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Integration of Functional Imaging to Guide Adaptive Treatment Planning for Lung SBRT

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ABSTRACT

Purpose: Hyperpolarized Xenon imaging is a recent FDA-approved MRI technique that can measure physiological changes in ventilation, membrane uptake, and red blood cell transfer of gas throughout the lung. The scope of this work is to demonstrate the feasibility of integrating this functional imaging technique with MRI-guided adaptive radiotherapy (MRIgART) to avoid highly functioning lung during treatment. For the purposes of this work, lung function was discretized into 5-functional tiers using the Xe imaging and a planning technique was developed called FA5T (Functional avoidance, 5 tiers) to minimize dose to the highest functioning lung.

Methods: Three Lung cancer patients receiving SBRT were retrospectively planned using FA5T in Monaco for the Elekta Unity MRLinac. Optimization objectives were assigned to the discretized functional levels in the FA5T scheme from published predictive dosimetric markers of radiation-induced pneumonitis that used ventilation or perfusion-based functional imaging metrics. Functional loss following treatment was estimated from the dose distributions from a standard, conformity-based SBRT treatment plan and compared to the FA5T optimization schema.

Results: The incorporation of functional imaging within the treatment planning optimization framework provides a method to preserve physiological function that would have otherwise been overlooked with standard treatment planning goals. The volume of high-functioning lung receiving at least 10 Gy was reduced between 40-54% using the proposed FA5T schema while still satisfying the dosimetric goals to their conventional SBRT counterparts. As a result of these dosimetric reductions, it was estimated that FA5T could preserve 1.6 to 2.6 times as much high-functioning lung volume compared to a standard SBRT treatment plan.

Conclusions: A clinical planning framework is presented to enable functionally adaptive MR-guided lung SBRT. The ability to integrate these markers into adaptive workflows represents a major opportunity to improve the efficacy of radiotherapy by adapting treatments based on functional as well as anatomical information.

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INTRODUCTION

Radiotherapy has advanced rapidly with MR- and CT-guided adaptive platforms that now enable enhanced visualization of the tumor while also accounting for daily changes in normal tissue anatomy, all of which can be performed within minutes while with the patient is on the table. However, these treatment methods are blind to the physiological response throughout an adaptive treatment course, which is a major shortcoming as this information may infer treatment response and toxicity. The central hypothesis driving this work is that radiation damage to regions of high-functioning lung carry the greatest risk of radiation-induced pneumonitis and fibrosis; standard SBRT planning practices ignores this spatial distribution.

Functional MRI imaging using hyperpolarized Xenon gas provides quantitative information about the underlying physiological mechanisms within the lung[1]. Changes to these biologic mechanisms hold significant potential to transform the field of radiotherapy as these imaging techniques can indicate early signs to changes in lung function and normal tissue damage[2]. The ability to integrate these markers into adaptive workflows, as illustrated in Figure 1, represents a major opportunity to improve the efficacy of radiotherapy by adapting treatments based on predicted biological response[3].

METHODS AND MATERIALS

A multiparametric schema, shown in Figure 1, was used to identify regions of high-functioning lung using Xenon MRI to provide functional measures of ventilation, gas exchange to the red blood cells (RBC:Mem), and the retention of inhaled gas within the membrane (Mem:Gas). Five discrete levels of lung function served as the basis for treatment planning optimization, in addition to the standard anatomical structures, and dose optimization objectives were set following the hierarchical approach in Figure 1.

A framework is proposed that maps specific dosimetric objectives inferred from longitudinal lung ventilation and perfusion studies that identified dosimetric markers associated with the development of radiation-induced pneumonitis and lung fibrosis. The optimization schema prioritizes sparing of the highest functioning lung, as it is hypothesized that these regions will become compensatory areas of hypertrophy to preserve overall lung function.

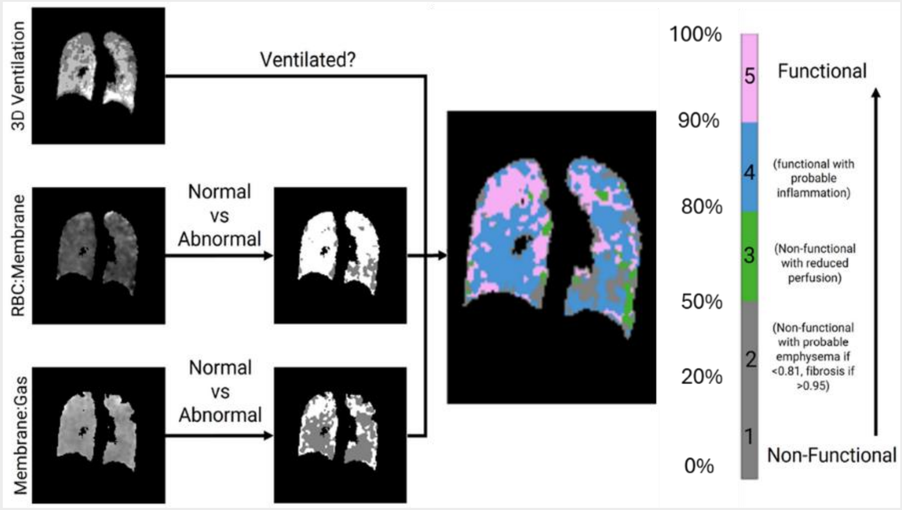

Figure 1: Schema combining multiple Xenon MRI functional measures to provide a spatial distribution of functional tiers. Dose objectives were assigned to each tier based on the expected physiological response to radiation damage (listed below).

Tier	Dose Goal	Physiological Reasoning
1 to 2	Conventional volumetric lung constraints	None functioning. Used in evaluation of conventional volumetric lung constraints.
3 to 5	$\bar{D} \leq 12.5$ Gy	Moderate gross inflammation throughout lung volume. Limit induced inflammation throughout lung airways to retain ventilation[4].
4 to 5	$V_{16.1\text{Gy}} \leq 17\ \%$	Minimize chronic loss of RBE transfer and acute membrane uptake in functional regions[5].
5 only	$V_{10\text{Gy}} \leq 10\%$	Spare top functional centers where compensatory hypertrophy is expected[6].

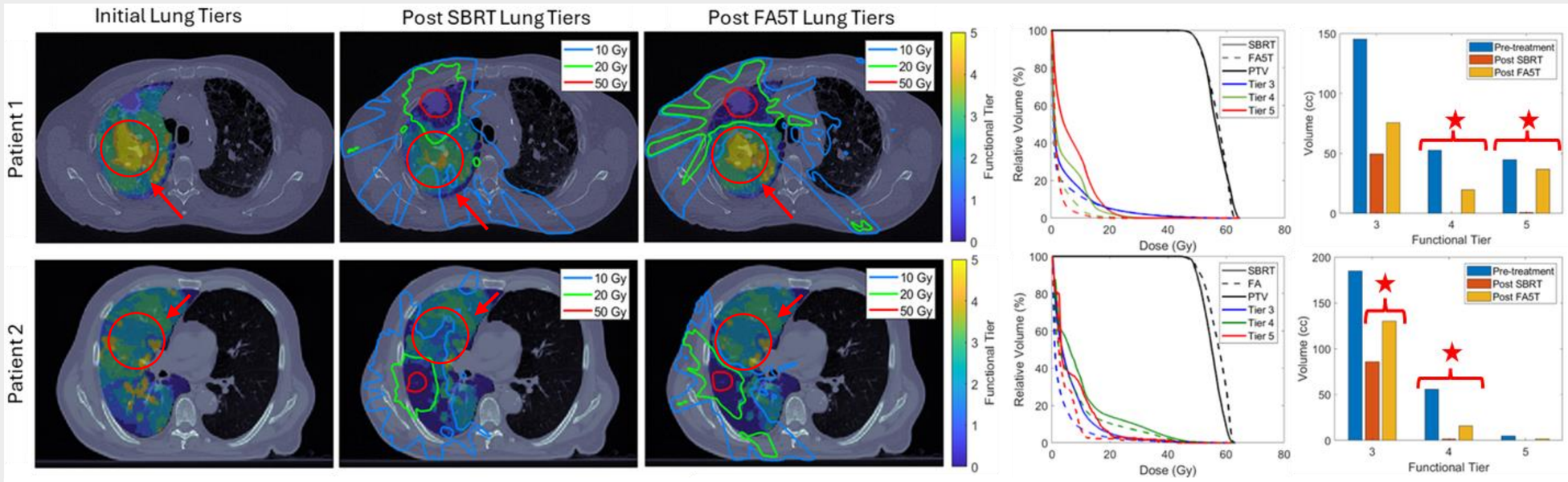

Figure 2: Treatment planning results for two lung SBRT treatments (50 Gy in 5 fractions) optimized using a conformity-based SBRT and a 5-tier functional avoidance (FA5T) approach. The initial measure of functional lung volume is shown along with the expected changes following treatment, dose shown with isodose lines. Dose-volume histograms are presented for the target and regions of high-functioning lung. FA5T is shown to preserve high-functioning lung (Tiers 3-5), which are highlighted with red arrows and circles for the cases presented. The dosimetric sparing of these structures shown in the DVH correspond to significant preservation of functional lung volume (starred) that is quantified in the bar graph for each tier.

RESULTS

Among the treatment plans investigated, treatment plans utilizing a functional avoidance-informed five-tier optimization schema (FA5T) preserved all traditional OAR constraints relative to standard SBRT-optimization strategies. Compared to standard SBRT treatment planning, FA5T-optimized treatments:

- Reduced the volume of high-functioning lung receiving more than 10 Gy by 46%
- Preserved 25% more of baseline function than conventional SBRT planning techniques

DISCUSSION

The following is a generalizable optimization strategy capable of translating a FA5T approach within conventional radiotherapy treatment planning methods. The pyramidal approach prioritizes the highest functioning lung with the strictest dose goals. Future work will focus on improving the reproducibility of the functional imaging technique and performing longitudinal monitoring studies to identify dosimetric markers that directly reflect our functional imaging technique and associate loss of pulmonary function.

CONCLUSIONS

This work presents the proof-of-concept use of a multiparametric mapping schema to enable an adaptive SBRT treatment planning framework using functional maps of ventilation, blood transfer between the alveoli membrane and blood stream obtained from Xenon MRI for lung. The use of these multiparametric maps form the basis of a novel hierarchy approach and initial set of dosimetric goals that reflect the organization of the functional tiered schema, which is aimed to prioritize the sparing of the regions of highest functioning lung.

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