MRI in interstitial lung disease (M-ILD): a momentum to innovate lung diagnostic

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The prevalence of interstitial lung disease (ILD) is high and progressively increasing.[1] Mortality and morbidity vary according to ILD subtype, but overall median survival is poor, ranging from 5 to 14 years.[2] Irrespective of classification and cause of lung fibrosis, several patients present with progressive-fibrosing ILD (PF-ILD), characterised by a rapid decline in lung function.[3]

A recent landmark study demonstrated a reduction in PF-ILD disease progression using costly antifibrotic drugs.[4] However, half of patients with ILD do not benefit from these expensive antifibrotic drugs but could be better treated with anti-inflammatory or combined treatment. Hence, there is an unmet need for a monitoring tool to phenotype patients with ILD by assessing the amount of pulmonary fibrosis and inflammation to guide treatment choices and monitor response.[3]

Current monitoring, namely, high-resolution CT (HRCT) and pulmonary function test, cannot differentiate between fibrotic lung disease and active inflammation.[3 5] Histology can make this distinction, but biopsy is a high-risk procedure not routinely performed in patients with ILD. Conversely, chest MRI can offer a one-stop-shop solution for ILD providing structural and functional information in a single examination, such as ventilation inflammation perfusion and structure (VIPS-MRI).[6] Using VIPS-MRI, both lung fibrosis and inflammation can be detected to select the best cost-effective treatment and to monitor its effect.[7]

In line with this concept, the interesting article published in this issue of *Thorax*, Weatherley and colleagues proposed a semiquantitative image measure of pulmonary perfusion based on the first pass of gadolinium-based contrast agent using dynamic contrast-enhanced MRI in a cohort of patients with PF-ILD. The study compares the full-width at half-maximum ($FWHM_{mean}$) of the dynamic contrast curve averaged over the whole lung as an estimate of global pulmonary perfusion response to IPF and possible change in disease severity between baseline and a 6-month follow-up study. A second semiquantitative measure of the IQR of the distribution of FWHM values over the whole lung (FWHM IQR) is used as a candidate measure of pulmonary perfusion heterogeneity. The study presents promising and clinically relevant first results of pulmonary perfusion quantification as measure of disease progression and response to treatment in PF-ILD. New biomarkers are needed to evaluate progression of PF-ILD at earlier stages of disease.[3] Previous studies on CT using quantitative methods, such as CALIPER, have clearly shown the close relationship between vascular pruning and progression of fibrosis.[8] Quantification of pulmonary vasculature and perfusion are therefore strong predictors of patient outcome in PF-ILD.[9] This strongly supports further development of MRI to assess pulmonary perfusion as a possible biomarker of early progression in PF-ILD.[7] Despite the small cohort, the $FWHM_{mean}$ shows reasonable repeatability, which is crucial for the selection of robust biomarkers, and that could be further improved by protocol refinement.

A few uncertainties remain. The use of a semiquantitative surrogate for pulmonary perfusion might be influenced by cardiac output, which in elderly population of PF-ILD can be quite variable, especially when another cardiac comorbidity is present. The biomarker proposed as measure of perfusion heterogeneity showed marginal repeatability, so $FWHM_{mean}$ seems a better candidate as image biomarker. Finally, it is unclear if the difference measured using $FWHM_{mean}$ between the two time points is related to progression of fibrosis rather than a reflection of true underlying vascular injury.

Said that, the study of Watherley and colleagues can generate *new momentum to innovate lung diagnostic of PF-ILD*. It would be important to coordinate a joint effort for a multicentre study in an adequately selected group of patients with PF-ILD including measures of disease activity (eg, Krebs-von-den-Lungen 6, also known as KL-6), patient-reported outcome (eg, King's Brief Interstitial Lung Disease) and quantitative HRCT biomarkers. Such validation will be crucial to introduce VIPS-MRI as a clinical tool for PF-ILD.

Acknowledgements P Wielopolski, MRI Physicist, Erasmus MC.

Collaborators Piotr Wielopolski, Radiology and Nuclear Medicine Department, Erasmus MC.

Contributors I've personally written the editorial.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

To cite Ciet P. *Thorax* 2021;**76**:108.

Accepted 16 November 2020
Published Online First 9 December 2020

Linked

► http://dx.doi.org/10.1136/thoraxjnl-2020-214924
► http://dx.doi.org/10.1136/thoraxjnl-2019-214375

Thorax 2021;**76**:108.
doi:10.1136/thoraxjnl-2020-216382

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