Optical Diagnostic Devices for Evaluating Skin Lesions Suspected of Malignancy
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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers dermatoscopy, using either direct inspection, digitization of images, or computer-assisted analysis as a technique to evaluate or serially monitor pigmented skin lesions to be investigational.*

Based on review of available data, the Company considers computer-based optical imaging devices e.g., multispectral digital skin lesion analysis (MSDSLA), as a technique to evaluate or serially monitor pigmented skin lesions to be investigational.*

Based on review of available data, the Company considers dermatoscopy and computer-based optical imaging devices for defining peripheral margins of skin lesions suspected of malignancy prior to surgical excision to be investigational.*

Background/Overview
There is interest in noninvasive 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.

Dermatoscopy
Dermatoscopy, also known as dermoscopy, describes a family of noninvasive techniques that allow in vivo microscopic examination of skin lesions and 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 transparent. Using a magnifying lens, the structures of the epidermis and epidermal-dermal junction can then be visualized. A handheld or stereomicroscope may 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.
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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 color, architecture, symmetry, homogeneity (CASH) algorithm. 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 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.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration
Dermatoscopic devices cleared by the U.S. 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.
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- 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 been cleared by 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 (ie, dermatologists) and only those who have additionally successfully completed training on the MelaFind device. The 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 nonpigmented 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., nonulcerated or nonbleeding 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 nonmelanoma skin cancers, so the dermatologist should rely on clinical experience to diagnose such lesions.”

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination (NCD).

Rationale/Source

As with any diagnostic tool, assessment of dermoscopy involves a determination of its sensitivity, specificity, and positive (PPV) and negative predictive values (NPV) in different populations compared with a reference standard and whether the results of the diagnostic tests are ultimately used to benefit health outcomes. The reference 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, dermoscopy is used in combination with clinical assessment, either based on direct visual inspection or review of photographs. Therefore, the diagnostic performance of dermoscopy combined with clinical assessment must be compared with clinical assessment alone and then to the reference standard of histology. There are 4 general clinical situations in which dermoscopy might be of benefit.

1. When patients present with a lesion with a low pretest possibility of malignancy, dermoscopy could potentially be used to determine which lesions did not require excision, ie, a deselection process. In this clinical situation, the NPV of dermoscopy is the most relevant diagnostic
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1. Accurate diagnosis of cutaneous melanoma relies on the recognition of specific morphological characteristics of pigmented skin lesions. These characteristics can aid in the selection of lesions for excision and also aid in the evaluation of lesions after excision. Optical diagnostic devices are used primarily to aid in the diagnosis of cutaneous melanoma.

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 PPV 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 PPV and NPVs 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.

Dermatoscopy for Selecting or Deselecting Lesions for Excision

Diagnostic Accuracy Compared With Naked Eye Examination

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. 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 for melanoma, for dermatoscopy compared with naked eye examination, was found to be 15.6 (range, 2.9-83.7). The removal of 2 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). (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 1 (which was conducted in Iran) were studies
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from Europe. A total of 9784 melanoma lesions were included in the review; of these, 8045 were analyzed by dermatoscopy and 2420 by CAD. The investigators conducted pooled analyses of studies, grouping them by the type of algorithm used for diagnosis (eg, pattern analysis, ABCD rule). The pooled sensitivity for dermatoscopy (30 analyses) was 88% (95% confidence interval [CI], 87% to 0.89%), and the pooled specificity was 86% (95% CI, 85% to 86%). For digital dermatoscopy with CAD, the pooled sensitivity was (12 analyses) 0.91 (95% CI, 88% to 93%), and the pooled specificity was 79% (95% CI, 77% to 81%).

A representative review of recent studies follows.

In 2014 Koelink et al conducted a cluster randomized trial on use of dermatoscopy in primary care. Patients from 48 general practices in the Netherlands were randomized to an intervention group using dermatoscopy in addition to naked eye examination or a control group using only naked eye examination. Eligibility included being at least 18 years old and presenting with a suspicious skin lesion. All patients underwent routine naked eye examination and those in intervention practices were also examined with a dermatoscope. The reference standard, in hierarchical order, for diagnosis, was pathologic diagnosis for excised lesions, diagnosis by a dermatologist for referrals, or diagnosis by trial dermatologist. A total of 170 patients in 26 practices were included in the intervention group and 211 patients in 22 practices were included in the control group. Overall, the percentage of correctly diagnosed lesions was 98 of 194 (50.5%) in the intervention group and 90 of 222 (40.5%) in the control group. The OR of a correct diagnosis in the intervention group compared with the control group was 1.51 (95% CI 0.96 to 2.37). Among melanoma lesions, the percentage of correct diagnoses was 8 of 13 (61.5%) in the intervention group and 2 of 9 (22.2%) in the control group (OR=5.52; 95% CI, 0.76 to 39.91). Neither of the differences was statistically significant. Because the study included relatively few melanoma lesions, there was a lack of precision in estimating the percentage of correct diagnoses.

Also in 2014, Unlu et al published a comparison of dermatoscopic diagnostic algorithms and clinical assessment using histological diagnosis as the reference standard. 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 4 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 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. 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. 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 (BCCs), and squamous cell carcinomas (SCCs). The process of analysis consisted of presenting 2 clinical images of each lesion (overview, 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. Receiver operator curve area under the 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).

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 may have similar diagnostic accuracy.
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Impact on Patient Management or Health Outcomes
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. 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 group that could use dermatoscopy, the number of lesions initially classified as suggestive or equivocal by naked eye examination was 158 or 311 (50.8%). After dermatoscopy, 28 of these 158 lesions (17.8%) were classified as suggestive or equivocal and were referred for excision. Thus, in the dermatoscopy group, a total of 28 of 311 (9.0%) lesions were referred for excision. The proportion of referrals was significantly lower than the naked eye only examination group, in which 47 of 302 (15.6%) lesions were referred for excision (p=0.013). Histologic analysis of excised lesions identified 3 melanomas in the naked eye examination only group and 2 in the combined examination group; the difference between groups was not statistically significant. No unexcised melanomas were identified in the 103 of 121 (85%) patients with clinically suspicious but dermatologically negative lesions who agreed to be reexamined several months later.

An RCT by Argenziano et al was published in 2006. 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). According to histopathologic analysis of equivocal lesions, 23 malignant lesions were missed by naked eye examination alone versus 6 missed lesions with dermatoscopy; the difference between groups was statistically significant (p=0.002).

In addition, the 2011 study by De Giorgi et al, previously described, addressed the issue of whether dermatoscopy leads to improved patient management. 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
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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 higher when dermatologic images were available in addition to clinical images (p<0.003) and there was not a statistically significant difference in specificity.

Section Summary
Several studies, including 2 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

Impact on Patient Management or Health Outcomes
No prospective comparative studies were identified that compared outcomes after managing patients over time with and without dermatoscopy. A meta-analysis of data from noncomparative studies was published in 2013 by Salerni et al. The authors identified 14 studies performed in a clinical setting. The studies included 5787 patients with a total of 52,739 lesions that were monitored using dermatoscopy (mean, 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 4388 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 with another technique for monitoring patients.

One study, published in 2009 by Menzies et al, 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) (ie, every 3 months). 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
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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 reevaluated 3 months later. At that time, 46 lesions were referred/excised, 6 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 SSDI 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 Before Surgery

Impact on Patient Management or Health Outcomes

One RCT was identified that compared dermatoscopy with other methods of defining peripheral margins. This was a 2013 trial published by Asilian and Momeni in which 60 patients with 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 before Mohs micrographic surgery. In all patients, a 3-mm 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 (standard deviation [SD]), the study's primary outcome, was 1.90 (0.55) in the curettage group, 1.55 (0.51) in the visual inspection group and 1.65 (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 nonrandomized study was published by Suzuki et al in 2014. 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 22 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 nonrandomized comparisons between clinical and dermatoscopic evaluation of suspected tumor margins. Most recently in 2012, Carducci et al evaluated outcomes in 94 patients with a suspected clinical diagnosis of SCC. 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 to 6 mm was chosen for SCC not located on the scalp, ears, eyelids,
nose, or lips. For lesions in those areas, margins of 6 to 10 mm were used. In the dermatoscopy group, clinical margins were first defined and outlined with a dermographic 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 with 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 BCC of the head or neck. A total of 84 patients were included. 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 BCC. 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 to 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 with 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 with 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.
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Computer-Based Optical Diagnostic Device for Selecting or Deselecting Lesions for Excision

Diagnostic Accuracy Compared With Naked Eye Examination

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

A total of 1393 patients with 1831 lesions were enrolled in the study. Of the 1831 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 postenrollment due to factors such as scarring. Histologic analysis determined that 127 of 1632 lesions (7.8%) were melanoma. The sensitivity of MelaFind for recommending biopsy of melanomas was 98.2% (125/127 melanomas) with a 95% lower 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 nonmelanoma 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 et al evaluated the diagnostic accuracy of MelaFind compared with the opinion of dermatologists. 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, 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, previously described. Dermatologists were given images of the lesions taken before 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% to 87%). Regarding specificity, MelaFind did not recommend biopsy for 2 of 24 benign lesions (specificity, 8%; 95% CI, 1% to 25%). In contrast, the biopsy specificity was 43% for dermatologists. In this study, the specificity of MelaFind was very low, ie, 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
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clinicians were not able to view lesions. Also, clinicians may not be representative of the average dermatologist, because they were part of a group that expressed interested in MelaFind and agreed to participate in company-sponsored research.

Section Summary
Only 1 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 with clinical examination for selecting suspicious lesions for excision.

Impact on Patient Management or Health Outcomes
A 2012 study by Rigel et al reported results of a simulation exercise with dermatologists attending an educational conference. A total of 179 practicing dermatologists participated in the exercise. They were asked to evaluate lesions before and after receiving information from MSDSLA 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 nonmelanoma 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% before 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 relook at the information might affect their biopsy recommendation.

Section Summary
There is insufficient evidence to draw conclusions about the effect of computer-based optical devices on patient management or health outcomes.

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 Before Surgery
No published studies were identified that addressed this topic.
Optical Diagnostic Devices for Evaluating Skin Lesions Suspected of Malignancy

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Ongoing and Unpublished Clinical Trials

- Post-Approval Study of MelaFind (NCT01700114): 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 Mar 2018.
- VivaNet Study. A Multicenter Study of Confocal Reflectance Microscopy in Telemedicine (EUNET) (NCT01385943): This is a multicenter European study that will include subjects 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.

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 randomized controlled trial 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.

There is less evidence on computer-based optical diagnostic devices for selecting or deselecting lesions for excision, and initial data suggest low specificity. There are 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 with 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 investigational 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 SCCs to guide surgical excision using dermatoscopic devices available in the United States. Thus, this application of dermatoscopy is considered investigational. 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.
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Policy History
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07/18/2002     Medical Policy Committee review
08/26/2002     Managed Care Advisory Council approval
12/07/2004     Medical Director review
01/31/2005     Managed Care Advisory Council approval
07/07/2006     Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
01/10/2007     Medical Director review
01/17/2007     Medical Policy Committee approval. Policy statement unchanged.
01/07/2009     Medical Director review
01/14/2009     Medical Policy Committee approval. No change to coverage.
01/07/2010     Medical Director review
01/20/2010     Medical Policy Committee approval. No change to coverage
01/06/2011     Medical Director review
01/19/2011     Medical Policy Committee approval. New investigational statement added.
02/02/2012     Medical Policy Committee review
02/15/2012     Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/03/2013     Medical Policy Committee review
01/09/2013     Medical Policy Implementation Committee approval. Title changed. Added a new investigational indication.
01/09/2014     Medical Policy Committee review
01/15/2014     Medical Policy Implementation Committee approval. No change to coverage.
01/08/2015     Medical Policy Committee review
01/21/2015     Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2015     Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
01/07/2015     Medical Policy Committee review
01/22/2016     Medical Policy Implementation Committee approval. No change to coverage. Policy archived.

Next Scheduled Review Date: Archived Medical Policy

Coding
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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

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