Author: Daniel Dresden

The need to measure

'My first substantial encounter with quantitative CT imaging has opened my eyes to what can be done', says David Langton, thoracic physician and associate professor at Monash University, Melbourne (Australia), speaking about the need to measure disease activity in patients with diverse airway diseases. 'At the moment, quantitative CT imaging is predominantly used in the research domain, but it is progressively moving to routine clinical practice. Quantitative CT imaging is clearly going to be the future.'

There is a saying: what gets measured, gets managed. This, of course, assumes management is possible. 'In the past, that measurement didn't make a lot of difference, because the treatments were the same anyway', says David Langton. 'Because of the introduction of new treatments, it in fact is important to differentiate within the spectrum of patients.' With more advanced interventions becoming available, physicians treating respiratory disease have found themselves in need of new, more sensitive forms of measurement.

SHORTCOMINGS OF FEV1

David Langton first encountered quantitative CT imaging while performing clinical research on asthma patients. 'We were trying to resolve the clinical paradox of why patients felt better after bronchial thermoplasty, which was clearly established in registries and clinical trials, when there didn't seem to be any improvement in FEV1. Either the patients were wrong, and they weren't any better at all, or alternatively the FEV1 was not detecting some other improvement that was happening.'

Although FEV1 is still considered the gold standard for the functional assessment of airway diseases, it does not give an accurate picture of local pathophysiology. 'We had worked out that the FEV1 only tests resistance in the large airways, but doesn't give us information what is happening in the small airways', David Langton added. 'Fittingly, the small airways are often called the silent zone of the lung. We thought that maybe something is happening there that is making the patient feel better, but it is not being detected by the FEV1.' It has long been

DAVID LANGTON

David Langton studied Medicine at Monash University in Melbourne. After graduation he completed the Royal Australasian College of Physician examinations and specialized in Intensive Care and Respiratory Medicine. He founded the ICU and Respiratory Units at Peninsula Health in Melbourne and later received an Order of Australia Medal for services to the community. In 2016 he completed a Master of Public Health, and more recently a PhD, studying the impact of bronchial thermoplasty in asthma. David Langton has extensive research experience in clinical trials and novel medications, particularly in the field of asthma.

clear that there is an unmet need for additional sensitive outcome parameters.

FIRST ENCOUNTER WITH QUANTITATIVE CT IMAGING

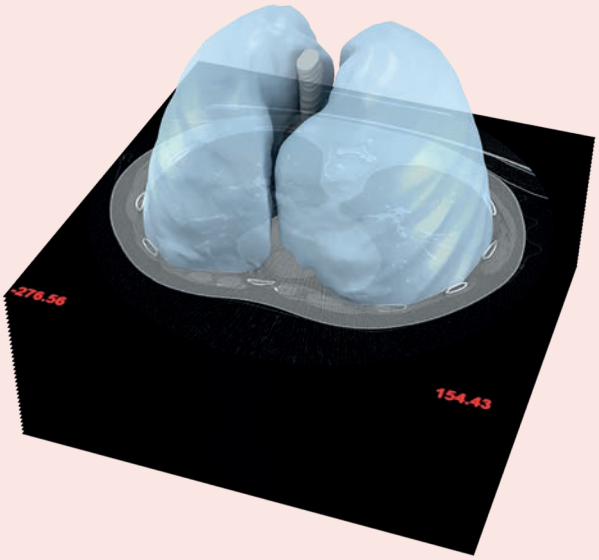
Functional respiratory imaging (FRI) provides regional information about the lung and allows for the measurement of changes at the level of the lobes and airways. Additionally, it offers the ability to describe how particles move through the airways, including accurate measurements of the regional deposition of inhaled drugs in the lungs.
That is why David Langton and colleagues embraced FRI. 'Using FRI, we were able to measure the volume of the smaller treated airways compared with the untreated airways, before and after bronchial thermoplasty. We were able to clearly show that the volume of the airways increased after the intervention. Now, when I look back, what we learned seemed obvious, which is good, because it makes it right. It wasn't obvious a couple of years ago. In the latest data, we treated the untreated lung and re-imaged again, so we had three time points. We were very happy with the reliability and repeatability of the measurements. For example, we obtained the same results over time in untreated portions of the lung when reimaged.'

MARRY THE INFORMATION

David Langton went on to describe the next step in this development process: 'We were able to marry the information we obtained from the quantitative CT scanning with more complex physiological measurements, to be able to prove that they were showing the same thing. Therefore, we had more than one technique, demonstrating that what we were finding, was correct.'
In performing these studies, David Langton found Fluidda, the company which developed FRI, 'a good company to work with. They were early responsive to our research questions and helping us to answer them. The reporting platform that they use, called broncholab, is very handy, clear, useful, and quickly allows you to compare multiple determinations for the same patient. So, they have got a good platform.'

APPLICATIONS IN CHRONIC OBSTRUCTIVE AIRWAY DISEASES

Quantitative CT imaging has predominately been used in a clinical research setting. Its use is progressively moving to include routine clinical practice. 'We are now rolling it out into daily clinical practice, for example in bronchial thermoplasty patients', David Langton said. 'This technique is so refined that we can now say: for every patient that we treat, we can determine if he or she has a benefit by comparing the CT scans before and after treatment. So, we have now a reliable tool for routine clinical practice that we can use in every case. At the same time, we are building our case numbers, so that we can learn more and answer other clinical questions in relation to asthma and bronchial thermoplasty.'
David Langton thinks the technique would find application routine clinical practice in other ways as well. 'For example, there is now a whole raft of monoclonal antibodies that we use for the treatment



> **There is a lot of interest in the world in interstitial lung diseases, like pulmonary fibrosis.**

of patients with asthma. It would be very interesting to look at what is happening in the airways before and after treatment. I bet the same thing is happening compared with bronchial thermoplasty.'

FURTHER APPLICATIONS: FIBROSIS AND POST-COVID

It is likely that there will be other applications of this sort of technology as well. 'We have focused on chronic obstructive airway disease, but obviously there is a lot of interest in the world in interstitial lung diseases, like pulmonary fibrosis', David Langton told. 'We know that these patients deteriorate, but the question is how to monitor them. We currently monitor them by asking how they feel and looking at their lung function. We perform serial CT scans, but we just visually decide whether they look the same or a little bit worse. Now, we are clearly possible to quantitative measure that could be used. The same applies for lung transplant patients.'
Another possible application of quantitative imaging, which David Langton finds interesting, is the potential use in post-COVID patients to monitor fibrosis and other lung lesions. 'We haven't looked at it, I do not think that anybody will have looked at it. It could be very interesting.'

LIVE HAPPIER AND HOPEFULLY LONGER

For personalized treatment, there is a need for improved understanding of disease pathophysiology and recognition of disease heterogeneity and complexity. According to David Langton, FRI is very useful in meeting this challenge. The ultimate goal is that with the guidance of quantitative imaging treatments can become more individualized, so that patients will live happier and hopefully longer. David Langton thinks that quantitative imaging has the potential to accomplish this goal.