Medical Coverage Policy

Effective Date.....12/15/2024
Next Review Date.....10/15/2025
Coverage Policy Number..... 0240

Reflectance Confocal Microscopy

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Related Coverage Resources

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy

will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses the use of reflectance confocal microscopy (RCM) as a technology that has been proposed for the early detection, screening, or surveillance of skin cancer.

Coverage Policy

Reflectance confocal microscopy (RCM) when used for the early detection, screening or surveillance of skin cancer is considered experimental, investigational or unproven.

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

General Background

There are two main types of skin cancer: nonmelanoma skin cancer and melanoma. Types of nonmelanoma skin cancer include basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). According to the National Comprehensive Cancer Network® (NCCN®), basal cell carcinoma (BCC) is the most common cancer in the United States with squamous cell carcinomas (SCCs) being the second most common type of skin cancer. When compared with SCC, BCCs are much less likely to metastasize, with a metastatic rate of <0.1% and generally have a good prognosis. Both BCC and SCC can produce substantial local destruction along with disfigurement and may involve extensive areas of soft tissue, cartilage, and bone. SCCs generally have a good prognosis, with 5-year survival of about 98% (NCCN, 2024). SCCs are usually a slow growing, nonaggressive cancer. However, 2%–5% can exhibit rapid growth and metastases with the rate of metastasis from all skin sites ranging from 0.5%–5.2% (Ferri, 2023). A precise estimate of the total number and incidence rate of nonmelanoma skin cancers is not possible because reporting to cancer registries is not required. However, it has been estimated that about three million individuals are diagnosed each year. That number exceeds all other cases of cancer estimated by the American Cancer Society for 2024, which is about 2million (National Cancer Institute [NCI], 2024).

Melanoma, also called cutaneous melanoma or malignant melanoma, is a malignant disease of the skin and one of the most dangerous forms of skin cancer. Although melanoma accounts for less than 5% of skin cancer cases, it accounts for approximately three-fourths of all skin cancer deaths. Early detection and treatment are the best strategies to reduce the mortality and morbidity associated with melanoma. Only 20 to 30 percent of melanomas are found in existing

moles, while 70 to 80 percent arise on normal skin with no associated nevus (Cymerman, 2016). Moles are common with the average person having 10–40. Puberty is a time when the size and number of nevi increase with very few moles developing after the age of 40 (Hooper and Goldman, 1999).

Risk factors for the development of single or multiple primary melanomas include male sex, age >60 years, phenotypic predisposition, personal medical history/comorbidities, genetic predisposition, and environmental factors (NCCN, 2024; NCI, 2024). High-risk individuals for melanoma include those with a personal history of prior primary melanoma, presence of pigmented lesions (e.g., atypical nevi, dysplastic nevi) or a first-(i.e. parent, sibling or child) or second-degree relative with melanoma (NCCN, 2024; NCI, 2024; Goodson, et al., 2010; Banky, et al., 2005; Oliveria, et al., 2004; Haenssle, et al., 2004). There are certain characteristics that place patients at higher risk of dying from melanoma. Despite there being a lower incidence of melanoma in Black patients, the five-year relative survival is lower than for white patients (69% vs. 93%) (Geller and Swetter, 2021; Cormier, et al., 2006). This trend has been observed in the Hispanic American population and is thought to be due to a greater likelihood of presenting with advanced disease compared to non-Hispanic white individuals (Cockburn, et al., 2006). The greater mortality in patients with skin of color may be due to several factors including delayed diagnosis due to a lower perceived risk of disease or lower rates of skin examinations, locations of melanoma in atypical non-sun-exposed areas (eg, leg, hip, and feet), a higher proportion of acral and nodular subtypes, and a decreased ability to seek care for localized disease (Carter, et al., 2021; Coups, et al., 2012; Myles, et al., 2012; Pollitt, et al., 2011). Almost 50 percent of melanoma deaths in the United States occur in white men over the age of 50 (Geller and Swetter, 2021). The poor survival rate in men may be due to differences in tumor biology and by differences in skin awareness, self-examination, and other early detection practices.

The assessment of suspicious skin lesions begins with a physical examination and visual inspection of the skin with the naked eye. Dermoscopy including digital epiluminescence microscopy (DELM) has evolved into an established technology used as an adjunct to a normal eye exam and is considered to be an integral part of the exam depending on the lesions being examined. Additional noninvasive technologies are proposed to provide better examination of lesions and assist the examiner in deciding whether a lesion should be biopsied. None of these devices can diagnosis skin cancer. Biopsy is considered the diagnostic "gold standard". Noninvasive technologies include: total-body photography (TBP); visual image analysis; electrical impedance devices; multispectral image analysis; ultrasound, optical coherence tomography [OCT]; and reflectance confocal microscopy (RCM). There is insufficient evidence in the peer-reviewed literature to support the use of these noninvasive technologies for the evaluation and surveillance of melanoma.

Reflectance Confocal Microscopy
Reflectance confocal microscopy (RCM), also known as confocal scanning laser microscopy (CSLM), uses a near infrared laser that emits near-infrared light (830 nm) to obtain images of the top layers of the skin. The images are magnified and information regarding cell structure and the architecture of the surrounding tissues is evaluated. Combinations of features are assessed to give a positive or negative diagnosis of melanoma. RCM is proposed to be comparable to conventional histology and proposed for use as an adjunctive diagnostic tool to examination and dermoscopy in difficult to diagnose lesions and therefore, aid in determining if a lesion is benign or is a melanoma. It enables high-resolution, noninvasive, real-time imaging of the epidermis and upper dermis at cellular resolution. Its primary field of application is the differential diagnosis of pigmented lesions. Studies evaluating the accuracy of confocal scanning laser RCM/CSLM in assessing skin lesions for melanoma have reported sensitivity, specificity, positive and negative predictive values ranging from 90.74% to 97.5%, 83% to 99%, 70.6% to 97.5%, and 98.17% to 99%, respectively.

RCM is considered an evolving technology with several limitations. The depth of imaging is confined to the epidermis and papillary dermis which may result in false negatives. Penetration of RCM light may be hampered by hyperkeratosis, reflective creams and surface particles. Another limitation is the challenge that the interpreter has of distinguishing between cells with similar reflection index and shape (e.g., Langerhans cells versus dendritic melanocytes at the spinous layer). RCM is a time consuming exam taking an average of seven minutes per lesion. Clinical-dermatoscopic skills are required, as well as adequate training and experience to read RCM images and make the correct interpretation. It has yet to be determined if the advantages of the clinical utility of RCM as an adjunctive diagnostic tool are greater than the risk of over-excising benign lesion and misdiagnosing melanomas as benign. In some cases RCM may be used for cosmetically sensitive areas to avoid excision (Hayes, 2019; Que, et al., 2016; Stevenson, et al., 2013; Gerger, 2008; Langley, 2007; Gerger, 2006). There is insufficient evidence to support the clinical utility of RCM.

U.S. Food and Drug Administration (FDA): Confocal microscopes are approved by the FDA 510(k) as a class II device. Examples of these devices include the VivaScope System 1500 and the handheld VivaScope 3000 (Lucid, Inc., Rochester, New York). The VivaScope is intended "to acquire, store, retrieve, display and transfer in vivo images of tissue, including blood, collagen and pigment, in exposed unstained epithelium and the supporting stroma for review by physicians to assist in forming a clinical judgment". The VivaScope 3000 is a hand-held device designed to access hard to reach areas such as nose, ears, or eyes. The 1500 and 3000 systems can be used alone or together. The SIAscope II (Astron Clinica Limited, Crofton MD) is FDA approved as a "non-invasive skin analysis system, which provides a synthesized 'image' showing the relative location of blood collagen and pigment" (FDA, 2008; 2003).

Literature Review: Pezzini et al. (2020) conducted a systematic review and meta-analysis to assess the accuracy of reflectance confocal microscopy (RCM) in diagnosing cutaneous malignant melanoma (MM) according to study design, lesion type and diagnostic modality. The meta-analysis included 32 studies (n=7352 lesions) that met the criteria of reporting RCM lesion classifications and included either histopathology diagnoses or long-term clinical follow-up data that verified the accuracy of the original diagnosis with evaluations that were performed by an expert/trained RCM investigator. Seven studies were prospective-non interventional, three were prospective interventional studies and 22 were retrospective reviews. Studies were excluded if they were case series/case reports with <10 lesions; pertained to special sites such as oral mucosa, lips, eyes, or genital area; or were for other types of skin cancers. The secondary outcome measure was a comparison of diagnostic accuracy to dermoscopy. The length of follow up was not reported. The pooled sensitivity was 92% with a pooled specificity of 70%. In regards to study design, the diagnostic sensitivity was high for all study types. The specificity was lower for prospective interventional studies. Diagnostic accuracy was high for all lesion types with the highest specificity reported in consecutive lesions (77%) highly suspicious for MM (65%). RCM diagnostic accuracy was 56% vs. dermoscopy at 38%. No serious adverse events were reported. Author noted limitations of the meta-analysis include heterogeneity of the inclusion and exclusion criteria of the studies, wide range of study designs, use of algorithms or scoring systems, and the range of RCM investigator expertise. Additional high quality studies with large patient populations and long term follow up are needed to validate the outcomes of this analysis and establish the clinical utility of RCM in the diagnosis of MM.

Edwards et al. (2016) conducted a systematic review and health technology assessment on the clinical effectiveness of the VivaScope 1500 and 3000 systems in the diagnosis of equivocal skin lesions. VivaScope 3000 was also evaluated for the assessment of lesion margin delineation prior to surgical excision of lesions. Eleven prospective observational studies and five retrospective reviews were included. No randomized controlled trials (RCTs) were found. One study suggested that VivaScope used subsequent to dermoscopy may improve diagnostic accuracy of equivocal

skin lesions compared with dermoscopy alone, especially for malignant melanomas. Another study reported that the sensitivity for dermoscopy plus VivaScope 1500 were the same (100%). Clinical data regarding margin delineation are scarce. The studies were too heterogeneous to be used in a meta-analysis. The authors noted that apart from diagnostic accuracy and lesion recurrence rate (only reported by one study), none of the outcomes specified in the protocol were reported in the outcomes and in some of the studies, there was paucity of reported data on number of patients with positive and negative test results. Other limitations of the studies included: lack of a comparator; retrospective study design; small patient populations; heterogeneity in cancer types (melanoma, basal cell and squamous cell carcinoma); and variation in reporting results as patient based or lesion based. The authors suggested that high-quality RCTs are required to assess diagnostic accuracy of dermoscopy plus VivaScope compared with dermoscopy alone in people with equivocal skin lesions, as well as the margin delineation accuracy of VivaScope compared with dermoscopy alone. RCTs focusing on clinical outcomes, test failure rates, number of biopsies performed, repeat biopsies, recurrence rates and morbidity associated with surgery are required.

Pellacani et al. (2014) conducted a prospective case series (n=1005) to assess the impact of reflectance confocal microscopy (RCM) in the routine diagnosis of melanoma. Patients had atypical moles and were initially referred to either no further examination or to RCM. The RCM group was further subdivided into RCM documentation (suspicious lesions already qualified for excision) or RCM consultation (i.e., RCM would determine if the lesion was excised or monitored with digital dermoscopy). RCM did not affect the outcome in patients already scheduled for excision. Patients referred for RCM had a higher number of nevi (>100 nevi; 19%) and atypical nevi (>5; 15%) compared to patients referred for RCM documentation and patients without RCM referral ($p<0.0001$). Personal and/or familial history of melanoma was recorded in approximately 8% of patients. A total of 493 lesions were referred to RCM of which 183 underwent RCM documentation and 308 RCM consultations. Histopathology identified 23 melanomas. RCM proposed the same diagnosis as histopathology in 82.6% of melanomas. A total of 109 of 308 RCM consultation lesions were excised, six cases of melanoma were diagnosed and five cases were confirmed as melanomas. Twenty-eight lesions deferred to follow-up were excised based on dermoscopic changes. Overall RCM proposed diagnosis was concordant with histopathological diagnosis in 76.3% of cases and reduced the number of excision by 46.5%. Limitations of the study include: 12.3% of patients were lost to follow-up; 11 patients either refused RCM or were unable to undergo RCM; and the study population was a low risk group referred for screening.

Stevenson et al. (2013) conducted a systematic review of the literature to determine the diagnostic accuracy of reflectance confocal microscopy (RCM) as an adjunctive tool to dermoscopy for the evaluation of melanoma. No systematic reviews or meta-analysis were found. Studies were primarily in the form of case series, case reports, and descriptive correlation studies that only described RCM features and narrative reviews. Five studies (n=909 lesions) met inclusion criteria and were eligible for meta-analysis. Meta-analysis returned a per lesion sensitivity of 93% (range 91%–97%) and a specificity of 76% (range 68%–86%). The average prevalence of melanoma was 36%. The authors noted that a weakness of the study was that the studies may not have focused on the pertinent patient populations to test the ability of RCM as an add-on test to dermoscopy. Limitations of the studies included use of various types of melanoma scoring systems and outcome measures, heterogeneity of lesion locations, and two studies did not list number of patients evaluated.

Professional Societies/Organizations

American Academy of Dermatology (AAD): In the guidelines for the management of primary cutaneous melanoma, AAD (2019) states that biopsy is the first step for a definitive diagnosis of cancer. In the discussion on emerging diagnostic technologies, the Academy notes that the use of noninvasive imaging/electrical data acquisition and evaluation tools including RCM, electrical impedance spectroscopy combined with digital dermoscopy, optical coherence tomography, cross-

polarized light and fluorescence photography, and high-frequency ultrasound are being investigated to further classify melanocytic lesions as either benign or malignant. AAD makes no recommendation on their use as evidence regarding effectiveness, clinical utility, and competing strategies is needed.

The AAD (2018) guidelines of care for the management of cutaneous squamous cell carcinoma (cSCC) do not address the use of noninvasive imaging/electrical data acquisition and evaluation tools. The Academy notes that the diagnosis of one cSCC puts the patient at risk for developing additional cSCC and other skin cancers such as basal cell carcinoma and melanoma.

In a position statement on reflectance confocal microscopy (RCM), the American Academy of Dermatology (ADA) (2019) states their support for "the use of RCM as a modality for in vivo microscopic examination of suspicious epidermal and superficial dermal skin lesions for diagnosing skin pathology when clinically appropriate." However, they recommend that additional research be conducted about the utility and efficacy of RCM in the diagnosis of skin lesions. The ADA's disclaimer states that the position statement is provided for educational and informational purposes only to offer physicians guiding principles and policies regarding the practice of dermatology not to establish a legal or medical standard of care.

National Cancer Institute (NCI): According to NCI (2024), squamous cell carcinoma and basal cell carcinoma are the most common forms of skin cancer. Both have a better prognosis as they are not as aggressive as melanoma. Risk factors for melanoma include sun exposure, pigmentary characteristics, multiple nevi, family and personal history of melanoma, immunosuppression and environment exposures. Fair-skinned individuals exposed to the sun are at high risk and certain types of pigmented lesions (dysplastic or atypical nevi), with several large nondysplastic nevi, with many small nevi, or with moderate freckling have a twofold to threefold increased risk of developing melanoma. Familial dysplastic nevus syndrome or the presence of several dysplastic or atypical nevi increases the risk of developing melanoma greater than fivefold. NCI stated that the only widely proposed screening procedure for skin cancer is visual examination of the skin, including both self-examination and clinical examination. More than 90% of melanomas can be recognized with the naked eye. A biopsy should be performed for any suspicious lesion.

National Comprehensive Cancer Network® (NCCN®): In the discussion for follow-up following diagnosis and treatment of melanoma, NCCN's Clinical Practice Guidelines in Oncology™ (2024) states that patients cured of an initial primary melanoma are at increased risk for a second melanoma. Patients with risk factors that increase the chance for recurrence (e.g., prior multiple primary melanomas, family history of melanoma and presence of atypical/dysplastic nevi) should be enrolled in a more intensive surveillance program and may benefit from adjuncts such as high-resolution total body photography. These risk factors include multiple primary melanomas, positive family history and the presence of multiple dysplastic nevi.

NCCN's Clinical Practice Guidelines in Oncology (2024) on squamous cell skin cancer (SCC) states that 13–50% of patients diagnosed with one SCC will develop another within five years. These patients are also at increased risk of developing cutaneous melanoma and basal cell cancer (BCC). Long term surveillance is required. The guidelines do not address the use of noninvasive imaging/electrical data acquisition and evaluation tools.

Noninvasive imaging/electrical data acquisition and evaluation tools are not mentioned in NCCN's Clinical Practice Guidelines in Oncology (2024) on basal cell skin cancer. Follow up for those patients with basal cell skin cancer includes a complete skin exam every 6–12 months for the first five years and then annually for life.

U.S. Preventive Services Task Force (USPSTF): In 2023, the USPSTF published an update to the 2016 systematic review on visual screening for skin cancer. The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of visual skin examination by a clinician to screen for skin cancer in adolescents and adults.

The 2016 systematic review included thirteen studies, mostly observational cohort studies and retrospective reviews (n=10), met inclusion criteria. Acceptable screening tests were defined as whole or partial visual skin examination with or without tools to aid examination (e.g., dermatoscopy, whole body photography). The report noted that definitive diagnosis of non-melanoma and melanoma skin cancer is made by shave, punch or excision biopsy depending on the type of skin cancer. The authors concluded that due to the limited evidence, no firm conclusions on skin cancer screening and melanoma mortality could be made. Noted limitations of the fair-quality studies included: various follow-up times; short-term follow-ups; noncomparative study design; subjects tended to be younger women even though the incidence of skin cancer is highest in older men; lack of complete data presented; and lack of rigorous studies on skin cancer screening conducted in the United States with an application in primary care or internal medicine settings.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD		No Determination found	
LCD		No Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
96932	Reflectance confocal microscopy (RCM) for cellular and sub-cellular imaging of skin; image acquisition only, first lesion

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4. American Academy of Dermatology (AAD). Guidelines of care for the management of cutaneous squamous cell carcinoma. Published Jan 10, 2018. Accessed Oct 7, 2024. Available at URL address: https://www.aad.org/member/clinical-quality/guidelines/scc

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Revision Details

Type of Revision	Summary of Changes	Date
Annual review	• Title change to Reflectance Confocal Microscopy • Removed all content except for reflectance confocal microscopy	10/15/2024
Annual review	• Updated to new template and formatting standards. • No changes to criteria.	10/15/2023