Name of Policy:
Optical Diagnostic Devices for Evaluating Skin Lesions Suspected of Malignancy

Policy #: 113
Category: Medicine
Latest Review Date: September 2014
Policy Grade: B

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**Description of Procedure or Service:**

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 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 three-point and seven-point checklists of dermatoscopy by Argenziano, the Menzies method, and the 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 multispectral digital skin lesion analysis (MSDLSA) device uses a handheld scanner to shine visible light on the suspicious lesion. The light is often wavelengths, varying from blue (430nm) and near infrared (950nm). The light can penetrate up to 2.5mm 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 Governing Bodies section) is intended only for suspicious pigmented lesions on intact skin and for use only by trained dermatologists.

**Total Body Photography**

Total Body Photography is another development for diagnosing and tracking melanoma but is separate and distinct from dermoscopy. This is a photographic display system on CD-ROM, designed to serve as an adjunct to the physical examination when following patients who are at high risk for developing cutaneous melanoma. This method is the MoleMapCD and marketed by DigitalDerm, Inc. This allows rapid display of 33 high-resolution color images of the patient’s skin surface and permits efficient comparison of the patient’s current condition with a set of baseline images. The use and focus of total body photography imaging is a significant change from the use of dermoscopy and should not be considered a component of dermoscopy or be evaluated as the same as MoleMap II, MS 500 B Micro-Scopeman, Moritex or any other instrument used for dermoscopy. Total Body Photography looks at the total body surface and dermoscopy looks at single moles. Dermatoscopy 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. Dermatoscopy may also be referred to as dermoscopy, skin surface microscopy, epiluminescence microscopy (ELM). This involves application of immersion oil to skin, which eliminates light reflection from the skin surface and renders the stratum corneum transparent.

Total Body Photography is a service that offers a comprehensive photographic archive of the patient’s skin surface at a particular time. A professional photographer takes a series of 33 images of the patient’s body. The images are forwarded on two compact disks to the physician. The physician keeps one disk and gives the other disk to the patient during the follow-up visit and may be instructed in the best use of the MoleMapCD for home self-examination.

**Policy:**

**Dermatoscopy**, using either direct inspection, digitization of images, or computer-assisted analysis as a technique to evaluate or serially monitor pigmented skin lesions **does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational**.

**Total (Whole) Body Photography** **does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage.

**Computer-based optical imaging devices** (e.g., multispectral digital skin lesion analysis) used as a technique to evaluate or serially monitor pigmented skin lesions **does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational**.
Dermatoscopy and computer-based optical imaging devices for defining peripheral margins of skin lesions suspected of malignancy prior to surgical excision do not meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered investigational.

"Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member’s contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination."

Key Points:
The first step in the evaluation of a diagnostic technology is to evaluate its performance in comparison to a gold standard. The assessment involves the determination of its sensitivity, specificity, and positive and negative predictive values in different populations compared to the gold standard, and whether the results of the diagnostic tests are ultimately used to improve health outcomes.

The gold standard for evaluation of pigmented skin lesions is excision with histologic evaluation and diagnosis by a pathologist. This method, depending on the skill of the pathologist, is considered to have a sensitivity and specificity of about 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 four 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 de-selection process. In this clinical situation, the NPV 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 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.

The American Cancer Society projected that one million cases of skin cancer will be diagnosed each year in the United States and that in 2004 about 55,000 new cases of melanoma will be detected with about 7,910 deaths. There are three main kinds of skin cancer: malignant melanoma, basal cell carcinoma and squamous cell carcinoma. Melanoma is the least common but the most deadly form of skin cancer. However, if detected early it is highly curable. Less than 5 percent of direct healthcare costs for melanoma are spent on diagnosis, more than 90 percent of the money for melanoma goes to treat advanced melanoma. This expense is attributable to fewer than 20 percent of patients with melanoma.

**Dermatoscopy for Selecting or Deselecting Lesions for Excision**

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; two were randomized controlled trials (RCTs) and the other seven 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). (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 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 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 (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, computer-aided diagnosis has only been used in experimental settings using preselected lesions.

A representative review of recent clinical studies follows:

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 four algorithms. These were the ABCD rule, the seven-point checklist, three-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 seven-point checklist, 19 (79%) by the three-point checklist, and 22 (92%) by the color, architecture, symmetry, homogeneity (CASH) algorithm. All melanomas with a Breslow thickness of at least 0.75mm 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 seven-point checklist, 79.1% and 62.6% for the three-point checklist and 91.6% and 64.8% for the CASH algorithm.

In 2011, De Giorgi and colleagues in Italy randomly selected eight dermatologists who had attended a basic dermatoscopy course six 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 <8.00mm). 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.

A 2011 study by Rosendahl and colleagues analyzed a consecutive series 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 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. 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 non-melanocytic 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. 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 seven-point checklist were sensitivity of 78% and specificity of 65%.

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.

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 two 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 one-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 histopathological analysis of equivocal lesions, 23 malignant lesions were missed by naked eye examination alone versus six 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 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.

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

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 colleague. 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 three 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 two-hour workshop and online training. Seventy-four physicians completed the training, and 63 of these (85%) then assessed 374 lesions (median of six 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 three 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 three 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 six months from the initial visit), referral/excision was recommended for two of the six SDDI lesions, and the other four returned to standard care. In addition, five 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

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) of 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 on 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. 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 two groups, e.g., 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). 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 6mm was chosen for SCC not located on the scalp, ears, eyelids, nose, or lips. For lesions in those areas, margins of 6 to 10mm 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 to three 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 eight of 40 (20%) histologic specimens excised after clinical evaluation and three of 44 (7%) specimens excised after dermatoscopic detection of margins; this difference was statistically significant, p<0.007. Seven of the eleven (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 1mm 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 to clinical assessment alone.

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

**Computer-based optical diagnostic device**

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. Food and Drug Administration (FDA) in the application for approval of the device. The study included patients with at least one 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 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 post-enrollment 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 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-approved 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 two of 24 benign lesions. 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.

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 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, five 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 five of the lesions; this rose to 70% after evaluation by the MelaFind system. The authors reported that the average biopsy sensitivity for the five 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. A stronger design would be to randomize clinicians to evaluate lesions with or without information from MelaFind and to compare the accuracy of each approach.

**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.

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.
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.

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 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.

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. 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 two-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 mention dermatoscopy. Biopsy is recommended for suspicious pigmented lesions.
The American Academy of Dermatology 2011 guidelines of care and treatment of melanoma do not mention dermatoscopy, e.g., in the discussion of determining surgical margins before surgery. The guidelines did not address evaluation of suspicious lesions.

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

Dermatoscopy is not a preventive service.

**Key Words:**
Dermoscopy, dermatoscopy, epiluminescence light microscopy, ELM, pigmented skin lesions, PSLs, and digital epiluminescence light microscopy, DELM, Episcope, Nevoscope, Dermascope, MoleMax, melanomagram, total body photography, optical diagnostic devices, computer-based optical imaging devices, MelaFind, MoleMapCD

**Approved by Governing Bodies:**

- MoleMapCD falls under FDA Code of Federal Regulations, Title 21, Volume 8, Revised as of April 1, 2003, as a medical storage device and as such is exempt from the premarket notification procedures.

Dermatoscopic devices cleared by the FDA include:

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

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 2mm and 22mm, 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 1cm 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.”

Benefit Application:
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP contracts: Special benefits consideration may apply. Refer to member’s benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity

Current Coding:
CPT codes:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>96904</td>
<td>Whole body integumentary photography, for monitoring of high risk patients with dysplastic nevus syndrome or a history of dysplastic nevi, or patients with a personal or familial history of melanoma</td>
</tr>
<tr>
<td>96999</td>
<td>Unlisted special dermatological service or procedure (This is the code that should be used for dermatoscopy)</td>
</tr>
</tbody>
</table>

Whole body photography represents one component of dermatoscopy. CPT code 96904 may also be submitted to describe whole body photography without dermatoscopy.

Previous Coding:
CPT codes:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0044T</td>
<td>Whole body integumentary photography, at request of a physician, for monitoring of high-risk patients with dysplastic nevus syndrome or familial melanoma (deleted 01/01/2007)</td>
</tr>
<tr>
<td>0045T</td>
<td>Whole body integumentary photography, at request of a physician, for monitoring of high-risk patients; with history of dysplastic nevi or personal history of melanoma (deleted 01/01/2007)</td>
</tr>
</tbody>
</table>

References:

Policy History:
Medical Policy Group, May 2003 (1)
Medical Policy Administration Committee, May 2003
Available for comment June 12-July 28, 2003
Medical Policy Group, June 2005
Medical Policy Administration Committee, June 2005
Available for comment June 18-August 2, 2005
Medical Policy Group, March 2009 (1)
Medical Policy Group, August 2009 (1)
Medical Policy Group, September 2010 (1): Updated Description, added non-coverage statement for dermatoscopy to define peripheral margins of basal cell carcinomas, updated Key Points
Medical Policy Administration Committee, September 2010
Available for comment September 22-November 5, 2010
Medical Policy Group, September 2011 (1): Update to Key Points and References
Medical Policy Panel, September 2012
Medical Policy Group, March 2013 (1): Update to Title, Description, Policy, Key Points, Key Words, Governing Bodies and References related to computer-based optical imaging devices and removing the specific phrase of basal cell carcinoma to the more generic phrase of skin lesions suspected of malignancy
Available for comment March 5 through April 18, 2013
Medical Policy Panel, October 2013
Medical Policy Group, October 2013 (3): 2013 Updates to Key Points & References; no change in policy statement
Medical Policy Panel, September 2014
Medical Policy Group, September 2014 (3): 2014 Updates to Description, Key Points & References; no change in policy statement

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case by case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.