Anthem

Medical Policy

Subject: Optical Detection for Screening and Identification of Cervical Cancer
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Description/Scope

This document addresses the use of optical detection for the screening and identification of cervical cancer.

Note: Colposcopy is considered the standard of care and is not addressed in this document.

Note: Please see the following related document for additional information:

- CG-MED-53 Cervical Cancer Screening Using Cytology and Human Papillomavirus Testing

Position Statement

Investigational and Not Medically Necessary:

The use of optical detection for the detection or identification of cervical cancer is considered **investigational and not medically necessary.**

Rationale

Optical Detection
On March 16, 2006 the U.S. Food and Drug Administration (FDA) granted pre-market approval (PMA) for the first optical detection system, the Luma™ Cervical Imaging System, for use as an adjunct to colposcopy for the identification of pre-cancerous and cancerous cervical lesions. The available data regarding this system is limited to a single study of 604 individuals undergoing colposcopy for evaluation of suspicious cervical lesions (Huh, 2004). The study involved the comparison of colposcopy results with those from the Luma Cervical Imaging System and histological findings. The authors reported 90% sensitivity for this method, stating that the use of the Luma device is predicted to identify 33% more high-grade cervical intraepithelial neoplasia (CIN) grade 2-3 lesions compared to colposcopy alone. While the results of this single study are promising, further evidence is needed to make an effective assessment of the utility of this device in clinical practice and on long-term clinical outcomes. In 2010, a post-market clinical trial of the Luma device was terminated due to withdrawal of the FDA PMA for the device; reason for withdrawal is not cited.

In 2014, a systematic review was conducted by Adelman with the objective of describing novel innovations and techniques for detecting high-grade cervical dysplasia. The inclusion criteria for published articles were (1) studies investigating noncolposcopic evaluation of the cervix for the detection of cervical dysplasia, (2) original research conducted within the past 10 years, (3) ability to calculate sensitivity and specificity from the data presented, and (4) available in the English language. A total of 32 articles met the inclusion criteria and were reviewed by the single author of the study. The author concluded:

> If a device is to eventually replace the colposcope, it will likely combine technologies to best meet the needs of the target population. As such, no single instrument may prove to be universally appropriate. None of the modalities discussed in this review are currently in a position to replace standard colposcopy…

In a 2018 systematic review and meta-analysis Yang and colleagues reported on nine studies which evaluated the accuracy of an optical detection system for cervical screening. The nine studies encompassed 2730 participants. Pooled sensitivity was found to be 76% (95% confidence interval [CI], 73-80%) and pooled specificity was 69% (95% CI, 67-71%). The analysis did not include the performance of an optical detection system for CIN II or higher. All studies were conducted in advanced areas and hospitals. Data collected from rural areas may lead to different conclusions. The studies were conducted in China and findings could not be generalized to other populations.

In 2021, Suchońska and colleagues reported on a single-center prospective study involving 130 individuals in Poland with abnormal Pap smear results. The aim of the study was to evaluate the efficacy and accuracy of an optoelectronic device in detecting CIN or cervical cancer. Participants underwent a cervical examination with a real-time optoelectronic scanner, which was followed by a colposcopy. For the 94 participants with an abnormal colposcopy, cervical biopsy was performed. Histopathological diagnosis was the reference standard method. Follow up was carried out for 4 years. The sensitivity and specificity for an abnormal cervical biopsy result were 65% and 55%, respectively; the positive predictive value was 58%. The authors concluded that an optoelectronic method might be useful as an initial cervical cancer screening, possibly in combination with other methods, in places like developing countries where standard methods of cervical cancer detection are not readily available. However, the relatively low specificity and high rate of false positive results were seen by the authors as disadvantages to the device.

In a 2021 single-center, prospective, case–control study in China by Wang and colleagues, the optoelectronic device was evaluated to determine its efficacy in detecting CIN and cervical cancer in individuals infected with high-risk human papillomavirus (HR-HPV). Among the 1344 individuals recruited for the study, 301 were determined to be HR-HPV positive. Optoelectronic examination was performed before performing standard colposcopy. The sensitivity and specificity of the device in identifying individuals with CIN grade 2 or worse (CIN2+) were 96.3% and 46.4%, respectively, compared with 85.2% and 40.5% for colposcopy, respectively. The high false positive rate was reduced when optoelectronic results were combined with HPV 16/18 genotyping (both positive) which gave the highest specificity at 83.6%. The authors concluded that the optoelectronic method is helpful for triage of HR-HPV positive individuals and "is suitable in regions where colposcopy and cytology are unavailable, patient follow-up is difficult or situations in which reducing the waiting time for results is crucial." They recommended further evaluation in larger populations to clearly establish the clinical utility of optoelectronic screening.

In another 2021 single-center, prospective study in China, Wei and colleagues sought to evaluate the clinical value of optoelectronic screening for CIN2+. A total of 458 individuals were recruited for cervical cancer screening including optoelectronic screening, HPV testing, and cytological testing using the ThinPrep cytology test (TCT). The sensitivity and specificity of the optoelectronic device were 83.78% and 78.86%, respectively, for CIN2+. The sensitivity of the optoelectronic device was similar to that of TCT (72.97%, p=0.344) and HPV testing (89.19%, p=0.754), while the specificity of the optoelectronic device was significantly higher than that of TCT

(55.58%, p<0.001) and HPV testing (50.59%, p<0.001). This study also compared the clinical performance of the optoelectronic device with that of TCT in detecting CIN2+ in 241 HR-HPV-positive individuals. The optoelectronic device showed a higher specificity (50%vs 39.9%, p=0.004), PPV (22.96% vs 18.83%, p<0.001), and NPV (98.11% vs 95.4%, p<0.001) than TCT for detection of CIN2+. The sensitivities of both methods were similar (93.94% vs 87.88%, for the optoelectronic device vs TCT, respectively, p=0.625). However, although TCT can grade cervical abnormalities, the optoelectronic device cannot. The authors concluded that there is potential for an optoelectronic device to be used as a screening tool for cervical cancer, but the study population was small, and the clinical value needs to be confirmed in a larger population.

None of the major authoritative organizations that address cervical cancer screening mention the use of an optical detection system as part of a cervical cancer screening recommendation. This includes the U.S. Preventive Services Task Force (USPSTF, 2018), the National Comprehensive Cancer Network (NCCN, 2023), the American College of Obstetrics and Gynecology (2021), the American Cancer Society (2020), and American Society for Colposcopy and Cervical Pathology (2018).

While the Luma system is no longer available in the United States, other optical detection systems are currently being studied and have been approved for use in Europe and Asia.

Background/Overview

According to the American Cancer Society, in 2023 there will be approximately 13,960 new cases of cervical cancer diagnosed in the United States and approximately 4310 deaths from the disease. Factors that increase the risk of developing cervical cancer include presence of the human papilloma virus (HPV), advanced age, and sexual history. HPV is a sexually transmitted virus that has been identified as the cause of the vast majority of cervical cancers. The more partners someone has had, the more likely they are to have been exposed to the virus. Individuals who regularly have cervical cancer screenings through the Pap smear test have a reduced likelihood of mortality due to cervical cancer. This is due to early identification of abnormal cells that may lead to cervical cancer and by early detection of existing cervical cancer.

Cervical cancer develops through a gradual, progressive series of well-defined pre-cancerous lesions. In some early phases of the process these pre-cancerous lesions can revert back to healthy tissue. In other moderately advanced phases, the lesions can persist for many years without progressing into cancer.

Screening and monitoring for cervical cancer is primarily done with Pap smear tests. This test is done by using a specialized brush and/or spatula to scrape cells from the surface of the cervix in order to view them under a microscope. Different phases of pre-cancerous and cancerous cells from the cervix look cytologically different from each other, allowing identification. If abnormal cells are found using a Pap smear test, the lesion with the abnormal cells can either be treated or monitored over time to prevent cervical cancer. Some lesions and cells are more difficult to identify than others. Under these circumstances additional work-up is required.

There are currently two methods for doing further evaluation of suspect or unidentified cells recommended by major medical societies. The first is to repeat the Pap smear test. The second is to test for HPV DNA. If such DNA is present, the likelihood that a lesion is pre-cancerous is greater than if it was not found.

At this time, the use of repeat Pap smears and detection of HPV DNA is considered the standard of care for follow-up investigation of unclear or suspect cervical lesions. Colposcopy, a technique that directly visually inspects the cervix following exposure to a mild acetic acid solution, is usually reserved for diagnosing the most difficult cases.

Another proposed method is optical detection which uses a specialized camera and light source connected to a computer to assess how different areas of the cervix respond to the light. The system uses an algorithm to process the cervical images and produce a color map of the cervix. This map indicates where the biopsy samples should be taken to maximize the likelihood of catching suspect lesions.

Definitions

Cervix: The opening of the uterus.

Dysplasia: Abnormal growth and potentially premalignant changes of squamous cells; also known as intraepithelial neoplasia.

Optical detection systems: Computerized image analysis systems that use specialized cameras and light sources to assess how different areas of the cervix respond to the light to aid in biopsy direction.

Papanicolaou (Pap) smear test: Involves examining a sample of cells from the cervix for evidence of malignancy and pre-cancerous changes.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

58999	Unlisted procedure, female genital system (nonobstetrical) [when specified as cancer screening or identification using an optical detection system]

ICD-10 Diagnosis

	All diagnoses

References

Peer Reviewed Publications:

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2. Huh WK, Cestero RM, Garcia FA, et al. Optical detection of high-grade cervical intraepithelial neoclassic in vivo: results of a 604-patient study. Am J Obstet Gynecol. 2004; 190(5):1249-1257.

3. Suchońska B, Gajzlerska-Majewska W, Wielgoś M. Evaluation of a real-time optoelectronic method in the diagnostics of CIN over four years of observations. PLoS One. 2021; 16(2):e0247702.
4. Wang Z, Kang Y, Yu F et al. TruScreen detection of cervical tissues for high-risk human papillomavirus-infected individuals during the COVID-19 pandemic. Future Oncol. 2021; 17(10):1197-1207.
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6. Wright TC Jr, Denny L, Kuhn L, Goldie S. Use of visual screening methods for cervical cancer screening. Obstet Gynecol Clin North Am. 2002; 29(4):701-734.
7. Yang H, Zhang X, Hao Z. The diagnostic accuracy of a real-time optoelectronic device in cervical cancer screening: A PRISMA-compliant systematic review and meta-analysis. Medicine (Baltimore). 2018; 97(29):e11439.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American College of Obstetricians and Gynecologists. Practice Bulletin Number. 168: Cervical Cancer Screening and Prevention. Obstet Gynecol. 2016; 128(4):e111-e130. Reaffirmed 2018.
2. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination: Screening pap smears and pelvic examinations for early detection of cervical or vaginal cancer. NCD #210.2. Effective June 19, 2006. Available at: http://www.cms.hhs.gov/mcd/index_list.asp?list_type=ncd. Accessed on December 7, 2023.
3. Fontham ETH, Wolf AMD, Church TR, et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. CA Cancer J Clin. 2020; 70:321–346.
4. NCCN Clinical Practice Guidelines in Oncology™ (NCCN). © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website at: http://www.nccn.org/index.asp. Accessed on December 7, 2023.
    - Cervical Cancer (V1.2024). Revised September 20, 2023.
5. Saslow D, Solomon D, Lawson HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin. 2012; 62(3):147-172.
6. U.S. Preventive Services Task Force. Screening for cervical cancer. August 2018. Available at: https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/cervical-cancer-screening. Accessed on December 7, 2023.

Websites for Additional Information

1. American Cancer Society (ACS). Guidelines for the prevention and early detection of cervical cancer. Updated April 22, 2021. Available at: https://www.cancer.org/cancer/cervical-cancer/detection-diagnosis-staging/cervical-cancer-screening-guidelines.html. Accessed on December 7, 2023.
2. American Cancer Society (ACS). Cervical cancer. Available at:https://www.cancer.org/cancer/cervical-cancer.html. Accessed on December 7, 2023.
3. Centers for Disease Control and Prevention (CDC). Cervical cancer. Reviewed on August 21, 2023. Available at: http://www.cdc.gov/cancer/cervical/. Accessed on December 7, 2023.
4. National Cancer Institute (NCI):
    - Cervical Cancer Home Page: Available at:https://www.cancer.gov/types/cervical/hp. Accessed on December 7, 2023.
    - Cervical Cancer Screening (PDQ®). Updated on April 21, 2023. Available at: https://www.cancer.gov/types/cervical/hp/cervical-screening-pdq. Accessed on December 7, 2023.
    - Cervical Cancer Treatment (PDQ®). Updated on October 17, 2023. Available at: https://www.cancer.gov/types/cervical/hp/cervical-treatment-pdq. Accessed on December 7, 2023.

Index

Cervical Cancer
Optical Detection Systems

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	02/15/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised Rationale, Background/Overview, References and Websites for Additional Information sections.
Reviewed	02/16/2023	MPTAC review. Updated Rationale, References and Websites for Additional Information sections.
Reviewed	02/17/2022	MPTAC review. Updated Rationale, Background/Overview, and References sections.
Revised	02/11/2021	MPTAC review. Title change to Optical Detection for Screening and Identification of Cervical Cancer. Removed cervicography and speculoscopy from the scope of the document. Updated Description/Scope, Position Statement, Rationale, Coding, Background/Overview, Definitions, References, and Index sections.
Reviewed	02/20/2020	MPTAC review. Updated Background/Overview and References sections.
Reviewed	03/21/2019	MPTAC review.
Reviewed	03/20/2019	Hematology/Oncology Subcommittee review. Updated Rationale, Background/Overview, References and Websites sections.
Reviewed	05/03/2018	MPTAC review.
Reviewed	05/02/2018	Hematology/Oncology Subcommittee review. The document header wording updated from “Current Effective Date” to “Publish Date.” Updated Rationale, References and Websites sections.
Reviewed	05/04/2017	MPTAC review.
Reviewed	05/03/2017	Hematology/Oncology Subcommittee review. Updated Background/Overview and References sections.
Reviewed	05/05/2016	MPTAC review.

Reviewed	05/04/2016	Hematology/Oncology Subcommittee review. Updated Background and References sections. Removed ICD-9 codes from Coding section.
Reviewed	05/07/2015	MPTAC review
Reviewed	05/06/2015	Hematology/Oncology Subcommittee review. Updated Rationale, Background/Overview, Definitions and Reference Sections.
Reviewed	05/15/2014	MPTAC review.
Reviewed	05/14/2014	Hematology/Oncology Subcommittee review. Updated References section.
Reviewed	05/09/2013	MPTAC review.
Reviewed	05/08/2013	Hematology/Oncology Subcommittee review. Updated References section.
Reviewed	05/10/2012	MPTAC review.
Reviewed	05/09/2012	Hematology/Oncology Subcommittee review. Updated References section.
Reviewed	05/19/2011	MPTAC review.
Reviewed	05/18/2011	Hematology/Oncology Subcommittee review. Updated References section.
Reviewed	05/13/2010	MPTAC review.
Reviewed	05/12/2010	Hematology/Oncology Subcommittee review. Updated References section.
Reviewed	05/21/2009	MPTAC review.
Reviewed	05/20/2009	Hematology/Oncology Subcommittee review. Updated References section.
	01/01/2009	Updated Coding section with 01/01/2009 CPT changes; removed CPT 0031T, 0032T deleted 12/31/2008.
Reviewed	05/15/2008	Medical Policy & Technology Assessment Committee (MPTAC) review.
Reviewed	05/14/2008	Hematology/Oncology Subcommittee review. Updated Rationale and References sections.
	02/21/2008	The phrase "investigational/not medically necessary" was clarified to read "investigational and not medically necessary." This change was approved at the November 29, 2007 MPTAC meeting.
Reviewed	05/17/2007	MPTAC review.
Reviewed	05/16/2007	Hematology/Oncology Subcommittee review. Coding updated; removed CPT 0003T deleted 12/31/2006.
Revised	06/08/2006	MPTAC revision. Title changed from “Cervicography and Speculoscopy” to “Imaging techniques for Screening and Identification of Cervical Cancer”. Added the Luma™ Cervical Imaging System as Investigational/Not Medically Necessary. Updated Rationale, Background/Overview, Definitions and References sections. Document number changed from RAD.00005 to MED.00087.
Revised	07/14/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-Merger Organizations	**Last Review Date**	**Document Number**	**Title**
Anthem, Inc.	06/16/2003	RAD.00005	Cervicography and Speculoscopy
WellPoint Health Networks, Inc.	04/28/2005	2.09.14	Cervicography
	04/28/2005	2.09.15	Speculoscopy

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