The ERS PROFILE.net Clinical Research Collaboration is dedicated to the set-up of an academic network to enhance imaging-based management of progressive pulmonary fibrosis

Julien Guiot[1] and Simon L.F. Walsh[2,3]

[1]Respiratory Medicine Department, University Hospital of Liège, Liège, Belgium. [2]National Heart and Lung Institute, Imperial College London, London, UK. [3]Royal Brompton Hospital, London, UK.

Corresponding author: Julien Guiot (j.guiot@chuliege.be)

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AI has the potential to revolutionise the way we diagnose and treat patients suffering from fibrotic ILDs. HRCT analysis and abnormalities quantification can facilitate diagnosis and monitoring of treatment response to assist clinicians. https://bit.ly/3rKI2Iq

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Interstitial lung disease (ILD) is a heterogeneous group of pulmonary disorders, characterised by diffuse parenchymal lung infiltration. Some ILD patients can develop a progressive fibrosing phenotype characterised by worsening fibrotic changes, decline in lung function over time, worsening symptoms and quality of life, and early mortality. Patients with this inexorable progression of disease are referred to as having progressive pulmonary fibrosis (PPF) [1]. This disease behaviour is associated with an autonomous progressive fibrotic evolution due to repetitive epithelial microinjuries, over-expression of fibrogenic growth factors, fibroblast proliferation and active collagen accumulation leading to progressive lung dysfunction [2, 3]. Although antifibrotic therapy does not stop progression, it slows the forced vital capacity (FVC) decline, making prompt identification of patients at high clinical risk of PPF crucial if lung function is to be preserved for as long as possible.

To date, the gold standard for the diagnosis of PPF is a holistic evaluation through a multidisciplinary team discussion (MDD), which commonly includes the analysis of clinical symptoms, pulmonary function test results and high-resolution computed tomography (HRCT) of the chest [4]. Current recommendations state that diagnostic criteria for PPF are a combination of two criteria, including: worsening symptoms over time, HRCT-proven fibrotic progression, and/or an absolute decline from baseline in FVC (⩾5%) or diffusing capacity of the lung for carbon monoxide (⩾10%) over 1 year of follow-up [5]. Determining the precise prevalence of PPF is challenging, although estimations can be made from retrospective data. In a large survey of international ILD physicians, it was estimated that 18–32% of patients diagnosed with non-idiopathic pulmonary fibrosis ILDs develop PPF and the time from symptom onset to death in these patients was 61–80 months [6]. The primary challenge of managing patients with PPF is that a period of lung disease progression, either in terms of symptoms, lung function decline or progression on HRCT, is required before initiating anti-fibrotic treatment. There is an urgent unmet need to develop reliable ways to identify patients at risk of PPF using their baseline clinical and imaging data to avoid unnecessary delays in treatment [7].

However, imaging of ILD is a field requiring expertise, and many centres lack the requisite radiology expertise to evaluate patients with suspected ILD. Medical imaging analysis and imaging-based biomarker detection has entered an accelerated phase of development with the advent of novel artificial intelligence (AI) technologies. AI offers an opportunity to develop decision support systems which democratise consistent and reproducible diagnosis. Exploring new reliable tools for quantifying disease severity on HRCT is also a growing area of interest for predicting PPF and monitoring treatment response in routine clinical practice, as well as for stratifying patients in treatment trials [4].

The main challenge in diagnosing fibrotic ILDs lies in the lack of noninvasive methods. Currently, the gold standard for diagnosis is a lung biopsy, which is invasive and carries a risk of complications. AI has the potential to change this by providing noninvasive methods for diagnosis, including multimodal inclusive clinical models or AI algorithms that can analyse imaging (*i.e.* HRCT scans), physiological and histopathological data concurrently. AI-based clinical decision support systems could greatly improve the speed and accuracy of diagnosis and facilitate MDD characterisation of disease without the need for invasive procedures. AI may also have a critical role stratifying patients based on the clinical risk of developing PFF, as well as predicting treatment response, thereby facilitating precision medicine. AI-based evaluation may also assist in the development of new treatment strategies. By analysing large amounts of data, such as genetic information and patient outcome, AI algorithms could identify potential targets for new therapies and subgroups of patients that can specifically benefit from early anti-fibrotic therapies [8].

One of the most promising applications of AI in fibrosing ILDs is the use of computer-aided diagnostic tools [9]. These approaches use machine learning algorithms, such as convolutional neural networks, to analyse medical images, such as HRCT scans, and identify characteristic patterns of ILD [10].

Two computer-based approaches of interest in the context of PPF are radiomics and deep learning (figure 1) [11, 12]. Radiomics analysis is based on the extraction of imaging features from the intended imaging area, or "region of interest", such as intensity, size, morphology and texture analysis. This enables a repeatable and measurable assessment of parenchymal alterations. The contribution of radiomics, as a reproducible and accurate imaging tool, represents an alternative way to explore AI-based decision support systems. Of interest, some studies have reported correlations between radiomic features in ILD and pulmonary function tests [13, 14]. Deep learning involves the training of neural networks on large quantities of well-annotated imaging data to identify patterns in the imaging that map to clinically relevant outcomes, such as diagnosis or prognosis. Deep learning has successfully been applied to CT phenotyping as well as quantification of disease on CT [15, 16].

While the potential of AI is exciting, there are also challenges to be addressed. The most important one being the acquisition of large imaging datasets to power machine AI research. A general and international consensus identifying the reproducible standards is yet to be established for an optimised interoperability of data between centres. Nowadays it is still difficult to have access to structured fibrotic ILD data, making high-quality datasets for AI algorithm training difficult and time-consuming to build. Another challenge is the lack of transparency and trustworthiness in AI algorithms. The decision-making process of AI algorithms is often opaque, making it difficult for doctors and patients to understand how a diagnosis or treatment recommendation was made. This lack of understanding could lead to mistrust and reluctance to use AI in healthcare. Therefore, we should aim to specifically increase the overall explainability of the process in order to be inclusive with clinicians and provide better understanding and trust in the tools.

Since 2013, the European Respiratory Society (ERS) Clinical Research Collaboration (CRC) programme has been providing support to more than 20 networks in different areas of respiratory health and ambitions to continue fostering international clinical research in areas where gaps have been identified [17, 18]. Our ERS CRC named PROFILE.net (PROgressive Fibrosing Lung diseasEs.network) aims to establish a multidisciplinary network of clinicians, radiologists, computer scientists and bioinformaticians to facilitate the development of clinical decision support tools for diagnosis and prognostication in patients with ILD.

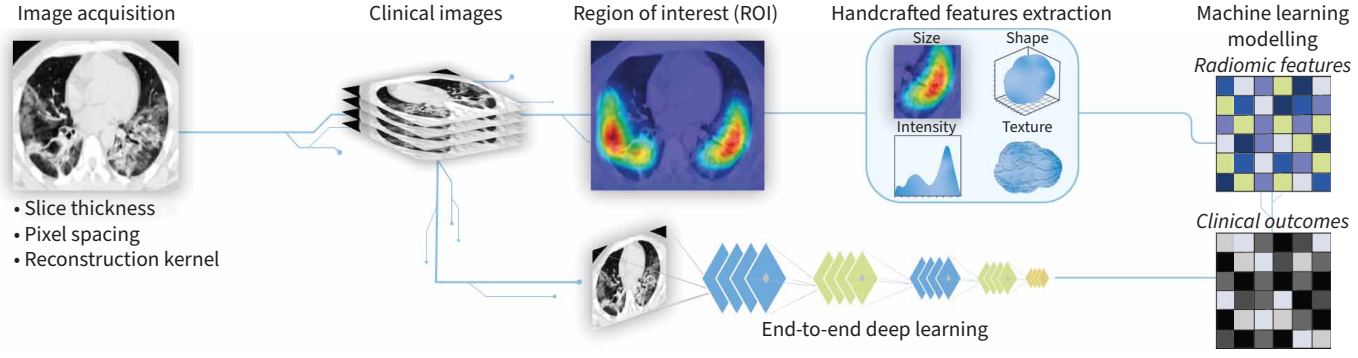

FIGURE 1 Scheme of the radiomics workflow for an artificial intelligence-based diagnosis model. Adapted from [11] with permission.

We designed our research plan with several steps and levels of prioritisation. We will start with the specific question of whether a reliable and reproducible method to evaluate HRCT can help clinicians to manage patients with systemic sclerosis (SSc)-associated ILD. Then, through a collaborative network between centres, we will develop imaging-based AI models specifically dedicated to addressing clinical questions in subgroups of patients suffering from rarer diseases. Being more difficult to identify, these phenotypes require deep clinical characterisation that is always challenging to gather on a large-scale basis, reinforcing the need for such clinical collaboration in parallel with a large strategic consortium like OSIC (Open Source Imaging Consortium: https://www.osicild.org/).

Our goal is to follow the general CRC vision and be as inclusive as possible in our approach. With this goal in mind, we will foster research relationships between patients and their advocacy groups, clinicians, translational scientists and industry partners. The involvement and training of early career researchers is also a core objective of our work, with which we fully engage.

In conclusion, AI has the potential to revolutionise the way we diagnose and treat patients suffering from fibrotic ILDs. Using radiomic and deep learning-based approaches to HRCT phenotyping and disease quantification will facilitate diagnosis and monitoring of treatment response, as well as assist in treatment decisions. Our ERS CRC will accelerate the development of these tools by increasing data sharing and promoting cross fertilisation of ideas across different stakeholder groups. Most importantly, our efforts will address an urgent unmet need in ILD, where treatment decisions rely on accurate and reliable diagnosis and early identification of patients at greatest clinical risk. The overall objective is to enhance a wide inclusive research collaboration aiming to specifically develop useful tools for imaging evaluation of patients suffering from ILDs, which we are trying to meet through this international collaboration. At the moment, two studies on SSc-ILD are being conducted to pave the way and open opportunities for other use-cases and pathological pathways to study.

Further information and the application procedure to join the CRC can be obtained on the dedicated ERS webpage (www.ersnet.org/science-and-research/clinical-research-collaboration-application-programme/profile-net-progressive-fibrosing-lung-diseases-network/).

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