

FRI0580 **QUANTITATIVE MRI OF SINGLE VS. MULTIPLE JOINTS IN JUVENILE IDIOPATHIC ARTHRITIS AS PREDICTIVE MEASURE OF CLINICAL OUTCOMES**

N. Tzaribachev¹, O. Kubassova², M. Hinton², M. Boesen³. ¹*Pediatric Rheumatology Research Institute, Bad Bramstedt, Germany;* ²*IAG, London, UK;* ³*Department of Radiology, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark*

Background: Clinical examination of juvenile idiopathic arthritis (JIA) patients does not always adequately reflect disease activity, whereas quantitative Dynamic Contrast Enhanced (DCE)-MRI based biomarkers extracted from images of multiple joints have been shown to reliably predict the course of the disease¹.

Objectives: To investigate the association between DCE-MRI measures of inflammation in a single and in multiple joints and the treatment related clinical changes.

Methods: 18 patients (12 girls, med. age 12.6 years, med. disease 1.2 years) with polyarticular JIA with more than 3 affected joints or intolerance to more than 3 months of MTX were given Etanercept. Their most clinically affected hand was imaged with DCE-MRI (0.2T Esaote C-Scan) at baseline, 3 and 6 months following the treatment. DCE-MRI was analysed using dedicated software package (DYNAMIKA, IAG). Dynamic Enhanced MRI Quantification (DEMRIQ-V) was calculated as the volume of enhancing voxels within Region of Interest placed around a single or multiple MCPJs. DEMRIQ-V was also weighted by the mean of Maximum Enhancement (ME) and Initial Rate of Enhancement (IRE), the parameters corresponding to the height and slope of the signal intensity vs time curves extracted from the enhancing voxels.² Clinical scores included active joint (AJ) count. Involvement of less than 3 AJ was considered a clinical response. The differences in DEMRIQ-V between the visits were analysed using t-test, assuming $p < 0.05^*$ to be statistically significant and $p < 0.025^{**}$ to be clinically meaningful.

Results: In all patients, in clinically unaffected joints, MRI was able to detect sub-clinical disease, and in all but 3 patients, significant and/or clinically meaningful changes were documented for DEMRIQ-ME. In 4 patients, DEMRIQ-V scores showed corresponding clinical changes whereas all other patients these markers were non-concordant. DEMRIQ-V score was predictive of clinical outcome:

- in 5 patients, improvement of DEMRIQ-V at month 3 predicted response to treatment at month 6;
- in 4 patients, increase or persistence of a high DEMRIQ-V at month 3 predicted non-response to treatment at month 6;
- DEMRIQ-V measured in a single most affected joint was as predictive as when it was measured in all MCPJs.

Conclusions: We conclude that DCE-MRI's ability to detect early disease can reliably support clinical examination. Use of DEMRIQ-V and DEMRIQ-ME scores, which either followed clinical response (DEMRIQ-ME) or predicted clinical outcomes at 6 months (DEMRIQ-V) in most patients can support early clinical and research decisions.

REFERENCES:

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FRI0581 **ULTRASONOGRAPHY IN THE DETECTION OF JOINT DESTRUCTION IN RA PATIENTS: A COMPARISON WITH CONVENTIONAL RADIOGRAPHY**

O. Alekseeva, A. Smirnov, S. Glukhova, A. Volkov, E. Nasonov. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia, Moscow, Russian Federation*

Background: RA evolves erosive polyarthritis resulting in destructive changes in the joints. Ultrasonography (US) is used in current practice as early diagnostic modality for identification of structural damage to the articular surfaces.

Objectives: To compare US and radiographic assessment of hands and feet joint destruction in RA patients, and to evaluate the contribution of early US detection of damage into long-term RA outcomes.

Methods: 75 patients with RA, mean age 54.0,^{44,0;} ^{62,0} disease duration ^{74;} ²⁰ months, were treated with MTX and biologics according to Treat-To-Target concept. Hands and feet US were analysed before initiation of treatment and in 3, 6, 9 and 12 months after. Deepening of the bony contour >2 mm in width and >1 mm

in depth, visualised in 2 orthogonal planes, was considered as the key US sign of destructive changes (erosions) according to OMERACT criteria. A binary scoring system (presence/absence of erosions) of the joints examined was used. Radiographs were obtained at baseline, at 12 month and 4 years, radiographic changes were assessed using Sharp/van der Heijde modified scoring method. Radiographic progression was documented based on Sharp/Van der Heijde modified score changes during the follow up.

Results: There was a significant correlation between the counts of joints with erosions obtained with two diagnostic methods – US and radiography. This correlation was moderate before initiation of therapy ($r=0,37$; $p=0,0008$), and weak – after 12 month follow up ($r=0,28$ $p=0,016$). During one year US showed increase in the count of joints with erosions (from 1 [0; 2] to 2^{1:3}) while radiography did not show any significant change (from 0 [0; 1] to 0 [0; 1]).

Bland-Altman analysis showed statistical agreement between the results obtained by two methods. Mean difference between the two modalities before initiation of treatment was $-0,42$ (95% CI $-0,68$; $-0,16$), and at 12 month follow up $-1,16$ (95% CI $-1,52$; $-0,80$), which is comparable with actual values. We identified the relationship between the difference in variables and the count of affected joints before and 12 month after initiation of treatment ($r=-0,35$, $r=-0,53$ respectively). 8% of variables were outside 2 standard deviations at baseline, and 4% – at 12 month. Logistic regression analysis showed no relationship between annual radiological progression and US diagnosed increasing count of joints with erosions at 3, 6 and 9 months follow up. However, dynamic radiographs assessment at 4 years revealed a correlation with US diagnosed count of joints with erosions at 6 month and 9 month follow up ($r=0,24$, $p=0,03$; $r=0,24$, $p=0,04$, respectively). Quality indicator of US diagnosed count of erosions at 6 month follow up: OR=2,8 95% CI 1.05–7,5, $p=0,037$, with 71% sensitivity and 54% specificity; Quality indicator of US diagnosed count of erosions at 9 month follow up: OR=2,73 95% CI 1.02–7,27, $p=0,041$, with 64% sensitivity and 61% specificity. Quantitative assessment of the dynamics at these time periods did not show any relationship.

Conclusions: Therefore, our study confirms the relevance of US in assessment of bone erosions in spite of weak agreement with radiography data. We found a prognostic value of US-diagnosed erosions during the first year of follow up for long-term (4 years) clinical outcomes, and the relevance of control assessment at 6 month after initiation of treatment.

Disclosure of Interest: None declared

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FRI0582 **CHANGE IN MUSCLE VOLUME AND MUSCLE FAT FRACTION AS POTENTIAL NON-INVASIVE BIOMARKERS OF DISEASE PROGRESSION: MACHINE LEARNING FRAMEWORK FOR QUANTITATIVE ANALYSIS OF MRI DATA**

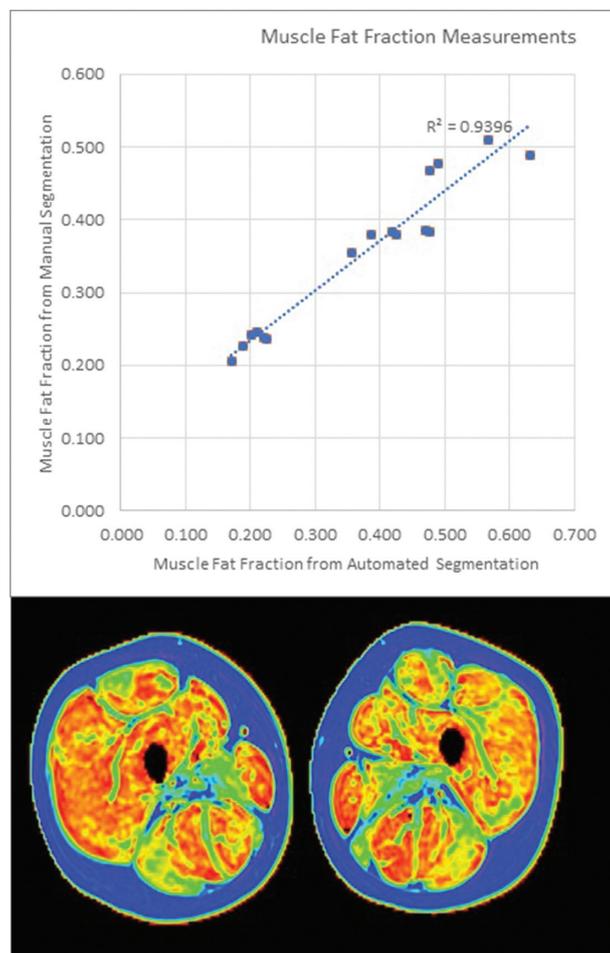
D. Fischer¹, P. Hafner¹, S. Schmidt¹, M. Hinton², J. Gonzalez², O. Kubassova². ¹*Division of Neuropaediatrics, University of Basel Children's Hospital, Basel, Switzerland;* ²*IAG, London, UK*

Background: Change in muscle volume and muscle fat fraction are potential non-invasive biomarkers of disease progression in a number of diseases, including sporadic inclusion body myositis¹ and osteoarthritis². Their measurement from magnetic resonance images (MRI) usually involves time consuming manual segmentations of the images by trained readers, which limits the use of these biomarkers in clinical research and practise.

Objectives: In this study, we present a novel unsupervised k-means-classifier based image processing framework, developed for machine learning approach to segmentation of thigh muscles from MRI and the subsequent calculation of fat fraction from Dixon images. Further, we present validation of the new approach against manual segmentation using longitudinal retrospectively acquired data.

Methods: Axial MR images from the upper thighs including in-phase and out of phase sequences were recorded in a group of 8 subjects at baseline and at a follow up. The 16 imaging time points were manually segmented by an expert reader, who delineated the muscle. For these regions the mean fat fraction was calculated from the in-phase and out of phase Dixon images. The fully automated segmentation was then run on the same images and the resulting fat fractions compared with the manual results. The proposed k-means approach classifies each image pixel according to signal intensity and creates image masks for bone, muscle and fat in three dimensions. The pixel counts from bone, muscle and fat are automatically measured to produce the volume and mean fat fraction.

Results: We compared the mean fat fraction for the two approaches and found linear correlation was good ($R^2=0.9396$). Manual segmentations typically took 40 min or more to execute, compared to the automated segmentations, which required less than 5 min on a standard desktop computer



Example Fat Fraction Map

Abstract FRI0582 – Figure 1. Example Fat Fraction Map

Conclusions: In the present study, we reported a segmentation framework based on unsupervised k-means to measure muscle volume and fat fraction. It offers time savings versus manual segmentations and correlates well with fat fraction measurements. This could be useful for muscle quantification in the fields of osteoarthritis, sports medicine and rehabilitation. Further studies are planned to compare sensitivity of automatically acquired measures to clinical progression.

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FRI0583

CLINICAL UTILITY OF ANA-ELIA VS ANA-IMMUNOFLUORESCENCE IN CONNECTIVE TISSUE DISEASE

O. Alsaed¹, L. Alamilah¹, O. Al-Radideh², M. Elkhalfa³, A.-W. Al-Allaf¹. ¹*Medicine/Rheumatology*; ²*Internal Medicine*; ³*laboratory medicine and pathology, Hamad Medical corporation, Doha, Qatar*

Background: Antinuclear antibody (ANA) detection by indirect immunofluorescence technique (ANA-IIF) is the standard test for connective tissue disease (CTD) screening for last 5 decades, which has low specificity and it is labour intensive. ANA detection by fluoroenzyme immunoassay (ANA-Elia) has been developed recently as an alternative method to include 17 ANA-targeted recombinant antigens.

Objectives: Compare the sensitivity and specificity of the new ANA-Elia with conventional ANA-IIF.

Methods: Randomly selected 1458 patient's sera from primary and secondary health care were tested for both the standard ANA-IIF (Diasorin S.P.A, saluggia, Italy) and the new ANA-Elia (Phadia GmbH, Ferieiburg, Germany). ANA-Elia is fluoroenzyme immunoassay performed on the Phadia-250 automated platform. It contains 17 ANA-targeted recombinant antigens; dsDNA, Sm-D, Rib-P, PCNA, U1-RNP (70, A, C), SS-A/Ro (52 and 60), SS-B/La, Centromere B, Scl-70, Fibril-larin, RNA Polymerase III, Jo-1, Mi-2, and PMScl. Result with ratio >1.0 considered positive for the new technique. For ANA-IIF our lab cut off for positive test is $\geq 1:80$. Patients were evaluated in our rheumatology clinic for fulfilling the corresponding international clinical criteria for various connective tissue diseases.

Results: 75.7% were females with mean age of 43 ± 13 years. 201 (11.5%) patients confirmed to have clinical CTD as follow: 142 SLE, 24 Sjogren's syndrome, 15 scleroderma, 7 MCT, 10 Myositis and 10 undifferentiated CTD. The specificity of ANA-Elia at cut off ratio of >1 and ANA-IIF at titer of $\geq 1:80$ was almost equal, 88.5% and 87.6% respectively. However, ANA-Elia has higher sensitivity (74.5%) as compared to ANA-IIF (61.6%). At a higher cut off ratio of >2 and titer of $\geq 1:160$, the specificity improved to 93.6%–92.6% respectively.

	ANA-Elia		ANA-IIF	
	>1	>2	$\geq 1:80$	$\geq 1:160$
Sensitivity	74.5%	67.6%	61.6%	50.7%
Specificity	88.5%	93.6%	87.6%	92.6%

Conclusions: The ANA testing with the newly developed, use friendly, fully automated and less labour intense method of ANA-Elia can replace the standard conventional ANA-IIF with better specificity.

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FRI0584

FLUORESCENCE OPTICAL IMAGING ENHANCEMENT IS ASSOCIATED WITH JOINT PAIN IN HAND OSTEOARTHRITIS

O. Maugesten¹, S. Ohrndorf², S.V. Hestetun¹, B. Slatkowsky-Christensen¹, T. K. Kvien¹, T. Uhlig¹, I.K. Haugen¹. ¹*Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*; ²*Dept. of Rheumatology and Clinical Immunology, Charité Univ.smedizin, Berlin, Germany*

Background: Joint inflammation plays a role in the pathogenesis of hand osteoarthritis (OA), and previous studies have presented an association between pain and synovitis detected by MRI and ultrasound. No previous hand OA studies have explored the validity of fluorescence optical imaging (FOI), a novel imaging technique demonstrating altered microcirculation in wrist and finger joints, as a sign of inflammation.

Objectives: The aims of the current study were to quantify the distribution of FOI findings in different joint groups in hand OA patients and explore the association between FOI findings and self-reported pain and tender joints on clinical examination.

Methods: The NOR-HAND study is an observational hand OA study, in which 251 patients (88% female, median age 61 (interquartile range 56–66) years) underwent FOI of both hands, bilateral clinical examination for tender joints on palpation and movement, and self-reported their pain in individual joints during the last 24 hours and the last 6 weeks on the homunculus. The FOI-scan was performed after the administration of an intravenous fluorescence dye (indocyanine green, ICG) and 360 images (1/second) were produced in 6 min. Based on the inflow and washing out of the dye the pictures were divided into 3 phases. Ultimately, the prima vista mode (PVM) represented a composite picture of the first 240 images of the examination. For each phase, fluorescence enhancement in the joints was graded from 0–3 based on signal intensity (grade 1=diffuse red, grade 2=intense red and diffuse white <50% of the joint, grade 3=intense white >50% of the joint). To study the association between FOI findings and pain in the same joint we applied logistic regression analyses with generalised estimating equations adjusting for age and sex. Separate models were applied for each of the FOI phases and pain outcomes.

Results: The median (interquartile range) number of DIP/PIP joints with FOI enhancement within each patient ranged from 0 (0–0) in phase 1, 14^{11-16} in phase 2, 3 (0–8) in phase 3 and 9^{7-11} in PVM. CMC-1 and MCP-joints showed no and uncommon enhancement on the examination, respectively, regardless of the phase, and the associations between FOI and pain were therefore analysed in the DIP and PIP joints only. FOI enhancement in the DIP and PIP joints was associated with pain in the same joint, consistent for all three pain outcomes. A dose-