-recurrences tended to remain at a constant level of SUV_{max} .

Incidental Lung Nodule and Mediastinal Node

An upper lobe lung nodule was incidentally discovered in one patient on the 3-month FDG-PET/CT scans. The SUV_{max} at 60, 90 and 120 minutes were 7.4, 8.3, and 10.0, resulting in a change of SUV_{max} slope of 0.8. Full body imaging FDG-PET/CT at 90 min revealed bilateral lung nodules. Our tumor board agreed that the lung nodules represented metastatic lesions from a HNSCC primary. Biopsy would require wedge resection and therefore was not recommended. Palliative chemotherapy was pursued, and the patient died 18 months later.

Another patient had right lower paratracheal nodal hypermetabolic activity on the 3-month FDG-PET/CT scan and FNA confirmed squamous cell carcinoma, consistent with metastasis. SUV_{max} at 60, 90 and 120 minutes were 4.7, 4.6, and 5.1, resulting in a change of SUV_{max} slope of 0.6. Palliative chemotherapy was recommended and the patient continues with follow-up. These incidental findings suggest that metastatic disease may also be accurately identified with second derivative analysis.

DISCUSSION

The use of post-RT FDG-PET/CT for response assessment in the management of head and neck cancer is a standard practice with previously demonstrated advantages over physical examination and serial CT imaging post-treatment (2, 3, 5, 22). Its utility has been studied extensively at our institution (6–11). However, previous research suggests FDG-PET/CT scans obtained post-RT suffer from relatively low PPV (approximately 50%), since inflammation results in a significant number of FP and equivocal scans (23). These require additional imaging and procedures, such as FNA, biopsies, and neck dissection. For example, one of our FP patients underwent biopsies under anesthesia, additional imaging and clinical visits amassing over \$17,000 in charges. Another FP patient underwent neck dissection with associated work-up and hospitalization resulting in over \$80,500 in charges. The charge for their post-RT PET/CT that led to the additional work-up was approximately \$6,750. Minimizing FP and equivocal scans and thus increasing the PPV of post-RT FDG-

PET/CT response assessment will immensely improve the quality of care for our patients (24, 25).

Several studies have demonstrated that FDG kinetics can differ significantly between inflammatory and malignant tissues (18, 26, 27) with several clinical applications of dual-time point FDG-PET/CT imaging in different body sites (20, 26, 28–32). One study even applied 9-time point scans to improve inter-scan accuracy (33). While these multiple time point imaging paradigms have significantly improved the ability to distinguish malignant from non-malignant tissues by calculating differences in tissue dynamics [% SUV_{max} change over time, and a “retention index” (SUV_{max} at delayed time point/ SUV_{max} at early time point)], the method applied in these studies calculates first order kinetics. We propose that malignant versus inflammatory tissue kinetics are better modeled as a second order function that includes wash-out from inflammatory tissue, and that change in SUV_{max} over 3 time points may be more effective at distinguishing recurrence from non-recurrence than a single time point or dual time point scan (Figure 3A–C). While our initial analysis is promising, it is based on small numbers and we cannot conclude that our proposed change in slope metrics is statistically different from optimized overall slope, SUV_{max60} , SUV_{max90} , or SUV_{max120} endpoints. Based on the trajectories as seen in Figure 1, it is also possible that SUV_{max} cut-offs of 5.0, or a more delayed single time point scan such as at 180 min may also differentiate patients in our study. However, our data suggests that patients such as H&N-074 and H&N-043 may not have accurate assessment of response using a single time point and that change in slope (SUV curvature) determined by three time points may help in this determination.

The change of SUV_{max} slope, a second order tissue dynamics indicator, is calculated through a dynamic triphasic scan and provides uptake curvature information along with slopes from the tissue dynamic data. This indicator measures FDG uptake change and more accurately identifies unique metabolic patterns of malignant and non-malignant tissues. Within HNSCC patients, the SUV_{max} slope change appears to more accurately identify tumor recurrence in patients presenting with lower SUV_{max} (H&N-043, Figure 1A) as well as others with higher SUV_{max} due to post-RT inflammation (H&N-074, Figure 1A). Ultimately, a multivariate model including change of SUV_{max} slope and overall slope may be the most accurate predictor of recurrence, as change of SUV_{max} slope by itself was not perfect.

In our trial, the time interval of 120 minutes after FDG injection was chosen because inflammatory tissue FDG uptake plateaus between 2–3 hours after FDG administration (19, 34). Our data confirmed FDG uptake in tumor and inflammatory tissues may continue to increase over time, but rate of uptake in inflammatory tissues appears to decrease after 90 minutes. Tumor recurrence shows constant or increasing FDG uptake kinetics after 90 minutes. The results demonstrated that data provided by a triphasic scan could improve PPV by eliminating FP and equivocal cases. As a small number of patients suffered recurrence at primary and nodal sites in this study, the generalizability of our results are limited. The suggested cut-off values were chosen empirically and require validation. However, these results are very encouraging and suggest further data collection using this novel approach is warranted.

The successful triphasic scanning of over 100 patients reveals that change of SUV_{max} slope is a clinically feasible metric to improve PPV. This technique is less prone to inter-institutional variation as each patient serves as their own internal control, mitigating problems associated with using absolute SUV_{max} as a cut-off to differentiate malignant from inflammatory lesions (17). Our preliminary data suggest this technique is effective for primary, nodal, and possibly distant sites, as measurements of SUV_{max} and calculation of SUV_{max} change are the same for all lesions, and can be applied to both definitive and post-operative patients.

One potential concern is the radiation exposure from additional imaging of the head and neck at the 60- and 120-minute time points. Total radiation exposure to the patient's head and neck region is estimated at 0.544 cGy; minuscule compared to the 5400–7400 cGy of therapeutic radiation to the head and neck. With the extra scans at 60 and 120 minutes, the additional time commitment from patients is approximately 30 minutes in addition to the routine 90-minute whole body FDG-PET/CT scan, and the scanner is occupied for an additional hour.

While the proposed technique improves the response assessment FDG-PET/CT PPV, there may also be opportunities to accurately detect patients with FN scans. To investigate this, we plan to retrospectively measure the SUV_{max} kinetics of the recurrence locations on the 3-month 60-, 90-, and 120-minute scans. There is also interest in investigating this dynamic triphasic technique in other organs such as lung, where discerning inflammation/infection from malignancy is also challenging.

In conclusion, we propose a novel method to distinguish post-RT inflammation versus malignancy with dynamic triphasic FDG-PET/CT by utilizing the change of SUV_{max} slope over time. Our data are encouraging but require further investigation and comparison to optimized single time point threshold techniques at standard as well as delayed times. By improving the accuracy of post-RT FDG-PET/CT, the number of unnecessary imaging and costly procedures in HNSCC patients will hopefully decrease. Accrual continues with 2 years of follow-up planned to capture additional head and neck recurrences.

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Figure 1.

(A) Recurrence (solid line) versus non-recurrence (dashed line) of triphasic FDG-PET/CT scans at the primary site. (B) Change of SUV_{max} slope of triphasic FDG-PET/CT scans at the primary site

Figure 2.

(A) Recurrence (solid line) versus non-recurrence (dashed line) of triphasic FDG-PET/CT scans at the nodal site. (B) Change of SUV_{max} slope of triphasic FDG-PET/CT scans at the nodal site

Figure 3.
Single time point (A) versus dual time point (B) versus triphasic (C) FDG-PET/CT scan

Table 1

Patient Characteristics (n=84)

Characteristics	No. of patients
Sex	
Male	63
Female	21
Intensity-modulated radiation therapy	
Definitive	59
With chemotherapy	51
Without chemotherapy	8
Postoperative	25
With Chemotherapy	12
Without Chemotherapy	13
Initial primary tumor site	
Hypopharynx	5
Larynx	20
Nasopharynx	3
Oral Cavity	16
Oropharynx	38
Salivary Gland	1
Unknown Primary	1
Histology	
Well-differentiated	1
Moderately-differentiated	36
Poorly-differentiated	37
Unknown	10
Initial T stage	
T0	2
T1	11
T2	25
T3	18
T4	28
Initial N stage	
N0	27
N1	9
N2a	5
N2b	27
N2c	13
N3	3
Smoking Status	

Characteristics	No. of patients
Never	14
Current	35
Quit at least 6 months	35

Table 2

Positive and equivocal scans patient characteristics

SID	Primary site	CT stage	CN stage	C stage	Definitive/post-op	Given chemotherapy?	(SUV120-90)-(SUV90-60)	(SUV120-SUV60)	90-min PET/CT clinical read	Recurrence/no Recur	F/U Time (months)
Primary											
H&N-008	Oral cavity	4a	2c	4	post-op	None	-0.3	0.3	EQ	no recur	30.30
H&N-009	Larynx	3	0	3	definitive	None	-0.7	0.9	EQ	no recur	31.73
H&N-013	Oropharynx	3	2b	4	definitive	Concurrent	-0.9	0.1	EQ	no recur	32.43
H&N-026	Larynx	3	0	3	definitive	Concurrent	-0.1	0.7	EQ	no recur	16.30
H&N-029	Oropharynx	2	2b	4	definitive	Concurrent	0	0	EQ	no recur	24.63
H&N-043	Oropharynx	4	0	4	definitive	Concurrent	0.4	1	EQ	recurrence	12.43
H&N-075	Oropharynx	2	2b	4	post-op	Concurrent	1.7	1.3	EQ	recurrence	12.73
H&N-077	Salivary gland	4b	0	4	definitive	Concurrent	0	0	EQ	no recur	13.13
H&N-092	Oropharynx	2	2b	4	definitive	Concurrent	-0.8	0	EQ	no recur	8.70
H&N-107	Oropharynx	2	2b	4	post-op	none	-0.1	0.7	EQ	no recur	4.10
H&N-023	Larynx	3	2b	4	definitive	Concurrent	-0.1	2.5	TP	recurrence	23.17
H&N-036	Oropharynx	3	2b	4	definitive	Concurrent	0	2.4	TP	recurrence	15.17
H&N-046	Oropharynx	4a	2b	4	definitive	Concurrent	0.2	1.6	TP	recurrence	13.30
H&N-064	Larynx	3	0	3	definitive	None	0	1.8	TP	recurrence	13.90
H&N-015	Larynx	4	0	4	definitive	Concurrent	-0.2	0	FP	no recur	32.30
H&N-032	Oropharynx	2	2b	4	definitive	Concurrent	-0.3	0.7	FP	no recur	25.03
H&N-074	Larynx	3	2c	4	definitive	Concurrent	-0.5	2.1	FP	no recur	13.63
H&N-078	Oral cavity	4	2b	4	definitive	Concurrent	-0.8	0.6	FP	no recur	12.73
Nodal											
H&N-007	Nasopharynx	4	3b	4	definitive	Concurrent	-0.7	0.5	EQ	no recur	24.83
H&N-013	Oropharynx	3	2b	4	definitive	Concurrent	0	-0.2	EQ	no recur	32.43
H&N-097	Oropharynx	4b	2c	4	definitive	Concurrent	-0.3	0.1	EQ	no recur	9.10
H&N-101	Larynx	3	2b	4	definitive	Concurrent	-0.3	-0.3	EQ	no recur	6.73
H&N-023	Larynx	3	2b	4	definitive	Concurrent	0.1	1.5	TP	recurrence	23.17

SID	Primar y site	CT stage	CN stage	C stage	Definiti ve/ post-op	Given chemoth erapy?	(SUV120- 90)- (SUV90-60)	(SUV120 -SUV60)	90-min PET/CT clinical read	Recurrence/ no Recur	F/U Time (months)
H&N-036	Oropharynx	3	2b	4	definitive	Concurrent	-0.1	2.7	TP	recurrence	15.17
H&N-008	Oral cavity	4a	2c	4	post-op	None	-0.1	-0.1	FP	no recurr	30.30
H&N-046	Oropharynx	4a	2b	4	definitive	Concurrent	-0.5	1.3	FP	no recurr	13.30
Distant											
H&N-018	Oral cavity	4a	2b	4	post-op	Concurrent	0.8	2.6	TP	recurrence	22.40
H&N-026	Larynx	3	0	3	definitive	Concurrent	0.6	0.4	EQ	recurrence	16.30

F/U—follow up; No Recurr—no recurrence; TP—True positive; FP—False Positive; EQ-Equivocal

Table 3

Change of SUV_{max} slope between -0.1 and 0

	Recurrences (SUV _{max} 120- SUV _{max} 90)- (SUV _{max} 90- SUV _{max} 60)	(SUV _{max} 120- SUV _{max} 60)		No Recurrences (SUV _{max} 120- SUV _{max} 90)- (SUV _{max} 90- SUV _{max} 60)	(SUV _{max} 120- SUV _{max} 60)
H&N -023	-0.1	2.5	H&N - 026	-0.1	0.7
H&N -036 (primary site)	0	2.4	H&N - 029	0	0
H&N -064	0	1.8	H&N - 077	0	0
H&N -036 (nodal site)	-0.1	2.7	H&N - 008	-0.1	-0.1
			H&N - 013	0	-0.2
			H&N - 107	-0.1	0.7
		all greater than 1			all less than 1