Optical Diagnostic Devices for Evaluating Skin Lesions Suspected of Malignancy

Description

There is interest in non-invasive devices that will improve the diagnosis of malignant skin lesions. One technique is dermatoscopy (dermoscopy, epiluminescence microscopy, in vivo cutaneous microscopy), which enables the clinician to perform direct microscopic examination of diagnostic features in pigmented skin lesions. Another approach is the use of computer-based light imaging systems. These techniques have the potential to improve diagnostic accuracy for suspicious skin lesions and may increase the detection rate of malignant skin lesions and/or reduce the rate of unnecessary biopsies.

Background

Dermatoscopy

Dermatoscopy, also known as dermoscopy, describes a family of noninvasive techniques that allow in vivo microscopic examination of skin lesions. It is intended to help distinguish between benign and malignant pigmented skin lesions. The technique involves application of immersion oil to the skin, which eliminates light reflection from the skin surface and renders the stratum corneum more transparent. Using a magnifying lens, the structures of the epidermis and epidermal-dermal junction can then be visualized. A handheld or stereomicroscope may also be used for direct visual examination. Digitization of images, typically after initial visual assessment, permits storage and facilitates their retrieval, is often used for comparison purposes if a lesion is being followed over time.

A variety of dermatoscopic features have been identified that are suggestive of malignancy, including pseudopods, radial streaming, the pattern of the pigment network, and black dots. These features in combination with other standard assessment criteria of pigmented lesions, such as asymmetry; borders; and color, have been organized into algorithms to enhance the differential diagnosis of pigmented skin lesions. Dermatoscopic images may be assessed by direct visual examination or by review of standard or digitized photographs. Digitization of images, either surface or dermatoscopic images, may permit qualitative image enhancement for better visual perception and discrimination of certain features, or actual computer-assisted diagnosis.
Interpretation of dermatoscopy findings have evolved over time. Initially, lesions were evaluated using pattern analysis. More recently several algorithms were developed, including the asymmetry, border, color and dermatoscopic structures (ABCD) rule of dermatoscopy, the 3-point and 7-point checklists of dermatoscopy by Argenziano, the Menzies method, and the CASH algorithm.\textsuperscript{1} There remains a lack of consensus in the literature regarding the optimal dermatoscopic criteria for malignancy.

Dermatoscopy is also proposed in the serial assessment of lesions over time and for defining peripheral margins prior to surgical excision of skin tumors.

### Computer-based optical diagnostic devices

A U.S. Food and Drug Administration (FDA)-approved multispectral digital skin lesion analysis (MSDSLA) device uses a handheld scanner to shine visible light on the suspicious lesion. The light is of 10 wavelengths, varying from blue (430 nm) and near infrared (950 nm). The light can penetrate up to 2.5 mm under the surface of the skin. The data acquired by the scanner are analyzed by a data processor; the characteristics of each lesion are evaluated using proprietary computer algorithms. Lesions are classified as positive (i.e., high degree of morphologic disorganization) or negative (i.e., low degree of morphologic disorganization) according to the algorithms. Positive lesions are recommended for biopsy. For negative lesions, other clinical factors are considered in the decision of whether or not to refer to biopsy. The FDA-approved system (see additional details in the Regulatory Status section) is intended only for suspicious pigmented lesions on intact skin and for use only by trained dermatologists.

### Regulatory Status

Dermatoscopic devices with 501 K clearance by the U.S. Food and Drug Administration (FDA) include:

- **Episcope™** (Welch Allyn, Inc., Skaneateles Falls, NY) approved in 1995, intended use is to illuminate body surfaces and cavities during medical examination.
- **Nevoscope™** (TRANSLITE, Sugar Land, TX) approved in 1996, intended use is to view skin lesions by either illumination or transillumination.
- **Dermascope™** (American Diagnostic Corp., Hauppauge, NY) approved in 1999, intended use is to enlarge images for medical purposes.
- **MoleMax™** (Derma Instruments, Austria) approved in 1999, intended use is to enlarge images for medical purposes.

One computer-based optical imaging device has PMA approval by the FDA:

MelaFind (MelaSciences, Inc. Irvington, NY) was approved in November 2011. Its intended use is to evaluate pigmented lesions with clinical or histological characteristics suggestive of melanoma. It is not intended for lesions with a diagnosis of melanoma or likely melanoma. MelaFind is intended for use only by physicians trained in the clinical diagnosis and management of skin cancer (i.e., dermatologists) and only those who have additionally successfully completed training on the MelaFind device. FDA documents further note:
“MelaFind is indicated only for use on lesions with a diameter between 2 mm and 22 mm, lesions that are accessible by the MelaFind imager, lesions that are sufficiently pigmented (i.e., not for use on non-pigmented or skin-colored lesions), lesions that do not contain a scar or fibrosis consistent with previous trauma, lesions where the skin is intact (i.e., non-ulcerated or non-bleeding lesions), lesions greater than 1 cm away from the eye, lesions which do not contain foreign matter, and lesions not on special anatomic sites (i.e., not for use on acral, palmar, plantar, mucosal, or subungual areas). MelaFind is not designed to detect pigmented non-melanoma skin cancers, so the dermatologist should rely on clinical experience to diagnose such lesions.”

Related Policies
None

Policy
*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Dermatoscopy, using either direct inspection, digitization of images, or computer-assisted analysis, is considered **not medically necessary** as a technique to evaluate or serially monitor pigmented skin lesions.

Computer-based optical imaging devices e.g., multispectral digital skin lesion analysis, are considered **not medically necessary** as a technique to evaluate or serially monitor pigmented skin lesions.

Dermatoscopy and computer-based optical imaging devices are considered **not medically necessary** for defining peripheral margins of skin lesions suspected of malignancy prior to surgical excision.

Rationale
As with any diagnostic tool, assessment of dermatoscopy involves a determination of its sensitivity, specificity, and positive and negative predictive values in different populations compared to a gold standard and whether the results of the diagnostic tests are ultimately used to benefit health outcomes. The gold standard for evaluation of pigmented skin lesions is excision with histologic diagnosis, in which, depending on the skill of the pathologist, sensitivity and specificity are considered near 100%. The relevant health outcome is early diagnosis of a malignancy. Clinically, dermatoscopy is used in combination with clinical assessment, either based on direct visual inspection or review of photographs. Therefore, the diagnostic performance of dermatoscopy combined with clinical assessment must be compared with clinical assessment alone and then compared to the gold standard of histology. There are 4 general clinical situations in which dermatoscopy may be of benefit:

1. When patients present with a lesion with a low pretest possibility of malignancy, dermatoscopy could potentially be used to determine which lesions do not require excision, i.e., a deselection process. In this clinical situation, the negative predictive value of dermatoscopy is the most relevant diagnostic parameter.

2. Some patients may present with multiple suspicious pigmented skin lesions such that excision of all or even some of them is not possible. In this clinical situation, a determination must be
made which of the lesions is most clinically suspicious and requires excision. In this setting, the positive predictive value of dermatoscopy is the most relevant diagnostic parameter.

3. Serial assessment of lesions over time, as a technique to prompt excision when a lesion changes shape or color, is commonly performed in patients with multiple pigmented lesions or for lesions in locations difficult to excise. Serial conventional and digital photography has been used for this purpose. Both the positive and negative predictive values of results are relevant.

4. Use in defining peripheral borders of basal cell or squamous cell cancers to guide surgery. If dermatoscopy combined with clinical assessment is more accurate than clinical assessment alone in defining tumor borders, then it might be possible to excise the tumor with a narrower margin, thus preserving a larger amount of normal skin.

**Literature Review**

The following is a summary of the key literature to date:

**Dermatoscopy**

Dermatoscopy for selecting or de-selecting lesions for excision

*Does dermatoscopy improve upon naked eye examination of lesions?*

A number of studies have reported on the diagnostic accuracy of dermatoscopy compared with clinical assessment, with histologic examination serving as the reference standard, and several meta-analyses have been published. In 2008, Vestergaard et al reviewed the literature on the accuracy of dermatoscopy for the diagnosis of melanoma compared with naked eye examination.2 Nine studies met the inclusion criteria; 2 were randomized controlled trials (RCTs) and the other 7 used a cross-sectional design. All of them were performed in an expert setting. There was variability across the studies in the following study characteristics: patient and lesion selections, naked eye criteria for melanoma, dermatoscopy criteria for melanoma, and follow-up. Hierarchical summary receiver operator curve (ROC) analysis was used to estimate the relative diagnostic accuracy for clinical examination with, and without, the use of dermatoscopy. The pooled relative diagnostic odds ratio (OR) for melanoma, for dermatoscopy compared with naked eye examination, was found to be 15.6 (range, 2.9-83.7). The removal of two small outlier studies changed this to 9.0 (range, 1.5-54.6) but the odds of identifying melanoma remained higher with dermatoscopy. The authors concluded that dermatoscopy is more accurate than naked eye examination for the diagnosis of cutaneous melanoma in suspicious skin lesions when performed in the clinical setting.

A 2009 meta-analysis by Rajpara et al reviewed studies on dermatoscopy using a handheld dermatoscope, as well as studies on digital dermatoscopy with computer-aided diagnosis (CAD).3 (The latter technique was called artificial intelligence in the article). The studies could be prospective or retrospective, evaluated dermatoscopy performed by experts, and used histology of excised lesions as the reference standard. Studies were not required to compare dermatoscopy with naked eye examination; thus, the study was not able to compare the diagnostic accuracy of dermatoscopy or digital dermatoscopy with CAD to clinical examination. The investigators identified 30 studies; all but
one (which was conducted in Iran) were studies from Europe. A total of 9784 melanoma lesions were included in the review; of these, 8045 were analyzed by dermatoscopy and 2420 by computer-aided diagnosis. The investigators conducted pooled analyses of studies, grouping them by the type of algorithm used for diagnosis (eg, pattern analysis, asymmetry, border, color, dermatoscopic structures [ABCD] rule). The pooled sensitivity for dermatoscopy (30 analyses) was 0.88 (95% confidence interval [CI], 0.87 to 0.89), and the pooled specificity was 0.86 (95% CI, 0.85 to 0.86). For digital dermatoscopy with CAD, the pooled sensitivity was (12 analyses) 0.91 (95% CI, 0.88 to 0.93), and the pooled specificity was 0.79 (95% CI, 0.77 to 0.81). The pooled specificity of the CAD diagnosis was significantly lower than the dermatoscopy analysis; pooled sensitivities did not differ significantly. There were no significant differences in overall diagnostic performance of different algorithms. The authors noted that, whereas dermatoscopy has been used by trained clinicians in a practice setting, CAD has only been used in experimental settings using preselected lesions.

A representative review of recent studies follows.

In 2014, Unlu et al published a comparison of dermatoscopic diagnostic algorithms and clinical assessment using histological diagnosis as the reference standard. (4) The study included 115 images of suspicious lesions. Three experienced dermatoscopists classified each of the lesions, in random order, as benign or malignant according to each of four algorithms. These were the ABCD rule, the 7-point checklist, 3-point checklist, and the CASH algorithm. The history and macroscopic images of the lesions were not provided to the dermatoscopists to avoid recall bias. According to histopathologic criteria, 24 lesions (20.9%) were classified as melanomas. A total of 18 (75%) of melanomas were correctly classified by clinical examination. In comparison, 22 (92%) of malignant lesions were correctly classified by the ABCD rule of dermatoscopy, 21 (88%) by the 7-point checklist, 19 (79%) by the 3-point checklist, and 22 (92%) by the color, architecture, symmetry, homogeneity (CASH) algorithm. All melanomas with a Breslow thickness of at least 0.75 mm were diagnosed correctly by the ABCD rule and the CASH algorithm. Overall, clinical examination had a sensitivity of 75% and specificity of 57%. The sensitivity and specificity of the dermatoscopic algorithms were 91.6% and 60.4% for the ABCD rule, 87.5% and 65.9% for the 7-point checklist, 79.1% and 62.6% for the 3-point checklist and 91.6% and 64.8% for the CASH algorithm.

In 2011, De Giorgi et al in Italy randomly selected 8 dermatologists who had attended a basic dermatoscopy course 6 months previously; none had extensive experience using dermatoscopy. (5) Each dermatologist was asked to examine separately clinical images only and then a combination of clinical images and dermatoscopic images of 200 melanocytic skin lesions (mean diameter <8.00 mm). All lesions had been histopathologically reviewed by a pathologist. Clinical images had been obtained with a digital camera, and dermatoscopy pictures were obtained using a dermatoscope. The dermatologists were asked to determine whether or not they thought the sample was a melanoma lesion (yes/no). Histopathologic diagnosis was used as the reference standard. The mean sensitivity was significantly increased when the clinician reviewed dermatoscopic images in addition to clinical images; specificity did not significantly change. The mean sensitivity and specificity of melanoma diagnosis using clinical image examination alone was 71.2% and 80.2%, respectively, and using the combined examination was 84.1% and 80.2%, respectively. The authors pointed out, unlike actual clinical practice, dermatologists were not given information about the lesion history and were not able to
examine other lesions from the same patient. In addition, while reviewing the dermatoscopy images, the dermatologists were also reviewing the clinical images for the second time.

A 2011 study by Rosendahl et al analyzed a consecutive series of 463 pigmented lesions from a single center in Australia. (6) All lesions had been photographed, and dermatoscopic images had been taken prior to excision. Histopathology was used as the diagnostic reference standard. Lesions were categorized as benign or malignant; the latter category consisted of melanomas, basal cell carcinomas, and squamous cell carcinomas. The process of analysis consisted of presenting two clinical images of each lesion (overview and close-up) to a blinded reviewer who then made a diagnosis. The reviewer was then shown the dermatoscopic image and asked to give another diagnosis. Histopathologically, 246 of 463 (53.1%) of the lesions were melanocytic, and a total of 138 (30%) lesions were malignant. The reviewer’s diagnosis matched the histopathologic diagnosis in 320 (69.1%) of cases using clinical images alone and in 375 (80.1%) of cases using clinical images and dermatoscopic images. At a fixed specificity of 80%, the sensitivity was 70.5% without dermatoscopic images and 82.6% with dermatoscopic images. ROC curve (AUC) analysis was also done to evaluate diagnostic accuracy. The AUC was significantly higher with dermatoscopy, 0.89, than without dermatoscopy, 0.83 (p<0.001). When melanocytic and nonmelanocytic lesions were examined separately, the difference in the AUC with and without dermatoscopy was statistically significant only for the melanocytic lesions (0.91 and 0.84, respectively, p<0.001).

A 2007 study by Annessi et al compared dermatoscopy using three algorithmic methods with clinical diagnosis in 198 consecutive atypical macular melanocytic lesions. (7) Compared with the reference standard of histopathologic diagnosis, dermatoscopy with pattern analysis and the ABCD method had similar sensitivity (85% vs 84%, respectively). Specificity (79% vs 75%, respectively) and PPV (80% and 76%, respectively) were modestly higher for pattern analysis. Results with the 7-point checklist were sensitivity of 78% and specificity of 65%.

Section Summary

Recent meta-analyses found that overall; the diagnostic accuracy of dermatoscopy was higher than clinical assessment/naked eye examination. However, most studies are retrospective, reported on the performance of clinicians who have extensive experience with dermatoscopic imaging and were conducted outside of the United States. There is a lack of consensus about a standard approach to evaluating dermatoscopic images, although a 2009 meta-analysis and a 2014 study found that several approaches might have similar diagnostic accuracy.

**Does dermatoscopy lead to changes in patient management or improve the net health outcome compared with standard practice?**

Several prospective comparative studies have evaluated the impact of dermatoscopy on patient management. In 2004, Carli et al published an RCT that included 913 consecutive patients referred to a pigmented lesion clinic in Italy for evaluation of skin lesions. (8) A total of 302 participants were randomized to standard naked eye examination and 311 to naked eye examination with the possibility of dermatoscopy at the clinician’s discretion. In both of these groups, there was mandatory excision of equivocal lesions. (A third study arm involved the option of digital follow-up without immediate excision).
Examinations were done by experienced dermatologists with expertise in dermatoscopy. In the comparison between naked eye examination alone and naked eye examination with dermatoscopy, a significantly higher proportion of patients in the naked eye examination only group were referred for excision compared with the group that included dermatoscopy (15.6% and 9.0%, respectively; p=0.013). Histologic analysis of excised lesions identified three melanomas in the naked eye examination only group and two in the combined examination group. The number of melanomas was too small for a between-group statistical comparison of diagnostic accuracy.

An RCT by Argenziano et al was published in 2006. (9) The trial addressed whether dermatoscopy improves the accuracy of primary care physicians in triaging lesions suggestive of malignancy. A total of 73 primary care physicians underwent a 1-day training course in dermatoscopy and were randomized to conduct examinations using naked eye examination only or naked eye examination plus dermatoscopy. Following the primary care evaluation, patients were re-evaluated by dermatologists who were expert in melanoma and all lesions considered suggestive of skin cancer were excised. Over a 16-month period, 1345 patients were evaluated using naked eye examination and 1197 also underwent dermatoscopy. The primary study outcome was referral accuracy. Physicians in both groups referred a similar proportion of patients to a specialty clinic, 30.3% in the naked eye only group and 31.5% in the dermatoscopy group, p=0.787. In their re-examinations, dermatologists considered 6.3% of lesions in the naked eye only group and 6.4% in the dermatoscopy group to be suspicious for skin cancer. The PPV of the primary care physicians’ recommendations was low in both groups, 11.3% in the naked eye only group and 16.1% in the dermatoscopy group. However, the NPV, the more clinically relevant outcome in this situation, was relatively high in both groups and was significantly higher in the dermatoscopy group than the naked eye only group, 98.1% versus 95.8%, p=0.004. Thus, in the group of primary care physicians using dermatoscopy, there was a low risk (1.9%) that patients with lesions suggestive of melanoma would not be referred for further evaluation.

In addition, the 2011 study by De Giorgi et al, previously described, addressed the issue of whether dermatoscopy leads to improved patient management.(5) The study asked dermatologists to decide whether or not they would recommend excision of lesions based on clinical images only and based on a combination of clinical images and dermatoscopic images. Dermatologists were told to simulate their practice setting and to attempt to minimize the number of negative lesions. Sensitivity and specificity were calculated based on whether any melanoma lesions would remain unexcised, with histopathologic findings as the reference standard. The mean sensitivity and specificity of the decision to excise using clinical image examination alone was 94.1% and 36.1%, respectively, and using the combined examination was 98.6% and 31.5%, respectively. The sensitivity was significantly high when dermatologic images were available in addition to clinical images (p<0.003).

Section Summary

Several studies, including two RCTs, have evaluated the impact of dermatoscopy on patient management. One RCT found a significantly lower rate of excision recommendations when dermatologists had access to dermatoscopy compared with naked eye examination alone. Another RCT found that primary care physicians did not refer fewer patients to specialists when used dermatoscopy in addition to naked eye examination but the NPV, a clinically relevant outcome, was significantly higher with dermatoscopy.
Dermatoscopy for evaluation of multiple suspicious pigmented lesions

No studies were found that specifically addressed the issue of dermatoscopy with patients who have multiple suspicious pigmented lesions to determine which lesions are most clinically suspicious and therefore require excision.

Dermatoscopy for serial assessments of lesions

Does serial assessment of lesions using dermatoscopy lead to improved patient management or improve the net health outcome compared to standard practice?

No prospective comparative studies were identified that compared outcomes after managing patients over time with and without dermatoscopy. A meta-analysis of data from non-comparative studies was published in 2013 by Salerni and colleagues. (10) The authors identified 14 studies performed in a clinical setting. The studies included 5,787 patients with a total of 52,739 lesions that were monitored using dermatoscopy (mean of 12 lesions per patient). Patients were followed for a mean of 30 months. During follow-up, the percentage of lesions excised per study ranged from 1.3% to 18.7%. A total of 4,388 lesions were excised (8.3%). There were 383 melanomas detected (<1% of lesions that were being followed). Of the melanomas detected, 209 (55%) were in situ and 174 (45%) were invasive. The meta-analysis did not evaluate data on dermatoscopy compared to another technique for monitoring patients.

One study, published in 2009 by Menzies and colleagues, compared an initial patient management decision with naked eye evaluation or dermatoscopy and then followed patients over time with short-term sequential digital dermatoscopy imaging (SDDI) (i.e., every 3 months). (11) The study was conducted in a general practice setting in Australia. Participating physicians were trained in the use of dermatoscopy with SDDI by means of a 2-hour workshop and online training. Seventy-four physicians completed the training, and 63 of these (85%) then assessed 374 lesions (median of 6 lesions per physician). Based on clinical assessment with the naked eye alone, all 374 lesions were assessed as requiring excision or referral. With dermatoscopy, lesions were triaged to 3 groups: 110 received immediate referral or excision, 192 were assigned to close follow-up with SDDI, and 72 were assigned to observation for change. The 192 SDDI lesions were re-evaluated 3 months later. At that time, 46 lesions were referred/excised, six were triaged to continue SDDI, and 140 were triaged to standard observation. At the third visit (a total of 6 months from the initial visit), referral/excision was recommended for 2 of the 6 SDDI lesions, and the other 4 returned to standard care. In addition, 5 of the lesions previously recommended for observation were triaged to referral/excision. Thus, in this group of 374 lesions that would all have been recommended for referral/excision with clinical examination alone, the combined dermatoscopy and SDDI intervention reduced the number of referrals/excisions by about half, to 163 (44%) of lesions. However, it is not known how many of the patients triaged to referral or excision would ultimately have had a biopsy.

Dermatoscopy for defining peripheral margins of cancerous skin lesions prior to surgery

Does dermatoscopy for defining peripheral margins lead to improved patient management or improve the net health outcome compared with standard of practice?
One RCT was identified that compared dermatoscopy to other methods of defining peripheral margins. (12) This was a 2013 trial published by Asilian and Momeni in which 60 patients with basal cell carcinoma (BCC) in the head and neck area were randomized to naked eye examination (n=20), dermoscopy (n=20) or curettage (n=20) to determine the extent of tumor extension prior to Mohs micrographic surgery. In all patients, a 3mm border was initially resected after the tumor margin was determined. If resection was found to be incomplete, patients received additional stages of Mohs surgery. The mean number of Mohs surgery resection stages, the study’s primary outcome, was 1.90 (SD: 0.55) in the curettage group, 1.55 (SD: 0.51) in the visual inspection group and 1.65 (SD: 0.49) in the dermoscopy group. The difference between groups was not statistically significant, p=0.10. Health outcomes such as rates of recurrence or mortality rates were not reported.

A prospective non-randomized study was published by Suzuki et al in 2014. (13) The study included 44 patients with melanoma and indications for Mohs micrographic surgery. All patients were assessed with naked eye examination and had surgical margins demarcated in a blue or black marker. The first 21 patients referred for surgery received only this naked eye examination and the remaining 223 patients were also assessed using dermatoscopy (margins drawn in red marker). Outcomes did not differ significantly in the 2 groups eg; Mohs surgery required a similar number of stages.

Several studies conducted in Italy have evaluated dermatoscopy used to define peripheral borders of skin tumors to guide surgical excision. All were non-randomized comparisons between clinical and dermatoscopic evaluation of suspected tumor margins. Most recently in 2012, Carducci and colleagues evaluated outcomes in 94 patients with a suspected clinical diagnosis of squamous cell carcinoma (SCC). (14) Prior to surgery, margins in 46 patients were determined by clinical evaluation and margins in 48 patients were determined with digital dermatoscopy. A lateral margin of 4-6 mm was chosen for SCC not located on the scalp, ears, eyelids, nose, or lips. For lesions in those areas, margins of 6-10 mm were used. In the dermatoscopy group, clinical margins were first defined and outlined with a dermatographic pencil. Then, dermatoscopy was performed, and the margins were redefined if pictures found that the margins were too near the pencil line. Histologic analysis of specimens was the reference standard. In the clinical evaluation group, 8 of 46 (17%) specimens showed incomplete margin excision compared to 3 of 48 (6%) in the digital dermatoscopy group. The difference between groups was statistically significant, p=0.015. The study was not randomized; the clinical evaluation group included patients who were evaluated before the introduction of digital dermatoscopy in that medical center.

In 2011 the Carducci research group published a similar study in patients with a suspected diagnosis of basal cell carcinoma of the head or neck. (15) A total of 84 patients were included who were referred for surgical excision and had a suspected diagnosis of basal cell carcinoma of the head or neck. Lesions were examined either clinically or with digital dermatoscopy to determine margins. Surgical excision was undertaken with a 3-mm surgical margin. Margin involvement was found in 8 of 40 (20%) histologic specimens excised after clinical evaluation and 3 of 44 (7%) specimens excised after dermatoscopic detection of margins; this difference was statistically significant, p<0.007. Seven of the 11 (64%) specimens found to have margin involvement were nodular basal cell carcinomas. Neither of the Carducci studies followed patients after surgical excision and reported health outcomes. Both of these studies used a digital Videocap dermatoscope which has not been cleared for use in the United States.
In 2010 by Caresana and Giardini that included 200 consecutive patients with basal cell carcinoma. (16) In the study, 2-mm excision margins were used. The margins were first marked using naked eye only, and then the borders were confirmed using dermatoscopy. (The type of device used in the study was not specified.) There was concordance in the peripheral margins drawn using the naked eye and dermatoscopy in 131 of 200 (66%) cases. In 69 cases, there was a larger margin with dermatoscopy, but this did not exceed 1 mm more than the clinical measurement in 55 (80%) of the 69 cases. According to histologic analysis, surgical excision using the 2-mm margin was found to be adequate in 197 of the 200 cases. After 10-30 months of follow-up, none of the 200 treated cases had signs or symptoms of recurrence. Because surgery was performed using the margins drawn with dermatoscopy in all cases, the study could not compare margins drawn using naked eye (clinical) assessment plus dermatoscopy to clinical assessment alone.

Section summary: There was been only 1 published RCT comparing margins drawn with and without the aid of dermatoscopy, and this study does not report superior outcomes using dermatoscopy compared to visual inspection or curettage. This RCT and other available published studies provide limited information on health outcomes. The published studies are all conducted outside of the United States and at least 2 did not use FDA-approved devices.

**Computer-based optical diagnostic device**

**Selecting or de-selecting lesions for excision**

*Does a computer-based optical diagnostic device improve upon naked eye examination of lesions?*

One published prospective study was identified that evaluated the diagnostic performance of MelaFind, an FDA-approved computer-based optical diagnostic device. This industry-sponsored study was published in 2011 by Monheit and colleagues, and included the data submitted to the FDA in the application for approval of the device. (17) The study included patients with at least 1 pigmented lesion scheduled for first-time biopsy. Lesions were between 2mm and 22mm in diameter. The following were exclusion criteria: the anatomic site was not accessible to the device, the lesion was not intact (e.g., open sores, ulcers or bleeding); the lesion was on a palmar, plantar or mucosal surface or under nails; the lesion was in an area of visible scarring and the lesion contained tattoo ink, splinter or other foreign matter. In addition, lesions with a pre-biopsy diagnosis of melanoma were excluded from the analysis. Histologic diagnosis was used as the reference standard.

A total of 1,393 patients with 1,831 lesions were enrolled in the study. Of the 1821 lesions, 1632 (90%) were eligible and evaluable. There were 165 lesions not evaluable by MelaFind due to reasons such as operator error and camera malfunction, and others were found to be ineligible post-enrollment due to factors such as scarring. Histological analysis determined that 127 of 1632 lesions (7.8%) were melanoma. The sensitivity of MelaFind for recommending biopsy of melanomas was 98.2% (125 of 127 melanomas) with a lower 95% CI bound of 95.6%. The average specificity (averaged over clinicians) of MelaFind for melanoma was 9.5%. The accuracy of clinician diagnosis was determined by randomly selecting 25 melanoma cases and matching them with 25 non-melanoma lesions. Clinicians were asked to classify the lesions into categories of melanoma, cannot rule out melanoma, or not melanoma. The specificity of clinician diagnosis, as determined by the proportion of melanomas among the total
number of lesions recommended for biopsy, was 3.7%, which was significantly lower than the specificity for MelaFind (p=0.02).

Using data from the industry-sponsored FDA-approval study, Wells and colleagues evaluated the diagnostic accuracy of MelaFind compared to the opinion of dermatologists. (18) A convenience sample of 39 dermatologists who had expressed interest in the MelaFind technology participated. The study was conducted over the internet. A total of 47 lesions (23 malignant melanomas and 24 benign lesions) were randomly selected from the repository of lesions that had been collected by MELA Sciences. Cases may have overlapped with the data used in the Monheit et al. study, described above. (20) Dermatologists were given images of the lesions taken prior to biopsy and case histories, but were not given MelaFind recommendations. The participants were asked whether or not they would recommend biopsy. MelaFind recommended biopsy of 22 of 23 melanoma lesions (sensitivity: 96%, lower limit of 95% CI: 83%). The average biopsy sensitivity for dermatologists was 80% (95% CI: 72-87%). Regarding specificity, MelaFind did not recommend biopsy for 2 of 24 benign lesions (specificity: 8% 95% CI: 1-25%). In contrast, the biopsy specificity was 43% for dermatologists. In this study, the specificity of MelaFind was very low i.e., findings suggested biopsy was needed for 22 of 24 benign lesions and the specificity of dermatologists’ reading was higher than in the Monheit et al. study. Limitations of the study methods include that it was conducted via the internet and clinicians were not able to view lesions. Also, clinicians may not be representative of the average dermatologist, since they were part of a group that expressed interest in MelaFind and agreed to participate in company-sponsored research.

Does analysis using a computer-based optical diagnostic device lead to changes in patient management or improve the net health outcome compared to standard practice?

A 2012 study by Rigel and colleagues reported results of a simulation exercise with dermatologists attending an educational conference. (19) A total of 179 practicing dermatologists participated in the exercise. They were asked to evaluate lesions before and after receiving information from multispectral digital skin lesion analysis using the MelaFind device and respond to the question of whether they would biopsy the lesion. There were 24 lesions, 5 known to be melanomas and 19 non-melanoma pigmented lesions. Before information from the computer-based system, 13% of participants said they would biopsy all 5 of the lesions; this rose to 70% after evaluation by the MelaFind system. The authors reported that the average biopsy sensitivity for the 5 melanoma lesions was 69% prior to receiving information from MelaFind and 94% afterwards. In addition, the biopsy specificity was 54% before information from MelaFind and 40% afterwards. Exact numbers were not reported. Potential biases in this analysis include that this was a simulation exercise and may not reflect clinical practice and that the exercise occurred at a meeting where the sponsorship was likely obvious. In addition, along with the information from MelaFind, the participants were evaluating the lesion for the second time, and this additional re-look at the information might affect their biopsy recommendation.

Computer-based optical imaging devices for serial assessments of lesions

No published studies were identified that addressed this topic.
Computer-based optical imaging devices for defining peripheral margins of cancerous skin lesions prior to surgery

No published studies were identified that addressed this topic.

Section summary: Only one published study has evaluated the accuracy of a computer-based optical diagnostic device. The study found that MelaFind was able to correctly identify 125 of 127 melanomas among evaluable samples; 10% of samples were not evaluable. One simulation study with a number of potential biases evaluated the potential impact on MelaFind on patient management decisions. The evidence is insufficient for evaluating the added benefit of using computer-based optical devices compared to clinical examination for selecting suspicious lesions for excision. Moreover, there is insufficient evidence to draw conclusions about the effect of computer-based optical devices on patient management or health outcomes. No studies were identified that addressed the use of computer-based optical imaging for serial assessment of lesions or for defining peripheral margins of lesions prior to surgery.

Ongoing Clinical Trials

Post-Approval Study of MelaFind (NCT01700114) (20): This multicenter industry-sponsored U.S.-based study is comparing the accuracy of dermatologists in correctly identifying melanomas or high-grade lesions when they do and do not have access to MelaFind data. Estimated enrollment is 720 patients and the expected date of completing data collection is February 2014.

VivaNet Study. A Multicenter Study of Confocal Reflectance Microscopy in Telemedicine (EUNET) (NCT01385943): (21) This is a multicenter European study that will include individuals with skin lesions considered suspicious for malignancy. Patients will have all of the following, on the same day (unless contraindicated): clinical photograph, dermatoscopic image, confocal reflectance microscopic image. In addition, they will undergo a tissue biopsy. Patients will return in 3 months for additional examination. The primary study outcome is the relative accuracy of the diagnostic methods. The estimated enrollment for this study is 500 with an estimated completion date of December 2015.

Practice Guidelines and Position Statements

In July 2007, the International Dermoscopy Society (IDS) embarked on creating a consensus document for the standardization and recommended criteria necessary to be able to effectively convey dermatoscopic findings to consulting physicians and colleagues. (22) The final items included in the document are as follows: (1) pertinent personal and family history (recommended); (2) clinical description of the lesion (recommended); (3) the 2-step method of dermatoscopy differentiating melanocytic from nonmelanocytic tumors (recommended); (4) the use of standardized terms to describe structures (recommended); (5) the dermatoscopic algorithm used (optional); (6) information on the imaging equipment and magnification (recommended); (7) clinical and dermatoscopic images of the tumor (recommended); (8) a diagnosis or differential diagnosis (recommended); (9) decision concerning the management (recommended); (10) specific comments for the pathologist when excision and histopathologic examination are recommended (optional).
The National Comprehensive Cancer Network (NCCN) melanoma guideline does not include dermatoscopy. Biopsy is recommended for suspicious pigmented lesions. (23)


**U.S. Preventive Services Task Force Recommendations**

Dermatoscopy is not a preventive service.

**Summary**

The literature regarding dermatoscopy for selecting or deselecting lesions for excision suggests that dermatoscopy is more accurate than naked eye examination when used in the expert clinical setting. The available evidence from prospective RCTs and other studies suggests that dermatoscopy used by specialists may lead to a decrease in the number of benign lesions excised and, when used by primary care physicians, may lead to fewer benign lesions being referred to specialists. The number of studies on the impact of dermatoscopy on patient management and clinical outcomes remains limited.

Although the literature regarding dermatoscopy is extensive, it is insufficient for determining whether use of the technique i.e., for selecting or de-selecting lesions for excision, leads to improvements in patient management or improved health outcomes. In simulated exercises, the accuracy of dermatoscopy has been reported as superior to clinician examination, but there are no prospective studies that demonstrate improvements in actual clinical care. There is less evidence on computer-based optical diagnostic devices for selecting or de-selecting lesions for excision. There is only one published study on diagnostic accuracy and no studies comparing patient management decisions and health outcomes with and without these devices. In addition, there is insufficient evidence on the impact of serial dermatoscopic monitoring on health outcomes compared to serial clinical monitoring and an absence of published studies evaluating computer-based optical devices for serial monitoring of lesions. Thus, dermatoscopy and computer-based optical diagnostic devices are considered **not medically necessary** for evaluating pigmented skin lesions suspected of malignancy and for serially monitoring pigmented skin lesions.

There are insufficient data on the added value of using dermatoscopy for defining peripheral margins of basal cell carcinomas or squamous cell carcinomas to guide surgical excision using dermatoscopic devices available in the United States. Thus, this application of dermatoscopy is considered **not medically necessary**. Due to the absence of evidence on computer-based optical devices for defining peripheral margins of lesions suspected of malignancy, the technology is considered investigational for this purpose.

**Medicare National Coverage**

No national coverage determination found.
References


Keywords

Dermoscopy
Dermatoscopy
Digital Epiluminescence Microscopy
Epiluminescence Microscopy
Molemax
MelaFind

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 5, 2014 and is effective January 15, 2015.

Signature on File
Deborah M. Smith, MD, MPH