Medical Coverage Policy | Reflectance Confocal Microscopy for Evaluating Skin Lesions for Suspected Malignancy

EFFECTIVE DATE: 01|01|2016
POLICY LAST REVIEWED: 03|06|2024

OVERVIEW

Reflectance confocal microscopy (RCM) is a relatively new technique that allows noninvasive imaging of the epidermis and superficial dermis to more accurately evaluate both melanocytic and nonmelanocytic skin lesions. RCM acquires images in the horizontal plane (en face), allowing assessment of tissue pathology underlying dermoscopic structures of interest at a cellular-level resolution.

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

Medicare Advantage Plans

Reflectance confocal microscopy is considered not covered as a technique to evaluate or serially monitor pigmented skin lesions as there is insufficient evidence to determine the effects of the technology on health outcomes.

Commercial Products

Reflectance confocal microscopy is considered not medically necessary as a technique to evaluate or serially monitor pigmented skin lesions as there is insufficient evidence to determine the effects of the technology on health outcomes.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage.

BACKGROUND

Reflectance Confocal Microscopy

Reflectance confocal microscopy, 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. 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 a 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) process. 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 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).

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.

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): 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.

National Cancer Institute (NCI): According to NCI (2022), 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™ (2022) 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 (2022) 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 (2022) 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): The USPSTF published a 2016 updated systematic review on visual screening for skin cancer. 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.

National Institute for Health and Clinical Excellence (NICE): The 2022 NICE guidelines (United Kingdom) on the assessment and management of melanoma included a review of the literature on dermoscopy and other visualization techniques. NICE stated that dermoscopy is an accepted practice but the accuracy and clinical utility depends on the experience of the practitioner who is using it and recommended its use in the assessment of lesions when performed by a trained professional. Based on the literature review, NICE did not recommend the routine use of confocal microscopy or computer-assisted diagnostic tools. NICE recommended that baseline photography (preferably dermoscopic) be used for a clinically atypical

melanocytic lesion that does not need excision and to review the clinical appearance with the images every three months. NICE noted that photography (mole mapping), might help to identify changes in moles but the quality is variable. The Guideline Development Group was uncertain about the most appropriate timing for sequential photography to detect significant changes in pigmented lesions to aide in the diagnosis of early melanoma.

Summary
Based on a systematic review of the literature, NICE stated that there is insufficient evidence to recommend the routine use of VivaScope 1500 and 3000 imaging systems to help decide whether to biopsy and excise skin lesions in people with suspected melanoma. Thirteen studies (randomized, prospective cohort and retrospective) met inclusion criteria and reported on the use of VivaScope or reflectance confocal microscopy (RCM) in diagnosing suspected or equivocal melanoma lesions and three reported its use in lesion margin delineation. Six studies used VivaScope 1500 and one used VivaScope 1500 or 3000. Six studies used earlier versions of VivaScope. Comparators included dermoscopy and histopathology. Meta-analysis could not be performed due to the heterogeneity of the studies including: study design; patient population (e.g., prior history of melanoma); and variation in reporting results as patient based or lesion based (NICE, 2015).

CODING

Medicare Advantage Plans and Commercial Products
The following codes are not covered for Medicare Advantage Plans and not medically necessary for Commercial Products:

96931 Reflectance confocal microscopy (RCM) for cellular and sub-cellular imaging of skin; image acquisition and interpretation and report, first lesion
96932 Reflectance confocal microscopy (RCM) for cellular and sub-cellular imaging of skin; image acquisition only, first lesion
96933 Reflectance confocal microscopy (RCM) for cellular and sub-cellular imaging of skin; interpretation and report only, first lesion
96934 Reflectance confocal microscopy (RCM) for cellular and sub-cellular imaging of skin; image acquisition and interpretation and report, each additional lesion (List separately in addition to code for primary procedure)
96935 Reflectance confocal microscopy (RCM) for cellular and sub-cellular imaging of skin; image acquisition only, each additional lesion (List separately in addition to code for primary procedure)
96936 Reflectance confocal microscopy (RCM) for cellular and sub-cellular imaging of skin; interpretation and report only, each additional lesion (List separately in addition to code for primary procedure)

RELATED POLICIES

None

PUBLISHED

Provider Update, May 2024
Provider Update, May 2023
Provider Update, July 2022
Provider Update, October 2021
Provider Update, December 2020

REFERENCES

1. Systematic review of diagnostic accuracy of reflectance confocal microscopy for melanoma diagnosis in patients with clinically equivocal skin lesions. Stevenson AD[1], Mickan S, Mallett S, Ayya M. http://www.ncbi.nlm.nih.gov/pubmed/24282659
2. American academy of Dermatology; Melanoma update: recent technological advances are helping dermatologists diagnose and treat early stage melanomas; https://www.aad.org/media/news-releases/melanoma-update-recent-technological-advances-are-helping-dermatologists-diagnose-and-treat-early-stage-melanomas

3. U.S. Preventive Services Task Force (USPSTF), Screening for Skin Cancer in Adults: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force, https://www.uspreventiveservicestaskforce.org/BrowseRec/Index
4. National Institute for Health and Clinical Excellence (NICE), VivaScope 1500 and 3000 imaging systems for detecting skin cancer lesions; https://www.nice.org.uk/guidance/dg19
5. NCBI; Noninvasive Diagnostic Techniques for the Detection of Skin Cancers
6. NICE; Diagnostic Assessment Programme, VivaScope 1500 and 3000 Imaging systems for detecting and monitoring skin cancer lesions; https://www.nice.org.uk/guidance/DG19/
7. Alarcon I, Carrera C, Palou J, Alos L, Malvehy J, Puig S. Impact of in vivo reflectance confocal microscopy on the number needed to treat melanoma in doubtful lesions. Br J Dermatol. 2014 Apr;170(4):802-8.
8. Que SK, Fraga-Braghiroli N, Grant-Kels JM, Rabinovitz HS, Oliviero M, Scope A. Through the looking glass: Basics and principles of reflectance confocal microscopy. J Am Acad Dermatol. 2015 Aug;73(2):276-84.
9. Gerger A, Hofmann-Wellenhof R, Langsenlehner U, Richtig E, Koller S, Weger W, et al. In vivo confocal laser scanning microscopy of melanocytic skin tumours: diagnostic applicability using unselected tumour images. Br J Dermatol. 2008 Feb;158(2):329-33.
10. Langley RG, Walsh N, Sutherland AE, Propperova I, Delaney L, Morris SF, Gallant C. The diagnostic accuracy of in vivo confocal scanning laser microscopy compared to dermoscopy of benign and malignant melanocytic lesions: a prospective study. Dermatology. 2007;215(4):365-72.
11. Pellacani G, Pepe P, Casari A, Longo C. Reflectance confocal microscopy as a second-level examination in skin oncology improves diagnostic accuracy and saves unnecessary excisions: a longitudinal prospective study. Br J Dermatol. 2014 May 29.
12. Hayes, Inc. Directory Report. Photographic surveillance for early detection of malignant melanoma. Lansdale, PA: Hayes, Inc. Mar 30, 2011. Reviewed Mar 2012–Feb 2015. Archived 2016.
13. Hayes, Inc. Evidence Analysis Research Brief. Reflectance confocal microscopy for diagnosis of melanoma. Hayes, Inc; Dec 20, 2019.
14. National Comprehensive Cancer NetworkR (NCCNR). Clinical Practice Guidelines in Oncology™. Basal Cell Skin Cancer V2.2022. Updated Mar 24, 2022. Accessed Sep 7, 2022. Available at URL address: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1416
15. National Comprehensive Cancer NetworkR (NCCNR). Clinical Practice Guidelines in Oncology™. Melanoma: cutaneous V 3.2022. Apr 11, 2022. Accessed Sep 7, 2022. Available at URL address: https://www.nccn.org/professionals/physician_gls/default.aspx#site
16. National Comprehensive Cancer NetworkR (NCCNR). Clinical Practice Guidelines in Oncology™. Squamous Cell Skin Cancer V 2.2022. May 2, 2022. Accessed Sep 7, 2022. Available at URL address: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1465
17. U.S. Food and Drug Administration (FDA). 510(k) premarket notification database. Accessed Sep 7, 2022. Available at URL address: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm
18. U.S. Food and Drug Administration (FDA). Premarket approval (PMA) database Accessed Sep 7, 2022. Available at URL address: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm
19. U.S. Food and Drug Administration (FDA). Nevisense. Premarket approval (PMA) database. Product code ONV. Accessed Sep 7, 2022. Available at URL address: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm
20. National Cancer Institute (NCI). Heath Professional. Genetics of Skin Cancer (PDQR). Updated Jun 28, 2022. Accessed Sep 7, 2022. Available at URL address: https://www.cancer.gov/types/skin/hp/skingenetics-pdq
21. National Cancer Institute (NCI). Heath Professional. Melanoma treatment (PDQR). Updated May 27, 2022. Accessed Sep 7, 2022. Available at URL address: https://www.cancer.gov/types/skin/hp/melanoma-treatment-pdq#section/all
22. National Cancer Institute (NCI). Heath Professional. Skin Cancer Screening (PDQR). Updated Sep 2, 2022. Accessed Sep 7, 2022. Available at URL address: https://www.cancer.gov/types/skin/hp/skinscreening-pdq

CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS