Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: Keystone First	**Submission Date**: 1/1/2024
Policy Number: ccp.1277	**Effective Date:** 4/2017 **Revision Date:** December 1, 2023
Policy Name: Fluorescence spectroscopy for prostate cancer diagnosis	

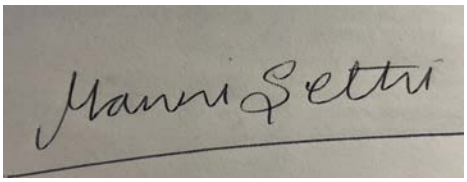
Type of Submission – Check all that apply:

- [ ] **New Policy**
- [x] **Revised Policy***
- [ ] **Annual Review – No Revisions**
- [ ] **Statewide PDL**

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

See tracked changes below.

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Keystone First
Family of Health Plans

Fluorescence spectroscopy for prostate cancer diagnosis

Clinical Policy ID: CCP.1277

Recent review date: 12/2023

Next review date: 4/2025

Policy contains: digital rectal examination, fluorometry, fluorescence spectroscopy, prostate specific antigen, spectrofluorometry.

Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First's clinical policies are not guarantees of payment.

Coverage policy

Fluorescence spectroscopy for prostate cancer diagnosis is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Digital rectal examination.
- Fine needle biopsy.
- Prostate specific antigen.
- Magnetic resonance imaging targeted prostate biopsy.
- Ultrasound guided transrectal biopsy.
- Ultrasound guided transperineal biopsy.

Background

In the United States, an estimated 288,300 new cases of prostate cancer and 34,700 deaths from prostate cancer will occur in 2023. Risk of prostate cancer is higher in men aged 65 or older and in non-Hispanic Black men (American Cancer Society, 2023a).

The most common means of diagnosing the disease is a Prostate Specific Antigen (blood) test, for which levels of 4.0 nanograms per milliliter or higher are considered abnormal, followed by a core needle biopsy (or sometimes an ultrasound) to confirm the presence and extent of cancer. Digital rectal exams may also detect prostate cancer (American Cancer Society, 2023b).

Prostate biopsy has limited ability to accurately diagnose cancer. After surgery, just 32.2% of cancers were found to be detected correctly with a 12-core prostate biopsy using the same mapping, and just 43.3% of cancers were assigned the same Gleason score (Serefoglu, 2013). Transrectal ultrasound and magnetic resonance imaging, performed alone or as fused images, may be used to improve detection of prostate cancer and improve the diagnostic accuracy of core needle biopsy (American Cancer Society, 2023b).

Transrectal ultrasound-guided prostate biopsies cannot differentiate cancer lesions from benign tissue and are only useful for locating boundaries of the gland to guide biopsy. About 90% of prostate cancer cores have been reported as benign, and thus targeting prostate cancer lesions and not benign tissue is desirable (Werahera, 2014).

Fluorescence spectroscopy is a non-invasive diagnostic tool that may improve cancer detection in real time using a type of electromagnetic spectroscopy to analyze biochemical tissue composition and structure. It uses a beam of light, typically ultraviolet, that causes electrons in molecules to emit light. The technique is also known as fluorometry or spectrofluorometry and employs two types of instruments (filter fluorometers and spectrofluorometers). It has been used for biochemical, chemical, and medical purposes (Francisco, 2014).

Findings

The American Urological Society's guideline on early detection for prostate cancer mentions multiparametric magnetic resonance imaging prior to initial biopsy, but not fluorescence spectroscopy, as a method for improving cancer detection (Wei, 2023). The American College of Radiology's most recent guideline on prostate cancer detection and staging does not list fluorescence spectroscopy as a means of staging prostate cancer (Akin, 2023). Finally, neither the U.S. Preventive Services Task Force guideline on prostate cancer screening nor the National Comprehensive Cancer Network guideline on prostate cancer mentions the method (National Comprehensive Cancer Network, 2023; U.S. Preventive Services Task Force, 2018).

No systematic reviews or meta-analyses on the topic exist. The current evidence consists of studies examining the technical feasibility of fluorescence spectroscopy in detecting cancerous prostate tissue. The evidence is insufficient to support an improvement in patient outcomes as a result of using the technology in the workup of prostate cancer.

Small *in vitro* studies (n = 12 and n = 20, respectively) of fluorescence spectroscopy used to differentiate malignant prostate tissues documented sensitivity and specificity above 85% (Masilamani, 2011) and above 90% (AlSalhi, 2012). Another showed fluorescence spectroscopy identified levels of tryptophan in spectra in advanced metastatic prostate cancers that exceeded moderately metastatic cancers and normal cells (Pu, 2013). Fluorescence spectrography has also calculated varying concentrations of fluorophores (a chemical that can re-emit light on light excitation) in prostate tissue according to disease state (Werahera, 2015).

A study of the contrast agents Cybesin and Cytate, measured with fluorescence spectroscopy, found differences in rotation time and fluorescence anisotropies differed between cancerous and normal prostate tissue. A preferential uptake exists for Cytate/Cybesin in cancerous tissues suggesting a new optical approach to detect cancerous from non-cancerous tissue areas in the prostate (Pu, 2011).

A study of 20 surgically excised prostate glands addressed the issue of most prostate cores reported as benign. After measuring fluorescence in 187 cores, 78 samples were malignant. Sensitivity and specificity were 86% and 87%, and negative and positive predictive values were 90% and 83% (Werahera, 2014).

A review of 724 capsular and parenchymal tissue samples from 37 patients with intermediate-to-high grade prostate cancer used auto-fluorescence lifetime spectroscopy and light reflectance spectroscopy to test the accuracy of the Gleason scale score. The study resulted in agreement of 87.9%, 90.1%, and 85.1% for parenchymal tissues, and 91.1%, 91.9%, and 94.3% when capsular tissues were included, for Gleason scores 7, 8, and 9, or high risk of the cancer spreading (Sharma, 2014).

One review used 50 prostate specimens from radical prostatectomy patients to obtain six punch biopsies from each, and four measurement points for each biopsy, making a total of 1,200 measurement points. Time-resolved fluorescence spectra resulted in a 93.4% correct classification (malignant versus non-malignant) of the 1,200 samples, suggesting a helpful diagnostic tool for both pathologists and surgeons (Gerich, 2011).

A study of concentrations of endogenous fluorophores in prostate tissue using an optical biopsy needle guided by fluorescence spectroscopy in 208 males undergoing prostatectomy surgery found 72% sensitivity and 66% specificity. The study also found a 93% negative predictive value to indicate benign tissue, leading authors to conclude that this technique can increase the diagnostic accuracy of prostate biopsies (Werahera, 2015).

A newly-constructed immunoassay system with surface plasmon field-enhanced fluorescence spectrometry that detected Prostate Specific Antigen levels was able to make distinctions between cases of prostate cancer and benign prostatic hypertrophy (Kaya, 2015).

A case-control study of 18 subjects, divided into those with and without prostate cancer, compared the autofluorescence of porphyrins in feces using fluorescence spectroscopy. A significant difference between groups was detected in the spectral region of 670 to 675 nanometers ($P = .000127$). No significant correlation between prostate-specific antigen levels and fecal porphyrins was observed (Gotardelo, 2018).

In 2022, we added a guideline on prostate cancer, which does not mention fluorescence spectroscopy as a diagnostic imaging alternative (National Comprehensive Cancer Network, 2022). No policy changes are warranted.

In 2023, we updated the references and guidelines, and added no newly relevant published studies to the policy. No policy changes are warranted.

References

On September 29, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “spectrometry, fluorescence” (MeSH), “prostatic neoplasms (MeSH), “fluorescence spectroscopy prostate,” “fluorometry,” and “spectrofluorometry.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

11/2016: initial review date and clinical policy effective date: 4/2017

11/2017: Policy references updated.

11/2018: Policy references updated.

12/2019: Policy references updated. Policy ID changed to CCP.1277.

12/2020: Policy references updated.

12/2021: Policy references updated.

12/2022: Policy references updated.

12/2023: Policy references updated.