Research article

Multispectral optoacoustic tomography might be a helpful tool for noninvasive early diagnosis of psoriatic arthritis

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A B S T R A C T

Currently used imaging methods for diagnosis of psoriatic arthritis (PsA) frequently come along with exposure to radiation and can often only show long-term effects of the disease. The aim of the study was to check the feasibility of a new optoacoustic imaging method to identify PsA. 22 psoriasis patients and 19 healthy volunteers underwent examination using multispectral optoacoustic tomography (MSOT). The presence of arthritis was assessed via quantification of optoacoustic signal intensity of the endogenous chromophores oxy- and deoxy-hemoglobin. We conducted high-resolution real-time ultrasound images of the finger joints. The semi quantitative analysis of the optoacoustic signals for both hemoglobin species showed a significant higher blood content and oxygenation in PsA patients compared to healthy controls.

Our results indicate that MSOT might allow detection of inflammation in an early stage. If the data is further confirmed, this technique might be a suitable tool to avoid delay of diagnosis of PsA.

1. Introduction

Psoriasis is a chronic inflammatory skin disorder affecting about 2–4 % of the Western populations [1]. About 20–30 % of all patients with psoriasis also suffer from psoriatic arthritis (PsA) [2]. PsA is associated with a substantial disease burden and has major socioeconomic impact [3]. For the therapist it is indispensable to know if a psoriasis patient is also affected by PsA in order to make the most appropriate decision about a treatment. There is increasing evidence that early diagnosis and management of PsA leads to better outcomes [4]. However, diagnosis of PsA might be challenging and on average five years elapse between the first symptoms of the disease and confirmation of the diagnosis [5,6]. PsA is classified according to the Classification of Psoriatic Arthritis (CASPAR) criteria, which provide high specificity and sensitivity [7]. Table 1 provides an overview of the items of the CASPAR criteria and the calculation of the score.

Laboratory parameters specific for PsA do not exist [8]. Elevation of C-reactive protein (CRP) above the normal range might be present, but is not specific to PsA [9]. CRP is a proinflammatory protein of hepatic origin and a useful biomarker of infection, tissue injury but also inflammation in general [10]. The reference range of CRP often varies between labs.

Imaging techniques to assess PsA include musculoskeletal ultrasound (US), conventional X-ray, magnetic resonance imaging (MRI), computed tomography (CT), bone scintigraphy, and experimental imaging procedures such as fluorescence optical imaging (FOI). There are advantages and disadvantages inherent in every imaging technique.

US is being increasingly used in the evaluation of PsA. No contrast agent is required, and no ionizing radiation is involved [11]. Power doppler US can visualize many of the peripheral heterogeneous tissue compartments affected by PsA like joints, tendons and entheses, but the visualization of blood flow is limited due to its dependency on the angle between the flow vector and the sound beam, and the disturbance of the blood flow by the probe pressure. Furthermore, US is highly operator-dependent and is characterized by suboptimal reproducibility [12,13].

Since conventional X-ray is a fast, easy accessible, relatively inexpensive and reliable imaging technique, it is still widely used to detect structural changes in joints and tendon attachments. The radiographic hallmark of PsA is the combination of destructive changes with bone proliferation [8,11,14]. However, these changes are only visible months or years after initial manifestation [8]. Further, X-ray is of little value in

Table 1
CASPAR criteria.

CASPAR criteria	
Evidence of psoriasis	
Current psoriasis	2 or
Personal history of psoriasis	1 or
Family history of psoriasis	1
Psoriatic nail dystrophy	
Pitting, onycholysis, hyperkeratosis	1
Negative test result for rheumatoid factor	1
Dactylitis	
Current swelling of an entire digit	1 or
History of dactylitis	1
Radiologic evidence of juxta-articular new bone formation	
Ill-defined ossification near joint margins on plain x-rays of hand and foot	1

Modified according to [7]. To meet the CASPAR criteria, a patient must have inflammatory articular disease (joint, spine, or entheseal) and score ≥3 points based on these categories.
Abbreviation: CASPAR, Classification Criteria for Psoriatic arthritis.

evaluation of soft tissues and is always associated with ionizing radiation, although the dose for peripheral joint examination is small [11].

MRI allows early detection of all the relevant pathologies of PsA and is more sensitive to inflammatory and destructive changes than X-ray and clinical examination [15]. However, its availability and costs limit the use of this technique in daily clinical practice [16].

CT plays a minor role in assessment of peripheral joints [14] and bone scintigraphy is becoming less important compared to other imaging techniques such as MRI and US due to its low specificity and higher radiation exposure [17].

Pilot data suggest, that indocyanine green (ICG)-enhanced fluorescence optical imaging (FOI) might allow a sensitive and valid assessment of inflammation in arthritis [18].

Multispectral optoacoustic tomography (MSOT) is an innovative noninvasive physical examination method based on the optoacoustic effect. It was first described by Alexander Graham Bell in 1880. MSOT enables molecular and functional imaging of the joints in conjunction with simultaneous gathering of anatomic data. Energy is applied to a medium in rapid sequences of light pulses. The emitted light pulses are primarily absorbed by the endogenous chromophore hemoglobin, which can be either oxygenated or deoxygenated. The absorption slightly heats structures containing these constituents, which leads to a small pressure build-up, generating sound waves that can be picked up by ultrasound transducers under suitable conditions. The created sound wave pattern is then converted into a high-resolution image [19]. Initial studies could demonstrate a successful use of optoacoustic imaging in arthritis, especially in rheumatoid arthritis [13].

However, to the best of our knowledge, up to now, there are no reports in the literature about the application of MSOT in the diagnostic of PsA. Thus, the aim of the current pilot study was to evaluate the feasibility of an MSOT imaging system for early diagnosis of PsA.

2. Material and methods

Patients undergoing care in the Department of Dermatology, Venereology and Allergology, University Hospital Essen were asked by their dermatologist to participate in this study. Healthy volunteers were recruited in person at the Department of Dermatology, Venereology and Allergology, University Hospital Essen. The study was performed between March 2019 and March 2020. Specific inclusion criteria for patients in the study were: age ≥ 18 years, diagnosis of psoriasis confirmed by a board-certified dermatologist, swelling or pain of at least one distal (DIP) or proximal interphalangeal (PIP) joint of the hands (see Fig. 1) in the context of previously diagnosed or suspected PsA (for reasons of simplicity in the following called "PsA patients"). Key exclusion criteria included: insufficient communication skills or lack of language skills in the German language and/or (functional) illiteracy. Participants'

Fig. 1. Experimental setting of optoacoustic imaging. The subject's hand is positioned in the water bath (29-31 °C). After an adaptation time of 5 min, imaging is performed using the ultrasound probe, which is similar to a conventional ultrasound transducer.
Abbreviations: DIP = Distal interphalangeal joint (finger end joint); PIP = Proximal interphalangeal joint (middle finger joint).

written, informed consent was obtained from all patients and healthy volunteers before inclusion in the study. Data were collected at a regular visit of the patients in the outpatient department of the Department of Dermatology, Venereology and Allergology, University Hospital Essen. The study was approved by the Ethics committee of the Medical Faculty of the University Duisburg-Essen (IRB protocol number 18-8287-BO) and registered at the German Clinical Trials Register (DRKS00021183). All experimental procedures were in accordance with the principles laid down in the Helsinki Declaration of 1975, as revised in 2008 in accordance with the ethical standards of the responsible committee on human experimentation.

2.1. Clinical evaluation

Data collected included basic demographics (age, sex, ethnicity), clinical data on psoriasis and PsA including the CASPAR score [7], existing diagnostic findings such as X-ray, and current anti-psoriatic treatment.

Participants were asked to rate their joint pain on the numeric rating scale (NRS) ranging from 0 (no pain) to 10 (maximal pain). The joints were physically examined and CRP was assessed at the central laboratory of the University Hospital Essen (Essen, Germany) as a marker of inflammation in psoriasis patients. The cut-off representing CRP values within the normal range is <0.5 mg/dl.

Two patients had a follow-up examination three months after induction of a systemic therapy.

2.2. Theory

2.2.1. Imaging system and acquisition

The imaging study was performed using a handheld 2-dimensional dual modality optoacoustic/ultrasound system (Acuity Echo research system, serial number SN 2-17-04, iThera Medical GmbH; Munich, Germany).

A device similar to the research system used in the current study, the MSOT Acuity v1 (optoacoustic device without active ultrasound), is CE marked. The imaging system used in the current study is based on the MSOT Acuity v1 CE version and adds active ultrasound imaging to the device.

For multispectral imaging, excitation wavelengths of 700, 730, 760, 780, 800, 875 nm were selected with pulsed class 4 laser at a repetition rate of 25 Hz, to allow discrimination of chromophores by spectral unmixing. A cylindrically focused, 256-element detector array (center frequency, 4 MHz; send/receive bandwidth, 52 %; resolution, approximately 190 µm) with 135° coverage provided 2-dimensional cross-sectional images with a field of view of 40×40 mm^2 and a pixel size of 62.5 µm. Laser light was delivered via a fiber bundle (CeramOptec GmbH). During the imaging process, examiners and patients had to protect their eyes with laser safety goggles. If eyes are well protected, side effects resulting from the laser energy are not to be expected. The examination of the finger joint took place with the subject's hand placed in a water bath. The water temperature was controlled to 29–31 °C during the examination. After an adaptation time of 5 min, the probe was placed over the finger joint to be examined, making use of the integrated ultrasound system that allows two-dimensional real-time visualization of the anatomical structures. One image of this area contained 8 repetitions and one frame per wavelength of the same position. The measurement of the optoacoustic signal took about 2–3 seconds.

2.2.2. Semi quantitative analysis

The acquired 2D-images images were reconstructed in real time with the help of the model-based algorithm supplied within the viewMSOT software suite (V3.8; iThera Medical) using standard backprojection. Multispectral illumination was utilized at the described wavelengths in order to separate individual contributions of absorbers. With the help of
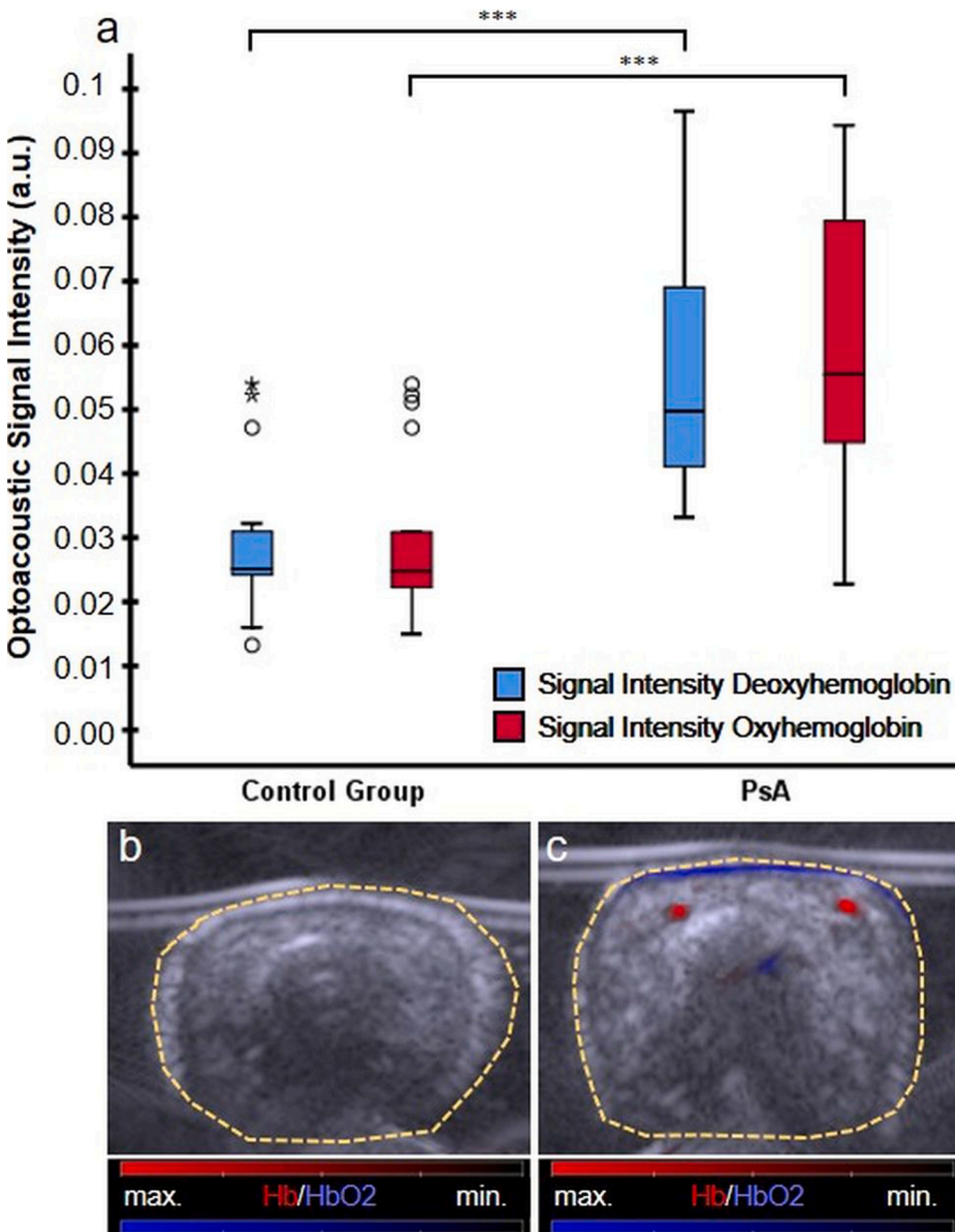

Fig. 2. Distribution of quantitative optoacoustic signals for hemoglobin species.
a) Boxplot diagram displays significantly lower signal intensity in healthy control population. Signal intensity displayed as a.u. (***p ≤ 0.001). b) Overlay of ultrasound and color-coded optoacoustic signal of a healthy control. c) Overlay of ultrasound and color-coded optoacoustic signal of a patient with known PsA. ROIs represented by yellow, dashed line.
Abbreviations: a.u., arbitrary units; PsA, psoriatic arthritis; ROI, region of interest.

linear regression spectral unmixing (negative values were discarded), known absorption spectra of the expected absorbers, oxygenated (HbO_2) and deoxygenated hemoglobin (Hb), were inverted and multiplied with the acquired images to reveal the spatial distribution of the absorber in separate component images. This was done on a pixel-by-pixel basis on the individual absorption spectra of those elements in the near-infrared window. After multispectral processing, the mean optoacoustic signal intensities in the region of interest (ROI) (area of the entire joint in cross section) for oxy- and deoxyhemoglobin were quantified and displayed in arbitrary units (a.u.). The optoacoustic signal intensities shown in the overlays (Fig. 2b and c) were compared between the PsA and the control group after assessing the same image thresholds. The transparency setting of the optoacoustic signal is linear to the signal intensity, so that areas with low optoacoustic signal intensity are completely transparent while the maximum signal is fully opaque.

2.2.3. Statistics

Data were analyzed with SPSS (Statistical Package for Social Science, SPSS Inc., Chicago) version 26 using Mann-Whitney *U* test. Correlations were tested using Spearman's rho. The AUC (area under the curve) values of the ROC (receiver operating characteristic) curves and the corresponding Youden index was assessed in order to investigate the diagnostic performance of MSOT imaging and to determine optimal cut-off values. P values <0.05 were considered statistically significant.

3. Results

22 psoriasis patients (n = 15 females, n = 7 males) fulfilling the above mentioned inclusion criteria were included in the analysis. Their average age was 52.9 years (standard deviation (SD) 13.9, range 26–73 years). 19 healthy volunteers (n = 15 females, n = 4 males) with a mean age of 31.9 (SD 4.2, range 26–45 years) were included in the study as a control group. All subjects were Caucasians. The characteristics of the study participants are shown in Table 2.

CASPAR classification criteria were satisfied in 20 out of 22 patients. The mean CASPAR score was 4.2 (SD 1.5, range 0–6). Mean CRP was 0.3 mg/dl (SD 0.6, range 0–1.9 mg/dl). Mean pain rating on the numeric rating scale (NRS) was 3.0 (SD 2.1, range 0–8).

In eight patients, results of an X-ray were available. In two of these X-rays signs of arthritis were detectable. In two patients bone scintigraphy

Table 2
Patient characteristics.

Patient characteristics				
	PsA		Healthy volunteers	
Age (years)	52.9 ± 13.9	range: 26−73	31.9 ± 4.2	range: 26−45
Female	15 (68.2 %)		15 (78.9 %)	
Male	7 (31.8 %)		4 (21.1 %)	
CASPAR score	4.18 ± 1.5		0	
CRP (mg/dL)	0.32 ± 0.57		N/A	
	MTX (mono)	5		
	MTX (add-on)	3		
	Adalimumab	2		
Systemic therapy	Ixekizumab	3	N/A	
	Secukinumab	4		
	Ustekinumab	3		
Intake of NSAIDs	12 (57.1 %)		0	
	None 12			
Prior imaging	X-ray 8		N/A	
	Bone scintigraphy 2			

Values are displayed as mean ± standard deviation where appropriate. Abbreviations: CRP, C-reactive protein; N/A, not applicable; NSAID, non-steroidal anti-inflammatory drugs; MTX; methotrexate (non-biologic disease modifying anti-rheumatic drug); mono = monotherapy; add-on = low-dose methotrexate in addition to biologic therapy; PsA, psoriatic arthritis; SD, standard deviation. Adalimumab, ixekizumab, secukinumab and ustekinumab belong to the group of biologics.

had been performed. Both results were compatible with psoriatic arthritis.

18 psoriasis patients were under non-biologic disease modifying anti-rheumatic drugs (chemically synthesized, so called 'traditional drugs', such as e.g. methotrexate), respectively biologic therapy (complex proteins produced from living organisms or containing components of living organisms, such as e.g. secukinumab) at the time point of participation in the study and 12 patients reported intake of pain-relieving non-steroidal anti-inflammatory drugs (NSAID) such as ibuprofen (Table 2).

3.1. Optoacoustic data and optoacoustic scoring

Using MSOT, high-resolution real-time images of the finger joints could be obtained. None of the study participants complained about side effects. In parallel, we were able to quantify blood content and oxygenation in the region under study. In PsA patients we detected significantly higher signal intensities of oxy- and deoxyhemoglobin compared to healthy controls (Fig. 2). The signal intensity of both hemoglobin species was found to correlate with higher pain ratings and deoxyhemoglobin signal intensity was shown to be associated with CRP levels (Fig. 3).

The AUC resulting from the optoacoustic signal was 0.921 (confidence interval (CI): 0.830–1.000) for deoxyhemoglobin and 0.900 (CI: 0.805 to 0.994) for oxyhemoglobin, respectively (Fig. 4) suggesting a high diagnostic accuracy. The optimal cutoff to distinguish PsA positive and PsA negative patients turned out to be at 0.033 arbitrary units (a.u.) for both hemoglobin species which resulted in a specificity of 0.842 and a sensitivity of 1.00 with regard to deoxyhemoglobin and a specificity of 0.955 and a sensitivity of 0.789 regarding oxyhemoglobin (Table 3).

Fig. 5 depicts exemplarily the pathologic optoacoustic signal in a painful DIP joint in a middle-aged psoriasis patient at first presentation in our clinic prior to initiation of systemic therapy. Fig. 6 shows an example of a middle-aged female psoriasis patient under systemic therapy with methotrexate with signs of insufficient therapeutic response as indicated by elevated signal intensity for deoxyhemoglobin and oxyhemoglobin. In X-ray, no signs of arthritis had been detectable in these two patients (Figs. 5 and 6).

Three months after induction of a therapy with secukinumab, respectively methotrexate, a follow-up imaging with MSOT was performed in two patients. In both patients, a decrease of signal intensity was detected. The decrease in signal intensity corresponded to a subjective pain relief. Fig. 7 depicts the optoacoustic imaging findings of the patient before and after three months of therapy with secukinumab.

4. Discussion

To the best of our knowledge, this is the first study showing evidence of the feasibility of an optoacoustic imaging system for assessment and monitoring of PsA. Using MSOT, we were able to visualize increased vascularization around the finger joints, a key feature of PsA [20], without applying any exogenous chromophores or contrast agent. The differences in blood content and oxygenation between healthy volunteers and PsA patients were statistically significant (p ≤ 0.001) (Fig. 2). We were able to determine a cutoff of the signal intensity for oxyhemoglobin and deoxyhemoglobin conceivably consistent with early signs of PsA.

Our results are consistent with previous studies that found an impaired oxygen saturation of synovial structures in proportion to the degree of inflammation in patients with inflammatory arthritis [21]. It is assumed, that the high metabolic demand resulting from the migration and proliferation of inflammatory cells, with an expansion of the distance between proliferating cells and nearby blood vessels leads to hypoxia [22]. This mechanism might explain the stronger correlation between the optoacoustic signal for deoxyhemoglobin and higher levels of CRP representing inflammatory activity (Fig. 3c, Table 3).
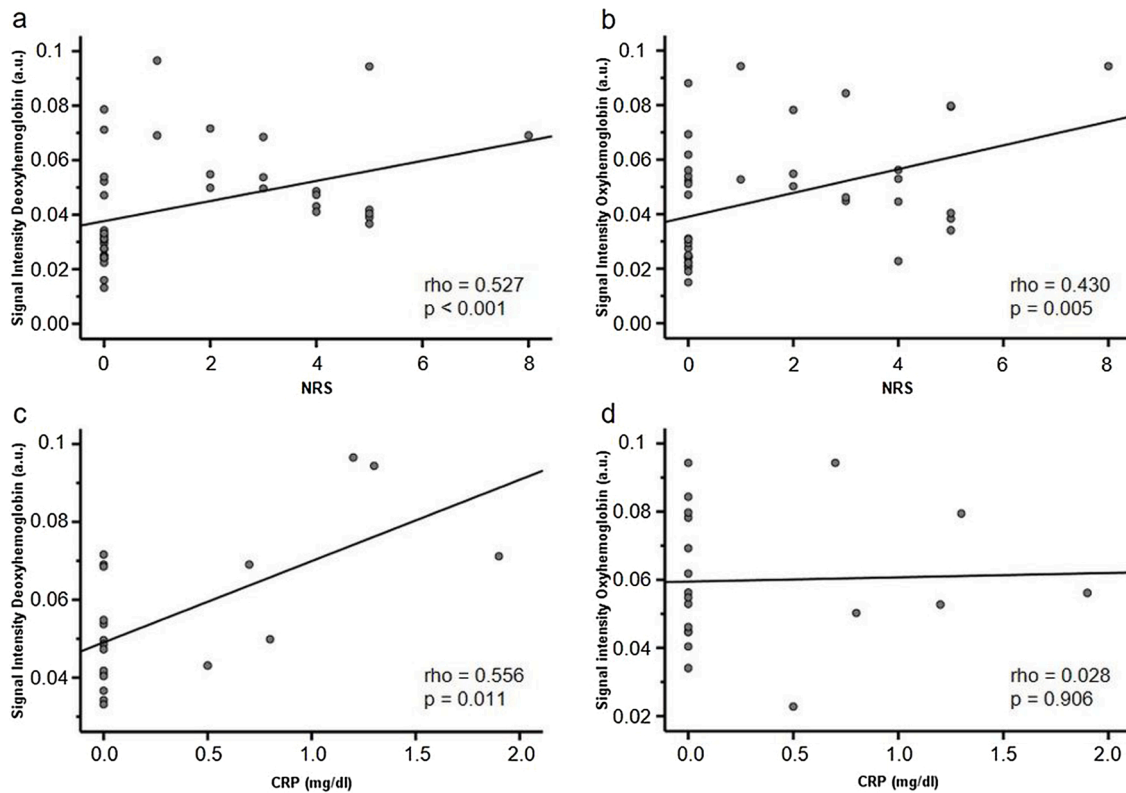
Fig. 3. Correlation of deoxyhemoglobin (a) and oxyhemoglobin (b) with NRS and correlation of deoxyhemoglobin (c) and oxyhemoglobin (d) with CRP. Abbreviations: a.u., arbitrary units; NRS, numeric rating scale; CRP, C-reactive protein.
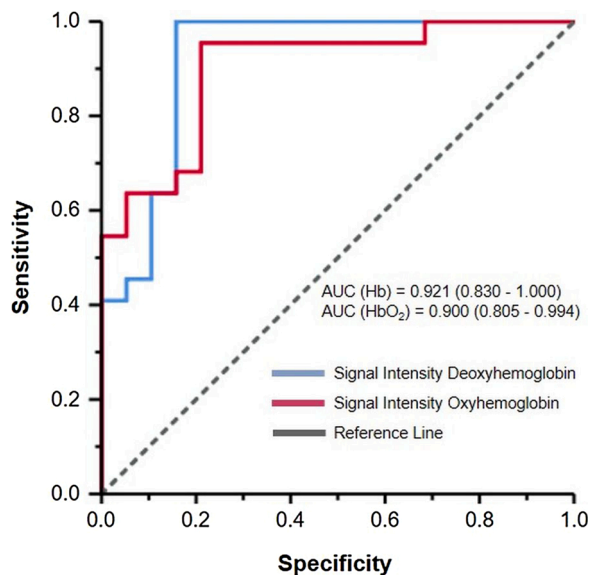

Fig. 4. Diagnostic performance of quantitative optoacoustic signals of hemoglobin species.
ROC curve analysis with corresponding AUC and 95 % confidence intervals displaying the diagnostic performance of optoacoustic signal of deoxyhemoglobin (blue) and oxyhemoglobin (red).
Abbreviations: ROC, receiver-operator characteristic; AUC, areas under the curves.

Increased optoacoustic signal intensities could also be detected in patients with no signs of PsA in X-ray. We assume that these patients were in such an early stage of PsA that morphological changes could not be detected by X-ray yet. This implicates that an earlier diagnosis of PsA

Table 3
Diagnostic accuracy of MSOT for Hb and HbO_2.

	Hb	HbO_2
Sensitivity	1.000	0.789
Specificity	0.842	0.955
PPV	0.880	0.840
NPV	1.000	0.938

Abbreviations: Hb = deoxyhemoglobin; HbO_2 = oxyhemoglobin; PPV = Positive predictive value; NPV = Negative predictive value.

might be possible with optoacoustic imaging. If the data is further confirmed, the decision for specific treatment might be made more quickly in the future.

One patient who already received therapy with MTX, exhibited strong optoacoustic signals, indicating an insufficient therapeutic response (Fig. 6). The follow-up imaging after three months of therapy with methotrexate, respectively secukinumab, showed a decrease of the optoacoustic signal for oxyhemoglobin and deoxygemoglobin species in both re-examined patients (Fig. 7). The results corresponded to a subjective regression of pain.

Our work has similarities with a study of van den Berg et al. [13] who evaluated the feasibility of a portable ultrasound and photoacoustic imaging (PAI) system in patients suffering from rheumatoid arthritis (RA). They examined inflamed and non-inflamed proximal interphalangeal joints of 10 patients suffering from RA compared with joints from 7 healthy volunteers using PAI scans and ultrasound power Doppler (US-PD). The amount of photoacoustic (PA) signal using a ROI drawn over the hypertrophic joint space was assessed. PAI response was significantly increased in inflamed joints in comparison with contralateral non-inflamed joints and with joints from healthy volunteers. Results of US-PD and PAI were strongly correlated.

RA and PsA both belong to the inflammatory rheumatic diseases and are both characterized by pain and swelling in the joints [23,24].
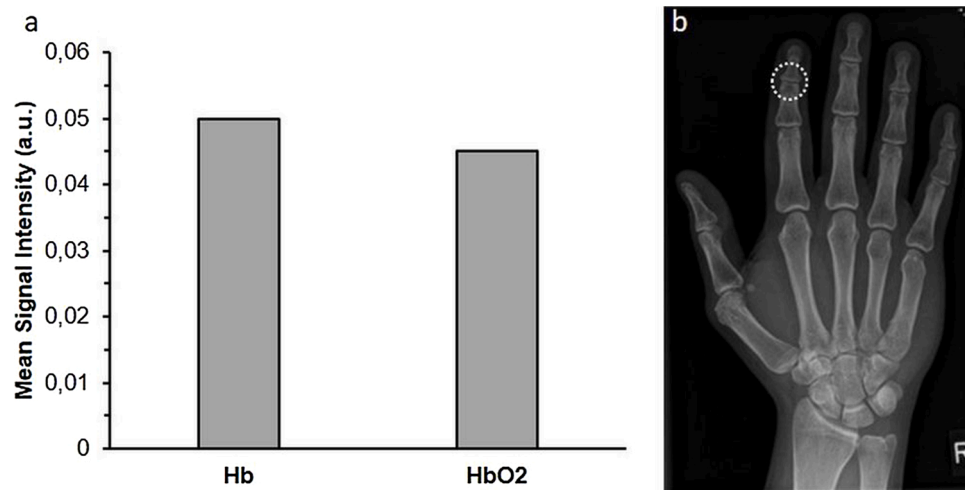
Fig. 5. Pathologic optoacoustic signal in a middle-aged patient with painful finger joints (NRS 3/10) prior to initiation of systemic therapy. a) Quantitative analysis of mean signal intensity shows increased amount of both hemoglobin species. b) X-ray displays no signs of arthritis. Dotted circle marks examined joint. Abbreviation: a.u., arbitrary units; NRS, numeric rating scale.
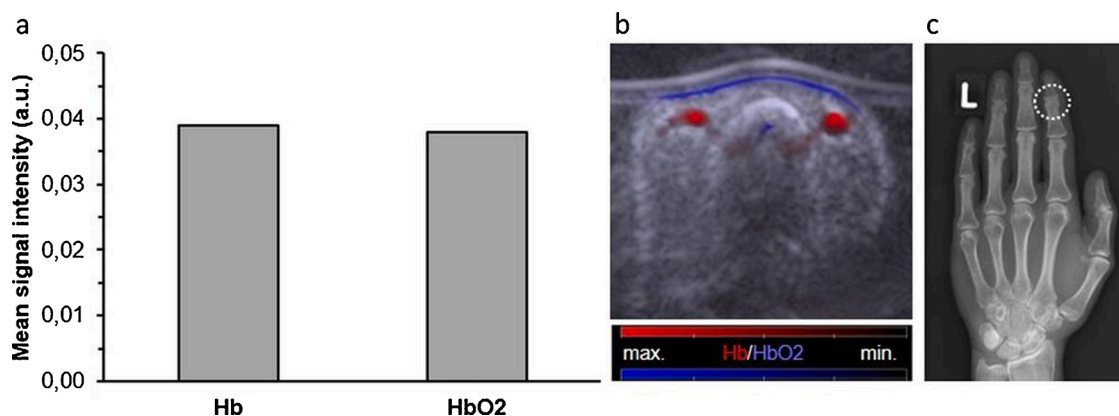

Fig. 6. Pathologic optoacoustic signal in a middle-aged female patient under therapy with methotrexate with painful finger joints (NRS 5/10). a) Quantitative analysis of mean signal intensity shows increased amount of both hemoglobin species. b) Overlay of ultrasound and color-coded optoacoustic signal showing visibly increased signal intensity. c) X-ray displays no signs of arthritis. Dotted circle marks examined joint. Abbreviation: a.u., arbitrary units; NRS, numeric rating scale.
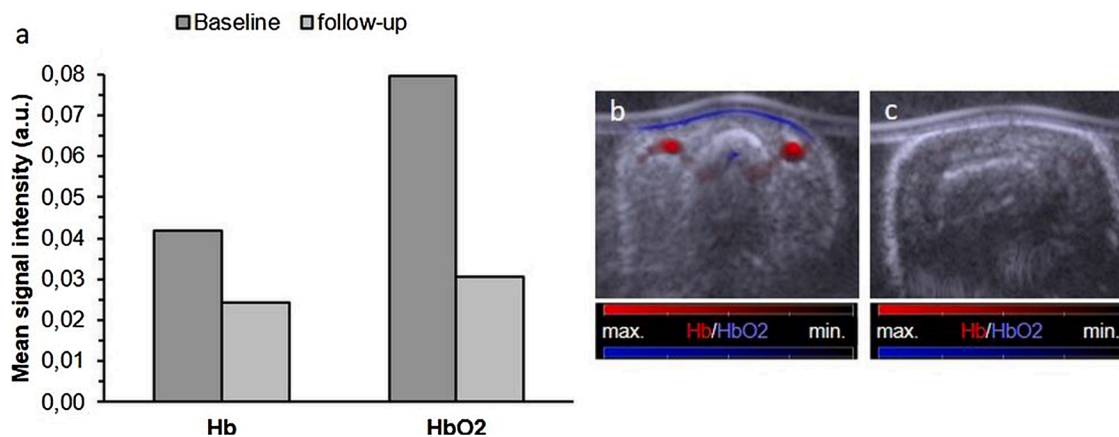

Fig. 7. Therapeutic effect in an elderly patient receiving a therapy with secukinumab with painful finger joints (NRS 5/10) at baseline and pain relief (NRS 0/10) at follow-up after 3 months. a) Quantitative analysis of mean signal intensity shows decrease of oxy- and deoxyhemoglobin representing reduced inflammatory activity in follow-up examination compared to baseline. b) Overlay of ultrasound and color-coded optoacoustic signal at baseline showing higher signal intensity compared to c) follow-up. Abbreviation: a.u., arbitrary units; NRS, numeric rating scale.

However, RA and PsA have key differences in pathogenesis and clinical presentation. In RA, the inflammatory processes primarily lead to thickening of the synovia, the tissue lining the joints. In PsA, the inflammatory process is thought to start at the entheses, the sites of insertion of tendons, ligaments, fascia, or capsules to bone, by the action of biomechanical stress leading to production of cytokines, which then enter synovial tissue, resulting in an articular inflammatory response [25].

In contrast to the study of van den Berg et al. in which a 805 nm single wavelength system was utilized, we used a multispectral optoacoustic approach, which allows separate detection of oxy- and deoxyhemoglobin. Thus, we were able to obtain additional information about the level of inflammation that is in general associated with a higher amount of deoxyhemoglobin. Further, we specified the ROI in a slightly different way compared to van den Berg et al. since they drew the ROI over the hypertrophic joint space, whereas we assessed the area of the entire joint in cross section. Due to the pathogenetic differences between RA (inflammation primarily of the synovia in the joint) and PsA (inflammation begins in the periarticular structures) this difference is reasonable. Considering the data of van Berg et al., the results of the current work fit in very well and support further research on optoacoustic imaging methods in diagnostic of arthritis.

However, there are still some limitations of optoacoustic imaging methods to consider. The acquisition costs of an optoacoustic device might be a relevant obstacle for the broad clinical use of the technology. An additional limitation of the technique is that the penetration depth of the laser is currently limited to 3–4 cm, hampering examination of the inflammatory activity of larger joints such as the knee joint or the spine [26]. Metallic foreign bodies such as osteosynthesis material can cause artifacts that significantly limit feasibility. Further, interpretation of optoacoustic images at the moment requires understanding of the physics and computations involved and a special training of the clinical examiner is needed [27].

While our work provides first evidence of MSOT detecting early signs of PsA, there also exist methodological limitations to this study. Firstly, the number of patients and healthy controls included in the study was small. Secondly, the technique is not specific for psoriasis associated inflammation of the joints, but detects inflammation in general. Thus, possible confounders might be activated arthrosis, rheumatoid arthritis and infectious inflammation. Specific confounding factors affecting vascularization or rheology must be considered prior to optoacoustic imaging. Diabetic angiopathy and peripheral vascular occlusive disease can affect the measurement leading to false-negative results. In such circumstances, it makes considerable sense to carry out a baseline examination and to correlate it with disease activity during subsequent treatment. The mean age of the healthy control group was significantly younger compared to the patients (31.9 vs. 52.9 years), which could have influenced the results. The older age of the PsA group might go along with a higher rate of (undiagnosed) diabetic angiopathy or peripheral vascular occlusive disease promoting false-negative results. However, the younger mean age of the control group might also be favorable since possible confounders such as activated arthrosis occur less frequently.

5. Conclusions

Our preliminary data indicate that MSOT with a handheld probe might be useful for early diagnosis of PsA and monitoring of therapeutic success, thus possibly facilitating therapy decisions in the future. Our results provide a basis for further research to investigate the potential benefits of optoacoustic imaging in diagnostic of PsA over other modalities.

Funding

Ethics approval

The study was approved by the Ethics committee of the Medical Faculty of the University Duisburg-Essen (IRB protocol number 18-8287-BO).

Consent to participate

Participants' written, informed consent was obtained from all patients and healthy volunteers before inclusion in the study.

Consent for publication

All authors approved the version to be published.

CRediT authorship contribution statement

Sandra Hallasch: Methodology, Formal analysis, Investigation, Writing - original draft. **Nina Giese:** Methodology, Writing - review & editing. **Ingo Stoffels:** Methodology, Writing - review & editing, Funding acquisition, Resources, Supervision. **Joachim Klode:** Conceptualization, Methodology, Formal analysis, Investigation, Writing - review & editing, Funding acquisition, Resources, Supervision. **Wiebke Sondermann:** Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

Dr. Sondermann reports personal fees from Almirall, personal fees from Abbvie, personal fees from UCB, personal fees from Janssen, personal fees from LEO Pharma, from Lilly, personal fees from Sanofi Genzyme, grants and personal fees from Novartis, personal fees from Celgene, personal fees from Pfizer, outside the submitted work. The other authors have nothing to declare.

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References

[1] M. Augustin, K. Reich, G. Glaeske, I. Schaefer, M. Radtke, Co-morbidity and age-related prevalence of psoriasis: analysis of health insurance data in Germany, Acta Derm. Venereol. 90 (2010) 147–151.

[2] M. Köhm, F. Behrens, Diagnosis and therapy of early psoriatic arthritis, Zeitschrift fur Rheumatologie 71 (2012) 46–52.

[3] M.A. Radtke, K. Reich, C. Blome, S. Rustenbach, M. Augustin, Prevalence and clinical features of psoriatic arthritis and joint complaints in 2009 patients with psoriasis: results of a German national survey, J. Eur. Acad. Dermatol. Venereol. 23 (2009) 683–691.

[4] D. Cretu, L. Gao, K. Liang, A. Soosaipillai, E.P. Diamandis, V. Chandran, Differentiating psoriatic arthritis from psoriasis without psoriatic arthritis using novel serum biomarkers, Arthritis Care Res. 70 (2018) 454–461.

[5] M.G. Lebwohl, H. Bachelez, J. Barker, G. Girolomoni, A. Kavanaugh, R.G. Langley, C.F. Paul, L. Puig, K. Reich, P.C. Van De Kerkhof, Patient perspectives in the management of psoriasis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey, J. Am. Acad. Dermatol. 70 (2014) 871–881, e830.

[6] M. Radtke, K. Reich, C. Blome, S. Rustenbach, M. Augustin, Prevalence and clinical features of psoriatic arthritis and joint complaints in 2009 patients with psoriasis: results of a German national survey, J. Eur. Acad. Dermatol. Venereol. 23 (2009) 683–691.

[7] W. Taylor, D. Gladman, P. Helliwell, A. Marchesoni, P. Mease, H. Mielants, Classification criteria for psoriatic arthritis: development of new criteria from a large international study, Arthritis Rheum. 54 (2006) 2665–2673.

[8] M.A. Radtke, K. Reich, F. Beikert, M. Augustin, Psoriasis arthritis. An interdisciplinary challenge, Hautarzt 62 (2011) 779–790, quiz 791-792.

[9] D. Cretu, L. Gao, K. Liang, A. Soosaipillai, E.P. Diamandis, V. Chandran, Differentiating psoriatic arthritis from psoriasis without psoriatic arthritis using novel serum biomarkers, Arthritis Care Res. (Hoboken) 70 (2018) 454–461.

[10] M. Boncler, Y. Wu, C. Watala, The multiple faces of C-reactive protein-physiological and pathophysiological implications in cardiovascular disease, Molecules (2019) 24.

[11] S.K. Felbo, L. Terslev, M. Ostergaard, Imaging in peripheral and axial psoriatic arthritis: contributions to diagnosis, follow-up, prognosis and knowledge of pathogenesis, Clin. Exp. Rheumatol. 36 (Suppl. 114) (2018) 24–34.

[12] M. Ostergaard, L. Eder, S.N. Christiansen, G.S. Kaeley, Imaging in the diagnosis and management of peripheral psoriatic arthritis-the clinical utility of magnetic resonance imaging and ultrasonography, Best Pract. Res. Clin. Rheumatol. 30 (2016) 624–637.

[13] P.J. Van Den Berg, K. Daoudi, H.J. Bernelot Moens, W. Steenbergen, Feasibility of photoacoustic/ultrasound imaging of synovitis in finger joints using a point-of-care system, Photoacoustics 8 (2017) 8–14.

[14] A. Spadaro, E. Lubrano, Psoriatic arthritis: imaging techniques, Reumatismo 64 (2012) 99–106.

[15] X. Baraliakos, A. Kleyer, D. Simon, M. Kohm, S. Ohrndorf, P. Sewerin, Imaging of psoriatic arthritis and aspects of radiographic progression, Z. Rheumatol. 79 (2020) 40–52.

[16] M. Gutierrez, E. Filippucci, F. Salaffi, L. Di Geso, W. Grassi, Differential diagnosis between rheumatoid arthritis and psoriatic arthritis: the value of ultrasound findings at metacarpophalangeal joints level, Ann. Rheum. Dis. 70 (2011) 1111–1114.

[17] P.J. Mease, Psoriatic arthritis: update on pathophysiology, assessment and management, Ann. Rheum. Dis. 70 (Suppl. 1) (2011) i77–84.

[18] S.G. Werner, H.E. Langer, S. Ohrndorf, M. Bahner, P. Schott, C. Schwenke, M. Schirner, H. Bastian, G. Lind-Albrecht, B. Kurtz, G.R. Burmester, M. Backhaus, Inflammation assessment in patients with arthritis using a novel in vivo fluorescence optical imaging technology, Ann. Rheum. Dis. 71 (2012) 504–510.

[19] Y. Jiang, A. Forbrich, T. Harrison, R.J. Zemp, Blood oxygen flux estimation with a combined photoacoustic and high-frequency ultrasound microscopy system: a phantom study, J. Biomed. Opt. 17 (2012) 036012.

[20] D.J. Veale, U. Fearon, The pathogenesis of psoriatic arthritis, Lancet 391 (2018) 2273–2284.

[21] C.T. Ng, M. Biniecka, A. Kennedy, J. Mccormick, O. Fitzgerald, B. Bresnihan, D. Buggy, C.T. Taylor, J. O'sullivan, U. Fearon, D.J. Veale, Synovial tissue hypoxia and inflammation in vivo, Ann. Rheum. Dis. 69 (2010) 1389–1395.

[22] F.P. Cantatore, N. Maruotti, A. Corrado, D. Ribatti, Angiogenesis dysregulation in psoriatic arthritis: molecular mechanisms, Biomed Res. Int. 2017 (2017), 5312813.

[23] B. Michelsen, R. Fiane, A.P. Diamantopoulos, D.M. Soldal, I.J.W. Hansen, T. Sokka, A. Kavanaugh, G. Haugeberg, A comparison of disease burden in rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis, PLoS One 10 (2015) e0123582-e0123582.

[24] J.F. Merola, L.R. Espinoza, R. Fleischmann, Distinguishing rheumatoid arthritis from psoriatic arthritis, RMD Open 4 (2018), e000656.

[25] J. Bagel, S. Schwartzman, Enthesitis and dactylitis in psoriatic disease: a guide for dermatologists, Am. J. Clin. Dermatol. 19 (2018) 839–852.

[26] A. Helfen, M. Masthoff, J. Claussen, M. Gerwing, W. Heindel, V. Ntziachristos, M. Eisenblätter, M. Köhler, M. Wildgruber, Multispectral optoacoustic tomography: intra- and interobserver variability using a clinical hybrid approach, J. Clin. Med. (2019) 8.

[27] A. Karlas, N.A. Fasoula, K. Paul-Yuan, J. Reber, M. Kallmayer, D. Bozhko, M. Seeger, H.H. Eckstein, M. Wildgruber, V. Ntziachristos, Cardiovascular optoacoustics: from mice to men – a review, Photoacoustics 14 (2019) 19–30.
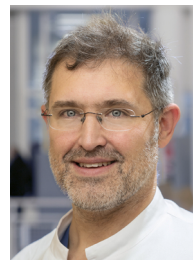
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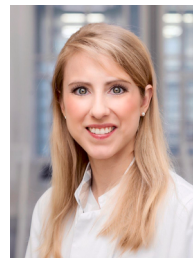

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