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Optical spectral transmission to monitor disease activity in arthritis patients: longitudinal follow-up comparison with clinical parameters

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Abstract

Objective: To examine the longitudinal associations of optical spectral transmission (OST) with clinical inflammatory arthritis activity markers in order to investigate its potential in monitoring disease activity.

Methods: OST measurements were performed in 1312 wrist and finger joints of 60 patients with clinical suspicion of inflammatory activity, within the context of known rheumatic inflammatory diseases at two separate time intervals. In each time point, patients underwent additional clinical and laboratory examinations. The change of OST values was statistically compared with changes in clinical activity parameters like DAS28 and swollen joint counts (SJC). Additionally, the diagnostic performance of OST was assessed in comparison to a historic control group (2508 joints of 114 healthy subjects) using receiver operating characteristics (ROC). The relationships between OST values, clinical and laboratory parameters, as well as patient characteristics, were evaluated through correlation analyses.

Results: Mean OST scores were significantly higher in the inflammatory arthritis group compared with the control group ($P < 0.001$). OST correlated significantly with clinical activity markers like DAS28, SJC and TJC in both time points (all; $P < 0.05$). Longitudinal changes of OST values (ΔOST) were significantly associated with changes in DAS28 (ΔDAS28) ($r = 0.377$; $P = 0.004$) and ΔSJC ($r = 0.488$; $P < 0.001$) over the same time period. The area under the curve of the baseline receiver operating characteristic curve was 0.781 (95%CI 0.82–0.94).

Conclusion: OST was able to reliably assess disease activity and correlated longitudinally with arthritis activity markers, showing promising potential during monitoring of inflammatory arthritis.

Keywords: optical spectral transmission, monitoring, inflammatory arthritis, disease activity.

Rheumatology key messages

- ΔOST values correlated significantly with ΔDAS28 over time, highlighting OST's potential to monitor disease activity.
- OST showed good diagnostic performance in differentiating inflammatory arthritis patients from controls.
- OST offers a non-invasive, efficient alternative for assessing disease activity, potentially complementing traditional clinical examinations.

Introduction

Tight control strategies are vital in the management of inflammatory arthritis, with the goal of achieving disease remission or maintaining low activity levels. This involves frequent monitoring, treatment adjustments and early intervention to minimize disease progression and prevent joint damage [1–4]. However, implementing such management approaches can be challenging, due to time constraints and inadequate rheumatologist resources. Furthermore, imaging techniques such as US rely heavily on the operator's experience, while MRI is expensive, not always accessible and often requires the use of contrast agents [5, 6]. Therefore, a new method that can assess disease activity frequently, quickly and objectively could be of value during monitoring disease activity in patients with inflammatory arthritis.

Over the past few years, new imaging technologies, including optical spectral transmission (OST) (HandScan®) [7–10] and fluorescence optical imaging (FOI) (Xiralite®) [11–13] have become more widely used within the field of rheumatology. OST offers the opportunity to detect inflammation in wrist and finger joints by using red and near-infrared light technology without the need of contrast agents or radiation, in contrast to FOI which requires the intravenous injection of indocyanine green with potential risks like allergic reactions [14]. Furthermore, OST allows for a non-invasive quantification of inflammation-associated changes in blood flow by measuring the blood-specific absorption of light transmitted through a tissue [15]. In conditions of inflammatory arthritis, neoangiogenesis leads to blood pooling and consequently decreased light transmission through the inflamed joints [15, 16]. Moreover, OST assessments can be easily performed by medical assistants and nursing staff after a brief training. Finally, OST results are automatically calculated via an integrated software, ensuring that the image interpretation is unaffected by the operator [7, 15].

However, there is still insufficient research data available on this diagnostic method. Most studies have evaluated the diagnostic performance of OST in comparison to clinical/US examinations at a singular time point in the course of the disease. Moreover, our group has examined diagnostic performance of OST *vs* joint US in patients during an arthritis flare before and after treatment with glucocorticoids [9]. Comparisons of OST with DAS28 across multiple patient visits before and after the application of additional RA medication have been examined until today in only one longitudinal study [17]. This creates a literature gap because frequent monitoring of disease activity using consistent reliable diagnostic methods in the follow-up of inflammatory arthritis is essential [18]. Therefore, the aim of our study was to investigate the longitudinal correlations between OST and clinical disease activity markers (DAS28/SJC/TJC) in real-world conditions in a longitudinal analysis and in comparison to controls.

Methods

Study population

This is a retrospective observational cohort study among patients with a diagnosis-related inflammatory arthritis activity who underwent at least two OST examinations across two corresponding hospitalization times in our inpatient rheumatology clinic since the installation of the HandScan® device. We analysed the data of all available patients ($n = 60$) with clinical suspicion of acute inflammatory arthritis activity. Suspicion of disease activity was defined as clinically assessed tenderness and/or synovial swelling of at least one wrist and/or MCP/PIP joint in the context of established systemic rheumatic diseases such as RA, PsA/peripheral SpA and gout.

Moreover, a historic cohort of 114 individuals without underlying inflammatory diseases, arthralgias or clinical signs of osteoarthritis consisting of clinic co-workers who had responded to an open call for study participation served as a control group.

Exclusion criteria for both groups included presence of joint prostheses/implants, severe hand deformities, pronounced ulnar deviation, recent trauma or surgery, a change in immunosuppressant therapy (glucocorticoids and/or DMARDs) between OST and clinical examination and a time interval of <6 months between both OST examinations.

Written informed consent was obtained from patients and HC, and the assessment has been approved by the ethics committee of the Rhineland Palatinate State Medical Council, Germany (EC number: 13042).

Data collection

In both study groups, demographics (such as age and sex), as well as weight and height to calculate BMI (in kg/m^2) were documented. During both hospitalization phases, patient disease activity was assessed using DAS28-ESR and DAS28-CRP scores. For that purpose, clinical examinations to calculate counts of tender (TJC) and swollen (SJC) joints along with laboratory assessments of inflammation markers (CRP, ESR) were performed, and visual analogue scale (VAS) was documented. Current medications (with a focus on immunosuppressants) and other patient-associated characteristics, as well as disease-associated antibodies such as RF and anti-CCP were reported. Finally, radiographs of the hands in two planes were examined by a radiology specialist to check for the presence of typical RA erosions (marginal) and osteophytes.

OST measurements

Measurements of OST were performed using the HandScan diagnostic device (Demcon/Hemics®, Eindhoven, The Netherlands) by trained nursing staff, blinded to the results of the clinical examinations and laboratory values. At the beginning of OST examinations, patient and control subjects placed their forearms on a glass surface into the HandScan device through two frontal openings that were fixed with pressure cuffs. Red and near-infrared laser light with wavelengths of 660 nm and 808 nm was used to illuminate the palmar side of the distal forearm, including both wrists, MCP, PIP joints and reference areas for every joint. A camera placed at the upper side of the device was used to record light transmitted through the hands [7].

A complete OST measurement lasted ~100 s and is divided into three phases: (i) a low-pressure phase, (ii) an increased pressure phase [55 mmHg (=7.3 kPa)] and (iii) a second low pressure phase. During the first phase, baseline transmission was measured. In the second phase, increased cuff pressure caused blood pooling in the examined joint areas. During the third phase, cuff pressure decreased, causing inversion of venous occlusion and blood pooling. An integrated software allowed the automatic identification of 'regions of interest' (ROI: wrists, MCP I-V and PIP I-V in both sides) and distally located reference areas. A comparison between the blood flow in the ROI and in the reference areas served as a control mechanism for the presence of impaired or increased peripheral blood flow due to systemic factors, such as body temperature, diabetes mellitus, nicotine use or vasoactive medication (Fig. 1).

Statistical analysis

We assessed the normality of data distribution using the Shapiro–Wilk test and graphical methods like quantile-quantile plots. For comparisons between patients across both timelines, McNemar's test was employed for categorical variables, Wilcoxon test for non-normally distributed metric parameters, and paired sample t test for normally distributed variables. For comparisons between patients and controls, Fisher's exact test was used for categorical variables, Mann–Whitney test for non-normally distributed metric parameters, and independent samples t test for normally distributed

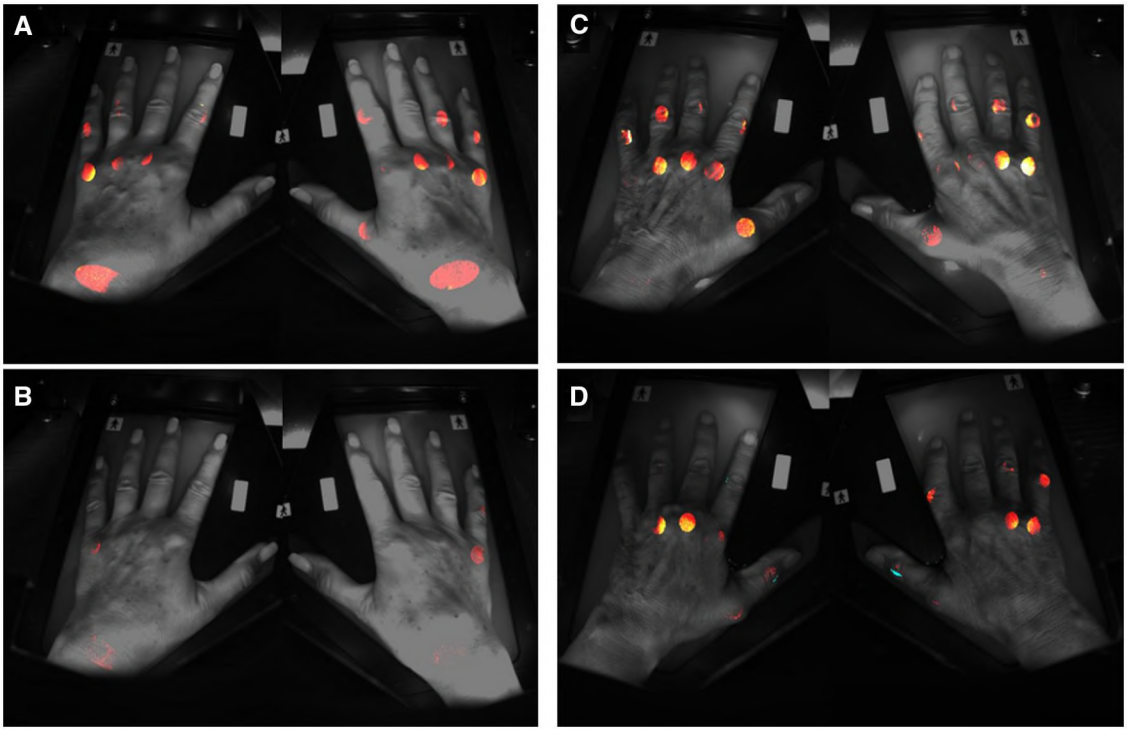

Figure 1. Assessment of the inflammation by optical spectral transmission (OST) in wrist and finger joints. (**A**) OST results of a female RA-patient before (OST = 15.93, DAS28 = 4.27) and (**B**) 9 months after the application of MTX (OST = 8.42, DAS28 = 2.86). (**C**) OST results of a male PsA-patient before (OST = 22.85, DAS28 = 5.10) and (**D**) 12 months after the application of Ixekizumab (OST = 12.42, DAS28 = 1.95). DAS28: 28-joint count disease activity score; MTX: methotrexate; OST: optical spectral transmission; PsA: psoriasis arthritis; RA: rheumatoid arthritis

variables. On each time point, correlations between OST, clinical parameters and other characteristics were examined using the Spearman correlation coefficient, while the Pearson correlation was used for normally distributed values. Moreover, we applied the Mann–Whitney *U* test to explore differences in the OST values in relation to binary categorical variables for inflammatory arthritis patients across both timelines.

To examine whether changes in OST are associated with changes in clinical parameters, linear regression analyses were performed at individual patient level, and the changes (slopes) in OST, DAS28, SJC and TJC values between both time intervals were separately calculated. Subsequently, Pearson's test was applied to assess the correlations between the slope values of OST, DAS28, SJC and TJC. A subgroup analysis including only RA patients was also performed to specially examine the relationship of RA clinical parameters on OST.

Further, comparisons of distributions of OST changes with DAS28-ESR, DAS28-CRP and SJC changes (ΔOST *vs* ΔDAS28-ESR, ΔOST *vs* ΔDAS28-CRP, ΔOST *vs* ΔSJC) between time points were performed using Bayesian posterior analysis with the Markov Chain Monte Carlo approach and a sample size of 100 000. Group differences were calculated as mean differences with accuracy ≥80% considered as significant ($^{*}P < 0.05$), ≥90% highly significant ($^{**}P < 0.01$) and ≥95% with the highest significance ($^{***}P < 0.001$). An 80% accuracy for differentiating between two groups is defined by a 20% probability of rejecting a true null hypothesis. This corresponds to a *P*-value of $P = 0.05$ [19], hence our cut-off. The BEST R package (https://jkkweb.sitehost.iu.edu/BEST/) was used for the estimation of the Bayesian posterior distributions.

Moreover, we performed several multivariate analyses to check for potential confounding effects on OST, including systemic factors such as arterial hypertension, diabetes mellitus, nicotine use and the effects of immunosuppressants, as well as patient-related parameters like age, sex and BMI. Furthermore, a subgroup analysis was conducted to examine the association between OST and control subject characteristics.

Finally, to evaluate the diagnostic performance of OST, receiver operating characteristic (ROC) analyses were conducted at the patient level. Comparisons included 'inflammatory arthritis *vs* controls' and cut-off values were calculated on both timelines. All tests were two sided and a significance level of 0.05 was considered. All statistical computations were carried out using SPSS software version 27.0.

Results

OST measurements were performed in a total of 1312 joints on time point (a) and the same 1312 joints on time point (b) in 60 patients with inflammatory arthritides [RA ($n = 40$), PsA/peripheral SpA ($n = 15$), gout ($n = 5$); time interval between OST measurements in months: median (IQR) = 16.5 (10.25–30.5)]. A total of 2508 joints of 114 control subjects were included for comparison with patient OST scores (female patients: 63.3% *vs* female controls: 77.2%, $P > 0.05$). A total of 16 joints of the patient group were automatically excluded by the OST software, due to anatomic anomalies. Descriptive statistics on both groups are presented in Table 1.

Mean OST values were significantly higher in the patient group in both time-points, compared with the control group [controls: 10.79 ± 4.20 *vs* patients at time-point (a): 15.89 ± 5.05, and patients at time point (b): 15.40 ± 5.53; both $P < 0.001$].

Correlations of OST with clinical activity markers and patient characteristics

At both examination time-points, OST correlated moderately with DAS28-ESR and DAS28-CRP scores: DAS28-ESR [(a): r = 0.346; $P = 0.007$, (b): r = 0.447; $P < 0.001$] and DAS28-CRP [(a): r = 0.365; $P = 0.004$, (b): r = 0.500; $P < 0.001$] (Fig. 2).

Similarly, OST showed significant correlations with SJC and TJC scores: SJC [(a): r = 0.400; $P = 0.002$, (b): r = 0.535; $P < 0.001$] and TJC [(a): r = 0.282; $P = 0.029$, (b): r = 0.458; $P < 0.001$]. The relationships between OST and blood inflammation markers such as ESR and CRP did not reach the appropriate level of statistical significance (Table 2).

The RA subgroup analysis also demonstrated significant correlations between OST and clinical examination parameters at both examination time points: DAS28-ESR [(a): r = 0.460; $P = 0.003$, (b): r = 0.487; $P = 0.002$], DAS28-CRP [(a): r = 0.486; $P = 0.002$, (b): r = 0.543; $P < 0.001$], SJC [(a): r = 0.373; $P = 0.018$, (b): r = 0.557; $P < 0.001$] and TJC [(a): r = 0.367; $P = 0.020$, (b): r = 0.459; $P = 0.003$].

In time point (a), male patients had significantly higher OST values than female patients [17.15 *vs* 14.08, $P = 0.009$]. Overall, there were no statistically significant relationships between OST and other factors such as BMI, visual analogue scale, arterial hypertension, diabetes mellitus, erosions in conventional radiographs, osteoarthritis and immunosuppressants or glucocorticoids intake (all $P > 0.05$; Table 2).

Association between changes in OST and clinical activity markers

The changes in clinical parameters as well as OST values between the two time intervals were measured using linear regression models for each patient. The median slope values were determined as 1.001 for OST, 1.011 for DAS28-ESR, 1.055 for DAS28-CRP, 0.761 for SJC and 1.044 for TJC (Table 3).

Statistical correlation analyses demonstrated significant correlations between slope values of OST and slope values of clinical activity parameters: DAS28-ESR (r = 0.377; $P = 0.004$), DAS28-CRP (r = 0.355; $P = 0.007$) and SJC (r = 0.488; $P < 0.001$) (Table 3, Fig. 2).

As for the RA subgroup analysis, correlations between slope values of OST and slope values of clinical activity parameters were also statistically significant: DAS28-ESR (r = 0.389; $P = 0.014$), DAS28-CRP (r = 0.439; $P = 0.006$) and SJC (r = 0.438; $P = 0.006$).

Bayesian statistics

The Bayesian statistical approach revealed no significant differences between the distributions of ΔOST and ΔDAS28-ESR,

Table 1. Descriptive characteristics of study participants

	Controls, $n = 114$	inflammatory arthritis cohort, $n = 60$	Significance (P) inflammatory arthritis vs controls
Age, yrs[b]	51.00 (35.00–57.00)	66.50 (56.25–74.75)	<0.001***
Sex (female), %	77.20	63.30	0.074
OST (time-point a)[a]	10.79 ± 4.20	15.89 ± 5.05	<0.001***
OST (time-point b)[a]	10.79 ± 4.20	15.40 ± 5.53	<0.001***
Nicotine use, %	19.40	15.00	0.530
Arterial HTN, %	19.40	68.30	<0.001***
Diabetes, %	1.90	13.30	0.005**
	Time-point (a)	Time-point (b)	Significance (P)
Patient count (n)	60	60	1.00
OST[a]	15.89 ± 5.05	15.40 ± 5.53	0.430
Age, yrs[b]	65.00 (55.00–72.00)	66.50 (56.25–74.75)	<0.001***
BMI,[b]	27.72 (25.06–31.98)	28.41 (25.32–31.70)	0.270
Disease duration, yrs[b]	4.00 (1.00–12.5)	6.00 (3.00–14.00)	<0.001***
ESR, mm/h[b]	25.50 (18.00–44.29)	22.00 (12.00–38.50)	0.081
CRP, mg/l[b]	5.23 (1.60–23.00)	4.20 (1.62–12.08)	0.113
RF, U/ml[b]	10.86 (8.85–55.20)	11.00 (9.22–52.23)	0.203
Anti-CCP, U/ml[b]	3.55 (1.10–96.50)	2.90 (1.60–54.30)	0.943
Tender joint count[b]	4.00 (1.00–12.75)	4.00 (0.00–10.00)	0.004*
Swollen joint count[b]	2.00 (0.00–6.00)	0.00 (0.00–4.00)	0.668
VAS, mm[b]	60.00 (40.00–70.00)	60.00 (50.00–80.00)	0.134
DAS28-ESR[a]	4.73 ± 1.38	4.51 ± 1.50	0.378
DAS28-CRP[a]	4.11 ± 1.39	3.98 ± 1.33	0.727
Erosions, %	18.80	20.00	0.625
Osteoarthritis, %[c]	60.40	65.10	1.00
NSAID, %	10.00	13.30	0.238
Immunosuppressants, %	40.00	43.30	0.845
csDMARD, %	23.30	23.30	1.00
bDMARD, %	21.70	21.70	1.00
JAK inhibition, %	6.70	8.30	1.00
glucocorticoids (low dose), %	53.30	69.00	0.022*
no DMARD, %	60.00	56.70	0.845

[a] Data are presented as mean ± standard deviation, as they are normally distributed.
[b] Data are presented as median (IQR), as they are not normally distributed.
[c] Distal interphalangeal joints excluded because they were not examined by OST.
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
anti-CCP: anticyclic citrullinated peptide antibodies; bDMARD: biologic DMARD; BMI: body mass index; CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying antirheumatic drugs; DAS28: 28-joint count disease activity score; ESR: erythrocyte sedimentation rate; HTN: hypertension; IQR: interquartile range; JAK: Janus kinase; OST: optical spectral transmission; RF: rheumatoid factor; VAS: visual analogue scale.

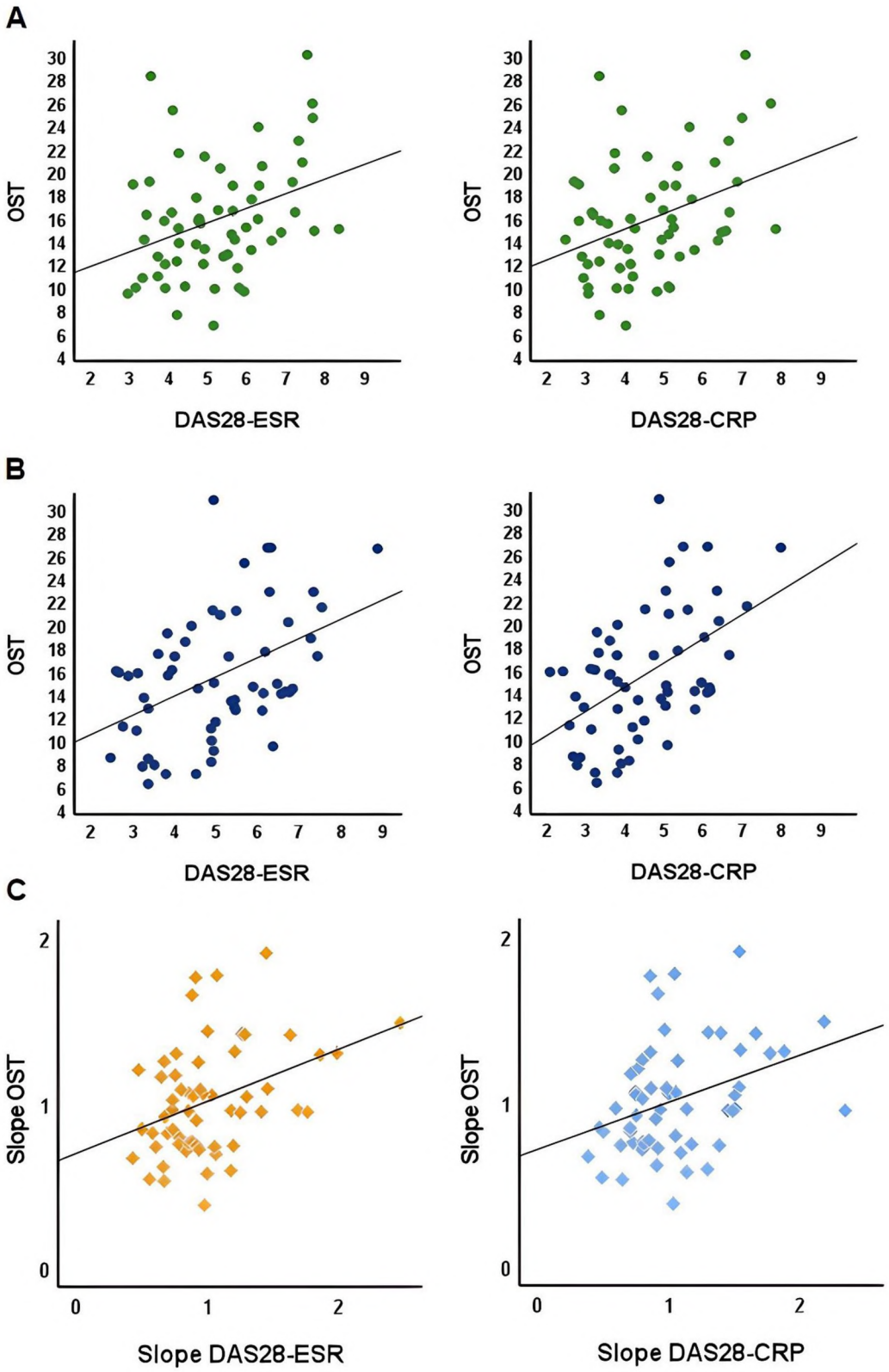

Figure 2. Associations of OST with DAS-28 scores. Correlations of OST and DAS28 values in time-point (**A**) and (**B**). (**C**) Associations of OST and DAS28 slope values indicate that changes in OST are significantly correlated with changes in DAS28 between the two timelines (all $*P < 0.05$). DAS28-CRP: 28-joint count disease activity score based on C-reactive protein; DAS28-ESR: 28-joint count disease activity score based on erythrocyte sedimentation rate; OST: optical spectral transmission

Table 2. Associations of OST with patient- and disease-associated characteristics

Metrical variables	Correlation coefficiency (Spearmann's rho/Pearson's r)	Significance (*P*) (2-sided)	Correlation coefficiency (Spearmann's rho/Pearson's r)	Significance (*P*) (2-sided)
	Time point (a)		Time point (b)	
Age, yrs[b]	rho=-0.045	0.731	rho=-0.122	0.354
BMI, kg/m[b]	rho = 0.118	0.370	rho = 0.016	0.906
TJC[b]	rho = 0.282	0.029*	rho = 0.458	< 0.001***
SJC[b]	rho = 0.400	0.002**	rho = 0.535	< 0.001***
VAS, mm[b]	rho=-0.119	0.363	rho = 0.022	0.866
ESR, mm/h[b]	rho = 0.149	0.255	rho = 0.109	0.416
CRP, mg/l[b]	rho = 0.168	0.203	rho = 0.119	0.373
DAS28-ESR[a]	r = 0.346	0.007**	r = 0.447	< 0.001***
DAS28-CRP[a]	r = 0.365	0.004**	r = 0.500	< 0.001***
Categorial variables	**Median OST (IQR)**	**Significance (*P*)**	**Median OST (IQR)**	**Significance (*P*)**
	Time point (a)		Time point (b)	
Sex: female	14.08 (10.91–16.52)	0.009**	14.57 (12.45–17.95)	0.939
Male	17.15 (14.69–21.01)		14.89 (11.03–20.15)	
Nicotine use: no	14.88 (12.01–18.80)	0.031*	14.21 (11.04–17.48)	0.016*
Yes	16.68 (14.87–23.67)		20.23 (15.48–22.03)	
Hypertension: no	15.51 (12.84–16.68)	0.956	15.62 (12.89–17.66)	0.455
Yes	14.88 (12.12–19.13)		14.21 (10.95–19.05)	
Diabetes: no	15.07 (12.07–19.03)	0.704	14.57 (11.31–17.62)	0.486
Yes	16.47 (13.79–18.88)		16.51 (11.28–25.32)	
Erosions: no	15.51 (12.24–19.11)	0.376	14.65 (10.85–17.29)	0.797
Yes	15.10 (9.80–18.80)		13.94 (10.02–24.72)	
Osteoarthritis: no[c]	15.93 (14.12–20.29)	0.062	15.62 (12.62–19.91)	0.452
Yes	14.12 (10.51–17.22)		14.49 (9.61–16.99)	
RF: negative	15.18 (11.47–19.01)	0.316	14.13 (10.94–16.99)	0.014*
Positive	15.51 (13.83–20.29)		17.27 (14.21–21.51)	
Anti-CCP: negative	15.18 (11.47–19.01)	0.336	14.19 (10.94–17.43)	0.023*
Positive	15.51 (13.83–20.29)		17.27 (14.48–22.85)	
Immunosuppressants: no	15.35 (12.64–20.00)	0.251	14.57 (11.17–18.06)	0.929
Yes	13.87 (11.91–18.54)		14.56 (11.82–19.34)	
Glucocorticoids: no	14.08 (10.84–18.54)	0.072	12.69 (8.95–17.74)	0.141
Yes	16.09 (13.25–20.68)		14.82 (17.78–20.45)	

[a] Pearson correlation tests were performed with normally distributed data (r: Pearson correlation index).
[b] Spearman correlation tests were performed with non-normally distributed data (rho: Spearman correlation index).
[c] Distal interphalangeal joints were excluded because they were not examined by OST.
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
anti-CCP: anticyclic citrullinated peptide antibodies; BMI: body mass index; CRP: C-reactive protein; DAS28: 28-joint count disease activity score; ESR: erythrocyte sedimentation rate; IQR: interquartile range; OST: optical spectral transmission; RF: rheumatoid factor; SJC: swollen joint count; TJC: tender joint count; VAS: visual analogue scale.

ΔDAS28-CRP, and ΔSJC across both time points (accuracy: DAS28-ESR: 59%; DAS28-CRP: 69.1%; SJC: 75%). Further details on these statistical analyses are provided in Supplementary Data S1, available at *Rheumatology* online.

Receiver operating characteristics

ROC analyses were performed to evaluate the comparison 'patients *vs* controls' via OST in both time points. The area under the curve (AUC) in time point (a) was 0.781 (95%CI 0.82–0.94), with a sensitivity of 0.750 and a specificity of 0.711, for an OST cut-off of 12.65 (Youden index 0.461). In time point (b) ROC revealed an AUC of 0.741 (95%CI 0.74–0.881), with a sensitivity of 0.717 and a specificity of 0.675, for an OST cut-off of 12.52 (Youden index 0.392) (Fig. 3).

Discussion

Our data indicates that changes of OST values are significantly associated with changes of clinical activity markers in patients with inflammatory arthritis. Bayesian analyses have further validated these findings. Furthermore, there was a significant difference in OST values between controls and patients and significant correlations between OST and several clinical activity markers.

To our knowledge, this is the first longitudinal study to examine the diagnostic value of OST in the long-term monitoring of patients with different types of inflammatory arthritides including RA, PsA and gout, while taking clinical disease activity parameters as a reference. Until now, there has been a further longitudinal study published on the topic, also including a validation cohort from our department. However, this investigated the diagnostic performance of OST in the direct follow-up monitoring of solely RA patients by examining OST associations with clinical activity parameters [17]. In this study, the longitudinal association of OST scores with DAS28 was investigated after the start of anti-inflammatory treatment (MTX for early RA, and TNFi for established RA) within a period of 6 months. In our study, the primary focus was to assess long-term effectiveness of HandScan to consistently identify inflammatory status independently of immunosuppressive treatment initiation.

Table 3. Correlations of the slope values of OST and clinical activity parameters

	Mean slope ± SD	R correlation index	Significance (*P*)
OST	1.001 ± 0.333	—	—
DAS28-ESR	1.011 ± 0.398	0.377	0.004**
DAS28-CRP	1.055 ± 0.417	0.355	0.007**
SJC	0.761 ± 1.508	0.488	< 0.001***
TJC	1.044 ± 1.372	0.241	0.095

Pearson correlation tests were performed to test correlations of the slope values (R: Pearson correlation index).
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
CRP: 28-joint count disease activity score based on C-reactive protein; DAS28-ESR: 28-joint count disease activity score based on erythrocyte sedimentation rate; DAS28- OST: optical spectral transmission; SD: standard deviation; SJC: swollen joint count; TJC: tender joint count.

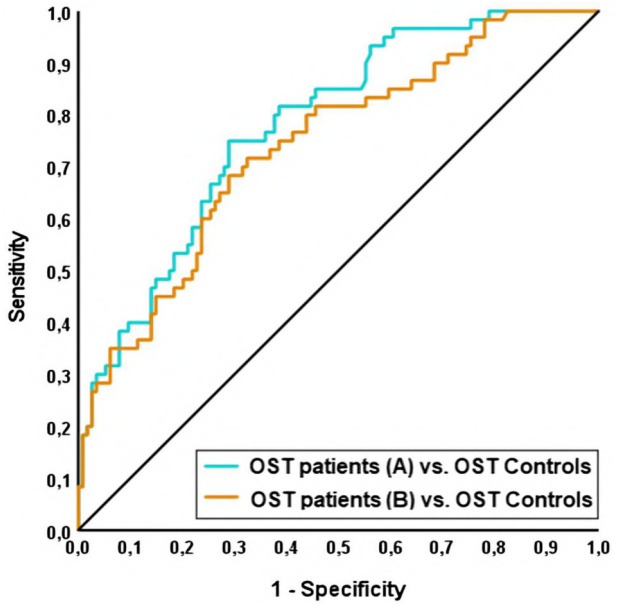

Figure 3. Evaluating the diagnostic performance of optical spectral transmission (OST) via receiver operating characteristics (ROC). For time point (**A**), ROC revealed an area under the curve (AUC) of 0.781 (95%CI 0.82–0.94), with a sensitivity of 0.750 and a specificity of 0.711, and an AUC of 0.741 (95%CI 0.74–0.881), with a sensitivity of 0.717 and a specificity of 0.675 for time point (**B**) (both, ***$P < 0.001$)

Similar to the study of Verhoeven *et al.* [17], a longitudinal association between OST scores and DAS28 could be found. In fact, our study showed that a change of OST values could be predicted by the changes of DAS28 and SJC within patients with inflammatory arthritis. In our previous longitudinal study to test the diagnostic performance of OST, we were similarly able to demonstrate no significant differences in the distributions of ΔOST values compared with the respective distributions of ΔUS (Grey Scale and Power Doppler US) activity parameters. This past study had focused primarily on evaluating the performance of OST in assessing therapy response after administration of glucocorticoids (GC) during an arthritis flare. Therefore, all patients included had an inherently high disease activity and were actively treated with glucocorticoids. OST examinations were performed before and within a maximum of 5 days after oral glucocorticoid administration, focusing on short-term therapy response. In contrast, the present study expands this scope by assessing the diagnostic ability of OST independently of disease activity and treatment status. To achieve this, we also included a different patient cohort also including patients with low disease activity where no treatment changes were performed. Furthermore, the current study extends the assessment period between both examinations to over 6 months, allowing for a longer-term analysis of OST performance.

Interestingly, the correlations between OST and DAS28-CRP were stronger than those with DAS28-ESR in both separate time points, respectively, possibly due to confounding factors such as age [20], anaemia [21] or hypergammaglobulinemia [22] that affect ESR independently of disease activity. Additionally, OST had a stronger correlation with SJC compared with TJC. This aligns with previous studies [7, 8, 23], supporting OST's ability in detecting solely the inflammatory aspect of arthralgia and not accompanying features of inflammation. However, OST did not show any significant correlation with inflammatory parameters such as ESR and CRP. A possible explanation is that these blood markers assess inflammatory activity throughout the entire body, whereas OST specifically measures inflammation in the finger and wrist joints. Additionally, OST did not show significant correlations with the patient global assessment via the VAS score. Similarly, this score reflects the patient's overall disease activity level and may vary significantly between individuals.

Importantly, there was a sex-based difference in OST values, with males having significantly higher scores than females. This supports our previous findings as well as those of other researchers [8, 9, 24]. However, this difference was not observed at time point (b). Our multivariate analysis indicated that this might be due to the sex-based difference in DAS28 scores at time point (b), where females had higher scores than males, potentially overshadowing the sex-specific difference in OST values, as OST positively correlates with disease activity parameters. Interestingly, also in control subjects, males had significantly higher OST scores than females. A possible explanation for this could be the fact that males may often have more robust bony, synovial or tendon structures than females, leading to increased light absorption and resulting in higher OST values.

These findings are important, given the known need for valid assessment tools of disease activity in the field of Rheumatology. As is well known, a tight clinical control strategy associates with a longer activity suppression and an improved overall prognosis [25]. Assessing disease activity using clinical scores in everyday practice remains of undisputable value and should always be considered both for the diagnosis and the follow-up of inflammatory arthropathies [26, 27]. However, assessment of clinical scores can be time-consuming, depends heavily on the examiner's expertise and may fail to depict subclinical inflammatory activity [28]. Therefore, having a tool with similar diagnostic performance to clinical examination and none of the mentioned disadvantages could greatly ease routine rheumatology practice.

Our study has certain limitations. Firstly, OST was compared with clinical, and not joint US activity markers. The reason for this was the fact that longitudinal correlations of OST with joint US have been thoroughly evaluated already by our group in previous works and were found to be statistically significant [9]. In this work we aimed to apply a slightly

different methodology and evaluate the utility of OST also in settings where only clinical and laboratory diagnostic assessments can be performed. For this purpose, we have used DAS28 as a clinical marker for disease activity in all included inflammatory arthritides, even though it is originally validated for RA. This decision was based on the fact that two-thirds of our patient group consisted of RA patients and that DAS28 has been previously utilized by other researchers, for example, for psoriatic arthritis/peripheral spondylarthritis [29, 30]. Moreover, we have performed a subgroup analysis only for RA patients, which showed even stronger longitudinal and concurrent correlations between OST and DAS28 scores compared with the entire inflammatory arthritis cohort. However, using DAS28 to assess clinical disease activity in non-RA inflammatory arthritides represents a limitation of our study.

A further limitation is the retrospective study design, compounded by the inclusion of patients with varying examination intervals and potential changes in immunosuppressive therapy during the study period. However, both OST and clinical examination were performed simultaneously at each time point under the exact same circumstances. This ensured that, for each individual patient, the intervals between the OST scans and the clinical examinations were identical. The same principle applies to changes in immunosuppressant therapy, which should cause the OST and clinical parameters like DAS28 to increase or decrease simultaneously. Therefore, a change in the OST score should be comparable to a change in the DAS28 score. Moreover, recruitment of all patients who have received OST in two different time points was done in a consecutive manner.

Correlation of changes can sometimes be misleading. In our study, we found weak-to-moderate correlations between DAS28 and OST value changes. Importantly, additional Bayesian analysis showed no significant differences in the distribution of values between OST and the other three disease activity parameters, further validating our findings from the slope correlation analyses. Nonetheless, the full potential of OST for long-term monitoring of patients with inflammatory arthritis requires further investigation.

Additionally, there was no matching performed between controls and patients for factors like age and sex, which might have acted as potential confounders for OST. However, our regression analyses show that even after accounting for these parameters, the difference in OST between patients and controls remained statistically significant at both time points. Interestingly, there was a significant age difference between the two groups, with patients being older than control individuals. This may be attributed to gout patients, who tend to be older. Finally, OST can detect inflammation of the wrist, MCP and PIP joints separately (excluding the DIP joints), with potentially unsimilar performance depending on the examined joints. This has been previously investigated by our group, comparing the performance of OST to joint ultrasound for each joint group separately, including the wrist, MCP and PIP joints [8]. The best performance was observed at the wrist joint level, followed by the MCP and PIP joints.

Conclusions

In summary, the here-presented data indicate a good diagnostic performance of OST in the long-term evaluation of patients with inflammatory arthritis. OST correlated significantly with clinical arthritis activity markers in both timelines. Therefore, OST has the potential to be a valuable non-invasive, time- and resource-saving tool to help in disease activity monitoring alongside clinical examination. Nonetheless, additional research involving larger and more diverse patient cohorts is essential to further validate these findings and help integrate OST into routine rheumatology practice.

The assessment was reviewed and approved by the Standing Committee for Clinical Studies of Rhineland-Palatinate, Germany, in adherence to the Declaration of Helsinki (Nr.: 13042). All patients gave their informed consent to the study.

Supplementary material

Supplementary material is available at *Rheumatology* online.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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