Medical Policy Manual Medicine, Policy No. 174

Skin Lesion Imaging and Spectroscopy

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Various non-invasive technologies, including multispectral image analysis, electrical impedance spectroscopy, optical coherence tomography, and reflectance confocal microscopy have been proposed for use in diagnosing skin lesions. These techniques have been proposed 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.

MEDICAL POLICY CRITERIA

The following skin lesion imaging and surveillance techniques are considered **investigational**:

A. Electrical impedance spectroscopy
B. Multispectral image analysis
C. Optical coherence tomography
D. Reflectance confocal microscopy
E. Fluorescent biotag imaging

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Gene Expression Profiling for Melanoma, Genetic Testing, Policy No. 29

BACKGROUND

SKIN CANCER DIAGNOSIS

The most common forms of skin cancer are keratinocyte carcinomas, which include basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC), and melanoma. Primary care providers evaluate suspicious skin lesions to determine who should be referred to dermatology. Factors considered include both a patient's risk for melanoma and other cancers as well as a visual examination of the lesion. The visual examination assesses whether the lesion has features suggestive of skin cancer. Primary care providers generally have a low threshold for referral to dermatology. A dermatologist may visualize the lesion using dermoscopy, a form of skin surface microscopy using incident light.

Skin cancers may be identified by providers based on certain lesion patterns and characteristics. Criteria for features suggestive of melanoma have been developed. One checklist is the ABCDE checklist:[1]

- Asymmetry;
- Border irregularities;
- Color variegation;
- Diameter ≥6 mm;
- Evolution.

Another criterion commonly used is the "ugly duckling" sign.[2] An ugly duckling is a nevus that is obviously different from others in a given patient. Melanoma is difficult to diagnose based on visual examination, and the criterion standard for diagnosis is histopathology. There is a low threshold for excisional biopsy of suspicious lesions for histopathologic examination due to the procedure's ease and low risk as well as the high probability of missing melanoma. However, the yield of biopsy is fairly low. The number of biopsies performed to yield one melanoma diagnosis has been estimated to be about 15 for U.S. dermatologists.[3] Therefore a test that could accurately identify those lesions not needing a biopsy (i.e., a rule-out test for biopsy) could be clinically useful. The purpose of evaluating a suspicious skin lesion is to inform a decision about whether to biopsy or excise the lesion.

ELECTRICAL IMPEDANCE SPECTROSCOPY

Electrical impedance spectroscopy (EIS) is a technology that measures the resistance to alternating electrical currents in a skin lesion. Electrical probes are used to generate a score that represents the irregularity of the skin cells. This has been proposed as a method for distinguishing melanoma from benign lesions.

- EIS devices include the Nevisense™ (Scibase AB, Stockholm, Sweden).

MULTISPECTRAL IMAGE ANALYSIS

Multispectral imaging (MSI) has been proposed as a technology that could improve melanoma detection and outcomes. A U.S. Food and Drug Administration (FDA)–approved MSI device uses a handheld scanner to shine a visible light on the suspicious lesion. The light is of 10

wavelengths, varying from blue (430 nm) to near-infrared (950 nm), and 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, and positive lesions are recommended for biopsy.

- MSI devices include the MelaFind®, SIAscope™ (Biocompatibles, Farnham, Surrey, UK) SIAscope II® and SIAscope V® (Astron Clinica Ltd., Cambridge, UK)

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) is a non-invasive technology that produces cross-sectional images of the layers of a skin lesion similar to ultrasound but based on the collection of reflected near-infrared light and a technique called interferometry. This allows for high-resolution microstructural and morphological imaging of the lesion, which can be converted into two- or three-dimensional images.

- OCT devices include the VivoSight® Dx (Michelson Diagnostics Inc. Atascadero, CA)

REFLECTANCE CONFOCAL MICROSCOPY

Reflectance confocal microscopy (RCM) is another type of microscopy that can be used for the non-invasive evaluation of skin lesions. RCM involves the focusing of reflected light from a single plane of tissue at a time, to a depth of 150 to 200 µm, which allows visualization of epidermis to the papillary dermis. This microscopy uses near-infrared light generated by a low-power laser and combines the planar data to create a three-dimensional image. Limitations of RCM include a loss of resolution beyond 150 µm in depth, making it less suitable for nodular or thickened lesions, and it may not detect deeper tumor margins. Visualization of a lesion by RCM requires more time than standard clinical and dermoscopic examination, and use of the instrumentation requires several months of formal training.[4]

- RCM systems include the VivaScope® 1500 and the VivaScope® 3000 (Lucid, Inc., Rochester, New York)

FLUORESCENT BIOTAG IMAGING

An imaging system by Orlucent™ for the evaluation of suspicious nevi includes a topically-applied fluorescent biotag. Incorporation of the biotag is used as a biomarker for tissue remodeling, which may be associated with the transition to atypia, a precursor to malignancy, and is assessed using a hand-held imager. This system is currently undergoing clinical trials and is marketed for research use only.[5]

EVIDENCE SUMMARY

Similar to other diagnostic tools, the assessment of skin lesion evaluation technology involves a determination of its diagnostic accuracy compared with a reference standard (clinical validity); then, it must be determined whether the results of the diagnostic tests can be used to improve health outcomes (clinical utility). The reference standard for evaluation of suspicious skin lesions is excision with histologic diagnosis, in which, depending on the skill of the pathologist, sensitivity and specificity are considered near 100%. Clinically, noninvasive techniques would be used in combination with clinical assessment, either based on direct

visual inspection or review of photographs. Therefore, the diagnostic performance of these technologies combined with clinical assessment should be compared with clinical assessment alone, and then a comparison should be made with the reference standard of histology. In addition, health outcomes in patients managed with these tools should be evaluated in comparison to standard care (clinical assessment alone or clinical assessment and dermoscopy).

CLINICAL VALIDITY

This evidence review is based primarily on series of Cochrane Reviews published in 2018 that evaluated new diagnostic technologies for skin cancers.[6-9]

Spectroscopy Technologies

A Cochrane Review published by Ferrante (2018) evaluated dermoscopy- and spectroscopy-based computer-assisted diagnosis (CAD) techniques.[6] The primary objectives of the review were to identify the diagnostic accuracy of CAD systems for melanoma, BCC, and cSCC. A comprehensive literature search through August 2016 was performed. Studies were excluded if they lacked an independent validation set (separate from the training set used to develop the test), used cross-validation approaches, or did not include an overall diagnosis of malignancy.

A total of 42 publications representing 19 patient cohorts were included in the analysis, of which, 18 publications representing 16 patient cohorts evaluated spectroscopy-based CAD (SPECT-CAD). These included both EIS (Nevisense™) and MSI devices (MSI-CAD, e.g., SIAscope™). Most of the studies were identified as having methodological concerns as assessed with the QUADAS-2 instrument, primarily regarding risk of bias and lack of applicability. Only a single study was reported as low concern for the applicability of its participant sample.

There were five MSI-CAD systems evaluated, including the MelaFind® and SIAscope™, while the Nevisense™ was the only EIS device evaluated. Eight datasets contributed to MSI-CAD meta-analysis (2,537 lesions, 296 melanomas), four of which were prospective. For the identification of melanoma or atypical melanocytic variants, the pooled sensitivity and specificity for the multispectral systems were 92.9% (95% confidence interval [CI] 83.7% to 97.1%) and 43.6% (95% CI 24.8% to 64.5%), respectively, and the pooled sensitivity and specificity from the two EIS studies (2,389 lesions, 368 melanomas) were 97% (95% CI 94.7% to 98.3%) and 33.6% (95% CI 31.6% to 35.7%), respectively. Six of the MSI-CAD studies also provided comparison data with dermoscopy (684 lesions, 220 melanomas and 8 BCC). An analysis of these data indicated that MSI-CAD was significantly more sensitive (difference of 22.7%, 95% CI 15.2% to 30.2%, $p<0.001$) but less specific (difference of −28.9%, 95% CI −56.3% to −1.48%, $p=0.039$). than dermoscopy. Only the Nevisense™ studies reported data on detection of cSCC and BCC, however the study populations were individuals with suspected melanoma, which limits the applicability of these findings.

The authors of the Cochrane Review reported the following conclusions:

- “Included studies inadequately address the review question due to an abundance of low-quality studies, poor reporting, and recruitment of highly selected groups of participants.
- CAD systems correctly identify melanoma in highly selected populations, but their low and very variable specificity suggest they are unreliable as stand-alone diagnostic tests,

especially in less selected populations.
- There is insufficient evidence to assess the accuracy of CAD systems in primary-care settings.
- Preliminary findings suggest CAD systems are at least as sensitive as assessment of dermoscopic images for the diagnosis of invasive melanoma and atypical intraepidermal melanocytic variants.
- The evidence base for individual systems is too limited to draw conclusions on which might be preferred for practice.
- Evidence of the ability of CAD to detect keratinocyte cancers is very limited and studies are confined to specialist settings."

Evidence on the diagnostic accuracy of EIS published since the Cochrane Review above is limited to a study by Sarac (2020) that prospectively evaluated 200 lesions in 101 patients for non-melanoma skin cancer, and reported a sensitivity, specificity, positive predictive value and negative predictive value of 94.2%, 41.9%, 78.3% and 76.5%, respectively.[10]

Optical Coherence Tomography (OCT)

A Cochrane Review by Ferrante (2018) evaluated the evidence for the use of OCT to diagnose skin cancer, including melanoma, atypical intraepidermal melanocytic variants, BCC or cSCC in adults.[7] Only studies that included a reference standard, such as histopathology or clinical follow-up, were eligible for inclusion, and the literature search was conducted through August 2016.

There were five studies with a total of 529 lesions (402 participants) that met the review inclusion criteria: four prospective case series and one study of unclear design (possibly case-control). Two of the studies evaluated pigmented lesions suspicious for melanoma and three evaluated non-pigmented lesions. The quality of the studies, as assessed by the QUADAS-2, were moderate to unclear, with concerns noted for the applicability of the results.

In the two pigmented lesion studies, there were 133 lesions evaluated and 36 melanomas detected. One of the studies used conventional swept-source OCT and reported a sensitivity of 89% (95% CI 52% to 100%) and specificity of 61% (95% CI 42% to 78%) at an attenuation coefficient of 5.4 mm^{-1}. The other study used high-definition OCT and reported a sensitivity of 74% (95% CI 54% to 89%) and specificity of 92% (95% CI 83% to 97%).

The three studies that evaluated non-pigmented lesions all used conventional swept-source OCT. BCC was detected in 237 of the 396 lesions analyzed. In one study that included 50 lesions, scoring of OCT characteristics provided a sensitivity of 97% (95% CI 82% to 100%) and specificity of 76% (95% CI 53% to 92%) at a Berlin score of 8 or greater. This study also detected nine cSCCs with a sensitivity of 56% (95% CI 21% to 86%) and specificity of 100% (91% to 100%) with the same score threshold. A meta-analysis of the 346 lesions from the other two studies yielded a pooled sensitivity of 95% (95% CI 91% to 97%) and pooled specificity of 77% (95% CI 69% to 83%) for BCC detection. These studies did not include cSCC. The author's concluded that data were insufficient to determine the accuracy of OCT for the detection of melanoma or cSCC. For BCC detection, they stated that, "initial data on OCT shows potential increased sensitivity and specificity compared with visual inspection and dermoscopy; however, the small number of studies and varying methodological quality means that no implications to guide clinical practice can currently be drawn."

Evidence on the diagnostic accuracy of OCT published since the Cochrane Review above is

limited to a cohort study by Sinx (2020), which evaluated OCT for the diagnosis of BCC in 250 lesions (182 patients) and reported that adding OCT to clinical examination resulted in an increase in the area under the receiver operating characteristic curve of 82.7% to 91.3% ($p<0.001$).[11]

Reflectance Confocal Microscopy (RCM)

Elshot (2023) published a systematic review and meta-analysis to evaluate surgical techniques and presurgical mapping with RCM in the treatment of lentigo malinga (LM) and lentigo maligna melanoma (LMM).[12] LM and LMM are subtypes of melanoma in situ and melanoma that are associated with increased risk for local recurrence. Forty-one studies involving 6330 skin lesions in 6278 patients were included. None of the studies were randomized controlled trials, and only six included RCM. RCM resulted in more negative histological margins when used prior to staged excision compared to staged excision alone ($p<0.0001$). When RCM was compared to Moh's micrographic surgery, the difference in negative histologic margins was not statistically significant ($p=0.69$). The analysis was limited by study heterogeneity and inconsistent follow-up reporting.

Two Cochrane Reviews, both by Dinnes (2018), were published evaluating the use of RCM to diagnose skin cancer: one specific to melanoma diagnosis,[8] and one focused on keratinocyte cancers (e.g., BCC and cSCC).[9]

<u>RCM for Keratinocyte Skin Cancers</u>

The review assessing RCM for diagnosis of cutaneous melanoma included both prospective and retrospective studies comparing RCM with a reference standard (ideally histopathologic diagnosis) in adult patients with pigmented lesions or lesions suspicious for melanoma.[8] There were 18 studies that met all inclusion criteria, for a total of 2,838 lesions, 658 of which were melanomas. Various algorithms were used to facilitate RCM diagnosis. The studies were found to generally be at high or unclear risk of bias across all domains and had high or unclear concern regarding applicability, using the QUADAS-2 checklist.

Eight publications included nine datasets that evaluated RCM for any lesions suspicious for melanoma that were scheduled for excision, including clinically obvious melanomas as well as equivocal or likely benign lesions. All were case series, and three included dermoscopy. RCM was performed with either the VivaScope® 1000 or VivaScope® 1500. Eight of the datasets used histology as the reference standard, and one used expert diagnosis based on clinical and dermoscopic criteria. The reported sensitivities from the studies ranged from 63% to 100% and specificities from 57% to 95%. A pooled analysis was used to produce a summary receiver operating characteristic that estimated a specificity of 82% at a fixed threshold of 90% sensitivity. The sensitivities for dermoscopy in the three studies that included it ranged from 86% to 91%, and the specificities ranged from 28% to 84%. In direct comparisons from these studies and in pooled RCM estimates, RCM accuracy was superior to dermoscopy with a predicted difference in specificity of 40% in the first comparison and 52% in the second at a fixed sensitivity of 90%.

Seven studies evaluated RCM diagnostic performance in equivocal lesions only, meaning that visual examination and dermoscopy did not provide sufficient information for management. All were case series and used the VivaScope® 1500, and three provided data on dermoscopy as well as RCM. Six studies used histology as the reference standard, while the participants in the remaining study underwent follow-up dermoscopic surveillance with searches in cancer

registries for any patients lost to follow-up. The sensitivities of RCM in these studies ranged from 80% to 100% and the specificities ranged from 67% to 95%. An analysis of the pooled results across the various thresholds and algorithms suggested a specificity of 86% at a fixed sensitivity threshold of 90%. Similar to the analyses of any suspicious lesions, the diagnostic accuracy of RCM for equivocal lesions was superior to that of dermoscopy.

Based on this review, the authors concluded that RCM "may have a potential role in clinical practice, particularly for the assessment of lesions that are difficult to diagnose using visual inspection and dermoscopy alone, where the evidence suggests that RCM may be both more sensitive and specific in comparison to dermoscopy. Given the paucity of data to allow comparison with dermoscopy, the results presented require further confirmation in prospective studies comparing RCM with dermoscopy in a real-world setting in a representative population."

Systematic reviews published since the Cochrane Review above include a review by Pezzini (2020), which included 34 studies on RCM for the diagnosis of melanoma (7,352 lesions), 32 of which contributed data to a meta-analysis.[13] In contrast to the Cochrane Review above, the study quality (as assessed by the QUADAS-2) was reported to be generally at low or unclear risk of bias and low for applicability concerns. There was a significant publication bias identified, with a funnel plot asymmetry coefficient of 11.19 (±4.03, 95% CI 2.97 to 19.43, $p<0.01$). The meta-analysis found a pooled sensitivity and specificity for RCM of 96% (95% CI 93% to 98%) and 56% (95% CI 52% to 60%), respectively, while the pooled sensitivity and specificity for dermoscopy was reported to be 90% (95% CI 86% to 93%) and 38% (95% CI 34% to 42%). The authors noted that "the scarcity, heterogeneity and bias associated with the data in literature should be considered when interpreting present conclusions."

In addition, a systematic review by Lan (2020) compared the diagnostic accuracy of RCM and dermoscopy for amelanotic/hypomelanotic melanoma in seven studies.[14] The meta-analysis found pooled sensitivities of 61% (95% CI 37% to 81%) and 67% (95% CI 51% to 81%) for dermoscopy and RCM, respectively, and pooled specificities of 90% (95% CI 74% to 97%) for dermoscopy and 89% (95% CI 88% to 92%) for RCM.

RCM for Keratinocyte Skin Cancers

The other Cochrane Review by the same group focused on RCM as a diagnostic tool for identifying keratinocyte skin cancers, including BCC and cSCC, in adults.[9] Inclusion criteria were similar to the other Cochrane Reviews discussed previously, with the primary target conditions defined as all subtypes of BCC and invasive cSCC (cSCC in situ and Bowen's disease were not considered as positive). A secondary target condition was defined as "any skin cancer, including BCC, cSCC, melanoma, or any rare skin cancer (e.g., Merkel cell cancer), as long as skin cancers other than melanoma made up more than 50% of the disease positive group."

Ten publications reporting on 11 patient cohorts were included in the review, with a total of 2,037 lesions with 464 BCCs included in the BCC datasets, and 834 lesions with 71 cSCCs included in the cSCC datasets. As in the previous reviews, studies were generally assessed as being at high or unclear risk of bias across many domains and had high or unclear concerns regarding applicability. Bias regarding participant selection was the most common, with two-thirds of the cohorts rating as high or unclear for this domain.

There were four studies that provided data on BCC diagnosis in patients with any lesion scheduled for excision (912 lesions, 107 BCCs). All were case series that used the VivaScope® 1500. Three of the studies used dermoscopy to guide RCM image acquisition. The combined sensitivity for the detection of BCC was 76% (95% CI 45% to 92%) and specificity was 95% (95% CI 66% to 99%).

Three studies, all case series that used the VivaScope® 1500, provided data on BCC diagnosis in patients with equivocal lesions (668 lesions, 148 BCCs). Two of the studies included lesions that were suspicious for melanoma, and one study included suspicious non-pigmented lesions. The combined sensitivity and specificity for BCC detection were 94% (95% CI 79% to 98%) and 85% (95% CI 72% to 92%), respectively. The non-pigmented lesion study included dermoscopy data and reported a nearly identical performance for dermoscopy and RCM.

Only two studies provided data on detection of cSCC, one of which included any lesion suspicious for melanoma and one that included only equivocal lesions. Reported sensitivities in these studies were 74% and 77%, and specificities were 92% and 98%, respectively. The study of equivocal lesions reported a similar accuracy for dermoscopy (sensitivity 77%, specificity 99%).

The review authors concluded that:

“It is unclear whether reflectance confocal microscopy (RCM) has a role in clinical practice for the diagnosis of basal cell carcinoma (BCC), although some studies suggest it has the potential to improve diagnoses. There are as yet insufficient data to support its use as a tool for avoidance of diagnostic biopsies in lesions with high clinical suspicion of BCC. In populations with a wider spectrum of lesions, there is potential for both missed BCCs and for misclassification of benign lesions, or other malignant skin cancers such as melanoma, as BCCs. Evidence for the detection squamous cell carcinoma (cSCC) is even more scarce; however, there is a clear suggestion that cSCCs could be missed with RCM. Importantly, data are lacking that compare RCM to usual practice (whether with or without dermoscopy), such that the diagnostic impact of RCM cannot be clearly estimated.”

Evidence on the use of RCM to diagnose keratinocyte cancers published since the Cochrane Review above includes a meta-analysis by Lupu (2019) that evaluated RCM for detection of BCC.[15] This review included 15 studies (4,163 lesions). Similar to the Cochrane Review, the studies were found to generally have high or unclear risk of bias and high or unclear applicability concerns based on the QUADAS-2. The pooled sensitivity and specificity for RCM were 92% (95% CI 87% to 95%) and 93% (95% CI 85% to 97%), respectively. The methodologic concerns and considerable heterogeneity of the studies limit the conclusions that can be drawn from this analysis.

Comparisons Between RCM, OCT, and Spectroscopic Technologies

A systematic review by Blundo (2021) compared the diagnostic accuracies of non-invasive alternatives to dermoscopy for melanoma detection.[16] The gold standard reference was histopathology, with dermoscopic diagnosis accepted only for benign lesions. A total of 62 papers were included in the review, 40 studies of optical-based technologies including MSI, OCT, and RCM, 12 studies of thermal-based technologies, and 10 studies of EIS. The included studies were assessed as having generally moderate to unclear quality based on the CASP checklist. Among the 38 studies that evaluated the diagnostic performance of a

technology, 32 were determined to have a high risk of bias based on the QUADAS-2, and similar results were found regarding applicability concerns, with 24 studies assessed as high concern. Meta-analysis for the diagnosis of melanoma produced a sensitivity of 88.2% (95% CI 80.3% to 93.1%) and specificity of 65.2% (95% CI 55.0 to 74.2%) for RCM, a sensitivity of 93% (95% CI 75.3% to 98.3%) and specificity of 71.2% (95% CI 17.6% to 96.6%) for MSI, and a sensitivity of 95% (95% CI 88.9% to 97.8%) and specificity of 48.9% (95% CI 30.5% to 67.6%) for EIS. There was insufficient OCT data for meta-analysis.

Fluorescent Biotag Imaging

No studies have been published on the clinical validity of fluorescent biotag imaging for the evaluation of suspicious skin lesions.

CLINICAL UTILITY

Direct evidence of the clinical utility of a spectroscopy or imaging technique will be demonstrated if its use leads to management changes that improve outcomes. Outcomes would ideally be evaluated in prospective randomized controlled trials examining health outcomes in patients presenting with pigmented lesions managed with and without the technology.

Pellacani (2022) published the results of a randomized clinical trial evaluating the impact of reflectance confocal microscopy (RCM) on diagnostic accuracy in melanoma patients.[17] A total of 3,165 patients were enrolled from three dermatology referral centers in Italy and randomly assigned 1:1 to standard therapeutic care (clinical and dermoscopy evaluation) with or without adjunctive reflectance confocal microscopy (RCM). The mean (SD) follow-up was 9.6 (6.9) months (range, 1.9 to 37.0 months). The diagnostic analysis included 3,078 patients, as 48 were lost, 39 refused excision. Compared with standard therapeutic care alone, adjunctive RCM was associated with a higher positive predictive value (18.9 vs. 33.3), lower benign to malignant ratio (3.7:1.0 vs. 1.8:1.0), and a number needed to excise reduction of 43.4% (5.3 vs. 3.0). Physicians' years of RCM experience correlated very highly with diagnostic accuracy (r=0.99; 95% CI 0.82 to 0.99; p=0.004) indicating prospective management decision-making is dependent on the RCM experience of the provider. The applicability of this trial is therefore limited to centers with RCM experience. The authors note "the results of this study cannot be attributed to RCM alone because the patient pathway for those without immediate excision foresaw additional dermoscopy and occasional RCM assessments."

Nonrandomized studies have evaluated whether the use of various technologies would lead to management changes.[18-21] Without health outcome data, studies of how physicians use medical tests, or how they may change behavior based on medical tests, do not provide significant additional data to inform clinical utility.

PRACTICE GUIDELINE SUMMARY

American Academy of Dermatology

The American Academy of Dermatology published guidelines on the management of primary cutaneous melanoma in 2019.[22] These guidelines do not make any recommendations regarding spectroscopy or imaging techniques, but state:

“Skin biopsy remains the first step to establish a definitive diagnosis of CM, although various molecular and imaging techniques have been studied as adjuncts to histopathologic assessment of melanocytic neoplasms. Once a lesion has been identified as clinically concerning, dermoscopy can improve diagnostic accuracy and/or help direct optimal and adequate tissue sampling in the case of very large lesions or those in cosmetically or functionally sensitive areas. Newer noninvasive techniques (eg, reflectance confocal microscopy [RCM], as well as electrical impedance spectroscopy, gene expression analysis, optical coherence tomography, and others [see the section Emerging Diagnostic Technologies]) can also be considered as these become more readily available.”

National Comprehensive Cancer Network (NCCN)

The NCCN treatment guidelines for cutaneous melanoma (v2.2023) include the following statement regarding the use of imaging technologies for follow-up surveillance after a melanoma diagnosis:[23]

“Pre-diagnostic clinical modalities (i.e., dermoscopy, total-body photography and sequential digital dermoscopy), non-invasive and other technologies (eg, reflectance confocal microscopy, electrical impedance spectroscopy) may aid in surveillance for new primary melanoma, particularly in patients with high mole count and/or presence of clinically atypical nevi.”

The NCCN guidelines for cancer risk management based on genetic test results (v1.2024) that indicate high melanoma risk from pathogenic *CDKN2A* variants do not address the use of electrical impedance spectroscopy, multispectral image analysis, optical coherence tomography, reflectance confocal microscopy, or fluorescent biotag imaging.[24]

SUMMARY

There is not enough research to show that newer skin lesion imaging and spectroscopy technologies can improve health outcomes for patients suspected of having skin cancer. The diagnostic accuracy of these tests has not yet been clearly determined. In addition, current clinical practice guidelines do not recommend their use. Therefore, the use of electrical impedance spectroscopy, multispectral image analysis, optical coherence tomography, and reflectance confocal microscopy are considered investigational for evaluation of skin lesions.

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CODES

NOTE: Dermoscopy is considered to be a part of a normal skin lesion evaluation and not separately reimbursable.

Codes	Number	Description
CPT	~~0470T~~	~~Optical coherence tomography (OCT) for microstructural and morphological imaging of skin, image acquisition, interpretation, and report; first lesion~~ (Deleted 01/01/2023)
	~~0471T~~	~~;each additional lesion (List separately in addition to code for primary procedure)~~ (Deleted 01/01/2023)
	0658T	Electrical impedance spectroscopy of 1 or more skin lesions for automated melanoma risk
	0700T	Molecular fluorescent imaging of suspicious nevus; first lesion
	0701T	Molecular fluorescent imaging of suspicious nevus; each additional lesion (List separately in addition to code for primary procedure)
	96931	Reflectance confocal microscopy (RCM) for cellular and sub-cellular imaging of skin; image acquisition and interpretation and report, first lesion
	96932	;image acquisition only, first lesion
	96933	;interpretation and report only, first lesion
	96934	;image acquisition and interpretation and report, each additional lesion (List separately in addition to code for primary procedure)
	96935	;image acquisition only, each additional lesion (List separately in addition to code for primary procedure)
	96936	;interpretation and report only, each additional lesion (List separately in addition to code for primary procedure)
	96999	Unlisted special dermatological service or procedure
HCPCS	None	

Date of Origin: *December 2021*