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First clinical evaluation of sagittal laser optical tomography for detection of synovitis in arthritic finger joints

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Abstract

Objective: To identify classifiers in images obtained with sagittal laser optical tomography (SLOT) that can be used to distinguish between joints affected and not affected by synovitis.

Methods: 78 SLOT images of proximal interphalangeal (PIP) joints II-IV from 13 patients with rheumatoid arthritis (RA) were compared with ultrasound (US) images and clinical examination (CE). Using light transmission measurements SLOT images that show the spatial distribution of scattering and absorption coefficients within the joint cavity were generated. The means and standard errors for seven different classifiers (operator score and 6 quantitative measurements) were determined from SLOT images with CE and US as diagnostic reference methods. For classifiers showing significant differences between affected and non-affected joints ROC-analysis was performed to calculate sensitivities and specificities for various cut-off parameters.

Results: For 5 classifiers used to characterize SLOT images the mean between affected and unaffected joints was statistically significant using US as diagnostic reference, while mean values of only 1 optical classifier showed statistically significant difference between affected and unaffected joints with CE as diagnostic reference. In general, high absorption and scattering coefficients in and around the joint cavity are indicative of synovitis. ROC-analysis showed that the minimal-absorption classifier yields the largest area under the curve (0.777; sensitivity and specificity 0.705 each) with US as diagnostic reference.

Conclusion: We have identified classifiers in SLOT images that show statistically significant differences between joints with and without synovitis. We demonstrated for the first time that it is possible to classify a joint as inflamed with SLOT, without the need for a reference measurement. Furthermore, SLOT based diagnosis of synovitis agrees better with US diagnosis than CE.

Key words: Rheumatoid arthritis, synovitis, finger joint, imaging methods, optical tomography
INTRODUCTION

Proximal interphalangeal (PIP) and metacarpo-phalangeal finger joints are usually among the first to be affected in rheumatoid arthritis (RA), and considered to be the best markers of overall joint damage in RA patients (1). Precise assessment of disease activity in RA is important for monitoring treatment efficiency and predicting the outcome of the disease. To use new RA treatment with TNF-alpha antagonists effectively it is important to establish an early diagnosis (2-4) and perform a sensitive follow-up analysis of synovitis to evaluate treatment efficiency (5). Therefore there is need for user friendly and inexpensive diagnostic techniques to fulfil these goals without side effects so that larger populations can be screened and benefit from new treatments.

The last decade has seen an increasing use of various imaging modalities such as computed tomography, ultrasonography (US), and magnetic resonance imaging (MRI) for diagnosis and assessment of RA (6). Conventional radiography as standard method of identifying progressive joint damage usually overlooks inflammatory soft tissue changes. MRI has shown strength in detecting early synovitis (6-9), but requires the use of contrast agents, is comparatively expensive, and involves long data acquisition times. US is particularly useful for the assessment of soft tissue structures and superficial bone lesions (10, 11), and it has been reported that Doppler US is sensitive for detecting active synovitis (9, 12-15). But Doppler US is not widely used yet for RA diagnostics, as the documentation is time consuming and accurate interpretation of US images requires considerable observer training.

Recently, optical methods that rely on transillumination measurements have emerged as potential new tools for detecting joint inflammation in RA (16-25). This technique uses low-level, non-ionizing near-infrared radiation and promises to provide a low cost, patient friendly joint imaging modality. In-vitro studies proved that there are significant differences in optical properties between normal and pathological joint tissue (16-18). Extensive numerical and experimental phantom studies suggested that these differences should be detectable with transillumination measurements in-vivo on the joint (19-25). In previous clinical studies, we showed that optical transmission measurements could be used for monitoring synovitis progression in RA patients (5, 26). In these studies, transillumination profiles of the joint obtained in subsequent visits were compared to transillumination profiles of the same joint obtained at the first visit. A determination concerning the status of joint inflammation, however, was not possible without the reference to an earlier measurement.

Klose et al. (25) have argued that the need for reference measurements could be overcome if tomographic images of the distribution of optical properties inside the joint were obtained. We therefore have recently developed a sagittal laser optical tomographic (SLOT) imaging setup that acquires transmission profiles and uses the data for tomographic image reconstruction of sagittal sections through the joint (27-29). SLOT images show the spatial distribution of two different optical properties (absorption coefficient, $\mu_a$, and scattering coefficient, $\mu_s$) inside the joint and surrounding tissues. In a small number of case studies, SLOT images could be used to distinguish between joints affected and not affected by synovitis, without a reference to a previous measurement on the same finger (28). Healthy joints showed a distinct reduction in $\mu_a$ and $\mu_s$ in the joint cavity as compared to the surrounding tissue, whereas joints with synovitis showed little variation in $\mu_a$ and $\mu_s$ across the joint (28).

The goal of the study at hand was to go beyond single case studies and identify classifiers in SLOT images that can be used to distinguish between joints with and without synovitis.
PATIENTS AND METHODS

Patients and clinical data
Thirteen patients (10 women and 3 men, mean age 46±12 years, range 17–63 years) with RA according to the ACR criteria (30) were included in the study. Patients were recruited from the Department of Rheumatology and Clinical Immunology, Charité University Hospital. All patients were under medication of cortisone and disease modifying antirheumatic drugs. Mean disease duration between onset of disease and inclusion into study was 4.3±3.3 years.

The clinically predominant hand was selected for clinical examination (CE) as well as SLOT and US examinations. Only PIP joints II–IV were included in the study since they were most easily accessible with optical scanning device and patients expressed some discomfort when placing other joints into our experimental setup. In total, 78 tomographical images were generated and compared to US and CE, which were performed by one investigator (AKS) blinded to the results. The study was approved by the local ethics committee and all patients gave informed consent prior to investigation.

Clinical examination of each PIP joint was performed by bi-manual palpation performed by a single physician (AKS) with long clinical diagnostic experience. Each PIP joint was examined and the clinical arthritis activity was classified from 0-3 (“degree of synovitis”). It was considered inactive (0) if the joints were not swollen or tender; moderately active (1); active (2); or very active (3), respectively (5). In addition, Disease Activity Score-28 (DAS-28) representing the overall disease activity was assessed at all consultations (31).

Imaging Methods
Conventional radiographs were taken of the hands of all patients. Since the study focuses on synovitis, we wanted to exclude possible interferences in optical measurements by bone lesions and therefore excluded patients with extensive bone erosions from the study.

Ultrasound imaging was performed with an ATL, HDI-3500 ultrasound system (Bothell, USA). We used a 10-5MHz hockey stick linear array transducer for examination of the PIP joints. Examples of US images taken from the palmar side are shown in Figure 1. No synovitis can be seen in Figure 1a, while Figures 1b-d shows joints with inflammation to different degree. In US, two criteria of active inflammation were evaluated: Joint effusion was visible as an anechoic area between the capsule and the bone in the proximal part from the palmar side of the hand (Figure 1b-d). Second, thickening of the synovial membrane could be visualized as hyper-echoic structures within the region affected by effusion (Figure 1c, d). The degree of joint effusion and hypertrophy was classified on a 4-grade semi-quantitative ultrasound examination score (USS) according to an adjusted score by Szkudlarek et al. (15) (Figure 1a-d). They described synovitis and effusion by separate scores (15). Since both processes mainly appear at the same time, we applied a combined score: When neither effusion nor synovial hypertrophy was visible a USS=0 was assigned. The larger the anechoic area and/or extent of synovial hypertrophy was, the higher was USS (USS=1 minimal, USS=2 moderate, USS=3 extensive effusion/hypertrophy). We performed US from palmar because we found that synovitis and effusion can best be evaluated from the palmar as opposed to the dorsal side. This is probably due to the small amount of tissue overlying the joint from the dorsal side.

Sagittal laser optical tomography (SLOT) was performed with an optical scanning setup recently developed in our laboratories (27-29). The system comprised a single laser-diode, a silicon photo detector, and an arrangement for hand and finger placement (Figure 2). A diode laser (wavelength $\lambda=675$nm) was focused to a spot of approximately 0.3mm in diameter dorsal with a photo detector palmar of the finger joint. Both were attached to stepping motor-driven translation stages. For measurements, the hand and finger was placed inside a specially designed box filled with water. For each laser-diode position, the detector was scanned along the sagittal plane to collect light transmission intensities from 16 positions (3cm range). After finishing the
detector scan, the laser-diode was moved a small distance and the photo-diode performed another scan, etc. This procedure was performed for 11 different laser-diode positions, so that multiple transmission profiles were obtained. Data acquisition (11 source positions, 16 detector positions) for each finger joint took about 3-4 minutes. The measurement data served as input to a model-based iterative image reconstruction (MOBIIR) scheme previously tested in our laboratories. This algorithm provides 2-dimensional images of the absorption and scattering coefficients ($\mu_a$ and $\mu_s$) in a sagittal plane through the joint (26-28; 32-36). The time needed for reconstruction of one image is approximately 2 hours on a 1.2 GHz Xenon processor.

The images of $\mu_a$ and $\mu_s$ distributions were analyzed in various different ways. Based on our previous experience (27, 28), images were assigned an optical operator score ranging from 1 to 5 to perform ROC analysis. A score of 1 was given to images that showed a pronounced drop of $\mu_a$ and $\mu_s$ in the joint cavity (Figure 3a). In our earlier pilot studies we found that to be an indication that a joint is “definitely not affected by synovitis”. A score of 5 was given when the image showed no spatial variation in optical properties or an increase in optical properties in the joint cavity (Figure 3e). This is usually a clear sign that a joint is “definitely affected by synovitis”. When there was some decrease in optical properties in the center of the joint, the image received a score of 2, 3, 4, depending on the strength and spatial extension of the decrease (Figures 3b-d). The clinical interpretation of these scores is “likely to be not affected” (score 2); “possibly affected” (score 3); “likely to be affected” (score 4). Scoring of SLOT images was performed by one investigator (AHH) without knowledge of USS or CE results.

In addition to the operator-dependent score, we determined further parameters, used as classifiers, for each image. These parameters include minimum and maximum scattering coefficients ($\text{Min}(\mu_s)$ and $\text{Max}(\mu_s)$), minimum and maximum absorption coefficients ($\text{Min}(\mu_a)$ and $\text{Max}(\mu_a)$), and the ratios of minimum divided by maximum scattering and absorption coefficients ($\text{Min}(\mu_a)/\text{Max}(\mu_a)$ and $\text{Min}(\mu_s)/\text{Max}(\mu_s)$), respectively. Instead of determining minima and maxima for the entire image, these values were determined for a region of interest depicted in Figure 3a. By choosing an area inside the finger, we excluded possible imaging artifacts that can appear in SLOT images near the sources and detector and near the surface of the finger.

**Statistics**

To compare SLOT images with CE and US, we calculated the mean and respective standard errors of all optical parameters (operator score, $\text{Min}(\mu_a)$, $\text{Min}(\mu_s)$, $\text{Max}(\mu_a)$, $\text{Max}(\mu_s)$, $\text{Min}(\mu_a)/\text{Max}(\mu_a)$, $\text{Min}(\mu_s)/\text{Max}(\mu_s)$) for all joints with CSS=0 or 1, CSS=2 or 3, respectively. The same was performed for fingers with USS=0 or 1, and USS=2 or 3. Mean values of each optical parameter for affected and non-affected joints were compared using the one side t-test. Difference in the mean values was considered significant if this test resulted in $p<0.05$. ROC analysis (37) was performed for optical parameters for which a significant difference in the mean between affected and non-affected joints was found. True-positive (TP), true-negative (TN), false-positive (FP) and false-negative (FN) values were calculated for all 7 optical classifiers taking USS and CSS as diagnostic references for determination of synovitis (unaffected: scores 0 and 1; affected: scores 2 and 3). Sensitivities and specificities were determined by calculating the true-positive rates TPR=TP/(TP+FN) and false-positive rates FPR=FP/(FP+TN) (sensitivity=TPR, specificity=1-FPR), for various thresholds for the 7 different classifiers.

Furthermore, for all ROC curves we determined the points with the maximal Youden index, defined as $J=$sensitivity+specificity-1 (38). For each classifier these points identify threshold values that lead to optimal sensitivity-specificity pairs.
RESULTS

All 13 patients were found with a moderate to high overall disease activity (mean DAS-28: 4.7±1.4) at time of examination. On the basis of CSS, 34 PIP joints were classified as Grade 0, 28 joints as Grade 1, 11 joints as Grade 2 and 5 PIP joints as Grade 3. Mean CSS for PIP joints II-IV were 0.8±0.9. Assuming CSS 0 and 1 as unaffected and CSS 2 and 3 as pathological, 16 of the 78 joints (20.5%) were affected, whereas 62 joints (79.5%) were not affected by synovitis.

Using USS, synovitis in PIP joints was classified as follows: 11 PIP joints were classified as Grade 0, 26 as Grade 1, 23 as Grade 2 and 18 PIP joints as Grade 3. Mean USS for PIP joints II-IV were 1.5±1.01. Assuming USS 0 and 1 as unaffected and USS 2 and 3 as pathological, 37 (47.4%) of the 78 joints were unaffected, whereas 41 joints (52.6%) were affected.

Table 1 summarizes the results for mean values and standard errors for all classifiers used to characterize SLOT images. In most cases there is a difference between the mean values for affected and unaffected joints as determined either by CE or US examination. But only in 6 of the 14 cases (Table 1) the differences in the mean were statistically significant (p<0.05). Five classifiers (operator score, Min(µs), Min(µa), and Min(µs)/Max(µs), and Min(µa)/Max(µa)) showed significant differences when optically derived parameters were compared to USS, while in only one case (Min(µa)) the difference was statistically significant when SLOT results were compared to CE (Table 1). The statistically most significant difference (p=0.005) was found for Min(µa) with USS as diagnostic reference.

For the cases showing statistically significant differences between mean values of affected and unaffected joints, we generated ROC curves. Assuming that a SLOT score of 4 or 5 is indicative of a joint with synovitis, while scores of 1, 2, and 3 identify a healthy joint, we find 17 true-positive cases, 31 true-negative cases, 6 false-positive cases, and 24 false-negative cases, when compared to USS. Choosing different cut-offs at which a finger is considered inflamed, different sensitivities and specificities were obtained (Figure 4). The same was performed using the six other classifiers (dashed lines in Figure 4). Assuming that a joint is inflamed if Min(µa)>0.210cm⁻¹, we receive a sensitivity of 0.638 and specificity of 0.6 (dotted blue curve in Figure 4).

In all these cases, the area under the ROC curve (AUC) was between 0.65 and 0.66. Better AUCs were obtained when instead of assuming a score of 0 and 1 as unaffected and 2 and 3 as affected, only cases of USS=0 were considered as unaffected and USS=3 as affected. Of the 78 fingers, 18 received USS=3 and 11 joints were scored 0. The mean value for the affected joints (CSS=3) was Min(µa)=0.268±0.056 cm⁻¹ and for the joints with CSS=0 we received Min(µa)=0.159±0.021 cm⁻¹ (p=0.038). The AUC was=0.744 compared to 0.680 in the case when CSS of 0, 1 were used to determine unaffected fingers and CSS of 2, 3 were used to identify affected fingers (ROC curve shown in Figure 5).

The best sensitivity-specificity pair was achieved when Min(µa) was used as classifiers and compared to USS as diagnostic reference. In this case we found sensitivity and specificity of 0.705 each when Min(µa)=0.272 cm⁻¹ was used as threshold (dotted blue curve in Figure 4) with a Youden index of 0.41. The same Youden index was found for a threshold of Min(µa)=0.241 cm⁻¹, for which the sensitivity slightly increased to 0.736, while the specificity decreases to 0.674.
DISCUSSION

The goal of this work was to find classifiers for SLOT images that can be used to distinguish PIP joints with synovitis from joints without synovitis in patients with RA. In previous case studies we had observed that SLOT images of joints without clinical signs of synovitis showed a clear decrease of scattering and absorption coefficients in the joint cavity, while joints with synovitis did not display this marked decrease (27-29). We now recruited 13 patients with active RA, and obtained images of 78 PIP joints that showed synovitis to different degree. Besides SLOT all joints were evaluated by CE and US to provide two diagnostic references.

The first important observation was that US classified more than twice as many joints (41 joints) as affected by synovitis than CE (16 joints). This discrepancy had been observed before by other groups that compared US and CE on finger (9, 10), shoulder (39) and knee joints (40). In all these studies CE classified a smaller number of joints with synovitis as compared to US.

Among the seven different classifiers that we chose from the SLOT images, we found five (operator score, Min($\mu_a$), Min($\mu_s$), and Min($\mu_a$/Max($\mu_a$), Min($\mu_s$/Max($\mu_s$))) that produced statistically significant differences between the mean values of affected and unaffected joints with US as diagnostic reference. Using CE as diagnostic reference only one classifier (Min($\mu_a$)) showed statistically significant differences in the mean between affected and unaffected joint. Statistically significant difference in the mean is a necessary condition for a classifier to be clinically useful, but it is not a sufficient condition. The distribution of joints affected and not affected by synovitis may still show substantial overlap with respect to a statistically significant classifier. To be clinically useful, the sensitivity and specificity for a certain cut-off value of a classifier have to be high. Therefore, once classifiers were identified, we investigated the clinical utility of these classifiers by ROC analysis. For all SLOT classifiers with significant differences in mean values, the AUC increased when only USS and CSS of 0 and 3, instead of 0,1 and 2,3 were used to classify joints. This appears logical since by omitting fingers from the statistical analysis that received scores of 1 or 2, we removed most cases that were borderline with respect of being involved or not involved. The best sensitivity-specificity pair was achieved when Min($\mu_a$) was used as classifier and compared to US giving a sensitivity and specificity of 0.705 each.

Overall, the results suggest that SLOT images agree better with US than with CE. The reason for that is not entirely clear. In this study, we chose to compare SLOT images to US since it is very sensitive in detecting soft tissue lesions (effusion and synovitis) (10). Different to normal effusion, which appears as a clear and colourless fluid, inflammatory effusion is turbid due to infiltration with inflammatory cells. Optical techniques are sensitive to these changes in the optical properties, which could be shown in previous in-vitro investigations (16-18). Furthermore, US is sensitive to hypertrophy of synovial membrane accompanied by neovascularization. It is well known from breast and brain imaging studies that blood dependent parameters strongly influence optical signals (27). Hence, tissue growth and neovascularization within the joint lead to an increase of scattering and absorption and will amplify the optical effects caused by effusion. False positive SLOT readings may be caused by non-inflammatory effusion, which still would get a USS of 2 or 3, but may look unaffected on SLOT images, since the fluid in joint cavity may be clear, similar to an unaffected joint. Swollen finger joints detected by CE may be indicative of effusion as well as increased blood volume. Since both affect optical properties one would expect a higher level of agreement between CE and SLOT imaging than we achieved. But palpation may miss more subtle cases and may lead to false-negative results. While there remain open questions, these results clearly constitute an advance over previous optical imaging studies involving finger joints. In contrast to earlier studies that relied on transmission profiles only (5, 26), we demonstrated for the first time that classifiers can be found for SLOT images showing significant differences between affected and unaffected joints based on a single measurement. This clearly shows the advantages of tomographic imaging over mere transmission measurements.
In general, we believe that different imaging methods as well as CE reflect multiple pathophysiological processes within the finger joints in different ways. Radiography is suitable for follow-up evaluation of bone erosions, but insensitive for detecting early erosive lesions and soft tissue swelling. US has strength in detecting joint effusion and synovitis, while it has difficulty to differentiate between inflammatory and non-inflammatory effusion (9). MRI is sensitive to active synovitis and early erosions (6-8). SLOT imaging, providing the poorest spatial resolution, may be sensitive to all three aspects of RA, since effusion, hypertrophy, and erosion all lead to changes in optical properties. While the results of the presented study support this hypothesis, further studies with improved instrumentation and larger patient groups are necessary to fully explore the contrast mechanisms and determine the ultimate clinical utility of SLOT. In this regard it will be useful to compare SLOT images to additional diagnostic references such as MRI. A clear separation of patient groups with different symptoms (e.g. patients with only synovitis, patients with synovitis and effusion, patients with synovitis, effusion and erosions) will also help to clarify contrast mechanisms in SLOT imaging. All this should lead to higher sensitivities and specificities that need to fall into the 0.85-0.95 range to support clinical use. Furthermore, it will be of great interest to use SLOT to study additional joints that are of clinical importance, such as MCP joints. At this point it appears unlikely that SLOT imaging will replace US or MRI imaging in RA diagnostic. But, we believe that a SLOT imager may supplement the clinical armamentarium of the rheumatologist in the future. SLOT, US, and MRI have different contrast mechanisms and sense different aspects of the disease. Therefore it appears that these different imaging modalities will complement each other, rather than make each other obsolete.

Concluding, we succeeded in identifying features in SLOT images that show statistically significant difference between joints with and without synovitis. Unlike in previous optical transillumination studies, we demonstrated for the first time that it is possible to classify a joint as inflamed using SLOT images without the need for a reference measurement. We confirmed that high absorption and scattering coefficients in and around the joint cavity are indicative of an inflammatory process. Furthermore, it was observed that SLOT-based diagnosis of synovitis agrees better with diagnosis based on US images than on CE.

Acknowledgements
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Tables

<table>
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<th></th>
<th>MEAN (±Std. Error)</th>
<th>score [1, ..., 5]</th>
<th>Min(µ_s) [cm⁻¹]</th>
<th>Min(µ_a) [cm⁻¹]</th>
<th>Max(µ_s) [cm⁻¹]</th>
<th>Max(µ_a) [cm⁻¹]</th>
<th>Min(µ_s)/Max(µ_s)</th>
<th>Min(µ_a)/Max(µ_a)</th>
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<td></td>
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<tr>
<td>affected joint</td>
<td>3.00 (±0.40)</td>
<td>5.91 (±1.01)</td>
<td>0.256 (±0.033)</td>
<td>16.26 (±0.97)</td>
<td>0.649 (±0.041)</td>
<td>0.388 (±0.074)</td>
<td>0.405 (±0.062)</td>
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<tr>
<td>unaffected joint</td>
<td>2.65 (±0.16)</td>
<td>5.07 (±0.51)</td>
<td>0.180 (±0.017)</td>
<td>16.43 (±0.49)</td>
<td>0.640 (±0.021)</td>
<td>0.347 (±0.037)</td>
<td>0.307 (±0.032)</td>
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<td>0.177</td>
<td>0.233</td>
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<td>0.436</td>
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<tr>
<td>affected joint</td>
<td>3.07 (±0.20)</td>
<td>6.12 (±0.62)</td>
<td>0.232 (±0.020)</td>
<td>16.08 (±0.60)</td>
<td>0.645 (±0.025)</td>
<td>0.412 (±0.045)</td>
<td>0.382 (±0.038)</td>
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<td>2.32 (±0.22)</td>
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<td>16.74 (±0.63)</td>
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Table 1

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<th>mean: score [1, ..., 5]</th>
<th>Min(µ_s) [cm⁻¹]</th>
<th>Min(µ_a) [cm⁻¹]</th>
<th>Max(µ_s) [cm⁻¹]</th>
<th>Max(µ_a) [cm⁻¹]</th>
<th>Min(µ_s)/Max(µ_s)</th>
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<tr>
<td>affected joint</td>
<td>3.50 (±0.32)</td>
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<td>0.140 (±0.038)</td>
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<td>0.265 (±0.084)</td>
<td>0.231 (±0.070)</td>
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<td>0.005</td>
<td>0.317</td>
<td>0.475</td>
<td>0.028</td>
<td>0.014</td>
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Table 2
Legend to the Tables and Figures

**Table 1:** Mean values and standard errors of various optical parameters (see methods section). The entries in bold identify cases in which the difference between the mean values found for the affected and unaffected joints are statistically significant (p<0.05).

**Table 2:** Mean values and standard errors of various optical parameters for finger joints that received an US score of 3 (affected by RA) and 0 (unaffected by RA). The entries in bold identify cases in which the difference in the mean values found for the affected and unaffected joints are statistically significant (p<0.05).

**Figure 1:** Ultrasound images, Grade 0 – 1 – 2 – 3
Figure 1 shows ultrasound images of PIP joint II (c, d) and IV (a, b) of patients with rheumatoid arthritis at different synovitis stages. In all images, bone surface is without irregularities, no erosions are visible. Images are taken from the palmar side, whereas the left side of the image is proximal and the right side distal of the hand. Effusion (ef) can be seen in images b)-d) with different extent. Close to the synovial membrane, synovial proliferation can be detected in images c and d. T = Tendon, JC = Joint cavity. According to an adjusted semiquantitative score to Szkudlarek et al. (15), images graded with regard to the degree of inflammation: Grade 0 = (a) = little; Grade 1 = (b) moderate; Grade 2 = (c) and Grade 3 = high (d); amount of inflammation interpreted by effusion and synovitis, respectively.

**Figure 2:** Experimental set-up for sagittal joint imaging.
The laser is positioned above and a photo detector is placed below the finger joint to be examined. Both, detector and diode laser are attached to stepping motor-driven translation stages that permits to independently control the position of the laser diode and photo detector relative to the joint. Detector and laser are connected to a personal computer, where data is collected.

**Figure 3:** Reconstructed cross-sections of the scattering coefficient for three different fingers typical for (a) category 1 - definitely no synovitis, (b) category 2 - likely no synovitis, (c) category 3 - possibly synovitis, (d) category 4 - likely synovitis, and (e) category 5 - definitely synovitis. The fingertip is located to the right of the images that show a 36 mm-wide section of the finger with the joint cavity located approximately in the center. The dotted rectangle in Figure 3a indicates the region for which Min(μs), Min(μa), Max(μs), Max(μa), Min(μs)/Max(μs), and Min(μa)/Max(μa), where calculated.

**Figure 4:** Receiver operating characteristics (ROC) curves with ultrasound scores of 0-unaffected and 3-affected as diagnostic reference (Case B) compared to ROC curves with ultrasound scores of (0,1)-affected and (2,3)-unaffected as diagnostic reference (Case A). The numbers in brackets are the area under the curve (AUC). Also given for each curve are the cut-off values that results in the largest Youden index.

**Figure 5:** ROC curves for min(μa) classifier with clinical scores as diagnostic reference. The two cut off values identify points on the curve for which the Youden index is maximal.
References


