Optical Coherence Tomography in Nail Research and Diagnosis

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Abbreviations

OCT	Optical coherence tomography
DLSO	Distal lateral subungual onychomycosis
D-OCT	Dynamic optical coherence tomography
MC	Myxoid cysts
NAPSI	Nail Psoriasis Severity Index
US	Ultrasonography

Background

Optical coherence tomography (OCT) is a noninvasive imaging tool enabling real-time imaging of skin, hair, and nails. It has also been widely investigated as a diagnostic tool in dermatology, particularly in non-melanoma skin cancer and inflammatory, bullous, nail, and hair diseases [1–3]. Nail disease diagnosis is based mainly on clinical examination, biopsies, and scrapings; however, noninvasive imaging technologies such as OCT may expedite diagnosis of pathologies in the nail unit [1, 4]. OCT is able to visualize the nail plate, bed, and matrix, as well as blood flow in nail bed [1, 3–5]. OCT provides clinicians with micrometer resolution images of morphological features of the nail and has been shown promising in exhibiting features characteristic of nail psoriasis, onychomycosis, nail hematoma, glomus tumor, and myxoid cysts.

Generally, OCT imaging is more accurate than existing ultrasonography and is approaching clinical utility much more rapidly. OCT images clearly provide more detail than a simple magnifying glass and are able to display both structural and functional aspects of the nail [5].

Technology

Optical Coherence Tomography

OCT is based on the principle of Michelson interferometry using infrared light (from an 830-nm superluminescence diode) to detect scattered light from target tissue and reconstruct the 2D/3D morphology [6]. The reflection of the light from tissue is measured and processed in order to improve the signal-to-noise ratio and transfer it to a computer-generated OCT image [7, 8]. As an imaging modality, it occupies a space between acoustic imaging and confocal microscopy in terms of its resolution and imaging depth, typically imaging to a depth of 0.4 to 2.00 mm with an optical resolution of 3 to 15 μm (Fig. 16.1).

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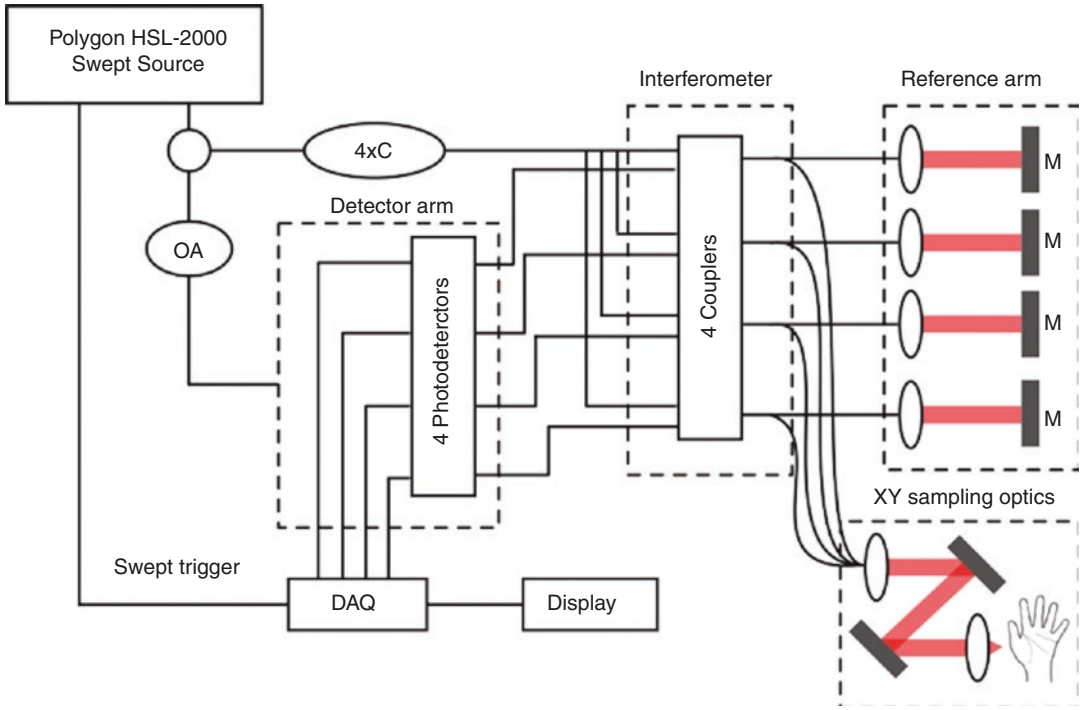

Fig. 16.1 Principle of optical coherence tomography. Schematic of multi-focus VivoSight optical coherence tomography. (Courtesy of Kamran Avanaki, PhD)

Dynamic Optical Coherence Tomography

A supplementary imaging technique, dynamic optical coherence tomography (D-OCT), allows the detection of vessels in transversal and en face/horizontal sections in real time to visualize the skin and nail bed microangiography [9–11]. D-OCT principles rely on detecting motion of blood cells during structural OCT scans by combining the image of the tissue structure with the blood vessel structures [9, 11].

Normal Nail

OCT visualizes images of the nail plate, the nail bed, and the matrix to a depth of 2 mm [4].

The nail plate is a modified form of stratum corneum, with a thick laminated keratinized structure overlying the nail bed and matrix. The nail plate is composed of 25 sheets of keratinized cells that can be divided into dorsal, intermediate, and ventral layers. Compared with the intermediate layer, the dorsal and ventral layers are thinner. The dorsal and ventral layers consist of harder skin-type keratin with lipids. In contrast, the intermediate layer is composed of hair-type keratin with few lipids, making the intermediate layer more flexible [12, 13]. OCT features of healthy nail plate are consistent with the above microscopic structure. The nail plate appears as a layered structure containing a varying number of horizontal homogeneous bands of varying intensity and thickness. The lunula contains distinct horizontal white band at the deep end of the nail plate. The nail bed is defined as the first change in OCT image intensity after the entrance signal, at the border of nail plate and nail bed (Fig. 16.2) [4].

Vascular changes coincide with structural features, nail fold, nail bed, and surrounding skin.

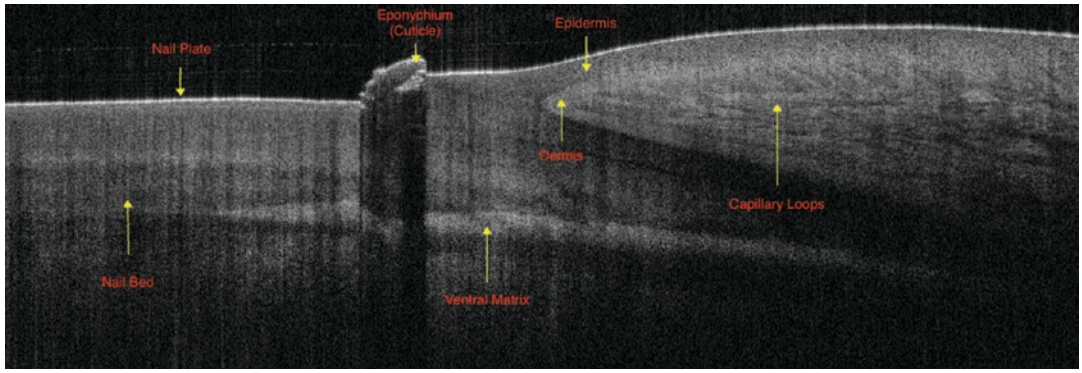

Fig. 16.2 Optical coherence tomography imaging of healthy nail and anatomic components of the normal nail unit. (Courtesy of Ali Rajabi-Estarabadi, MD, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA)

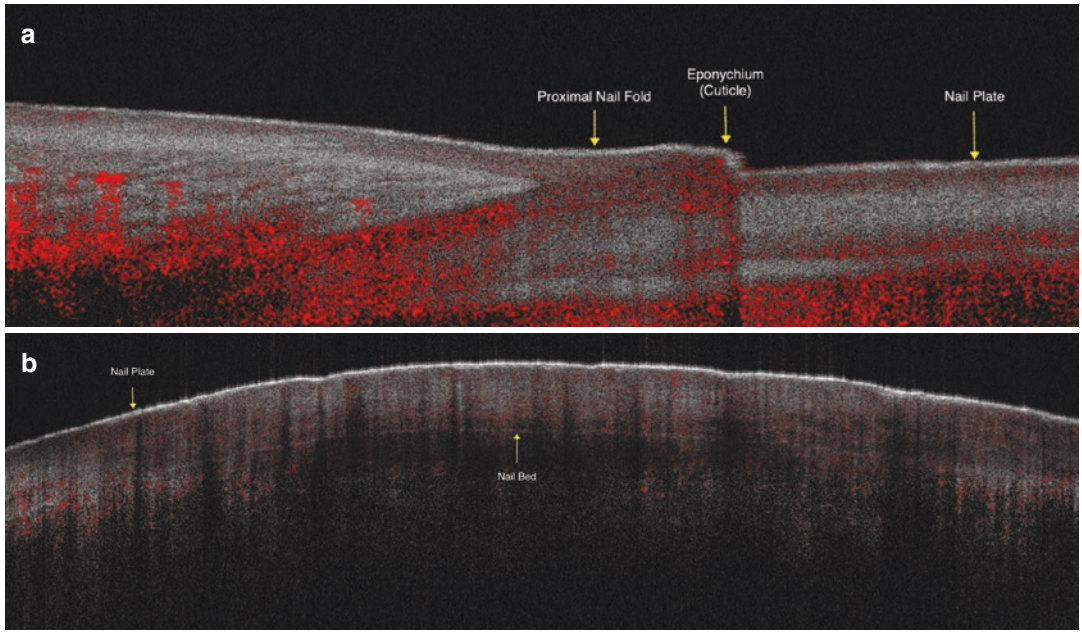

Fig. 16.3 Dynamic optical coherence tomography of healthy nail unit and vascular distribution at nail bed: (**a**) en face view, (**b**) trans-sectional view. (Courtesy of Ali Rajabi-Estarabadi, MD, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA)

The capillary loops of the proximal nail fold appear aligned compared to random distribution within the adjacent skin, and vessels in the nail bed appear more aligned along its leading edge. This is evidence that vascular traits and tissue structures are invariably linked [12] (Fig. 16.3).

Nail Psoriasis

Nail psoriasis most commonly involves the nail bed or nail matrix. Recently, the use of OCT has been incorporated in describing the characteristics of nail psoriasis. The first report on the

utility of OCT in nail psoriasis was in 2011 [7]. The researchers of this study not only described the morphological features of nail psoriasis on OCT imaging but also compared them to high-resolution ultrasonography (US). They found that OCT confirmed the ultrasonographic findings of a decreased trilaminar appearance of nails, which caused the nail plate to appear as one hyperechoic layer. However, OCT demonstrated higher resolution and specifically exhibited an inhomogeneous, eroded, and unevenly fused ventral plate.

The same authors subsequently studied 18 patients with at least 1 psoriatic nail compared to 12 healthy controls with both OCT and US. On OCT, leukonychia appeared as linear white stripes angled downwards in the proximal to distal direction [14]. Other white structures such as hyperreflective dots and thickening and irregularity of the superficial nail plate were also observed. These hyperreflective lesions on OCT demonstrated the highest sensitivity of all morphologic features mentioned (41.1%). Nail pitting correlated to small regions of sclerosis on OCT, which occasionally resulted in a shadow under the pit, whereas milder pitting demonstrated wavy abnormalities of the superficial nail. While the sensitivity of pitting and/or waving of the superficial layer was low (13.9%), the specificity was excellent (100%) (Fig. 16.4). Overall, the absolute agreement between OCT and clini-

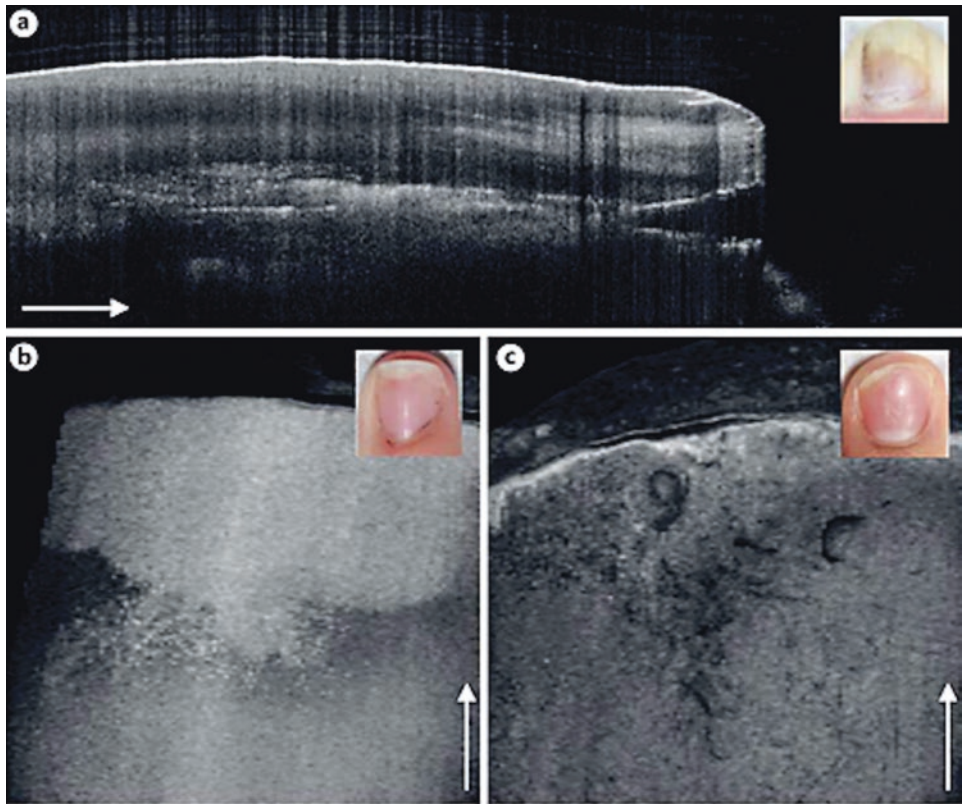

Fig. 16.4 Optical coherence tomography imaging of nail psoriasis vs healthy nail unit. Nail psoriasis: (**a**) Cross-sectional OCT image of a distal psoriatic nail: a wavy nail plate with white streaks and significant onycholysis overlying a highly reflective and irregular nail bed with white tufts. (**b**) En face view of a distal psoriatic nail demonstrating pronounced leukonychia and extensive speckling (depth 0.16 mm). (**c**) En face view of a distal psoriatic nail showing pitting (depth 0.30 mm). Healthy nail: (**d**) Cross-sectional view of a distal normal nail unit: a smooth nail surface, normal distribution of white speckles, and a linear regular nail bed proximal to the hyponychium. En face views at 0.16 mm (**e**) and 0.30 mm (**f**) in depth. (Reproduced with permission of [15])

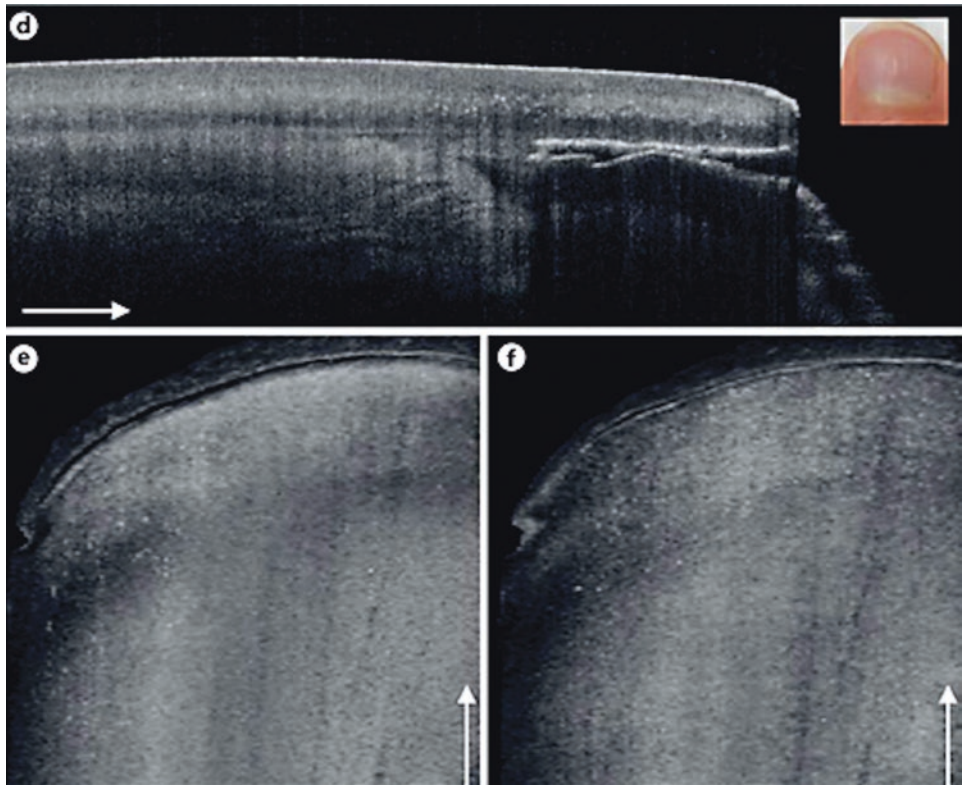

Fig. 16.4 (continued)

cal evaluation was 76.3% with a kappa value of 0.49 ($p < 0.0001$). OCT was able to identify abnormalities in 12 of 58 clinically normal nails in psoriatic patients compared to 5 of 120 nails of healthy controls. This suggests that OCT is able to detect subclinical nail involvement and may thereby have a role in identifying patients without obvious psoriatic lesions.

Furthermore, the specific vascular features of nail psoriasis have also been investigated using OCT. In a study of 16 psoriatic nails and 16 control nails, psoriatic nails exhibited significantly more blood flow at the proximal nail plate despite an increased nail thickness [15]. Psoriatic nails were also more likely to display dilated vessels with a haphazard architecture at the proximal nail fold (Fig. 16.5).

Other studies have highlighted the utility of OCT in assessing the therapeutic response of various treatments for nail psoriasis. Currently, the Nail Psoriasis Severity Index (NAPSI) is the most commonly used method of evaluating psoriatic nails and response to treatment. However, this tool is relatively subjective. Abignano and colleagues evaluated OCT changes occurring in 40 psoriatic fingernails before and after a 6-month treatment with apremilast [16]. The researchers developed a scoring system with OCT that included the presence or absence of leukonychia, pitting, diffuse surface waving, onycholysis, and subungual hyperkeratosis. Concurrently, a dermatologist blinded to these findings provided a NAPSI score for each nail. In general, the authors found that OCT identified more baseline abnormalities in nails than the clinical tool was able to detect. However, the outcomes of the clinical and imaging assessments were consistent in demonstrating improvement or worsening of nail psoriasis. The only exceptions were two cases where OCT demonstrated improvement in nails marked as "stable" by NAPSI and three cases where OCT found mild irregularities in nails marked as "normalized" by NAPSI.

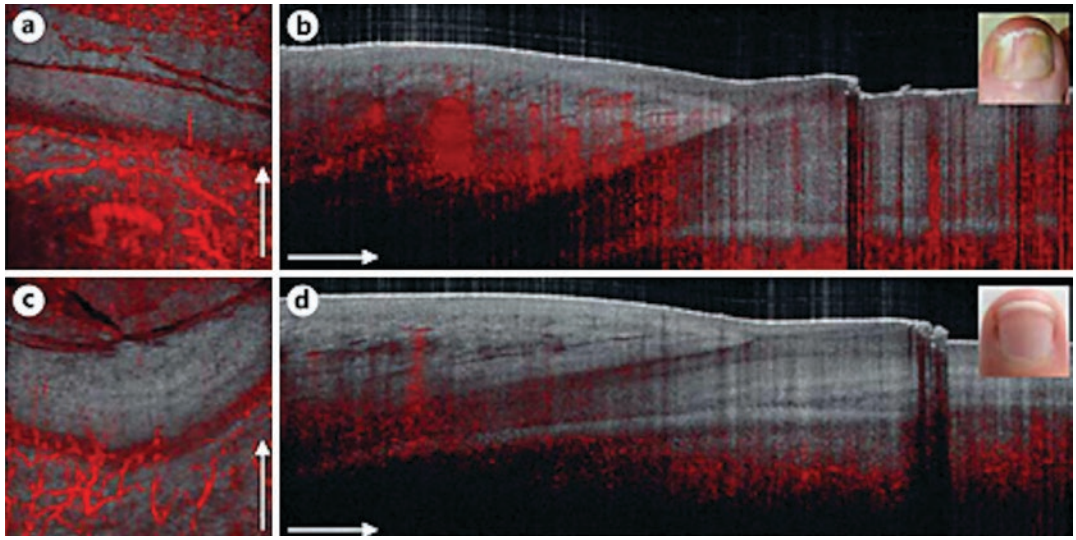

Fig. 16.5 Dynamic optical coherence tomography (D-OCT) of nail psoriasis vs healthy nail unit. Vascular features of nail psoriasis in the proximal nail fold: (**a**) En face view of a psoriatic nail: dilated vessels in a haphazard orientation (depth 0.6 mm). (**b**) Cross-sectional view: an increased density of blood vessels protruding superficially. Vascular features of healthy nail: (**c**) En face view of a healthy nail (depth 0.6 mm). (**d**) Cross-sectional view of the same healthy nail. (Reproduced with permission of [15])

Overall, these studies suggest that OCT may provide a more objective, quantitative, and structure-specific evaluation of nail psoriasis than pre-existing clinical tools. The clinical use of OCT may have prognostic potential as well, such as whether subclinical nail disease detected on OCT may predict arthritis. Ultimately, prospective studies with larger numbers are needed to clarify its potential role as a marker for nail psoriasis.

Onychomycosis

Onychomycosis occurs when a nail is infected with a fungal organism, most commonly dermatophytes such as *Trichophyton rubrum*, but can also occur secondary to yeast and non-dermatophyte molds. While a KOH preparation is the preferred initial test for suspected onychomycosis, OCT has recently demonstrated promise as a method of confirmation. As onychomycosis is the most common nail disorder seen in clinical practice, the application of OCT for this condition has been studied relatively more than for other nail disorders. Studies incorporating OCT have described the morphological characteristics of onychomycosis and have demonstrated the utility of this tool in increasing the diagnostic sensitivity.

A classic finding of onychomycosis is thickening of the nail plate, which can be visualized on OCT. This thickening is due to reactive subungual hyperkeratosis of the infected nail. OCT may also demonstrate a decrease in differentiation of scattering parallel layers of the nail plate [17]. Fungal elements typically appear as elongated, high-scattering structures, representing groups of hyphae, surrounded by low-scattering areas, correlating to the lacunas of the hyperkeratotic nail plate. This pattern is due to the high chitin concentration of fungal elements, which reflect more light and thus generate a higher signal intensity on OCT than the surrounding regions. Other reports describe fungal elements as white lengthy or thready structures or round aggregated white structures [18]. In addition to the presence of hyperreflective lines, hyperreflective dots, and irregular surfaces, more recent studies suggest that the morphologic features of onychomycosis on OCT can be further subdivided per clinical subtypes. For example, it has been reported that onychomycosis presents with diffusely demar-

cated lines rather than sharply demarcated lines and tends to lack surface irregularity [5]. In addition, distal lateral subungual onychomycosis (DLSO) commonly portrays hyperreflective dots. In a series that included 12 cases of onychomycosis demonstrating hyperreflective dots, DLSO was the only clinical subtype to specifically display clustered dots [5]. The authors of this series postulated that clustered dots may represent a proximal spread of infection, as the hyphae are not condensed to the point of forming clear-cut lines. More specifically, OCT has also been utilized to visualize complications of onychomycosis, such as dermatophytoma. A dermatophytoma is a thick, localized area of infection in the nail plate that is composed of dermatophytes compacted into a fungal ball. In a series of six cases, it was found that dermatophytomas typically appear as well-demarcated avascular masses with jagged borders, located above the vascular nail bed and below a disorganized nail plate [2] (Fig. 16.6).

While the terminology and diagnostic criteria for OCT in onychomycosis are still being developed, studies suggest that the above morphologic features may assist in increasing the sensitivity of diagnosis. In a pilot study of ten patients with histologically proven onychomycosis, OCT demonstrated fungal elements in all patients [17]. In contrast, KOH preparations and fungal cultures revealed positive results in only five and six patients of the ten patients, respectively. These results indicate that OCT is a reliable method of diagnosing onychomycosis, even in cases of false-negative KOH preparations and cultures. In contrast, Rothmund and colleagues determined OCT to be ineffective in diagnosing onychomycosis due to a high number of false-positive results. They found that the specificity of diagnosing onychomycosis with OCT was lower than KOH preparation, culture, PAS staining, PCR, and confocal laser scanning microscopy. The researchers attributed the poor specificity to the low resolution of the machine, which did not allow for precise differentiation of hyphae and other nail structures, as well as possible artifacts that may appear similarly. Although the specificity of OCT was not impressive in this study, the authors found that its sensitivity was second best to PCR (94.9% vs 92.3%).

Furthermore, understanding the characteristics of onychomycosis on OCT may aid in obtaining optimal nail scrapings. Olsen and colleagues recommend that areas appearing as dark bands on OCT should not be targets of nail scrapings, as these low-scattering regions generally represent lacunae and not fungal elements [5]. Using OCT as an adjunct may thereby increase the sensitivity of nail scrapings. In addition, OCT may serve useful in determining whether a mycotic

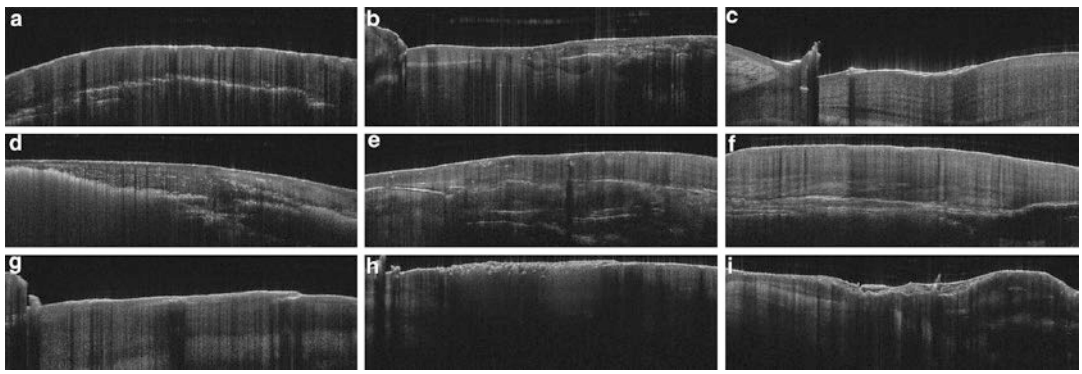

Fig. 16.6 Optical coherence tomography feature of onychomycosis. Cross-sectional view of proximal nail: (**a**) Sharply demarcated hyperreflective lines. (**b**) Clustered hyperreflective dots. (**c**) Dark band and a mildly irregular surface. (**h**) Moderately irregular surface. (**g**) Mildly irregular surface. Cross-sectional view of distal nail: (**d**) Diffusely demarcated hyperreflective lines and clustered hyperreflective dots. (**e**) Singular hyperreflective dots and sharply demarcated hyperreflective lines. (**f**) Disturbed architecture and sharply demarcated hyperreflective lines. (**i**) Severely irregular surface. (Reproduced with permission of [5])

cure has been accomplished. Some reports have even highlighted the use of OCT specifically for performing and monitoring laser treatment for onychomycoses [19]. Overall, while the use of OCT in this disorder is still relatively new with questionable specificity, its potential role in the management of onychomycosis is wide-ranging, spanning from diagnosis to therapeutic monitoring.

Subungual Myxoid Cysts

Myxoid cysts (MCs) of digits generally present as firm, translucent nodules arising from the dorsum of the digit and located between the crease of the distal interphalangeal joint and the proximal nail fold. De Berker classified MCs into three subtypes based on the location of the lesions: (a) located on the dorsum of the digit and between the crease of the distal interphalangeal joint and the proximal nail fold, (b) located beneath the proximal nail fold, and (c) extending beneath the nail matrix.

Type B and C create a space-occupying lesion that can affect microvasculature, nail matrix function, and nail shape and integrity. A longitudinal groove in the nail plate can be seen in MCs located distal or beneath the nail fold. Subungual MCs are more difficult to recognize than the more superficial variety, and the characteristic mucoid discharge is rare in this location [20].

OCT imaging of subungual MCs can demonstrate nail changes including cystic lesions beneath the nail (represented by hypointense areas), alteration in blood flow due to local pressure of the space-occupying cystic lesions, and a disorganized nail plate (Figs. 16.7 and 16.8).

Onychomatricoma

Baran and Kint first described onychomatricoma in 1992 [21]. Onychomatricoma is a rare, benign, slow-growing, and painless neoplasm of the nail matrix that clinically presents as a longitudinal whitish or yellowish band (longitudinal leuk-

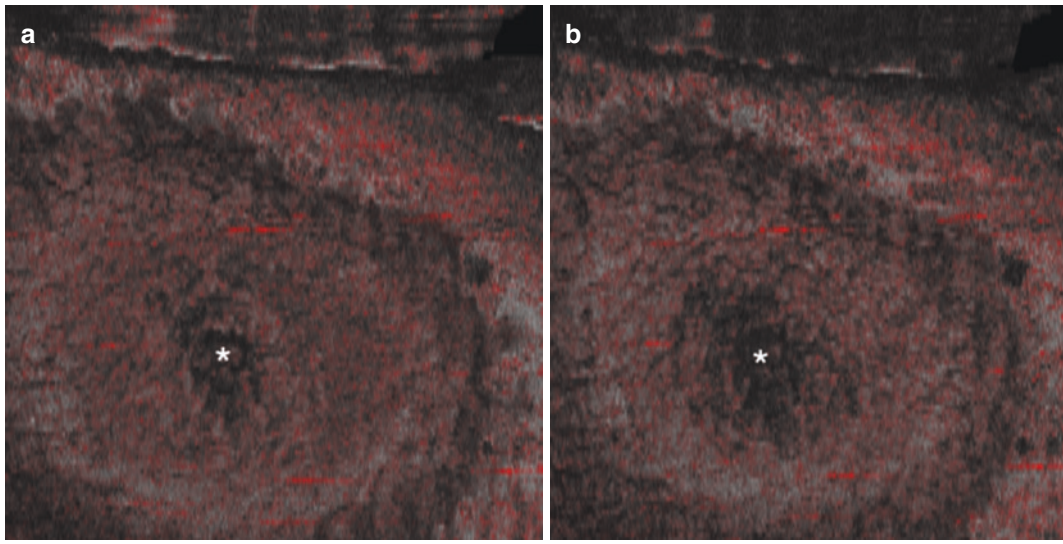

Fig. 16.7 OCT en face view of subungual myxoid cysts: well-circumscribed, oval-shaped soft tissue mass with peripheral rim enhancement, central enhancement, and lack of internal vascularity. Central hypointense area suggests fluid accumulation inside the surrounding tissue at different depths (**a**: 0.25 mm, **b**: 0.30 mm, **c**: 0.35 mm, **d**: 0.40 mm, **e**: 0.45 mm, and **f**: 0.50 mm). (Courtesy of Antonella Tosti, MD, and Ali Rajabi-Estarabadi, MD, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA)

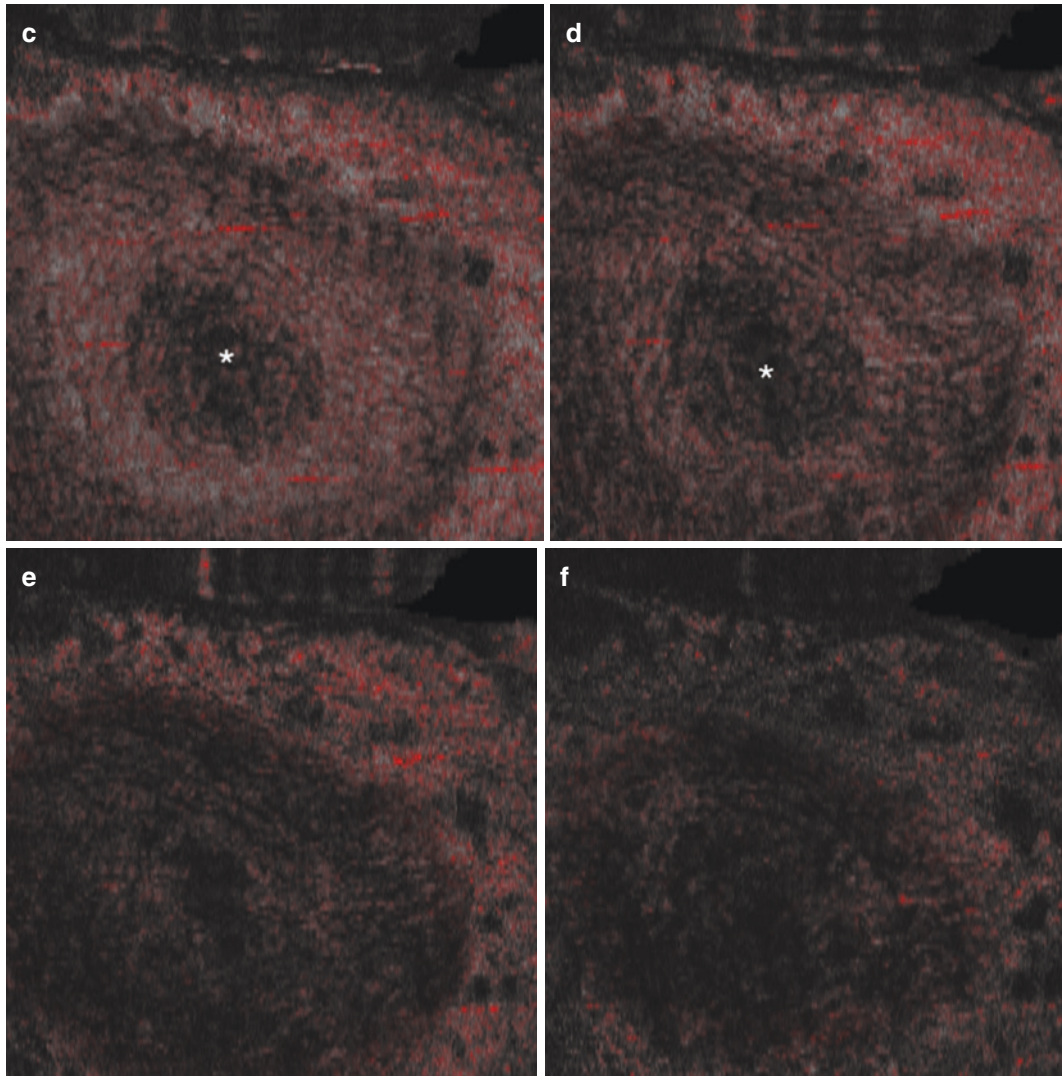

Fig. 16.7 (continued)

onychia or xantonychia) with a thickened nail plate and splinter hemorrhages at the proximal end [22, 23]. Cinotti et al. described OCT features of onychomatricoma in 2018. OCT visualized the tumoral cavities as multiple hypointensive oval-shaped cavities inside the nail plate with curvature of the nail plate [22]. D-OCT also can visualize splinter hemorrhages in the proximal part of the nail (Fig. 16.9).

Glomus Tumor

Glomus tumors are painful, benign perivascular neoplasms of the glomus body. The glomus body is a perivascular temperature-regulating structure consisting of an afferent arteriole, anastomotic vessel, primary collecting vein, intraglomerular reticulum, and a capsular portion. It is located in the stratum reticularis of the

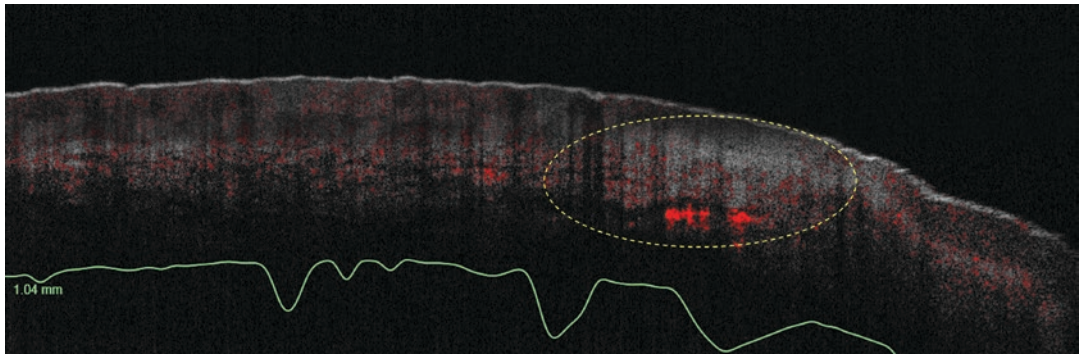

Fig. 16.8 OCT cross-sectional view of subungual myxoid cysts – space-occupying lesion with uniform enhanced density and increased peripheral blood flow. (Courtesy of Antonella Tosti, MD, and Ali Rajabi-Estarabadi, MD, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA)

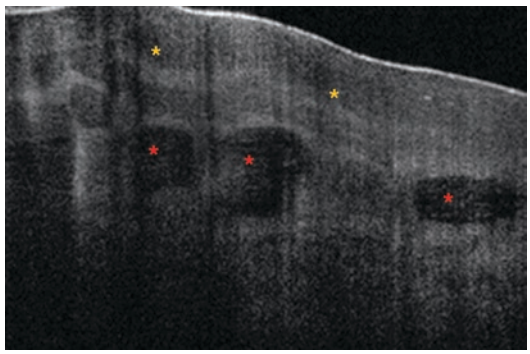

Fig. 16.9 Onychomatricoma: optical coherence tomography of the free edge of a nail shows multiple hypointensive oval-shaped cavities inside the nail plate (red asterisk) with curvature of the nail plate cavities inside the nail plate (yellow asterisk). (Reproduced with permission of [22])

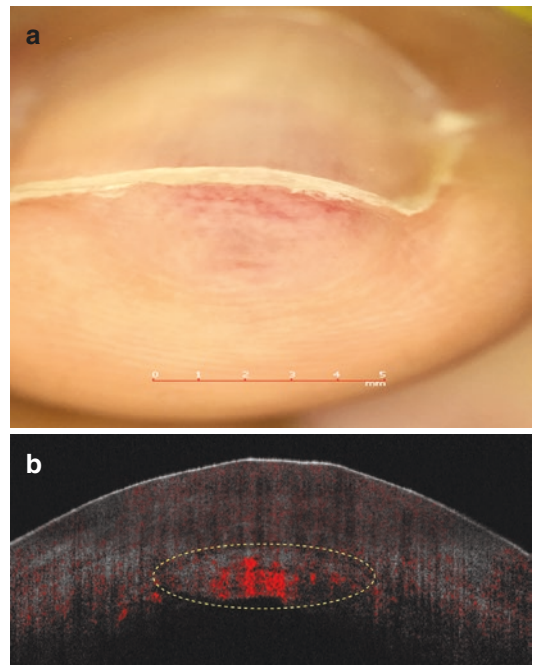

Fig. 16.10 Glomus tumor. (**a**) Dermatoscopy. (**b**) OCT cross-sectional view: vascular oval-shaped mass with a significant increase in blood flow, consistent with the angiomatous subtype of the glomus tumor. (Courtesy of Antonella Tosti, MD, and Ali Rajabi-Estarabadi, MD, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA)

dermis [1]. *Masson* et al. defined four histological types of glomus tumors: (I) an angiomatous form, (II) one with fewer vessels and a larger proportion of Musculoendothelial stroma, (III) one composed largely of nerve fibers, and (IV) a degenerative form showing either edema or hyaline and mucoid changes [24].

D-OCT is well-suited as an outpatient diagnostic imaging modality for glomus tumors and may help distinguish angiomatous subtypes from less vascular tumors (*Masson* subtype 2). In 2019, Rajabi-Estarabadi et al. described the OCT features of glomus tumors. OCT demonstrated destruction of the lunula (by mass effect) and longitudinal ridging. In two cases, dynamic blood flow evaluation revealed a vascular tumor with a significant increase in blood flow, consistent with the angiomatous subtype of the glomus tumor (Fig. 16.10) [1].

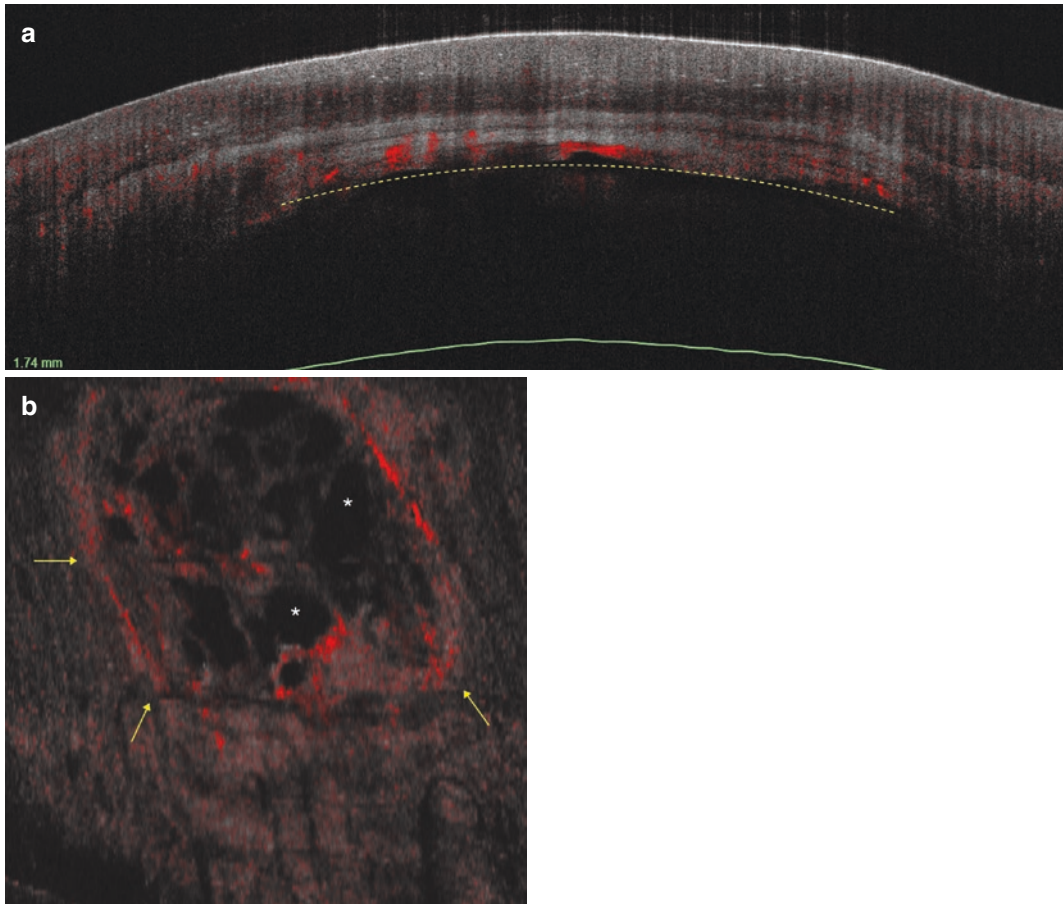

Fig. 16.11 Glomus tumor. (**a**) Cross-sectional view: area of hyperreflective with minimal tumoral core vascularity and increased peripheral vascularity. (**b**) En face view of the same lesion with minimal vascular flow and larger proportion of musculoendothehal stroma, representing Masson histopathological subtype II. (Courtesy of Antonella Tosti, MD, and Ali Rajabi-Estarabadi, MD, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA)

Additionally, it can be presented with ovoid area of hypointensity with minimal tumoral core vascularity and increased peripheral vascularity in OCT imaging which is representing *Masson* histopathological subtype II (Fig. 16.11) [1].

Summary

OCT effectively complements other imaging modalities by visualizing blood flow and providing images with a sufficient depth and a high resolution. OCT enables fast detection of specific vascular features of nail psoriasis and subclinical morphologic nail changes. OCT is a reliable diagnostic method in onychomycosis, even in cases of false-negative KOH preparations and cultures. The use of OCT may be helpful in avoiding multiple biopsies and can measure the therapeutic efficacies in the treatment of several nail disorders such as nail psoriasis and onychomycosis. D-OCT offers distinct advantages in imaging nail diseases and can aid in the differentiation of various subtypes of glomus tumors. Overall, OCT is a remarkable addition to other imaging techniques in dermatology and offers a noninvasive, high-resolution diagnostic approach.

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