

Morphological Evaluation of Facial Pigmented Lesions with Line-Field Confocal Optical Coherence Tomography: Correlation with Reflectance Confocal Microscopy. A Pilot Study

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ABSTRACT Introduction: Facial pigmented lesions pose significant challenges for diagnosis and treatment planning due to their anatomical topography and complexity. Traditional methods like dermoscopy have limitations, and while reflectance confocal microscopy (RCM) offers in-vivo cellular resolution, it is hindered by shallow penetration. The recently developed line-field confocal optical coherence tomography (LC-OCT) combines the benefits of OCT and RCM, providing deeper penetration and three-dimensional cellular imaging.

Objectives: This study aims to assess the ability of LC-OCT in displaying morphological features correlated and compared with RCM and histopathological findings.

Methods: Over a period of 1-year, various pigmented facial lesions were selected, including solar lentigo, seborrheic keratosis, lichen planus-like keratosis, pigmented actinic keratosis, basal cell carcinoma, compound nevus, lentigo maligna, and invasive melanoma. LC-OCT and RCM were used

for imaging, and their morphological features were compared. Lesions, except solar lentigo and compound nevus, were excised for histopathological evaluation. Morphological criteria from imaging were correlated with histopathological findings.

Results: LC-OCT matched RCM in spatial resolution while providing deeper tissue penetration and three-dimensional visualization. This advantage was particularly notable in pigmented actinic keratosis and basal cell carcinoma, where LC-OCT's vertical imaging offered unique diagnostic insights. It also enhanced the understanding of the architecture of melanocytic lesions.

Conclusion: LC-OCT adds new insight into the imaging and diagnosis of facial pigmented lesions, offering additional morphological features. This pilot study highlights its potential to improve diagnostic accuracy and patient care, with further research needed to assess its broader clinical applications.

Introduction

Proper management of facial skin lesions in daily dermatology practice poses peculiar challenges due to anatomical, cosmetic, diagnostic, and therapeutic considerations. Dermatologists must handle these difficulties to ensure accurate diagnosis and effective treatment while preserving function and achieving optimal cosmetic outcomes. Being the most continuously sun-exposed area of the human body, facial skin is a privileged localization for the development of skin cancer for which early management is paramount. Besides their own clinical expertise, dermatologists rely on auxiliary diagnostic tools such as dermoscopy, imaging, and histopathology to enhance diagnostic accuracy and guide appropriate treatment choices [1, 2]. Yet, despite all these techniques at their disposal, facial lesions remain tricky for various reasons, such as the high number of lookalikes or simulators of different biological origin and prognosis, and the difficulty of characterizing the malignancy potential of some lesions, melanocytic ones in particular. Among these developing imaging devices, reflectance confocal microscopy (RCM) is has been widely used for several years to examine the skin *in vivo* at a cellular resolution and its added value in patient management has already been established especially regarding pigmented lesions [3-5]. However, it allows only horizontal view of the skin, lacks penetration depth (maximum 300 microns), and its interpretation requires thorough specific training and experience particularly for equivocal lesions. Line-field confocal optical coherence tomography (LC-OCT) was recently developed as an imaging technology that combines the benefits of standard OCT and RCM. It displays high resolution, 1.2- μm in axial and 1.3- μm in lateral, with 500 μm penetration depth and visualization of the vertical plane similar to histopathology. It is also the first skin imaging device able to produce tridimensional pictures of the skin with cellular resolution, allowing appreciation of micro-architectural morphology as well as cytological aspects [6-11]. LC-OCT has been studied for its potential use in the management of various skin lesions after describing

morphologic criteria and assessing diagnostic performance [12-19]. However, the added value of this technique for pigmented facial lesions remains to be defined.

Objectives

The main objective of this pilot study is to describe the correlation between LC-OCT and RCM as well as the tridimensional anatomy of the most frequently encountered facial pigmented lesions in order to compare the quality of images provided by the 2 techniques and to determine if LC-OCT could potentially bring useful insight to increase diagnostic accuracy and management performance.

Methods

From January to June 2023, we prospectively evaluated adult patients with pigmented facial and scalp lesions and selected one case for each entity, namely solar lentigo (SL), seborrheic keratosis (SK), lichen-planus like keratosis (LPLK), pigmented actinic keratosis (AK), pigmented basal cell carcinoma (BCC), pigmented compound nevus, lentigo maligna (LM), and invasive melanoma (MM). For each case we gathered clinical and dermoscopic images with a camera equipped with a dermoscopic lens and polarized light (Casio). Subsequently, each lesion was examined with RCM (Vivascope 1500TM, Mavig Corp, Munich, Germany). This device integrates a dermoscopic tool which allows to navigate precisely in the corresponding confocal image. For each case multiple mosaic-like pictures (4x4 mm Vivablocks) were acquired at different layers of the epidermis and the dermis. Additionally, we collected images using the LC-OCT device (deepLiveTM, DAMAE Medical, Paris, France), exploring the lesion in vertical view with its videodermoscopy camera and acquired several tridimensional blocks (1,2x0,5x0,4 mm) from the regions of interest. From these tridimensional blocks we selected horizontal pictures of the examined area and correlated them with the best corresponding RCM Vivablocks showing features shared by both LC-OCT and

RCM. The analysis of horizontal LC-OCT acquisitions was based on criteria and morphologic features already described and established in RCM and LC-OCT literature. Moreover, except for the SL, SK and pigmented compound nevus, which were without doubt benign either clinically, dermatoscopically and/or after imaging examination, all other lesions were either biopsied or excised for diagnostic as well as therapeutic purpose. In these cases, we also selected the best matching correlation between the features seen in LC-OCT vertical view and the histopathological equivalent, also based on morphologic criteria well-established in the pathology literature. No horizontal histopathological section was performed due to the sample processing that would impair the diagnostic and prognostic assessment which is crucial especially in equivocal melanocytic tumors.

Results

Solar Lentigo

Horizontal mode of LC-OCT displays the same typical features of SL that have been described in RCM examination i.e. a regular honeycomb pattern and intertwined dermal papillae with elongated cord-like rete ridges corresponding to the lentiginous pigmented keratinocyte proliferation, preserving follicular integrity [3, 4, 20]. It is the same pattern that

translates into the typically regular pigment network with fingerprint-like areas in dermoscopy [1]. Nuclei of keratinocytes are more clearly identified in LC-OCT than in RCM as regular roundish dark shapes inside the cells, although the granular melanin pigmentation appears more finely contrasted in RCM. The vertical view combined with tridimensional display in LC-OCT allows the clinician to appreciate the architecture of SL with more histopathological-like and real-life perspective. The cord-like rete ridges are distributed in a regular fashion in the papillary dermis and the keratinocytes are monomorphous and evenly pigmented at the basal layer, without hyperkeratosis nor acanthosis (Figure 1).

Seborrheic Keratosis

SK belongs to the same spectrum of lesion as SL, sometimes arising from one, and as such it shares common morphological features with SL in RCM [20] and LC-OCT. Epidermal architecture remains regular and shows a typical honeycomb pattern with coiled dermal papillae and thickened cord-like rete ridges. In the left part of these acquisitions, which focuses on a more acanthotic and keratotic area of the SK, we can observe hyperreflective horn cysts filled with keratin. LC-OCT signal penetrates deeper in the lesion and reaches the lower ridge of the horn cyst observed on tridimensional reconstruction. This view also forthrightly emphasizes the

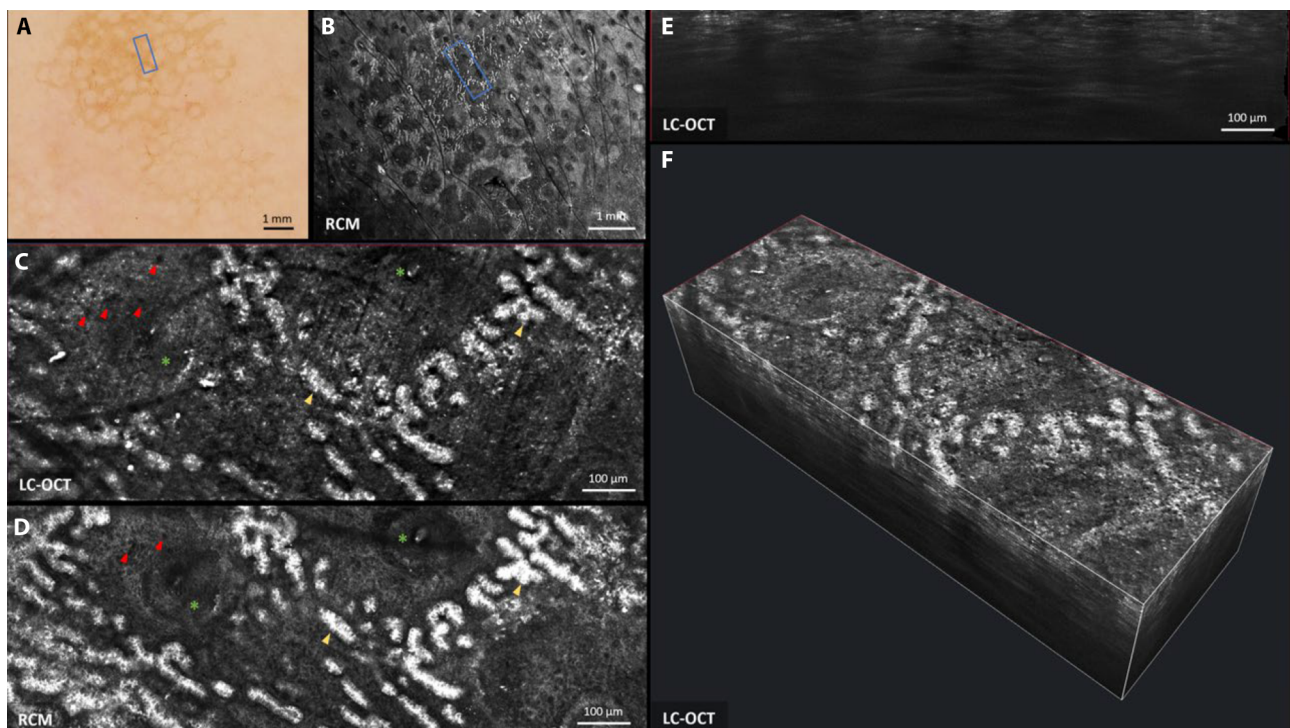


Figure 1. LC-OCT imaging and corresponding RCM features of solar lentigo (SL). (A) Dermoscopic and (B) RCM Vivablock overviews; (C) matching horizontal LC-OCT and (D) RCM (D) views; and (E) vertical histology-like and (F) tridimensional LC-OCT views. Intertwined dermal papillae and elongated rete ridges (yellow arrows) are visible in all the acquisitions and indicate lentiginous keratinocytic proliferation, preserving follicular integrity (green stars). Horizontal LC-OCT view shows a regular honeycomb pattern similar to RCM. Nuclei of keratinocytes appear as roundish dark shapes more clearly in LC-OCT than in RCM (red arrows) while melanin pigment is more finely defined in RCM.

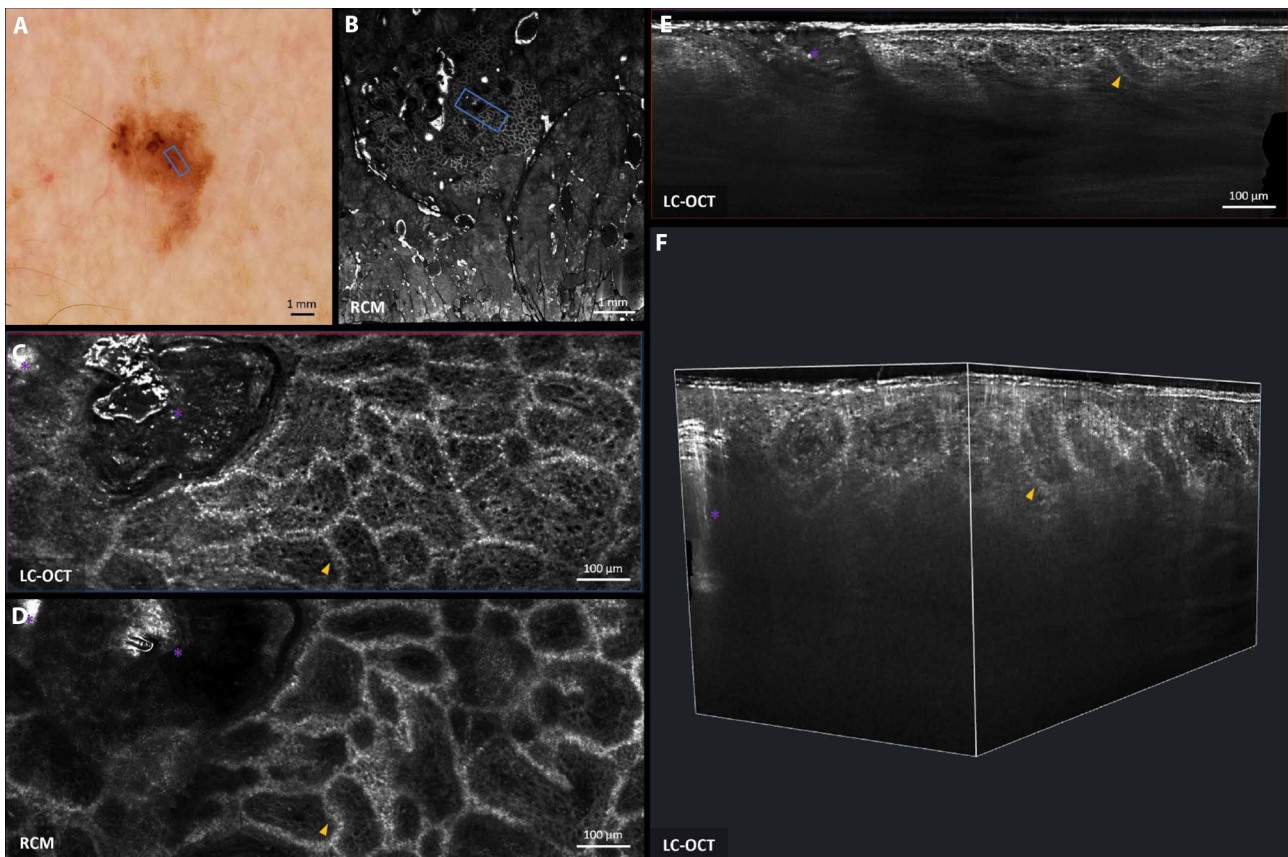


Figure 2. LC-OCT imaging and corresponding RCM features of seborrheic keratosis (SK). (A) Dermoscopic and (B) RCM Vivablock over-views; (C) matching horizontal LC-OCT and (D) RCM views; and (E) vertical histology-like and (F) tridimensional LC-OCT views. Regular honeycomb pattern coiled dermal papillae and thickened cord-like rete ridges with lentiginous keratinocytic proliferation (yellow arrows) are seen in all acquisitions. The left part of the lesion shows a hyperreflective horn cyst filled with keratin (purple stars), wholly and clearly observed in LC-OCT.

regularity and homogenous distribution of the epidermal projections. (Figure 2).

Lichen Planus-Like Keratosis

LPLK arises from SL or SK, and as such they all share common features in dermoscopy, histopathology and *in vivo* skin imaging. The regular honeycomb pattern is largely preserved and the same cord-like rete ridges that we see in SL and SK are observed in both LC-OCT and RCM as described before. Vertical view of LC-OCT provides additional features such as the bright horizontal line just underneath the dermoepidermal junction (DEJ), underlining a large band of marked elastosis as seen in histopathology. Furthermore, we can best appreciate the focal loss of sharp demarcation between the epidermis and the dermis in vertical histology-like display of LC-OCT, which reflects the lichenoid interface inflammation that contains multiple bright plump cells and bright dots scattered throughout the dermis corresponding to melanophages and lymphocytes. These are observed with greater depth penetration than in RCM (Figure 3).

Pigmented Actinic Keratosis

Pigmented AK, mostly found on the face and scalp, is one of the several described subtypes of AK, though it is the only one that can be confused with an atypical melanocytic lesion and hence the most crucial to accurately diagnose. The main feature observed upon horizontal view of LC-OCT just like in RCM is pigmented keratinocytic pleomorphism, known as atypical honeycomb pattern. Although RCM brings finer brightness contrast related to the degree of melanic pigmentation as well as better-defined interkeratinocytic cell junctions, LC-OCT shows highly defined nuclei corresponding to the black roundish and oval shapes inside the keratinocytes. Moreover, keratinocytic pleomorphism is more precisely assessed in vertical and tridimensional view of LC-OCT thanks to the projection of the whole epidermal thickness on one scan. We can easily appreciate the degree and topography of atypia with nuclei of irregular shape and size compared to the previously described SL, mostly noticeable in the lower half of the epidermis in this case, which is diagnostic of low-grade AK. The enlarged atypical keratinocytes of the basal

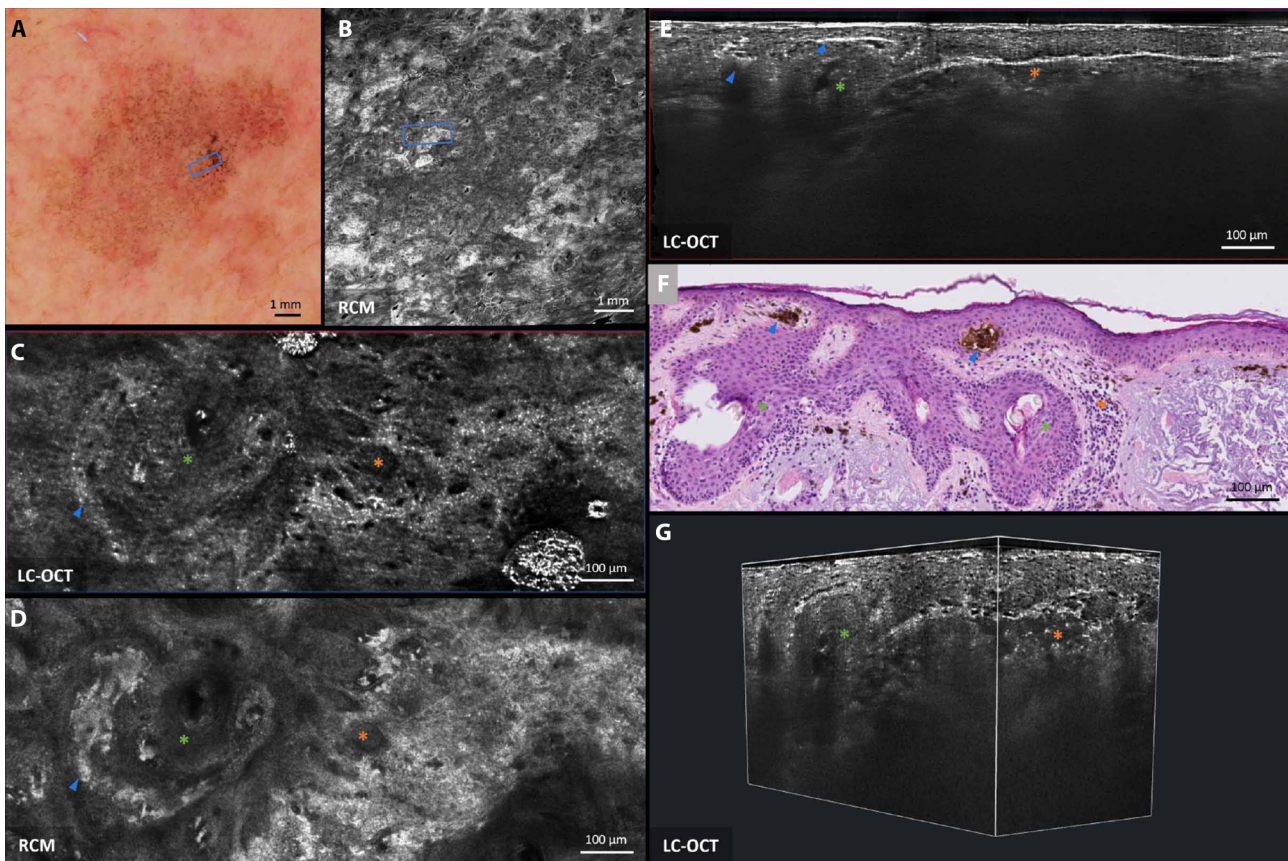


Figure 3. LC-OCT imaging, corresponding RCM features, and histopathology of lichen planus-like keratosis (LPLK). (A) Dermoscopic and (B) RCM Vivablock overviews; (C) matching horizontal LC-OCT and (D) RCM views; and (E) vertical LC-OCT, (F) histopathology and (G) tridimensional LC-OCT views. Focal loss of sharp demarcation between epidermis and dermis is visible in LC-OCT and RCM with vertical view of LC-OCT providing a more histology-like perspective. It corresponds to lichenoid interface inflammation (orange stars), with plump cells and bright dots representing melanophages (blue arrows) as well as lymphocytes scattered throughout the dermis, more deeply observed than in RCM. The vertical view of LC-OCT highlights a bright horizontal line just beneath the DEJ, indicating marked elastosis as confirmed in histopathology. Follicles (green stars) are preserved.

layer focally appear pigmented, but do not dive into the follicles, and there are no dendritic and pagetoid bright cells in the upper layers of the epidermis. Underneath the flattened DEJ, we can observe the same fine bright horizontal line that we saw in the LPLK covering a homogenous grayish papillary dermis that displays marked elastosis in histopathology (Figure 4).

Pigmented BCC

The pigmented variant of BCC, more commonly found on the face and scalp area, shares most of its features with all the other subtypes of BCCs in RCM and LC-OCT, in addition to some more specific signs that we can observe in this case. The lobules appear as cohesive cord-like structures, containing several plump bright oval-shaped elements, corresponding to melanophages, pigmented melanocytes and Langerhans cells. Vertical as well as tridimensional display in LC-OCT is highly superposable with histology and we can effortlessly observe the tumor lobules, of which the connection

to the epidermis appears more obvious than in RCM. The deep tumor borders also emerge as much better-defined in LC-OCT, with a clear picture of clefting revealed underneath the lobules, echoing the well-established eponym histological feature (Figure 5).

Pigmented Compound Naevus

Melanocytic nevi of the face present as variably pigmented lesions depending on the depth and pigmentation degree of melanocytic proliferation. The typically described ring-pattern as observed in RCM and LC-OCT horizontal view of LC-OCT of pigmented nevi is not strikingly observed in this compound nevus on the cheek of a young patient due to the physiological flattening of the DEJ in facial skin. However, we can observe several monomorphous bright structures surrounding small papillae, forming nests corresponding to benign melanocytes. These are visible mainly along the DEJ in both RCM and LC-OCT, but the combination of vertical view and tridimensional display in LC-OCT

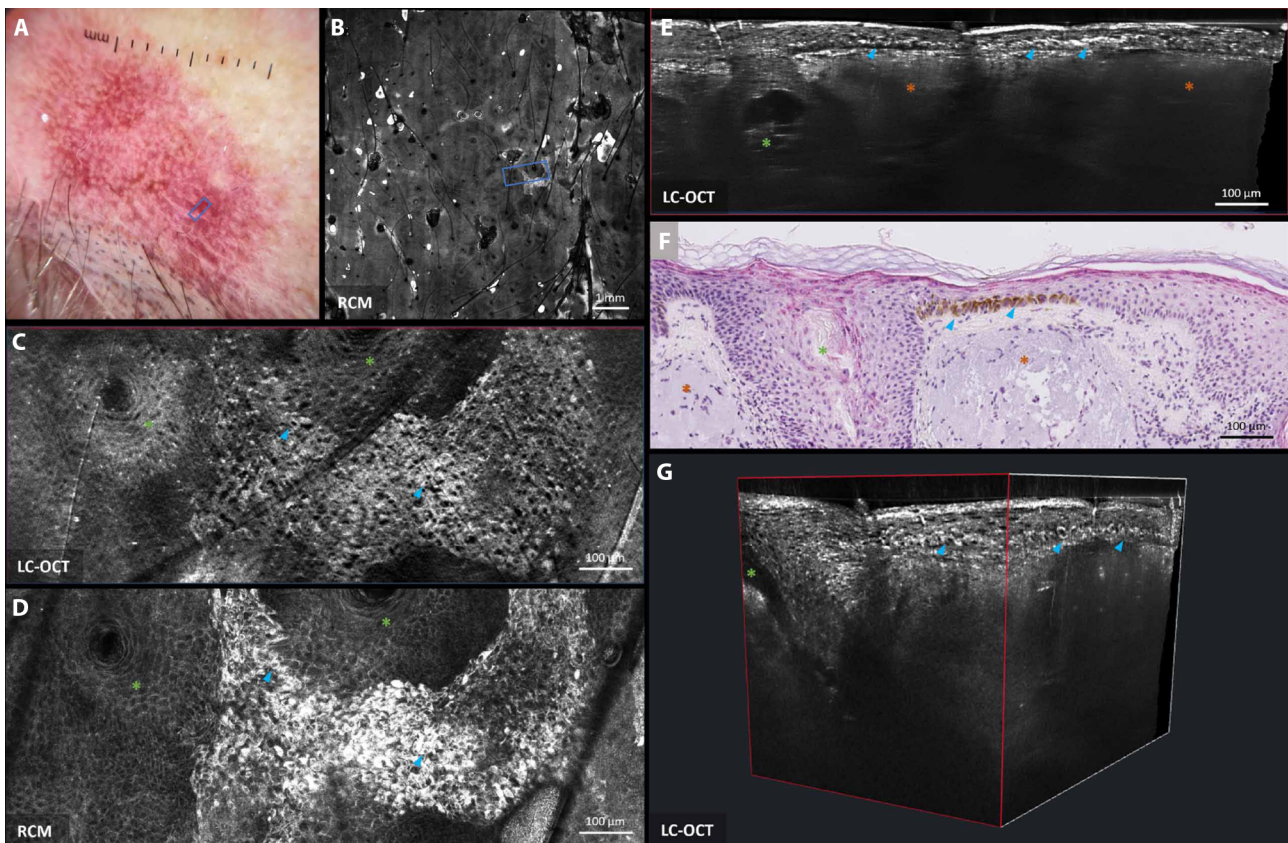


Figure 4. LC-OCT imaging, corresponding RCM features, and histopathology of pigmented actinic keratosis (AK). (A) Dermoscopic and (B) RCM Vivablock overviews; (C) matching horizontal LC-OCT and (D) RCM views; and (E) vertical LC-OCT, (F) histopathology, and (G) tridimensional LC-OCT views. Horizontal views of both RCM and LC-OCT display an atypical honeycomb pattern corresponding to pigmented keratinocytic pleomorphism (blue arrows). Vertical view of LC-OCT clearly confirms the basal localization of this atypical proliferation. While visible in both techniques, features such as nuclear shape and pleomorphism are more easily observed in LC-OCT as irregular black oval structures, while cellular shape and pleomorphism, interkeratinocytic cell junctions as well as melanin pigment are more finely contrasted in RCM. The flattened DEJ, best observed in vertical view of LC-OCT, underlines a fine bright horizontal line indicative of marked elastosis (orange stars) as confirmed in histopathology.

facilitates the understanding of the global architecture, here well-preserved, in terms of size, shape, location and distribution of the melanocytic proliferation. Moreover, the absence of large, bright, roundish and dendritic cells emphasizes the benign character of the lesion (Figure 6).

Lentigo Maligna

LM is the most common subtype of melanoma on the face and scalp and RCM has already been proven significantly valuable for its diagnosis and surgical treatment planning. Horizontal view of LC-OCT can display just like RCM the most prominent diagnostic criterion of LM which is the presence of atypical melanocytes in the shape of large and pleomorphic bright cells. They appear as large roundish cells with abundant cytoplasm and can project numerous dendrites visible in the epidermis, with better vertical resolution in LC-OCT than in RCM. Those melanocytes are seen proliferating in a contiguous manner along the basal membrane, diving inside the follicles as well as spreading to the upper layers of the epidermis in a pagetoid fashion. The

straightforward visualization of the DEJ in vertical view or tridimensional setting of LC-OCT allows to evaluate the integrity of the basal membrane throughout the whole lesion as seen in this *in situ* melanoma (Figure 7).

Superficial Spreading Melanoma

Invasive melanomas of the face and scalp share most of their morphological features with the *in situ* counterparts from which they develop over time. The same large pleomorphic roundish and dendritic bright cells are observed in both RCM and LC-OCT. They are numerous, isolated or grouped in nests of variable size along the junction and in the epidermis, including the follicles. The DEJ, best assessed in vertical view and tridimensional reconstruction of LC-OCT, appears blurry and correlates with the histological picture of breached basal membrane, signing the invasive aspect of the lesion. Moreover, disarrangement of both the honeycomb and meshwork patterns underlines the consumption of the epidermis and its altered architecture. (Figure 8).

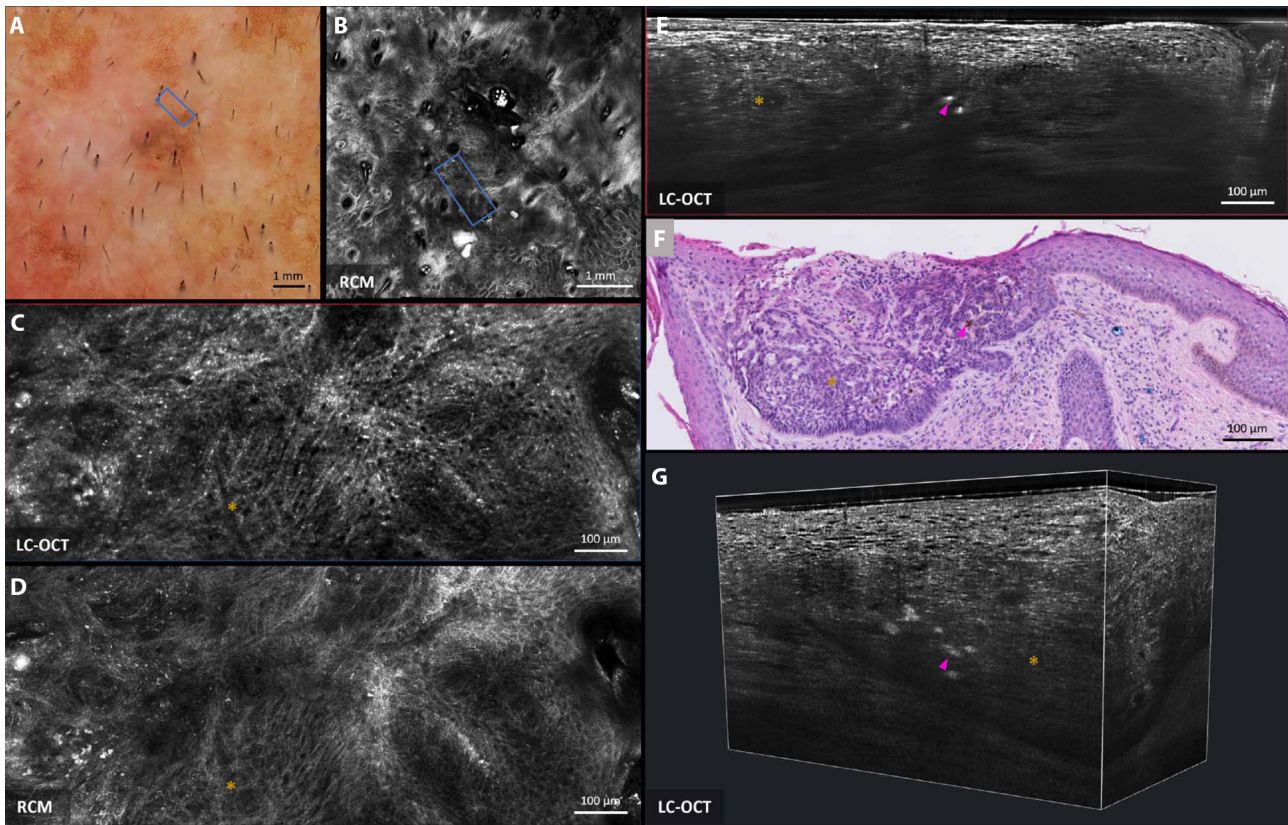


Figure 5. LC-OCT imaging, corresponding RCM features, and histopathology of pigmented basal cell carcinoma (BCC). (A) Dermoscopic and (B) RCM Vivablock overviews; (C) matching horizontal LC-OCT and (D) RCM views; and (E) vertical LC-OCT, (F) histopathology, and (G) tridimensional LC-OCT views. Both RCM and LC-OCT demonstrate lobular structures typical of BCC (orange stars), containing plump bright oval-shaped elements, identified as melanophages, pigmented melanocytes, and Langerhans cells (purple arrows). Vertical and tridimensional LC-OCT views closely mirror histological findings, depicting the tumor lobules, the clefting visible beneath them and their connection to the epidermis, in a more intuitive manner than in the horizontal view of RCM for the pathology-trained eye.

Discussion

Morphologic features and diagnostic criteria for most skin lesions have been extensively described in histopathology which remains the gold-standard to this day. More recently, RCM offered a high-resolution horizontal perspective, and a new range of descriptive patterns and criteria were published over the years to help dermatologists achieve a more precise *in vivo* characterization of suspicious lesions. Finally, LC-OCT was developed with the aim of combining the benefits of RCM in terms of spatial resolution with the deeper signal penetration and the vertical imaging of conventional OCT. As such, it is the first skin imaging technology able to provide *in vivo* histology-like pictures of skin lesions with cellular resolution. With adequate training the dermatologist can therefore be expected to recognize features described in both RCM and histopathology when examining a skin lesion with LC-OCT. This proves especially helpful in lesions such as AK and BCC where vertical and tridimensional imaging provide the most clear-cut and straightforward diagnostic criteria. Moreover, LC-OCT can potentially help specify the

histological subtype of these lesions with more ease and precision than in the sole horizontal view provided by RCM. In the case of AK, besides allowing to grade the degree of atypia in the different epidermal layers as is done routinely in histopathology, this can be typically useful to detect *in vivo* the proliferative subtype of AK (pigmented or not), which is known to be the most aggressive and at risk of developing into SCC. Same goes regarding BCC where the distinction between indolent and aggressive subtypes has already been proven significantly efficient in LC-OCT, allowing better treatment planning, much appreciated in an area as essential as the face. In the case of melanocytic pigmented lesions of the face where assessment of global architecture and distribution of the melanocytic proliferation is paramount in the diagnostic process, LC-OCT also brings valuable additional information. Though RCM can already display the overall horizontal architecture of the lesion, LC-OCT shows with more clarity the location and the connection of melanocytic cells and nests with the epidermis, the follicles, the basal membrane and the dermis, allowing better assessment of the tridimensional architecture. Moreover, thanks to the vertical

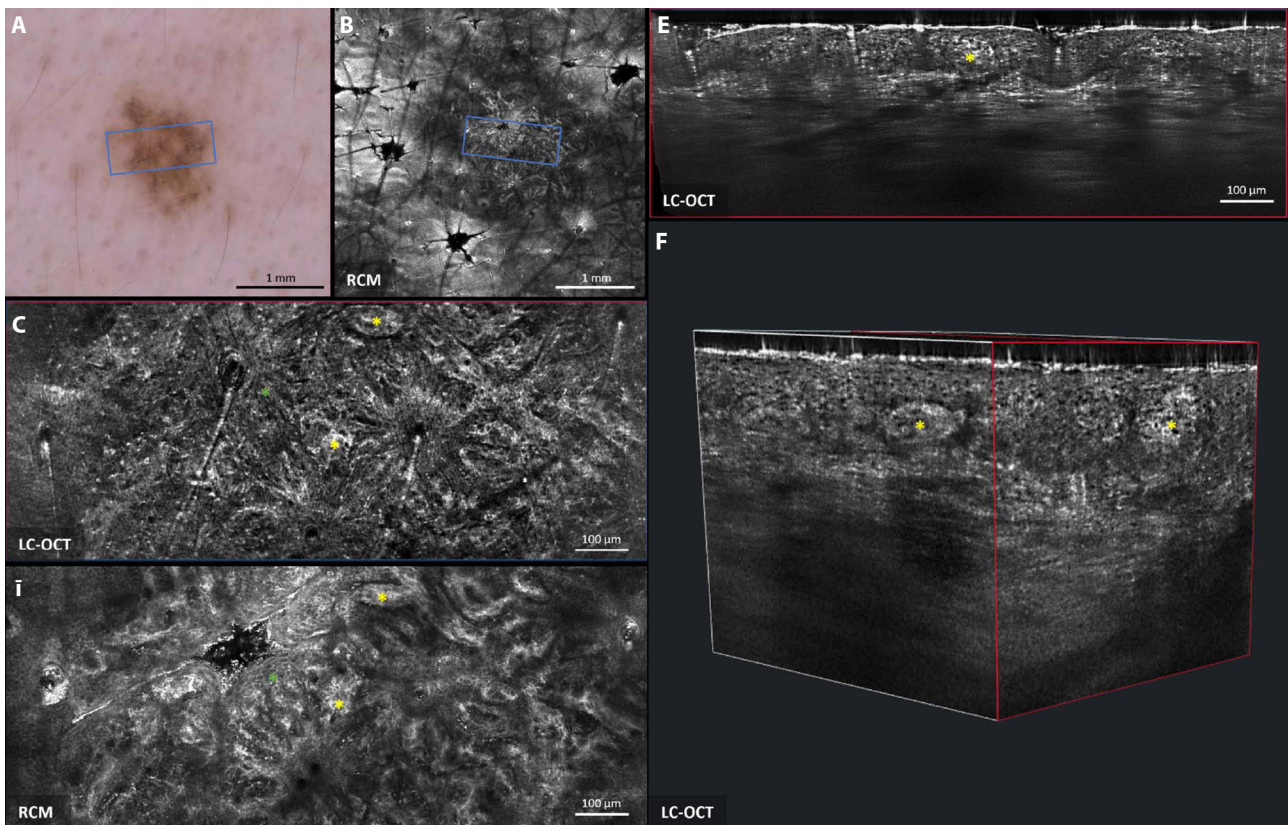


Figure 6. LC-OCT imaging and corresponding RCM features of a pigmented compound nevus. (A) Dermoscopic and (B) RCM Vivablock overviews; (C) matching horizontal LC-OCT and (D) RCM views; and (E) vertical and (F) tridimensional LC-OCT views. Both RCM and LC-OCT horizontal views reveal monomorphous bright structures forming nests of benign melanocytes around small papillae (yellow stars), predominantly along the DEJ. The vertical and tridimensional LC-OCT views provide a clearer understanding of the lesion's architecture, showing well-preserved global structure in terms of size, shape, location, and distribution of the melanocytic proliferation. Green stars indicate follicles, which are preserved.

display and deeper penetration of LC-OCT compared to RCM, the papillary dermis becomes more accessible for *in vivo* analysis and can reveal additional relevant features. The bright horizontal line particularly well visible in LPLK and pigmented AK just underneath the epidermis seems to correlate with marked elastosis in histopathology, probably due to an increased difference of signal absorption and reflection than in normal skin between the epidermis and the dermis. Inflammatory cells in the form of plump bright cells and small bright dots are also effortlessly observed, particularly in the LPLK where they are numerous. In terms of spatial resolution, LC-OCT appears to provide similar performances to RCM but with subtle differences in the projected structures. Cell nuclei are more clearly visible in LC-OCT than in RCM images: in particular, LC-OCT allows an easy appreciation of the degree of nuclear pleomorphism, especially in AK or LM cases. Of converse, the melanin pigment and the interkeratinocytic cellular junctions appear with more contrast in RCM than in LC-OCT. Regarding large dendritic cells

which are prominent mostly in atypical melanocytic lesions, both techniques display them efficiently, with finer contrast in RCM but better vertical resolution in LC-OCT where the dendrites can easily be followed from one horizontal plane to the next.

Limitations

As for the limitations of the study, it should be reminded that the findings resulting from those correlations were obtained based on the analysis of a single lesion for each type of diagnosis. Except for SL, each lesion was selected after being deemed clinically equivocal and for which the *in vivo* examination showed the clearest features as previously established in LC-OCT, RCM and histopathology literature. It is therefore possible that some of these diagnoses may present with varying morphological features that were not exhaustively described in this study. For example, regarding BCC, the infiltrative subtype is known to be the most difficult to

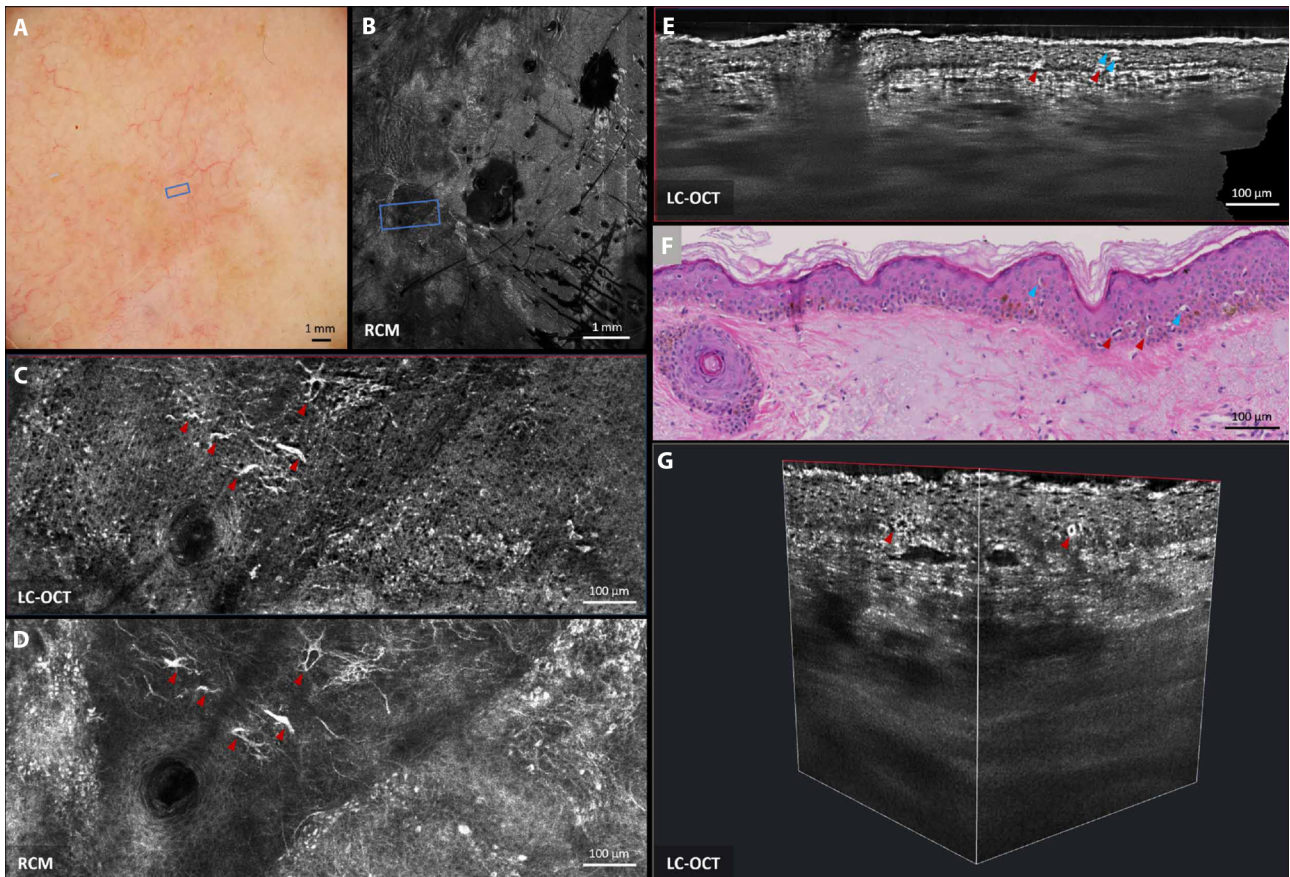


Figure 7. LC-OCT imaging and corresponding RCM features of lentigo maligna (LM). (A) Dermoscopic and (B) RCM Vivablock overviews; (C) matching horizontal LC-OCT and (D) RCM views; and (E) vertical LC-OCT, (F) histopathology, and (G) tridimensional LC-OCT views. Horizontal views of both RCM and LC-OCT highlight the presence of confluent atypical melanocytes (red arrows) reaching the follicle nearby. These melanocytes proliferate along the basal membrane as clearly observed in vertical view of LC-OCT. Some are seen in the upper layers of the epidermis (blue arrows). Vertical and tridimensional LC-OCT views enable clear visualization of the DEJ and assessment of basal membrane integrity in this *in situ* lesion.

diagnose in dermoscopy as well as in skin imaging, and a skin biopsy is usually necessary to confirm the suspected diagnosis. However, the main features described in each lesion are expected to be observed in most cases routinely seen in dermatology consultation and their relevance was certainly also shaped by our own real-life experience as skin imaging consultants. It is evident that further studies are needed to evaluate each sign's value in terms of sensibility and specificity as diagnostic criteria, as has been done for other diagnostic technologies in the past.

Conclusions

With LC-OCT being a recent technology, continuously developing and adapting tools to aid the dermatologist in achieving better *in vivo* diagnostic performance, we can expect it to fulfill some yet unmet needs particularly in the difficult

field of pigmented facial lesions. This first-of-its-kind pilot study comparing superposable pictures of LC-OCT and RCM of the most common pigmented facial lesions is a first step in determining the added value of this new technology. Its ability to project horizontal pictures with similar spatial resolution to RCM as well as to display histology-like and tridimensional view of skin lesions allows to integrate the previously described and well-established morphological criteria from both RCM and histopathology for each lesion. Moreover, the ongoing development of artificial intelligence as well as algorithms that provide a clear assessment of key structures like the DEJ and the microvascular environment may lead to a better understanding of how these lesions develop in facial skin. Finally, LC-OCT could represent a major step closer to the ideal of a technology that would one day be able to provide a full tridimensional *in vivo* reconstruction of a whole lesion.

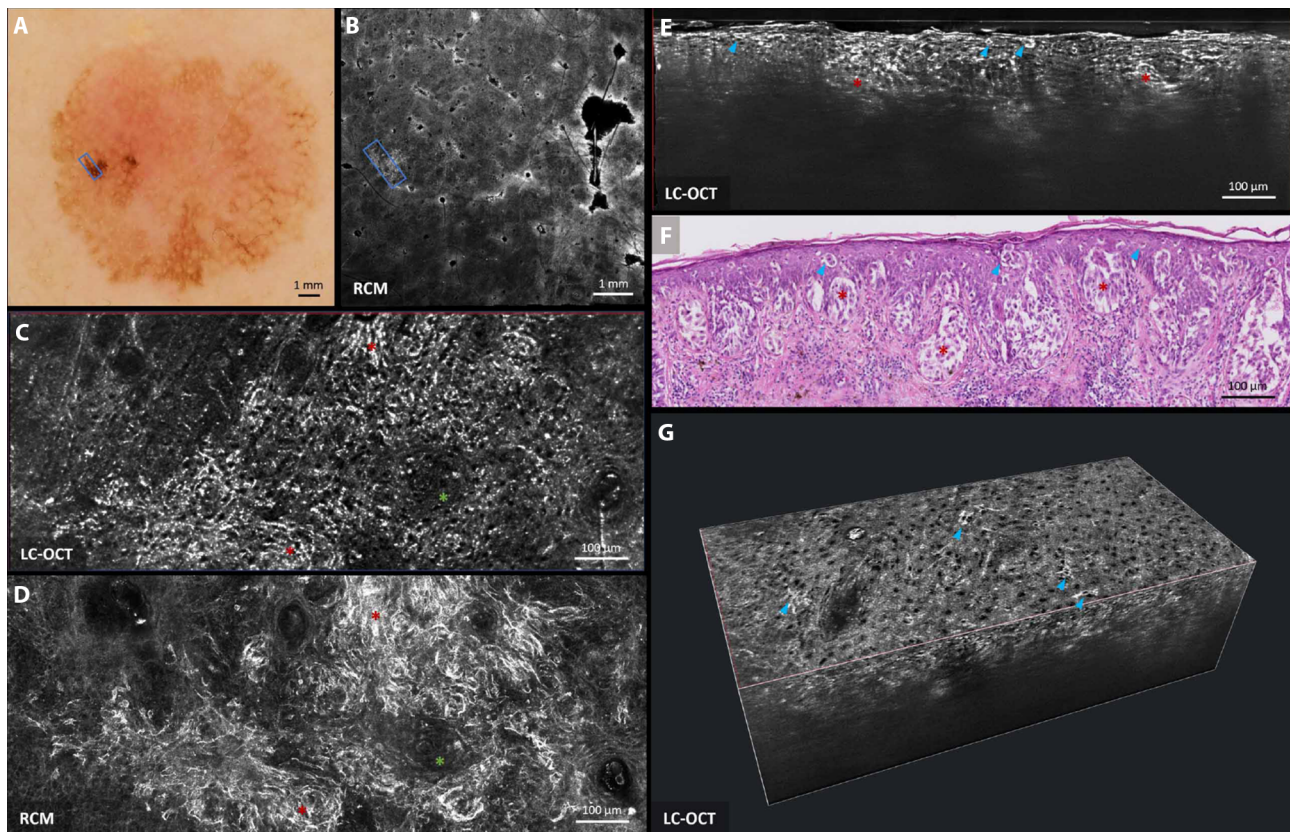


Figure 8. LC-OCT imaging and corresponding RCM features of invasive melanoma. (A) Dermoscopic and (B) RCM Vivablock overviews; (C) matching horizontal LC-OCT and (D) RCM views; and (E) vertical LC-OCT, (F) histopathology, and (G) tridimensional LC-OCT views. Horizontal views from both RCM and LC-OCT show numerous large pleomorphic roundish and dendritic bright cells, isolated or in nests (red arrows), along the junction, including follicles (green stars) and focally spreading in the upper layers of the epidermis (blue arrows). Disarrangement of the honeycomb and meshwork patterns highlights the consumption of the epidermis and its altered architecture. The DEJ is best visualized in vertical and tridimensional LC-OCT views and appears blurry, indicating invasiveness.

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