Quantification of human skin biomarkers for disease characterization by optoacoustic mesoscopy with machine learning

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Abstract: We introduce optoacoustic mesoscopy with machine learning analysis pipeline to quantify morphological and microvasculature skin features that cannot be achieved before. We found those features can be used for disease characterization, which are strongly correlated to physician observations and histology, demonstrating great clinical potential.

Introduction

Non-invasive quantification of the anatomical features of human skin can lead to improved identification of vascular and other features associated with a number of diseases. Ultra-wideband raster-scan optoacoustic mesoscopy (RSOM) is a novel modality that has demonstrated unprecedented ability to visualize epidermal and dermal features in vivo. This ability can be used to prognose dermatological diseases and monitor treatment responses in a non-invasive manner based on quantified skin anatomical and microvasculature features. However, automatic and quantitative analysis of three-dimensional RSOM datasets remain a challenge.

Methods

To address this challenge, we have developed a deep learning-based framework, termed Deep Learning RSOM Analysis Pipeline (DeepRAP), to analyze and quantify morphological skin features recorded by RSOM and extract imaging biomarkers for disease characterization. DeepRAP uses a two-layer segmentation strategy based on a convolutional neural network with a transfer learning approach. This strategy enabled automatic recognition of the skin layers according to their morphological structure and subsequent segmentation of the dermal microvasculature with an accuracy equivalent to human assessment.

Results/Discussion

We demonstrate DeepRAP by applying it to automatically segment RSOM images obtained from 25 psoriasis patients (Fig. 1) under treatment and the quantified RSOM biomarker is applied to characterize the disease severity and progression, showing excellent agreement with manual segmentation and histology. In addition, we test DeepRAP using a more challenging problem, namely the assessment of cutaneous microvascular endothelial function by analyzing a sequence of RSOM volumetric images acquired during post-occlusive reactive hyperemia process, i.e. an image sequence with significant contrast variations. Results show that DeepRAP accurately captures and quantifies the strong dynamic changes of skin microvasculature features, in higher detail and accuracy compared to Laser Doppler flowmetry or tissue spectrometry. We found DeepRAP to perform well, even at varying signal intensities due to tissue inhomogeneity at different skin depths or from different skin conditions. Having validated DeepRAP in datasets with known performance, we applied it to explore the rate of microvasculature change as a function of age in a group of 75 healthy volunteers (Fig. 2). DeepRAP extracted five vessel features, which were examined for their relationship to age progression. The analysis indicates that small vessels in the 10-40 micrometers range were most prominently affected by age, with a reduction rate that appeared most prominent in the 20-65 years' age range.

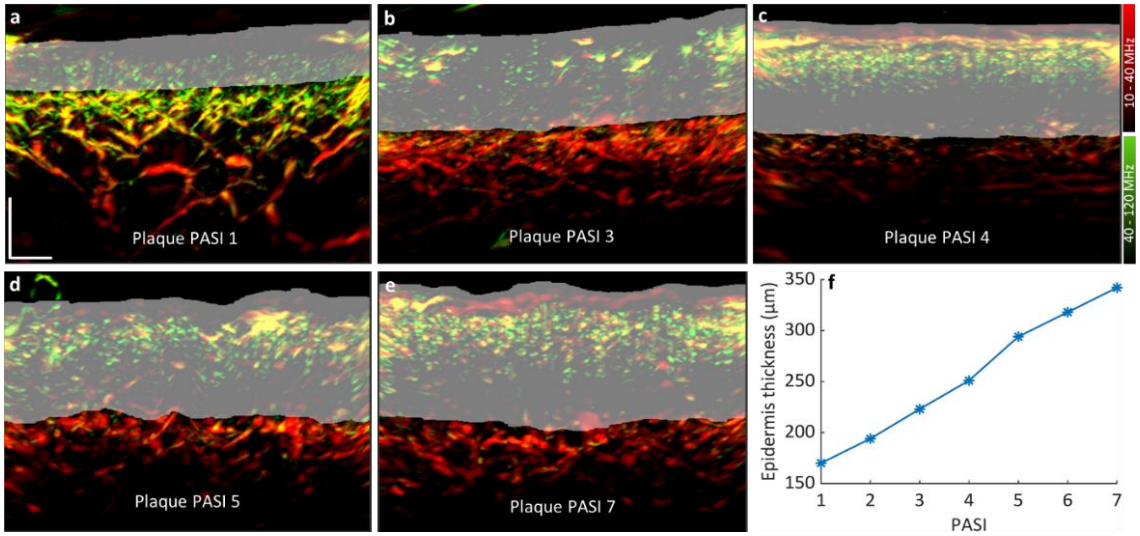

Fig. 1 Epidermis segmentation of psoriasis skin. (a)-(e) Cross-sectional RSOM images of psoriasis skin lesions with various PASI scores, where the epidermal thickness is segmented and marked by the grey areas. (f) Correlation between the PASI score and the epidermal thickness. Scale bar: 500 μm.

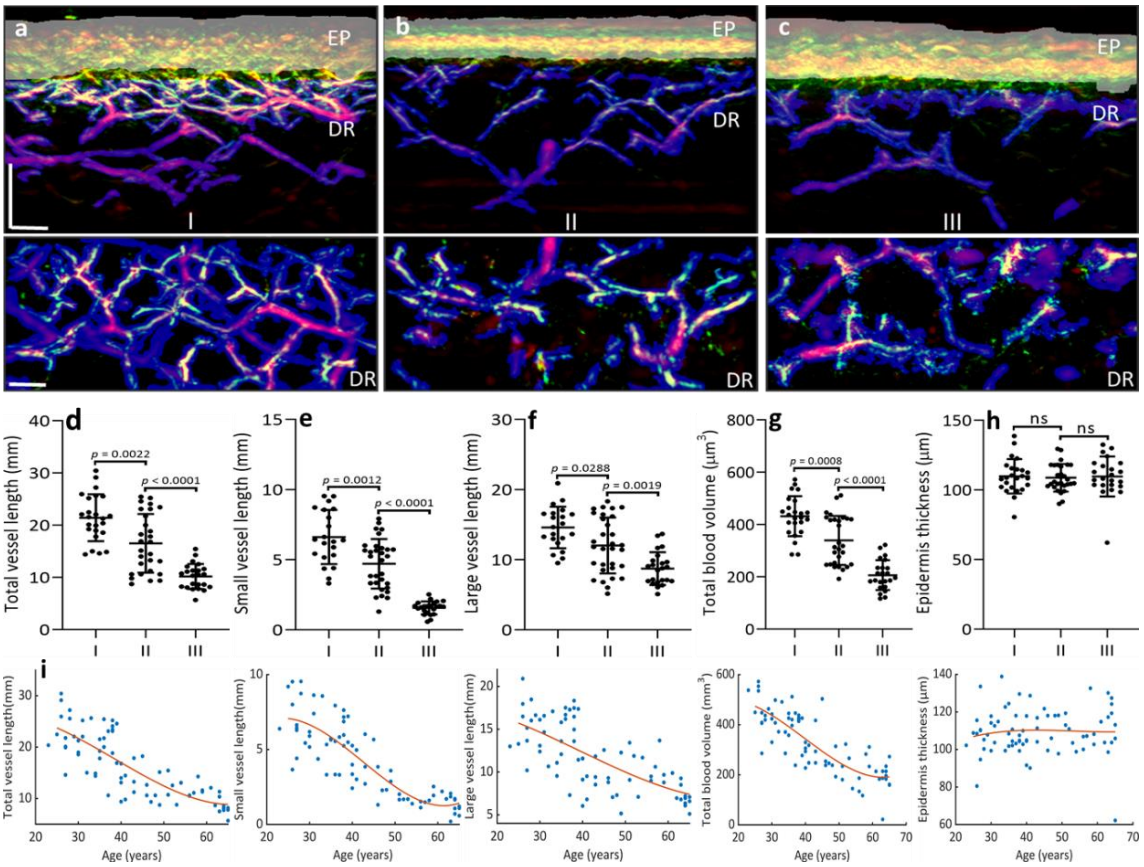

Fig. 2 Comparisons of skin features among healthy volunteers in three age groups. The healthy volunteers were divided into three groups based on their ages: I (n=24, 29.5 ± 3.5 years), II (n= 28, 41.1 ± 4.1 years) and III (n=23, 59.5 ± 4.9 years). Three cross-sectional RSOM images of each group and corresponding dermal vessels from the top-view are shown in (a-c), where the epidermis (EP) and dermal (DR) vessels were segmented by the DeepRAP. (d-h). Skin features were computed and compared among the three groups including: (d) total vessel length, (e) small vessel length (vessels with diameter < 40 μm), (f) large vessel length (vessels with diameter ≥ 40 μm), (g) total blood volume and (h) epidermal thickness. (i) the distributions of these five skin features with increment of volunteer aging. ns: not significant. Scale bar 500 μm.

Conclusions

The newly developed ability of DeepRAP to enable rapid study of human skin morphology and microvasculature in-vivo, a task that has been so far possible only with laborious studies typically based on biopsied samples, has further increased the translational potential of RSOM.