**Results:** The microtissues presented a core of SSc fibroblast as revealed by vimentin staining and an external layer of keratinocytes as revealed by cytokeratin 10 staining, mimicking the human skin architecture. Gene expression analysis following TGFβ stimulation displayed induced expression of extracellular matrix gene *COL1A1* (p=0.044) and the myofibroblast marker *ACTA2* (p=0.018), indicating that the microtissues were able to develop a fibrotic response. Microtissues, where H19X was silenced, displayed reduced gene expression of *COL1A1* and *ACTA2* after TGFβ stimulation (*COL1A1* p=0.007, *ACTA2* p=0.045). Additionally, H19X silencing led to lower levels of αSMA protein expression (p=0.009) and pro-collagen1α1 secretion (p=0.039) in the supernatant of the microtissue cultures as revealed by Western Blot and ELISA, respectively. *FN1* expression and fibronectin protein levels were not significantly reduced in the microtissues after H19X silencing.

**Conclusion:** We were able to produce a 3D microtissue resembling skin architecture that can respond to fibrotic stimuli. Knockdown experiments of pro-fibrotic lncRNA H19X confirmed the potential of the model as screening platform for novel pro-fibrotic effectors. A future aim will be to optimize the model for high-throughput automated screening platforms.

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## OP0249 SERUM PROTEOMIC BIOMARKERS DEFINE PATIENTS WITH SYSTEMIC SCLEROSIS WITH INTERSTITIAL LUNG DISEASE

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**Background:** Systemic sclerosis (SSc) is a systemic condition affecting multiple organs and thus being burdened by high morbidity and mortality; disease management is based largely on the early detection of organ involvement, particularly in the case of interstitial lung disease (ILD), ideally through noninvasive biomarkers. Beside serum autoantibodies associated with diffuse SSc, there is currently no reliable serum marker to predict the onset of SSc organ involvement, monitor its progression, and foresee the response to treatments. Proteomic analysis based on aptamer technology is a powerful method with the potential to address this unmet need in SSc.

**Objectives:** To identify serum biomarkers associated with ILD in SSc.

**Methods:** Serum samples from 6 women with SSc (3 with ILD at high-resolution pulmonary CT scan) and 7 age-matched female healthy controls (HC) were analyzed using the SOMAscan platform (SomaLogic, Inc., Boulder, CO, USA) to test more than 1300 proteins even at femtomolar concentration. Subsequent validation of candidate proteins was performed using ELISA in an independent cohort of 88 patients with SSc and 48 HC. Statistical analysis included Student's t-test and was assessed using the SomaSuite software (SomaLogic, Boulder, CO, USA).

**Results:** The proteomic analysis identified 33 proteins with significantly different serum levels in SSc cases compared to HC and 9 proteins differentiating SSc patients according to ILD (Table 1). Compared to HC, SSc sera manifested an altered expression of proteins involved in extracellular matrix formation and cell-cell adhesion (with higher Calpain, EphA5, IDS, MATN2, MMP-12, TNR4, and lower desmoglein-1, SNP25), angiogenesis (with higher anti-angiogenetic factors as angiopoietin-2 and kininogen high molecular weight) lymphocyte recruitment, activation, and signaling (with higher CXCL-1, LAG3 and lower SH21A) with an overall inhibition of neutrophil function (with lower G-CSF-R, CD177, calgranulin B).

**Table 1. Significantly altered proteins at serum proteomic analysis of systemic sclerosis (SSc) with or without interstitial lung disease (ILD) and healthy controls (HC)**

| SSc versus healthy controls | | SSc with ILD versus SSc without ILD and healthy controls | |
|---|---|---|---|
| Increased | Reduced | Increased | Reduced |
| Aldolase A | Adrenomedullin | FCRL3 | BAFF |
| Angiopoietin-2* | ASGR1 | IL-22BP** | DERM |
| C1QR1 | C1s | MCP-3 | |
| Calpain | C5 | PDE11 | |
| COLEC12 Eotaxin | Calgranulin B | PGP9.5 | |
| EphA5 | CD177 | sICAM-5 | |
| Fractalkine/CXCL-1 | Desmoglein-1 | Stratifin | |
| Granulins | Flt-3 ligand | | |
| IDS Kininogen, HMV | G-CFS-R | | |
| LAG-3 | IL-1Ra | | |
| Lamin-B1 | Leptin | | |
| LRP1b | Lypd3 | | |
| MATN2 | SH21A | | |
| MMP-12 | SNP25 | | |
| STAT1 TMR4 | TPBS2 | | |

*significantly increased also at ELISA** significantly increased at ELISA only in SSc with ILD versus HC

The majority of proteins with higher levels in SSc with ILD compared to SSc without ILD were involved in intracellular signaling and cell cycle (FCRL3, PDE11, Stratifin), along with higher MCP-3, a monocyte chemoattractant, and sICAM-5, ligand for the leukocyte adhesion protein LFA-1. Of note, we found that increased IL-22BP, antagonist of IL-22, and decreased BAFF levels characterized SSc with ILD.

**Conclusion:** Aptamer proteomic analysis allowed to define serum profiles differentiating SSc patients from healthy controls and SSc with ILD from SSc without ILD; the proteins identified are involved in SSc pathogenic pathways and after further investigation on larger cohorts they can be used as reliable biomarkers.

**Characters from table content including title and footnotes:** 631

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# Imaging in axial spondyloarthritis – what is new?

## OP0250 MRI VERTEBRAL CORNER INFLAMMATION AND FAT DEPOSITION ARE ASSOCIATED WITH WHOLE SPINE LOW DOSE CT DETECTED SYNDESMOPHYTES: A MULTILEVEL ANALYSIS

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**Background:** A few studies have shown an association between vertebral corner inflammation (VCI) and vertebral corner fat deposition (VCFD) on MRI and syndesmophyte formation on cervical and lumbar conventional radiography.

**Objectives:** To investigate whether magnetic resonance imaging (MRI) patterns of VCI, VCFD and a combination of both are associated with the development of new or grown syndesmophytes as detected by whole spine low dose computed tomography (ldCT), thereby studying these associations also in the thoracic spine.

**Methods:** Patients in the Sensitive Imaging in Ankylosing Spondylitis cohort underwent MRI at baseline, 1 year and 2 years, and ldCT at baseline and 2 years. MRI lesions were scored by 3 central readers, using the SPARCC method for VCI and the CanDen method for VCFD, and coded as absent or present per timepoint and per reader. MRI patterns over time (Table) were based on patterns studied by Machado et al.[1] and deemed present if seen by ≥2 out of 3 readers. The patterns reflect hypothetical associations between presence and absence of VCI and VCFD, independently and combined, on ldCT detected new or grown syndesmophytes. Individual reader change scores were used for ldCT images, scored by 2 central readers with the Computed Tomography Syndesmophyte Score. New (CTSS 0 to 1, 2 or 3) and grown (CTSS 1 to 2 or 3; 2 to 3) syndesmophytes were grouped together to represent bone formation. Corners not at risk

for the outcome due to presence of a bridged syndesmophyte at baseline were excluded. Multilevel generalized estimated equations were used, with separate models per MRI pattern, accounting for correlations within patients and between ldCT readers.

**Table 1. Effect of vertebral corner inflammation and vertebral corner fat deposition on syndesmophyte formation**

| Patterns of lesions over time on MRI | Corners with VCI/ VCFD pattern N(%) | OR (95% CI) |
|---|---|---|
| 1. VCI at any TP, irrespective of VCFD | 691 (15.0%) | **2.37 (1.49-3.78)** |
| 2. VCFD at any TP, irrespective of VCI | 1080 (23.5%) | **2.58 (1.97-3.39)** |
| 3. VCI on ≥1 TP and absence of VCFD on all TPs | 372 (8.1%) | **1.90 (1.15-3.13)** |
| 4. VCFD on ≥1 TP and absence of VCI on all TPs | 754 (16.4%) | **1.87 (1.41-2.48)** |
| 5. VCI precedes VCFD | 43 (0.9%) | 2.20 (0.83-5.86) |
| 6. VCI precedes or coincides with VCFD. VCFD does not precede VCI | 198 (4.3%) | **2.33 (1.47-3.69)** |
| 7. Absence of VCI and VCFD on all TPs | 3108 (67.6%) | **0.35 (0.25-0.49)** |

VCI, vertebral corner inflammation; VCFD, vertebral corner fat deposition; TP, timepoint.

**Results:** 50 patients were included, contributing a total of 4600 vertebral corners. Their mean age was 49.3 years (SD 9.8), 86% were male and 78% were HLA-B27+. Presence of VCI and VCFD patterns ranged from 43 (0.9%) to 3108 (67.6%) corners (Table), with the lowest frequency being for VCI preceding VCFD. Protection against syndesmophyte development was seen in case of absence of both VCI and VCFD (OR 0.35) and positive associations with ORs ranging from 1.87-2.58 were observed for various VCI/VCFD patterns. Nevertheless, out of all corners with a new or grown syndesmophyte, 47.3% of corners according to reader 1 and 43.9% according to reader 2 had neither VCI nor VCFD preceding the bone formation.

**Conclusion:** Presence of VCI or VCFD and combinations of the two, measured yearly on MRI, increased odds of bone formation 2 years later, whereas absence of both VCI and VCFD decreased the odds, showing that VCI and VCFD have some role in the development of syndesmophytes. However, almost half of all bone formation occurred in corners without VCI or VCFD, suggesting the presence of these lesions in yearly MRIs does not fully explain the development of syndesmophytes. This study confirmed that there is an association between VCI and VCFD and bone formation also for the thoracic spine and on ldCT compared to conventional radiography.

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## OP0251 DATA-DRIVEN DEFINITIONS BASED ON INFLAMMATORY LESIONS FOR A POSITIVE MRI OF THE SPINE CONSISTENT WITH AXIAL SPONDYLOARTHRITIS

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**Background:** The ASAS definition of a positive MRI for inflammation in the spine (ASAS-MRIspine+) is intended for classification of patients as having axSpA but is often misused for diagnostic purposes. This is problematic because bone marrow edema (BME) in the spine may occur in 20-40% of those with mechanical back disorders. The ASAS MRI group has generated updated consensus lesion definitions which have been validated on MRI spine images from the ASAS Classification Cohort.

**Objectives:** We aimed to identify quantitative cut-offs based on numbers of vertebral corners that define ASAS-MRIspine+, there being two gold standards: A. majority central reader decision as to the presence of spine MRI findings consistent with axSpA B. rheumatologist expert opinion diagnosis of axSpA.

**Methods:** Eight ASAS-MRI readers recorded MRI lesions in the spine according to recently updated ASAS definitions from 62 cases in an eCRF that comprises global assessment (MRI consistent with axSpA? (yes/no)), and detailed scoring of lesions for all sites in the spine. We calculated sensitivity and specificity for numbers of vertebral corners with BME where a majority of readers (≥5/8) agreed as to the presence of MRI findings consistent with axSpA. We selected cut-offs with ≥95% specificity. These cut-offs were analyzed for their predictive utility for rheumatologist diagnosis of axSpA by calculating positive and negative predictive values (PPV, NPV) and selecting cut-offs with PPV ≥95%. Both criteria were considered requirements for designation of MRI cut-offs defining ASAS-MRIspine+.

**Results:** MRI findings consistent with axSpA were observed by majority read in 8 (20%) of 40 cases diagnosed with axSpA, and 0 (0%) of 19 cases without axSpA. Cut-offs achieving specificity of ≥95% for MRI findings consistent with axSpA were 4 vertebral corners (sensitivity 75%) for all cases, 3 vertebral corners (sensitivity 37.5%) for cases with ≥1 additional location with inflammation, 1 vertebral corner (sensitivity 62.5%) in cases with ≥2 vertebral corner fat lesions (Table 1). All of the above cut-offs also had very high PPV (≥95%) for diagnosis of axSpA in cases diagnosed by the rheumatologist (Table 2).

**Table 1. Majority readers agree MRI findings consistent with axSpA are present is the gold-standard external reference**

| MRI cut-offs | Sensitivity (95%CI) | Specificity (95%CI) |
|---|---|---|
| BME in ≥2 vertebral corners | 87.5 (47.3 - 99.7) | 87.0 (75.1 - 94.6) |
| BME in ≥ 3 vertebral corners | 87.5 (47.3 - 99.7) | 94.4 (84.6 - 98.8) |
| **BME in ≥4 vertebral corners** | **75.0 (34.9 - 96.8)** | **98.2 (90.1 - 100.0)** |
| **Cases with ≥1 additional non-corner site inflammatory lesion** | | |
| BME in ≥2 vertebral corners | 37.5 (8.5 - 75.5) | 94.4 (84.6 - 98.8) |
| **BME in ≥3 vertebral corners** | **37.5 (8.5 - 75.5)** | **98.2 (90.1-100.0)** |
| **Cases with ≥2 vertebral corner fat lesions** | | |
| **BME in ≥1 vertebral corner** | **62.5 (24.5 - 91.5)** | **100.0 (93.4-100.0)** |
| BME in ≥2 vertebral corners | 62.5 (24.5 - 91.5) | 100.0 (93.4-100.0) |

**Table 2. Predictive values of cut-offs for number of vertebral corners with BME according to the diagnostic ascertainment of the rheumatologist**

| MRI cut-offs | Sensitivity (95%CI) | Specificity (95%CI) | PPV | NPV |
|---|---|---|---|---|
| MRI findings consistent with axSpA ≥any 2 readers | 52.5 (36.1 - 68.5) | 94.7 (74.0 - 99.9) | 95.5 (75.3 - 99.3) | 48.6 (40.2 - 57.2) |
| MRI findings consistent with axSpA ≥majority read | 20.0 (9.1 - 35.6) | 100.0 (82.4 - 100.0) | 100.0 | 37.3 (33.7 - 40.9) |
| **BME in ≥ 4 vertebral corners** | **17.5 (7.3 - 32.8** | **100.0 (82.4 - 100.0)** | **100.0** | **36.5 (33.3 - 39.9)** |
| **Cases with ≥1 additional inflammatory lesion** | | | | |
| **BME in ≥ 3 vertebral corners** | **10.00 (2.8 - 23.7)** | **100.00 (82.4 - 100.0)** | **100.0** | **34.5 (32.2 - 36.9)** |
| **Cases with ≥2 vertebral corner fat lesions** | | | | |
| **BME in ≥1 vertebral corner** | **12.50 (4.2 - 26.8)** | **100.00 (82.4 - 100.0)** | **100.0** | **35.2 (32.6 - 37.9)** |

**Conclusion:** A cut-off of BME in ≥4 vertebral corners, or ≥3 corners in the setting of additional inflammatory lesions at other locations or corner fat, are primary candidates for defining ASAS-MRIspine+. These cut-offs apply to typical patients referred to a rheumatologist with a high index of suspicion of axSpA and may not be appropriate in other populations.

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## OP0252 ARTHRITIS AND ENTHESITIS IN THE HIP AND PELVIS REGION IN SPONDYLOARTHRITIS – VALIDATION OF TWO WHOLE-BODY MRI METHODS

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