Prostate-Specific Antigen (PSA) Tests for Color's Prostate Cancer Screening Programs

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Executive Summary

Prostate cancer is the most common cancer among males and is one of the top causes of cancer-related deaths.[1] As a result, efficient screening methods have become critical to detecting cancer early and improving patient outcomes. The Prostate-Specific Antigen (PSA) test has been a cornerstone in prostate cancer screening since 1994 when it was first approved by the FDA.[2] Traditionally PSA testing has relied on blood samples collected through a venous blood draw in a healthcare provider's office. However, venous blood draws have limitations, including the need for trained personnel and logistical challenges in remote or resource-limited settings.

PSA testing via self-collected devices, such as liquid blood microsamples and dried blood spots (DBS), has emerged as a promising alternative for collecting and testing blood samples for various health assessments. For prostate cancer, liquid blood microsamples and DBS both offer advantages for improving access and potentially reducing the cost of screening.

This technical document describes the two self-collected PSA tests available through Color's Cancer Screening & Prevention Program:

- Liquid blood microsample-based PSA test using the Abbott Alinity ci-series i module system with the FDA-approved Alinity i Total PSA assay. This test is validated for use in Color's laboratory with capillary blood collected using the Tasso+ blood collection device and BD Microtainer® blood collection tube.
- Dried blood spot-based PSA test using the Beckman Coulter DXI 800 chemistry analyzer with the FDA-approved Access Hybritech PSA assay. This test is validated for use with capillary dried blood collected with the AdvanceDx 100 Serum collection (DBS) card at our partner laboratory, US Speciality Labs (USSL).

Introduction

Prostate-Specific Antigen (PSA) testing is a recommended way to screen for prostate cancer.

The American Cancer Society (ACS) recommends that males who are at average risk for prostate cancer consider screening starting at age 50.[3] For those who are at increased risk, screening may begin as early as age 40. The frequency with which to continue screening depends on the PSA level – individuals with more elevated PSA levels are encouraged to screen more frequently.

When detected early, prostate cancer is largely treatable. Those diagnosed with early stage prostate cancer have a threefold higher 5-year survival rate than those diagnosed at a late stage (5-year survival rate: >99% vs. 32%).[4]

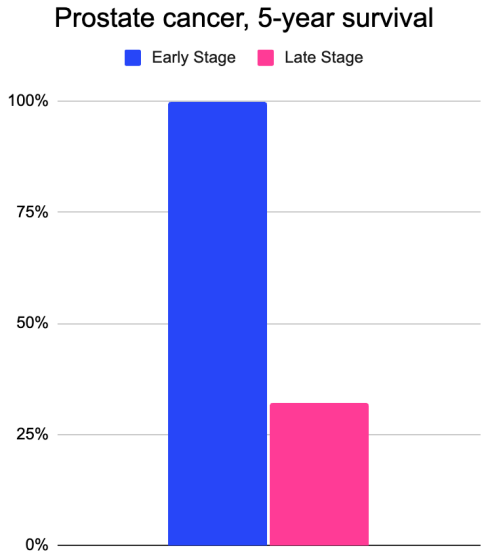

Figure 1. 5-year survival rate of early vs. late stage prostate cancer

Utilization of prostate cancer screening is low.

About 2 in 3 males who are eligible for screening are not up-to-date with recommended prostate cancer screening. In fact, over the past decade, there has been an increase in metastatic prostate cancer incidence and prostate cancer-related deaths.[5] This rise in incidence and mortality has been attributed to a decline in prostate cancer screening rates. In addition, individuals of lower socio-economic status, individuals in rural communities, and individuals who have lower access to healthcare have been disproportionately impacted by prostate cancer due to low uptake of standard prostate cancer screening and low follow-through with a diagnostic biopsy.

Alternative sample collection modalities can increase access to screening.

PSA testing is typically done during an outpatient blood draw visit. However, sample collection by a clinician can create access barriers that may unnecessarily discourage screening according to guidelines.

The use of self-collected biological specimens for health screening has several advantages:

1. Self-collection requires less healthcare provider staff to supervise the collection of specimens.
2. Self-collection can be less invasive and can make for a better patient experience and decrease discomfort.
3. Self-collection can greatly increase access to testing – one of the major bottlenecks to sufficient testing in the United States.
4. Self-collection can decrease tester wait times for access to in-person testing and results where wait times for doctor appointments can be up to several months.

How it works

Step 1: Self-collection of blood

Liquid blood microsample (upper arm)

The liquid blood microsample (upper arm) kit contains all of the materials needed to collect a sample (Figure 2). The Tasso+ device attaches to the upper arm, uses a small lancet to create a nick, and applies gentle vacuum pressure to collect roughly 400uL of blood. Blood is collected in a BD Microtainer® with lithium heparin additive to prevent coagulation. Instructions for collecting a sample can be found here: https://support.color.com/en/articles/8426651-blood-sample-collection-upper-arm

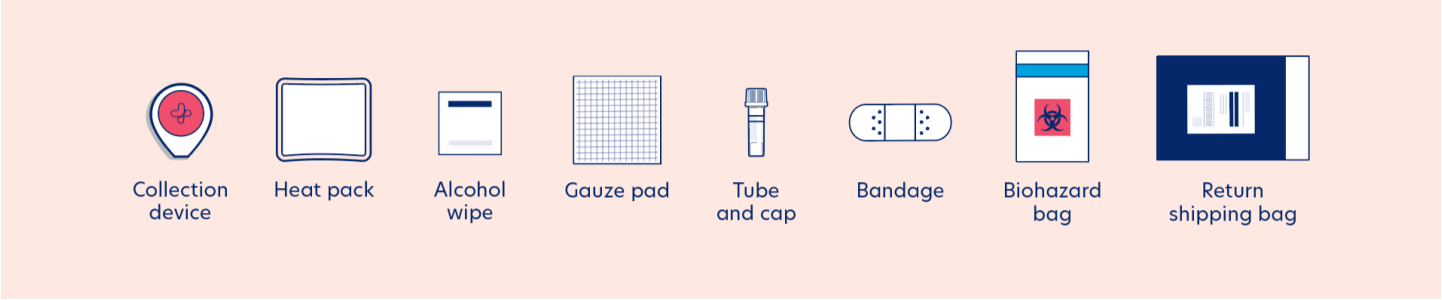

Figure 2. Liquid blood microsample (upper arm) collection kit components

Dried Blood Spot (fingertip)

Color's Dried Blood Spot collection (DBS) kit contains all of the materials needed to collect a sample (Figure 3). Blood samples are self-collected with a lancet and the AdvanceDx 100 Serum collection (DBS) card. Approximately four drops of capillary blood from the fingertip are needed for this test. The card must be air dried and returned to the laboratory within 24 hours of collection. Instructions for collecting a fingertip blood sample can be found here: https://support.color.com/en/articles/7996561-how-do-i-collect-my-blood-sample-for-my-at-home-te

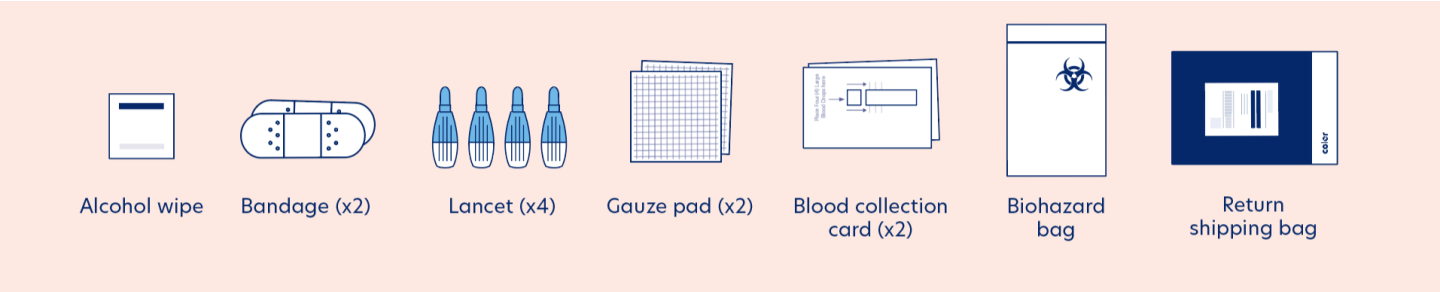

Figure 3. Dried Blood Spot (fingertip) collection kit components

Step 2: Analysis of the self-collected blood sample

Liquid blood microsample (upper arm)

The liquid blood microsample-based PSA test is performed at the Color Diagnostics laboratory using the Abbott Alinity ci-series i module system with the FDA-approved Alinity i Total PSA assay. This test is validated for use in Color's laboratory with capillary blood collected using the Tasso+ blood collection device and BD Microtainer® blood collection tube.

Dried Blood Spot (fingertip)

The DBS-based PSA test is performed at US Speciality Labs (USSL) using the Beckman Coulter DXI 800 chemistry analyzer with the FDA-approved Access Hybritech PSA assay. This test is validated for use with capillary dried blood collected with the AdvanceDx 100 Serum collection (DBS) card.

Step 3: PSA test results

The PSA tests used in Color's Cancer Screening & Prevention Program measure PSA levels in capillary blood. Clinical samples will be reported as shown in Table 1.

Result	Meaning
High	Total PSA levels > 4.0
Normal	Total PSA within normal range (0.0-4.0 ng/mL)
Sample unsuitable for analysis	Reason for Sample Rejection: Quantity not sufficient

Table 1. Possible PSA test results from Total PSA Tests.

Technical Details of the Liquid Blood Microsample-based PSA test

The Color Total PSA Test is an extension of the FDA-approved Alinity i Total PSA assay. Beyond the validation performed by the test manufacturer, the validity of the assay on capillary blood collected with the Tasso+ device into BD Microtainers was further evaluated for analytical sensitivity, accuracy, precision, analytical specificity, reportable range, and reference interval. Here we present the results of the LDT validation study.

Method Comparison

A total of 47 paired clinical samples (capillary blood collected in the BD Microtainer device and a standard venous blood draw) were collected. Derived serum was assayed for Total PSA levels on the Alinity i Total PSA assay to establish equivalency. Sample values spanned the analytical measurement range measured between 0.00 - 14.00 ng/mL. Total PSA levels were plotted and paired concentrations were compared using linear regression analysis. The study returned an R^2 correlation coefficient of 0.995.

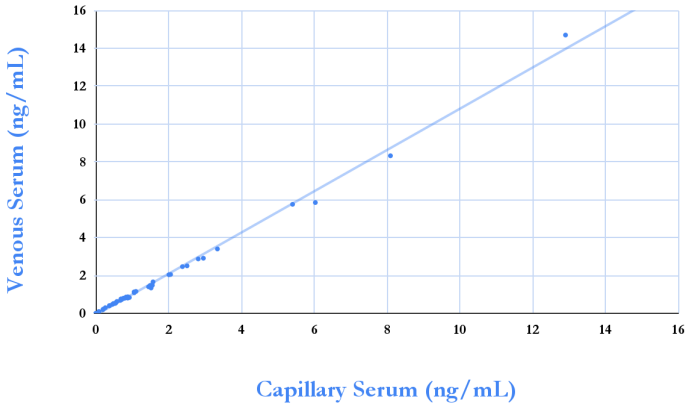

Figure 4. Method comparison. PSA measurement comparison between capillary serum and venous serum with a $R^2 = 0.995$.

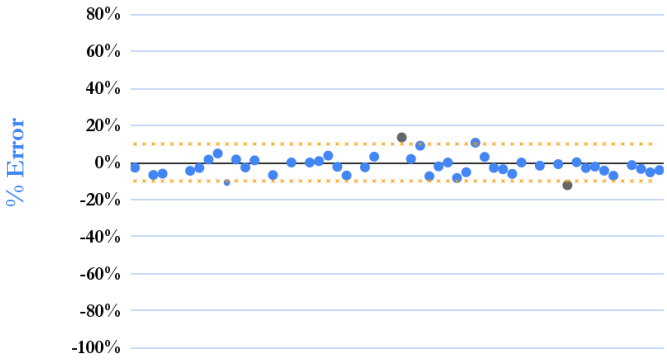

Figure 5. Accuracy results. Blue dots representing capillary serum samples have Total PSA measurement within 10% error or 0.1 ng/mL total error from the venous serum sample. Black dots indicate samples failed both the % error and total error criteria.

Accuracy

Additionally, accuracy was evaluated against standard "Total Allowable Error" criteria set by the College of American Pathologists. The study demonstrated an average percent error of <2% and met acceptability criteria with a passing rate of 95.74% where total PSA measurements in capillary serum samples are within 10% for % error or 0.1 ng/mL for total error when compared to venous serum samples.

Additional Studies

The reproducibility of the Color Total PSA Test was evaluated using a three-level quality control (QC) material. Simple precision samples were run in triplicate in three runs. Total precision samples were processed in triplicate over the span of three days by three different operators.

An analytical specificity study demonstrated robust tolerance against potentially interfering substances, Hemoglobin and Bilirubin, at the highest acceptable concentration validated by the manufacturer. Less than 10% interference to the total PSA measurement was observed when these substances were added to two serum samples separately. The reportable range was verified via reference materials with known concentrations at 5 difference levels and a previously quantified sample with concentration above 100 ng/mL followed by serial dilutions. An R^2 correlation of 0.998 was observed.

The reference interval study assessed 43 reference individuals with prostates to verify the pre-established reference range and confirmed the reference range is ≤ 4.0 ng/mL.

Finally, shipping stability was evaluated at multiple temperatures demonstrating that the measured PSA levels were accurate for at least 10 days at temperatures up to 86°F (30°C) and can endure temperatures up to 95°F (35°C) for at least 6 days.

Technical Details of the Dried Blood Spot-based PSA test

The DBS-based Total PSA Test is an extension of the FDA-approved Access Hybritech PSA assay. Beyond the validation performed by the test manufacturer, the validity of the assay on capillary blood collected with the AdvanceDX 100 serum collection card performed by US Specialized Labs is summarized here.

Method Comparison

Whole blood collected on the AdvanceDx 100 Serum collection card paired with serum collected by venipuncture were assayed on the Beckman Coulter DXI 800 chemistry analyzer. The amount of the Prostate Specific Antigen in ng/mL was plotted and paired concentrations were compared using linear regression analysis. The study returned an R^2 correlation coefficient of 0.9819 with samples measured between 0.00 - 6.00 ng/mL for Total PSA.

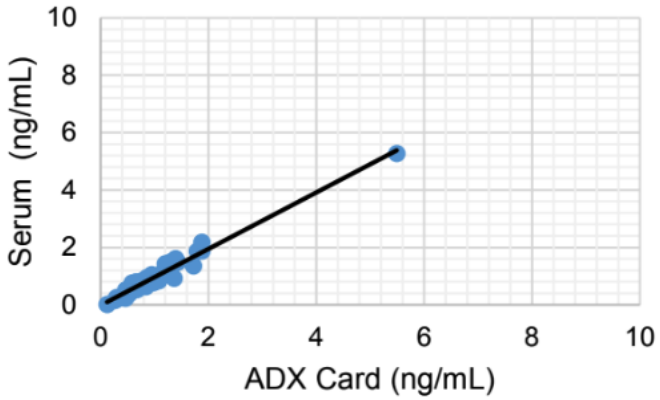

Figure 6. Accuracy results. Linear regression graph comparing DBS serum and venous serum in Total PSA measurement.

Analytical Specificity

The Access Hybritech PSA assay from USSL has confirmed no significant interference by bilirubin, hemolysis, or lipemia.

Reportable Range and Reference Interval

The validated reportable range of the USSL Access Hybritech PSA assay is 0.00-20.00 ng/mL. The reference interval of the assay is verified to be 0.00-4.00 ng/mL.

References

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2. Prostate-Specific Antigen (PSA) Test. National Cancer Institute. Published March 21, 2022. Accessed November 7, 2023. https://www.cancer.gov/types/prostate/psa-fact-sheet

3. American Cancer Society Recommendations for Prostate Cancer Early Detection. Accessed November 7, 2023. https://www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/acs-recommendations.html

4. Surveillance Research Program, National Cancer Institute. SEER*Explorer: An interactive website for SEER cancer statistics. Data source(s): SEER Incidence Data, November 2022 Submission (1975-2020), SEER 22 registries. Published April 29, 2023. Accessed May 31, 2023. Available from: https://seer.cancer.gov/statistics-network/explorer/

5. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin.* 2023;73(1):17-48.