Università di Brescia

Dipartimento di Scienze Cliniche e Sperimentali

Dottorato di Ricerca in
«Intelligenza Artificiale in Medicina e Innovazione nella Ricerca clinica e metodologica»

Coordinatore: Prof. Domenico Russo

Integrating Radiomic and Flow Cytometry Biomarkers for Predicting Disease Progression and Pulmonary Hypertension secondary to Interstitial Lung Disease associated to Connective Tissue Diseases

MOSCHETTI LIALA

CICLO XLI

Supervisor: Prof. Ilaria Cavazzana

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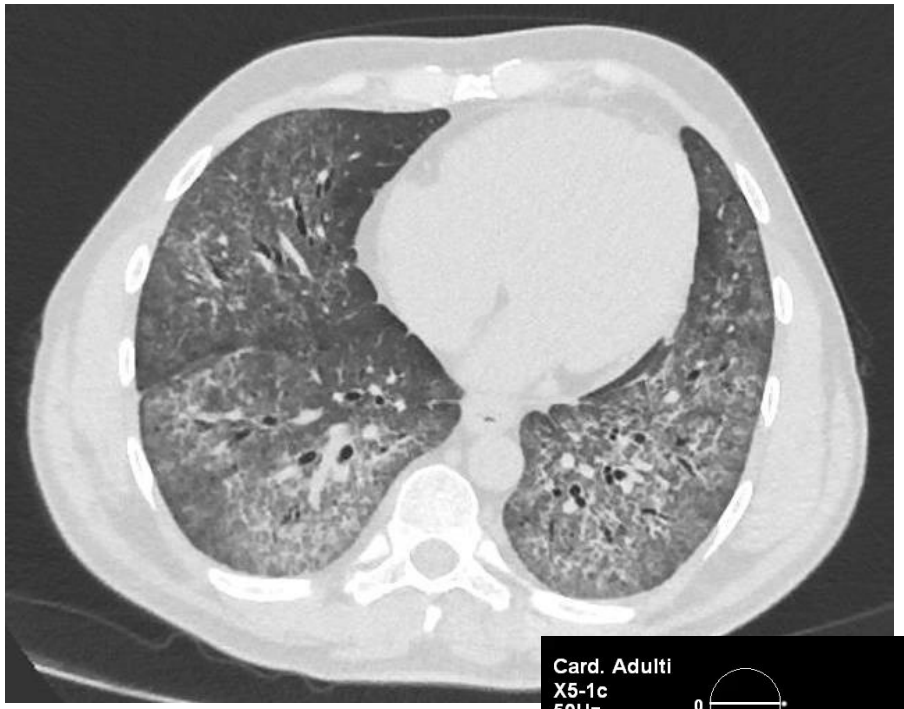
Clinical background

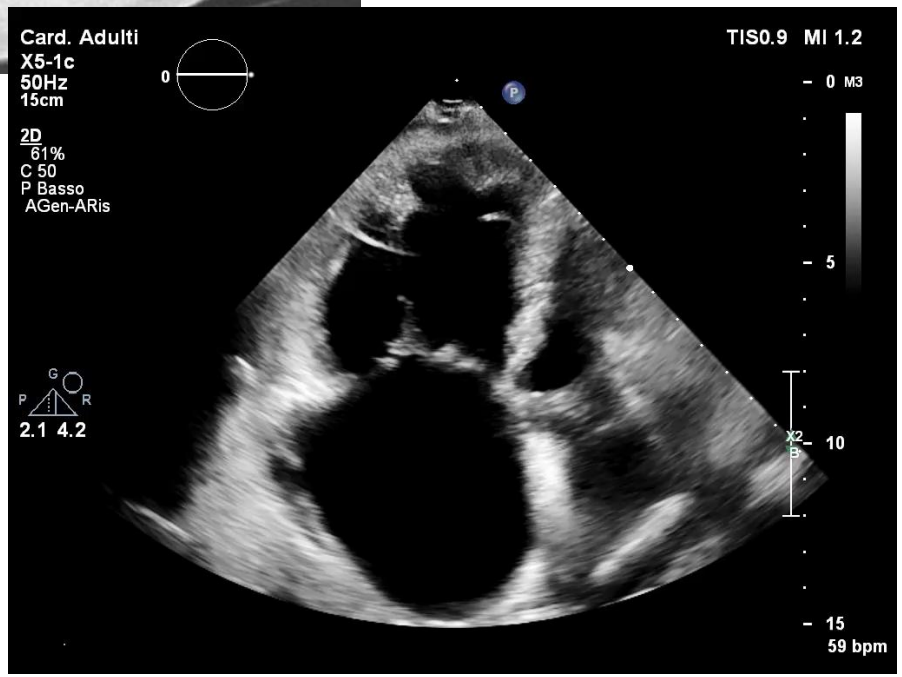
Interstitial lung disease (ILD) is one of the most frequent and severe pulmonary manifestations of connective tissue diseases (CTD)

ILD is particularly relevant in systemic sclerosis (**SSc**), idiopathic inflammatory myopathies (**IMM**), and rheumatoid arthritis (**RA**)

ILD progression significantly affects morbidity, mortality, and quality of life

Pulmonary hypertension (PH) may complicate RA/CTD-ILD and is associated with worse prognosis





Why this project

Current clinical tools often detect disease progression only after relevant functional or structural damage has already occurred

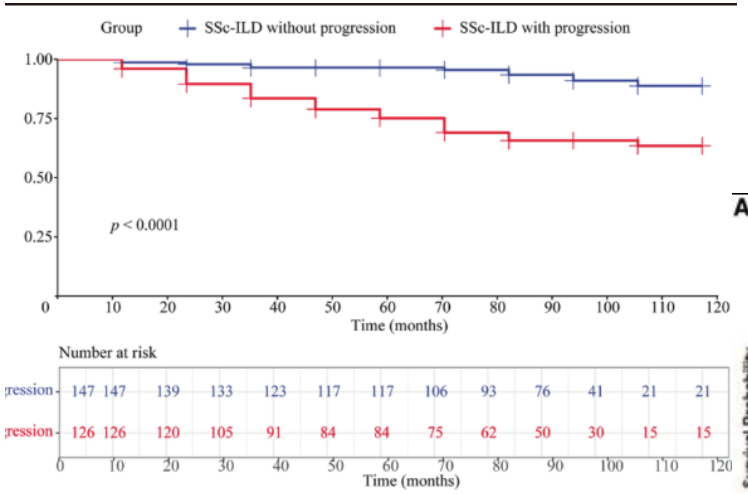
HRCT is the gold standard for ILD assessment, but conventional interpretation may be partly subjective
Radiomics allows quantitative and reproducible extraction of parenchymal and vascular imaging features

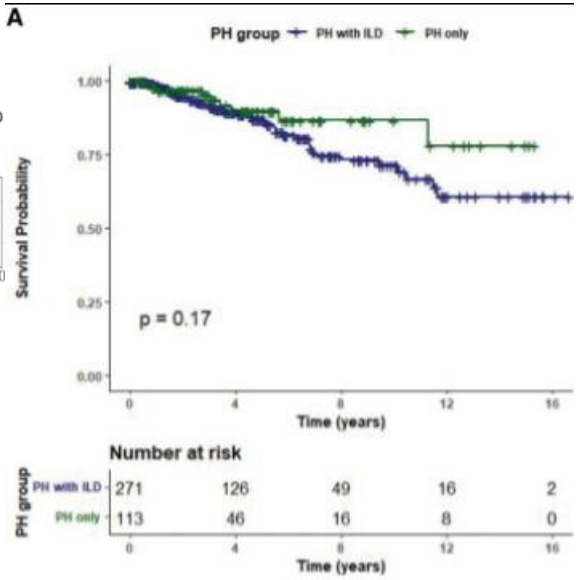
Endothelial progenitor cells (EPCs) and angiogenic T cells (Tang) may reflect vascular injury and repair mechanisms

Integrating these biomarkers may improve early risk stratification

Table 4. Definition of Progressive Pulmonary Fibrosis

Definition of PPF
In a patient with ILD of known or unknown etiology other than IPF who has radiological evidence of pulmonary fibrosis, PPF is defined as at least two of the following three criteria occurring within the past year with no alternative explanation*:
1 Worsening respiratory symptoms
2 Physiological evidence of disease progression (either of the following): a. Absolute decline in FVC ⩾5% predicted within 1 yr of follow-up b. Absolute decline in D_{LCO} (corrected for Hb) ⩾10% predicted within 1 yr of follow-up
3 Radiological evidence of disease progression (one or more of the following): a. Increased extent or severity of traction bronchiectasis and bronchiolectasis b. New ground-glass opacity with traction bronchiectasis c. New fine reticulation d. Increased extent or increased coarseness of reticular abnormality e. New or increased honeycombing f. Increased lobar volume loss





Aim of the project

To identify radiomic and flow-cytometry biomarkers for predicting:
- ILD progression
- development of PH in RA/CTD-ILD patients

Specific objectives
- To extract radiomic features related to lung parenchymal abnormalities and vascular remodeling
- To assess EPCs and Tang cell populations
- To evaluate *longitudinal* changes in imaging and cellular biomarkers
- To develop integrated predictive models combining radiomic, flow-cytometry, and clinical data

Study design

Single-center study
Patients will be recruited at the Rheumatology and Clinical Immunology Unit, ASST Spedali Civili of Brescia.

Two-cohort design
Prevalent cohort: retrospective longitudinal cohort of RA/CTD-ILD patients with available chest HRCT scans acquired up to study start included for longitudinal radiomic evaluation.
Incident cohort: prospective longitudinal cohort of newly diagnosed RA/CTD-ILD patients enrolled from study start onward, with serial HRCT assessment and prospective flow-cytometry analysis during follow-up.

Population
Adult patients with RA/CTD-associated ILD
Diseases included: SSc, IMM, RA

Methods

Clinical and functional data collection

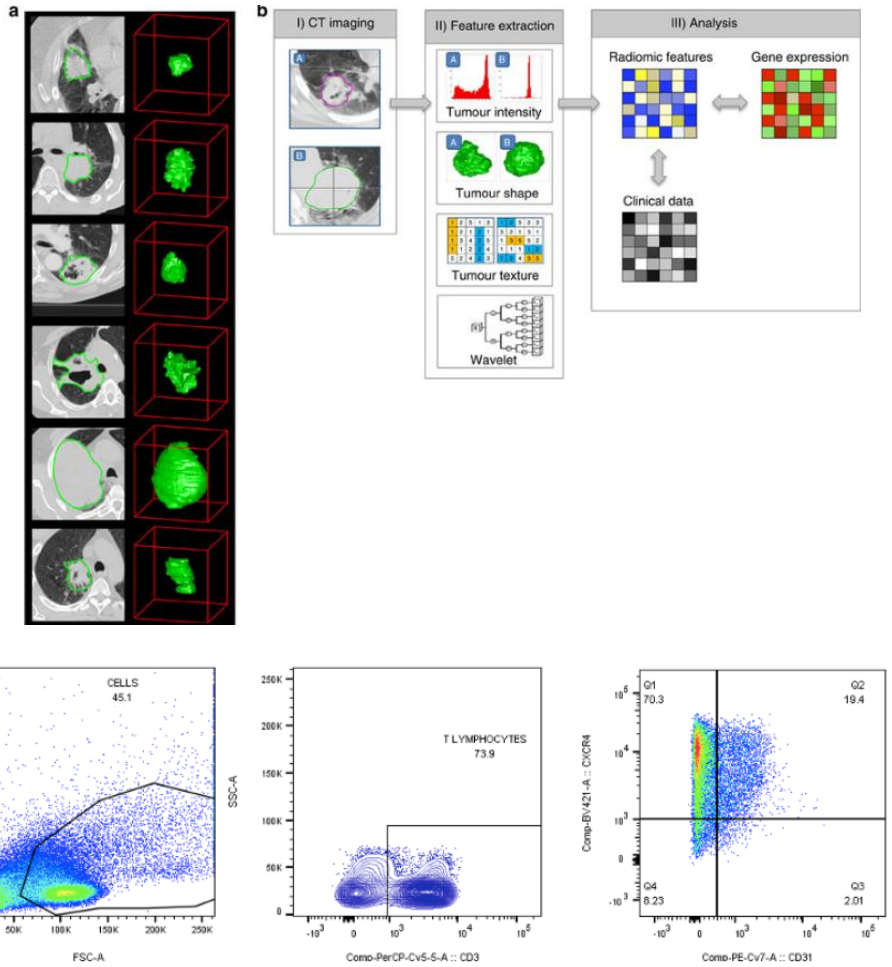
-demographic and clinical features
-ongoing and previous therapies, with focus in immunosuppressive, antifibrotic and vasoactive
-serological biomarkers
-pulmonary function tests, 6-minute walking test
-ECG, echocardiography, and right heart catheterization

Radiomic analysis [in collaboration with Radiology Unit 2 of ASST Spedali Civili of Brescia]

-longitudinal analysis of thoracic HRCT scans
-semi-automatic segmentation of lung and vascular structures
-extraction of parenchymal and vascular quantitative features

Flow cytometry [Research Laboratory affiliated with the Rheumatology Unit, ASST Spedali Civili of Brescia and the University of Brescia (WKG-0143, ERC field=LS6_2-Adaptive Immunity), in collaboration with the Nocivelli Laboratory]

-assessment of T-cell subsets, Tang cells, and EPCs
-evaluation at baseline and follow-up



Current status

Completed
Scientific rationale defined
Study protocol developed
Submission to the Ethics Committee completed

Ethics approval currently pending

Immediate next steps
Activation of retrospective data collection
Radiomic pipeline standardization
Cytofluorimetry panel set up
Start of prospective patient enrollment

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GRAZIE PER L'ATTENZIONE

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