Breathing room

Medical engineer and health researcher Dr Andreas Fouras discusses the challenges posed to global health by lung diseases, and the promising new solution he has developed to improve diagnosis.

You are based at the Laboratory for Dynamic Imaging (LDI) at Monash University. Can you summarise the lab’s key objectives?

At LDI we aim to make a global impact on human health through the development of a new generation of functional imaging tools to augment research and diagnostic capability. Our goal is to advance novel imaging technology and build on fundamental mechanics in order to meet critical needs in healthcare.

By what means is your research uncovering the interaction between diseases and regional lung motion?

We have developed a 4D X-ray lung imaging technology, which is patented under the start-up medical technology company – 4DX – that I founded with members of my LDI research team. This technology uniquely and non-invasively measures the natural patterns of motion within moving, breathing lungs; and using it, we have discovered that functional deficits in the lung can be sensitively detected through local differences in the patterns of movement.

We have been applying our technology to the widest possible array of lung conditions, including asthma, chronic obstructive pulmonary disease, cystic fibrosis and cancer, to name just a few. In each case, we are learning something different about the lungs and how they respond to various challenges. Lungs are incredibly resilient; when small parts of the organs are unable to function at normal levels, nearby regions automatically compensate, maintaining our capacity to breathe.

Ironically, this incredibly useful feature also makes early diagnosis of lung diseases much more difficult; often, diseases aren’t detected until they have progressed so far that the lungs can no longer compensate. By then, it is usually too late.

How is the technology viewed by potential consumers?

As it happens, one of 4DX’s executive directors, Steve Peuschel OAM, suffers from lung disease, and is therefore in the position of being able to comment on the technology from a consumer viewpoint. He said: “As a cystic fibrosis sufferer and recipient of a double lung transplant, this technology provides individuals affected by a range of chronic lung conditions with the ability to better understand the health of our lungs with the prospect of more effective treatment pathways. This level of detailed regional lung function data also represents an enormous opportunity to better detect early-stage lung disease and provide for more effective drug development in a range of chronic lung conditions.”
Could you briefly discuss the experience of being involved from the initial stages of a research project to the final stages of commercialisation?

This has been an amazing experience that I would highly recommend to any other researcher. The depth of knowledge and passion that comes from developing a technology from the very beginning provides the ideal qualifications for a researcher hoping to take a concept all the way through to commercialisation.

I have been fortunate in having a great team of highly skilled individuals with a passion and commitment to changing outcomes for people suffering from lung diseases. Our ongoing relationship with Monash University has been extremely valuable, as has the support we’ve received from the clinical and business communities, which understand the enormous social and commercial opportunities presented by this technology.

Looking beyond the scope of this project, will your team aim to develop further similar technologies over the coming years?

We have discovered that much of what we have learnt looking at the lungs is also applicable to other parts of the body – such as the heart. I’m therefore hoping that after we’ve made an impact on lung disease, we can continue to engineer healthcare solutions well into the future.

To what extent are you engaged in science dissemination?

I actively pursue science communication activities whenever I can. This includes engaging with the public through lectures and visits to schools, as well as interacting with governmental bodies at all levels.

Most importantly, I am also an executive member of the Early- and Mid-Career Researcher Forum of the Australian Academy of Science. The Forum is the national voice of Australia’s emerging scientists, representing researchers who are up to 15 years post-PhD (or other research higher degree), irrespective of their professional appointment. It examines critical issues including career structure, job security, funding, education, training and gender equity.
Lung capacity

Medical imaging experts at Monash University in Melbourne, Australia, have been responsible in recent years for the discovery of several new methods for investigating the lungs with unprecedented clarity and definition.

The human lung is an extremely efficient, flexible and versatile organ. Chronic diseases of the lung, which include asthma, chronic obstructive pulmonary disease and bronchopulmonary dysplasia, restrict airflow during the respiratory process and therefore take a significant toll on the patients they affect. All of these diseases can be associated with structural ‘remodelling’ within the lungs, which affects their normal motion. Though these alterations can facilitate the detection of such diseases, subtle changes in the organ’s structure are difficult to distinguish. This, and the lung’s ability to automatically compensate for regions that are unable to function at normal levels, means that early diagnosis is a challenge and diseases often go undetected until the lungs are no longer able to offset their negative effects.

Its capacity for change is not the lung’s only strength that couples as a weakness; some of the features that make it most efficient also inhibit attempts to investigate the organ non-invasively. The internal structure of the lung is governed by the need to absorb as much oxygen as possible; it is a low-density network of branching air sacs with large air/tissue interfaces spread over numerous small structures. These interfaces disrupt ultrasound waves, and the low density of the tissue confounds magnetic resonance imaging (MRI). In addition, the small size of the air sacs stretches X-ray methods to the upper limit of their resolution, and the general complexity of the organ ensures that most imaging methods will be unsuitable for gaining an insight.

A moving target

There are two main tools that a medical professional can use to gain an insight into the internal workings of a patient’s lungs: computed tomography (CT) and spirometry. CT scanning uses X-rays – which are absorbed at varied rates by different tissues – to create a series of 2D images that then combine to form a 3D model. The disadvantages associated with use of CT are that X-rays are damaging in themselves, and may lead to a higher risk of developing cancer in the future, and that the scan is unable to provide dynamic information about the way the lung moves, which is often important for diagnostics. Spirometry, conversely, provides useful functional information on the lung as a whole – for example, how it is performing – but cannot offer similar information on a regional basis.

One team at Monash University’s Laboratory for Dynamic Imaging (LDI) may have developed a solution to this problem. Dr Andreas Fouras leads a research group dedicated to ushering in a new age of medical imaging, beginning with a non-invasive technology to enable the 4D X-ray imaging of lungs – effectively combining the best aspects of both spirometry and CT scanning. The researchers believe their innovative technology will provide the clearest picture ever of how the lung functions, both in a healthy and diseased state: “Despite the prevalence and cost of respiratory diseases, new diagnostic technologies have been slow to develop; we saw an opportunity to alleviate this burden,” Fouras explains.

CTXV

In the last few years, the Australian team has developed several entirely new types of imaging technology with the lung in mind – but of these, perhaps the most important is computed tomographic X-ray velocimetry (CTXV). This method, first demonstrated in 2010, combines velocimetry with phase-contrast X-ray imaging (PCXI) to give an excellent picture of the lungs and how they move. PCXI has the advantage of using a lower dose than most X-ray imaging methods, and is therefore better suited to long-term or dynamic imaging processes whereby a patient may need to be scanned several times in succession. In 2011, the group published a paper in which they described how conventional CT and MRI scanning techniques are unsuitable for determining lung motion, and proposed CTXV as a useful alternative.

The merits of their method were confirmed by laboratory tests on mice. After treating the mice with bleomycin, an essential medicine that causes pulmonary fibrosis, the researchers examined their subjects using the imaging system at 36 hours and six days from their first exposure. The results were very promising: where the mice would not have presented functional physiological symptoms until 21 days after exposure, the novel imaging system allowed Fouras and his team to identify significant changes in regional lung motion from the earliest test point. Interestingly, other measurements of lung function, such as tidal volumes and inflation pressures, remained largely unchanged. It was the accurate measure of their motion that allowed the researchers to detect the presence of infection, demonstrating the importance of altered lung motion as a sensitive indicator of lung disease.

Cystic fibrosis

More recently, the scientists have developed a number of projects surrounding this new imaging method, some of which are designed to increase its value beyond its already extensive clinical potential. In one such proposal, for example, they highlight the opportunity to...
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Augment lung and breath modelling methods by synthesising them with this new and more comprehensive approach to imaging. Despite the importance of this biomechanical system, the lungs are still poorly understood by medical science – and a basic appreciation of how the organ operates in healthy and diseased states can be provided by combining computer modelling and accurate imaging.

Another related project focuses specifically on the value of CTXV in cystic fibrosis (CF) – the most common fatal genetic condition during early life for Caucasians. Diagnosis of CF takes place via screening programmes that rely on tests of overall lung function – so, like many other lung diseases, it is difficult to catch early. New methods are particularly crucial in CF because the dosage of ionising radiation associated with a standard CT scan is too high for young patients. This may, therefore, be one of the most important applications of the group’s new imaging method.

**Bench to Bedside**

In order to maximise the impact of their research, Fouras and members of his LDI research team founded start-up company 4Dx to enable them to translate their technology from the laboratory to the clinic. The researchers have already set the wheels in motion towards the goal of validating CTXV’s clinical utility – especially with regard to radiotherapy in oncology. Using information provided by dedicated clinical partners around the world, the team will be able to gain real insight into how helpful the technique could be in catching lung cancer early in its development – a crucial factor, since lung cancer has a high recurrence rate caused by the limited symptoms of its initial stages.

The data gathered at the clinical centres consists of images collected from existing hospital equipment, and therefore requires no additional cost in time or effort for the practitioners, and no extra doses of radiation for the patient. A number of leading clinicians are on 4Dx’s advisory board, and are able to aid with the interpretation and analysis of the data received. “This provides us with critical feedback regarding use and application of the technology in the clinical setting,” Fouras enthuses. In the near future, the company expects to expand this clinical engagement even further in preparation for the introduction of its new technology to practice.

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**THE ROAD TO COMMERCIALISATION**

**An idea with the practical potential of CTXV needs an efficient vehicle to bring it to the commercial market. For the Monash University team, this is their medical technology company – 4Dx**

Founded in December 2012 by Dr Andreas Fouras, it took only four months for the company to raise the money required to commence operations; AUS $1 million was provided by angel investors confident in the technology. Two months later, in June 2013, 4Dx secured an exclusive commercial use licence for technologies from Monash University, an allowance that would enable them to use multiple patents across all their target geographical areas.

The company commenced commercial operations in July the same year. Many researchers who had been involved in the development of the imaging techniques were eager to join the organisation and, with their help, the first successful preclinical trials were carried out before the end of the year.

Clinical pilot studies around the world are now in their advanced stages – and 4Dx members have increasingly devoted their time to attending big conferences, including the American Thoracic Society conference in San Diego, USA, and the Radiology Society of North America’s annual conference in Chicago, USA.