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Physics Contribution

Regional Lung Function Profiles of Stage I and III Lung Cancer Patients: An Evaluation for Functional Avoidance Radiation Therapy

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Summary

The development of clinical trials is under way to use 4DCT-ventilation imaging to preferentially spare functional portions of the lung. We present a 118-patient retrospective study aimed at characterizing dosimetric and functional profiles for patients with different stages of lung cancer. We developed metrics to evaluate regional lung function, compared functional profiles

Purpose: The development of clinical trials is underway to use 4-dimensional computed tomography (4DCT) ventilation imaging to preferentially spare functional lung in patients undergoing radiation therapy. The purpose of this work was to generate data to aide with clinical trial design by retrospectively characterizing dosimetric and functional profiles for patients with different stages of lung cancer.

Methods and Materials: A total of 118 lung cancer patients (36% stage I and 64% stage III) from 2 institutions were used for the study. A 4DCT-ventilation map was calculated using the patient's 4DCT imaging, deformable image registration, and a density-change—based algorithm. To assess each patient's spatial ventilation profile both quantitative and qualitative metrics were developed, including an observer-based defect observation and metrics based on the ventilation in each lung third. For each patient we used the clinical doses to calculate functionally weighted mean lung doses and metrics that assessed the interplay between the spatial location of the dose and high-functioning lung.

Results: Both qualitative and quantitative metrics revealed a significant difference in functional profiles between the 2 stage groups ($P<.01$). We determined that 65% of

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of different stage groups, and characterized dose-function trends. The presented data provide valuable guidance for the design of functional avoidance clinical trials.

stage III and 28% of stage I patients had ventilation defects. Average functionally weighted mean lung dose was 19.6 Gy and 5.4 Gy for stage III and I patients, respectively, with both groups containing patients with large spatial overlap between dose and high-function regions.

Conclusion: Our 118-patient retrospective study found that 65% of stage III patients have regionally variant ventilation profiles that are suitable for functional avoidance. Our results suggest that regardless of disease stage, it is possible to have unique spatial interplay between dose and high-functional lung, highlighting the importance of evaluating the function of each patient and developing a personalized functional avoidance treatment approach.

Introduction

A new and exciting form of functional imaging has been developed that uses 4-dimensional computed tomography (4DCT) images to calculate 4DCT-based lung ventilation maps. Four-dimensional CT-ventilation is attractive to use in radiation oncology because patients routinely get 4DCT imaging as part of the standard simulation process, therefore calculating 4DCT-ventilation does not burden the patient with an extra imaging procedure. Four-dimensional CT-ventilation has been validated against nuclear medicine single-photon emission computed tomography ventilation—perfusion images (1-3), hyperpolarized helium—based magnetic resonance imaging (4), positron emission tomography imaging (5), and pulmonary function test data (3, 6) and was found to have reasonable correlation when compared with other lung function assessment modalities.

Several clinical applications have been proposed for 4DCT-ventilation imaging, including diagnosis of non-oncologic lung disease (7) and evaluation of lung function throughout and after radiation therapy (8-10). The most frequently proposed use of 4DCT-ventilation is for functional avoidance radiation therapy, which implies designing the radiation treatment plan to avoid functional portions of the lung (as measured by 4DCT-ventilation) (11-13). The idea is that if functional portions of the lung received less dose, the probability of developing thoracic radiation—related side effects (radiation pneumonitis, for example) would decrease (11, 14). The development of prospective clinical trials is under way to use hyperpolarized helium magnetic resonance imaging for functional avoidance and to evaluate 4DCT-ventilation as a functional imaging modality for functional avoidance (15).

An important practical topic that remains to be thoroughly addressed is how to evaluate which patients should be eligible for functional avoidance. Two critical considerations for functional avoidance should be the patient's functional and dosimetric spatial distributions. If a patient has homogenous lung function, there are no regions to preferentially spare. Conversely, if a patient's ventilation image is heterogeneous and displays a major ventilation defect, functional avoidance can preferentially deposit dose in the defect area as opposed to the functional area. Dosimetrically, the spatial dose distribution of stereotactic body radiation therapy (SBRT) plans will have much steeper dose gradients when compared with conventionally fractionated plans. Because of the unique functional and dosimetric profiles of patients with different stages of lung cancer disease, studies are needed that assess spatial lung function and dose-function dosimetry for both late- and early-stage lung cancer patients. The purpose of this work was to retrospectively characterize and compare 4DCT-ventilation—based function and dose-function profiles of patients with stage I and stage III lung cancer. Specifically, we compared functional profiles and presented dose-function metrics for stage I and stage III lung cancer patients.

Methods and Materials

Study population

A total of 118 lung cancer patients from 2 institutions (MD Anderson Cancer Center and University of Colorado) treated from 2004 to 2012 were used for the study. The study included 36% stage I patients and 64% stage III patients. The stage III patients were treated with a median dose of 63 Gy (range, 45-72 Gy) in 35 fractions (range, 25-40). The stage I cohort was treated with SBRT with a median dose of 52.5 Gy (range, 34-60 Gy) in 3 fractions (range, 1-5). Each patient underwent 4DCT imaging simulation as part of their radiation treatment planning. Each 4DCT image was manually reviewed, and patients were excluded from the study if their 4DCTs had significant volume averaging artifacts.

4DCT-ventilation image generation

A 4DCT-ventilation image was calculated using the patient's 4DCT imaging data. The Hounsfield unit (HU) calculation technique was used to calculate ventilation (8, 16, 17). Briefly, the first step is to segment the lungs in the end-inhalation and end-exhalation image. Deformable image registration was then performed to link lung voxel elements from inhale to exhale. The spatial accuracy of the deformable registration algorithm used for the study was evaluated and found to be on the order of 1.25 mm for thoracic registration (18). Each deformation field was manually