RESEARCH TOPIC CLI11

Advanced Imaging and Multimodal Biomarkers for Predicting Disease Progression and Guiding Precision Medicine in Interstitial Lung Diseases

Research area
Medical area

Clinical Unit name
Pneumology 1, Humanitas Research Hospital, Rozzano

Supervisor
Dr. Francesco Amati francesco.amati@hunimed.eu

Co- Supervisor
Prof. Stefano Aliberti stefano.aliberti@hunimed.eu

Abstract
Interstitial lung diseases (ILDs) represent a heterogeneous group of diffuse parenchymal lung disorders characterized by varying degrees of inflammation and fibrosis, frequently leading to progressive respiratory failure and reduced survival. Despite important advances in antifibrotic therapies and diagnostic strategies, ILDs remain associated with delayed diagnosis, substantial interobserver variability, and highly heterogeneous clinical trajectories. These challenges are particularly relevant in idiopathic pulmonary fibrosis (IPF) and progressive fibrosing ILDs, where early identification, accurate risk stratification, and timely therapeutic intervention are critical determinants of outcome. In this context, there is a growing need for integrated, multidisciplinary, and data-driven approaches capable not only of improving diagnostic accuracy, but also of identifying predictive biomarkers and developing robust algorithms for disease progression and patient stratification.

This PhD project is embedded within a structured and comprehensive research program focused on ILDs, in which our institution plays a central coordinating role. The primary aim of this doctoral work is to develop and validate integrated clinical, radiological, and epidemiological frameworks to enhance disease characterization, improve early diagnosis, and refine prognostic stratification across the ILD spectrum. A central objective of the project will be the identification and validation of predictive biomarkers and imaging-based algorithms able to recognize patients at higher risk of progression and to support a more precise stratification of disease behavior over time. This aspect is particularly relevant for both clinical decision-making and translational research, as it may provide tools to enrich clinical trials, optimize treatment selection, and support the development of novel antifibrotic therapies.

A core component of the project is the coordination of prospective multicenter registries. Our institution will act as the coordinating center for all registries, ensuring methodological consistency, data harmonization, and high-quality data collection across participating sites. The first initiative is a large-scale registry that has been designed and has already enrolled patients with ILD to systematically capture clinical, radiological, and functional data across a

broad spectrum of ILD subtypes. This registry provides a robust real-world dataset enabling comprehensive phenotyping, longitudinal assessment of disease progression, evaluation of treatment patterns and outcomes, and, importantly, the development of predictive models for progression and patient stratification based on multidimensional clinical and imaging variables.

In parallel, two specialized multicenter registries were recently approved by the Ethics Committee and will further explore key aspects of ILD pathogenesis and prognosis. The first focuses on familial pulmonary fibrosis (FPF), a condition with a recognized genetic component but still incompletely understood clinical course. This registry aims to evaluate the impact of pharmacological treatments, including antifibrotic therapies, as well as other prognostic factors on five-year outcomes such as lung function decline, disease progression, and survival. By leveraging coordinated multicenter data, the study will contribute to a more precise understanding of FPF and support the development of tailored management strategies, including improved prognostic algorithms for identifying patients with more aggressive disease trajectories. The second registry addresses environmental and occupational exposures, which are important but often underrecognized contributors to ILD development and progression. Through systematic exposure assessment, this study will evaluate the prevalence of relevant exposures across ILD subtypes and analyze their impact on disease behavior and outcomes. Integrating exposure data with clinical and radiological variables will improve etiological classification and may also refine predictive models of progression by identifying modifiable and non-modifiable risk factors influencing disease course.

Another key objective of this PhD is the prospective evaluation of multidisciplinary discussion (MDD) in ILDs. MDD, involving pulmonologists, radiologists, and pathologists, is considered the diagnostic gold standard; however, its real-world impact on diagnostic accuracy, interobserver agreement, prognostic stratification, and clinical decision-making requires further quantification. This project will assess the role of MDD in improving diagnostic confidence, guiding therapeutic choices, and optimizing patient management, while also identifying factors that may enhance its effectiveness, including the integration of advanced imaging modalities and predictive biomarkers capable of supporting disease classification and progression-risk assessment.

Innovative imaging technologies represent a further pillar of this research. Within this PhD, several prospective imaging studies based on CT have already been initiated and are currently ongoing, with preliminary analyses already providing promising and clinically relevant insights. These imaging studies pursue four main objectives. First, they aim to evaluate the added value of new innovative CT techniques in improving the diagnostic identification of IPF patterns during MDD. Second, they focus on the early detection of radiological biomarkers associated with the progressive fibrosing phenotype, with the goal of identifying patients at higher risk of disease progression at an earlier stage. Third, they aim to develop and validate predictive imaging biomarkers and integrated algorithms for disease progression and patient stratification, combining radiological features with clinical and functional data. Fourth, they investigate screening strategies for ILD in patients with autoimmune diseases, particularly Sjögren's syndrome and rheumatoid arthritis, where early lung involvement is often subclinical but clinically significant.

Humanitas University – Via Rita Levi Montalcini, 4 – 20072 Pieve Emanuele (MI) Italy
CF 97692990159 – Tel. 02.8224.3777 – info@hunimed.eu – hunimed.eu

Methodologically, this PhD will integrate prospective cohort analyses, advanced imaging interpretation, and statistical modeling. Multivariate and longitudinal analyses will be used to identify independent predictors of outcomes, while exploratory data-driven approaches will be employed to integrate complex datasets and generate predictive algorithms for progression and patient stratification. The coordinated structure of the registries, combined with high-resolution imaging data, will allow for a multidimensional characterization of ILDs and the validation of clinically meaningful biomarkers capable of supporting personalized management.

The expected impact of this research is substantial. By coordinating multicenter registries, the project will generate high-quality, standardized datasets that can inform clinical practice and future guidelines. The integration of clinical, environmental, and imaging data will enhance understanding of disease heterogeneity and progression. Furthermore, the evaluation of new CT techniques has the potential to refine diagnostic pathways, improve early detection, and identify predictive imaging signatures associated with fibrotic progression. The development and validation of progression biomarkers and stratification algorithms are also expected to have a strong translational value, as they may support antifibrotic drug development by enabling better patient selection, enrichment of clinical trials, and more accurate monitoring of treatment response. This is particularly relevant for emerging therapeutic strategies, including TG2-targeted approaches, where confirming the role of TG2 in lung fibrosis and identifying patients more likely to benefit from pathway-specific interventions may represent a major step toward precision medicine in ILDs.

In conclusion, this PhD project addresses critical unmet needs in ILDs by combining large-scale coordinated data collection, multidisciplinary clinical research, and innovative imaging technologies. Through these integrated efforts, it aims not only to contribute to earlier diagnosis and improved prognostic assessment, but also to develop predictive biomarkers and algorithms for disease progression and patient stratification, thereby supporting more personalized management strategies and facilitating future antifibrotic drug development.

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Type of contract

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CF 97692990159 – Tel. 02.8224.3777 – info@hunimed.eu – hunimed.eu