Dermatology Practical & Conceptual

Noninvasive Imaging Markers for Acne Treatment Response Monitoring: A Pilot Study During Use of a Topical Product Containing Silybum Marianum Fruit Extract

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Introduction

High-resolution noninvasive imaging techniques such as reflectance confocal microscopy (RCM) and optical coherence tomography (OCT) have provided valuable insights into the morphological changes occurring in non-lesional and lesional skin during the acne cycle [1]. RCM generates *en face* (horizontal) real-time images of the epidermis, dermo-epidermal junction, and papillary dermis (maximum depth: 200–250 µm), allowing the visualization of cellular structures at near-histologic resolution (1 µm) [2]. In addition, the interferometric OCT imaging technique, which penetrates deeper into the skin (maximum depth: 1 mm, but with lower lateral [7.5 µm] and axial [5 µm] resolution), has been used to generate 2D and 3D vertical (cross-sectional) and horizontal images of the stratum corneum, epidermis, sebaceous glands, and dermal vessels in acne skin [2]. When used in the dynamic mode, OCT can also provide information on dermal blood flow [2]. The combined use of RCM and OCT has led to the definition of a precise set of microscopic features that characterize developing and resolving acne lesions (Figure 1) [1,2]. Monitoring of RCM and OCT parameters has also shown potential for evaluating the effectiveness of new and existing topical acne treatments [6].

Clinical data have shown that topical application of a dermocosmetic product containing *Silybum marianum* fruit extract (SMFE) leads to reductions in the percentage of hair follicles with microcomedones and subsequently the number of visible inflammatory and non-inflammatory acne lesions [7]. This pilot study further evaluated the effects of SMFE by identifying the RCM and OCT characteristics of developing subclinical and clinical acne lesions and their resolution before and during SMFE use.

Case Presentation

Lesion-prone skin on the cheek and forehead of five patients (aged 15–25 years with mild comedogenic acne) was monitored by dermoscopy, then by RCM and OCT at baseline (W0), initiation of twice-daily SMFE application (W1), and after two weeks of SMFE use (W2-W3). Several typical RCM and OCT features of comedogenesis (W0 and W1) and comedolysis (W2-W3) were identified (Table 1). Comedogenesis was characterized by inflammatory infiltrate accumulation, keratin plug formation, and increased infundibular diameter as well as by increased comedone depth and vascularization. Comedolysis was characterized by disappearance of the keratinized plug and hyperkeratinized border, reduced inflammation and comedone number, and decreases in infundibular diameter (Figure 2).

Conclusions

These findings define the microscopic and mesoscopic markers of comedogenesis and comedolysis in SMFE-exposed acne-affected skin. RCM was used alongside clinical scoring in a previous study evaluating the therapeutic response to SMFE in subjects with acne, revealing that reductions in total lesion counts after 60 days of treatment were accompanied by significant reductions in inflammatory and non-inflammatory lesion infundibular diameter [8]. The current study, using both RCM and OCT, identified additional noninvasive imaging markers of comedogenesis and comedolysis in SMFE-treated acne skin, which can be applied to further studies evaluating product effectiveness. This study also further demonstrates how RCM and OCT can be used as efficient and reproducible methods to assess therapeutic responses to acne treatment in clinical trials and provide a better understanding of acne pathophysiology.

Ethical Statement: All patients included in this pilot study provided informed consent for the publication of their clinical data and photographs for research purposes and before undergoing any type of clinical examination. All patients received standard treatment and were followed up using routine noninvasive imaging techniques.

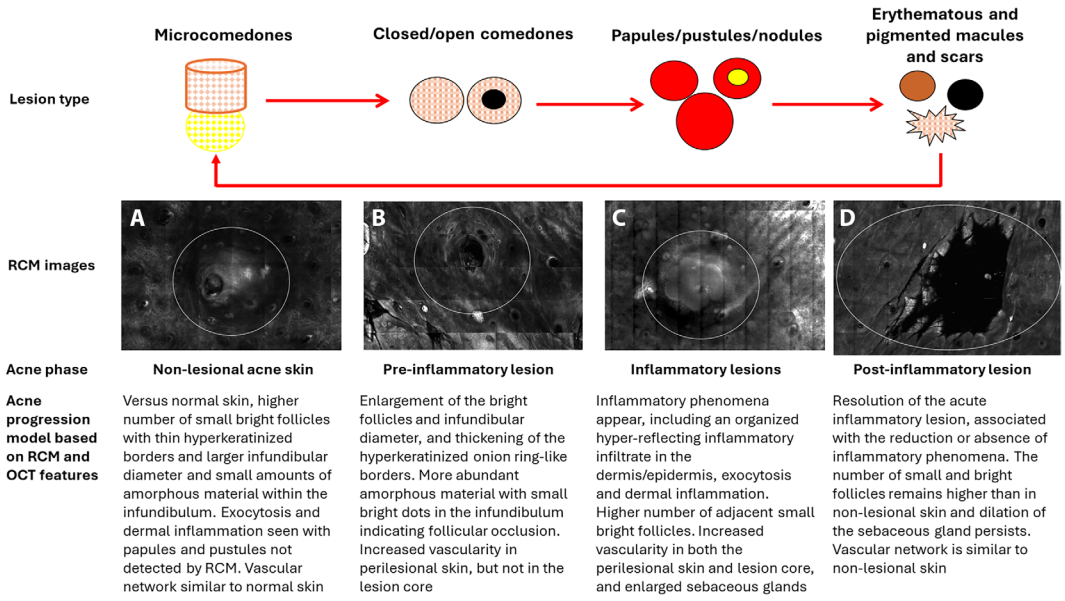

Figure 1. Progression model for lesions during the acne cycle based on the features observed from longitudinal noninvasive imaging of acne-prone skin. The schematic representation of the acne cycle is based on the model proposed by J-H Saurat [9]. RCM images (scale: 500 µm) show typical (A) microcomedone, (B) open comedone, (C) pustule, and (D) scar acne lesions. The acne progression model and description of RCM and OCT features are based on the results of the study by Manfredini et al. [2].

Table 1. Reflectance confocal microscopy and optical coherence tomography markers of comedogenesis and comedolysis in response to twice-daily application of a *Silybum marianum* fruit extract (SMFE)-containing dermocosmetic product.

COMEDOGENESIS (W0 and W1)	RCM	OCT
Inflammatory infiltrate	✓	
Keratin plug	✓	✓
Increased diameter of the infundibular opening	✓	✓
Increased comedone depth		✓
Increased vascularization		✓
COMEDOLYSIS (W2 and W3)	RCM	OCT
Comedone with an empty appearance	✓	✓
Disappearing onion ring-like hyperkeratinized border	✓	
Decreased diameter of the infundibular opening	✓	✓
Reduction in inflammation	✓	
Reduction in the number of comedones	✓	✓

OCT, optical coherence tomography; RCM, reflectance confocal microscopy; W, week.

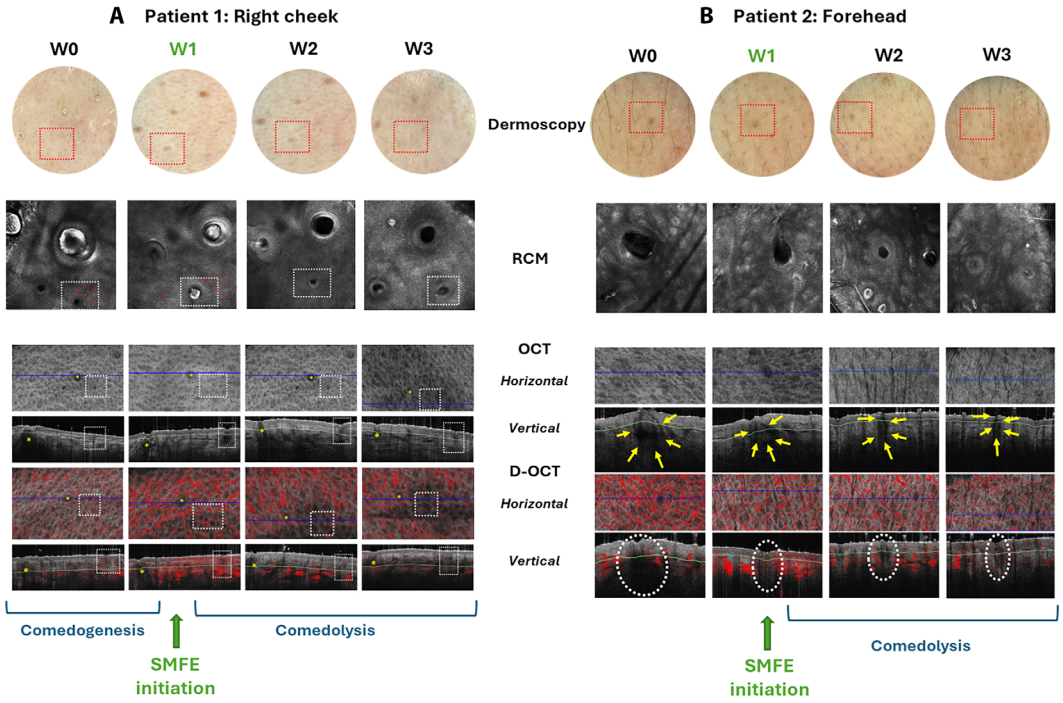

Figure 2. Typical dermoscopy, RCM, and OCT images of the right cheek (A) and forehead (B) of two patients with comedonal acne included in the SMFE pilot study. Noninvasive imaging techniques were used alongside dermoscopy to assess acne-prone skin at baseline (1 week prior to use of the SMFE product; W0), at the initiation of topical SMFE application (W1), and after one and two weeks of twice-daily application of the SMFE product (W2 and W3). Dermoscopy images were taken using a dermascope (VivaCam D200, VivaScope, GmbH, Munich, Germany) integrated into the confocal microscope. RCM images (lateral resolution 0.5 µm for detection of microscopic features such as inflammatory cells, follicular hyperkeratosis, diameter of the infundibular structures) were taken using a VivaScope 3000 microscope (VivaScope 1500 & VivaScope 3000, VivaScope GmgH, Munich, Germany). (A) Red arrows indicate the area of interest (forming comedone). OCT and D-OCT images were taken using a VivoSight microscope (Michelson Diagnostics Ltd, Maidstone UK). Yellow asterisks indicate the point of reference (existing comedone visible by RCM) and dashed boxes indicate the area of interest (the forming and resolving comedone). (B) Yellow arrows (vertical OCT) and dashed ellipses (vertical D-OCT) indicate the area of interest (the forming and resolving comedone). Blue (horizonal OCT and D-OCT) and green (vertical OCT and D-OCT) lines indicate the reference imaging plane. Abbreviations: D-OCT, dynamic mode optical coherence tomography; OCT, optical coherence tomography; RCM, reflectance confocal microscopy; SMFE, *Silybum Marianum* Fruit Extract; W, week.

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