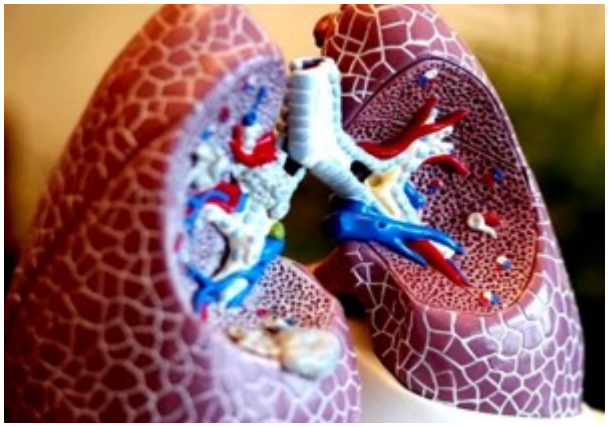
The authors from UK and Germany conducted this pilot prospective study to evaluate hyperpolarized (HP) pulmonary xenon 129 (129Xe) magnetic resonance imaging (MRI) measurements of the pulmonary red blood cell (RBC)-to–alveolar tissue barrier ratio as a surrogate of abnormal gas exchange in a small group of nonhospitalized and posthospitalized participants with long COVID symptoms. The results revealed an abnormal gas exchange (129Xe MRI RBC-to–alveolar tissue barrier ratio) in long COVID patients.

The World Health Organization defines post COVID or long COVID condition as “usually three months from the onset of COVID-19, with symptoms that last at least two months”. Although over 200 symptoms have been reported, the most common are breathlessness, fatigue, and brain fog. Symptomatic patients with long COVID typically have normal pulmonary function test results, and in some cases, they have normal or mildly abnormal diffusing capacity of the lung for carbon monoxide (DLCO). In some patients with long COVID, chest CT (computerized tomography) scans have revealed fibrotic lung abnormalities that may be partially responsible for respiratory symptoms.



Hyperpolarized 129Xe MRI pulmonary measurements are driven by the unique properties of inhaled 129Xe gas, which in the healthy human lung instantaneously fills the terminal bronchi and lung parenchyma, participates in transmembrane diffusion through the alveolar-capillary membrane, and binds to RBCs in the pulmonary capillaries. This pulmonary functional imaging method provides a noninvasive way to simultaneously capture a subvoxel snapshot in time of inhaled gas delivery, flow, diffusion, and RBC binding throughout the entire lung.

HP129Xe MRI scans provides regional information on pulmonary vasculature integrity. It may enable the assessment of ventilation and gas transfer across the alveolar epithelium into RBCs even when CT scans and lung function test results were normal or nearly normal.

About the study

The authors investigated HP 129Xe MRI measurements of the pulmonary RBC-to–alveolar tissue barrier ratio as a surrogate of abnormal gas exchange in small groups of nonhospitalized (NHLC) and posthospitalized (PHC) participants with long COVID. They also performed chest CT scans to analyze post-COVID interstitial lung disease severity using a previously published scoring system and full-scale airway network (FAN) modeling. The participants also had spirometry, measurement of hemoglobin level, Dyspnea-12 score and a 1-minute sit-to-stand test.

Thirty-six participants were enrolled, including 11 participants with long COVID who had never been hospitalized, 12 who had been hospitalized for acute COVID-19, and 13 healthy volunteers who had not been infected. In the PHC group, participants had proof of SARS-CoV-2 infection by reverse transcription–polymerase chain reaction, and they had no history of intubation. In the NHLC group, participants had proof of SARS-CoV-2 infection by reverse transcription–polymerase chain reaction or positive antibodies. Both groups had no evidence of interstitial lung or airways disease or history of smoking more than 10 pack-year.

Participants were enrolled between June 2020 and August 2021. The mean time from infection was 287 days ± 79 days for NHLC participants and 143 days ± 72 days for PHC participants.

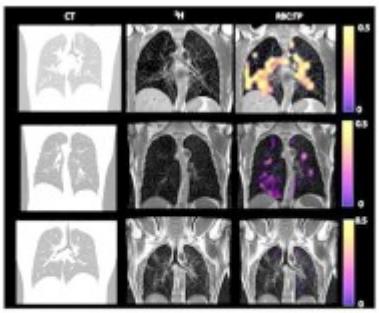
The results showed that NHLC and PHC participants had breathlessness, with mean Dyspnea-12 scores of 9 ± 5 and 10 ± 5, respectively. There was no evidence that oxygen saturations changed before or after the mBORG sit-to-stand test. The mean hemoglobin level for NHLC and HLC participants was 144 g/L ± 15 and 145 g/L ± 14, respectively. CT findings were normal or nearly normal.

There were no significant differences in spirometry measurements between the two subgroups. The mean DLCO was normal but significantly lower in the NHLC subgroup than in the PHC subgroup.

Importantly, results showed that NHLC and PHC subgroups had significantly lower 129Xe MRI RBC-to–alveolar tissue barrier ratio than healthy volunteers, but there was no difference between measurements in the NHLC and PHC subgroups. The measured abnormality on HP129Xe MRI scans appears to be only marginally greater in the PHC participants than in the NHLC participants.

A relationship between RBC-to-barrier and DLCO was observed in both NHLC and PHC

subgroups, which suggests that RBC-to-barrier provides a surrogate measure of gas transfer.



CT, proton (^{1}H), and proton and RBC:TP imaging from post-hospitalized COVID patients. There is minimal damage on CT, and yet highly heterogeneous and low RBC:TP in the lungs of post-hospitalized COVID-19 patients.

Picture from the original article of Grist et al.

The authors noted that pathophysiological mechanisms that underlie the changes in HP129Xe MRI after COVID-19 infection remain unresolved. They said that a lower 129Xe MRI RBC-to-barrier ratio suggests that SARS-CoV-2 infection may have caused some microstructural abnormality to one or two volumes, leading to a decrease in blood volume, for example due to pulmonary embolism, changes in pulmonary blood flow, a thickening of the alveolar membrane. These factors are expected to cause a decrease in diffusing capacity.

Although the CT scans were normal or near normal in the PHC participants, prior COVID-19 pneumonia, may partially explain the abnormal RBC-to–alveolar tissue barrier ratio and pulmonary gas transfer values.

The pathophysiological basis for abnormalities detected in the NHLC cohort may be different. All CT scans in the NHLC participants were normal, and none of the participants had evidence of previous pneumonia (it is possible that they were not imaged during their acute infection). In addition, DLCO, which also measures pulmonary vascular integrity, was lower in the NHLC group than in the PHC group, and correlated with the RBC-to–alveolar tissue barrier ratio. The nature of this abnormality needs further investigation.

In conclusion, this study found that both PHC and NHLC participants had lower MRI RBC-to-barrier ratios than healthy volunteers. The reported abnormal 129Xe MRI RBC-to–alveolar tissue barrier ratios suggest abnormal oxygen and carbon dioxide gas exchange.

The underlying pathophysiological mechanisms behind long COVID symptoms are not well understood, which makes treatment decisions hard, if not impossible.

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