CT-Based Quantitative Analysis of Lung COPD Phenotype Progression in Thoracic Reirradiation

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ABSTRACT

Purpose: As thoracic reirradiation becomes more common in clinical practice, the changes of underlying lung comorbidities due to multiple treatments are relatively unknown. Parametric response mapping (PRM) has shown promise as a method of tracking COPD phenotype changes due to clinical factors. This study investigates the changes in PRM-measured lung comorbidity classifications in a reirradiation cohort. Methods: Inspiration/expiration CTs were acquired during pre-treatment simulation for 20 patients before each of their 2-3 courses of thoracic radiotherapy, which were on average 0.99 years apart. Patient scans were processed using a commercially available PRM platform, classifying lung voxels as normal, functional small airways disease (fSAD), emphysema, or parenchymal disease (PD). The percentage of each classification was reported for the overall lung volume as well as for subdivisions representing a third of each lung. The classification percentages were compared to the prior PRM timepoint, noting the lung thirds that were treated during the prior treatment. Results: An overall decrease of normal lung classification was observed in 15 patients between their first and second treatment courses, 6 having a decrease ≥10%. Decrease in normal lung classification translated to increased fSAD, emphysema, or PD in 13, 6, and 11 patients, respectively. Increased PD was observed in the previously treated lung third in 11 patients and often resulted in a distinct region of new PD surrounding the previously treated target. Additional small decreases in normal lung classification were observed in 2 of 3 patients with 3 PRM timepoints. Conclusions: A commercial PRM tool showed the progression of underlying lung comorbidities between courses of radiotherapy, with 6 of 20 patients showing notable conversion of normal-classified lung to abnormal classification after their first treatment course. More study is warranted to investigate the impact of reirradiation on the development of PD and progression of COPD.

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INTRODUCTION

Reirradiation is becoming more common as cancer treatments improve and the population ages. A recent study showed that 14.8% of all patients treated at an academic medical center were reirradiation patients that required a special medical physics consult due to concern for cumulative dose toxicity, with the thorax being one of the most common reirradiation sites[1]. This patient population is known to be at a risk of toxicity due damage from cumulative dose[2]. In addition, patients with pulmonary dysfunction, such as interstitial lung disease (ILD), are also known to be at higher risk of pulmonary toxicity, making underlying pulmonary comorbidities potentially of high interest in reirradiation[3]. Parametric Response Mapping (PRM) has shown promise as an approach for pulmonary comorbidity mapping and tracking changes due to treatment[4]. PRM utilizes paired full inspiration/expiration CT scans to identify voxels of lung as normal lung, functional small airways disease (fSAD), emphysema, or parenchymal disease (PD). Studies have suggested that elevated levels specific PRM classifications, such as PD or emphysema, may be related with elevated pulmonary toxicity risk[5,6]. This study investigates how PRM pulmonary comorbidity classifications change for thoracic reirradiation patients between courses of treatment.

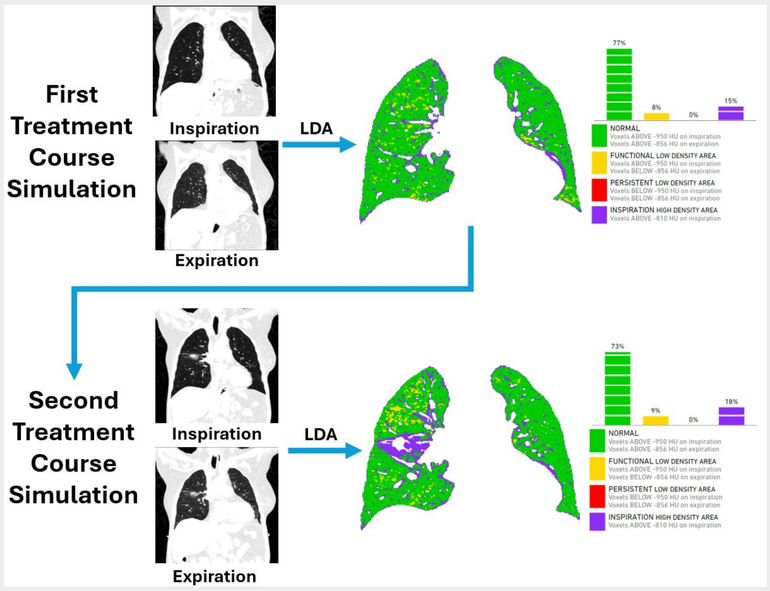

Figure 1. Outline of the LDA acquisition workflow. Paired full inspiration and full expiration CT scans were acquired at the time of CT simulation in addition to the patient's treatment planning CT. The LDA system was used to perform PRM in an automated fashion, resulting in classification maps and calculations of the percentages of the classifications within the lung volume. This process was repeated at subsequent treatment courses for the patients in the cohort, allowing for calculation of quantitative changes in the classification percentages between courses of treatment as well as observation of qualitative changes in 3D classification maps.

METHODS AND MATERIALS

Paired inspiration/expiration CTs were acquired during CT simulation for 20 patients before each of their 2-3 courses of thoracic radiotherapy (**Figure 1**). Patient treatment courses were on average 12 months apart, with a range of 1 to 37 months. Scans were processed with the Lung Density Analysis (LDA, Imbio, Minneapolis, MN), a commercial PRM system. LDA performs a PRM-based process in an automated fashion and classifies lung voxels as normal lung, functional low density (FLD), which represents fSAD, persistent low density (PLD), which represents emphysema, and inspiration high density (IHD), which represents PD, fibrosis, and potential ILD. The percentage of each classification in the patient's lungs were calculated for the full volume of both lungs, each individual lung, and subdivisions representing a third of each lung. The changes in LDA classifications between treatments were calculated for the entire lung volume and each of the lung thirds. Also, the thirds of the lung that was treated in the prior treatment course was manually identified on the prior treatment planning CT.

RESULTS

Out of the 20 patients, 15 patients displayed a decrease in the percentage of normal lung classification after their first course of treatment. Six of these patients had a decrease of normal lung of at least 10% of the total lung volume. Of the 15 patients with decreased normal lung, 13 had increased in FLD, 6 had increased PLD, and 11 had increased IHD. The percentage of the previously treated lung thirds classified as IHD increased in 11 patients at the time of their second course of treatment. These patients often showed a distinct region of IHD classification surrounding the previous target, with an example of this shown in **Figure 2**. Two of the three patients that had three courses of treatment that included LDA CT scans showed additional reduction in normal classification lung percentage between the second and third courses of treatment.

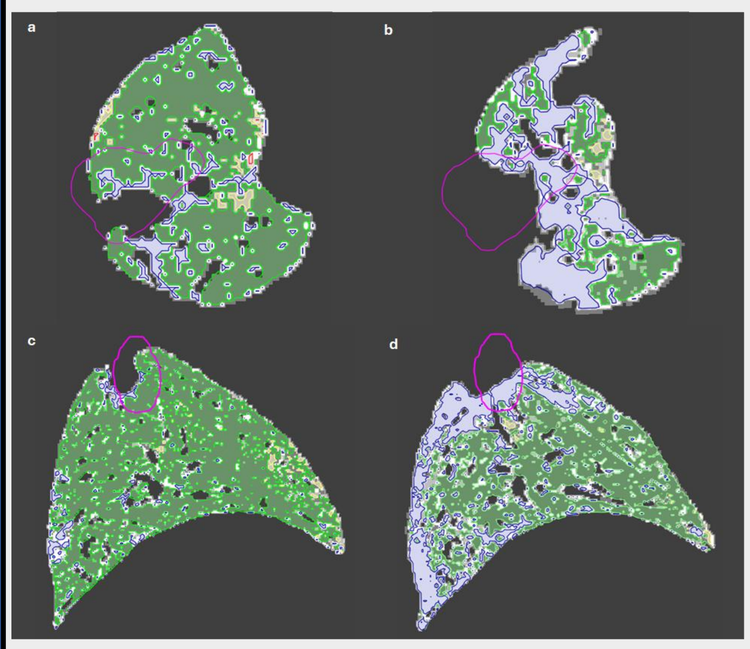

Figure 2. PRM results before the first course of treatment (a and c) and the patient's second course of treatment 18.3 months later (b and d), showing the PRM classifications of normal (green), FLD/SAD (yellow), PLD/emphysema (red), and IHD/PD (purple). The magenta contour shows the location of the planning target volume (PTV) for the first course of treatment overlaid on the output of the commercial PRM system. This case showed an 11% overall decrease in normal classification and a 13% overall increase in IHD/PD between time points with a 28% increase of IHD/PD in the upper third of the right lung where the target was located.

DISCUSSION

A notable finding in this study was that the majority of the patients in this thoracic reirradiation cohort showed a distinct decrease in normal lung and an increase in FLD and/or IHD, suggesting that the condition of these patients' fSAD and PD comorbidities worsened between courses of treatment. The distinct increase of IHD surrounding the previously treated targets also suggests that these regions are developing into potential regions of PD or fibrosis. The increase of IHD is of particular interest since in a recent publication it was found that IHD over a certain threshold was related to higher risk of pulmonary toxicity after radiotherapy[5]. These results suggest that thoracic reirradiation patients could more commonly exceed this high-risk IHD threshold than in a *de novo* setting due to the decrease of normal classification lung and increase percentage of IHD after the first course of treatment.

CONCLUSIONS

A commercial PRM software showed that patients' lungs did generally show a shift from normal classification to pulmonary comorbidity classifications between courses of treatment. Some of these comorbidity classifications have been associated with increased risk of pulmonary toxicity. The impacts of these changes in underlying lung comorbidities between treatment warrants further study in a larger cohort. Also, the association of dose to specific PRM classifications and its potential relationship to toxicity risk requires further investigation, especially in a high-risk population such as reirradiation patients.

REFERENCES

1. Paradis KC et al. Reirradiation Special Medical Physics Consultations: Lessons Learned From Nearly 3000 Courses of Treatment. Int J Radiat Oncol Biol Phys. 2025 Aug;122(5):1327-1336.
2. Gabrys D et al. Re-irradiation for intra-thoracic tumours and extra-thoracic breast cancer: dose accumulation, evaluation of efficacy and toxicity based on a literature review. Br J Radiol. 2022 Apr;95(1132):20201292
3. Saha A et al. Is Thoracic Radiotherapy an Absolute Contraindication for Treatment of Lung Cancer Patients With Interstitial Lung Disease? A Systematic Review. Clin Oncol (R Coll Radiol). 2022 Dec;34(12):e493-e504.
4. Galbán CJ et al. Computed tomography-based biomarker provides unique signature for diagnosis of COPD phenotypes and disease progression. Nat Med. 2012 Nov;18(11):1711-5.
5. Miller SR et al. Quantitative lung tissue functional analysis for pulmonary adverse event risk assessment prior to thoracic radiotherapy. Phys Imag Radiat Oncol. 2026 Apr; In Press
6. Owen DR et al. Investigating the Incidence of Pulmonary Abnormalities as Identified by Parametric Response Mapping in Patients With Lung Cancer Before Radiation Treatment. Adv Radiat Oncol. 2022 Apr; 7(4):100980

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