Non-invasive in vivo metabolic profiling of inflammation in joints and entheses by optoacoustic imaging

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Background:

- An in-depth metabolic characterization of joints and entheses at the tissue level can help in the early diagnosis and treatment selection for patients with inflammatory arthritis (1).
- However, current knowledge about the metabolic profiles of synovitis and enthesitis is limited.
- Multispectral optoacoustic tomography (MSOT), a novel metabolic imaging technology, could be used to undertake metabolic profiling of joints and entheses non-invasively using near-infrared multispectral laser to stimulate tissues and detect the emitted acoustic energy, enabling quantification of tissue components in vivo based on differential absorbance at multiple wavelengths (2, 3).

Objectives:

- To explore the metabolic characteristics of arthritis and enthesitis using MSOT.

Methods:

- Cross sectional study in healthy controls (HC), patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA).
- Participants underwent clinical, ultrasound (US), and MSOT examination of different anatomical regions (metacarpophalangeal joints, wrists, entheses of lateral epicondyles, patellar, quadriceps and Achilles tendons).
- MSOT-derived hemoglobin, oxygen saturation, collagen and lipid levels were measured.
- We calculated scaled mean differences (SMD) between affected and unaffected joints and entheses as defined by clinical examination or US using linear mixed effects models.

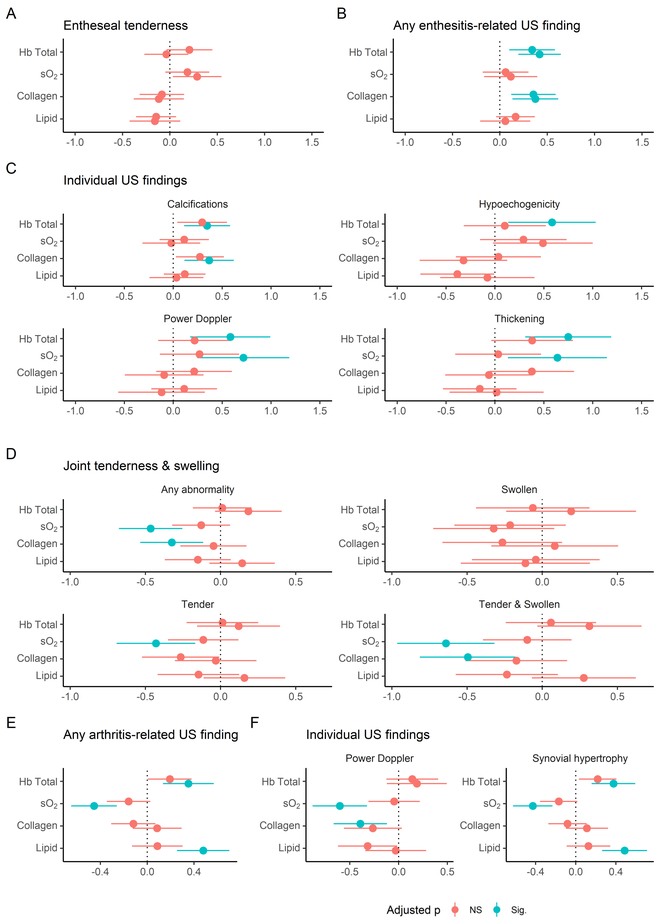

Figure 1: Scaled differences and 95% confidence intervals of MSOT-measured metabolite values by clinical and ultrasonographic findings of enthesitis (A-C) and arthritis (D-F).

Enthesitis plots are depicted in A-C and arthritis plots in D-F. Two differences are plotted for each metabolite indicating two multispectral processing algorithms used for estimation. P values were adjusted for multiple testing using a false discovery rate of 5%.

NS, not significant. sO2, oxygen saturation.

Results:

- We obtained 1535 MSOT and 982 US scans from 87 participants (36 HC, 34 PsA, 17 RA) (**Table 1**).
- Entheseal tenderness was not associated with metabolic changes, whereas US enthesitis was associated with increased total hemoglobin, oxygen saturation and collagen content.
- In contrast, clinical and US arthritis showed increased hemoglobin levels but reduced oxygen saturation and reduced collagen content.
- Synovial hypertrophy was associated with increased articular lipids (**Figure 1**).

Table 1 Baseline characteristics.

	Overall	Healthy	PsA	RA
N	87	36	34	17
Age, mean (SD)	47.0 (15.7)	34.7 (12.0)	52.4 (11.5)	62.5 (9.1)
Tender joints, median (IQR)	0 (0-2)	0 (0-0)	1 (0-5)	2 (1-6)
Swollen joints, median (IQR)	0 (0-1)	0 (0-0)	0 (0-2)	2 (1-6)
Tender entheses, median (IQR)	0 (0-2)	0 (0-0)	1 (0-3)	0 (0-0)
csDMARD, n (%)	22 (25.3)	-	13 (38.3)	9 (53.0)
b-tsDMARD, n (%)	31 (35.6)	-	20 (58.8)	11 (64.7)

SD, standard deviation; IQR, interquartile range; csDMARD, conventional synthetic disease modifying anti-rheumatic drug; b-tsDMARD, biologic or targeted synthetic disease modifying anti-rheumatic drug.

Conclusion:

- MSOT allows non-invasive characterization of metabolic changes in arthritis and enthesitis.
- Our findings can be interpreted as a reflection of increased synovial cellularity, collagen degradation, and metabolic demand in synovitis, and of an increased tissue apposition and vascularization in enthesitis.
- Our results suggest that synovitis and enthesitis do not only differ at the clinical and anatomical-functional level, but also exhibit divergent metabolic changes.

References:

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