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Positron Emission Tomography for Assessing Local Failure After Stereotactic Body Radiotherapy for Non-Small-Cell Lung Cancer

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Abstract

Purpose—We analyzed whether positron emission tomography (PET)/computed tomography standardized uptake values (SUVs) after stereotactic body radiotherapy (SBRT) could predict local recurrence (LR) in non-small-cell lung cancer (NSCLC).

Methods and Materials—This study comprised 128 patients with Stage I ($n = 68$) or isolated recurrent/secondary parenchymal ($n = 60$) NSCLC treated with image-guided SBRT to 50 Gy over 4 consecutive days; prior radiotherapy was allowed. PET/computed tomography scans were obtained before therapy and at 1 to 6 months after therapy, as well as subsequently as clinically indicated. Continuous variables were analyzed with Kruskal-Wallis tests and categorical variables with Pearson chi-square or Fisher exact tests. Actuarial local failure rates were calculated with the Kaplan-Meier method.

Results—At a median follow-up of 31 months (range, 6–71 months), the actuarial 1-, 2-, and 3-year local control rates were 100%, 98.5%, and 98.5%, respectively, in the Stage I group and 95.8%, 87.6%, and 85.8%, respectively, in the recurrent group. The cumulative rates of regional nodal recurrence and distant metastasis were 8.8% (6 of 68) and 14.7% (10 of 68), respectively, for the Stage I group and 11.7% (7 of 60) and 16.7% (10 of 60), respectively, for the recurrent group. Univariate analysis showed that SUVs obtained 12.1 to 24 months after treatment for the Stage I group ($p = 0.007$) and 6.1 to 12 months and 12.1 to 24 months after treatment for the recurrent group were associated with LR ($p < 0.001$ for both). Of the 128 patients, 17 (13.3%) had ipsilateral consolidation after SBRT but no elevated metabolic activity on PET; none had LR. The cutoff maximum SUV of 5 was found to have 100% sensitivity, 91% specificity, a 50% positive predictive value, and a 100% negative predictive value for predicting LR.

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Conflict of interest: none.

Conclusions—PET was helpful for distinguishing SBRT-induced consolidation from LR. SUVs obtained more than 6 months after SBRT for NSCLC were associated with local failure.

Keywords

Stereotactic body radiotherapy; Non-small-cell lung cancer; ^{18}F -fluorodeoxyglucose positron emission tomography; Local recurrence

Introduction

Lung cancer is the leading cause of cancer death throughout the world and accounts for 28% of all cancer deaths in the United States (1). Approximately 15% to 20% of patients with non-small-cell lung cancer (NSCLC) present with early or localized disease that could be treated with surgery (2). Stereotactic body radio-therapy (SBRT) delivers an ablative biologic effective dose (>100 Gy) to the target while minimizing toxicity to normal tissues, and SBRT can produce excellent local control ($>95\%$) and potentially improved survival (3–5). The Radiation Therapy Oncology Group Trial 0236 reported that patients with inoperable NSCLC who received SBRT had a 3-year survival rate of 55.8% and a 3-year primary tumor control rate of 97.6% (6). SBRT is emerging as a standard treatment option for medically inoperable Stage I disease (4, 5) and for isolated recurrence of NSCLC (7).

As more patients are treated with SBRT, means of evaluating treatment response and predicting failure are needed so that salvage treatment could be applied early if needed. Computed tomography (CT) images are routinely obtained after definitive radiotherapy, but post-radiotherapy changes can make the findings hard to interpret (8). Positron emission tomography (PET) is increasingly used to stage NSCLC, with reported sensitivity and specificity superior to those of CT (9) and promising predictive indices for clinical response, recurrence, and survival in NSCLC (10, 11). However, the role of PET/CT in predicting clinical outcome, particularly local recurrence (LR), after SBRT remains controversial, mainly because of residual avidity on PET after this form of treatment (12, 13). We sought to clarify this issue by investigating the prognostic utility of the maximum standardized uptake value (SUV_{max}) on PET/CT by analyzing PET/CT findings in patients with Stage I NSCLC or isolated lung parenchyma recurrent NSCLC before and after SBRT.

Methods and Materials

Study design

One hundred twenty-eight patients were identified as having been treated with image-guided SBRT through our institutional SBRT program at The University of Texas MD Anderson Cancer Center between August 2004 and December 2008. Only cases with cytology- or biopsy-proven NSCLC—either Stage I that was not resectable for medical reasons or patient refusal ($n = 68$) or isolated pulmonary recurrence after prior definitive therapy (surgery or radiotherapy) for NSCLC ($n = 60$)—were included. All lesions measured less than 4 cm, and patients with direct invasion of the bronchial tree or mediastinal structures were excluded. Disease in all cases was staged with chest CT, brain magnetic resonance imaging, and PET/CT within 3 months before SBRT. (Typically, a standard uptake value [SUV] of 2.5 or higher than background was considered to indicate avidity.) Patients were required to have had no radiographic evidence of mediastinal or hilar nodal involvement or to have negative biopsy findings if suggestive imaging findings were present. Patients who had received systemic therapy or prior radiotherapy were eligible. Lesions within 2 cm of the bronchial tree or mediastinal structures were considered central; all other lesions were considered peripheral.

Treatment planning

All patients underwent 4-dimensional CT-based planning and daily in-room CT-guided SBRT. Techniques for patient immobilization and treatment planning are described elsewhere (7). The clinical target volume was created by expanding the envelope of tumor motion (internal gross tumor volume) with an isotropic 8-mm margin that was edited to account for tumor spread as judged by the treating physician. A further expansion of 3 mm was added to create the planning target volume to account for residual setup error and patient motion after the image-guided setup. Patients were treated with six to nine 6-megavolt X-ray beams. The prescribed dose of SBRT was 50 Gy to 95% of the planning target volume prescribed to between the 75% and 90% isodose line, delivered over 4 consecutive days.

Semiquantitative analysis by ^{18}F -fluorodeoxyglucose–PET

Patients were injected with 10 to 20 mCi of ^{18}F -fluorodeoxyglucose (FDG), and images were acquired 60 minutes later with PET/CT scanners (Discovery ST; GE Healthcare, Milwaukee, WI). Scans were all acquired in two-dimensional mode at 5 minutes per field of view, and noncontrast CT images were used for attenuation correction. Patients had fasted for at least 6 hours and had a measured blood sugar level of less than 150 mg/dL at the time of injection. SUVs of the primary tumor and the regional lymph nodes were calculated as $\text{SUV} = \text{Activity concentration (in microcuries per milliliter)} / (\text{Injected dose [in millicuries]} / \text{Body weight [in grams]})$. Delta SUV was calculated by subtracting the post-SBRT SUV at 2 to 6 months from the pre-SBRT SUV.

Follow-up

Follow-up care consisted of CT imaging and clinical examination every 3 months for the first 2 years after SBRT, then every 6 months for the third year, and annually thereafter. Post-treatment FDG-PET scans were obtained at MD Anderson at 1 to 6 months after SBRT and subsequently as clinically indicated. Rates and times of LR, intrathoracic regional lymph node recurrence, and distant metastasis (DM) were recorded and calculated from the date of completion of SBRT to the last available follow-up. The timing of recurrence was scored as the time at which the first image (PET or CT) showed abnormalities. LR (*i.e.*, in-field recurrence) was defined as progressive abnormalities on CT images corresponding to one or more avid lesions on follow-up PET scans or positive biopsy findings within the planning target volume plus 1 cm to count for anatomic changes after SBRT during the follow-up interval.

Statistical analysis

Data were analyzed with SAS version 9.2 (SAS Institute, Cary, NC). One- to three-year actuarial local control rates were calculated with the Kaplan-Meier method. Each factor was tested individually for possible association with LR. Continuous variables were analyzed with Kruskal-Wallis tests and categorical variables with Pearson chi-square or Fisher exact tests. We considered p values of less than 0.05 to be statistically significant. Cutoff values for PET SUV_{max} were determined with receiver operating characteristic curves. Sensitivity, specificity, positive predictive value, and negative predictive value were reported.

Results

Patient characteristics

A total of 128 patients were identified, with 140 biopsy-proven NSCLC tumors; 12 patients had 2 lesions that were considered synchronous primary tumors. Of the patients, 68 had Stage I disease and 60 had isolated lung parenchyma recurrent or new primary NSCLC after

a previous diagnosis of and treatment for NSCLC. Most recurrences had occurred after surgical resection, but 10 lesions recurred after prior radiotherapy (7 within or close to the previous field). All lesions had been treated with image-guided SBRT to a total dose of 50 Gy delivered in 4 fractions. When an SUV of 2.5 was used as a cutoff value, 24 patients showed no PET avidity before treatment; no LR occurred in these 24 patients. Patient and tumor characteristics are listed in Table 1.

Patterns of failure after SBRT

At a median follow-up of 31 months (range, 6–71 months), in-field LR had developed after SBRT in 8 patients (9 lesions). Of 102 lesions with at least 24 months of follow-up, only 1 failed locally. Seven lesions with LR in seven patients were confirmed by biopsy, and the other two lesions in one patient were diagnosed by PET/CT but were not biopsied because of contemporaneous multiple DM. The actuarial 1-, 2-, and 3-year local control rates were 100%, 98.5%, and 98.5%, respectively, in the Stage I group and 95.8%, 87.6%, and 85.8%, respectively, in the recurrent group. Of the 9 recurrent lesions, 2 appeared within 9 to 12 months after completion of treatment, 5 within 15 to 18 months, and 2 within 22 to 26 months. Of the 68 patients treated for Stage I disease, 2 (3%) had regional nodal failure plus DM, 4 (6%) had isolated nodal failure without DM, and 10 (15%) had DM only. Of the 60 patients treated for recurrent disease, 4 (7%) had regional nodal failure plus DM, 7 (12%) had isolated nodal failure without DM, and 10 (17%) had DM only. In the Stage I group the single recurrence after SBRT was treated surgically; that patient survived for 19 more months before dying of unknown causes. In the recurrent group, 4 patients received chemotherapy alone, 2 received chemotherapy and palliative radiotherapy, and 1 received surgery. The median survival time for the 7 patients with LR in the recurrent group was 15 months (range, 5–23 months); the 1 patient who had salvage surgery was still alive at the time of analysis without evidence of disease (17 months after surgery). Four patients were alive with disease, and two patients died at 9 and 12 months.

PET/CT SUVs before and after SBRT and LR

A total of 506 FDG-PET scans were obtained for all 128 patients during the staging workup and follow-up periods. All of the quantitative SUVs were analyzed in the Department of Diagnostic Radiology and verified by the coauthors. All of the patients underwent pretreatment PET scanning within 3 months before SBRT, and the median duration of PET follow-up was 26 months (range, 2–68 months). As noted earlier, 8 patients (9 lesions) had LR: 1 patient in the Stage I group and 7 patients (8 lesions) in the recurrent group (Table 2). Univariate analysis showed that sex, age, histology, tumor location, tumor size, gross tumor volume, and SUVs on baseline PET scans or on PET scans obtained 2 to 6 months after SBRT were not associated with LR, and this was true for both treatment groups (Table 3). However, significant associations were found between LR and SUV_{max} on post-treatment PET/CT scans. For the group treated for recurrent disease, the median SUV_{max} was 6.6 in patients with LR vs. 3.1 in those without LR at 6.1 to 12 months after SBRT ($p < 0.001$), and at 12.1 to 24 months, the median SUV_{max} was 7.3 in patients with LR vs. 2.8 in those without LR ($p < 0.001$) (Tables 2 and 3, *p*Figs. 1A and 1B). For those patients treated for Stage I disease, only the SUV from the PET scans obtained at 12.1 to 24 months showed a significant difference ($p = 0.007$) between patients with and without LR; however, only 1 patient in that group had LR, which appeared at 15 months after SBRT. Representative cases of a tumor that did not recur and a tumor that did recur are shown in Fig. 2.

The cutoff SUV for all 140 lesions in terms of association with LR was found to be 5 by use of receiver operating characteristic curves. With this value, the sensitivity was 100%, specificity was 91%, positive predictive value was 50%, and negative predictive value was 100%. Among all lesions that later recurred locally, 4 of 8 had PET SUV_{max} greater than 5

at 2 to 6 months after SBRT, 8 of 8 at 6.1 to 12 months, and 7 of 7 at 12.1 to 24 months. Among all lesions that did not recur locally, 24 of 126 had PET SUV greater than 5 at 2 to 6 months after SBRT, 3 of 36 at 6.1 to 12 months, and 7 of 73 at 12.1 to 24 months. The numbers of patients varied because PET was not obtained at all follow-up visits. The delta SUV from before to 2 to 6 months after SBRT was not associated with LR after SBRT for Stage I or recurrent disease (Table 3).

Post-SBRT consolidation

Of the 128 patients, 17 (13%) had evidence of consolidative changes on CT within the planning target volume or in the SBRT beam path after SBRT. These masses, evident on anatomic imaging, could be mistaken for LR or interpreted as “possible local recurrence” or “local recurrence cannot be ruled out” on diagnostic radiologic assessment. However, the SUVs of those solid masses declined over time, suggesting that they were not recurrent tumors (Fig. 3A). Some post-SBRT consolidation eventually disappeared, wholly or in part (Fig. 3B), and no evidence of recurrence was noted on serial follow-up by PET/CT, biopsy, or both.

Discussion

To our knowledge, this is the first report to show an association between PET SUV_{max} and LR after SBRT for NSCLC. We found that having an SUV_{max} greater than 5 at 6 or more months after SBRT was associated with LR after SBRT for Stage I disease or isolated recurrent parenchymal NSCLC. A limited number of studies have used PET to evaluate response after SBRT. A pilot study by Henderson *et al.* (12) reported low-grade activity in the treated lung that persisted for up to 1 year after SBRT. In that study serial PET/CT images were obtained from 14 patients given SBRT to 60 to 66 Gy in 3 fractions (without heterogeneity correction). Patients with high pretreatment SUVs were more likely to have SUV decline than were patients with low pretreatment SUVs. However, this study had small numbers of patients, relatively short follow-up, and no local failure events, which limit or preclude the ability to assess the significance of residual PET activity with regard to LR. In contrast, our study included 128 patients (140 lesions) and 9 LRs (7 proven by biopsy) and had a median follow-up of 31 months. The local control rate after SBRT was lower in the patients treated for recurrent disease than in the Stage I group (3-year actuarial rate of 85.8% vs. 98.5%). In all 8 of the LRs after SBRT for recurrent NSCLC, the primary tumors had been treated with surgical resection and not radiation. It is possible that recurrent disease may have aggressive genomic phenotypes that result in radiation resistance. Of the 10 patients in the recurrent group whose primary tumors (before SBRT) had been treated with radiotherapy, 7 lesions had recurred close to or within the prior radiation field. Interestingly, although those lesions seemed to have higher SUV background (perhaps because of the prior radiation), none of those 7 lesions recurred after SBRT, as confirmed by serial CT, PET/CT, and biopsy.

In cases of LR after SBRT, the SUV_{max} was significantly higher on PET scans obtained more than 6 months—but not less than 6 months—after SBRT. This finding suggests that PET scans would be most helpful for identifying LR if they are obtained no sooner than 6 months after SBRT; indeed, an SUV_{max} greater than 5 on scans obtained more than 6 months after SBRT should raise suspicion of LR. We did find some residual PET activity on scans taken more than 6 months after SBRT for some lesions that did not recur. Therefore PET scanning should not be used as the only tool to evaluate LR; biopsy should be considered if salvage chemotherapy, radiotherapy, or surgery would be used in the event of an LR. Although biopsy was strongly recommended to confirm LR in this study, only 7 of the 9 lesions that recurred after SBRT were confirmed by biopsy. However, all lesions were followed by serial imaging, and only those lesions that showed progressive increases in size

and SUV were considered to be LR. Lesions that initially showed avidity after SBRT but subsequently showed declines in size and SUV were considered to reflect consolidative changes, not recurrence. This approach has been used in Radiation Therapy Oncology Group trials, because not all LRs will be biopsied, particularly for patients in poor general condition, with tumors in difficult locations, or with concurrent DM.

Because some post-SBRT lesions did show residual PET activity, the conventional SUV cutoff point of 2.5 to 3.5 may not be appropriate. If a cutoff point of 5 were used instead, the positive predictive value of PET at 6.1 to 12 months after SBRT in our study was 50% and the negative predictive value was 100%. Thus, having an SUV lower than 5 would be reassuring in terms of low risk of LR, and having an SUV_{max} greater than 5 after SBRT should prompt a biopsy to rule out LR. Our findings, like those in the study by Henderson *et al.* (12), indicate that pretreatment SUV did not predict LR after treatment of Stage I disease or recurrent disease. The cumulative regional nodal recurrence rate was low (9%) in the Stage I group, and the isolated nodal recurrence rate was 6%. All isolated nodal recurrences were detected by PET, and most were salvaged with systemic and local treatment, indicating that PET has another important role during follow-up.

No consensus has been reached as to the optimal timing of PET after SBRT (12, 13), but our findings suggest that this timing is crucial. Six patients in our study had LR but could not be distinguished from patients without LR based on PET scans obtained within the first 6 months after SBRT. However, a difference became evident on scans obtained after that time, extending up to 48 months after SBRT. It is possible that PET activity within the first 6 months after therapy reflects an inflammatory response, residual metabolic activity of dying cancer cells, or both and that that activity resolves over time. Therefore we recommend that post-treatment PET scans be obtained no sooner than 6 months after SBRT to evaluate treatment response.

Traditionally, CT has served as the basis for treatment planning and response assessment; however, this technology is limited in its ability to identify small tumor deposits or tumor extension and to distinguish scar tissue or radiation necrosis from malignancy. SBRT in particular can lead to solid consolidations of lung parenchyma, inside or outside target volumes, that can be mistaken for residual or recurrent tumor on CT scans. However, in our cases PET showed no increased activity, and further follow-up including biopsy ruled out recurrence, suggesting—as have Mac Manus *et al.* (11)—that PET is a better predictor of treatment response after radiotherapy than CT. The large radiation fractions used in SBRT may produce segmental atelectasis or focal fibrosis that would result in the appearance of post-SBRT consolidations on imaging and be interpreted as possible LR on diagnostic radiology. Other investigators have found that SBRT produces radiographic changes that can confound CT-based evaluations of treatment response in 60% to 100% of cases (9, 14). The ability of PET to distinguish malignancy from atelectatic or normal tissue would improve the accuracy of the treatment response assessment and avoid unnecessary biopsy and attendant patient anxiety.

In summary, we found that SBRT produced 3-year actuarial local control rates of 98.5% in the Stage I NSCLC group and 85.8% in the recurrent group. SUVs on PET scans obtained more than 6 months after SBRT are associated with LR in NSCLC. High SUVs (>5) more than 6 months after SBRT should raise suspicion of LR; however, because false-positive findings on PET are possible, biopsy in such cases is still recommended to confirm the recurrence if that would change the management strategy. We further found that SBRT can produce consolidative changes that mimic LR on CT scans. PET scans can be helpful to distinguish such SBRT-induced consolidation from LR and avoid unnecessary biopsy.

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Summary

Positron emission tomography was helpful for distinguishing consolidation induced by stereotactic body radiotherapy (SBRT) from local recurrence in non-small-cell lung cancer. Standard uptake values obtained more than 6 months after SBRT for non-small-cell lung cancer were associated with local recurrence. A maximum standardized uptake value greater than 5, especially at more than 6 months after SBRT, should prompt biopsy to rule out local recurrence.

Fig. 1.

Maximum standardized uptake value (SUV_{max}) for lesions with vs. without local recurrence (LR). (A) Distribution of median SUV_{max} before stereotactic body radiotherapy (SBRT) for patients who did or did not have LR. No difference was found between the group treated for Stage I disease ($p = 0.242$) and the group treated for recurrent disease ($p = 0.355$). The box length is the interquartile range. The circles and asterisks are the outliers. The asterisks represent extreme outliers (>3 times the interquartile range). The circles represent outliers with values between 1.5 and 3 times the interquartile range. (B) Changes in median SUV_{max} over time after SBRT in the group treated for recurrent disease. The solid line indicates standard uptake values (SUVs) for lesions that recurred locally; the dashed line indicates

SUVs for lesions that did not. (C) Distribution of median SUV_{max} at 6.1 to 12 months after SBRT for Stage I disease or recurrent disease for lesions with or without LR. PET = positron emission tomography.

Fig. 2. Stereotactic body radiotherapy plans and axial positron emission tomography (PET)/computed tomography scans obtained before and 6 months after treatment for a patient with a tumor that did recur (A) and for another patient with a tumor that did not recur (B).

Fig. 3. Development of post-treatment consolidation in patients without local recurrence. (A) Median maximum standardized uptake value (SUV_{max}) and tumor size at various times after stereotactic body radiotherapy (SBRT). (B) Axial positron emission tomography/computed tomography scans and treatment plan illustrate typical post-SBRT consolidation and its resolution over time.

Table 1Patient ($n = 128$) and tumor ($n = 140$) characteristics

Characteristic	Stage I disease ($n = 68$)	Isolated recurrences ($n = 72$)
Sex		
Female	30	32
Male	38	40
Race		
White	62	64
Black	5	2
Hispanic	0	3
Asian	0	1
Other	1	2
Age (yr)		
Median	72.5	70
Range	55–91	59–89
ECOG performance score		
0–1	46	58
2–3	22	14
Histology of SBRT lesions		
Adenocarcinoma	37	47
Squamous	19	21
Other/unidentified	12	4
Location of SBRT lesions		
Peripheral	56	62
Central	12	10
Tumor size (cm)		
Median	1.75	1.4
Range	0.5–3.8	0.4–3.3
GTV (cm ³)		
Median	10.7	9.6
Range	1.4–53.2	1.2–52.4
PET/CT follow-up (mo)		
Median	27	25
Range	2–68	2–67
Clinical follow-up (mo)		
Median	31	30
Range	6–71	6–70

Abbreviations: ECOG = Eastern Cooperative Oncology Group; SBRT = stereotactic body radiotherapy; GTV = gross tumor volume; PET/CT = positron emission tomography/computed tomography.

SUV_{max} on PET/CT scans obtained before and after SBRT in lesions that did ($n = 9$) or did not ($n = 131$) recur locally

Table 2

Time of PET/CT scan	SUVs in patients with LR after SBRT for Stage I disease ($n = 1$)			SUVs in patients without LR after SBRT for Stage I disease ($n = 67$)			SUVs in patients with LR after SBRT for recurrent disease ($n = 8$)			SUVs in patients without LR after SBRT for recurrent disease ($n = 64$)		
	Median	Range	No. of patients scanned	Median	Range	No. of patients scanned	Median	Range	No. of patients scanned	Median	Range	No. of patients scanned
Staging PET (before SBRT)	6.5	NA	1	6.5	0.5–32.6	67	6.8	2.8–11.3	8	4.9	0.4–28.9	59
2–6 mo after SBRT	4.6	NA	1	2.9	1–7.7	49	5.9	1.4–7.2	7	3.2	0.9–10.4	47
6.1–12 mo after SBRT	6.2	NA	1	3	1.2–7.3	28	6.6	5.1–10.8	7	3.1	0.4–7.2	34
12.1–24 mo after SBRT	7.2	NA	1	2.2	0.8–7.3	37	7.3	5.8–16.6	6	2.8	0.8–12.2	33

Abbreviations: SUV_{max} = maximum standardized uptake value; PET/CT = positron emission tomography/computed tomography; SBRT = stereotactic body radiotherapy; LR = local recurrence; NA, not applicable.

Table 3

Univariate analysis of factors related to local recurrence of SBRT lesions ($n = 140$)

Variables	Lesions in patients treated for Stage I disease ($n = 68$, 1 LR)			Lesions in patients treated for recurrent disease ($n = 72$, 8 LRs)		
	No. with LR (%)	Median (range)	p Value	No. with LR (%)	Median (range)	p Value
Sex			0.865			0.131
Female	0/30 (0)			4/32 (12.5)		
Male	1/38 (2.6)			4/40 (10.0)		
ECOG performance score			0.122			0.490
0–1	1/46 (2.2)			7/58 (12.1)		
2–3	0/22 (0)			1/14 (7.1)		
Lesion location			0.506			0.232
Peripheral	1/56 (1.8)			6/62 (9.7)		
Central	0/12 (0)			2/10 (20.0)		
Lesion histology			0.480			0.287
Squamous cell carcinoma	1/19 (5.3)			3/21 (14.3)		
Non-squamous/unidentified	0/49 (0)			5/51 (9.8)		
Patient age (yr)		72.5 (55 to 91)	0.849		70 (59 to 89)	0.111
Tumor size (cm)		1.75 (0.5 to 3.8)	0.623		1.4 (0.4 to 3.3)	0.578
Gross tumor volume (cm ³)		10.7 (1.4 to 53.2)	0.345		9.6 (1.2 to 52.4)	0.217
Median SUV _{max} on staging PET (before SBRT)		6.5 (0.5 to 32.6)	0.242		5.8 (0.4 to 28.9)	0.355
Median SUV _{max} on PET 2–6 mo after SBRT		3.0 (1.0 to 7.9)	0.057		3.3 (0.9 to 10.4)	0.296
Median SUV _{max} on PET 6.1–12 mo after SBRT		3.2 (1.2 to 7.3)	0.146		3.4 (0.4 to 10.8)	<0.001 *
Median SUV _{max} on PET 12.1–24 mo after SBRT		2.2 (0.8 to 9.5)	0.007 *		3.2 (0.8 to 16.6)	<0.001 *
Delta SUV _{max} [†]		4.1 (5.8 to 26.3)	0.703		3.1 (–7.3 to 28.9)	0.722

Abbreviations: SBRT = stereotactic body radiotherapy; LR = local recurrence; ECOG = Eastern Cooperative Oncology Group; SUV_{max} = maximum standardized uptake value; PET = positron emission tomography.

* Statistically significant.

[†]Delta SUV_{max} = SUV_{max} at 2 to 6 months after treatment – Staging SUV_{max}.