PROJECT

Supervisor: Lorenzo Dagna

Advanced imaging techniques to disclose and quantify lung involvement in Systemic Sclerosis-associated Interstitial Lung Disease

Curriculum: Clinical and Experimental Medicine

Link to the personal page of the University or relevant hospital site website: https://www.unisr.it/docenti/d/dagna-lorenzo

https://www.hsr.it/dottori/lorenzo-dagna

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Systemic sclerosis (SSc) is a rare autoimmune disease marked by immune dysregulation, vasculopathy, and progressive fibrosis. Interstitial lung disease (ILD) is the most frequent and life-threatening visceral complication, with a 10-year mortality of up to 40%. Around 30% of patients show progression within a year, making early identification a major unmet clinical need. Several circulating biomarkers have been associated with ILD progression. However, high-resolution computed tomography (HRCT) is the gold standard for diagnosing and monitoring SSc-ILD, but repeated exposure to ionizing radiation is a concern, particularly in younger patients requiring serial assessment. Additionally, it struggles to distinguish inflammation from fibrosis or detect subclinical microvascular changes. On the other hand, MRI is radiation-free but limited by suboptimal resolution. Finally, despite these advances, a multimodal framework integrating imaging, vascular, and circulating biomarkers is still lacking.

Rationale and hypothesis

Photon-counting detector CT (PCD-CT) and high-field (3T) MRI offer enhanced resolution and functional characterization with reduced radiation. Preliminary data from our centre suggest PCD-CT detects early ILD changes, including perfusion defect, even without overt fibrosis; optimized 3T MRI with T2-STIR sequences may differentiate inflammation from fibrosis. Vascular assessment by nailfold video capillaroscopy (NVC) can bridge nailfold vasculopathy with parenchymal imaging changes, while serial KL-6 provides complementary monitoring value. Blood-based multi-omic profiling of plasma and PBMCs, integrating proteomics and gene expression, may identify inflammatory vs. fibrotic profiles whose

alignment with imaging phenotypes enables precision stratification We hypothesize that combining PCD-CT, 3T MRI, NVC, KL-6, and multi-omic profiling can improve staging, prognosis, and monitoring of SSc-ILD.

Aims and specific Objectives

The primary aim is to validate novel imaging biomarkers from PCD-CT and 3T MRI for characterizing and monitoring SSc-ILD.

Specific objectives:

Compare PCD-CT and 3T MRI in staging ILD activity and severity.

Identify imaging biomarkers of early inflammation, microvascular damage and fibrosis

Determine what biomarkers best predict rapidly progressive ILD.

Define multi-omic profiles (inflammatory vs. fibrotic) and test their association with imaging phenotypes, NVC pattern, and KL-6 trajectory.

Assess the multimodal biomarker panel in predicting and monitoring treatment response.

Expected outcomes

This project will validate non-invasive imaging biomarkers for early and active SSc-ILD, providing mechanistic insights into the inflammation-fibrosis balance. Multi-omic profiling will indeed molecularly validate imaging phenotypes, identifying patients most likely to benefit from anti-inflammatory and antifibrotic strategies. This approach may minimize radiation exposure and guide personalized treatment.

Skills that the student should acquire (max. 600 characters including spaces):

The student will acquire advanced skills in thoracic imaging, including PCD-CT and 3T MRI acquisition and interpretation, as well as expertise in radiomics, artificial intelligence, and quantitative image analysis. Moreover, she/he will develop skills in clinical data integration, translational research methodology, and multidisciplinary collaboration across radiology, rheumatology, and pulmonology. The student will also gain proficiency in performing and interpreting NVC. Laboratory and bioinformatic skills including PBMC isolation, targeted proteomic, gene expression profiling and multi-omic data integration will be acquired.

References (max. 15)

1) Denton CP, Khanna D. Systemic sclerosis. Lancet. 2017;

2) Roofeh D. et al. Systemic sclerosis associated interstitial lung disease:a conceptual framework for subclinical, clinical and progressive disease. Rheumatology (Oxford) 2023;

3) Ledda RE and Campochiaro C. High resolution computed tomography in systemic sclerosis: From diagnosis to follow-up. Rheumatol Immunol Res 2024;

4) Hoffmann-Vold AM et al. The identification and management of interstitial lung disease in systemic sclerosis: evidence-based European consensus statements Lancet Rheum 2020;

5) Raghu G et al. Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults: An Official ATS/ERS/JSR/ALAT Clinical Practise Guideline. Am J Respir Crit Care Med 2022;

6) Jungblut L et al. Assessment of interstitial lung disease in a systemic sclerosis patient cohort using photon-counting detector CT with ultra-high resolution and a 1024 pixel image matric. Br J Radiol 2024;

7) Jungblut L et al. Potential of Photon-Counting Detector CT for Radiation Dose Reduction for the Assessment of Interstitial Lung Disease in Patients With Systemic Sclerosis. Invest Radiol 2022;

8) Dupont A et al. Dual-energy CT lung perfusion in systemic sclerosis; preliminary experience in 101 patients. Eur Radiol 2023;

9) Lanzetti L et al. Magnetic resonance imaging of interstitial lung disease: a state-of-art review. Respir Med 2019;

10) Pinal-Fernandez et al. Fast 1.5 T chest MRI for the assessment of Interstitial Lung Disease extent secondary to systemic sclerosis Clin Rheumatol 2016;

11) Velauthapillai A et al. Longitudinal association between nailfold capillaroscopy and incident interstitial lung disease: A EUSTAR database analysis. J Scleroderma Relat Disord 2025;

12) Volkmann ER et al. Treatment Response Biomarkers for Systemic Sclerosis–Associated Interstitial Lung Disease. Arthritis Care Res 2025;

14) Zinellu A et al. Vascular endothelial growth factor as a potential biomarker in systemic sclerosis: a systematic review and meta-analysis. Front Immunol 2024;

15) Shimagami H. *et al.* Single-cell analysis reveals immune cell abnormalities underlying the clinical heterogeneity of patients with systemic sclerosis. Nat Commun 2025;