

Imaging Lung Inflammation in Interstitial Lung Disease (ILD) with ^{99m}Tc-Maraciclalide – a Therapy Selection Tool?

D. Burch^{3,4}, G. Dixon¹, D. Little², S. Cade², J. Barnett³, J. C. Rodrigues², K. Tsaneva-Atanasova⁵, S. L. Barratt⁶, T Garrood⁷, C. J. Scotton¹, M. A. Gibbons⁸

1. Department of Clinical & Biomedical Sciences, University of Exeter, Exeter (United Kingdom)
2. Royal United Hospitals Bath NHS Foundation Trust, Bath (United Kingdom)
3. Serac Healthcare Ltd, London (United Kingdom)
4. John Radcliffe Hospital, Oxford (United Kingdom)
5. Department of Mathematics and Statistics, Faculty of Environment, Science and Economy, University of Exeter, Exeter (United Kingdom)
6. Bristol Interstitial Lung Disease Service, North Bristol NHS Trust, Bristol (United Kingdom)
7. Department of Rheumatology, Guy's and St Thomas' NHS Foundation Trust, London (United Kingdom)
8. Exeter-South West Peninsula ILD Network, Royal Devon University Healthcare, Exeter (United Kingdom)

Background/Purpose

Differentiating between inflammatory and fibrotic stages of interstitial lung disease (ILD) is critical. Optimal patient management depends on determining the two, which have distinct pathophysiological mechanisms, prognostic implications, and therapeutic requirements.

High-Resolution Computed Tomography (HRCT) provides a structural view of the lungs and can map fibrotic patterns, but there is currently no reliable non-invasive way to identify inflammation.

The molecular imaging agent ^{99m}Tc-maraciclalide binds to $\alpha_v\beta_3$ integrin which is upregulated in vascular endothelial cells during angiogenesis, a cardinal feature of inflammation. The agent has demonstrated diagnostic promise in other inflammatory conditions such as endometriosis¹ and RA² Proof of concept of the potential of ^{99m}Tc-maraciclalide to identify inflammation in the lungs of subjects with RA has been established, with lung uptake observed in subjects with RA-associated ILD (RA-ILD) but not in those without (Figure 1).

We investigated SPECT-CT ^{99m}Tc -maraciclalide imaging of $\alpha_v\beta_3$ integrin expression in subjects with idiopathic pulmonary fibrosis (IPF), fibrotic hypersensitivity pneumonitis (fHP) and age- and sex-matched healthy controls (HCs).

Methods

HCs, IPF and fHP patients (n=5 per group) were administered 740 MBq of ^{99m}Tc -maraciclalide via intravenous injection. SPECT-CT scans were acquired 2 hours post-injection, with a scan duration of 20 minutes. Fused images were evaluated by both nuclear medicine and thoracic radiologists, who classified them based on the observed radiological patterns as well as on distribution and intensity of standardized uptake values (SUV). The maximum lung SUV (SUV_{max}) was compared to the minimum lung SUV (SUV_{min}) to determine the target-to-background ratio (TBR), and the mean lung SUV was calculated for each patient.

Results

The HC showed minimal basal uptake in the lungs, whereas both IPF and fHP patients showed distinct uptake. The mean (+/- SD) TBR was numerically higher in the IPF and fHP cohorts vs HCs (2.4 +/-0.48, 4.0 +/- 1.77 and 2.2 +/- 1.24, p=0.08, respectively); with the mean lung SUV significantly higher in the fHP cohort vs HCs (1.2 +/- 0.18 vs 0.75 +/- 0.09, p=0.02) and numerically higher for IPF (0.95 +/- 0.2, p=0.18). This is biologically plausible as inflammation is expected in fHP patients but not usually with IPF.

Conclusion

These encouraging Phase 2 results show that SPECT-CT imaging with ^{99m}Tc -maraciclalide has the potential to meet a number of unmet clinical needs:

1. Differentiate inflammation from fibrosis in subjects with ILD and help inform critical treatment decisions.
2. Identifying those patients with co-existent inflammation alongside fibrosis may help inform treatment approaches in fibrotic-ILD.
3. Provide a screening tool for ILD in subjects with RA based on established risk factors.

4. Early identification of subjects with RA-ILD followed by monitoring of their condition for progression and therapy response.

Phase 3 studies are warranted.

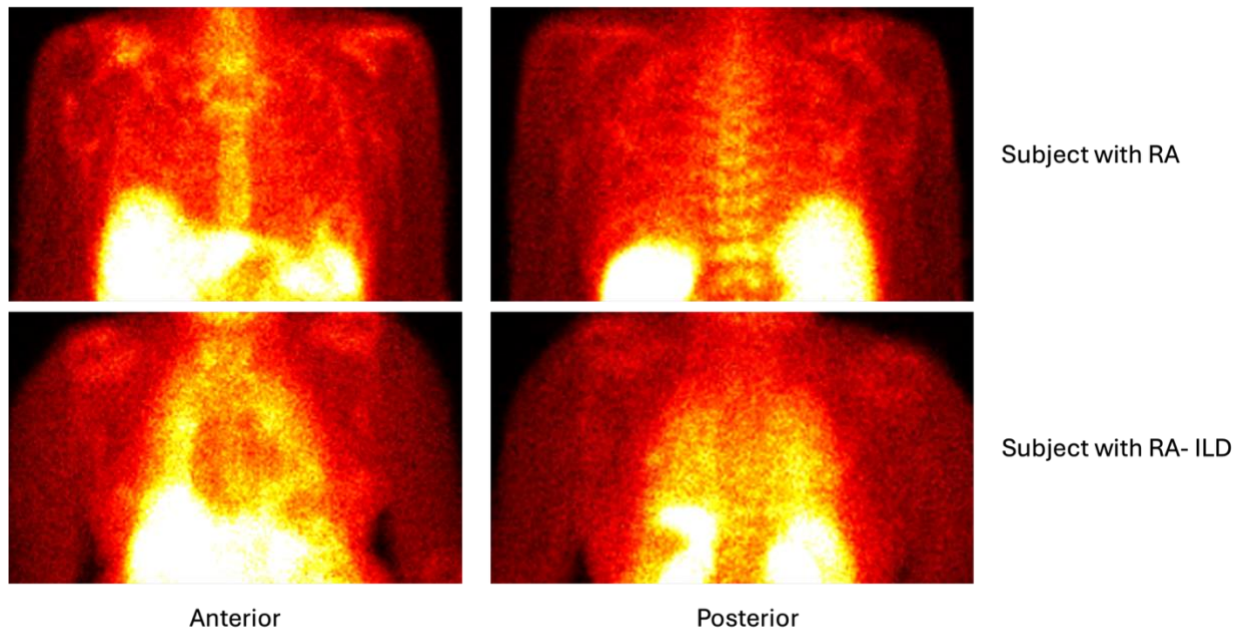


Figure 1. Planar ^{99m}Tc -Maraciclalide lung images of RA subjects with and without RA-ILD

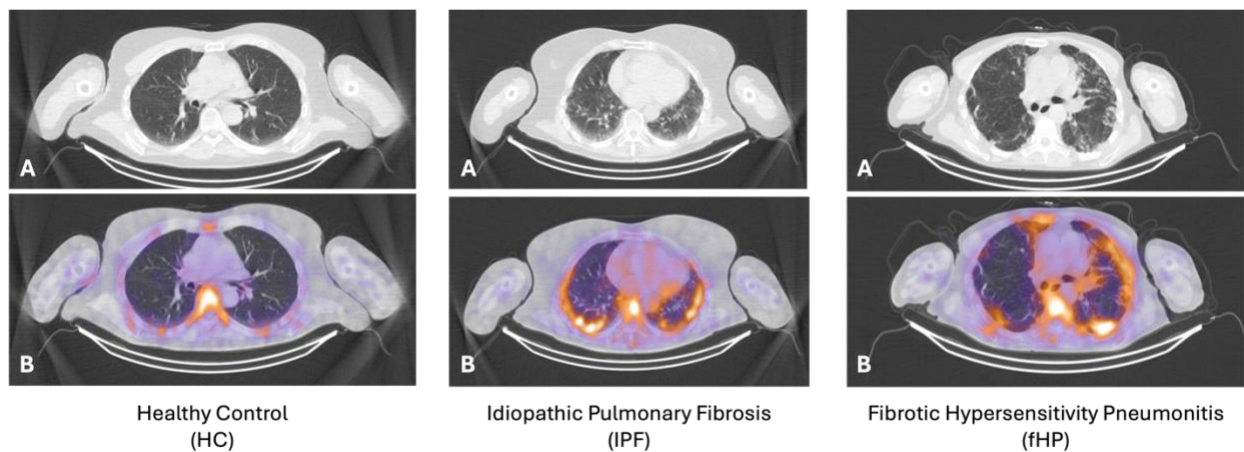


Figure 2. Sample images from each participant group: A: CT only; B: fused SPECT-CT ^{99m}Tc -Maraciclalide

References

1. Barnett J, Ghesani M, Gibbons T, Burch D, Cade S, Graham R, Patel N, Zondervan K, Becker C. Visualisation of Superficial Peritoneal Endometriosis with ^{99m}Tc -maraciclalide. *Eur J Nucl Med Mol Imaging* **51** (Suppl 1), 1–1026 (2024).

2. Attipoe L, Subesinghe S, Blanco-Gil C, Opena M, Norton S, Rosser M, Cope AP, Cook GJR, Garrod T. Imaging Neoangiogenesis in Rheumatoid Arthritis (INIRA) Part II: Whole-body Synovial Uptake of ^{99m}Tc -maraciclalide is Highly Correlated with Power Doppler Ultrasound. *Acad Radiol.* 2025 Aug 4:S1076-6332(25)00561-6. doi: 10.1016/j.acra.2025.06.013.

Notes:

D Burch and G Dixon are joint first authors.

C Scotton and M Gibbons are joint senior authors.

Disclosures: G. Dixon, ; D. Little, ; S. Cade, ; J. Barnett, None; D. Burch, None; J. C. Rodrigues, ; K. Tsaneva-Atanasova, ; C. J. Scotton, ; S. L. Barratt, ; T Garrod, ; M. A. Gibbons, .