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Editorial for "Elevated Lung Water Density (LWD) Measured with MRI in Individuals Previously Infected with COVID-19: A Cross-Sectional Study"

Persistent symptoms following COVID-19 are common and can be accompanied by radiological abnormalities, particularly in patients with more severe acute infection(1). While CT imaging remains the gold-standard for lung parenchymal imaging, significant advancements in lung MRI make it a promising alternative to CT for the assessment of lung structural abnormalities. Lung MRI may be particularly beneficial in situations where limited exposure to ionizing radiation is desirable, such as during patient follow-up.

The use of ultra-short echo times to overcome low lung signal to noise ratio, due to short lung T_2^* has permitted substantial improvements in the ability of lung MRI to visualise structural abnormalities. UTE imaging combined with quantitative analysis techniques are now approaching the quality of lung CT(2). Lung Water Density (LWD) quantification is an innovative image analysis technique proposed by Meadus et al(3) that solves two important post-processing problems. It allows normalisation of lung signal without depending on manual, user-dependent, input and it also permits an empirical B_1 inhomogeneity correction, based on the assumption that tissue outside the lung is of a uniform density. This method provides a meaningful move towards more accurate tissue signal quantification of lung UTE images.

In this issue of JMRI, Authors et al(4) employ LWD imaging to quantitatively evaluate lung structure in 185 participants who have had COVID-19 and 109 healthy controls. Two different acquisition variations were used in this study. The consistency between the two methods was measured by acquiring LWD maps in 39 post-COVID participants using both pulse sequence variants. The two acquisition variants showed excellent agreement, with intra-class correlation coefficient values >0.98. This demonstration of the robustness of the method to variation in acquisition parameters suggests promise for its application to multi-site studies and further clinical translation.

Interestingly, this paper reported increased LWD (>1.96 standard deviations from healthy mean values in at least one lung) in participants who have had COVID-19 when compared to the control cohort, with 37% of men and 24% of women having elevated LWD. Elevated LWD was associated with hospitalisation during the acute phase of COVID-19, as well as elevated C-reactive protein and white blood cell count, suggesting an association with systemic inflammation. It has been previously shown that there is an association between C-reactive protein and residual lung abnormalities identified using CT in post-COVID patients(5). Elevated LWD imaging may be identifying residual lung abnormalities in some of the patients in this study, although without corresponding CT imaging this can only be speculated. However, as up to 11% of patients are estimated to be at risk of residual lung abnormalities following hospitalisation due to COVID-19(6), further work establishing whether LWD imaging

could be an effective tool for longitudinal monitoring of lung parenchymal changes in those patients is warranted.

A key limitation of this work is a disparity in the prevalence of comorbidities between the healthy volunteers and the post-COVID participants, preventing clear conclusions about the independent effects of comorbidities and COVID-19 infection. In addition, the paper does not evaluate the relationship between patient reported symptoms or outcome measures and LWD, which limits what conclusions can be drawn around the clinical implications of this paper's findings. However, these limitations are communicated explicitly by the authors, who interpret their data pragmatically with careful consideration to these limitations. Analysis with patients with comorbidities grouped separately shows that post-COVID participants with comorbidities had significantly higher LWD than controls and post-COVID participants without comorbidities, with LWD differences between controls and post-COVID participants without comorbidities only found in the right lung in men.

The authors also report that LWD correlated with BMI in both control and post-COVID cohorts. One cause of this may be that patients with obesity, particularly patients with a central fat distribution, have reduced functional residual capacity(7) which we would expect to lead to an increased proton density within the lung when imaged during free breathing. Further work characterising the relationship between LWD and comorbidities, in particular obesity, in healthy populations is needed and this work is an important first step towards understanding these associations.

The findings in this paper add to the growing body of evidence that UTE imaging, and the LWD post-processing pipeline in particular, shows promise as an effective, quantitative tool for assessing lung structural abnormalities in patient cohorts or circumstances where exposure to ionizing radiation should be avoided. LWD imaging provides quantitative structural information that would be well suited to being employed alongside functional lung MRI imaging techniques, such as Fourier Decomposition or hyperpolarised gas MRI methods, and would therefore be a valuable addition to a lung MRI imaging protocol.

In conclusion, this work demonstrates that LWD imaging can visualise and quantify lung density differences in post-COVID patients and that elevated LWD was associated with inflammatory plasma biomarkers and acute disease severity. In addition, this work highlights the importance of understanding the impact of comorbidities on lung MRI biomarkers, such as LWD, if markers are to transition into clinical practice.

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