92nm) in SSc compared to OA ($p < 0.05$) and in the range of MV (230-510 nm) (figure below). Finally, we observed a positive association between HLA-G+ with Erythrocyte Sedimentation Rate (ESR) ($\beta = 0.34$; $p < 0.01$).

Abstract THU0344 – Figure 1

Conclusion: In our study, limited cutaneous SSc showed different EVs concentrations from controls: SSc tends to have less exosomes and more MV than OA. Moreover, environmental stimuli (e.g. PM exposure) are confirmed to be able to influence HERV-w+ MV release both in SSc and controls. Finally, in SSc patients PM exposure could significantly alter the release of HLA-G+ MV that has been correlated to the process of self-tolerance maintenance. Further studies are required to fully unlock the role of PM and EVs in SSc.

Disclosure of Interests: None declared

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THU0345 TEXTURE-BASED RADIOMICS FEATURES DISCRIMINATE DIFFERENT STAGES OF EXPERIMENTAL INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a life-threatening complication of systemic sclerosis (SSc). There is an unmet need for validated, routinely available biomarkers for disease staging and individualized patient stratification. In that respect, high-resolution computed tomography (HRCT), routinely performed in the work-up of SSc-ILD patients, has great potential as a source for non-invasive imaging biomarkers. Recently, radiomics, the quantitative extraction of hundreds of radiologic image features, has emerged as a powerful tool for biomarker research and precision medicine approaches; however, so far, it has been applied predominantly in oncology.

Objectives: To evaluate the performance of CT-based radiomics for disease detection, staging and as surrogate marker for tissue pathophysiology in the model of bleomycin (BLM)-induced lung fibrosis.

Methods: To mimic different stages of SSc-ILD, small-animal CT imaging was performed at days 3, 7, and 14 after instillation of BLM or saline solution, respectively (n=5-6 mice/group). Trained observers manually segmented the left and right mouse lungs in the CT images, and 154 radiomics features were extracted including 17 histogram- and 137 texture-based features using the in-house developed software Z-Rad (Python 2.7). To link the radiomics features with the underlying pathophysiology, Pearson correlation analysis between radiomics and histological features (Ashcroft score, Sirius red and CD45 staining positivity) was performed.

Results: CT imaging visualized morphological changes of the lung architecture in BLM-treated mice, as evidenced by a time-dependent increase of grey areas on chest CT images and a gradual increase in tissue density on density-masked lungs. Accordingly, 6 out of 17 classical histogram

features (e.g. mean CT density, skewness and kurtosis) precisely distinguished diseased from healthy mice with area under the curve values (AUCs) of >0.87 ($p < 0.05$) and thus detected lung remodelling. However, histogram-based features failed to differentiate between the different time points and thus stages of experimental lung fibrosis as investigated by receiver operating characteristic curve analysis and by hierarchical clustering. In contrast, 59 out of 137 texture-based radiomics features, including features describing image homogeneity or contrast detected ILD and distinguished the different stages with excellent accuracy (AUCs >0.84 ; $p < 0.05$) thus outperforming the classical histogram features.

In addition, texture-based, but not histogram-based features were associated ($R^2 > 0.5$, $p < 0.05$) with histological parameters, thereby possibly reflecting changes in lung (micro-)architecture, which may result from both inflammatory and/or fibrotic changes.

Conclusion: If confirmed in human SSc-ILD, texture-based radiomics features have great potential to provide biological and stage-specific quantitative information on lung (micro-)architecture and thus could serve as quantitative imaging biomarkers for guided decision making in SSc-ILD.

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THU0346 EVALUATION OF A NOVEL PARTICLE-BASED ASSAY FOR DETECTION OF MYOSITIS SPECIFIC ANTIBODIES

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Background: Myositis specific antibodies (MSA) represent important diagnostic tools and also help stratify idiopathic inflammatory myositis (IIM) patients with particular clinical features, treatment responses, and disease outcomes. Standardization of MSA detection is of high importance because these antibodies also have the potential to be used in classification criteria.

Objectives: The objective of this study was to evaluate the clinical performance of a novel particle based multi-analyte technology (PMAT) for the detection of MSA as an aid in the diagnosis and also in the differentiation of IIM subtypes.

Methods: The study included 464 patient samples collected at Hospital Vall d'Hebron, Autonomous University of Barcelona, most of whom had a diagnosis of IIM (n=264). As controls, samples from patients with myositis like conditions (ML, n=20), rheumatoid arthritis (RA, n=33), systemic lupus erythematosus (SLE, n=40), Sjögren's syndrome (SjS, n=25), infectious diseases (ID, n=40) and healthy individuals (HI, n=42) were included. All samples were tested using a novel fully automated particle-based multi-analyte technology (PMAT, Inova Diagnostics, research use only; Jo-1, PL-7, PL-12, EJ, Mi-2b, NXP2, SAE, TIF1y, MDA5, HMGCR, SRP) which utilizes paramagnetic particles with unique signatures and a digital interpretation system.

Abstract THU0346 –Table 1.

Analyte	IIM Subtype	Sensitivity (95% CI)	Specificity (95% CI)	Odds Ratio (95% CI)
Jo-1	ASS (n=67)	71.6% (59.9-81.0%)	98.0% (94.9-99.2%)	121.9 (40.8-360.0)
PL-7	ASS	10.4% (5.2-20.0%)	100.0% (98.1-100.0%)	+++ (5.8-+++)
PL-12	ASS	7.5% (3.2-16.3%)	100.0% (98.1-100.0%)	+++ (4.0-+++)
EJ	ASS	3.0% (0.8-10.2%)	99.5% (97.2-99.9%)	6.0 (0.7-46.8)
Mi-2	DM (n=70)	21.4% (13.4-32.4%)	97.9% (94.8-99.2%)	13.0 (4.3-38.7)
NXP2	DM	7.1% (3.1-15.7%)	98.5% (95.6-99.5%)	4.9 (1.3-19.1)
SAE	DM	11.4% (5.9-21.0%)	99.0% (96.3-99.7%)	12.4 (2.9-52.9)
TIF1y	DM	15.7% (9.0-26.0%)	96.2% (92.0-98.3%)	4.8 (1.7-13.0)
TIF1y	cDM (n=35)	62.9% (46.3-76.8%)	96.2% (92.0-98.3%)	43.2 (15.1-122.8)
MDA5	CADM (n=21)	71.4% (50.0-86.2%)	97.1% (94.2-98.6%)	84.3 (25.7-277.5)
HMGR	IMNM (n=16)	50.0% (28.0-72.0%)	96.8% (93.8-98.4%)	30.0 (9.2-98.2)

ASS = Anti-Synthetase Syndrome, DM = Dermatomyositis, cDM = Cancer Associated Dermatomyositis, CADM = Amyopathic Dermatomyositis

Results: The sensitivity/specificity of the individual MSA were: 19.7%/100% (Jo-1), 7.2%/100.0% (Mi-2), 3.0%/99.0% (NXP2), 3.8%/100.0% (SAE), 2.7%/100.0% (PL-7), 1.9%/99.5% (PL-12), 1.1%/100.0% (EJ), 15.5%/99.5% (TIF1y), 8.3%/98.5% (MDA5), 6.1%/99.0% (HMGR) and 1.9%/98.5% (SRP). The overall clinical performance was: sensitivity 68.2% (95% confidence interval 62.3-73.5%), specificity 94.0% (95% CI 89.8-96.5%) and odds ratio 33.8. In the table below, the sensitivity and specificity of each analyte for IIM subtypes was calculated along with odds ratio.

Conclusion: The novel PMAT used to detect a spectrum of MSA in IIM on a fully automated system showed good sensitivity and specificity in line with the known associations of MSA. Sensitivities and specificities of the individual MSA are within expected ranges. Lastly, the individual markers help to stratify patients into IIM subtype which is important for management of the patients.

Disclosure of Interests: Michael Mahler Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Kishore Malyavantham Employee of: Inova Diagnostics, Michaelin Richards Employee of: Inova Diagnostics, Chelsea Bentow Employee of: INOVA Diagnostics, Silvia Casas Employee of: Inova Diagnostics, Eva Balada: None declared, Maite Sanz: None declared, M. Angeles Martinez: None declared, Albert Selva-O'Callaghan: None declared

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THU0347 TESTING THE IN VITRO EFFECTS OF NINTEDANIB ON CIRCULATING FIBROCYTES AND RESIDENT SKIN FIBROBLASTS FROM THE SAME SYSTEMIC SCLEROSIS PATIENTS: PRELIMINARY RESULTS

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Background: The fibrosis in systemic sclerosis (SSc) progresses from microvascular alterations, immune system activation, and increased extracellular matrix protein synthesis into the skin and internal organs, primarily mediated by myofibroblasts.¹ Myofibroblasts are characterized by a higher expression of α -smooth muscle actin (α SMA) and by the overproduction of type I collagen (COL1) and fibronectin (FN).² Although myofibroblasts primarily derive from fibroblasts differentiation and transition, circulating fibrocytes represent a further important source.³ Nintedanib is a tyrosine kinase inhibitor that interacts with several inflammatory and profibrotic pathways implicated in the pathogenesis of fibrosis, including those of platelet derived growth factor receptors, vascular endothelial growth factor receptors and fibroblast growth factor receptors.⁴

Objectives: To investigate, in primary cultures, the effects of nintedanib on the differentiation of circulating fibrocytes and on the profibrotic activity of skin fibroblasts isolated from the same SSc patients.

Methods: Circulating fibrocytes and fibroblasts were obtained from peripheral blood and skin biopsies, respectively, from three untreated SSc patients with diffuse skin involvement (mean age 55±6 yrs). To investigate the complete differentiation, fibrocytes were maintained in DMEM at 20% of foetal bovine serum, either with or without treatment with nintedanib at the concentrations of 0.1µM and 1µM for 8 days.⁵ Fibrocytes were characterized as CD45⁺CXCR4⁺COL1⁺cells, and their percentage was detected by Flow Cytometry analysis.⁶ Fibroblasts were grown until the

3rd culture passage and then maintained in normal growth medium with or without nintedanib treatment for 4, 24 and 48 hours. The gene expressions of α SMA, COL1 and FN were evaluated by qRT-PCR.

Results: Nintedanib reduced the percentage of differentiated SSc fibrocytes (CD45⁺CXCR4⁺COL1⁺cells), already at the concentration of 0.1µM compared with untreated fibrocytes. In cultured SSc skin fibroblasts, nintedanib 1µM downregulated α SMA, COL1 and FN expressions already after 4 hours of treatment, and this effect was also maintained after 24- and 48-hours' treatment. Nintedanib 0.1µM downregulated the α SMA expression at all timepoints, whereas the downregulation of COL1 and FN expressions was observed at 4 and 24 hours, with no more effect at 48 hours of treatment compared with untreated cells.

Conclusion: Initial experiments seem to indicate an evident *in vitro* concentration-dependent antifibrotic activity of nintedanib on SSc fibrocytes and skin fibroblasts from the same SSc patients; in particular by reducing the fibrocyte differentiation as potential source of myofibroblasts and contrasting the profibrotic activity of already activated fibroblasts/myofibroblasts. These results have translational implications in clinical trials using nintedanib in SSc patients.

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THU0348 IDENTIFICATION OF CIRCULATING CELLS WITH AN HYBRID M1/M2 MACROPHAGE PHENOTYPE IN SYSTEMIC SCLEROSIS PATIENTS AND CORRELATIONS WITH SELECTED CLINICAL ASPECTS

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Background: Systemic sclerosis (SSc) is characterized by immune system alterations, vascular damage and fibrosis (1). Macrophages seem to have an emerging role in SSc, and the characterization of their polarized phenotype, starting from the dichotomic definition of classically activated (M1) or alternatively activated (M2) macrophages, is a recent research topic of interest (2).

Objectives: The study investigated a possible imbalance in the distribution of circulating cells expressing M1 and M2 markers in SSc patients (pts) compared to healthy subjects (HSs), and the presence of circulating cells co-expressing M1 and M2 surface markers. Possible correlations between their percentage and selected SSc clinical aspects were investigated.

Methods: In the study 55 SSc pts (50 females/5 males, mean age 64 ±13 yrs), fulfilling the new EULAR/ACR criteria for SSc diagnosis, and 27 age-matched HSs (25 females/2 males, mean age 57±7 yrs) were enrolled after written informed consent. Nailfold videocapillaroscopy (NVC), evaluation of SSc-related antibodies and pulmonary functional tests were performed. In particular, circulating cells belonging to the leukocyte and monocyte populations (CD45⁺ and CD14⁺ cells) were investigated by flow cytometry (FC) using the surface markers characterizing M1 (CD80, CD86, TLR2, TLR4) and M2 phenotypes (CD204, CD206, CD163). Statistical analysis was performed using Mann-Whitney and Kruskal-Wallis tests, and correlations were explored by bivariate Pearson's analysis.

Results: Increased circulating cells showing an M2 phenotype and characterized as CD204⁺CD206⁺CD163⁺ cells was observed in SSc pts compared to HSs (p<0.0001), whereas no difference in CD80⁺CD86⁺TLR2⁺TLR4⁺(M1) cell percentage was observed. A significant higher percentage of circulating cells showing a hybrid M1/M2 phenotype (CD204⁺CD206⁺CD163⁺TLR4⁺CD80⁺CD86⁺ cells) was observed in SSc pts compared to HSs. These hybrid M1/M2 cells were significantly increased in SSc pts either treated with steroids or under no immunosuppressive treatment (p<0.01; p<0.05), as well as in Scl70⁺ pts (p<0.05 vs. Scl70⁺ pts)