
Proceedings Paper:
Tahir, B.A. orcid.org/0000-0003-0531-3519, Hughes, P.J.C. orcid.org/0000-0002-7979-5840, Astley, J.R. et al. (4 more authors) (2024) 1614: MRI V/Q for assessing radiation-induced changes in regional lung function in lung cancer patients. In: Radiotherapy and Oncology. ESTRO 2024, 03-07 May 2024, Glasgow, United Kingdom. , S5062-S5066.

https://doi.org/10.1016/S0167-8140(24)01981-9

Utility of MRI V/Q for assessment of radiation-induced changes in regional lung function in lung cancer patients

Tahir BA[1,2], Hughes PJ[1], Astley JR[1,2], Biancardi A[1], Marshall H[1], Wild JM[1,2] and Hatton MQ[1]

[1]Division of Clinical Medicine, University of Sheffield, UK and [2]Insigneo Institute for in silico medicine, University of Sheffield, UK

Main text: 738/750 words

Background and Purpose:

Radiotherapy (RT) is a cornerstone in treating non-small cell lung cancer (NSCLC). Although there have been advancements in RT techniques, such as the introduction of stereotactic ablative RT, survival rates remain poor. A contributing factor to this is radiation-induced lung damage, which is further aggravated by pre-existing diminished pulmonary function prior to RT [1]. Presently, NSCLC patients' lung function prior to RT is evaluated using standard pulmonary function tests (PFTs), which are somewhat limited in scope as they offer global, whole-lung metrics and lack sensitivity to early alterations [2].

The lungs primarily serve the purpose of gas exchange, making both ventilation (V) and perfusion (Q) critical for a comprehensive understanding of lung function, ideally on a regional level. Traditional methods for assessing regional lung function have included radionuclide scintigraphy or single-photon emission computed tomography, despite their limitations in spatial and temporal resolution [3]. As an alternative, MRI offers the capability for high-resolution imaging of regional lung function, as demonstrated by dynamic contrast-enhanced (DCE) perfusion proton (^{1}H) MRI and hyperpolarised gas ventilation MRI [4].

In this study, we develop and apply an imaging acquisition and analysis workflow to evaluate the impact of radiation dose on regional lung function, as determined by MRI V/Q, in NSCLC patients undergoing a course of RT.

Materials and Methods:

Patient and imaging data

12 NSCLC patients receiving RT underwent pre-RT free-breathing CT as standard-of-care and inspiratory breath-hold CT at functional residual capacity (FRC)+1L. Helium-3 (^{3}He) (3D SSFP) and ^{1}H-MRI (3D SPGR) were acquired in the same breath and inflation state as inspiratory CT [5] following inhalation of 200ml hyperpolarised ^{3}He and 800ml N_2. Imaging was performed at 1.5T (GE HDx) using a ^{3}He transmit-receive vest coil (CMRS). Patients were repositioned in an 8-channel cardiac coil with DCE-MRI acquired using a 3D SPGR sequence and parallel imaging [6]. All MRI scans were repeated 3-4 months post-RT.

Image registration

Images were segmented using previously described methods [7, 8]. Free-breathing CT, planned dose distribution and RT contours were deformably registered to inspiratory CT. Pre-RT inspiratory CT, the

warped dose distribution and RT contours, post-RT ^{3}He-MRI and pre- and post-RT DCE-MRI were registered to the spatial domain of pre-RT ^{3}He-MRI [9]. The registration workflow is shown in Figure 1.

Dosimetric and image analysis

A threshold of ≥20Gy was applied to the warped dose distribution minus the gross tumour volume; this threshold was selected as it has been validated as a predictive marker for radiation pneumonitis [10]. All lung function metrics described below were computed in this dose region.

Ventilation and perfusion defect percentages (VDP, QDP, respectively) were computed from the ratios of the ventilated and perfused lung segmentations over the pre-RT ^{1}H-MRI thoracic cavity volume. The spatial overlap of ventilated and perfused defects was computed via the Dice similarity coefficient (DSC) to assess global V/Q matching (DSC(V/Q)). Fractional ventilation (FV) [11], pulmonary blood volume (PBV), pulmonary blood flow (PBF) and mean transit time (MTT) [12] were computed as previously described. The V/Q ratio (FV/PBV) was used as a surrogate of gas exchange [13].

Statistical analysis

Wilcoxon signed-rank tests were used to assess differences in imaging biomarkers pre- and post-RT.

Results

9 of the 12 patients underwent all imaging tests required to be included in this study. Statistically significant differences between the VDP, QDP and DSC(V/Q) before and after RT were only observed for DSC(V/Q). Figure 2 summarises the results for the V/Q metrics. Although PBF was the only metric to exhibit a statistically significant difference between pre- and post-RT, trends towards significance were observed for FV and PBV. The significant changes in vascular response to radiation as observed by pre- and post-RT PBF measurements are in line with preclinical studies in irradiated rats [14, 15]; radiation induces endothelial injury which exposes basement membrane, resulting in platelet adhesion and vascular obstruction, thus limiting blood flow [15].

Conclusion

Quantitative evaluation of dose-associated alterations in MRI V/Q-derived biomarkers can be effectively conducted utilising a specialised acquisition and analysis framework. Significant dose-dependent decrease in the overlap of ventilation and perfusion following RT suggests that MRI V/Q holds potential as a diagnostic tool for identifying radiation-induced pulmonary damage in patients receiving thoracic RT.

References:

1. Robnett TJ, Machtay M, Vines EF, et al. Factors predicting severe radiation pneumonitis in patients receiving definitive chemoradiation for lung cancer. Int J Radiat Oncol Biol Phys. 2000;48:89-94.
2. Que C, Cullinan P, Geddes D. Improving rate of decline of FEV1 in young adults with cystic fibrosis. Thorax. 2006;61:155-7.
3. Marks LB, Spencer DP, Bentel GC, et al. The utility of SPECT lung perfusion scans in minimising and assessing the physiologic consequences of thoracic irradiation. Int J Radiat Oncol Biol Phys. 1993;26(4):659-68.
4. Ireland RH, Din OS, Swinscoe JA, et al. Detection of radiation-induced lung injury in non-small cell lung cancer patients using hyperpolarised helium-3 magnetic resonance imaging. Radiother Oncol. 2010;97(2):244-8.

5. Tahir BA, Hughes PJC, Robinson SD, et al. Spatial comparison of CT-based surrogates of lung ventilation with hyperpolarised helium-3 and xenon-129 gas MRI in patients undergoing radiation therapy. Int J Radiat Oncol Biol Phys. 2018;102(4):1276-86.
6. Johns CS, Swift AJ, Rajaram S, et al. Lung perfusion: MRI vs. SPECT for screening in suspected chronic thromboembolic pulmonary hypertension. 2017;46(6):1693-7.
7. Hughes PJC, Horn FC, Collier GJ, et al. Spatial fuzzy c-means thresholding for semiautomated calculation of percentage lung ventilated volume from hyperpolarised gas and ^{1}H MRI. J Magn Reson Imaging. 2018;47(3):640-6.
8. Schiwek M, Triphan SMF, Biederer J, et al. Quantification of pulmonary perfusion abnormalities using DCE-MRI in COPD: comparison with quantitative CT and pulmonary function. Eur Radiol. 2021. DOI: 10.1007/s00330-021-08229-6
9. Tahir BA, Swift AJ, Marshall H, et al. A method for quantitative analysis of regional lung ventilation using deformable image registration of CT and hybrid hyperpolarised gas/^{1}H MRI. Phys Med Biol. 2014;59(23):7267-77.
10. Palma DA, Senan S, Tsujino K, et al. Predicting radiation pneumonitis after chemoradiation therapy for lung cancer: an international individual patient data meta-analysis. Int J Radiat Oncol Biol Phys. 2013;85(2):444-50.
11. Tzeng YS, Lutchen K and Albert M. The difference in ventilation heterogeneity between asthmatic and healthy subjects quantified using hyperpolarised ^{3}He MRI. J Appl Physiol. 2009;106(3):813-22.
12. Sourbron SP and Buckley DL. Classic models for dynamic contrast-enhanced MRI. NMR Biomed. 2013:26(8):1004-27.
13. Hughes PJC, Tahir BA, Horn FC, et al. Quantitative ventilation-perfusion imaging using co-registered hyperpolarised gas and contrast enhanced ^{1}H perfusion MRI. ISMRM 2017.
14. Peterson LM, Evans ML, Graham MM, et al. Vascular response to radiation injury in the rat lung. Radiation Research. 1992:129(2):139-48.
15. Peterson LM, Evans ML, Thomas KL, et al. Vascular response to fractionated irradiation in the rat lung. Radiation Research. 1992:132(2):224-6.

Figures

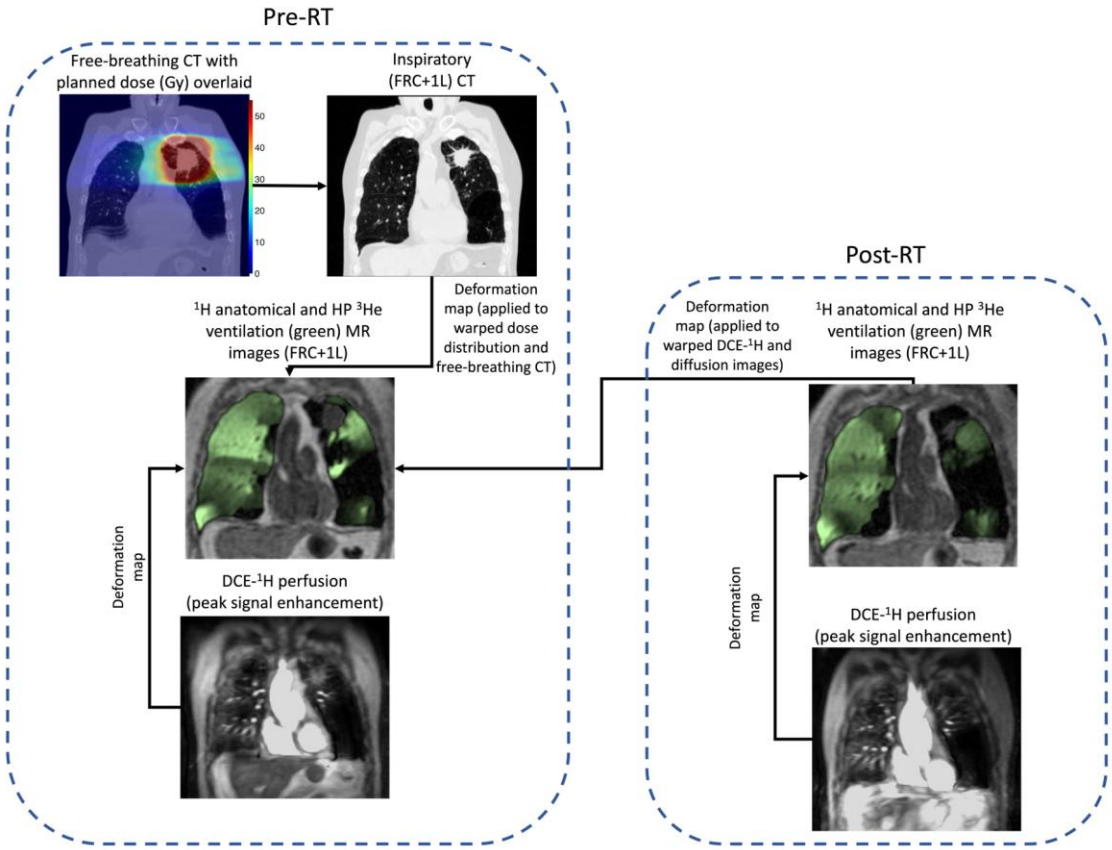

Figure 1. Multi-modal image registration workflow to facilitate quantification of dose-related changes in regional lung function pre- and post-RT.

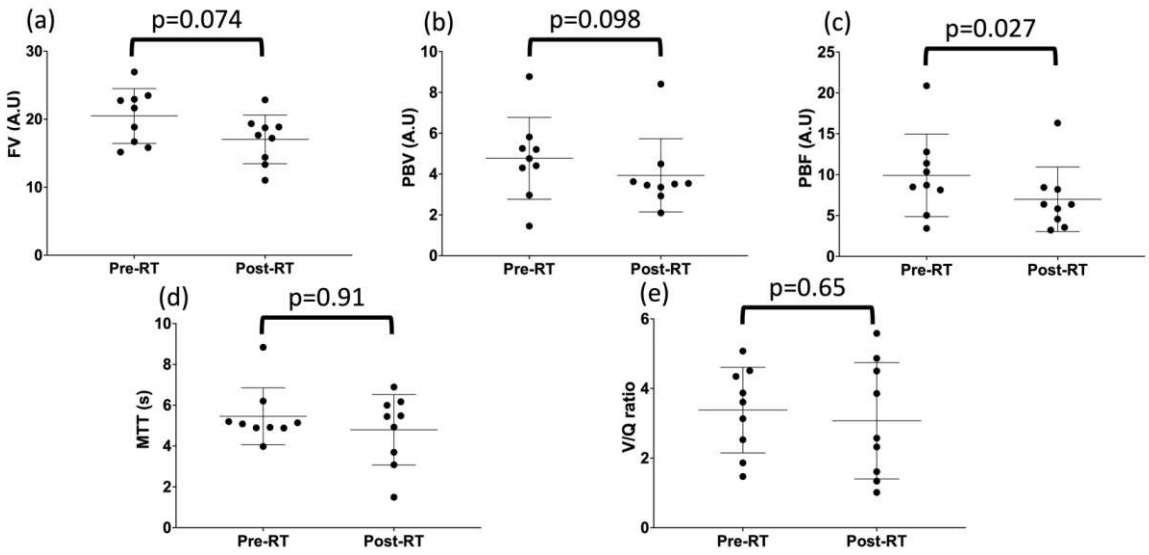

Figure 2. Box plots of (a) FV, (b) PBV, (c) PBF, (d) MTT and (e) V/Q ratio. Individual data points are shown for all patients along with the mean±SD. Wilcoxon signed-rank p-values are provided. A.U = arbitrary units.