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Progress and prospect of non-invasive detection techniques in the therapeutic evaluation of melasma

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Melasma is a common, chronic, acquired, and refractory hyperpigmentation, the etiopathogenesis of which is multifactorial.[1,2] Current treatments include topical or systemic agents, chemical peels, laser- and light-based therapies, and traditional Chinese medicine.[3] At present, the therapeutic evaluation of melasma can be mainly summarized into four categories: (1) Patient self-assessments[4]; (2) Scoring systems used by dermatologists[5]; (3) Non-invasive detection techniques[6,7]; (4) Histopathological and immunohistochemical assessments.[8] Providing a non-invasive, objective, and reproducible methodology to evaluate treatment efficacy in melasma has become the focus of many researchers. In the current review, the commonly used and the latest non-invasive detection techniques which have been applied in the therapeutic evaluation of melasma in recent years are discussed.

Skin Color Measurement Techniques

Based on different principles, measurement instruments can be classified into four types, namely, scanning reflectance spectrophotometers, tristimulus colorimeters, narrow-band reflectance spectrophotometers, and visible-spectrum reflectance colorimeters.[9] Among these, three kinds of instruments, including the Chromameter, Mexameter, and Dermacatch, have been widely applied in clinical efficacy evaluations. Some researchers simultaneously applied two kinds of instruments for more objective assessments of clinical outcome. For example, the Chromameter combined with the Mexameter,[10] and the Mexameter along with the Dermacatch.[11]

Skin Imaging Techniques

Skin imaging technique is a general term for various imaging technologies based on laser, ultrasound, and electromagnetic waves.[12] The techniques which have been commonly used in the diagnosis, classification, severity assessment, and therapeutic evaluation of melasma in recent years, are mainly summarized as the following five types.

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Ultraviolet optical imaging and quantitative analysis technology

To objectively quantify the severity of pigmentary skin disease, especially melasma, Onseok *et al*[13] utilized an air cooling scientific complementary metal-oxide-semiconductor charge-coupled devices [Figure 1A] to acquire images from where melasma tended to occur [Figure 1B], on the basis of the characteristics of ultraviolet light for the diagnosis and classification of melasma. The authors adopted the gradient mask algorithm to segment the target images in the region of interest (ROI) and correct the facial curvature, and developed a quantitative evaluation method of darkness and homogeneity by calculating the arithmetic mean of the gray level and the coefficient of variation per pixel of the normal area and pigment lesion area under ultraviolet conditions. The red, green and blue (RGB) color model was converted to the L*a*b* color model in normal and pigment lesion areas under visible light conditions, and L*a*b* and ΔE values were used.

VISIA

It is a complexion analysis system (Canfield Scientific., Fairfield, NJ, USA), the evaluation indexes of which include the skin phototype and eight parameters involving spots, wrinkles, texture, pores, ultraviolet spots, brown spots, red areas, and porphyrins on the forehead and both cheeks.[14] Feng *et al*[15] calculated the correlation between the melasma area and severity index (MASI) score and the VISIA analysis, and found that both the eigenvalues and scores for spots, red areas and brown spots were positively associated with MASI score.

Antera 3D

It uses reflectance mapping of seven different light wavelengths spanning the entire visible spectrum. The acquired spectral data are used to map the distribution and concentration of melanin and hemoglobin.[16] Ana *et al*[16] compared the Antera 3D (Miravex Limited, Ireland) with the Mexameter MX-18 (Courage and Khazaka Electronic

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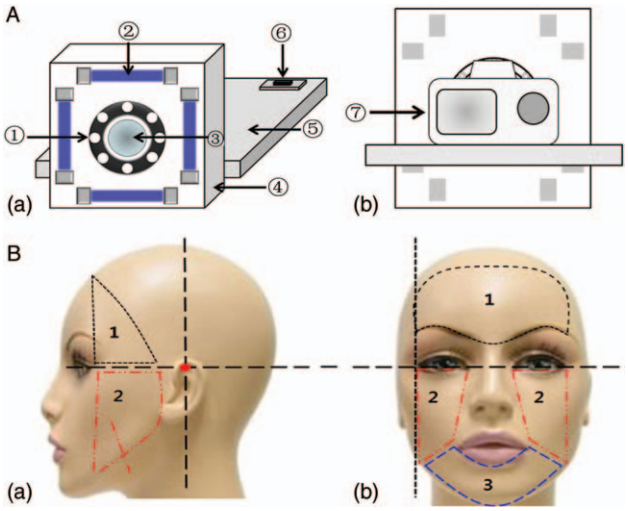

Figure 1: (A) The optical imaging system with the air cooling scientific complementary metal-oxide-semiconductor (sCMOS) charge-coupled devices (CCD) camera under ultraviolet (UV) light. (a) Front and (b) rear views of the manufactured optical imaging system, which consists of ring-shaped white light light emitting diodes (LEDs); four UV-A lamps; base plate; imaging box; optical filter for polarization imaging, digital camera, and air cooling sCMOS CCD camera; switches to control the LEDs and UV-A lamp; target window. (B) Partitioning the regions of interest (ROIs). (a) Lateral and (b) front, four target measurement areas.

GmbH, Cologne, Germany) and Colorimeter CL-400, and found that the Antera 3D possessed better sensitivity and specificity than the Mexameter MX-18 regarding the melanin parameter, while a similar sensitivity was found for erythema determination. Moreover, good correlations were observed for all the parameters analyzed, and the Antera 3D had a higher repeatability.

Dermoscopy

It allows visualization of melanin color intensity as well as pigment network regularity, and provides information concerning the density of melanin and its localization.[17] Moreover, it can be used to observe changes in blood vessels in a timely and dynamic manner.[18] Naglaa *et al*[19] performed the evaluations using modified MASI (mMASI) and dermoscopy. The dermoscopic examination showed a decrease in the density of pigmentation and a decrease in the severity of skin telangiectasia after treatment and at the follow-up.

Reflectance confocal microscopy (RCM)

RCM, which correlates well with dermoscopy, can be used to observe the structure of the entire epidermis and the superficial layer of the dermis, as well as the pigment distribution, and to evaluate the size and superficial location of the blood vessels. Its resolution can reach the cellular level, and has a good correlation with the histopathological manifestations.[12,20,21] Ardigo *et al*[22] performed a semi-quantitative assessment of the degree of pigmentation in different skin layers in melasma patients. Hee *et al*[23] scored the parameters of epidermal pigmentation, dendritic cells or melanophages, and solar elastosis to quantify their changes, and counted the number of vessels per image to identify vascularity. They found that the distribution of melanophages in melasma was not homogeneous, and counting vessels was difficult.

Combined applications

Huang *et al*[24] adopted RCM to evaluate the quantity and distribution of melanin, and to observe the morphology of melanin and dendritic melanocytes. Dermoscopy was performed to assess the quantity and morphology of blood vessels. The authors considered that assessing morphological changes in melanin made the evaluation results more objective and specific, and the observation through dermoscopy could offset the difficulty with RCM in counting blood vessels. Morphological changes in dendritic cells could be used to evaluate their activity, which might be helpful for clinical treatment. Some researchers have simultaneously applied several kinds of skin imaging techniques to evaluate efficacy more objectively, such as VISIA combined with Antera 3D,[25] or a combination of RCM, VISIA, and dermoscopy.[26]

Conclusions

Although the treatment of melasma is varied, it is still a challenge for dermatologists, since it is related to many factors, with complicated pathogenesis and recurrence. The therapeutic evaluation of melasma is an ongoing area of research interest.

At present, there are numerous methods to evaluate the efficacy of melasma treatment. An increasing number of researchers, however, have realized that self-evaluation by patients or visual observation by clinicians will lead to a lack of objective indicators. Although pathological evaluations can be qualitative and semi-quantitative, trauma and scar formation are caused by biopsies. As a consequence, non-invasive detection techniques have become the focus of many researchers. Because of the small probes and limited measurement area of skin color measurement instruments, the positioning and repeatability of the target before and after treatment are affected.

All of the pieces of equipment have their advantages owing to the different principles. Therefore, combinations of skin color measurement techniques and/or skin imaging techniques for clinical detection can improve on the deficiencies of previous evaluation methods. Some researchers have utilized the characteristics of ultraviolet light to characterize and classify melasma, acquired overall images from the ROI and quantitatively analyzed the normal area and the pigment lesion area. These studies, which observed the severity and therapeutic effect of melasma in a real-time and dynamic way with follow-up visits, may become a research trend.

Numerous studies have confirmed that correlations between lesions and histopathology, as well as related histopathologic changes, can be directly or indirectly reflected by skin imaging techniques, especially RCM technology, which can be used to locate, characterize, and visualize the target and make quantitative analyses. The collection of these characteristics may form the basis for future research into the non-invasive detection and therapeutic evaluation of melasma.

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Conflicts of interest

None.

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