FLUIDDA
Respiratory solutions for better patient care

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FRI offers early and rapid detection of lung diseases

MAARTEN LANCLUS
Maarten Lanclus, PhD graduated from the Catholic University of Leuven, Belgium, as a biomedical engineer. He received his MSc degree specializing in artificial intelligence within the biomedical space. He received his PhD degree at the University of Antwerp, focusing on the application of AI algorithms to FLUIDDA's Functional Respiratory Imaging technology. His work has been published in international, peer-reviewed journals. After managing the company's R&D team, Maarten recently became the CTO of FLUIDDA. In this role, he is responsible for managing the technical department to optimize the structure, workflow, and communication between the subdepartments. With his team, he focuses on strategizing future development steps and integrating them at the core of the company.

MINAL PATEL
Minal Patel, PhD is a Clinical Science Liaison with a medical degree and a decade of successful experience in inpatient and outpatient clinical research trial management in all phase studies in pulmonary and critical care, mainly in pulmonary arterial hypertension, COPD, and idiopathic pulmonary fibrosis. She has served as the primary point of contact and liaison between patients, providers, specialty pharmacies, and health insurers regarding needs for education, resources, and support for a pulmonary hypertension program, and assisting pulmonologists in process improvement and the achievement of desired team outcomes.

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Lung diseases often lead to irreversible damage. Early detection and start of the right treatment are therefore crucial. Functional Respiratory Imaging (FRI) makes rapid diagnosis and treatment possible. And more than that: FRI will greatly add to our knowledge of lung diseases and their heterogeneity. In both scientific research and clinic practice, FRI is on the verge of a breakthrough.

"A characteristic of most lung diseases is a permanent, irreparable loss of lung volume," explained Minal Patel, physician and Clinical Science Liaison for FLUIDDA in the United States. "The lung also has a surprising capacity for compensation. This means that early stages of lung diseases cannot be detected with the traditional measurements of lung function. Only when the structural damage to the lung is so extensive that compensation no longer succeeds do lung function measurements start to deviate. The irreparable damage has already occurred by then."

WHAT IS FRI?

It would be invaluable to be able to diagnose lung diseases earlier in the disease process, before severe structural damage has occurred. Functional Respiratory Imaging (FRI) enables just that. Maarten Lanclus, Chief Technology Officer at FLUIDDA, explained. "The basis for FRI is high-resolution CT scans. We developed software that extracts quantitative and functional information from these scans and relates it to the lung's anatomy. This allows us to document various lung tissues and structures in detail." The technique reveals, amongst others, the volume of large and small airways and blood vessels in the lung down to a resolution of half a millimeter.

But FRI reveals more than just the lung structures: it also estimates functional parameters. For this purpose, FLUIDDA uses a technique from the aerospace industry: Computational Fluid Dynamics. Lanclus stated about the three most important functional parameters, "First, we measure resistance in the airflow in the lung. We find areas with increased resistance. Second, we can prepare a ventilation chart of the lung, which shows which parts of the lung are functioning abnormally due to a reduced airflow. Finally, we can measure the ventilation-perfusion of a lung when we combine the ventilation data with our blood vessel segmentation. Specifically, we employ an algorithm that splits the vascular system into small, mid-sized, and large blood vessels, depending on their cross-sectional surface area. This provides very detailed insight into the lung's perfusion. Such functional parameters make the characterization of lung diseases and their follow-up more sensitive and concrete."

GOLDMINE OF DATA

According to Lanclus, one of the strongest points of FLUIDDA is the enormous mountain of data that the company has gathered. "We have been collecting CT scans and the associated medical and demographic data for 15 years. We use these data for research: we can answer questions with it for a range of stakeholders in the field of lung diseases, like hospitals, universities and insurers. We are busy working on an extensive database to provide our customers with information."

APPLICATION TO COVID-19

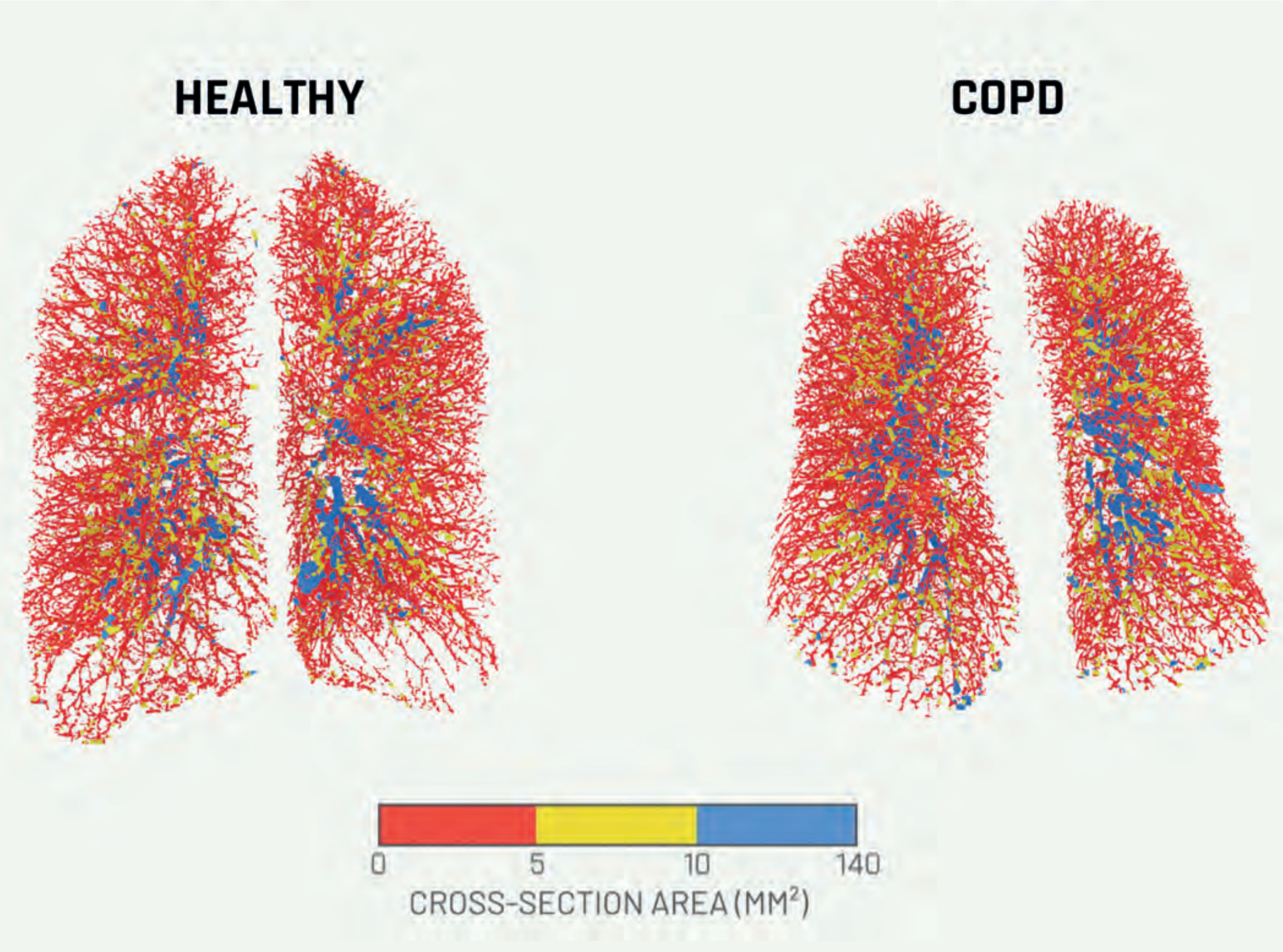
FLUIDDA discovered serendipitously using FRI that patients with severe COVID-19 have a much lower volume of small blood vessels in their lungs than healthy people. "We saw these changes even in an early stage of the epidemic, some 8-9 months before this knowledge became mainstream," said Lanclus. (You can read more about FRI and COVID-19 in the article published elsewhere in this magazine.)

FRI has proven its utility in scientific research into COVID-19, as well as lung diseases like asthma, COPD, pulmonary hypertension, pulmonary fibrosis, cystic fibrosis, and bronchial pulmonary dysplasia. Patel mentioned the important benefits of FRI in clinical trials. "Techniques like spirometry are the current golden standard in clinical scientific research. Because spirometry is not sensitive enough to detect early or small changes in the lung, many patients and much time are required to notice an effect in clinical trials. With FRI such an effect is visible faster, enabling faster trials to be conducted with fewer patients."

FOREST FIRES

One example of a study set up by FLUIDDA together with UC Davis Medical Center in Sacramento, USA, involved fire department personnel. Lanclus said, "At UC Davis a few years ago, a group of Rhesus macaques were exposed to the smoke from a forest fire. Years later CT scans were done of the lungs of these macaques and compared with the scans of apes who had never been exposed to smoke. The analysis with FRI revealed large changes in the lungs of apes who had been exposed to smoke." The question was whether these findings could be extrapolated to humans, said Lanclus. "The population of California is regularly exposed to smoke from forest fires. How does that influence the development of children's lungs? We are working on a study of firemen to ascertain how smoke influences the health of their lungs. With FRI this damage can be discovered sooner than with spirometry."

Lanclus and his colleagues are conducting more research that targets the everyday clinical practice. "We analyse CT scans made on the first visit to a hospital," stated Lanclus. "With artificial intelligence we try to predict disease, stage, prognosis and suitable treatment as precisely as possible for various lung diseases. With FRI we have been successful in predicting the course of the disease whereas the predictive value of spirometry for these patients is very low due to its low sensitivity."



CLINICAL PRACTICE

"Slowly but surely, everyone in the field of lung diseases is open to another approach instead of the current lung function measurements," said Lanclus. "Doctors have realized that spirometry is subject to an intrinsic variability. As more and more quantitative CT parameters become available, we can diagnose lung diseases digitally. The CT scans also provide more information, enabling phenotyping of diseases and revealing new phenotypes. The change to the diagnostic paradigms will be gradual, but ultimately, qCT and FRI will be mainstream techniques," added Lanclus.

"A traditional lung function measurement provides only an average impression of the lungs' function," continued Patel. "FRI gives detailed information about the local structural damage. The technique is thus suited for the early diagnosis and phenotyping of lung diseases. Because FRI reveals changes in the lung faster, we can see sooner if there is a response to therapy and what its extent is. Doctors can then choose the optimal therapy sooner with this information."

BRONCHOLAB

With Broncholab, FLUIDDA is taking the first step towards the clinic. Lanclus stated, "Broncholab is an online platform with which we want to involve doctors with FRI in their clinical practice. The doctor uploads a scan of a patient about whom he or she wants to obtain more information. We analyze the scan and send the results back to the doctor." Patel added, "Broncholab provides more information than the standard diagnostic information, enabling the doctor, for example, to monitor the effect of the therapy." Broncholab has now received approval in the US from the FDA for use as a diagnostic tool. In Canada, Broncholab has been approved for Emergency Covid-19 Care.

To make FRI more easily applicable in clinical practice, FLUIDDA is working on far-reaching automation based on artificial intelligence. Lanclus said, "Our team in Portugal currently analyses the CT images partly automatically and partly manually. The manual aspect is needed to ensure a highly detailed image of all structures in the lung. Using artificial intelligence it is becoming increasingly easier to analyze images fully automatically, although

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manual quality controls remain necessary. We are getting closer to the point at which the automatic analysis is so good that manual quality controls will no longer be needed. When that time comes, we can integrate FRI into the Picture Archiving and Communications System (PACS) of hospitals in a fully automated way. Then every doctor can have CT scans of the lungs analyzed by clicking on a button via our fully automated cloud-application."

MORE PARAMETERS

Currently, for regulatory standards in clinical trials, FLUIDDA focuses on one prominent FRI parameter for each lung disease. "It is a parameter that is prominent in the disease and capable of describing the progression of the disease or the effect of a clinical intervention. One example we are working on is the specific central surface area-volume in interstitial lung diseases. In principle, every parameter from the CT images can be used as a biomarker. As the use of big data becomes more important in medicine also, I predict that in the future we shall no longer work with just one but rather with a set of biomarkers. A set describes the heterogeneity of a disease better."

Patel also sees a great future for the technique. "For many lung diseases, it is a diagnostic golden standard, depending on where and by whom the research is done. FRI supplies objective and reproducible data. Take, for example, right ventricle catheterization for the diagnosis of pulmonary hypertension. The cost of FRI is minimal compared to that for catheterization, while the results of FRI are objective and reproducible."

"We are working now with Broncholab to generate product recognition for FRI," continued Patel. "In the coming ten years we shall see that FRI helps with the diagnosis and phenotyping of lung diseases, including pulmonary hypertension, and the effect of the treatment of these diseases."

BETTER CARE

Will there be room for spirometry in ten years' time? "Hopefully not," said Lanclus. "Consider how specialty fields like cardiology and neurology are already dependent on digital solutions with CT scans for accurately evaluating the health of the heart and brain." Patel added, "As a clinician I saw the consequences of a subjective analysis with spirometry on the choice of treatment. There are also people with severe lung diseases who are not always capable of undergoing the test. With FRI we avoid this subjectivity, and it is clear sooner whether the choice of a medicine is correct. No one product is capable of repairing the lung damage; at best, it can inhibit further degeneration. Faster diagnostics and a faster choice for the right treatment enable earlier intervention in lung diseases while they are still mild, and thus prevent severer forms of the disease. FRI makes this possible."