

# Noninvasive Imaging Tools in Dermatology

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## PRACTICE POINTS

- There are several new noninvasive imaging tools in dermatology that can be utilized to aid in the diagnosis and management of skin disease, including dermoscopy, reflectance confocal microscopy, and optical coherence tomography.
- Among these tools, there are several differences in cost, clinical integration, reimbursement, and accuracy.

The diagnosis of skin disease relies on visual inspection, often followed by biopsy and histopathologic examination, which remains the gold standard in diagnosis. New imaging tools, including dermoscopy, reflectance confocal microscopy (RCM), and optical coherence tomography (OCT), can provide noninvasive diagnoses while sparing unnecessary biopsies. We discuss dermoscopy, RCM, and OCT, and compare cost, clinical integration, reimbursement, and accuracy of these imaging modalities.

*Cutis.* 2019;104:108-113.

Traditionally, diagnosis of skin disease relies on clinical inspection, often followed by biopsy and histopathologic examination. In recent years, new noninvasive tools have emerged that can aid in clinical diagnosis and reduce the number of unnecessary benign biopsies. Although there has been a surge in noninvasive diagnostic technologies, many tools are still in research and development phases, with few tools widely adopted and used in regular clinical practice. In this article, we discuss the use of dermoscopy, reflectance confocal

microscopy (RCM), and optical coherence tomography (OCT) in the diagnosis and management of skin disease.

## Dermoscopy

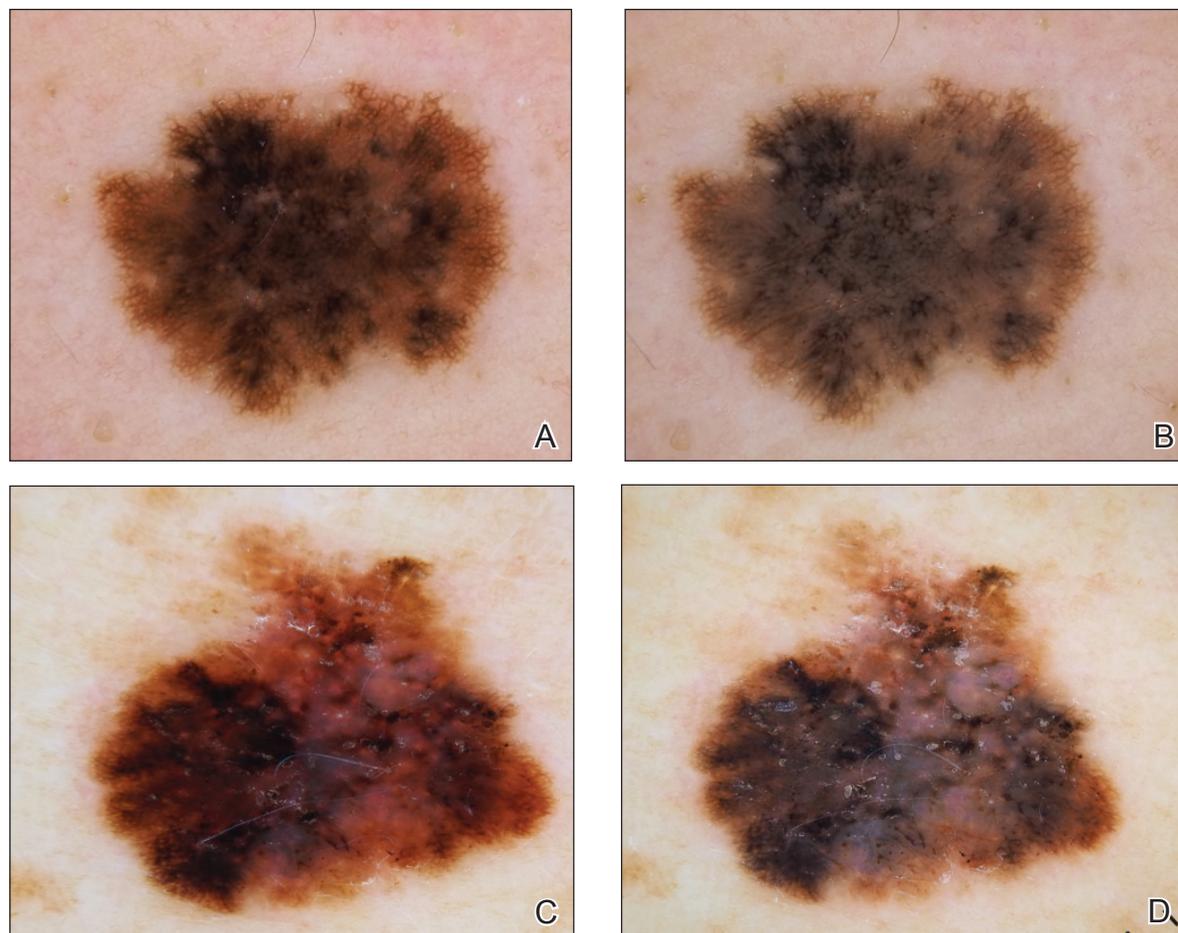
Dermoscopy, also known as epiluminescence light microscopy and previously known as dermatoscopy, utilizes a  $\times 10$  to  $\times 100$  microscope objective with a light source to magnify and visualize structures present below the skin's surface, such as melanin and blood vessels. There are 3 types of dermoscopy: conventional nonpolarized dermoscopy, polarized contact dermoscopy, and nonpolarized contact dermoscopy (Figure 1). Traditional nonpolarized dermoscopy requires a liquid medium and direct contact with the skin, and it relies on light reflection and refraction properties.<sup>1</sup> Cross-polarized light sources allow visualization of deeper structures, either with or without a liquid medium and contact with the skin surface. Although there is overall concurrence among the different types of dermoscopy, subtle differences in the appearance of color, features, and structure are present.<sup>1</sup>

Dermoscopy offers many benefits for dermatologists and other providers. It can be used to aid in the diagnosis of cutaneous neoplasms and other skin diseases. Numerous low-cost dermatoscopes currently are commercially available. The handheld, easily transportable nature of dermatoscopes have resulted in widespread practice integration. Approximately 84% of attending dermatologists in US academic settings reported using dermoscopy, and many refer to the dermatoscope as “the dermatologist’s stethoscope.”<sup>2</sup> In addition, 6% to 15% of other US providers, including family physicians, internal medicine physicians, and plastic surgeons, have reported using dermoscopy in their clinical practices.

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Ms. Srivastava and Dr. Manfredini report no conflict of interest. Dr. Rao serves as a consultant for Caliber ID.

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**FIGURE 1.** A, Melanocytic nevus using nonpolarized contact dermoscopy. B, Melanocytic nevus using polarized contact dermoscopy. C, In situ malignant melanoma using nonpolarized contact dermoscopy. D, In situ malignant melanoma using polarized contact dermoscopy.

Limitations of dermoscopy include visualization of the skin surface only and not deeper structures within the tissue, the need for training for adequate interpretation of dermoscopic images, and lack of reimbursement for dermoscopic examination.<sup>3</sup>

Many dermoscopic structures that correspond well with histopathology have been described. Dermoscopy has a sensitivity of 79% to 96% and specificity of 69% to 99% in the diagnosis of melanoma.<sup>4</sup> There is variable data on the specificity of dermoscopy in the diagnosis of melanoma, with one meta-analysis finding no statistically significant difference in specificity compared to naked eye examination,<sup>5</sup> while other studies report increased specificity and subsequent reduction in biopsy of benign lesions.<sup>6,7</sup> Dermoscopy also can aid in the diagnosis of keratinocytic neoplasms, and dermoscopy also results in a sensitivity of 78.6% to 100% and a specificity of 53.8% to 100% in the diagnosis of basal cell carcinoma (BCC).<sup>8</sup> Limitations of dermoscopy include false-positive diagnoses, commonly seborrheic keratoses and nevi, resulting in unnecessary biopsies, as well as false-negative diagnoses, commonly amelanotic and nevoid melanoma, resulting in delays in skin cancer

diagnosis and resultant poor outcomes.<sup>9</sup> Dermoscopy also is used to aid in the diagnosis of inflammatory and infectious skin diseases, as well as scalp, hair, and nail disorders.<sup>10</sup>

### Reflectance Confocal Microscopy

Reflectance confocal microscopy utilizes an 830-nm laser to capture horizontal en face images of the skin with high resolution. Different structures of the skin have varying indices of refraction: keratin, melanin, and collagen appear bright white, while other components appear dark, generating black-and-white RCM images.<sup>11</sup> Currently, there are 2 reflectance confocal microscopes that are commercially available in the United States. The Vivascope 1500 (Caliber ID) is the traditional model that captures 8×8-mm images, and the Vivascope 3000 (Caliber ID) is a smaller handheld model that captures 0.5×0.5-mm images. The traditional model provides the advantages of higher-resolution images and the ability to capture larger surface areas but is best suited to image flat areas of skin to which a square window can be adhered. The handheld model allows improved contact with the varying topography of skin; does not require an adhesive

window; and can be used to image cartilaginous, mucosal, and sensitive surfaces. However, it can be difficult to correlate individual images captured by the handheld RCM with the location relative to the lesion, as it is exquisitely sensitive to motion and also is operator dependent. Although complex algorithms are under development to stitch individual images to provide better correlation with the geography of the lesion, such programs are not yet widely available.<sup>12</sup>

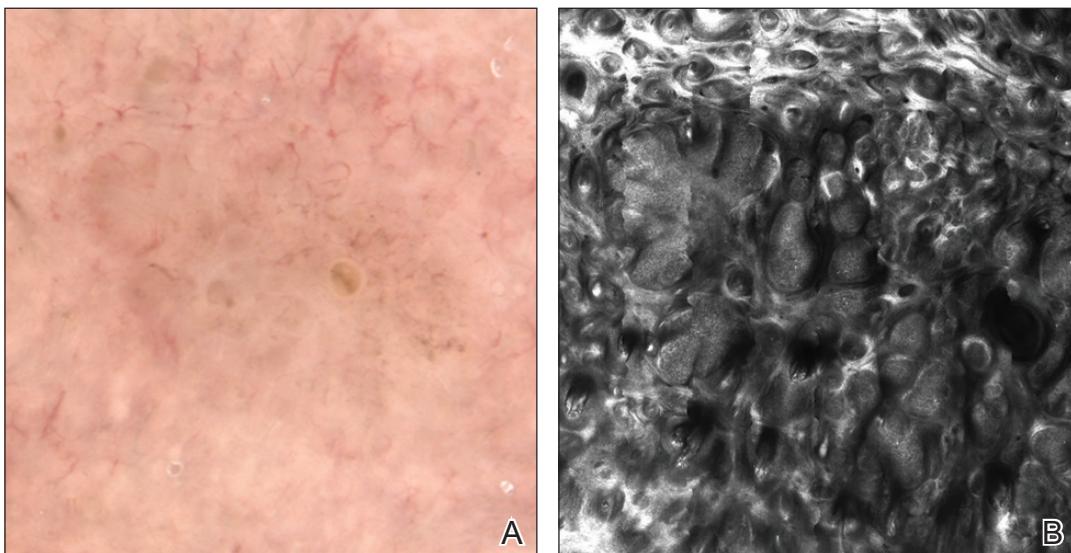
Reflectance confocal microscopy affords many benefits for patients and providers. It is noninvasive and painless and is capable of imaging *in vivo* live skin as compared to clinical examination and dermoscopy, which only allow for visualization of the skin's surface. Reflectance confocal microscopy also is time efficient, as imaging of a single lesion can be completed in 10 to 15 minutes. This technology generates high-resolution images, and RCM diagnosis has consistently demonstrated high sensitivity and specificity when compared to histopathology.<sup>13</sup> Additionally, RCM imaging can spare biopsy and resultant scarring on cosmetically sensitive areas. Recently, RCM imaging of the skin has been granted Category I *Current Procedural Terminology* reimbursement codes that allow provider reimbursement and integration of RCM into daily practice<sup>14</sup>; however, private insurance coverage in the United States is variable. Limitations of RCM include a maximum depth of 200 to 300  $\mu\text{m}$ , high cost to procure a reflectance confocal microscope, and the need for considerable training and practice to accurately interpret grayscale *en face* images.<sup>15</sup>

There has been extensive research regarding the use of RCM in the evaluation of cutaneous neoplasms and other skin diseases. Numerous features and patterns

have been identified and described that correspond with different skin diseases and correspond well with histopathology (Figure 2).<sup>13,16,17</sup> Reflectance confocal microscopy has demonstrated consistently high accuracy in the diagnosis of melanocytic lesions, with a sensitivity of 93% to 100% and a specificity of 75% to 99%.<sup>18-21</sup> Reflectance confocal microscopy is especially useful in the evaluation of clinically or dermoscopically equivocal pigmented lesions due to greater specificity, resulting in a reduction of unnecessary biopsies.<sup>22,23</sup> It also has high accuracy in the diagnosis of keratinocytic neoplasms, with a sensitivity of 82% to 100% and a specificity of 78% to 97% in the diagnosis of BCC,<sup>24</sup> and a sensitivity of 74% to 100% and specificity of 78% to 100% in the diagnosis of squamous cell carcinoma (SCC).<sup>25,26</sup> Evaluation of SCC and actinic keratosis (AK) using RCM may be limited by considerable hyperkeratosis and ulceration. In addition, it can be challenging to differentiate AK and SCC on RCM, and considerable expertise is required to accurately grade cytologic and architectural atypia.<sup>27</sup> However, RCM has been used to discriminate between *in situ* and invasive proliferations.<sup>28</sup> Reflectance confocal microscopy has wide applications in the diagnosis and management of cutaneous infections<sup>29,30</sup> and inflammatory skin diseases.<sup>29,31-33</sup> Recent RCM research explored the use of RCM to identify biopsy sites,<sup>34</sup> delineate presurgical tumor margins,<sup>35,36</sup> and monitor response to noninvasive treatments.<sup>37,38</sup>

### Optical Coherence Tomography

Optical coherence tomography is an imaging modality that utilizes light backscatter from infrared light to produce grayscale cross-sectional or vertical images and horizontal *en face* images.<sup>39</sup> Optical coherence tomography



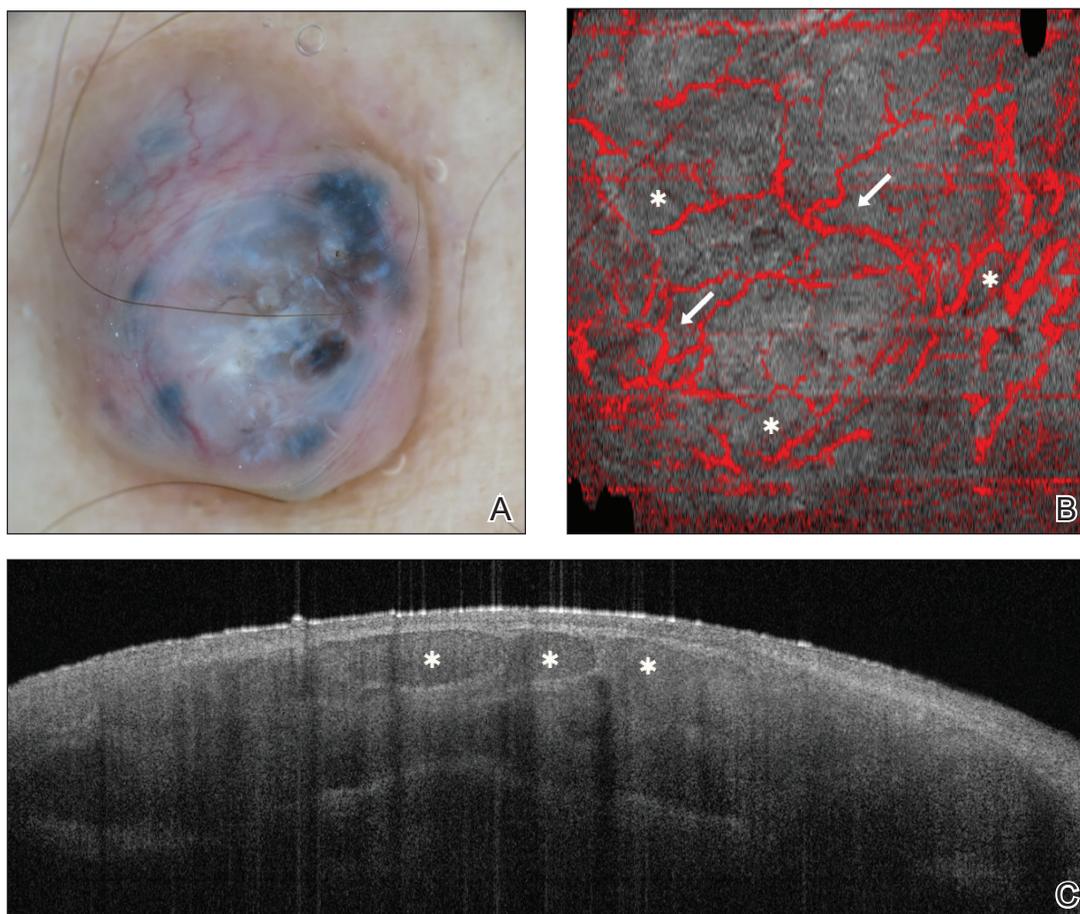
**FIGURE 2.** A, Nonpolarized contact dermoscopy of a suspicious lesion showed prominent vessels, irregular pigmentation, and prominent follicular openings, which are not classic features of basal cell carcinoma. B, A reflectance confocal microscopy mosaic of the same lesion showed well-defined tumor nodules, resulting in a diagnosis of basal cell carcinoma.

can visualize structures in the epidermis, dermoepidermal junction, and upper dermis.<sup>40</sup> It can image boundaries of structures but cannot visualize individual cells.

There are different types of OCT devices available, including frequency-domain OCT (FD-OCT), or conventional OCT, and high-definition OCT (HD-OCT). With FD-OCT, images are captured at a maximum depth of 1 to 2 mm but with limited resolution. High-definition OCT has superior resolution compared to FD-OCT but is restricted to a shallower depth of 750  $\mu\text{m}$ .<sup>39</sup> The main advantage of OCT is the ability to noninvasively image live tissue and visualize 2- to 5-times greater depth as compared to RCM. Several OCT devices have obtained US Food and Drug Administration approval; however, OCT has not been widely adopted into clinical practice and is available only in tertiary academic centers. Additionally, OCT imaging in dermatology is rarely reimbursed. Other limitations of OCT include poor resolution of images, high cost to procure an OCT device, and the need for advanced training and experience to accurately interpret images.<sup>40,41</sup>

Optical coherence tomography primarily is used to diagnose cutaneous neoplasms. The best evidence of the diagnostic accuracy of OCT is in the setting of BCC, with a recent systematic review reporting a sensitivity of 66% to 96% and a specificity of 75% to 86% for conventional FD-OCT.<sup>42</sup> The use of FD-OCT results in an increase in specificity without a significant change in sensitivity when compared to dermoscopy in the diagnosis of BCC.<sup>43</sup> Melanoma is difficult to diagnose via FD-OCT, as the visualization of architectural features often is limited by poor resolution.<sup>44</sup> A study of HD-OCT in the diagnosis of melanoma with a limited sample size reported a sensitivity of 74% to 80% and a specificity of 92% to 93%.<sup>45</sup> Similarly, a study of HD-OCT used in the diagnosis of AK and SCC revealed a sensitivity and specificity of 81.6% and 92.6%, respectively, for AK and 93.8% and 98.9%, respectively, for SCC.<sup>46</sup>

Numerous algorithms and scoring systems have been developed to further explore the utility of OCT in the diagnosis of cutaneous neoplasms.<sup>47,48</sup> Recent research



**FIGURE 3.** A, A nonpolarized contact dermoscopy image of a nodular pigmented basal cell carcinoma showed large blue-gray ovoid nests, arborizing vessels, and small fine telangiectases. B, A microvascular en face dynamic optical coherence tomography image (size, 6×6 mm; depth, 300  $\mu\text{m}$ ) of the same lesion revealed circumscribed areas (asterisks) and branching/arborizing vessels (arrows). C, A cross-sectional optical coherence tomography image of the same lesion showed ovoid structures (asterisks) corresponding with tumor nests with dark peripheral borders and thinning of the epidermis above them.

investigated the utility of dynamic OCT, which can evaluate microvasculature in the diagnosis of cutaneous neoplasms (Figure 3)<sup>49</sup>; the combination of OCT with other imaging modalities<sup>50,51</sup>; the use of OCT to delineate presurgical margins<sup>52,53</sup>; and the role of OCT in the diagnosis and monitoring of inflammatory and infectious skin diseases.<sup>54,55</sup>

## Final Thoughts

In recent years, there has been a surge of interest in non-invasive techniques for diagnosis and management of skin diseases; however, noninvasive tools exist on a spectrum in dermatology. Dermoscopy provides low-cost imaging of the skin's surface and has been widely adopted by dermatologists and other providers to aid in clinical diagnosis. Reflectance confocal microscopy provides reimbursable in vivo imaging of live tissue with cellular-level resolution but is limited by depth, cost, and need for advanced training; thus, RCM has only been adopted in some clinical practices. Optical coherence tomography offers in vivo imaging of live tissue with substantial depth but poor resolution, high cost, need for advanced training, and rare reimbursement for providers. Future directions include combination of complementary imaging modalities, increased clinical practice integration, and education and reimbursement for providers.

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