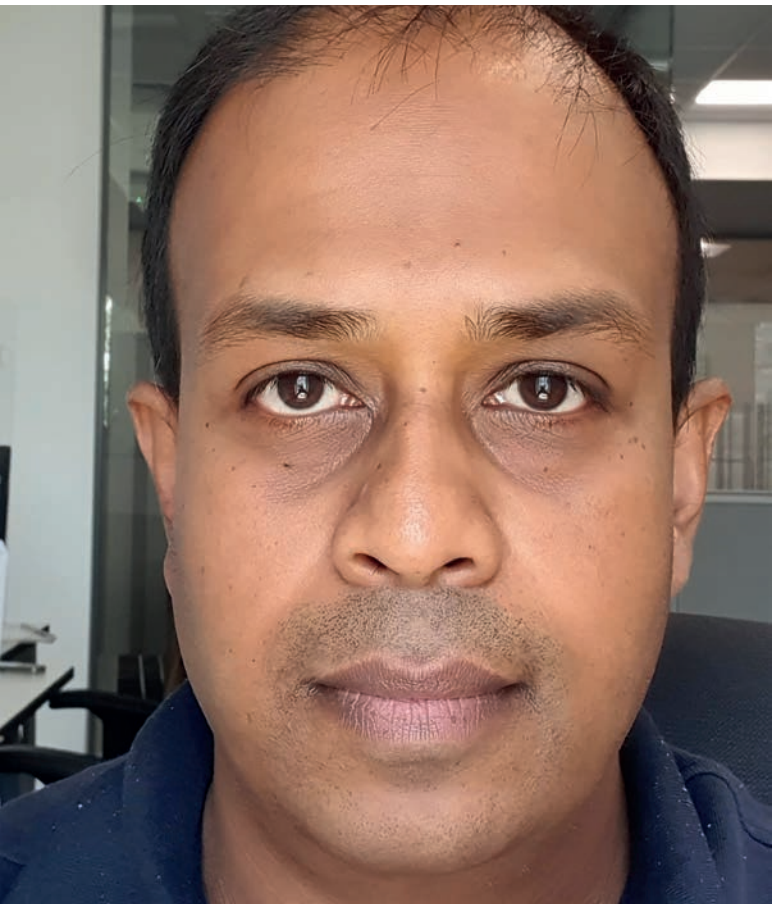

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FRI adds an important dimension to conventional imaging techniques

MUHUNTHAN THILLAI

Muhunthan Thillai (BA PhD MBBS MRCP) graduated from St Mary's Medical School in 2002. He began his training as a junior doctor in London and Oxford, where he gained membership of the Royal College of Physicians. He was then appointed as the Infectious Diseases Fellow on the Map of Medicine project at NHS Connecting for Health. Three years of research into sarcoidosis culminated in a PhD in Immunology and Proteomics from Imperial College London in 2012.

Dr. Thillai continued his medical training at Papworth and Addenbrooke's Hospital. He subsequently completed an observership in sarcoidosis at the Cleveland Center (USA), before being appointed as a Consultant within the Papworth Interstitial Lung Diseases Unit with a specific interest in sarcoidosis in 2015. He continues to attend a regular outpatient clinic at Addenbrooke's Hospital and maintains ongoing research links with Imperial College London.

Dr. Thillai is the co-founder and CEO of Qur8 (www.qureight.com), an imaging platform for analyzing large clinical data sets using FRI, among other techniques. Qur8's main focus is on respiratory medicine; its primary goal is to analyze clinical trial data in innovative ways.

There are two reasons why Dr. Muhunthan Thillai is highly interested in functional respiratory imaging (FRI) and uses it in his research. First, because he is a pulmonologist specializing in pulmonary fibrosis; and secondly, because he is the co-founder and CEO of Qur8, an imaging platform where FRI is a helpful tool for analyzing large clinical sets of data. He details two very recent studies – of fibrosis and of COVID-19 patients – in which FRI has played a pivotal role.

Dr. Thillai emphasizes the added value of FRI compared with more conventional techniques measuring lung function and volume. 'FRI can by no means replace those techniques; what it does is add an important dimension. FRI allows you to quantify disease level over a period of time to demonstrate whether the disease is improving, stabilizing or deteriorating. As FRI is based on an image at a set point in time, there is less variability than with conventional measures. In addition, FRI can quantify large amounts of volume data that lung function testing cannot.' FRI offers improved visualization of airways, blood vessels and other anatomical structures. It provides detailed information not only about lung and lobar volume, but also on airway resistance, internal airflow distribution, aerosol deposition, nodule volume, and many other variables.

> **FRI was found to be a safe, robust mechanism for assessing airway volume.**

FRI IDENTIFIES IPF PROGRESSION

One of the fields of research where Dr. Thillai uses FRI is idiopathic pulmonary fibrosis (IPF). Options for determining the disease course in patients with IPF are limited. A recent study Dr. Thillai was involved in hypothesized that FRI could identify patients with more progressive IPF between two CT time points.[1] Two separate cohorts of IPF patients were identified: 12 patients with stable IPF and 12 patients with progressive disease. FRI was found to be a safe, robust mechanism for assessing airway volume. Thillai explains: 'It was shown for the very first time that specific airway volume (siV_{aw}) can be used to help identify IPF patients with progressive disease. Obviously, we need to do a lot more research, but we have shown that airway volumes increase in progressing patients, whereas they do not change in stable patients. This seems to be a useful additional piece of information; measuring siV_{aw} is by no means meant to replace existing assessment tools.' Dr. Thillai explains that this information can be used to monitor disease course; to help determine which patients are progressing and may therefore be candidates for certain treatments; and to help evaluate the effectiveness of any of these therapies. 'As some of the available drugs are very expensive, they are reserved for patients who get worse. However, when patients are relatively well, it may be difficult to establish whether they are deteriorating. Serial FRI measurements could be sufficiently sensitive to show that patients are progressing microscopically.'

HYPOXEMIA IN COVID-19 PATIENTS

In 2020, Dr. Thillai has also been involved in COVID-19-related studies. One of these studies, he explains, originated from the observation that some patients with COVID-19 have relatively normal lung capacity and lung function, but they still have significant hypoxemia different from typical acute respiratory distress syndrome (ARDS). 'We hypothesized that insufficient blood supply was contributing to the low levels of oxygen in these patients.[2] We used FRI to calculate pulmonary blood volume.' FRI was performed on CT scans from intubated patients with COVID-19 (n = 10) and compared with data from matched intubated ARDS patients (n = 7) and a retrospective group of healthy controls (n = 107). Volumes of blood were computed from the cross-sectional area of each vessel: <5 mm^2 was defined as small. Dr. Thillai notes: 'FRI allowed us to observe differences in blood volume distribution between the three groups. The small blood vessels in the lungs were highly constricted in COVID-19 patients, but not in the other two groups. That may explain the hypoxemia in these patients.'
Dr. Thillai and his group gathered additional lung CT scans that allow for longitudinal analysis of the lung blood vessels, which they are now performing. 'We want to know if changes in the lung vessels correlate with the clinical condition of patients over time: if they recover, do the blood vessels in the lungs also return to normal?' Thillai speculates that the increased vascular resistance observed may be caused either by vasoconstriction of distal pulmonary arteries or by the presence of numerous microthrombi.
Apart from helping to gain insight into the mechanisms of COVID-19, the results of this study may have various clinical implications. They confirm that high positive end-expiratory pressure (PEEP) alone is not enough to oxygenate these patients. 'If microthrombi play a causative role, perhaps stronger anticoagulation should be given; if vasoconstriction is the main cause, the use of pulmonary vasodilators should perhaps be considered. These issues should be addressed in future research.'

NUMEROUS APPLICATIONS

Imaging techniques will gain in importance in lung diseases, Dr. Thillai expects. 'Since both the radiation dose and the cost have come down, CT scans will play an even bigger role in lung imaging. FRI provides valuable additional information to assist the radiologist, the pathologist, the pulmonologist. The applications are manifold: diagnostics, clinical trials, personalized medicine, et cetera. With personalized medicine on the rise, FRI data can help physicians determine if a treatment is effective in trials and continues to be so afterwards. Everybody gains: patients, physicians and society at large, because expensive drugs can be confined to those patients in which they really work.'

REFERENCES

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