Test Specific Guidelines

Decipher Prostate Cancer Classifier

MOL.TS.294.A
v1.0.2023

Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedures addressed by this guideline	Procedure codes
Decipher Prostate Cancer Classifier	81542

What Are Gene Expression Profiling Tests for Prostate Cancer?

Definition

Prostate cancer (PC) is the most common cancer in men, and metastatic prostate cancer is a leading cause of cancer-related deaths worldwide. It is considered a heterogeneous disease with highly variable prognosis.[1]

At the time of diagnosis of localized PC, patients typically undergo a prognostic risk assessment with routine clinical and pathological tests to assess the probability of subsequent progression or metastasis. These prognostic assessments help to identify lower risk patients with indolent disease who may opt for active surveillance (AS), or higher risk patients with more aggressive disease who may benefit from a treatment intervention.

High-risk prostate cancer (PC) patients treated with radical prostatectomy (RP) also undergo risk assessment to assess future disease prognosis and determine optimal treatment strategies. Post-RP pathology findings, such as disease stage, baseline Gleason score, time of biochemical recurrence (BCR) after RP, and PSA doubling-time, are considered strong predictors of disease-associated metastasis and mortality. Following RP, up to 50% of patients have pathology or clinical features that are considered at high risk of recurrence and these patients usually undergo post-RP treatments, including adjuvant or salvage therapy or radiation therapy, which can have serious risks and complications. According to clinical practice guideline recommendations, high risk patients should undergo 6 to 8 weeks of radiation therapy (RT) following RP. However, approximately 90% of high-risk patients do not develop metastases or die of prostate cancer, and instead may be appropriate candidates for alternative treatment approaches, including AS. As such, many patients may be subjected to unnecessary follow-up procedures and their associated complications, highlighting the need for improved methods of prognostic risk assessment.[2,3]

Several genomic biomarkers have been commercially developed to augment the prognostic ability of currently available routine clinical and pathological tests and identify those patients either at the time of diagnosis of localized PC or after radical prostatectomy (RP) most and least likely to benefit from a specific treatment strategy. Prognostic genomic tests, including gene expression profiling tests, may help to avoid overtreatment by reclassifying those men originally identified as high risk, but who are unlikely to develop metastatic disease. Genomic biomarkers may also play a role in assisting clinicians to tailor personalized and more appropriate treatments for subgroups of PC patients, and improve overall health outcomes.[2,3]

Test Information

Gene expression profiles (GEPs) evaluate the expression of several genes using one sample. Gene expression is determined through RNA analysis, using either reverse transcriptase (RT) polymerase chain reaction (PCR) or DNA microarrays.[4]

According to the manufacturer, "Decipher® uses an oligonucleotide microarray to measure the expression of up to 1.4 million RNAs (e.g., mRNA, lncRNA) extracted from formalin-fixed, paraffin-embedded (FFPE) prostate specimens. Decipher testing on tumor specimens provides the probability of high-grade disease at radical prostatectomy (biopsy specimens only), 5-year probability of clinical metastasis, and 10-year prostate cancer specific mortality. A gene expression signature is used to generate the Decipher score, which ranges from 0 to 1.0."[5]

Decipher Prostate Biopsy

Decipher Prostate Biopsy results are "intended for use as an adjunct to conventional clinical risk factors for determining metastatic potential and prognosis of patients diagnosed with localized prostate cancer."[6]

"Decipher Prostate Biopsy predicts a patient's risk for metastasis or prostate cancer mortality, as well as adverse pathology at RP, using the gene expression profile of FFPE prostate cancer tissue samples collected at biopsy. Decipher Prostate Biopsy classifies as low risk those who may be safely followed with active surveillance, or as high risk those who would potentially benefit from immediate treatment."[5]

Decipher Prostate Radical Prostatectomy (RP)

Decipher Prostate RP results are intended as "an adjunct to conventional clinical variables and models currently used for determining prognosis and treatment of prostate cancer patients after radical prostatectomy."[7] Clinical validity studies have evaluated patients designated as very low-, low-, favorable intermediate-, unfavorable intermediate, high, and very high risk per the National Comprehensive Cancer Network (NCCN) risk groups for prostate cancer.

Decipher Prostate RP "predicts a patient's risk for metastasis or prostate cancer mortality for men with adverse pathology or PSA persistence / recurrence

following RP using the gene expression profile of FFPE prostate cancer tissue samples collected at RP. Decipher Prostate RP classifies as low risk those who may be safely observed, or as high risk those who would potentially benefit from treatment or treatment intensification." [5]

Guidelines and Evidence

American Association of Clinical Urologists

The American Association of Clinical Urologists (AACU) has issued a position statement on genomic testing in prostate cancer that states the following:[8]

"The AACU supports the use of tissue-based molecular testing as a component of risk stratification in prostate cancer treatment decision making."

American Society of Clinical Oncology

The American Society of Clinical Oncology (ASCO, 2020) issued a guideline on molecular biomarkers in prostate cancer. This guideline states:[9]

"Are there molecular biomarkers to diagnose clinically significant prostate cancer?"

"Recommendation 2.1. Commercially available molecular biomarkers (ie, Oncotype Dx Prostate, Prolaris, Decipher, and ProMark) may be offered in situations in which the assay result, when considered as a whole with routine clinical factors, is likely to affect management. Routine ordering of molecular biomarkers is not recommended (Type: Evidence based; Evidence quality: Intermediate; Recommendation: Moderate)."

"Recommendation 2.2. Any additional molecular biomarkers evaluated do not have sufficient data to be clinically actionable or are not commercially available and thus should not be offered (Type: Evidence based; Evidence quality: Insufficient; Strength of recommendation: Moderate)."

"Are there molecular biomarkers to guide the decision of postprostatectomy adjuvant versus salvage radiation?"

"Recommendation 3.1. The Expert Panel recommends consideration of a commercially available molecular biomarker (eg, Decipher Genomic Classifier) in situations in which the assay result, when considered as a whole with routine clinical factors, is likely to affect management. In the absence of prospective clinical trial data, routine use of genomic biomarkers in the postprostatectomy setting to determine adjuvant versus salvage radiation or to initiate systemic therapies should not be offered (Type: Evidence based; Evidence quality: Intermediate; Strength of recommendation: Moderate)."

"Recommendation 3.2. Any additional molecular biomarkers evaluated do not have sufficient data to be clinically actionable or are not commercially available

and thus should not be offered (Type: Evidence based; Evidence quality: Insufficient; Strength of recommendation: Moderate)."

American Urological Association and American Society of Radiation Oncology

The American Urological Association and American Society for Radiation Oncology (AUA/ASTRO, 2022) published an evidence-based guideline on localized prostate cancer endorsed by the Society of Urologic Oncology (SGO) that stated:[10]

"Clinicians may selectively use tissue-based genomic biomarkers when added risk stratification may alter clinical decision-making. (Expert Opinion)"

"Clinicians should not routinely use tissue-based genomic biomarkers for risk stratification or clinical decision-making. (Moderate Recommendation; Evidence Level: Grade B)"

"Regarding tissue-based genomic biomarkers, several currently available commercial tests, including Prolaris, Oncotype Dx, and Decipher, variously offer prediction of adverse pathology as well as the risks of biochemical recurrence, metastasis, and prostate cancer death. However, most of the reported studies to date that evaluated the prognostic ability of these genomic tests did not meet inclusion criteria for the systematic review as the studies used surgical (ie, prostatectomy) rather than biopsy specimens."

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2022) Clinical Practice Guidelines on Prostate Cancer stated the following regarding molecular assays:[11]

"Patients with low or favorable intermediate-risk disease and life expectancy >10 y may consider the use of the following tumor-based molecular assays: Decipher, Oncotype DX Prostate, and Prolaris. Patients with unfavorable intermediate- and high-risk disease and life expectancy >10 y may consider the use of Decipher and Prolaris tumor-based molecular assays."

"Retrospective studies have shown that tumor-based molecular assays performed on prostate biopsy or RP specimens provide prognostic information independent of NCCN or CAPRA risk groups. These include, but are not limited to, likelihood of death with conservative management, likelihood of biochemical progression after RP or EBRT [external beam radiation therapy], and likelihood of developing metastasis after RP or salvage radiotherapy."

"These molecular biomarker tests have been developed with extensive industry support, guidance, and involvement, and have been marketed under the less rigorous FDA regulatory pathways for biomarkers. Although full assessment of their clinical utility requires prospective randomized clinical trials, which are unlikely to be done, the panel believes that men with low or favorable intermediate disease and life expectancy greater than or equal to 10 years may

consider the use of Decipher, Oncotype DX Prostate, or Prolaris during initial risk stratification."

With regard to the use of Decipher post-radical prostatectomy (RP), NCCN stated:[11]

"The panel recommends use of nomograms and consideration of age and comorbidities, clinical and pathologic information, PSA levels, PSADT, and Decipher molecular assays to individualize treatment discussion."

"Decipher molecular assay is recommended if not previously performed to inform adjuvant treatment if adverse features are found post-RP." (category 2B)

"Adverse laboratory/pathologic features include: positive margin(s); seminal vesicle invasion; extracapsular extension; or detectable PSA."

Selected Relevant Publications

The majority of the evidence for Decipher retrospectively evaluates the association between the Decipher score and adverse pathology, biochemical recurrence, or metastasis in men post-RP.[12-33] There is a paucity of evidence evaluating test performance in men at initial biopsy. Several decision impact studies suggest Decipher results may influence clinical decision-making; however, it remains unclear if Decipher-based decision-making ultimately leads to improvements in patient health outcomes. Future trials should prospectively evaluate the impact of Decipher testing on clinical decision-making in large independent cohorts of men and include sufficient follow-up to capture patient-relevant outcomes (e.g., mortality, recurrence, and metastasis)

Clinical trials may be ongoing. Additional information can be found at https://clinicaltrials.gov.

Criteria

Decipher Prostate RP

No previous gene expression profile testing performed for this diagnosis of cancer, AND

Member is post-radical prostatectomy, AND

Post-surgical PSA is undetectable (below 0.2mg/dl), AND

No evidence of lymph node metastasis identified, AND

One or more of the following adverse features identified in the surgical specimen:

positive surgical margin(s), or

extracapsular extension, or

seminal vesicle invasion, AND

Test is being requested to inform adjuvant treatment decisions.

Decipher Prostate Biopsy

This test is considered investigational and/or experimental.

Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.

In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

References

Bostrom PJ, Bjartell AS, Catto JW, et al. Genomic predictors of outcome in prostate cancer. *Euro Urol.* Dec 2015;68(6):1033-1044.

Marrone M, Potosky AL, Penson D, Freedman AN. A 22 gene-expression assay, Decipher® (GenomeDx Biosciences) to predict five-year risk of metastatic prostate cancer in men treated with radical prostatectomy. *PLoS Curr.* Nov 17 2015;7.

Moschini M, Spahn M, Mattei A, Cheville J, Karnes RJ. Incorporation of tissue-based genomic biomarkers into localized prostate cancer clinics. *BMC Med.* Apr 04 2016;14:67.

AHRQ. Gene expression profiling for predicting outcomes in patients with stage II colon cancer. 2012.

Decipher website. Available at: http://deciphertest.com/

Decipher Biosciences. Decipher Prostate Biopsy Test Report. Decipher Biosciences website. Available at: https://decipherbio.com/about-us/resource-publications/#test-reports

Decipher Biosciences. Decipher Radical Prostatectomy Report. Decipher Biosciences website. Available at: https://decipherbio.com/about-us/resource-publications/#test-reports

American Association of Clinical Urologists, Inc. (AACU) website. Position statement: genomic testing in prostate cancer. Available at: https://aacuweb.org/wp-content/uploads/2022/02/Position-Statement-Tissue-based-genetic-testing-in-prostate-cancer-Endorsement-02-26-18.pdf

Eggener SE, Rumble RB, Armstrong AJ, et al. Molecular biomarkers in localized prostate cancer: ASCO Guideline. *J Clin Oncol*. 2020;38(13):1474-1494. doi: 10.1200/JCO.19.02768

Eastham JA, Auffenberg GB, Barocas DA et al: Clinically localized prostate cancer: AUA/ASTRO guideline part I: introduction, risk assessment, staging and risk-based management. *J Urol*. 2022;208(1):10-18. doi: 10.1097/JU.0000000000002757. Epub 2022 May 10

NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. V3.2022 Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf

Tomlins SA, Alshalalfa M, Davicioni E, et al. Characterization of 1577 primary prostate cancers reveals novel biological and clinicopathologic insights into molecular subtypes. *Eur Urol.* Oct 2015;68(4):555-567.

Knudsen BS, Kim HL, Erho N, et al. Application of a clinical whole-transcriptome assay for staging and prognosis of prostate cancer diagnosed in needle core biopsy specimens. *J Mol Diagn.* May 2016;18(3):395-406.

Den RB, Santiago-Jimenez M, Alter J, et al. Decipher correlation patterns post prostatectomy: initial experience from 2 342 prospective patients. *Prostate Cancer Prostatic Dis.* Dec 2016;19(4):374-379.

Badani KK, Thompson DJ, Brown G, et al. Effect of a genomic classifier test on clinical practice decisions for patients with high-risk prostate cancer after surgery. *BJU Int.* Mar 2015;115(3):419-429.

Nguyen PL, Shin H, Yousefi K, et al. Impact of a Genomic classifier of metastatic risk on postprostatectomy treatment recommendations by radiation oncologists and urologists. *Urology.* Jul 2015;86(1):35-40.

Nguyen PL, Haddad Z, Ross AE, et al. Ability of a genomic classifier to predict metastasis and prostate cancer-specific mortality after radiation or surgery based on needle biopsy specimens. *Eur Urol*. 2017;72(5):845-852.

Berlin A, Murgic J, Hosni A, et al. Genomic classifier for guiding treatment of intermediate-risk prostate cancers to dose-escalated image guided radiation therapy without hormone therapy. *Int J Radiat Oncol Biol Phys*. 2019;103(1):84-91.

Olleik G, Kassouf W, Aprikian A, et al. Evaluation of new tests and interventions for prostate cancer management: a systematic review. *J Natl Compr Canc Netw*. 2018;16(11):1340-1351.

Gore JL, du Plessis M, Zhang J, et al. Clinical utility of a genomic classifier in men undergoing radical prostatectomy: The PRO-IMPACT Trial. *Pract Radiat Oncol*. 2019 Nov 20. pii: S1879-8500(19)30305-4. doi: 10.1016/j.prro.2019.09.016. [Epub ahead of print]

Hu JC, Tosoian JJ, Qi J, et al. Clinical utility of gene expression classifiers in men with newly diagnosed prostate Cancer. *JCO Precision Oncology*. 2018(2):1-15.

Spratt DE, Zhang J, Santiago-Jiménez M, et al. Development and validation of a novel integrated clinical-genomic risk group classification for localized prostate cancer. *J Clin Oncol*. 2018;36(6):581-590.

Herlemann A, Huang H-C, Alam R, et al. Decipher identifies men with otherwise clinically favorable-intermediate risk disease who may not be good candidates for active surveillance. *Prostate Cancer P D*. 2019:1-8.

Muralidhar V, Zhang J, Wang Q, et al. Genomic validation of 3-Tiered clinical subclassification of high-risk prostate cancer. *Int J Radiat Oncol Biol Phys*. 2019;105(3):621-627.

Kim HL, Li P, Huang H-C, Deheshi S, et al. Validation of the Decipher Test for predicting adverse pathology in candidates for prostate cancer active surveillance. *Prostate Cancer and Prostatic Diseases*. 2019;22(3):399-405.

Tosian JJ, Birer SR, Jeffrey Karnes R, et al. Performance of clinicopathologic models in men with high risk localized prostate cancer: impact of a 22-gene genomic classifier. *Prostate Cancer Prostatic Dis*. 2020:[Epub ahead of print]. doi: 10.1038/s41391-020-0226-2

Jambor I, Falagario U, Ratnani P, et al. Prediction of biochemical recurrence in prostate cancer patients who underwent prostatectomy using routine clinical prostate multiparametric MRI and decipher genomic score. *J Magn Reson Imaging*. 2019. doi: 10.1002/jmri.26928

Goldberg H, Spratt D, Chandrasekar T, et al. Clinical-genomic characterization unveils more aggressive disease features in elderly prostate cancer patients with low-grade disease. *Eur Urol Focus*. 2020. doi: 10.1016/j.euf.2020.02.008

Feng FY, Huang H-C, Spratt DE, et al. Validation of a 22-gene genomic classifier in patients with recurrent prostate cancer: An ancillary study of the NRG/RTOG 9601 randomized clinical trial. *JAMA Oncol*. 2021;7(4):544-552. doi: 10.1001/jamaoncol.2020.7671

Jairath NK, Pra AD,Vince R, et al. A systematic review of the evidence for the Decipher Genomic Classifier in prostate cancer. *Eur Urol*. 2021 Mar;79(3):374-383. doi: 10.1016/j.eururo.2020.11.021

White C, Staff I, McLaughlin T, et al. Does post prostatectomy decipher score predict biochemical recurrence and impact care? *World J Urol*. 2021. doi: 10.1007/s00345-021-03661-1

Press BH, Jones T, Olawoyin O, et al. Association between a 22-feature genomic classifier and biopsy Gleason upgrade during active surveillance for prostate cancer. *Eur Urol Open Sci*. 2022;37:113-119. doi: 10.1016/j.euros.2022.01.008

Vince RA, Jr., Jiang R, Qi J, et al. Impact of Decipher Biopsy testing on clinical outcomes in localized prostate cancer in a prospective statewide collaborative. *Prostate Cancer Prostatic Dis*. 2021. doi: 10.1038/s41391-021-00428-y