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Cost Analysis of PET/CT Versus CT as Surveillance for Stage III Non–Small-Cell Lung Cancer After Definitive Radiation Therapy

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Abstract

We estimated and compared the costs of positron emission tomography (PET)/computed tomography (CT) versus CT for surveillance of patients with stage III non–small-cell lung cancer and identified patient and provider demographic characteristics associated with preference for PET/CT. PET/CT was associated with higher costs for 18 months post-treatment, but the difference was borderline statistically significant at 24 months. Consistent with national guidelines, PET/CT surveillance was not cost-saving and did not provide an economic benefit over CT.

Introduction: A previous study showed that use of positron emission tomography (PET)/computed tomography (CT) for surveillance after treatment of non–small-cell lung cancer (NSCLC) does not yield a detection or survival benefit over the use of chest CT. However, PET/CT remains a common method of follow-up imaging. Here we estimated and compared the costs of PET/CT versus CT for surveillance of patients with stage III NSCLC and identified patient and provider demographic characteristics associated with preference for use of PET/CT.

Patients and Methods: We reviewed 178 patients with stage III NSCLC who had received 1 PET/CT scan within 6 months of completing radiotherapy (n = 89) or had received CT after radiotherapy (n = 89) from 2000 to 2011. Costs were measured according to Medicare payments converted from institutional billing records. Total and imaging costs were analyzed at 6, 12, 18,

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The authors have stated that they have no conflicts of interest.

Supplemental Data

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and 24 months after the end of treatment. Patient and provider demographic characteristics were also evaluated for potential associations with PET/CT use.

Results: Total costs in the PET/CT group were higher during the first 18 months after treatment ($P = .002$ at 6 months, $P = .019$ at 12 months, and $P = .018$ at 18 months) but was marginally significant ($P = .05$) at 24 months. In univariate analysis of demographic variables, patients who lived in a state different from the treatment center might have been more likely to receive PET/CT (odds ratio [OR], 1.76; $P = .051$). In multivariate analysis, patients treated in 2007 to 2010 (OR, 29.9; $P < .001$) or 2003 to 2006 (OR, 11.6; $P = .002$) were more likely to receive PET/CT than patients treated in 1999 to 2002. In addition, radiation oncologists with > 10 years of experience were more likely to use PET/CT than those with less experience, although this result might be confounded by the small number of providers.

Conclusion: Use of PET/CT was associated with higher costs for 18 months after treatment, but the difference was at the borderline of statistical significance at 24 months.

Keywords

Benefit; Clinical cost; Non-small-cell lung carcinoma; Radiotherapy; Recurrence

Introduction

Despite recent advances in cancer therapy, lung cancer remains the most common cause of cancer-related death worldwide¹ owing to late detection, therapeutic resistance, and disease relapse.² Non-small-cell lung cancer (NSCLC) represents the highest proportion of lung cancer subtypes, representing 80% to 85% of diagnosed lung cancer cases.² Recommended surveillance guidelines for stage III NSCLC include chest computed tomography (CT) imaging every 3 to 6 months for 3 years, then chest CT imaging every 6 to 12 months for 2 years, followed by annual chest CT imaging thereafter.³ Positron emission tomography (PET)/CT has theoretical benefits over CT scanning for surveillance (primarily in earlier detection of recurrence) that might be expected to enhance survival. A previous study compared PET/CT versus CT for surveillance in patients after (chemo)radiation treatment for stage III NSCLC with regard to several outcomes, including overall survival (OS) and the detection of local and distant recurrence; no differences in outcomes were found according to surveillance modality.⁴ Those results were concordant with the fact that PET/CT is not currently recommended for NSCLC surveillance imaging⁵ because of lack of evidence indicating a clinical benefit over CT. Nevertheless, PET/CT remains a preferred modality of surveillance among some providers, and PET/CT usage has increased substantially from 1997/1998 to 2005.^{6, 7}

Because PET/CT continues to be chosen for surveillance in clinical practice despite the lack of evidence supporting its use and contrary to national recommendations, we sought to evaluate the burden of PET/CT versus CT-only surveillance. As a secondary aim, we assessed the characteristics of patients and providers associated with use of PET/CT technology. Specifically, our objectives were to: (1) evaluate differences in total and imaging-only costs between PET/CT and CT-only surveillance; (2) identify the patient characteristics that favor PET/CT use; and (3) identify the provider characteristics that favor

PET/CT use. We conducted a descriptive study to evaluate the cost of PET/CT scan surveillance compared with CT imaging as well as the specific patient and provider characteristics that are associated with PET/CT use.

Patients and Methods

Cohort Ascertainment

This study was approved by the institutional review board at our center and carried out in concordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). Patient cohorts were previously analyzed for survival outcomes, and patient, disease, and treatment characteristics were described in detail in the previous publication⁴ for the study time frame of 2000 to 2011 (see Supplemental Table 1 in the online version). Patterns of local and distant metastases as well as covariates of interest with respect to outcome are also detailed in Supplemental Table 2 in the online version and Supplemental Table 3 in the online version for the original cohort of $n = 200$. From the original study ($n = 200$), we ascertained our cohorts using imaging records between 1 month and 6 months after the end of treatment. Patients with stage III NSCLC who had completed radiation therapy were considered to have had PET/CT for surveillance if 1 of the first 2 follow-up scans was a PET/CT or CT-only if both of the first 2 follow-up scans was CT. The rationale for designating the modality of surveillance on the basis of only the first 2 imaging studies was the wide variation in practice patterns after approximately 6 months (eg, 2 scans). This variability largely depended on the presence or absence of disease recurrence or suspicion thereof, rather than provider preference for one modality over another. Twenty-two of the 200 patients from the original cohort were excluded from the current analysis because they only had 1 imaging record or had no imaging record during the observation time (possibly because of referrals), resulting in a PET/CT cohort of $n = 89$ and a CT-only cohort of $n = 89$.

Construction of Cost Data and Cost Analysis

We obtained charge information from institutional billing records for each group. Because charges tend to be highly inflated, we used nationally representative cost measures as a proxy of costs. We quantified cost by converting charges to Medicare payments using billing codes in the billing records, including Current Procedural Terminology (CPT) codes for professional charges and outpatient technical charges, and Diagnosis-Related Group (DRG) codes for inpatient technical charges. Using CPT codes, we obtained Medicare reimbursement rates from the 2015 Physician Fee Schedule Final Rule.⁸ We also used the 2015 Addendum B in the Ambulatory Payment Classification for CPT codes included in the Hospital Outpatient Prospective Payment System,⁹ the 2015 Average Sales Price Drug Price File¹⁰ for the drug-related codes, and the 2015 Clinical Laboratory Fee Schedule for laboratory services.¹¹ Anesthesia reimbursement rates were calculated using the Anesthesia Base Units, conversion factors,¹² and minutes spent for procedures. Rates were multiplied by the associated unit quantity in each billing record. For records without CPT codes (7.6%), we divided the average Medicare payment with CPT codes by the average charges of the corresponding codes to impute the “average” cost-to-charge ratio, and applied it to the amount of charges. For hospitalized patients, we obtained mean costs for each DRG code

from the Healthcare Cost and Utilization Project¹³ and normalized to 2015 US dollars by Consumer Price Index.

With those rates, we estimated mean costs of total and imaging-only at 6 months, 12 months, 18 months, and 24 months after the end of treatment. Professional and technical costs were combined for total costs, and imaging-only costs included PET and CT. The study period was from the treatment end date to the date of relapse or death, whichever occurred first. Observations without experiencing either of these 2 events by the end of our data collection were considered censored.

Factors Associated With PET/CT Use

We also attempted to identify patient and provider characteristics that were associated with the use of PET/CT. For that analysis, we assessed all 200 patients from the previous publication⁴ and collected the following variables: tumor histology (small-cell carcinoma [SCC] vs. non-SCC), sex, race (white vs. nonwhite), age (≥ 65 years vs. < 65 years), geographic location (≥ 200 miles from treatment center vs. < 200 miles from treatment center; out-of-state vs. in-state), marital status, Karnofsky performance status (≥ 80 vs. < 80), insurance (private vs. Medicare/Medicaid), and treatment era (2007-2010 vs. 1999-2002 and 2003-2006 vs. 1999-2002). The number of years in practice for the providers was assessed as years since completing residency (≥ 10 vs. < 10) for radiation oncologists and years since completing fellowship (≥ 10 vs. < 10) for medical oncologists.

Statistical Analysis

To estimate total and imaging costs, we used censored data methods for 6-month, 12-month, 18-month, and 24-month time horizons. We accumulated converted Medicare reimbursement rates for each patient according to time horizon. We weighted accumulated rates by the inverse probability of being observed, then adjusted correlation at censoring for total and imaging costs.¹⁴ Estimates for the difference between 2 groups were also obtained.^{14, 15}

Logistic regression modeling was used to evaluate for patient and provider factors associated with PET/CT use. Each patient and provider characteristic was evaluated separately for association with PET/CT use via univariate analyses. Patient and provider characteristics showing a potential trend ($P < .025$) were subsequently incorporated in the multivariate logistic regression analysis. Statistical analyses were conducted with SPSS (IBM SPSS Statistics for Windows, Version 23.0; IBM Corp, Armonk, NY).

Results

Surveillance Imaging Characteristics

The PET/CT group received 863 re-staging scans before recurrence or last contact date, of which 763 were PET/CT scans (88.4%; 308 PET scan [35.7%] and 455 CT scan of chest [52.7%]; Table 1). In the CT group, 919 restaging scans were provided, of which 675 were CT scans (73.5%) and 149 were PET scans (16.2%). The median event-free survival time was 20.04 months (range, 6.18-125.53 months), and the median OS time was 37.24 months (range, 6.81-125.53 months).

Cost Comparisons of CT versus PET/CT

We compared imaging costs between the CT-only group and the PET/CT group at 6 months, 12 months, 18 months, and 24 months after the final radiation treatment. The PET/CT group consistently incurred higher costs for imaging at all 4 time points ($P < .001$; Figure 1A). However, the comparison of total costs indicated that although the PET/CT group had higher costs at 6 months, 12 months, and 18 months (mean, \$1259, $P = .002$; \$1280, $P = .019$; and \$1569, $P = .018$, respectively; Figure 1B), the difference was marginally statistically significant by 24 months ($P = .05$).

The specific breakdowns of the frequencies of professional services in the CT-only and PET/CT groups are shown in Table 1. The number of clinical encounters associated with office visits, rediagnosis, re-staging, and re-treatment were recorded for both groups; all were nearly equivalent in the 2 groups. The most frequent category of health care utilization in both groups was office visits, followed by re-staging (Figure 2A and B). This pattern also held true for outpatient technical charges in both groups (Figure 2C and D). The high concordance of frequencies of health care resource utilization between the CT-only and PET/CT groups shows that the calculated total costs (Figure 1B) were not dominated by a particular category of service use in one group.

Factors Associated With PET/CT Surveillance

We next investigated patient and provider characteristics associated with the use of PET/CT for surveillance. In univariate analysis, we found that patients who lived in a state different from their treatment center (odds ratio [OR], 1.76 [95% confidence interval (CI), 1.039-3.46]; $P = .051$; Figure 3A) were more likely to have PET/CT surveillance. A preference for use of PET/CT was also noted for patients treated in 2007 to 2010 (OR, 22.8 [95% CI, 5.0-103.8]; $P < .001$) and those treated in 2003 to 2006 (OR, 9.3 [95% CI, 2.1-42.3]; $P = .004$) versus 1999 to 2002. Analysis of provider demographic characteristics revealed that radiation oncologists with ≥ 10 years of experience were more likely to prescribe PET/CT surveillance (OR, 1.9; $P = .037$). In multivariate analysis accounting for radiation oncologist experience, in-state status, patient sex, and treatment era, the 2 factors that maintained significance were: radiation oncologist experience ≥ 10 years (OR, 2.7 [95% CI, 1.3-5.4]; $P = .007$; Figure 3B) and treatment era (Figure 3C).

Discussion

In this study of the costs and potential predictors of using PET/CT versus CT for surveillance in locally advanced NSCLC, our key findings were as follows. First, PET/CT was more expensive at the 1.5-year time point, but the costs between the PET/CT and CT groups reached only marginal statistical significance at the 2-year time point. Second, patient characteristics associated with the use of PET/CT surveillance were living out of state and treatment period (2007 to 2010 or 2003 to 2006 vs. 1999 to 2002). Third, the sole provider characteristic associated with PET/CT surveillance was having ≥ 10 years of experience among the radiation oncologists.

Although the literature evaluating the efficacy of PET/CT for surveillance in NSCLC is increasing,¹⁶ the evidence regarding the clinical or economic benefits of PET/CT over CT is inconclusive. In one prospective assessment of patients with stage IV NSCLC, PET/CT scanning at 3 months after radical radiotherapy was able to detect asymptomatic progression amenable to curative therapy in 2% of patients.¹⁷ However, the cost-effectiveness analysis in that report had a high degree of uncertainty because it was modeled after a small prospective cohort and indicated that PET/CT was cost-effective in only a subgroup of asymptomatic patients, which could not necessarily be identified a priori.¹⁷ Similar studies have had small sample sizes ($n < 100$)¹⁸⁻²² and have focused primarily on the clinical advantages of PET/CT without characterizing overall costs for PET/CT versus CT or directly comparing the 2 groups. The previous study of patients with stage III NSCLC was the largest to date to directly examine the differences between PET/CT and CT for post-treatment surveillance in such patients.⁴

Unfortunately, drawing definitive economic conclusions from the existing literature is difficult, because cost-effectiveness studies must evaluate the clinical benefits of a certain imaging modality in conjunction with its cost comparisons. An economic evaluation of PET/CT versus CT conducted in Germany assessed the cost-effectiveness of PET/CT from a staging perspective and showed that PET/CT was a relatively cost-effective option per quality-adjusted life-year, although its incremental cost-effectiveness ratio (ICER) exceeded the commonly accepted threshold of approximately €50,000 for reimbursement.²³ However, that study evaluated the clinical benefit of PET/CT for staging in only a small subset of patients ($n = 77$), which might have skewed calculations of ICERs.²³ A similar investigation of the staging capabilities of PET suggested that a PET-based management strategy for NSCLC staging would yield a cost savings of \$1455 per person, but again this study was performed from a diagnostic perspective.²⁴ Even for diagnosis, the purported cost-effectiveness of PET is controversial, with use of early PET scans reducing the number of mediastinoscopies but having only a cost-neutral effect.²⁵ These diagnostic results are not directly comparable with ours, because they do not investigate the economics of PET/CT versus CT at the level of post-treatment surveillance. Studies of other cancer types have explored the cost-effectiveness of PET/CT versus CT for cancer surveillance, but with predictably mixed conclusions depending on cancer type and the tissue-specific course of disease. Briefly, neither PET/CT nor CT produced a clinical or economic benefit for patients with asymptomatic diffuse large B-cell lymphoma in remission.²⁶ For patients with head and neck squamous cell carcinoma, PET/CT-guided surveillance was noninferior to the standard of care (neck dissection), but resulted in a savings of £1492 per patient.²⁷ For patients with ovarian cancer, serial imaging, including PET/CT, in combination with carcinoma antigen 125 monitoring detected the highest number of cases of progressive disease, but at substantial financial cost.²⁸

Our data and our patient groups are unique and meaningful in that they draw on a data set of patients with stage III NSCLC for whom the clinical advantage of PET/CT over CT surveillance had already been refuted.⁴ In line with the current Medicare fee schedule, PET/CT scans were more expensive than CT scans, but when the total costs of the 2 groups were considered, the difference was only borderline statistically significant 2 years after treatment. Longer follow-up data are required to draw further conclusions, but our study

suggests that the PET/CT group initially sustained higher total costs because of the higher cost associated with PET/CT, but the total cost difference could possibly level off with time.

The patient characteristics associated with increased use of PET/CT were out-of-state status and treatment era. We can infer from these findings that patients from out of state might have been more likely to either request PET/CT or be assigned to receive extra PET/CT technology because they had traveled a larger distance to treatment center or because they sought a more advanced surveillance modality for reassurance. These results are concordant with recent findings indicating a significant increase in PET/CT use over the past 2 decades.^{6, 29, 30} Interestingly, the provider characteristic associated with use of increased PET/CT technology was 10 years of experience for radiation oncologists, which might signify a time-related dissociation from standard practice guidelines. Our findings contribute to the literature by elucidating the differences (or lack thereof) in charges for PET/CT versus CT for surveillance and by identifying the patient and provider qualities correlated with a preference for PET/CT in a group of patients with concordant clinical data.⁴

Although our results are limited by the small sample size, numerous demographic variables were available for patients as well as providers, allowing us to assess different correlations with PET/CT versus CT between groups. Nevertheless, our data set had a limited number of providers and is therefore susceptible to factors that inherently influence decision-making; a larger provider cohort is needed to overcome the influence of individual provider preference, although we included relevant variables such as provider experience and date range of treatment in our analyses. Finally, it is important to emphasize that we are not drawing conclusions on the “misuse” of any imaging modality, because many factors might have warranted the use of a certain modality, which were not captured in the existing data. Rather, we are reporting pilot data that can be further explored in terms of patient and provider characteristics leading to increased use of an advanced technology. Another strength of our study is that our approach is applicable to other surveillance technologies as well as to novel surgical procedures and radiation techniques.

One limitation of the study is that because of the statistical modeling that was used and because of the size of the patient cohort, some results that appeared clinically significant did not show statistical significance. For example, we found a borderline *P* value (*P* = .05) despite a potentially clinically significant cost difference of \$1745 between the PET/CT and CT group total cost at 2 years. Note that in doing the analysis, we determined that the relationship between clinical significance and statistical significance was stronger at earlier time points, and as such we included data only up to 2 years. As described in our previous report,⁴ we triaged our patients according to their first 2 surveillance scans, because our long follow-up period resulted in highly heterogeneous surveillance patterns that were difficult to interpret across patients. In addition, many patients did not have multiple post-treatment scans, and it was therefore challenging to detect surveillance imaging patterns after the first 2 scans. Therefore, although we acknowledge the limitation of using only the imaging within the first 6 months in assigning the patient group, because of the high rate of recurrence and unpredictable nature of lung cancer within the first 2 years after diagnosis, this method limits the rate of clinically indicated “crossover” between groups because of suspicion on imaging or subsequent events. We thus believe that this approach serves to

answer our primary question of the effect of selection of surveillance regimen on patient outcomes.

Furthermore, the PET/CT group was defined according to the use of PET/CT as surveillance within the first 6 months of follow-up after radiation, and it is unclear if a different time frame for cohort classification would influence our results. Thus, although we believe that there are implications from these findings with regard to choosing a surveillance regimen, the effect of the specific *P* values should be de-emphasized, as should extrapolation to later time periods. Future work with expanded cohorts will determine whether cost differences are maintained at longer follow-up.

Conclusion

In tandem with a previous report that PET/CT surveillance did not provide a clinical benefit over CT surveillance for patients with NSCLC, the present study showed that PET/CT surveillance also was not cost-saving (ie, did not provide an economic benefit over CT surveillance). Our results are thus consistent with national guidelines, which do not recommend PET/CT as a surveillance modality. We also identified characteristics associated with increased use of PET/CT technology at a tertiary cancer hospital, which should be explored further in multi-institutional reports that include larger numbers of patients and providers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Clinical Practice Points

- Recommended surveillance guidelines for NSCLC include chest CT every 3 to 6 months for the first 2 years after curative-intent treatment, followed by annual chest CT imaging thereafter.
- Use of PET/CT imaging has theoretical benefits over CT scanning for surveillance that might be expected to enhance survival, although a previous study compared PET/CT versus CT for surveillance in stage III NSCLC patients after (chemo)radiation treatment with regard to several outcomes, including OS and the detection of local and distant recurrence, and found no differences in outcomes according to surveillance modality.
- We estimated and compared the costs of PET/CT versus CT for surveillance of patients with stage III NSCLC and identified patient and provider demographic characteristics associated with preference for use of PET/CT.
- Use of PET/CT was associated with higher costs for 18 months post-treatment, but the difference was at the borderline of statistical significance at 24 months.
- Consistent with national guidelines, PET/CT surveillance was not cost-saving and did not provide an economic benefit over CT surveillance.

Incurred Higher Overall Costs in the 6 Months, 12 Months, and 18 Months ($P = .002$, $P = .019$, and $P = .018$), the Difference Between Groups Was Only at Borderline Statistical Significance at 2 Years ($P = .05$). All Estimated Costs Were Rounded to the Nearest US Dollar. Reimbursement Rates Are Used As a Proxy of Cost

Figure 2. Relative Frequencies of Categories of Professional Charges (Panels A and B) and Technical Charges for Outpatient Services (Panels C and D) for Patients Who Underwent Computed Tomography (CT) versus Positron Emission Tomography (PET)/CT for Surveillance. Among the Professional Charges of Physician Services, the Most Common in Both Groups Was Office Visits, Followed by Re-staging. Among the Categories of Technical Charges for Outpatient Services, Which Occurred Without Hospital Admission, the Most Common Was Again for Office Visits, Followed by Outpatient Re-staging, in Both Groups

Figure 3. Demographic Characteristics Associated With Receipt of Positron Emission Tomography (PET)/Computed Tomography (CT) Over CT for Surveillance in Stage III Non-Small-Cell Lung Cancer (NSCLC). (A) The PET/CT Group Might Have Been More Likely to Live out of State Relative to the Treatment Center ($P = .051$). (B) Patients Were More Likely to Undergo PET/CT If They Had Been Treated in 2007 to 2010 ($P < .001$) or 2003 to 2006 ($P = .002$) versus 1999 to 2002. (C) Analyses of Years of Experience Revealed That Radiation Oncologists With ≥ 10 Years of Experience Were More Likely to Prefer PET/CT for Surveillance ($P = .007$). Bars Indicate Odds Ratios at the 95% CI

Table 1

Frequencies of Recorded Professional Charges From the End of Treatment to Date of Relapse or Last Contact for 178 Patients Who Received Chemoradiation Therapy for Stage III Non–Small-Cell Lung Cancer

Category	CT Group (n = 89)		PET/CT Group (n = 89)		Total	
	n	%	n	%	n	%
Office Visit	2177	15.98	1933	14.19	4110	30.16
Consultation, inpatient	34	0.25	31	0.23	65	0.48
Consultation, office and outpatient	115	0.84	70	0.51	185	1.36
Follow-up, inpatient	306	2.25	348	2.55	654	4.8
Follow-up, office and outpatient	1722	12.64	1484	10.89	3206	23.53
Re-diagnosis	151	1.11	161	1.18	312	2.29
Core biopsy specimen (pathology code)	97	0.71	91	0.67	188	1.38
Cytology (pathology code)	37	0.27	43	0.32	80	0.59
Fine needle aspiration/CT-guided biopsy	17	0.12	27	0.20	44	0.32
Video-assisted thorascopic surgery	0	0.00	0	0.00	0	0.00
Core/open biopsy	0	0.00	0	0.00	0	0.00
Re-staging	919	6.74	863	6.33	1782	13.08
Bronchoscopy	22	0.16	36	0.26	58	0.43
CT scan of the chest	675	4.95	455	3.34	1130	8.29
CT scan of head	12	0.09	9	0.07	21	0.15
Magnetic resonance imaging	50	0.37	49	0.36	99	0.73
Mediastinoscopy	0	0.00	1	0.01	1	0.01
PET scan	149	1.09	308	2.26	457	3.35
Whole body bone scan	11	0.08	5	0.04	16	0.12
Retreatment	56	0.41	61	0.45	117	0.86
Chemotherapy	0	0.00	0	0.00	0	0.00
Radiation therapy (including SABR)	38	0.28	48	0.35	86	0.63
Surgery—less than lobar resection	0	0.00	0	0.00	0	0.00
Surgery—lobar resection	0	0.00	0	0.00	0	0.00
Surgery—surgical pathology	18	0.13	13	0.10	31	0.23

Category	CT Group (n = 89)		PET/CT Group (n = 89)		Total	
	n	%	n	%	n	%
Surgery—pneumonectomy	0	0.00	0	0.00	0	0.00
Surgery—not otherwise specified	0	0.00	0	0.00	0	0.00
Others (uncategorized)	3678	26.99	3628	26.62	7306	53.61
Total	6981	51.23	6646	48.77	13,627	100.00

Abbreviations: CT = computed tomography; PET = positron emission tomography; SABR = stereotactic ablative radiation therapy.