CHEST

Assessing the Usefulness of ^{18}F-fluorodeoxyglucose PET-CT Scan After Stereotactic Body Radiotherapy for Early-Stage Non-small Cell Lung Cancer

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BACKGROUND: Although stereotactic body radiation therapy (SBRT) is an established treatment option for early-stage lung cancer, there are no guidelines for reassessing patients for local treatment failure or intrathoracic recurrence after treatment. This study reports the sensitivity, specificity, and positive and negative predictive values for ^{18}F-fluorodeoxyglucose (FDG) PET-CT scanning when used to evaluate patients after SBRT.

METHODS: Charts were reviewed of all patients who received SBRT and a subsequent FDG PET-CT scan at a university hospital over a 5-year period. Pretreatment and 3-month post-treatment tumor characteristics on PET-CT scan and outcome data (adverse events from SBRT, need for repeat biopsy, rate of local treatment failure and recurrent disease, and all-cause mortality) were recorded.

RESULTS: Eighty-eight patients were included in the study. Fourteen percent of patients (12 of 88) had positive 3-month PET scans. Of the positive results, 67% (eight of 12) were true positives. Eighty-six percent (76 of 88 patients) had negative 3-month FDG PET-CT scans, with 89% (68 of 76) true negatives. FDG PET-CT scan performed 3 months after SBRT for non-small cell lung cancer (NSCLC) had a sensitivity of 50% (95% CI, 0.26-0.75), a specificity of 94% (95% CI, 0.89-1.0), a positive predictive value of 67% (95% CI, 0.4-0.93), and a negative predictive value of 89% (95% CI, 0.83- 0.96).

CONCLUSIONS: FDG PET-CT scan 3 months after treatment of NSCLC with SBRT was a specific but insensitive test for the detection of recurrence or treatment failure. Serial CT scans should be used for early surveillance following SBRT, whereas FDG PET-CT scans should be reserved to define suspected metastatic disease or to evaluate new abnormalities on CT scan, or for possible reassessment later in the follow-up period after radiation-related inflammation subsides.

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ABBREVIATIONS: 4D = four-dimensional; FDG = ^{18}F-fluorodeoxyglucose; ITV = internal target volume; MUSC = Medical University of South Carolina; NSCLC = non-small cell lung cancer; PTV = planning target volume; SBRT = stereotactic body radiation therapy; SUVmax = maximal standard uptake value; TPS = treatment planning system

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Lung cancer is the third most common cause of cancer and the leading cause of cancer death among men and women in the United States. Unfortunately, lung cancer is detected in an advanced stage approximately 70% of the time, with a 16% 5-year survival rate.[1] Surgical resection is the treatment of choice for early-stage non-small cell lung cancer (NSCLC), with a 70% 5-year survival rate and a 55% to 75% recurrence rate. In patients who are medically inoperable or who decline surgery, stereotactic body radiation therapy (SBRT) has emerged as a noninvasive treatment option with a 97.6% 3-year primary tumor control rate.[2-5] Although SBRT is an established treatment, there is a paucity of data on how and when to reassess patients radiographically after treatment to detect local treatment failure or intrathoracic recurrence.

The Radiation Therapy Oncology Group 0236 trial followed patients with CT scans every 3 months during the first 2 years after treatment and then every 6 months for 2 more years. ^{18}F-fluorodeoxyglucose (FDG) PET (FDG PET) scanning was used only if CT scans showed progressive soft tissue abnormalities.[6] Despite this protocol, many physicians in clinical practice use FDG PET-CT scanning for interval follow-up. FDG PET-CT scanning is 72% to 94% sensitive and 77% to 92% specific for evaluating malignancy in lung nodules.[7] It is superior to CT scan for detecting mediastinal metastasis, with a sensitivity and specificity of 77% and 86%, respectively.[8] However, it is unclear whether routine FDG PET-CT scanning improves the detection of recurrence following SBRT for early-stage NSCLC during the period when postradiation-related inflammation increases the maximal standard uptake value (SUVmax) measurements and may degrade the sensitivity of the FDG PET-CT scans.

The aim of this study was to determine the rate of treatment failure and recurrence for 88 consecutive patients who had an FDG PET-CT scan 3 months after SBRT completion. These data were used to determine the sensitivity, specificity, and positive and negative predictive value of FDG PET-CT scanning in this setting.

Materials and Methods

Patients

The Medical University of South Carolina (MUSC) Institutional Review Board (Pro00013650) and the MUSC Hollings Cancer Center Protocol Review Committee approved this study. A retrospective chart review was performed for patients aged ≥ 18 years who underwent SBRT at MUSC for stage I or II NSCLC between July 9, 2008, and January 12, 2012. The diagnosis of cancer was made based on tissue biopsy for all patients except for 10 in whom the risk of morbidity or mortality from a biopsy was too high. In these cases, a presumptive diagnosis was based on a review of clinical and radiographic data by a multidisciplinary thoracic tumor board. Staging was performed using the seventh edition TNM classification and, if any uncertainty arose, via review by a multidisciplinary tumor board.[5] Patients with more than one lung nodule were included if each nodule represented a synchronous primary lung cancer. However, only data from the first cancer treated were analyzed. Exclusion criteria included the following: (1) SBRT for malignancies other than early-stage NSCLC, (2) palliative SBRT in the setting of advanced-stage lung cancer, (3) absence of pretreatment FDG PET-CT scan for comparison, (4) failure to return for 3-month follow-up PET-CT scan and (5) FDG PET-CT scan performed at another facility and unavailable for review.

SBRT Treatment Protocol

For treatment simulation, the patient's upper thorax was positioned in a customizable mold that overlapped a head rest and indexed wing-board. Several helical CT scans were taken through the chest. The first CT scan taken through the involved region was used to triangulate and mark the treatment isocenter on the patient's skin. This was followed by a four-dimensional (4D) CT scan that extended from the chin inferiorly to include the extent of the lung volume. The 4D CT scan was reconstructed to generate 10 CT image sets, each representing a different respiratory phase. The medical physicist reviewed these image sets under a cine display to inspect for artifacts and adequacy of the images before transferring them via digital imaging and communications in medicine to the treatment planning system (TPS) (PINNACLE v 9.0; Philips Healthcare). The reference CT scan was an average-intensity projection CT image set generated from raw, untagged 4D CT scan projection data. The average-intensity projection and 10 phase-based image sets were registered in the TPS by aligning their common digital imaging and communications in medicine origin. The motion exhibited on the phase-based image sets permitted the radiation oncologist to delineate the internal target volume (ITV) that included all respiratory-induced motion of the gross tumor volume. An intermediate margin to define a clinical target volume was not applied. An isotropic setup margin of 5 mm was added to the ITV to generate the planning target volume (PTV). Normal tissue structures contoured included the left and right lungs, heart, esophagus, trachea, skin, great vessels, and spinal canal. The brachial plexus was contoured in instances in which it was in proximity to the PTV. No block margin was used axially, but a 3-mm margin in addition to the PTV in the craniocaudal direction improved coverage, thereby reducing high-and intermediate-dose spillage. Heterogeneous dose calculations were performed by the collapsed-cone convolution algorithm available in the TPS.

Plan evaluation criteria and normal tissue constraints followed were consistent with currently available protocols, including Radiation Therapy Oncology Group 0618, 0813, and 0915. Prescription doses were either 50 Gy in five fractions or 48 Gy in four fractions. No more than two fractions were delivered per week. Standard practice was to separate fractions by ≥ 2 or 3 days but ≤ 5 days. Treatment plans consisted of eight to 11 static 6-MV photon beams in a mix of noncoplanar and coplanar beam arrangements, although several included dynamic conformal arcs. In rare circumstances in which the PTV abutted a critical structure, an intensity-modulated radiation therapy treatment plan was created allowing only two to three segments per beam and a minimum of 30 MU per segment to reduce the effect of respiratory motion on dose-delivery error.

Before each treatment, each patient was set up by triangulating the treatment isocenter marked during simulation, using the room lasers. This was followed by a cone-beam CT scan to facilitate image-guided patient setup. The visualized ITV in the cone-beam CT images was registered with its position in the reference CT images at the treatment