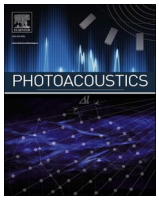
Photoacoustics 38 (2024) 100611

Contents lists available at ScienceDirect

Photoacoustics

journal homepage: www.elsevier.com/locate/pacs



Structural and functional imaging of psoriasis for severity assessment and quantitative monitoring of treatment response using high-resolution optoacoustic imaging

Xiuting Li [a], Yik Weng Yew [b,1], Keertana Vinod Ram [a,1], Hazel H. Oon [c], Steven Tien Guan Thng [b,*], U.S. Dinish [a,*], Malini Olivo [a,*]

[a] A*STAR Skin Research Labs (A*SRL), Agency for Science, Technology and Research (A*STAR), 31 Biopolis Way, #07-01 Nanos, Singapore 138669, Republic of Singapore
[b] National Skin Centre, Singapore
[c] National Skin Centre and Skin Research Institute of Singapore (SRIS), Singapore

ARTICLE INFO

Keywords:
Psoriasis
Multispectral optoacoustic imaging
Oxygen saturation
Epidermis thickness
Total blood volume
Treatment response
Objective assessment

ABSTRACT

Psoriasis is a chronic inflammatory skin disease, characterized by thick scaly plaques. It imposes a notable disease burden with varying levels of severity affecting the quality of life significantly. Current disease severity assessment relies on semi-objective visual inspection based on the Psoriasis Area and Severity index (PASI) score that might not be sensitive to sub-clinical changes. Histology of psoriasis skin lesions necessitate invasive skin biopsies. This indicates an unmet need for a non-invasive, objective and quantitative approach to assess disease severity serially. Herein, we employ multispectral Raster-Scanning Optoacoustic Mesoscopy (ms-RSOM) derived structural and microvascular functional imaging metrics to examine the lesional and non-lesional skin in psoriasis subjects across different severities and also evaluate the treatment outcome in a subject with topical steroids and biologics, such as adalimumab. ms-RSOM derived structural metrics like epidermal thickness and total blood volume (TBV) and microvascular functional information such as oxygen saturation (sO_2) are evaluated by spectrally resolving the endogenous chromophores like melanin, oxy-, and deoxy-hemoglobin. Initial findings reveal an elevated sO_2 and TBV with severity in lesional and non-lesional psoriasis skin, thus representing increasing inflammation. An increase in epidermal thickness is also noted with the degree of severity, corresponding to the inflammation and increased abnormal cell growth. As a marker to evaluate the treatment response, we observed a decrease in epidermal thickness, sO_2, and TBV in a psoriasis patient post-treatment, which is consistent with the decrease in the PASI score from 4.1 to 1.9. We envision that ms-RSOM has a huge potential to be translated into routine clinical setting for the diagnosis of severity and assessment of treatment monitoring in psoriasis subjects.

1. Introduction

Psoriasis is a chronic skin disease with well-demarcated scaly plaques affecting the scalp, trunk and limbs. It is a result of a dysregulation of the skin immune system that causes a rapid replacement of the skin [1]. Dysregulation of the immune system can occur due to genetic risk factors, immune suppressant medications like steroids, immune responses such as allergies or due to autoimmunity [2]. Psoriasis is an inflammatory skin disorder where the immune cells known as T cells attack normal healthy skin cells in the body which release signals to recruit other immune cells creating an inflammatory environment within the skin [3]. This causes the body to generate keratinocytes at an undesirable faster rate which results in keratinocytes stacking on top of each other [3]. There are many types of psoriasis, some common types of which include plaque, scalp, nail, guttate, and inverse psoriasis, while less common types include localized pustular, generalized pustular, palmoplantar and erythrodermic psoriasis [1]. There is variation with disease severity and psoriatic comorbidities include metabolic disorders, ischemic heart disease, inflammatory bowel disease, and uveitis [1,4]. Psoriasis may also result in psoriatic arthritis which affects one's daily

* Corresponding authors.
E-mail addresses: steventhng@nsc.com.sg (S.T.G. Thng), dinish@asrl.a-star.edu.sg (U.S. Dinish), Malini_Olivo@asrl.a-star.edu.sg (M. Olivo).
[1] These authors contributed equally

https://doi.org/10.1016/j.pacs.2024.100611
Received 26 January 2024; Received in revised form 19 April 2024; Accepted 22 April 2024
Available online 23 April 2024

life [5]. Additionally, psoriasis may be associated with psychological comorbidities such as low self-esteem, anxiety or depression [5]. Given that psoriasis can affect one's health to a great extent, affecting the quality of life, it is important to have an objective tool that can accurately and non-invasively identify and evaluate psoriasis's severity at an early stage, so that early treatment can be initiated to reduce the cumulative life course impairment [6].

Currently, the severity of psoriasis is assessed clinically using the Psoriasis Area and Severity Index (PASI) score [7], which involves visual examination of the skin, scalp and nails for signs of psoriasis, and through questionnaires directed to the patients to better understand their health and disease history [1,8]. Dermoscopy offers a horizontal view, revealing the vascular pattern and enhanced visibility of the skin and blood vessels, where psoriatic lesions would show uniformly distributed 'dotted' or 'pinpoint' capillaries, along with coiled vessels, against a light red background with white diffuse scales [8]. Analyzed skin lesions of psoriasis are then recorded and stored in a computer under standardized conditions using video dermoscopy. But the PASI score and dermoscopy currently used still have many drawbacks. Although, PASI may seem like a well-developed form of scoring measurement, it is semi-objective as it relies entirely on the doctor's experience in examining the skin condition [9]. Research has shown that there is substantial difference between the PASI scores calculated by experienced and inexperienced physicians, which raises concerns for its reliability [10]. Additionally, PASI lacks sensitivity as erythema, desquamation, and induration within the four body region are scored with equal weightage [10]. This should not be the case as occurrences at the palm and soles can affect a patient from work and other life activities more greatly than if it occurs at the trunk. In addition, PASI only involves surface level examination of the skin which fails to reflect what is happening beneath the skin surface, which may be of greater concern. Similar to the PASI score, dermoscopy examination also primarily entails surface level skin information and depends highly on the clinicians' expertise in interpreting thermoscopic images which can be subjective.

To comprehend the underlying pathophysiology non-invasively, optical coherence tomography (OCT) typically using and other imaging modalities offer insights without resorting to invasive procedures like skin biopsy [11]. Skin biopsy's invasive nature, involving tissue removal, poses risks such as bleeding and damage to surrounding tissues [12], making it less favorable among patients. OCT is based on low-coherence interferometry, collects a small portion of the light that reflects from sub-surface features when an optical beam is directed at the tissue. It capable of imaging 1–2 mm beneath the skin surface, provides detailed information on structural and microvascular changes in real-time [13,14]. While widely used in early-stage skin cancer diagnosis and excelling in deep vertical slice imaging, OCT has less cellular resolution (a few μm) as compared to confocal microscopy (~1 μm), and lacks the ability to image pigmented lesions [14,15]. A recent version of OCT, Line-field confocal optical coherence tomography (LC-OCT) merges the strengths of both, achieving an impressive spatial resolution of ~1 μm, and penetration depth of ~500 μm, revealing structural details of the skin, but fails in providing functional and hemodynamic information, which poses as a limitation to treatment monitoring applications [16,17]. Given these constraints, a non-invasive diagnostic method that sensitively detects skin changes with minimal bias is essential for comprehensive assessment and monitoring of psoriasis treatment responses [18]. Accurate monitoring is crucial for optimizing medication usage during treatment, ensuring effectiveness while avoiding adverse effects [19]. In this context, optoacoustic (photoacoustic) imaging (OAI) which has a similar spatial resolution to OCT (~10 μm) emerges as a potential non-invasive objective diagnosis method that provides functional information [20].

OAI employs short-pulsed laser excitation of tissue to cause transient temperature rise leading to thermoelastic expansion generating acoustic waves that are detected using an ultrasonic transducer [20]. Tissue thermoelastic expansion, resulting from light absorption by chromophores, facilitates image generation [21]. OAI, uniquely capable of assessing infectious pigmented skin lesions, surpasses OCT in this regard [22]. Various OAI versions include macroscopic optoacoustic tomography and optoacoustic microscopy. Optoacoustic tomography, employing lower central frequency detector to collect ultrasound signals, enables deeper penetration in centimeters with macroscopic-scale resolution. This technique is used for detecting hemodynamic changes in foot vessels and assessing breast tumor margins [23,24]. Conversely, optoacoustic microscopy, also known as photoacoustic microscopy (PAM), utilizing a higher central frequency detector to capture the ultrasound signals from superficial smaller structures, encounters limitations in imaging depth due to the frequency-dependent ultrasonic attenuation in tissue. In PAM, the dual foci of the optical excitation and ultrasonic detection are typically configured confocally to optimize sensitivity. Depending on whether the optical or ultrasonic focus is finer, PAM is further categorized into optical-resolution (OR) and acoustic-resolution (AR) PAM [25,26]. In OR-PAM, optical focus is much tighter than the acoustic focus, providing a high lateral resolution at the subcellular or cellular scale ranging from a few hundred nanometers to a few micrometers [25]. In contrast, in AR-PAM, the acoustic focus is finer than the optical focus. Despite diffuse optical excitation, diffraction-limited acoustic detection ensures lateral resolution in the tens of micrometers range. This capability persists at depths beyond the optical diffusion limit, reaching a few millimeters [26]. PAM is beneficial for stem cell monitoring, imaging of breast tumor, gastrointestinal tumor and eye etc. [27–29].

In this study, we used innovative multi-spectral raster-scanning optoacoustic mesoscopy (ms-RSOM), operating in wide broadband detection mode spanning 11 ~ 99 MHz. It effectively balances the depth and resolution, providing up to ~ 2 mm with a lateral resolution of ~40 μm, which is well-suited for skin imaging [30–32]. To enable advanced imaging of various skin chromophores and derive functional information, ms-RSOM utilizes a high repetition rate laser at four distinct wavelengths. This setup facilitates spatial visualization and unmixing of different chromophores [20]. In our previous study focused on imaging of atopic dermatitis (AD), ms-RSOM effectively differentiated between lesional and non-lesional skin, providing valuable insights into oxygen saturation (sO_2) and revealing nuanced morphological and physiological aspects across varying severities[20].

Historically, investigations have predominantly employed single-wavelength OAI to elucidate structural details in human subjects. The application of functional imaging, however, has been primarily confined to studies involving animals. Aguirre J. et al. have showcased the application of single wavelength RSOM to visualize skin morphology and vascular patterns in the dermal and sub-dermal layers of six psoriasis patients. Their results were validated with corresponding histopathology samples in terms of epidermal thickness and vessel diameter. This method enabled the quantification of inflammation and other psoriasis biomarkers without the need for contrast agents [32]. Benedikt H. et al. proposed a study that involved 80 measurements of 20 psoriatic skin plaques under diverse treatments, underscored the potential of optoacoustic mesoscopy in delivering label-free assessments of inflammation biomarkers through three-dimensional, high-resolution images of human skin [33]. Additionally, Wang et al. emphasized the capacity for high-resolution anatomical structure visualization of human skin using optoacoustic dermoscopy [34]. In the pursuit of monitoring therapeutic responses in psoriasis plaque, K. Ossadnik et al. investigated the pathological changes in vascular structures of patients using OAI and confocal laser scanning microscopy [35]. In a pioneering initiative, Luo et al. designed a broadband, high-frequency ultrasonic transducer for functional OAI to explore psoriasis progression in a small animal model [36]. Our study marks the first integration of both structural and functional imaging to assess the degree of inflammation as a surrogate indicator of lesional psoriasis severity, and quantitatively monitor treatment responses through high-resolution OAI. This approach holds promise for gaining insights into various treatment protocols and topical applications.

In this research, we introduce a novel approach by combining functional information such as sO_2 in the skin microvasculature with structural information, including epidermal thickness and total blood volume (TBV). These parameters, for the first time, serve as biomarkers to assess the degree of inflammation in psoriasis in both lesional and non-lesional areas. Additionally, we showcase the objective quantification of the structural and functional metrics for treatment response using topical steroids and the biologic adalimumab. The collective information on skin microvasculature emerges as a promising and objective biomarker, offering non-invasive imaging capabilities for investigating inflammatory skin diseases and their treatment responses.

2. Methods

2.1. Subjects

The study included eight psoriasis patients recruited from the National Skin Centre, Singapore, comprising two mild, three moderate, and three severe cases. Average PASI scores were 3.1 ± 1.48 for mild, 8.9 ± 3.8 for moderate, and 20.3 ± 4.3 for severe cases. All subjects had Fitzpatrick scores of types III to IV, minimizing external confounding factors. OAI using ms-RSOM was performed on the ventral forearm, capturing images from a 5 mm×3 mm area over a representative psoriasis skin lesion and a non-lesional area at least 2 cm away. The study was approved by the National Healthcare Group (NHG) Domain Specific Review Board (DSRB), Singapore (Ref No. 2020/00079), with patient consent obtained in compliance with institutional approvals.

2.2. Multi-spectral RSOM imaging workflow

The ms-RSOM system (RSOM Explorer ms-C50, iThera Medical GmbH, Munich, Germany) has been meticulously devised to achieve high-resolution clinical visualization of superficial microvasculature, presenting intrinsic optical tissue contrast at mesoscopic scales. Demonstrating an axial and lateral resolution of up to 10 μm and 40 μm respectively at penetration depths of 2 mm, as expounded in our previous publication [20]. This innovative system integrates a nanosecond Raman laser with four distinct wavelengths (532, 555, 579, and 606 nm) and an ultra-broadband transducer (center frequency 50 MHz, bandwidth 11–99 MHz), shown in Fig. 1. The absorption of light by different chromophores leads to the production of pressure waves, detectable through an ultrasound transducer, subsequently reconstructed into single-wavelength images. To enhance visualization, a frequency separation approach is implemented such that the lower frequency band, spanning 11–33 MHz corresponds to larger structures, while the higher frequency band, ranging from 33 to 99 MHz represents smaller vascular structures [20]. Employing spectral unmixing, a linear regression algorithm incorporating non-negative constraints is employed to discern distinct skin chromophores based on their respective absorption spectra within the induced light wavelengths. Multiple wavelengths' illumination facilitates the reconstruction of a three-dimensional spatial map of skin chromophores, including melanin, oxy-hemoglobin (HbO_2) and deoxy-hemoglobin (Hb) by spectral unmixing. It affords the quantification of functional information, such as sO_2 in microvasculature. The system's unique capability to calculate sO_2 in individual vessels distinguishes it from other optical imaging techniques, providing unprecedented insights into tissue oxygenation states.

2.3. Quantitative analysis of specific imaging metrics

In our investigation, we employed ms-RSOM images derived four metrics to explore changes in the vascular structure and function, including (1) sO_2, (2) relative difference of sO_2 between lesional and non-lesional area (δsO_2), (3) TBV, and (4) epidermal thickness (ET). Min-max normalization was implemented to scale the metric values within the range of 0 to 1. We quantitatively analyzed normalized sO_2, δsO_2, TBV, and ET across different severity levels in psoriasis patients. Furthermore, we evaluated these four imaging metrics along with three clinical skin physiology metrics (a) TEWL, (b) skin moisture, and (c) pH for monitoring the treatment response in one mild psoriasis patient. Detailed calculations for each metric have been previously elucidated in our publication [20,30], with a brief overview provided here.

sO_2 is determined by the equation $\frac{HbO_2}{(Hb+HbO_2)}$, and the contributions of HbO_2 and Hb in the dermis are obtained through spectral unmixing based on the absorption coefficients of skin chromophores from individual wavelength images. TBV was derived by summing the non-zero number of voxels within the segmented 3D dermal region after applying a threshold. In our study, epidermis thickness was taken as the distance from the skin surface to the bottom of the melanin layer, considering melanin's predominant presence in the basal epidermal layer [30]. We computed the average of all pixels in the x-y plane along the z-axis of the unmixed melanin 3D image stacks. Then, we identified the center of the melanin layer as the first dominant peak and determined the bottom edge of the melanin layer using the full width at half maximum. For better visual representation, the epidermis thickness is indicated by white arrows as in Fig. 2.

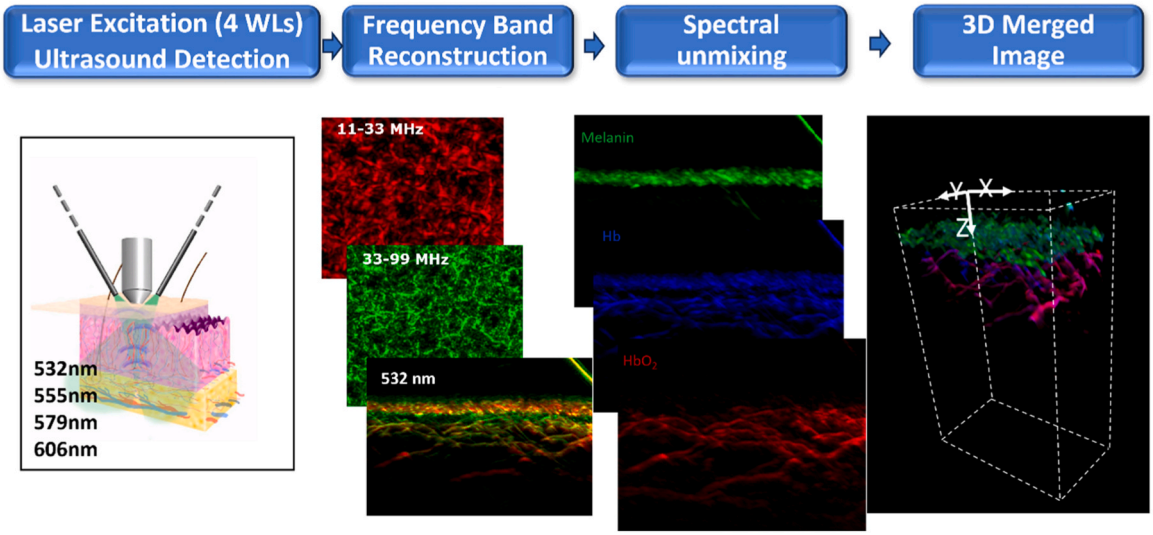


Fig. 1. Schematic imaging workflow of ms-RSOM.

2.4. Treatment response

We conducted imaging in a mild psoriasis patient with a baseline PASI value of 4.1. Imaging was conducted before and four-months after the treatment period involving topical steroids and biologic, adalimumab. High-resolution 3D vascular structural images were acquired from both non-lesional and lesional areas of the patient, and subsequently, image metrics were systematically calculated. This method allowed for a detailed examination of the effects of the specified treatment regimen on the psoriatic skin condition.

3. Results and discussions

3.1. Image visualization across psoriasis severity

Based on the absorption of light by the different chromophores, Fig. 2A, B, and C present 3D spatial map of lesional psoriasis skin revealing different vasculatures and morphology among mild, moderate, and severe cases. Distinguishing the epidermis from the surrounding skin, melanin is depicted in green, while the dermis showcases a robust vascular network denoted by blue for Hb and red for HbO_2 content. The skin surface epidermal layer in all severities displays a robust green signal indicative of the melanin present. In Fig. 2B and C, the depiction of the HbO_2 chromophore in red is notably lower for mild cases compared to moderate and severe cases. Additionally, the presence of blood vessels towards the surface is observed in severe cases. This suggests heightened inflammation corresponding to increased severity [37]. Maximum intensity projections of 3D images obtained with a 532 nm laser and then subjected to analysis through low and high-frequency bands, are depicted in Fig. 2D, E, and F. As the severity increases, the low-frequency band, representing blood flow and indicating inflammation, demonstrates an escalated blood flow on the surface. This observation aligns with the elevated inflammation portrayed in Fig. 2C. Additionally, the 2D image in Fig. 2F exhibits capillary loops present only in the severe psoriasis case [37,38].

3.2. Quantitative analysis of image-derived metrics across psoriasis severity

As represented in Fig. 3A, the mean value of normalized sO_2 in lesional psoriasis increases by 27% from mild (0.35 ± 0.04) to moderate (0.45 ± 0.26) and 63% from moderate to severe (0.73 ± 0.24) psoriasis patients. As inflammation intensifies with increasing severity, there is a concurrent rise in HbO_2, consequently increasing the levels of sO_2 and TBV in lesional skin, as also depicted in Fig. 2. This finding is consistent with prior studies that have demonstrated an increase in sO_2 with inflammation [39]. It is intriguing to observe that in non-lesional psoriasis, there is a rise in normalized sO_2 with severity, with a 50% rise from mild (0.09 ± 0.06) to moderate (0.13 ± 0.11), and a remarkable 393% surge from moderate to severe (0.67 ± 0.30). This shows that while non-lesional skin is less inflamed than lesional skin, it is significantly affected in severe psoriasis cases. This finding could serve as an early indicator of future disease progression in the region, aligning with a previous histopathological study [40]. It also supports earlier research suggesting that even non-lesional psoriasis skin displays inflammation characteristics [41]. Fig. 3B delineates normalized δsO_2, denoting the disparity between lesional and non-lesional regions in each patient. The ascending trajectory, correlating with the severity spectrum from mild to severe, aligns with heightened inflammation observed in localized lesional psoriasis. This trend persists even after adjusting for the concurrent elevation in the non-lesional regions. Specifically, a 47% escalation in δsO_2 is evident from mild to severe conditions, with a more pronounced 96% increase noted from moderate to severe manifestations.

Another metric indicative of inflammation is the TBV, as depicted in Fig. 3C, which increases as blood vessels dilate to enhance the nutrient supply to inflamed regions [20]. The average value of normalized TBV demonstrated a 10% increase from mild (0.54 ± 0.13) to moderate (0.60 ± 0.29) and a 5% increase from moderate to severe (0.63 ± 0.28) in lesional psoriasis. This ascending pattern is also observed in non-lesional skin, with a 17% increase from mild (0.21 ± 0.30) to moderate (0.25 ± 0.13) and a substantial 93% from moderate to severe (0.49 ± 0.44). The notable and consistent upward trend observed in non-lesional skin from

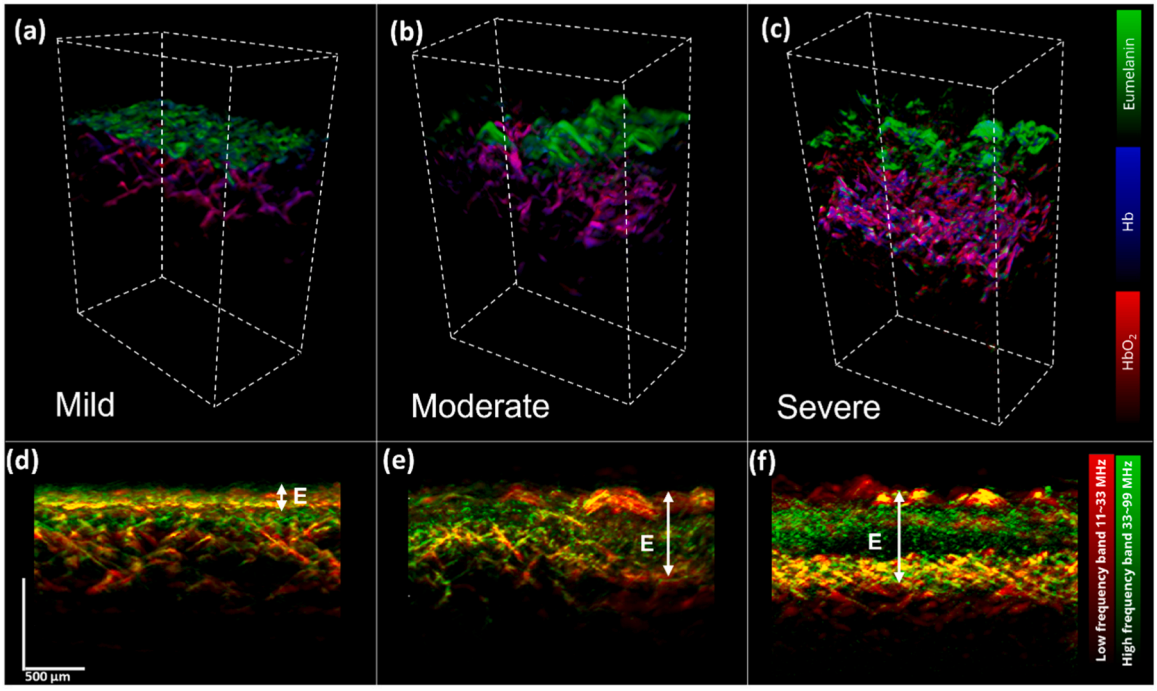


Fig. 2. 3D spatial mapping of skin chromophores, including melanin(green), oxy-(red) and deoxy-hemoglobin(blue) from lesional psoriasis areas of mild (left), moderate (center) and severe (right) subjects in (a) (b) (c); The corresponding maximum intensity projection of 532 nm images with frequency band separation low in red, high in green in (d)(e)(f). The representative epidermis (E) is indicated by white arrows. Scale bar; 500 μm.

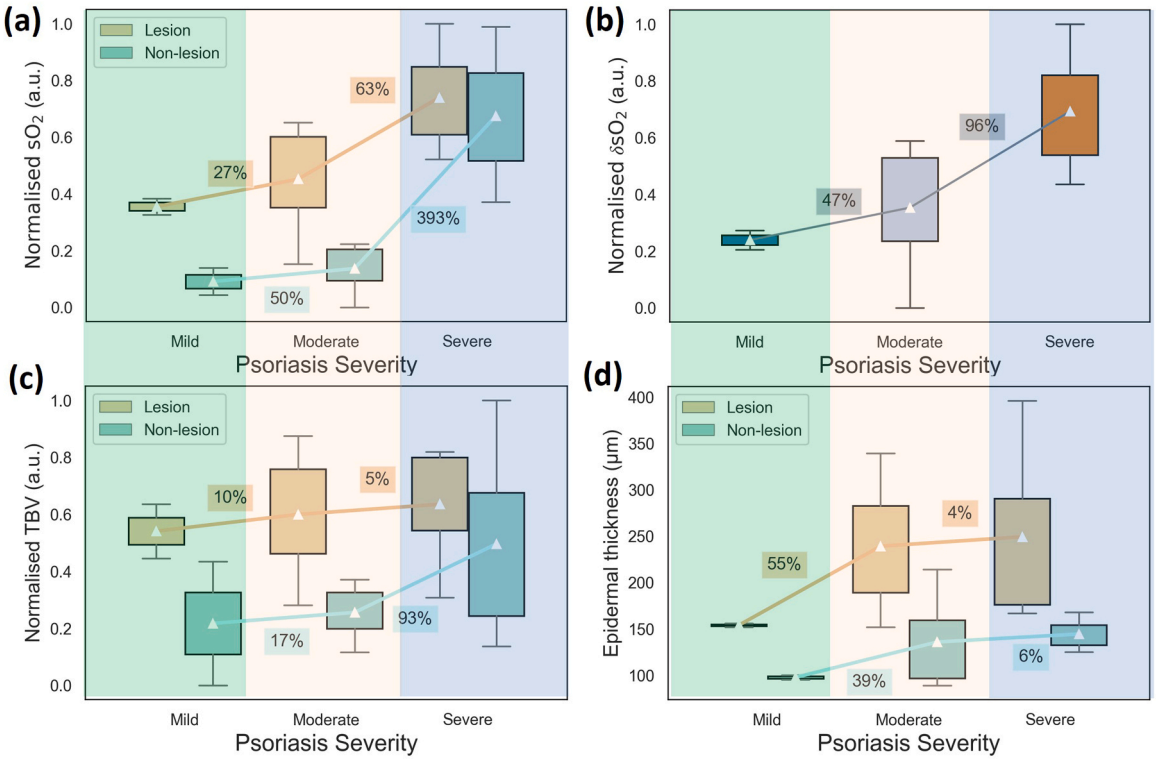


Fig. 3. Quantitative analysis of image-derived metrics with varying psoriasis severity, illustrating normalized (a) sO_2, (b) δsO_2 (difference between lesional and non-lesional data in each patient), (c) TBV, and (d) epidermal thickness.

moderate to severe severity range suggests that inflammation intensifies, reaching a level comparable to that of lesional skin in severe psoriasis patients. This, along with the increasing ESR values, indicates that inflammation rises with increasing severity. Furthermore, non-lesional psoriasis skin shows sub-clinical symptoms, not visible to naked eye, which suggests the potential for these areas to evolve into lesional regions over time.

The epidermal thickness in skin inflammatory conditions such as AD and psoriasis has been documented to surpass that of healthy skin [20,42]. This increased thickness, denoted as epidermal hyperplasia, is attributed to inflammatory processes and abnormal cellular proliferation [43]. Specifically, empirical evidence indicates that lesional regions exhibit a thicker epidermis compared to non-lesional areas. With escalating severity in psoriasis, the epidermal thickness demonstrates an ascent, as depicted in Fig. 3D. In lesional skin, the epidermis is 55% thicker in moderate cases (239 ± 94 μm) than in mild cases (153 ± 3 μm), and 39% thicker (135 ± 68 μm) than in mild (97 ± 3 μm) in non-lesional skin. Hence, a substantial elevation is evident from mild to moderate, whereas a more modest rise of 4% (249 ± 127 μm) is observed for lesional, and 6% (144 ± 22 μm) for non-lesional conditions from moderate to severe psoriasis cases. This suggests a relatively limited difference in epidermal thickness between moderate and severe cases. Severe psoriasis cases might be dictated mainly by dermal inflammation. It can also be noted that the increase in the epidermal thickness is more pronounced in lesional cases than in non-lesional ones from mild to moderate, indicating that epidermal dysregulation is less prominent in the non-lesional skin. This aligns with an earlier study asserting that non-lesional psoriasis skin exhibits properties intermediate between healthy and lesional skin [41]. Additionally, the epidermal thickness in the non-lesional skin across all severities, ranges between 100 to 160 μm indicating that non-lesional skin doesn't display prominent epidermal dysregulation in psoriasis, contrary to earlier documented results in AD [20]. In this preliminary study aiming to assess psoriasis severity, many results and their interpretations align with previous studies and the understanding of physicians. However, they cannot be fully endorsed without further investigation involving an increased number of subjects, which could yield statistically significant results.

3.3. Treatment response monitoring

3.3.1. Clinical skin physiology measurements

TEWL serves as an indicator of the quantity of water loss from the epidermis, which tends to increase with heightened barrier dysfunction [44]. Given that barrier dysfunction is a secondary phenomenon of psoriasis, individuals with psoriasis typically exhibit higher TEWL values. [45–47]. Following treatment, TEWL decreases by 18% from 10.4 g/m^2h to 8.4 g/m^2h as represented in Fig. 4A. This decline signifies the anticipated restoration of the skin barrier. Fig. 4B shows a 13% increase in skin moisture from 17.3 to 19.6 post-treatment compared to the pre-treatment measurement. The rise in skin moisture corresponds to the decrease in TEWL as they are expected to exhibit opposite trends. Skin pH also plays a crucial role in the pathogenesis of psoriasis influencing the barrier function, inflammation, and overall balance of the skin homeostasis [48]. The skin pH value decreased by 9%, transitioning from 5.7 to 5.17 after treatment. Healthy skin is characterized by a more acidic pH and this regulates the skin barrier properties [49,50]. This explains the less acidic pH before treatment as compared to after treatment.

3.3.2. Image visualization and quantitative analysis

Fig. 5A and B depict 3D spatial mapping of lesional skin in a mild psoriasis patient before and after treatment, respectively. The reduction in melanin (green), which serves as an estimate for epidermal thickness, is evident after treatment. Despite the anticipated decrease in the blood vessel network, associated with reduced inflammation and diminished blood flow post-treatment, this phenomenon is not evident in Fig. 5B. This discrepancy could be attributed to the mild nature of the psoriasis case, where the inflammation may not be significant.

Fig. 6A illustrates an 18% reduction in tissue sO_2 following treatment in lesional psoriasis skin, accompanied by a 22% decrease in non-lesional skin. Although statistically nonsignificant, this reduction

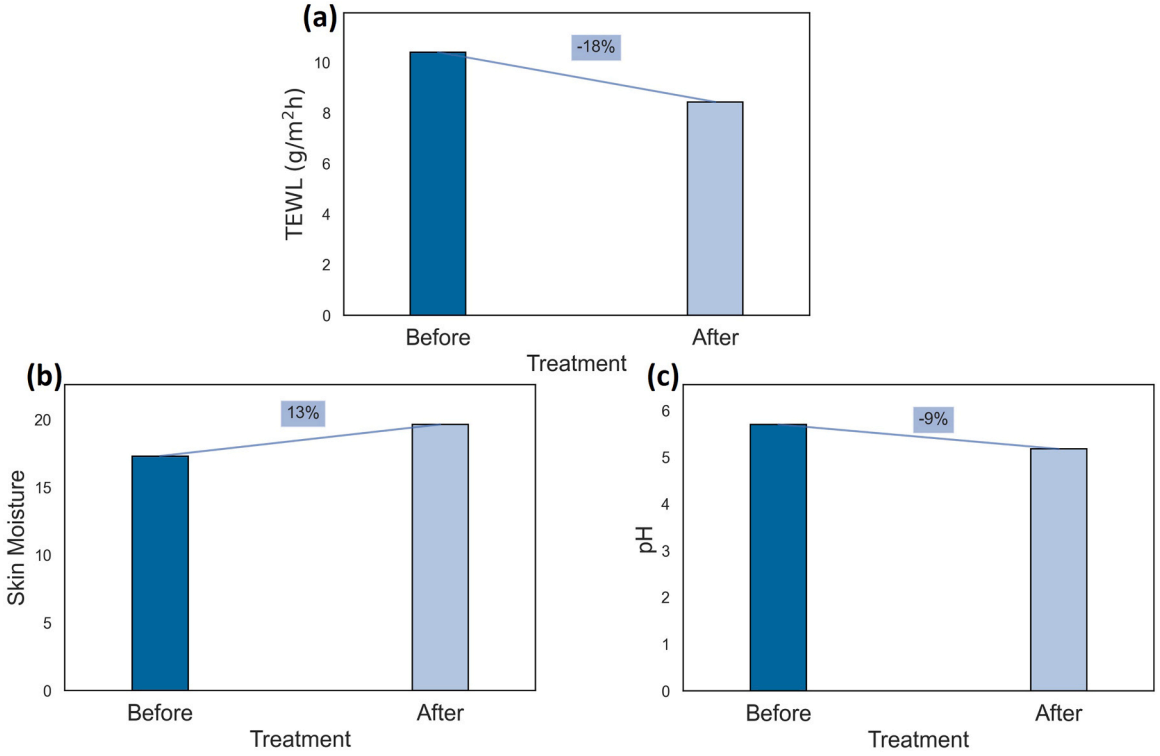


Fig. 4. Clinical skin physiology metrics (a) TEWL, (b) Skin moisture, and (c) pH in a psoriasis subject before and after treatment.

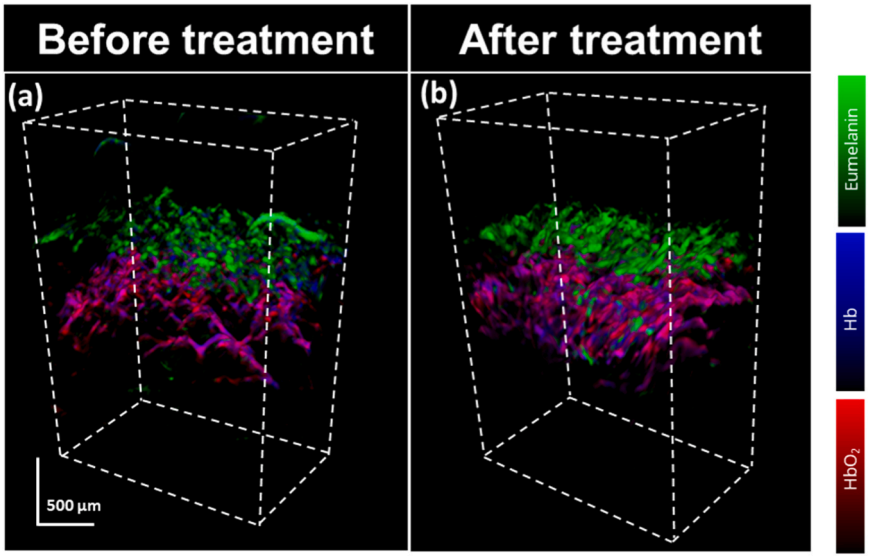


Fig. 5. 3D spatial mapping of lesional area of a mild psoriasis patient (a) before and (b) after treatment.

aligns with the anticipated inflammation mitigation [51]. In Fig. 6B, the δsO_2 trend demonstrates a mere 2% decrease from pre-treatment to post-treatment, potentially attributed to the relatively mild nature of the patients' psoriasis condition. In Fig. 6C, a 20% decrease in TBV is observed in lesional skin, and a 39% decrease is noted in non-lesional skin, indicative of reduced inflammation. The visually apparent reduction in epidermal thickness in Fig. 5A and B is confirmed by the quantitative metric in Fig. 6D post-treatment. Lesional psoriasis skin exhibits a more substantial 12% reduction from 172 μm to 151 μm, in contrast to non-lesional skin, which displays a 5% decrease from 101 μm to 95 μm post-treatment. These metrics effectively reflect the improvement in the psoriasis condition post-treatment, corroborating the concurrent decline in the patient's PASI score from 4.1 to 1.8, respectively.

With the imaging of a skin inflammatory condition like psoriasis using ms-RSOM we can compare the morphological and functional features of subjects across different clinical severities and for treatment monitoring. While direct validation with histopathological images was not conducted in this study, the structural features observed with ms-RSOM were corelated in a prior study using histology and capillaroscopy [52]. The results for sO_2 and TBV successfully indicate the inflammation symptoms exhibited in psoriasis skin escalating with increased severity. Although the absorption due to melanin from the thickened epidermis is a considerable constraint, the results follow the expected trends as documented in previous studies. Here, it is worth noting that the recruited subjects were within a fixed Fitzpatrick score range. The 3D images obtained through ms-RSOM boast high resolution

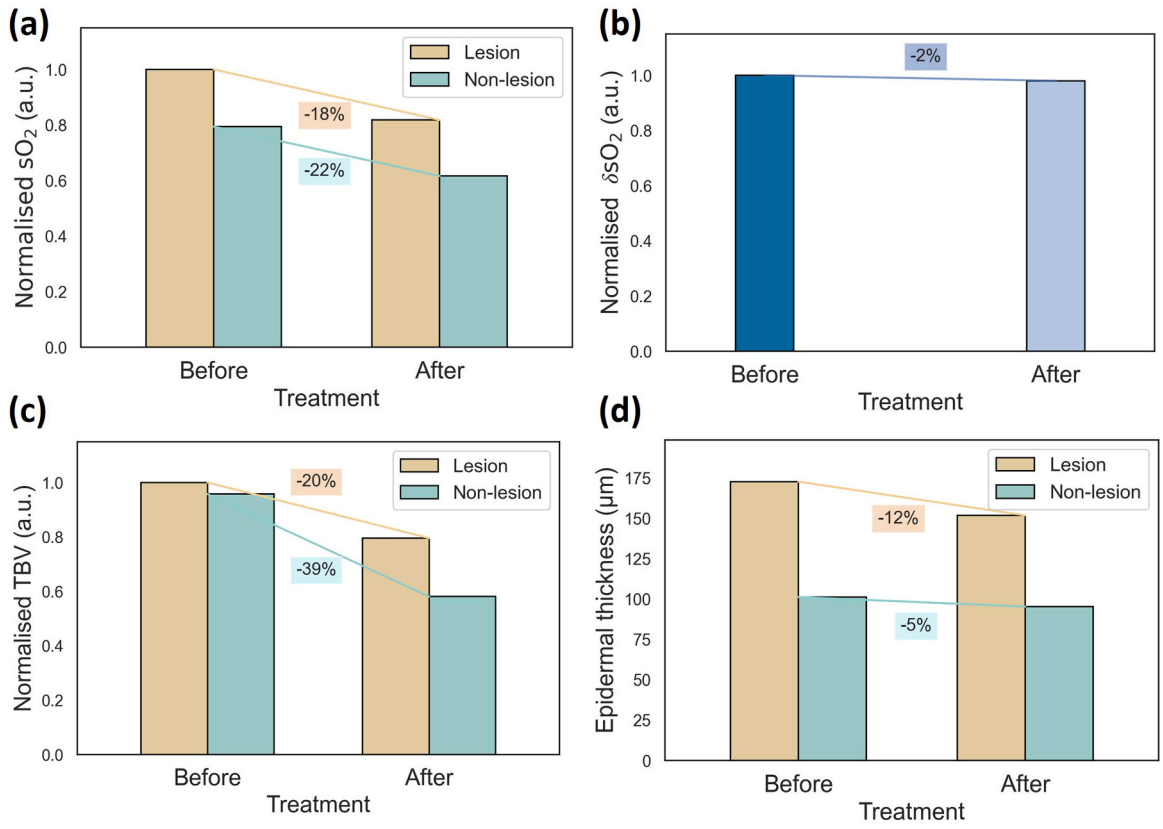


Fig. 6. Quantitative analysis of image-derived metrics in a mild psoriasis subject before and after treatment, illustrating normalized (a) sO_2, (b) δsO_2, (c) TBV, and (d) Epidermal thickness.

and can penetrate deep, enabling the measurement of the vascular network in the dermis and quantification of morphological metrics like epidermal thickness. This proves highly advantageous for skin imaging. While the benefits of utilizing ms-RSOM based objective structural and functional metrics are well elucidated in this study, it is essential to note that the treatment response results are derived from only one patient. Further investigations in our ongoing study with an expanded sample size are warranted to substantiate these findings in this field.

4. Summary

This study represents a pioneering study of both lesional and non-lesional skin in psoriasis subjects across different severities, utilizing high-resolution and non-invasive optoacoustic image-derived metrics. The investigation extends to the monitoring of treatments involving topical steroids and biologics, including adalimumab. Notably, 3D spatial mapping of skin chromophores like melanin, oxy-, and deoxy-hemoglobin provides objective insights into both the morphological and functional aspects of psoriatic skin. The observed elevation in tissue oxygen saturation and TBV with increasing psoriasis severity signifies heightened inflammation, while their reduction post-treatment indicates the efficacy of the interventions. The documented increase in epidermal thickness aligns with severity-related cell proliferation, and post-treatment reductions are coherent with subjective PASI scores. The monitoring of treatments yields valuable insights for designing patient-specific protocols. These findings highlight the potential integration of structural and functional information as an innovative, non-invasive and unbiased means of psoriasis assessment and real-time treatment monitoring, suggesting its potential integration into the clinical settings. This study, however, is preliminary in nature due to the limited sample size and can be further substantiated through our ongoing studies with a larger number of subjects.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

Acknowledgments

This work was supported by the National Medical Research Council [grant number NMRC OF-IRG Grant OFIRG18nov-0101], funding support from the Agency for Science, Technology and Research's (A*STAR) BMRC Central Research Fund (CRF) and Translational Biophotonics Innovation Platform IAF PP grant (H19H6a0025). Authors would like to acknowledge intern Teo Yu Xuan, National Skin Centre research coordinators Kyreen Lee, Emily QY Tang, Cheng Yi Kwa, Zhi Qing Lin, Veron Lu, and the support from iThera Medical as a part of the SBIC-iThera Medical joint lab.

References

[1] C.E.M. Griffiths, A.W. Armstrong, J.E. Gudjonsson, J.N.W.N. Barker, Psoriasis, Lancet 397 (2021) 1301–1315, https://doi.org/10.1016/S0140-6736(20)32549-6.
[2] A.W. Armstrong, C. Read, Pathophysiology, clinical presentation, and treatment of psoriasis: a review, JAMA 323 (2020) 1945–1960, https://doi.org/10.1001/jama.2020.4006.
[3] S. Quah, G.M. Sundaram, G. Subramanian, C. Vaz, J.S.L. Tan, R.F. Kabir, J.M. R. Ong, H.H. Oon, C. Theng, P. Sampath, IL-17-mediated downregulation of miR-101 facilitates the expression of EZH2 to promote epidermal hyperplasia in psoriasis, J. Invest Dermatol. 144 (2024) 403–407.e7, https://doi.org/10.1016/j.jid.2023.07.013.

[4] W.M.M. Chan, Y.W. Yew, T.S.C. Theng, C.F. Liew, H.H. Oon, Prevalence of metabolic syndrome in patients with psoriasis: a cross-sectional study in Singapore, Singap. Med J. 61 (2020) 194–199, https://doi.org/10.11622/smedj.2019152.

[5] D.S. Lim, A. Bewley, H.H. Oon, Psychological profile of patients with psoriasis, Ann. Acad. Med Singap. 47 (2018) 516–522.

[6] C.C. von Stülpnagel, M. Augustin, L. Düpmann, N. da Silva, R. Sommer, Mapping risk factors for cumulative life course impairment in patients with chronic skin diseases - a systematic review. J. Eur. Acad. Dermatol. Venereol. 35 (2021) 2166–2184, https://doi.org/10.1111/jdv.17348.

[7] T. Fredriksson, U. Pettersson, Severe psoriasis–oral therapy with a new retinoid, Dermatology 157 (1978) 238–244, https://doi.org/10.1159/000250839.

[8] I.-A. Grajdeanu, L. Statescu, D. Vata, I.A. Popescu, E. Porumb-Andrese, A.I. Patrascu, T. Taranu, M. Crisan, L.G. Solovastru, Imaging techniques in the diagnosis and monitoring of psoriasis (Review), (2019). https://doi.org/10.3892/etm.2019.7957.

[9] R.G. Langley, C.N. Ellis, Evaluating psoriasis with psoriasis area and severity index, psoriasis global assessment, and lattice system physician's global assessment, J. Am. Acad. Dermatol. 51 (2004) 563–569, https://doi.org/10.1016/j.jaad.2004.04.012.

[10] Validity of Outcome Measures, in: Clinical Review Report: Guselkumab (Tremfya): (Janssen Inc.): Indication: For the Treatment of Adult Patients with Moderate-to-Severe Plaque Psoriasis Who Are Candidates for Systemic Therapy or Phototherapy [Internet], Canadian Agency for Drugs and Technologies in Health, 2018. https://www.ncbi.nlm.nih.gov/books/NBK534046/ (accessed November 23, 2023)..

[11] M. Mogensen, L. Thrane, T.M. Joergensen, P.E. Andersen, G.B.E. Jemec, Optical Coherence Tomography for Imaging of Skin and Skin Diseases, Semin. Cutan. Med. Surg. 28 (2009) 196–202, https://doi.org/10.1016/j.sder.2009.07.002.

[12] S. Wahie, C.M. Lawrence, Wound complications following diagnostic skin biopsies in dermatology inpatients, Arch. Dermatol. 143 (2007) 1267–1271, https://doi.org/10.1001/archderm.143.10.1267.

[13] M.A. MS, H.D. BS, M.S.J.J. MD, Optical Coherence Tomography Imaging of Normal, Chronologically Aged, Photoaged and Photodamaged Skin A Systematic Review, (2015). https://doi.org/10.1097/dss.0000000000000457.

[14] B.H. Oh, K.H. Kim, K.Y. Chung, Skin imaging using ultrasound imaging, optical coherence tomography, confocal microscopy, and two-photon microscopy in cutaneous oncology, Sec. Dermatol. 6 (2019), https://doi.org/10.3389/fmed.2019.00274.

[15] F. Latriglia, J. Ogien, C. Tavernier, S. Fischman, M. Suppa, J.-L. Perrot, A. Dubois, Line-field confocal optical coherence tomography (LC-OCT) for skin imaging in dermatology, Life (Basel) 13 (2023), https://doi.org/10.3390/life13122268.

[16] A. Dubois, O. Levecq, H. Azimani, D. Siret, A. Barut, M. Suppa, V. del Marmol, J. Malvehy, E. Cinotti, P. Rubegni, J.-L. Perrot, Line-field confocal optical coherence tomography for high-resolution noninvasive imaging of skin tumors, JBO 23 (2018) 106007, https://doi.org/10.1117/1.JBO.23.10.106007.

[17] J. Ogien, C. Tavernier, S. Fischman, A. Dubois, Line-field confocal optical coherence tomography (LC-OCT): principles and practical use, Ital. J. Dermatol. Venereol. 158 (2023), https://doi.org/10.23736/S2784-8671.23.07613-2.

[18] R.J. Chalmers, Assessing psoriasis severity and outcomes for clinical trials and routine clinical practice, Dermatol. Clin. 33 (2015) 57–71, https://doi.org/10.1016/j.det.2014.09.005.

[19] D. Balak, E. Hajdarbegovic, Drug-induced psoriasis: clinical perspectives, Psoriasis.: Targets Ther. Volume 7 (2017) 87–94, https://doi.org/10.2147/ptt.s126727.

[20] X. Li, M. Moothanchery, C.Y. Kwa, W.L. Tan, Y.W. Yew, S.T.G. Thng, U.S. Dinish, A.B.E. Attia, M. Olivo, Multispectral raster-scanning optoacoustic mesoscopy differentiate lesional from non-lesional atopic dermatitis skin using structural and functional imaging markers, Photoacoustics 28 (2022) 100399, https://doi.org/10.1016/j.pacs.2022.100399.

[21] M.W. Schellenberg, H.K. Hunt, Hand-held optoacoustic imaging: a review, Photoacoustics 11 (2018), https://doi.org/10.1016/j.pacs.2018.07.001.

[22] T.V.O.N. KNORRING, N.M. Israelsen, V. Ung, J.L. Formann, M. Jensen, M. Haedersdal, O. Bang, G. Fredman, M. Mogensen, Differentiation between benign and malignant pigmented skin tumours using bedside diagnostic imaging technologies: a pilot study, Acta Derm. -Venereol. 102 (2022), https://doi.org/10.2340/actadv.v101.571.

[23] Y. Goh, G. Balasundaram, M. Moothanchery, A. Attia, X. Li, H.Q. Lim, N.C. Burton, Y. Qiu, T.C. Putti, C.W. Chan, P. Iau, S.A. Buhari, M. Hartmann, S.W. Tang, C.W. Q. Ng, Y.H. Chan, F.J. Pool, P. Pillay, W. Chua, J. Kapur, P. Jagmohan, E. Sterling, S.T. Quek, M. Olivo, Ultrasound guided optoacoustic tomography in assessment of tumor margins for lumpectomies, Transl. Oncol. 13 (2020) 254–261, https://doi.org/10.1016/j.tranon.2019.11.005.

[24] J. Yang, G. Zhang, Q. Shang, M. Wu, L. Huang, H. Jiang, Detecting hemodynamic changes in the foot vessels of diabetic patients by photoacoustic tomography, J. Biophotonics 13 (2020), https://doi.org/10.1002/jbio.202000011.

[25] L.V. Wang, Multiscale photoacoustic microscopy and computed tomography, Nat. Photonics 3 (2009) 503, https://doi.org/10.1038/nphoton.2009.157.

[26] L.V. Wang, S. Hu, Photoacoustic tomography: In vivo imaging from organelles to organs, Science 335 (1979) (2012) 1458–1462, https://doi.org/10.1126/science.1216210.

[27] N. Sun, S. Hu, Chapter 13 - Intravital photoacoustic microscopy of microvascular function and oxygen metabolism, in: Z.S. Galis (Ed.), The Vasculome, Academic Press, 2022, pp. 151–161, https://doi.org/10.1016/B978-0-12-822546-2.00002-2.

[28] J. Yao, L.V. Wang, Sensitivity of photoacoustic microscopy, Photoacoustics 2 (2014), https://doi.org/10.1016/j.pacs.2014.04.002.

[29] M. Seong, S.-L. Chen, Recent advances toward clinical applications of photoacoustic microscopy: a review, Sci. China Life Sci. 63 (2020) 1798–1812, https://doi.org/10.1007/s11427-019-1628-7.

[30] X. Li, U.S. Dinish, J. Aguirre, R. Bi, K. Dev, A.B.E. Attia, S. Nitkunanantharajah, Q. H. Lim, M. Schwarz, Y.W. Yew, S.T.G. Thng, V. Ntziachristos, M. Olivo, Optoacoustic mesoscopy analysis and quantitative estimation of specific imaging metrics in Fitzpatrick skin phototypes II to V, J. Biophotonics 12 (2019), https://doi.org/10.1002/jbio.201800442.

[31] M. Omar, D. Soliman, J. Gateau, V. Ntziachristos, Ultrawideband reflection-mode optoacoustic mesoscopy, Opt. Lett. 39 (2014), https://doi.org/10.1364/ol.39.003911.

[32] J. Aguirre, M. Schwarz, N. Garzorz, M. Omar, A. Buehler, K. Eyerich, V. Ntziachristos, Precision assessment of label-free psoriasis biomarkers with ultra-broadband optoacoustic mesoscopy, Nat. Biomed. Eng. 1 (2017) 0068, https://doi.org/10.1038/s41551-017-0068.

[33] B. Hindelang, T. Nau, L. Englert, A. Berezhnoi, F. Lauffer, U. Darsow, T. Biedermann, K. Eyerich, J. Aguirre, V. Ntziachristos, Enabling precision monitoring of psoriasis treatment by optoacoustic mesoscopy, Sci. Transl. Med. 14 (2022) eabm8059, https://doi.org/10.1126/scitranslmed.abm8059.

[34] Z. Wang, F. Yang, W. Zhang, S. Yang, Quantitative and anatomical imaging of human skin by noninvasive photoacoustic dermoscopy, Bio-Protoc. 12 (2022) 1–12, https://doi.org/10.21769/BioProtoc.4372.

[35] K. Ossadnik, S. Philipp, W. Bost, M. Fournelle, H. Richter, J. Lademann, Application of photoacoustic methods and confocal microscopy for monitoring of therapeutic response in plaque psoriasis, Ski. Pharmacol. Physiol. 31 (2018) 308–315, https://doi.org/10.1159/000492474.

[36] X. Luo, D. Wang, B. Wang, H. Shan, Y. Xie, X. Sun, C. Fei, Z. Chen, Broadband high-frequency ultrasonic transducer based functional photoacoustic mesoscopy for psoriasis progression, IEEE Trans. Ultrason., Ferroelectr., Freq. Control 69 (2022) 1926–1931, https://doi.org/10.1109/TUFFC.2021.3136870.

[37] R. Tammi, K. Paukkonen, C. Wang, M. Horsmanheimo, M. Tammi, Hyaluronan and CD44 in psoriatic skin. Intense staining for hyaluronan on dermal capillary loops and reduced expression of CD44 and hyaluronan in keratinocyte-leukocyte interfaces, Arch. Dermatol. Res 286 (1994) 21–29, https://doi.org/10.1007/BF00375839.

[38] R. Archid, A.P. M.d, S.S. Ahmad, W. Sterry, J.M. Lademann, B. Lange-Asschenfeldt, M. Ulrich, E. Stockfleth, S. Philipp, Confocal laser-scanning microscopy of capillaries in normal and psoriatic skin, JBO 17 (2012) 101511, https://doi.org/10.1117/1.JBO.17.10.101511.

[39] M. Oi, T. Maruhashi, K. Kumazawa, S. Iwakawa, Y. Kurihara, J. Wato, Y. Niimi, A. Takeda, Y. Asari, Diagnosis of skin and soft tissue infections using near-infrared spectroscopy, Acute Med. Surg. 8 (2021) e642. https://doi-org.ejproxy.a-star.edu.sg/10.1002/ams2.642.

[40] A. Lemini-López, L. Flores-Romo, A. Arévalo-López, I. Meza, Altered morphology and distribution of cellular junction proteins in non-lesional psoriatic epidermis: an insight into disease severity, Arch. Med. Res. 37 (1) (2006) 36–44, https://doi.org/10.1016/J.ARCMED.2005.07.003.

[41] A. Nosbaum, K. Dahel, C. Goujon, J. Nicolas, V. Mengeaud, M. Vocanson, Psoriasis is a disease of the entire skin: non-lesional skin displays a prepsoriasis phenotype, Eur. J. Dermatol. 31 (2021) 143–154, https://doi.org/10.1684/ejd.2021.4015.

[42] M. Alper, A. Kavak, A. Parlak, R. Demirci, I. Belenli, N. Yesildal, Measurement of epidermal thickness in a patient with psoriasis by computer-supported image analysis, Braz. J. Med. Biol. Res. 37 (2004) 111–117, https://doi.org/10.1590/S0100-879×2004000100015.

[43] J.G. Krueger, J.F. Krane, D.M. Carter, A.B. Gottlieb, Role of growth factors, cytokines, and their receptors in the pathogenesis of psoriasis, J. Invest. Dermatol. 94 (1990) s135–s140, https://doi-org.ejproxy.a-star.edu.sg/10.1111/1523-1747.ep12876121.

[44] H. Gu, N. Li, Y. Tu, Q. Pang, L. He, Dysfunction of epidermal barrier in psoriasis, Chin. J. Dermatol. 45 (2012) 134–135, https://doi.org/10.3760/CMA.J.ISSN.0412-4030.2012.02.024.

[45] A. Orsmond, L. Bereza-Malcolm, T. Lynch, L. March, M. Xue, Skin Barrier Dysregulation in Psoriasis, Int. J. Mol. Sci. 22 (2021) 10841, https://doi.org/10.3390/ijms221910841.

[46] M. Ramos-e-Silva, C. de-Moura-Castro Jacques, Epidermal barrier function and systemic diseases, Clin. Dermatol. 30 (2012) 277–279, https://doi.org/10.1016/j.clindermatol.2011.08.025.

[47] U.S. Dinish, Y.W. Yew, K. Vinod Ram, R. Bi, A.B.E. Attia, V. Teo Xinhui, P. Rajarahm, H.H. Oon, S.T.G. Thng, M. Olivo, Non-invasive biochemical analysis and comparison of atopic dermatitis and psoriasis skin using handheld confocal Raman spectroscopy, J. Biophotonics 16 (2023) e202300191, https://doi.org/10.1002/jbio.202300191.

[48] P.L. Bigliardi, Role of Skin pH in Psoriasis, in: C. Surber, H. Maibach, C. Abels (Eds.), pH of the Skin: Issues and Challenges, S. Karger AG, 2018: p. 0. https://doi.org/10.1159/000489524.

[49] Formulating at pH 4–5: How Lower pH Benefits the Skin and Formulations, Cosmetics & Toiletries (2013). https://www.cosmeticsandtoiletries.com/research/literature-data/article/21836958/formulating-at-ph-4–5-how-lower-ph-benefits-the-skin-and-formulations (accessed January 22, 2024).

[50] M. Lukic, M. Filipovic, N. Pajic, D. Lunter, D. Bozic, S. Savic, Formulation of topical acidic products and acidification of the skin–Contribution of glycolic acid, Int. J. Cosmet. Sci. 43 (2021) 419–431, https://doi-org.ejproxy.a-star.edu.sg/10.1111/ics.12707.

[51] R. Bissonnette, J. Tardif, F. Harel, J. Pressacco, C. Bolduc, M. Guertin, Effects of the Tumor Necrosis Factor-&agr; Antagonist Adalimumab on Arterial Inflammation Assessed by Positron Emission Tomography in Patients with Psoriasis: Results of a Randomized Controlled Trial, Circ.: Cardiovasc. Imaging 6 (2013) 83–90, https://doi.org/10.1161/CIRCIMAGING.112.975730.

[52] M. Hughes, T. Moore, N. O'Leary, A. Tracey, H. Ennis, G. Dinsdale, A. Murray, C. Roberts, A.L. Herrick, A study comparing videocapillaroscopy and dermoscopy

in the assessment of nailfold capillaries in patients with systemic sclerosis–spectrum disorders, Rheumatology 54 (2015) 1435–1442, https://doi.org/10.1093/rheumatology/keu533.

Xiuting Li received her Ph.D. degree in Physics and Applied Physics from School of Physical and Mathematical Sciences (SPMS), Nanyang Technological University (NTU), 2013. She is currently a senior scientist I at Translational Biophotonics Laboratory of A*STAR Skin Research Labs (A*SRL), A*STAR. Her current research focuses on design and development of clinical applications in the realms of photoacoustic, biomedical image processing and analysis facilitated artificial intelligence.

Yik Weng Yew (Asst Prof) is a Consultant Dermatologist at the National Skin Centre (NSC) with strong clinical and research interests in atopic dermatitis (AD), psoriasis dermato-epidemiology and disease outcomes research, with close to 60 peer reviewed scientific publications. He is currently the deputy head of the NSC Research Division and head of Eczema clinic, NSC. He obtained his MBBS from the Yong Loo Lin School of Medicine, NUS in 2006 and completed his training as a dermatologist in 2014 at NSC. After his dermatology training, he obtained a Master of Public Health to further his training in epidemiology research from the Harvard School of Public Health, USA in 2015 as part of his Health Manpower Development Plan award. He was awarded the National Healthcare Group Clinician Scientist Career Scheme award in 2016 and started his PhD studies at Lee Kong Chian School of Medicine, NTU, Singapore to study disease prevalence and risk factors associations of atopic dermatitis in a general adult population cohort. He has also obtained numerous grants, notably the National Medical Research Council (NMRC) New Investigator Grant in 2018 to study treatment of nail psoriasis with microneedles and recently the NMRC Transitional Award in July 2020 to investigate the effects of adiposity on skin barrier function in a general population cohort. He is active in various types of research in AD and collaborates with various local and overseas institutes on population-based cohort studies, clinical trials, basic and translational AD research on omics, skin microbiome and skin bioimaging.

Keertana Vinod Ram received her master's by research (MEng) degree in biomedical engineering from the National University of Singapore, Singapore, in 2022. Currently, she holds the position of Research Officer at the Translational Biophotonics Laboratory, Agency for Science, Technology, and Research (A*STAR) in Singapore and works on the application of Raman spectroscopy, diffuse reflectance spectroscopy, and photoacoustic imaging for the skin. Keertana's professional interests encompass biophotonics and biomedical spectral and image analysis, with a particular emphasis on developing medical applications that are easily translatable.

Hazel H. Oon heads the Psoriasis Unit and Acne Clinic at the National Skin Centre, Singapore. She is Chair of the Chapter of Dermatologists of Singapore, Councilor at the International Psoriasis Council, Regional Coordinator for the Global Psoriasis Atlas, Clinical Educator Lead for undergraduate dermatology in Singapore, Principal Lead for dermatology at Lee Kong Chian School of Medicine and Clinical Lecturer at Yong Loo Lin School of Medicine. Her special interests are psoriasis, acne, hidradenitis suppurativa, rosacea photo dermatology and medical education.

Steven Tien Guan Thng(Prof) graduated from National University of Singapore in 1992 and went on to pursue his interest in Humanitarian and Disaster medicine with the Singapore Armed Forces from 1992 to 2002. After completing his dermatology training in Singapore, Dr Steven Thng went on to Amsterdam Medical Centre, Netherlands, to continue his training in pigmentary disorder, under Professor Westerhof. Upon returning from his training, Dr Steven Thng started the pigment clinic in National Skin Centre as well as set up the melanocyte culture lab to start his work on cultured melanocytes grafting for vitiligo patients. Currently, Dr Thng is the head of the pigment clinic, in charge of managing all complex pigmentary disorders in National Skin Centre, and he is also the principal surgeon for tissue grafting for vitiligo. In 2012, he has also started a research clinic for hyperpigmentary disorders exploring novel ways to manage difficult hyperpigmentary conditions. He took over as Executive Director of Skin Research Institute of Singapore from Jan 2017 to Feb 2020, and was responsible for the transformation of SRIS from a virtual institute to a dynamic institute, working on 4 main multi-institutional, interdisciplinary research programs of chronic wound, acne, skin microbiome and atopic dermatitis. His current research interest is on skin pigmentary disorder, novel drug delivery systems, as well as advanced imaging for skin cancer and skin diseases. He has translated much of his research to improve patient care in dermatology. He has been serving as the Chief Dermatologist of Skin Research Institute of Singapore from Feb 2020. For his dedication in research and patient care, he was awarded Excellence in Public Service Award in 2013, Healthcare Humanity Award in 2014, Singapore Clinician Investigator Award in 2015 and 2016

U. S. Dinish serves as a group leader in the Translational Biophotonics Laboratory, A*STAR Skin Research labs, A*STAR Singapore. Additionally, he holds a joint adjunct faculty position at the School of Physical and Mathematical Sciences (SPMS), Nanyang Technological University (NTU), Singapore. Dinish possesses extensive expertise in the development of biophotonics technologies, encompassing photoacoustic imaging (PAI), diffuse reflectance spectroscopy, Raman spectroscopy, surface-enhanced Raman scattering (SERS), fluorescence imaging, and multimodal imaging techniques for diverse preclinical and clinical studies. Dinish assumes the role of PI or Co-PI on numerous national and international research grants. He serves as the PI of the joint virtual international lab called 'FiberMed,' which is an esteemed collaboration between A*STAR, CNRS, and the University of Limoges, France. Additionally, he has contributed to the development of 25 patents/patent applications and has published around 160 significant journal papers and conference proceedings. In 2015, he co-edited a book titled 'Frontiers in Biophotonics for Translational Medicine' (Springer). Currently, Dinish serves as an editorial board member for 'Scientific Reports' (Nature Publishing Group) and acts as a consulting editor for the 'International Journal of Nanomedicine' (Dove Press). Furthermore, he holds the position of a series editor for Springer's book series titled 'Progress in Optical Science and Photonics'.

Malini Olivo (Prof) is the Distinguished Principal Scientist of A*STAR Skin Research Labs (A*SRL) where she spearheads the Translational Biophotonics Laboratory. Concurrently, she is also an Adjunct Professor at the Lee Kong Chian School of Medicine, NTU; Department of Obstetrics & Gynaecology, National University Health System, NUS, Singapore; and Royal College of Surgeons Ireland, Dublin, Ireland. She obtained a PhD degree in Bio-Medical Physics in 1990 from University Malaya/University College London (UCL) and did her post-doctoral training between 1991 and 1995 at UCL, UK and both McMaster University and University of Toronto, Canada. Her current research interest is in Medtech and nano-biophotonics and its applications in translational medicine. Her efforts include bridging the gap between cutting edge optical technologies and unmet clinical needs by developing in-house photonics-based devices for various industries. She has succeeded in obtaining competitive research funding of over USD 25 million to support her research in Singapore and overseas. She has published over 500 papers, three books and 20 book chapters, and filed close to 50 patents on technology platforms and devices. She is also the co-founder of three Medtech companies. Furthermore, she holds many advisory international roles and is well recognised internationally for her research in biophotonics for her pioneering research contributions. She has conferred as the Fellow of Optical Society of America (OSA), Fellow of American Institute of Medical Bioengineering (AIMBE) and Fellow of Institute of Physics, UK.