SAT0656 OPTICAL IMAGING OF PHAGOCYTE MIGRATION REPRESENTS A NOVEL METHOD TO DETERMINE DISEASE ACTIVITY IN CIA

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Background: Recruitment and migration of phagocytes to the site of inflammation are key events in the onset of inflammation. Albeit crucial for pathogen elimination, tissue repair and restoration of tissue homeostasis, dysregulated phagocyte infiltration can also cause severe inflammatory disorders. Therefore, targeting and modulation of phagocyte infiltration represents a promising new approach to fight inflammatory disorders and diseases, such as rheumatoid arthritis. Additionally, non-invasive tracking of phagocyte migration to the site of inflammation could extend both scientific knowledge as well as the repertoire of diagnostic strategies in clinical use.
Objectives: The aim of this study was to establish a fluorescence reflectance imaging (FRI) based system to visualize and analyze migration properties of different cell populations in inflammatory disease models, like experimental arthritis, *in vivo*.
Methods: Immortalized murine myeloid progenitor ER-HoxB8 cells were differentiated to neutrophils or monocytes (1). Cells were labeled with the membrane-selective fluorescent dyes DIR (2) or DID, respectively. We analyzed viability and functionality of stained cells *in vitro* and investigated their ability to migrate to sites of inflammation *in vivo* in several mouse models - particularly in a collagen induced arthritis (CIA) mouse model - via fluorescence reflectance imaging (FRI). Using CRISPR-Cas9 technology we introduced targeted gene deletions for main adhesion molecules.
Results: Differentiated ER-HoxB8 cells could effectively be labeled with DIR or DID. Labeling of monocytes or neutrophils did not affect cellular viability or functionality *in vitro*. Subsequent *in vivo* imaging experiments allowed the visualization of migrated labeled phagocytes in different murine disease models, thereby cells could be detected at sites of inflammation with high sensitivity and specificity. In a CIA mouse model the amount of immigrated cells could even be associated closely to disease score and disease severity. Thus, the detection of immigration of labeled cells might also give hints about new inflammatory spots that are about to settle up before they can be detected macroscopically. Furthermore, differential cell labeling allowed direct quantitative comparison of differences in migration rates of wildtype and CD18 or CD49d knockout cells *in vivo*.
Conclusions: Specific and distinguishable labeling of diverse cell types allows *in vivo* tracking and subsequent quantification of migrated cells within the same animal. Targeted gene deletion allows analysis of molecular mechanisms relevant for leukocyte recruitment during different stages of arthritis. Correlation of the amount of immigrated cells to disease severity offers new opportunities to non-invasively detect and monitor inflammatory sites *in vivo*.
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SAT0657 CAN VASCULAR INFLAMMATION IN RA BE DETECTED USING CONTRAST ENHANCED MRI? PRELIMINARY RESULTS

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Background: In rheumatoid arthritis (RA) vascular inflammation may contribute to excess cardiovascular (CV) risk. Contrast enhanced MRI has been used to detect vascular inflammation in Takayasu's arteritis. In RA, its utility has not been studied but it may provide a method of identifying and monitoring vascular inflammation and effects of therapy.
Objectives: We sought to compare carotid artery wall enhancement on contrast enhanced MRI in RA patients and controls and evaluate association with circulating markers of inflammation, endothelial activation and CV risk factors.
Methods: Patients and age/sex matched controls underwent clinical and serological assessment (details in Table 1) and a screening carotid ultrasound. Those with wall thickening>2mm had a carotid MRI. T_1-weighted images were acquired before and after gadopentate injection on a 3T scanner. Increase in mean signal intensity (SI) in the carotid vessel wall normalised to adjacent skeletal muscle provided a global enhancement metric (WE_G). Histograms of distribution of SIs on pre-and post- contrast images were generated and bimodal Gaussian distributions fitted to explore patterns of enhancement within the wall. MRI measurements were compared between groups and association with serological markers tested using non-parametric statistics.
Results: 27 patients and 10 controls underwent MR imaging. Key characteristics are seen in Table 1. There was no difference in WE_G between groups and no association with serological markers. However a bimodal distribution of SI in vessel wall was observed (Figure 1) and in exploratory analysis these two components were analysed separately. For the low-signal component enhancement (WE_{low}) correlated with ESR, I-CAM, e-selectin (r=0.39,p=0.03;r=0.44,p=0.01;r=0.37,p=0.04). There was a trend towards correlation with CRP (r=0.30,0.08) and towards higher values in patients (median 0.20 (0.15, 0.33) vs 0.14 (0.11, 0.22),p=0.051). Enhancement in the high-signal component (WE_{high}) was not associated with serological markers or RA status.

Table 1.Key characteristics (median (IQR) or frequency (%) where*)

	Cases	Controls	P value
Age (yrs)	61.0 (56.5, 64.6)	55.4 (54.0, 57.0)	0.07
Female*	22 (81)	5 (50)	0.06
LDL (mmol/L)	2.7 (2.25, 3.23)	3.80 (3.24, 4.53)	0.08
Glucose (mmol/L)	4.8 (4.6, 5.0)	5.8 (5.3, 6.0)	0.01
Hs-CRP (mg/l)	3.34 (2.04, 5.75)	0.81 (0.39, 4.58)	0.047
ESR (mm/hr)	18 (10, 35)	7 (5, 10)	0.01
ICAM (ng/ml)	161.5 (134.8, 213.4)	151.3 (106.9, 220.8)	0.51
V-CAM1 (ng/ml)	398 (352, 473)	376 (353, 390)	0.52
E-selectin (ng/ml)	7.55 (5.79, 21.1)	4.71 (3.01, 7.76)	0.11
WE_G	0.23 (0.23, 0.28)	0.25 (0.18, 0.27)	0.62
WE_{low}	0.20 (0.15, 0.33)	0.14 (0.11, 0.22)	0.05
WE_{high}	0.32 (0.22, 0.50)	0.33 (0.29, 0.38)	0.73

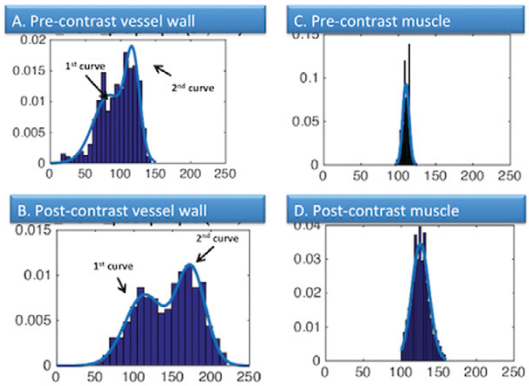

Figure 1. Distribution of signal intensity (SI) within the vessel wall and muscle referent before and after contrast injection (x axis signal intensity (a.u), y axis relative frequency). Gaussian curves were fitted and mean of fit values for each curve were calculated. A bimodal distribution with low and high signal intensity components can be seen in vessel wall (panel A & B) compared with a single curve in muscle (panel C& D). For each curve the difference between pre- and post- contrast mean SI was calculated (with normalisation to muscle signal). This provided a wall enhancement measurement for the 2 separate curves (WE_{low} and WE_{high})

Conclusions: Simple global SI measurement on MRI did not suggest vascular inflammation in RA. However, the bimodal SI distribution may represent different wall components e.g. intima and adventitia. The differential enhancement, and association of WE_{low} with inflammation, endothelial activation and RA status, warrants further investigation.
Disclosure of Interest: None declared
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SAT0658 THE STIFFNESS OF MEDIAN NERVE MEASURED BY ELASTOSONOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Carpal tunnel syndrome (CTS) is the most frequent neuropathy of all entrapment neuropathies in the general population. Rheumatoid arthritis (RA) is one of the disease generate secondary CTS. The pathophysiology of CTS of RA might be different from idiopathic CTS. RA is a disease that has the characteristics to generate inflammatory synovial proliferation of the joint and also tendon. Although inflammation of the wrist joint and synovial tissue of the flexor tendons can cause increased pressure in the carpal tunnel, there is a possibility that even RA patients without symptoms of CTS also have subclinical median nerve damage because of the synovial proliferation and inflammation.
Objectives: The aim of this study was to assess and compare the stiffness of the median nerve measured by quantitative elastosonography between patients with RA without symptom of CTS and controls.
Methods: Four hundred two hands in 201 patients with RA and 222 hands in controls were included. All participants were examined both wrists. Ultrasound (US) examination was performed by using a 5- to 18-MHz linear array transducer (HI VISION Ascendus; HitachiAloka Medical,Tokyo, Japan). As a reference medium, an acoustic coupler (EZUTECPL1; HitachiAloka Medical) with a standardized

elasticity was attached to the transducer during the elastosonography. The inlet of the carpal tunnel at the scaphoidpisiform level and the proximal portion of the carpal tunnel inlet were scanned in a transverse plane. The crosssectional area (CSA) and the elasticity of the median nerve, which was measured as the acoustic coupler/median nerve strain ratio, were evaluated. The measurements were repeated two times, and the average strain ratio was used for analysis.

Results: We analyzed 342 hands in 177 RA patients (139 female, mean age: 63.5±11.6 years) and 158 hands in 81 non-RA (68 female, mean age: 71.5±14 years) finally. There were no significant differences in the cross-sectional area of median nerve (left: 8.9 vs 8.7 mm^2, p=0.91, right: 8.2 vs 8.4 mm^2, p=0.62) or the circumference of median nerve (left: 13.1 vs 13.4 mm, p=0.41, right: 13.7 vs 13.7 mm, p=0.95) within carpal tunnel between RA group and non-RA group. Strain ratio within carpal tunnel in RA group was higher than that of non-RA group (left: 2.6 vs 2.1, p=0.002, right: 2.7 vs 2.2, p=0.003). There were no significant differences in the cross-sectional area of median nerve (left: 7.5 vs 8.1 mm^2, p=0.07, right: 8.8 vs 8.3 mm^2, p=0.6), the circumference of median nerve (left: 13.1 vs 13.5 mm, p=0.3, right: 13.7 vs 13.9 mm, p=0.71) and strain ratio (left: 2.1 vs 2.0, p=0.88, right: 2.3 vs 2.1, p=0.01) at the entrance of the carpal tunnel between RA group and non-RA group.

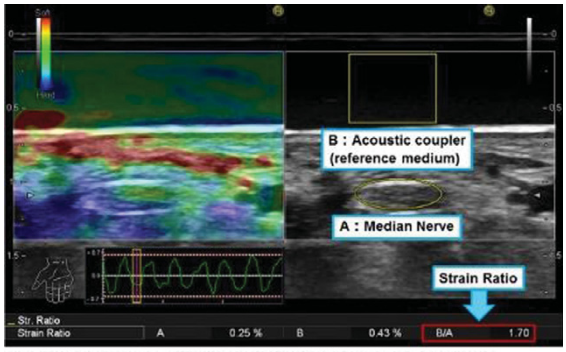

Figure: The images of acoustic coupler /median nerve strain ratio.

Conclusions: Real-time Elastosonography showed the stiffness of the median nerve with RA patients without any symptoms of CTS was higher than controls. It suggests that inflammation of flexor tenosynovitis and wrist joint may generate fibrotic change of median nerve in patients with RA.

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SAT0659 COMPARISON BETWEEN EIGHT DIFFERENT ULTRASONOGRAPHIC SCORES FOR HAND ASSESSMENT IN RHEUMATOID ARTHRITIS -A CROSS-SECTIONAL STUDY

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory condition associated with well-recognised inflammatory joint features, which are amenable to ultrasound (US) examination. The implementation of US scoring systems in addition to clinical examination could help standardise the way RA is monitored; however, due to variation in local availability of US and sonographer expertise, different scoring systems have been used in clinical practice (1). Despite significant research progress in supporting the role of US in RA, there is no consensus as to which scoring system is most useful.

Objectives: To assess whether simplified US protocols for hand examination correlate significantly with a 22 hand joint US score in patients with established rheumatoid arthritis, and correlate the US examination with the disease activity score (DAS-28 score).

Methods: This is a cross-sectional study of 224 RA patients stratified based on their DAS-28 scores and assessed using eight preselected US examination protocols including 22, 18, 16, 14, 10, 8 and two different combinations of 4 joints, respectively. Student T, Mann-Whitney U and Kuskal-Wallis tests were employed for analysis of clinical, laboratory and US parameters in the RA patient groups ($P<0.05$ was considered significant). Spearman's coefficients were used to correlate permutations of pairs of US scores, and US and DAS-28 scores.

Results: We found a significant difference between different US hand scores and their ability to detect the presence of active and chronic inflammation in RA patients. The DAS-28 scores correlated very well (R=0.89–1, $P<0.05$) with the total Power Doppler (PD) scores generated by all US protocols irrespective of patients' disease activity. Simplified US scores missed information on presence of erosions ($P<0.05$), but were equivalent to the extensive 22 joint score in appreciating the amount of chronic and active inflammation compared to the extensive 22 joint score (P=0.15, P=0.11, respectively).

Conclusions: This study showed that preselected simplified US scores could be used in clinical practice to appreciate reliably the disease activity in patients with established RA; however they are less reliable in appreciating the disease burden when compared with an extended protocol for US examination of 22 hand joints. All the simplified US scores correlated very well with DAS-28 scores.

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Acknowledgements: S. Hussain and P. Sivakumaran contributed equally to the study.

Disclosure of Interest: None declared

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SAT0660 SAFETY, FEASIBILITY AND TOLERABILITY OF PERFORMING CONSECUTIVE MINIMAL INVASIVE ULTRASOUND-GUIDED SYNOVIAL BIOPSY PROCEDURES ON THE SAME WRIST IN A PROSPECTIVE RHEUMATOID ARTHRITIS STUDY

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Background: Studies on synovial tissue retrieved using the minimal invasive ultrasound-guided synovial biopsy (USG-SB) method have led to major advances in the understanding of Rheumatoid Arthritis (RA). The method is now used in multicenter RA studies and recommended in the phases of RA drug development. Only to biopsy disease active joints at start and end of a study, can lead to biopsies being retrieved from different joints. This can make interpretation of the changes in the synovial tissue and gene-expression profile difficult, as synovial histology patterns can vary between joints. We here present an approach where we biopsied the wrist with disease activity at presentation and the same wrist after six month of disease duration. We use the wrist, as it is the joint most commonly involved in the upper extremity in RA. The joint is easily accessible for USG-SB and therefore ideal to use to follow disease activity/treatment response/biomarker change in prospective RA studies.

Objectives: To assess the safety, tolerability and feasibility to perform repeated synovial biopsies from the same wrist, using a minimally invasive USG-SB technique in patients suffering from RA.

Methods: Patients with newly diagnosed untreated RA or longstanding (>5 years) RA and at least one clinically swollen wrist, underwent x-ray, magnetic resonance imaging (MRI) and ultrasound examination of the affected wrist and hand on the day of the biopsy. This was repeated 6 months later, where the second biopsy from the same wrist was taken. EULAR guidelines for RA treatment were followed in the 6 months between biopsies. Patient-reported outcomes (PRO) included a standard questionnaire given to all patients on the day of the biopsy as well as 2 weeks after the biopsy. Tolerability and the patient-reported willingness to repeat the procedure was assessed using the 5-point Likert scale.

Results: 38 RA patients (22 early, 16 longstanding) underwent USG-SB procedure at inclusion and after 6 months. One patient was excluded and did not have second biopsy due to diagnosis of CPPD. All patients have undergone first biopsy and at present time and 50% second biopsy. At the EULAR congress complete data will be presented. At present time, at both first and second biopsy no worsening in PRO of the biopsied joints was reported 2w after the biopsy, as compared before the biopsy. No infection, hemorrhage, nerve or tendon damage has currently been observed. One patient developed a tenosynovitis after biopsy (the CPPD patient), successfully treated with glucocorticoid injection. 10% of the patients were somewhat or very unlikely to have another biopsy procedure after the first procedure, and 6% after the second. All included RA patients accepted to have a second biopsy. Detailed data on differences in tolerability between early untreated RA patients versus patients with longstanding RA, will be presented at the conference.

Conclusions: To our knowledge, we are the first, to demonstrate that retrieving synovial tissue using the USG-SB method on the same wrist, at start and end of a prospective RA study, is safe and well tolerated.

Disclosure of Interest: None declared

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SAT0661 FINGER JOINT CARTILAGE THICKNESS EVALUATED BY ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: Joint destruction in RA includes both bone and cartilage lesions. By X-ray examination, cartilage destruction is evaluated as a joint space narrowing (JSN). However, joint space narrowing is not a direct evaluation of cartilage.

Objectives: We aimed to examine the finger joint cartilage thickness (CT) by ultrasound (US) imaging and clarify its clinical significance in patients with RA.

Methods: We enrolled 121 RA patients in low disease activity or clinical remission