Test Definition: PHI11

Prostate Health Index Reflex, Serum

Overview

Useful For

As an aid in distinguishing prostate cancer from benign prostatic conditions in men aged 50 years and older with total PSA between 4.0 and 10.0 ng/mL and digital rectal examination findings that are not suspicious for cancer

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
PHI13	Prostate Health Index (phi) Reflex	No	No

Testing Algorithm

This test begins with the analysis of prostate-specific antigen (PSA). If the PSA concentration is between 2.0 and 10.0 ng/mL, then the reflex test will be performed at an additional charge.

If the initial PSA concentration is between 2.0 and 10.0 ng/mL, then free PSA and [-2]pro-PSA isoform results will be reported.

If the initial PSA concentration is between 4.0 and 10.0 ng/mL, then the percent free PSA result and prostate health index (*phi*) will be calculated and reported.

If the initial PSA concentration is between 2.0 and 4.0 ng/mL, then the percent free PSA result and prostate health index (*phi*) will not be calculated or reported.

Highlights

Prostate health index (*phi*) may be used to determine the probability of prostate cancer on biopsy in men with total prostate-specific antigen (PSA) in the 4.0 to 10.0 ng/mL range.

Free PSA, [-2]proPSA, % free PSA, and *phi* will only be reported when the initial total PSA value is between 4.0 and 10.0 ng/mL.

Method Name

Immunoenzymatic Assay

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Patient Preparation:

1. Specimens for testing should be collected prior to prostate manipulations such as digital rectal examination, prostatic massage, transrectal ultrasound, and prostatic biopsy.
2. A 6-week waiting period between needle biopsy and specimen collection is recommended.
3. Specimens **should not** be collected from patients receiving therapy with high biotin (vitamin B7) doses (ie, >5 mg/day) until at least 8 hours following the last biotin administration.

Supplies: Sarstedt Aliquot Tube 5 mL (T914)
Collection Container/Tube: Red top (serum gel/SST are **not acceptable**)
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL Serum
Collection Instructions:

1. Within 3 hours of collection, centrifuge, aliquot serum into a plastic vial, and refrigerate.
2. Freeze serum within 24 hours of collection.
3. Send frozen.

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

Serum: 0.75 mL

Reject Due To

Gross hemolysis	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Frozen (preferred)	150 days	
	Ambient	24 hours	
	Refrigerated	24 hours	

Clinical & Interpretive

Clinical Information

Prostate-specific antigen (PSA) is a glycoprotein produced by the prostate gland, the lining of the urethra, and the bulbourethral gland. Normally, very little PSA is secreted in the blood. In conditions of increased glandular size and tissue damage, PSA is released into circulation. Measurement of serum PSA is useful for determining the extent of prostate cancer and assessing the response to prostate cancer treatment. PSA is also used as a screening tool for

prostate cancer detection, although its use in screening has become controversial in recent years. While an elevated serum PSA is associated with prostate cancer, a number of benign conditions, such as benign prostatic hyperplasia and prostatitis might lead to elevated serum PSA concentrations. As a consequence, PSA lacks specificity for prostate cancer detection.

Several PSA isoforms have been identified that can further increase the specificity of PSA for prostate cancer. In particular, the [-2] form of proPSA (p2PSA) shows improved performance over either total or free PSA for prostate cancer detection on biopsy. The prostate health index (*phi*) is a formula that combines all 3 PSA forms (total PSA, free PSA, and p2PSA) into a single score. *phi* is calculated using the following formula: (p2PSA/free PSA) x square root of PSA.

In a multicenter study that compared the performance of total PSA, free PSA, p2PSA, and *phi* in men undergoing prostate biopsy due to a serum PSA concentration between 4.0 and 10.0 ng/mL, *phi* was the best predictor of any prostate cancer, high-grade cancer, and clinically significant cancer. At 95% clinical sensitivity, the clinical specificity of *phi* was 16.0%, compared to 8.4% for free PSA and 6.5% for total PSA.

Reference Values

PROSTATE-SPECIFIC ANTIGEN (PSA)
Males:
<40 years: < or =2.0 ng/mL
40-49 years: < or =2.5 ng/mL
50-59 years: < or =3.5 ng/mL
60-69 years: < or =4.5 ng/mL
70-79 years: < or =6.5 ng/mL
> or =80 years: < or =7.2 ng/mL

Females: Not applicable

PERCENT FREE PSA
Males:
When PSA is in the range of 4.0-10.0 ng/mL

% Free PSA	Probability of cancer
< or =10%	56%
11-15%	28%
16-20%	20%
21-25%	16%
>25%	8%

Females: Not applicable

PROSTATE HEALTH INDEX (phi)
Males:
When PSA is in the range of 4.0-10.0 ng/mL

phi range	Probability of cancer	95% Confidence interval
0-26.9	9.8%	5.2-15.4%
27.0-35.9	16.8%	11.3-22.2%

36.0-54.9	33.3%	26.8-39.9%
> or =55.0	50.1%	39.8-61.0%

Females: Not applicable

Interpretation

The prostate health index (*phi*) may be used to determine the probability of prostate cancer on biopsy in men aged 50 years and older with total prostate-specific antigen (PSA) in the 4.0 to 10.0 ng/mL range. Low *phi* scores are associated with a lower probability of finding prostate cancer on biopsy, and higher *phi* scores are associated with an increased probability of finding prostate cancer on biopsy. The choice of an appropriate *phi* score to be used in guiding clinical decision-making may vary for each patient and may depend on other clinical factors or family history. The table below indicates the probability of finding prostate cancer on biopsy when total PSA is in the range of 4.0 to 10.0 ng/mL and may be used as guidance for interpreting the *phi* score.

***phi* range**	**Probability of cancer**	**95% Confidence interval**
0-26.9	9.8%	5.2%-15.4%
27.0-35.9	16.8%	11.3%-22.2%
36.0-54.9	33.3%	26.8%-39.9%
55.0+	50.1%	39.8%-61.0%

Cautions

Specimens for [-2]pro-prostate-specific antigen (p2PSA) testing should be collected prior to prostate manipulations such as digital rectal examination (DRE), prostatic massage, transrectal ultrasound, and prostatic biopsy. DRE may cause a transient increase in p2PSA, free prostate-specific antigen (PSA), and PSA.

Transrectal needle biopsy has also been shown to cause transient increases in p2PSA, free PSA, and PSA elevations, thus a 6-week waiting period between needle biopsy and p2PSA, free PSA, and PSA sampling is recommended.

The prostate health index (*phi*) results should be interpreted in light of the total clinical presentation of the patient, including symptoms, clinical history, data from additional tests, and other appropriate information. The *phi* should not be interpreted as absolute evidence for the presence or absence of prostate cancer. Elevated PSA concentrations, increased *phi*, or decreased free PSA may be observed in patients with nonmalignant disorders, as well as those with prostate cancer.

Routine use of 5 alpha-reductase inhibitor drugs typically lower PSA, free PSA, and p2PSA levels in patients. Other drugs used to treat benign prostatic hyperplasia may also affect PSA levels. Care should be taken in interpreting results from patients taking these drugs.

For patient samples containing elevated levels of total protein (>8 g/dL), the possibility exists for interference by total protein. Carefully evaluate the results of patients suspected of having elevated total protein levels.

Free PSA specimens can potentially be falsely decreased by biotin. Biotin should not strongly affect total PSA or p2PSA values.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human

anti-mouse antibodies (HAMA) or heterophile antibodies), which may cause interference in some immunoassays. Caution should be used in interpretation of results and the laboratory should be alerted if the result does not correlate with the clinical presentation.

The use of the prostate health index (phi) has not been validated when PSA values are outside of the range of 4.0 to 10.0 ng/mL

Clinical Reference

1. Catalona WJ, Partin AW, Sanda MG, et al. A multicenter study of [-2]pro-prostate-specific antigen combined with prostate-specific antigen and free prostate-specific antigen for prostate cancer detection in the 2.0 to 10.0 ng/mL prostate-specific antigen range. J Urol. 2011;185(5):1650-1655
2. Pecoraro V, Roli L, Plebani M, Trenti T. Clinical utility of the (-2)proPSA and evaluation of the evidence: a systematic review. Clin Chem Lab Med. 2016;54(7):1123-1132. doi:10.1515/cclm-2015-0876
3. Loeb S, Catalona WJ: The Prostate Health Index: a new test for the detection of prostate cancer. Ther Adv Urol. 2014 Apr;6(2):74-77. doi:10.1177/1756287213513488
4. Fan YH, Pan PH, Cheng WM, et al. The Prostate Health Index aids multi-parametric MRI in diagnosing significant prostate cancer. Sci Rep. 2021;11(1):1286. doi:10.1038/s41598-020-78428-6
5. Sekine Y, Arai G, Kito H, et al. The Complementary Roles of the Prostate Health Index and Multiparametric Magnetic Resonance Imaging in Optimizing the Detection of Clinically Significant Prostate Cancer in Patients With Prostate-Specific Antigen Levels Below 10?Ng/mL. Int J Urol. 2026;33(9):e70625. doi:10.1111/iju.70625

Performance

Method Description

Prostate-specific antigen:
The Access Hybritech PSA (prostate-specific antigen) assay is a 2-site immunoenzymatic ("sandwich") assay. A sample is added to mouse monoclonal anti-PSA alkaline phosphatase conjugate and paramagnetic particles coated with a second mouse monoclonal anti-PSA antibody. The PSA in the sample binds to the immobilized monoclonal anti-PSA on the solid phase while the monoclonal anti-PSA alkaline phosphatase conjugate reacts with a different antigenic site on the sample PSA. After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. The chemiluminescent substrate Lumi-Phos* 530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of PSA in the sample and is determined from a stored, multipoint calibration curve.(Package insert: Access Hybritech PSA/Prostate-Specific Antigen Instructions for Use. Beckman Coulter Inc; 08/2023)

Free PSA:
The Access Hybritech free PSA assay is a 2-site immunoenzymatic ("sandwich") assay. A sample is added to mouse monoclonal anti-free PSA-alkaline phosphatase conjugate and paramagnetic particles coated with a second mouse monoclonal anti-PSA antibody. The free PSA in the sample binds to the immobilized monoclonal anti-PSA on the solid phase while the monoclonal anti-free PSA-alkaline phosphatase conjugate reacts with different antigenic sites on the free PSA molecule. After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. The chemiluminescent substrate Lumi-Phos 530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of

free PSA in the sample and is determined from a stored, multipoint calibration curve.(Package insert: Access Hybritech free PSA/Free Prostate-Specific Antigen Instructions for Use. Beckman Coulter Inc; 06/2020)

[-2]ProPSA:
The Access Hybritech p2PSA ([-2]proPSA) is a 2-site immunoenzymatic ("sandwich") assay. A sample is added to mouse monoclonal anti-PSA-alkaline phosphatase conjugate, paramagnetic particles coated with a mouse monoclonal anti-[-2]proPSA antibody, and a blocking reagent. The [-2]proPSA in the sample binds to the immobilized monoclonal anti-[-2]proPSA on the solid phase while the monoclonal anti-PSA-alkaline phosphatase conjugate reacts with different antigenic sites on the [-2]proPSA molecule. After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. The chemiluminescent substrate Lumi-Phos*530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of [-2]proPSA in the sample and is determined from a stored, multipoint calibration curve.(Package insert: Access Hybritech p2PSA/[-2]proPSA Instructions for Use. Beckman Coulter Inc; 10/2023)

Percent free PSA:
This is a calculated result. The percentage is provided only when the total PSA is in the range of 4.0 to 10.0 ng/mL. The following equation is used to calculate the percent free PSA:
Percent free prostate-specific antigen (PSA) = free PSA/total PSA * 100(Package insert: Access Hybritech PSA/Prostate-Specific Antigen Instructions for Use. Beckman Coulter Inc; 08/2023)

Prostate health index:
Prostate health index (*phi*) is calculated in the laboratory information system and provided only when the total PSA is in the range of 4.0 to 10.0 ng/mL. The following equation is used to calculate the prostate health index:
(p2PSA /free PSA) x square root (PSA).(Package insert: Access p2PSA/[-2]proPSA Instructions for Use. Beckman Coulter Inc; 10/2023)

PDF Report
No

Day(s) Performed
Monday through Saturday

Report Available
1 to 3 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

84153 - Total PSA
84154 - Free PSA (if appropriate)
86316 - [-2]ProPSA (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PHI11	Prostate Health Index Reflex, S	53764-7

Result ID	Test Result Name	Result LOINC® Value
PHI12	Prostate Specific Antigen, S	83112-3