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Optical Diagnostic Devices for Evaluating Skin Lesions Suspected of Malignancy

Policy # 00025

Original Effective Date: 06/05/2002

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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, 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.

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

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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.

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 (MSDSL) 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 (FDA)

Dermatoscopic devices cleared by the U.S. FDA include:

- EpiscopyTM ‡ (Welch Allyn, Inc., Skaneateles Falls, NY) approved in 1995; intended use is to illuminate body surfaces and cavities during medical examination.
- NevoscopeTM ‡ (TRANSLITE, Sugar Land, TX) approved in 1996; intended use is to view skin lesions by either illumination or transillumination.
- DermoscopeTM ‡ (American Diagnostic Corp., Hauppauge, NY) approved in 1999; intended use is to enlarge images for medical purposes.
- MoleMaxTM ‡ (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 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



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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.”

Centers for Medicare and Medicaid Services (CMS)
No National Coverage Determination found.

Rationale/Source

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 might 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 did 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

This policy was originally created in 2001 and was updated regularly with searches of the MEDLINE database. The most recent literature search was performed for the period July 2012 through August 27, 2013. Following is a summary of the key literature to date.



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Dermatoscopy

Dermatoscopy for selecting or deselecting lesions for excision

Does dermatoscopy improve upon naked eye examination of lesions?

A variety of studies have reported on the diagnostic parameters of dermatoscopy criteria compared to clinical assessment with histologic examination serving as the gold standard. However, most studies are retrospective, and most compare clinical assessment only to dermatoscopy instead of the more clinically relevant comparison of clinical assessment alone compared with combined clinical and dermatoscopic assessment. In addition, the studies do not subcategorize lesions into varying levels of pretest probabilities. Moreover, there is a lack of consensus in the literature regarding the optimal dermatoscopic criteria for malignancy and the optimal method of using the criteria to assess malignancy. For example, dermatoscopic images may be evaluated qualitatively, with semiquantitative scoring according to algorithms, evaluated using statistical methods to assess risk of malignancy, or evaluated using artificial neural networks. Dermatoscopic criteria for malignant melanoma have undergone multiple modifications, with questions raised regarding their validity and reproducibility. As recently as 2009, even in papers that advocate for the widespread use of dermatoscopy, the accuracy of algorithms developed to differentiate between various types of pigmented lesions has been questioned. This variety of methods obviously complicates the evaluation of the data.

Another important issue is that the majority of the studies report on the performance of clinicians who have extensive experience with dermatoscopic imaging, and it is not clear whether these results can be duplicated in a community setting or what kind of formal training would be required. A 2010 article reiterates that the generalizability of study findings to the general practice setting is still not known.

Several meta-analyses of studies on the diagnostic accuracy of dermatoscopy have been published; findings of recent meta-analyses are described below:

In a 2008 meta-analysis, Vestergaard et al. reviewed studies on the diagnostic accuracy of dermatoscopy for the diagnosis of melanoma compared with naked eye examination. All of the studies were performed in an expert setting. Nine studies met the inclusion criteria; 2 were randomized controlled trials (RCTs); 7 used a cross-sectional design. The authors compared the diagnostic accuracy of dermatoscopy with naked eye examination using a reference test on consecutive patients with a defined clinical presentation. 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); removal of 2 small outlier studies changed this to 9.0 (range: 1.5–54.6). 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. The limitations of this meta-analysis include 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.

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



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dermatoscopy performed by experts, and used histology of excised lesions as the reference standard. Studies were not required to compare dermatoscopy to 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 9,784 melanoma lesions were included in the review; of these, 8,045 were analyzed by dermatoscopy and 2,420 by computer-aided diagnosis. The investigators conducted pooled analyses of studies, grouping them by the type of algorithm used for diagnosis e.g., pattern analysis, ABCD rule, etc. The pooled sensitivity for dermatoscopy (30 analyses) was 0.88 (95% confidence interval [CI]: 0.87-0.89), and the pooled specificity was 0.86 (95% CI: 0.85-0.86). For digital dermatoscopy with CAD, the pooled sensitivity was (12 analyses) 0.91 (0.88-0.93), and the pooled specificity was 0.79 (95% CI: 0.77-0.81). 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, computer-aided diagnosis has only been used in experimental settings using preselected lesions.

A representative review of recent clinical studies follows.

In 2000, Ascierto and colleagues reported on a series of 8,782 subjects with 15,719 skin lesions evaluated dermatoscopically. Based on dermatoscopic assessment, the lesions were further classified from very low to very high risk for malignant melanoma. Excision was advised for all high-risk lesions. In medium- and low-risk lesions, excision was justified for "cosmetic or functional" reasons. The sensitivity and specificity of dermatoscopy were then compared to the histologic results of the 2,731 excised lesions. For very high- and high-risk lesions, the positive and negative predictive values of dermatoscopy were 86.4% and 96.6%, respectively. In the low-risk group, the positive and negative predictive values were 93.1% and 95.4%, respectively. This study did not compare the performance of dermatoscopy, alone or in combination with clinical assessment, to clinical assessment alone.

A 2007 study by Annessi et al. compared dermatoscopy using 3 algorithmic methods with clinical diagnosis in 198 consecutive atypical macular melanocytic lesions. Compared against the gold 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 positive predictive value (80% and 76%, respectively) were modestly higher for pattern analysis. Results with the 7-point checklist were sensitivity of 78% and specificity of 65%.

In 2007, Langley et al. conducted a study to evaluate the diagnostic accuracy of confocal scanning laser microscopy (CSLM) compared to dermatoscopy in a prospective examination of benign and malignant melanocytic lesions. Patients (n=125) with suspicious pigmented lesions were prospectively recruited to undergo a clinical, dermatoscopic and CSLM examination. All patients had lesions studied; 88 melanocytic nevi and 37 melanomas. Dermatoscopy had a sensitivity of 89.2%; specificity of 84.1%; positive predictive value of 70.2%; negative predictive value of 94.9%. CSLM was found to have a sensitivity of 97.3%; specificity of 83.0%; positive predictive value of 70.6%; negative predictive value of 98.6%. No melanomas were misidentified when both techniques were used together. The authors concluded that CSLM had a



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relatively higher sensitivity than dermatoscopy. However, they noted that, the specificity was similar with CSLM and dermatoscopy, suggesting that the 2 techniques are complementary.

In 2011, De Giorgi and colleagues 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 gold 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.

Rosendahl and colleagues 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 gold 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 2 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. Receiver operating characteristic 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, $p < 0.001$).

The generalizability of the results of the above studies may be limited in that clinical assessment consisted only of photographs of the lesions; other clinical information was not available. As stated in a recent review article, research studies may artificially inflate the sensitivity of dermatoscopy for several reasons, including that they generally compare dermatoscopy to naked eye evaluation of morphology, which does not reflect actual clinical assessment that also takes history and context, e.g., patient's degree of sun damage, into consideration.

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Does dermatoscopy to aid in selection of lesions for excision lead to changes in patient management or improve the net health outcome compared to standard practice?

No prospective comparative studies were identified that compared patient management with and without dermatoscopy. One study that addressed the issue of whether dermatoscopy leads to improved patient management was the 2011 study by De Giorgi and colleagues, described above. 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 gold 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, $p < 0.003$.

Section summary: Recent meta-analyses found that overall; the diagnostic accuracy of dermatoscopy was higher than clinical assessment/naked eye examination. However, definitive conclusions could not be drawn on the impact of dermatoscopy on health outcomes. There is a lack of controlled studies comparing patient management decisions and health outcomes with and without dermatoscopy. Most of the studies of diagnostic accuracy were not performed in the clinical setting but rather using photographs of lesions with and without dermatoscopy in the research setting. Increased accuracy of diagnosis in the research setting may not translate to changes in clinical decision making, such as the decision to perform a skin biopsy. In addition, most studies have been conducted outside the U.S and have included clinicians with extensive experience in dermatoscopy, creating concerns for generalizability of the results.

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 result in 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 noncomparative studies was published in 2013 by Salerni and colleagues. 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.

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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). 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 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 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 improve the net health outcome compared to standard practice?

One RCT was identified that compared dermatoscopy to other methods of defining peripheral margins.

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.

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 and colleagues evaluated outcomes in 94 patients with a suspected clinical diagnosis of squamous cell carcinoma (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 4-6 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



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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. 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 basal cell carcinoma. 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 U.S. 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: the



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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 prebiopsy 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 1,831 lesions, 1,632 (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 1,632 lesions (7.8%) were melanoma. The sensitivity of MelaFind for recommending biopsy of melanomas was 98.2% (125 of 127 melanomas) with a 95% lower confidence interval (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 and colleagues evaluated the diagnostic accuracy of MelaFind compared to 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 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. 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. 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



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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 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% 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): 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): 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.



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Summary

Although the literature regarding dermatoscopy is extensive, it is insufficient for determining whether use of the technique i.e., for selecting or deselecting 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 deselecting lesions for excision, and initial data suggests 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 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 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 squamous cell carcinomas 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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CPT	96904
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ICD-9 Diagnosis	All relevant diagnoses
ICD-9 Procedure	No codes

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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
12/14/2004 Medical Policy Committee review. Format revision. Coverage eligibility unchanged.
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.
Next Scheduled Review Date: 01/2015

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