Lung Perfusion Imaging Can Risk Stratify Lung Cancer Patients for the Development of Pulmonary Complications after Chemoradiation

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Introduction: We investigated the value of lung perfusion imaging in predicting the risk of developing pulmonary complications after chemoradiation (CRT) or radiation therapy (RT) for lung cancer.

Methods: Fifty patients who underwent lung perfusion imaging before RT for lung cancer were included. Planar and single photon emission computed tomography/computed tomography images of the lungs were obtained. Lung perfusion score (LPS) was developed to visually grade localized perfusion defect per lung on a scale of 0 to 4 and perfusion pattern in the remaining lungs on a scale of 1 to 4. The LPS is the sum of the score for the localized perfusion defect in each lung plus the score for the remaining lungs perfusion. LPSs were correlated with pulmonary function tests and the patients were followed for 8 months after therapy to determine the incidence of grade 2 to 5 symptomatic therapy related pulmonary complications according to the common terminology criteria for adverse events (CTCAE 3.0).

Results: Thirty-four patients underwent CRT and 16 underwent RT. The mean total radiation dose delivered was 56.1 ± 10.4 Gy. Eighteen patients (36%) suffered from pulmonary complications at a mean interval of 3.4 months after therapy. Nine patients had grade 2, 7 had grade 3, 1 had grade 4, and 1 had grade 5 pulmonary complications. The mean LPS was 4.9 in patients who developed pulmonary complications versus 3.5 in patients who did not ($p = 0.01$). There were no significant difference between pulmonary function tests in the patients with pulmonary complications and the patient without. In addition, there were no significant differences between the mean lung radiation dose, the volume of lung irradiated or the percentage of lung receiving greater than 20 Gy between the two groups.

Conclusions: LPS using lung perfusion imaging is useful for predicting possible pulmonary complications after CRT or RT in lung cancer patients.

Key Words: Lung perfusion imaging, SPECT-CT, Lung cancer, Pulmonary complications.

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Although the main aim of radiation therapy (RT) is to deliver sufficient radiation to the targeted tumor, the inclusion of surrounding tissues and organs is unavoidable. This becomes a challenge when the surrounding tissues or organs are diseased or compromised by a prior surgical resection or prior RT. Lung cancer patients, who frequently suffer from underlying chronic obstructive pulmonary disease (COPD) or prior resections and/or radiation, present a major population where RT faces this challenge. RT must be carefully and conservatively planned for such patients to minimize comorbidities and complications related to surrounding lung injury. The reported incidence of radiation pneumonitis has varied widely in clinical studies ranging from 0 to 54%.[1] This wide range is probably the result of differences in the total radiation doses, number of fractions and fraction dose, and the differences in associated chemotherapy regimens.

Multiple tests and imaging procedures were proposed to guide RT planning or to predict the effect of radiation dose on pulmonary function or degree of tissue damage and fibrosis in patients with lung cancer.[2–6] These procedures included computed tomography (CT), pulmonary function tests (PFTs), differential pulmonary function mapping, lung perfusion and/or ventilation imaging, and oxygen enhanced magnetic resonance imaging.[7,8] Single photon emission computed tomography (SPECT) perfusion and/or ventilation imaging of the lungs provides functional information that is not provided by CT.[9] Different areas of the lung may have different degrees of perfusion and function as demonstrated using SPECT lung perfusion imaging but appearing of the same lung density on CT. Also an area of inflammation or

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fibrosis on CT may appear smaller than the actual associated functional perfusion defect on lung perfusion imaging.[10,11] Sparing of the better perfused regions of the lung during RT planning would be ideal if the tumor size and location allow modification of RT beams. Lung perfusion SPECT has been demonstrated to add important functional lung information for RT planning for different tumors in the chest.[12,13] Also, multiple investigators have also demonstrated a decrease in pulmonary function after RT using PFTs.[14–19] Previous attempts at using lung perfusion scanning to predict post-RT pulmonary function in comparison with PFTs have been reported with suboptimal results.[20–22] These reports used planar quantitative lung perfusion images to estimate the residual post-RT pulmonary function as used for prediction of residual postoperative pulmonary function after lung resection.

To our knowledge, the ability of lung perfusion imaging to predict clinical patient outcome after chemoradiation (CRT) or RT alone to the chest has not been investigated. A method of prospectively identifying patients who cannot tolerate the changes related to radiation pneumonitis and the fibrotic permanent late effect of RT is needed. Therefore, in this study, we investigated the value of lung perfusion SPECT CT in predicting pulmonary morbidity and complications after CRT or RT alone in patients with lung cancer. We developed a lung perfusion score (LPS) that reflects the degree of loss of perfusion before initiation of RT and correlated the results with the patients' clinical outcomes.

MATERIALS AND METHODS

After obtaining approval of the study from The University of Texas M.D. Anderson Cancer Center Institutional Review Board, 50 consecutive patients with lung cancer who underwent lung perfusion SPECT CT scanning were obtained from a prospectively collected data base in the nuclear medicine department. The scans were performed within 6 weeks before the initiation of RT (mean = 12 days) except in one patient it was performed 83 days before RT. The SPECT-CT scans were considered baseline scans for future repeat scans to evaluate the extent of lung damage caused by the RT field. RT planning was performed using simulation CT. Data regarding the total RT dose, mean lung dose, total irradiated lung volume and percentage lung volume receiving greater than 20 Gy (V20) were collected from the RT plans.

Lung Perfusion SPECT CT

The patients were administered 185 MBq of Tc-99m Macroaggregated Albumin particles intravenously while lying in the supine position over a flat-bed imaging table. The Tc-99m Macroaggregated Albumin dose was thoroughly shaken immediately before intravenous administration. With the arms above the head, anterior and posterior static images were subsequently obtained for 700K counts. This was followed by a SPECT CT acquisition using a 6 slice Symbia T6 (Siemens Medical Solutions) equipped with a low-energy high-resolution collimators. The CT scans were acquired during shallow breathing using 130 kVp, 90 mAs, 6 × 2 mm collimation, and pitch 1.2. The SPECT scans were acquired using a noncircular orbit and step-and-shoot mode over a 360 degrees arc, in 128 frames, 19 sec/frame at 3-degree angles into 128 × 128 matrices. After attenuation and scatter correction, the SPECT slices were reconstructed using three-dimensional ordered-subset expectation maximization iterative reconstruction with resolution, scatter and attenuation correction. Regions of interest were drawn around each lung on planar views to obtain the geometric means of counts and split lung perfusion percentage in each lung and in three zones over each lung (apex, mid, and base).

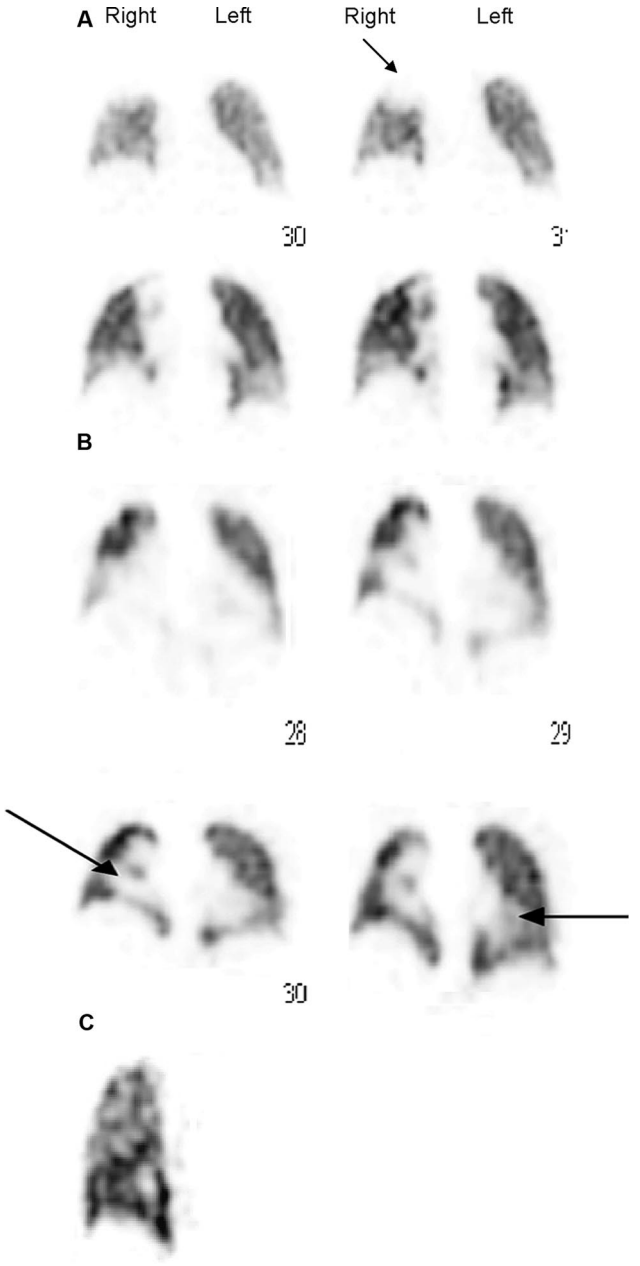

FIGURE 1. Coronal slices from lung perfusion SPECTs demonstrating *A,* Localized perfusion defect in the right upper lung (arrow) equivalent to a score of 1 on the LPS. *B,* Localized perfusion defect in the left lung equivalent to a score of 2 (short arrow) and in the right lung (long arrow) equivalent to a score of 3 on the LPS. *C,* Absent left lung after pneumonectomy equivalent to a score of 4 on the LPS.

