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RESEARCH ARTICLE

A correlation and red, amber, green (RAG) analysis of Boditech i-CHROMA™ Prostate Specific Antigen (PSA) Point of Care Test (POCT) Method and Roche PSA laboratory methods

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Abstract

***Background*:** This study evaluated and compared the performance of the Boditech i-CHROMA™ point-of-care testing (POCT) method for the quantification of prostate-specific antigen (PSA) against traditional laboratory PSA method (Roche Methods – Roche Cobas c303/501/502/503, Roche Cobas e402/ e801 and Roche Cobas e411) using external quality control material from RIQAS.

***Materials and method*:** External quality control distributions from RIQAS were analysed using the Boditech i-CHROMA™ PSA method; these were then compared with the results of the Roche Methods – Roche Cobas c303/501/502/503, Roche Cobas e402/ e801 and Roche Cobas e411 provided by participants in the scheme. The mean results of the Roche methods were compared using linear regression and Red Amber Green (RAG) analysis, a scoring system where red is indicative of a raised PSA (>6.0 ng/mL), amber is indicative of a slightly raised PSA (5.0 – 6.0 ng/mL). Green indicates a normal PSA (<5.0 ng/mL).

***Results*:** The data showed that between the Boditech i-CHROMA™ PSA results and the Roche Cobas c303/501/502/503, there was an excellent correlation (r^2 = 0.9843). The RAG analysis showed the Boditech i-CHROMA™ PSA method identified 26 reds, two ambers, and six greens compared with 27 reds, two ambers, and six greens determined by the Roche Cobas c303/501/502/503 method. The data showed an excellent correlation between the Boditech i-CHROMA™ PSA results and the Roche Cobas e402/ e801 PSA methods (r^2 = 0.9842). The RAG analysis showed the Boditech i-CHROMA™ PSA method identified 30 reds, three ambers, and eight greens compared with 31 reds, two ambers, and eight greens identified by the Roche Cobas e402/ e801 PSA methods. The data showed an excellent correlation between the Boditech i-CHROMA™ PSA results and the Roche Cobas e411 PSA methods (r^2 = 0.9851). The RAG analysis showed the Boditech i-CHROMA™ PSA method identified 30 reds, three ambers, and eight greens compared with 31 reds, two ambers, and eight greens identified Roche Cobas e411 PSA methods.

***Conclusion*:** The data showed that the Boditech i-CHROMA™ PSA method is comparable to the Roche Cobas c303/501/502/503, Roche Cobas e402/ e801 and Roche Cobas e411 PSA methods. This could effectively reduce the turnaround time to make prompt decisions on diagnosing, treating, and monitoring of patients with prostate-related disorders.

Keywords: *PSA*; *POCT*; *iCHROMA*; *Roche*; *Prostate Cancer*

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The epithelial cells within the prostate gland are responsible for the secretion of prostate-specific antigen (PSA), an enzymatic protein belonging to the serine protease category. The PSA test is essential to screen benign prostate hyperplasia and malignant prostate carcinoma as a laboratory procedure. Recognised as a benchmark, PSA plays a crucial role in diagnosing these conditions related to the prostate. Its levels include screening, diagnosis, treatment guidance, monitoring, and prognosis assessment.

Prostate cancer ranks as the second most prevalent cancer among men globally [1]. Notably, the incidence of prostate cancer among African populations surpasses that among Caucasians [2]. This may be linked to genes, and

other factors such as age, socioeconomic status, and accessibility to healthcare facilities contribute to the potential challenge of delayed detection of prostate cancer.

In healthcare, there has been a notable surge in the adoption of point-of-care testing (POCT), particularly evident in general practitioner (GP) settings, where rapid test results are pivotal for informed diagnostic and treatment determinations.

The NHS Centre for Evidence-Based Purchasing assessed three quantitative techniques—Qualigen FastPack, VEDALAB PSA-CHECK-1, and Mediwatch PSAwatch and Bioscan systems—alongside one semi-quantitative approach, the SureScreen PSA test. As part of the NHS Prostate Cancer Risk Management Programme, none of these POCT PSA tests met the acceptable performance standards for use when testing asymptomatic males [3].

Recently, a study presented compelling evidence of a robust association between quantitative results obtained from the OPKO 4Kscore test utilising a finger-stick of whole blood and laboratory evaluations over clinically relevant PSA levels, including extremely low PSA concentrations. POCT PSA methods such as the FREND PSA Plus [4]. Another article showed that the PSAwatch and Bioscan systems correlated well ($r^2 = 0.88$) with laboratory results [5].

Recent advancements have yielded a range of POCT devices dedicated to diagnosing prostate cancer. Noteworthy examples include the PSA SPOT test [6], Cube™ [7], concile® Ω100 POC reader [8], and i-CHROMA™ PSA Plus. These devices have undergone comparative evaluation against traditional central laboratory apparatus. Their sensitivity and specificity stand at 89.1 and 93%, respectively, although variations in performance emerged due to the duration of testing. Notably, the Cube™ demonstrated a strong correlation of 0.95 with the IMMULITE total PSA assay. Similarly, the concile® Ω100 POC reader exhibited correlations of 0.72 (Immulite®) and 0.63 (Centaur®) when matched against laboratory-based testing.

This study aims to compare and establish a correlation in the performance of the Boditech i-CHROMA POCT system and conventional laboratory-based analysers, specifically diverse models of Roche autoanalyser.

Materials and methods

i-CHROMA™

The i-CHROMA™ POCT PSA method is a quantitative assay for measuring total PSA in serum, plasma, or whole blood using fluorescence immunoassay technology to assess total PSA in serum, plasma, or whole blood. The technique uses the sandwich immuno-detection principle, whereby the fluorescence-labelled detector antibody binds the target protein in the sample.

The fluorescence-labelled antigen-antibody complex is then transferred to a test strip, where it is caught by a second antibody incorporated into the solid phase. The quantity of PSA present correlates with the recorded complex's fluorescence signal intensity, allowing the estimation of sample PSA concentration via a pre-programmed calibration process. The reader shows the test's outcome as nanograms per millilitre (ng/mL).

In brief, 75 µL of serum was mixed with a pre-measured volume of detection buffer containing fluorescence-labelled anti-PSA monoclonal antibodies and anti-rabbit IgG. A small volume, 75 µL, of the mixture was then loaded into the sample well of the test strip, and the cartridge was incubated at room temperature for 15 min. The intensity of the captured fluorescence-labelled PSA-antibody complexes was measured using the supplied meter, and the concentration of PSA in the sample was calculated. Assay accuracy and precision during the study were assessed using the manufacturer's internal quality control (IQC) material. The PSA sample cartridge and i-CHROMA reader are seen in Fig. 1.

Fig. 1. PSA sample cartridge containing fluorescence-labelled anti-PSA monoclonal antibodies and anti-rabbit IgG with an i-CHROMA™ reader.

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RIQAS

The Randox International Quality Assessment Scheme (RIQAS). The RIQAS material was analysed using the i-CHROMA™ POCT method and Cobas auto analysers for total PSA concentrations: Cobas® e402/e801 (n = 41), Cobas® e411 (n = 41), Cobas® c303/501/502/503 (n = 35), and i-CHROMAä (n = 35; n = 41).

Red Amber Green analysis

The Red Amber Green (RAG) analysis score used was correlated with the level of PSA concentration. The red, amber, and green represent PSA concentrations of >6.0 ng/l, 5.0 – 6.0 ng/mL, and <5.0 ng/mL, respectively. These values represent normal (green), slightly abnormal (amber), and abnormal (red).

Statistical analysis

Data was analysed using SPSS (Statistical Package for the Social Sciences)® 22 software (IBM, Chicago) and GraphPad Prism 10. The Pearson correlation coefficient measured the strength of a linear relationship between two variables. A correlation coefficient of 1 represents a perfect positive correlation. Bland-Altman plot was used to analyse the agreement between the methods used.

Results

Evaluation of correlation (i-CHROMA™ versus Cobas, N = 35)

The i-CHROMA™ POCT method showed an excellent correlation with the COBAS c303/501/502/503 (r^2 = 0.9843) in Fig. 2.

Bland-Altman plot

The bland-Altman graph illustrates the mean and difference of Cobas c303/501/502/503 and Boditech i-CHROMA™ testing platforms. The plot's scatter increases as the total PSA concentration increases beyond 15 ng/mL. There were two outliers seen beyond the concentration of 20 ng/mL (Fig. 3).

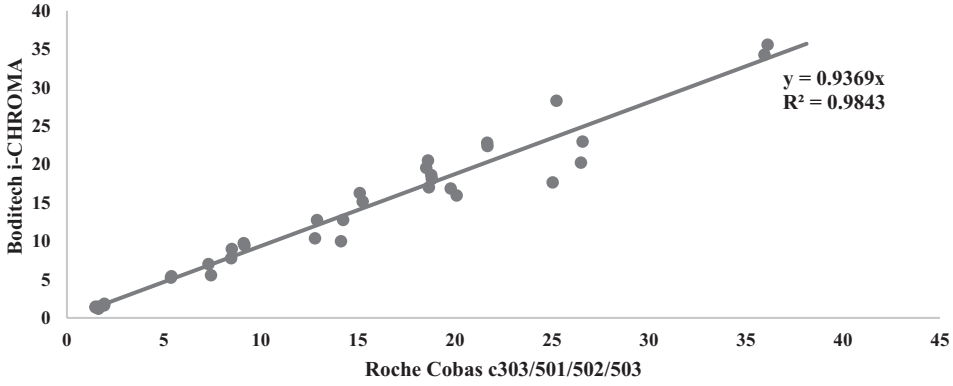

Fig. 2. The scatter plot shows the observations of Roche Cobasc303/501/502/503 (Reference method) and Boditech i-CHROMA (Test Method) for evaluating total PSA.

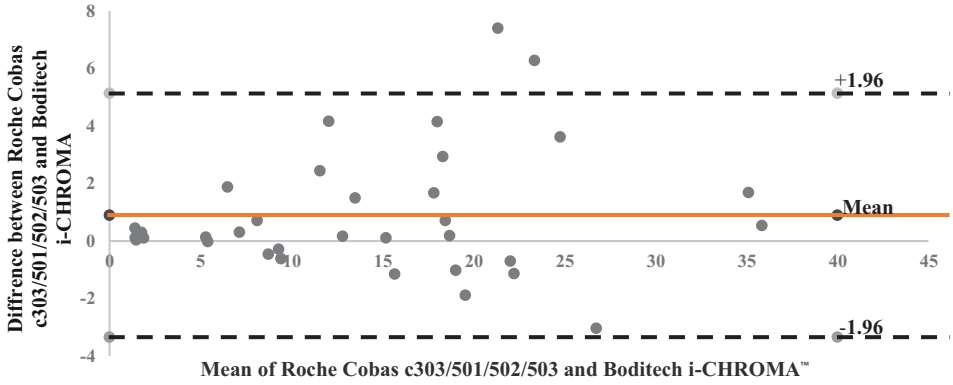

Fig. 3. Bland-Altman plot of Roche Cobas c303/501/502/503 and Boditech i-CHROMA™. The mean is 0.9 ng/mL with a confidence of 95% limits of agreement on both sides of the mean. 35 samples were evaluated. The upper limit of agreement (5.13 ng/mL) and lower limit agreement (−3.33 ng/mL).

RAG analysis

The RAG analysis was used to stratify different samples according to the concentration of total PSA concentration (ng/mL) into normal, slightly abnormal, and abnormal on both platforms. The i-CHROMA™ method identified 26 individuals with abnormal results (red) compared with 27 individuals on the Cobas c303/501/502/503. The i-CHROMA™ method identified three individuals with slightly abnormal (amber) results compared to two on the Cobas method. The i-CHROMA™ method and Cobas methods identified six individuals with normal (green) results, as seen in Table 1.

Table 1. Red Amber Green analysis for PSA using Roche Cobas c303/501/502/503 and i-CHROMA™

	Green	Amber	Red.	Total
Roche Cobas c303/501/502/503	6	2	27	35
Boditech i-CHROMA™	6	3	26	35

Evaluation of correlation (i-CHROMA™ vs. Cobas, N = 41)

The i-CHROMA™ POCT method positively correlated with the COBAS e402/e801 (r^2 = 0.9842) as illustrated in Fig. 4.

Bland-Altman plot

The Bland-Altman graph illustrates the mean and difference of Cobas e402/e801 and Boditech i-CHROMA™ testing platforms (Fig. 5). The plot's scatter increases as the total PSA concentration increases beyond 15 ng/mL. There were two outliers seen beyond the concentration of 20 ng/mL.

RAG analysis

The RAG analysis was used to stratify different samples according to the concentration of total PSA concentration (ng/mL) into normal, slightly abnormal, and abnormal on both platforms. The i-CHROMA™ method identified 30 individuals with abnormal results (red) compared with 31 individuals on the Cobas e402/e801. The i-CHROMA™ method identified three individuals with

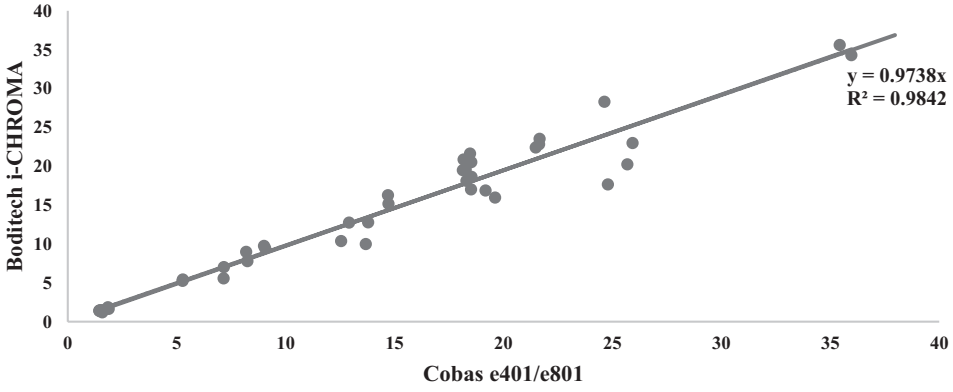

Fig. 4. The scatter plot shows the observations of Roche Cobas e401/e801(Reference method) and Boditech i-CHROMA (Test Method) for evaluating total PSA.

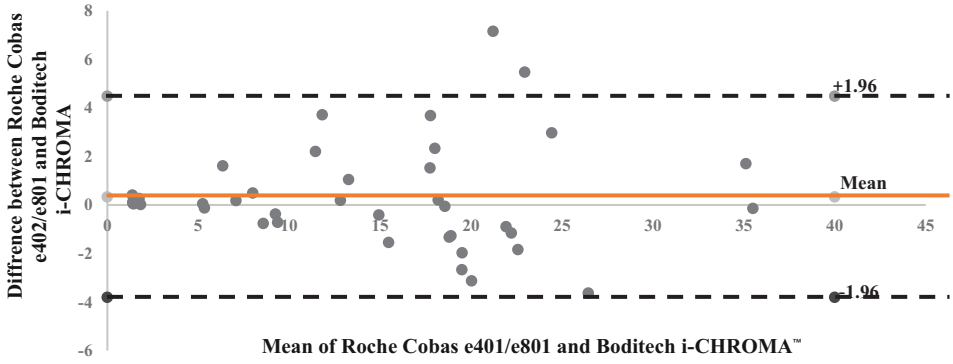

Fig. 5. Bland-Altman plot of Roche Cobas c303/501/502/503 and Boditech i-CHROMA™. The mean is 0.33 ng/mL with a confidence of 95% limits of agreement on both sides of the mean. 41 samples were evaluated. The upper limit of agreement (4.48 ng/mL) and lower limit of agreement (−3.81 ng/mL) [n = 41].

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slightly abnormal (amber) results compared to two on the Cobas method. Both the i-CHROMA™ method and the Cobas method identified eight individuals with normal (green) results (Table 2).

Evaluation of correlation (i-CHROMA™ vs. Cobas)

The i-CHROMA™ POCT method positively correlated with the COBAS e411 ($r^2 = 0.9851$) Fig. 6.

Bland-Altman plot

The Bland-Altman graph illustrates the mean and difference between Cobas e411 and Boditech i-CHROMA™ testing platforms. The plot's scatter increases as the total PSA concentration increases beyond 15 ng/mL, as seen in Fig. 7.

Table 2. Red Amber Green analysis of PSA using Roche Cobas e402/e801 and i-CHROMA™, $n = 41$

	Green	Amber	Red	Total
Roche Cobas e402/e801	8	2	31	41
Boditech i-CHROMA™	8	3	30	41

RAG analysis

The RAG analysis was used to stratify different samples according to the concentration of total PSA concentration (ng/mL) into normal, slightly abnormal, and abnormal on both platforms. The i-CHROMA™ method identified 30 individuals with abnormal results (red) compared with 31 individuals on the Cobas e402/e801. The i-CHROMA™ method identified three individuals with slightly abnormal (amber) results compared to two on the Cobas method. The i-CHROMA™ method and Cobas methods identified eight individuals with normal (green) results (Table 3).

Discussion

This study aimed to evaluate and compare the performance of the Boditech i-CHROMA™ POCT method for measuring PSA with traditional laboratory PSA methods provided by Roche (Cobas c303/501/502/503, Cobas e402/e801, and Cobas e411). This study utilised external

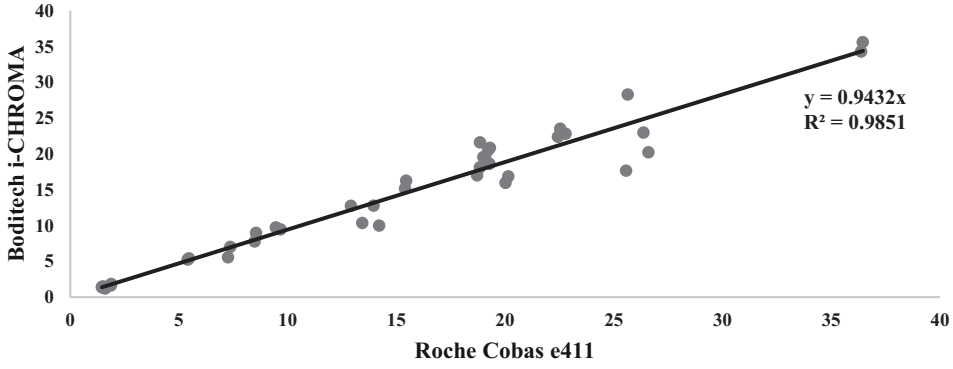

Fig. 6. The scatter plot shows the observations of Roche Cobas e411 (Reference method) and Boditech i-CHROMA (Test Method) for evaluating total PSA [$n = 41$].

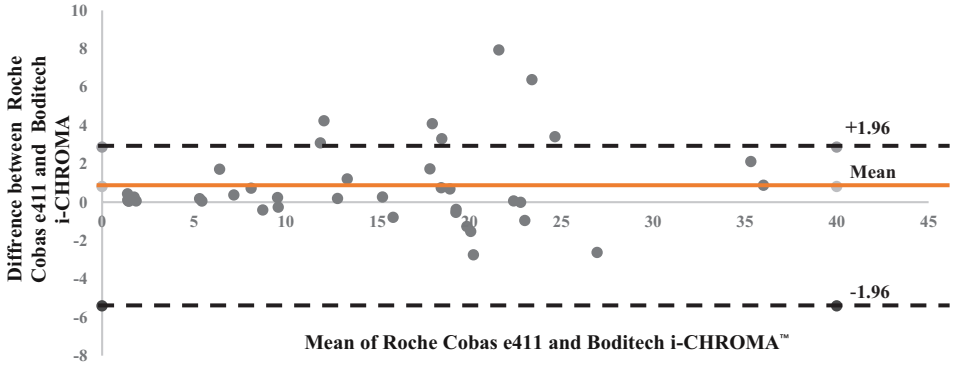

Fig. 7. Bland-Altman plot of Roche Cobas e411 and Boditech i-CHROMA™. The mean is 0.33 ng/mL with a confidence of 95% limits of agreement on both sides of the mean. 41 samples were evaluated. The upper limit of agreement (2.87 ng/mL) and lower limit agreement (−5.41 ng/mL).

Table 3. Red Amber Green analysis of PSA using Roche Cobas e411 and i-CHROMA™, *n* = 41

	Green	Amber	Red	Total
Roche Cobas e411	8	2	31	41
Boditech i-CHROMA™	8	3	30	41

quality control material from RIQAS to analyse correlations and perform RAG analysis, classifying PSA concentrations as normal, slightly abnormal, or abnormal.

The comparison started with evaluating the correlation between the Boditech i-CHROMA™ PSA method and the Roche Cobas c303/501/502/503 PSA methods. The correlation was excellent (r^2 = 0.9843), indicating a strong relationship between the results obtained from these methods. Additionally, RAG analysis revealed comparable results between the two approaches, with slight variations in the number of individuals categorised as red, amber, or green.

Similar results were observed when comparing the Boditech i-CHROMA™ PSA method with Roche Cobas e402/e801 PSA and Roche Cobas e411 PSA methods. The correlation was excellent (r^2 = 0.9842 and r^2 = 0.9851, respectively), suggesting consistent agreement between the results obtained from the Boditech i-CHROMA™ method and the Roche methods. RAG analysis again showed similar classifications between the Boditech and Roche methods, with a few differences in the number of individuals falling into each category.

The Bland-Altman plot showed that most data points were around the mean for Cobas c303/501/502/503 and Cobas e402/e801 compared to i-CHROMA. These data points were within 2 SD limits on both sides of the mean. However, outliers (4.9%) exceeded the 2 SD limits. In contrast to the Cobas e411 and i-CHROMA methods, there were more outliers (12%) beyond the 2 SD limits compared to other Cobas testing platforms, around 12–25 ng/mL of PSA.

A similar study done at OAUTH by Ajala and his colleagues showed a good correlation between the i-CHROMA™ and the Accubind® Enzyme Linked Immuno-Sorbent Assay (ELISA) (r = 0.956) [9]. A previous study done by our team showed that the Abbott Architect PSA laboratory method and the i-CHROMA™ PSA method had a good correlation (r^2 = 0.90845) using venous and finger-prick samples [10]. Another study by our group also showed a good correlation (r^2 = 0.9841) between the i-CHROMA™ PSA assay and the Cobas e602 PSA assay for total PSA [11].

The findings highlight the strong correlation and comparable results between the Boditech i-CHROMA™ and the various Roche PSA methods. This indicates that the i-CHROMA™ method is reliable and comparable to the Roche methods for total PSA testing.

The Bland-Altman plot in this study revealed a bias between −3.33 and +5.13 ng/mL with a mean value of +0.9 ng/mL for Cobas c303/501/502/503, with a mean of +0.33 ng/mL, the bias for Cobas c303/501/502/503 ranged from −3.81 to +4.48 ng/mL. Furthermore, Cobas e411's bias ranged from −5.41 to +2.87 ng/mL, with a mean value of +0.33 ng/mL. The positive bias was less than 1.0 ng/mL for the i-CHROMA™ method.

Our previous study determined the performance of the i-CHROMA™ using the RIQAS and UKNEQAS quality control schemes with other PSA methods (Abbott Architect, Beckman Access standardised to WHO, Beckman DXI standardised to Hybritech, Ortho Vitros, Roche Modular E-170, Roche Elecsys, Siemens Advia Centaur, Siemens Immulite 1000, Roche Cobas, Abbott Axsym Monoclonal, Abbott Axsym polyclonal, BioMerieux Vidas, Siemens Centaur XP/XPT/Classic, Siemens/Dade Dimension, Siemens Immulite 2000/2500, Siemens Immulite 1000, Siemens Immulite 2000/2500 3rd generation, DiaSorin, Liaison, Monobind Inc. ELISA/CLIA, Roche COBAS® 4000/e411, Beckman DXI standardised to WHO IRP96/670) exhibited a bias in RIQAS that was on the order of −2.99 to +6.8 ng/mL, with an average of +0.88 ng/mL. The UKNQEAS, on the other hand, displayed bias between +0.53 and +2.58 ng/mL, with an average of +1.46 ng/mL [12]. Over 50% of the RIQAS and UKNEQAS approaches revealed a positive bias greater than 1.0 ng/mL for all the methods used. Both studies showed positive bias, but this present study revealed lower positive bias, below 1.0 ng/mL.

The i-CHROMA™ PSA method was simple to use, requires no regular maintenance processes, and showed no performance issues throughout the study. The sample preparation protocol is straightforward because the manufacturer clearly outlines all instructions. Furthermore, all reagents are supplied ready to use. However, one potential source for error is that the sample application well is not unambiguously labelled, and it is possible to apply this directly onto the cartridge membrane by mistake. The method is relatively straightforward, although some specific features introduce potential sources for error, which could be minimised with comprehensive operator training. The assay is carried out in room temperature and all the reagents are kept at room temperature apart from the detection buffer.

In conclusion, this study successfully demonstrated the comparable performance of the Boditech i-CHROMA™ PSA method with Roche Cobas c303/501/502/503, Cobas e402/e801, and Cobas e411 PSA methods. The correlation analysis and Bland-Altman plot validate the i-CHROMA™ method's accuracy and reliability, making it a valuable alternative for PSA testing in clinical practice. This could effectively reduce the turnaround time to

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make prompt decisions on diagnosing, treating, and monitoring patients with prostate-related disorders. However, bias should be considered because this may incorrectly categorise a healthy or an unhealthy individual.

Conflict of interest and funding

JB works as an Independent Consultant for Boditech and supports the products in the UK. TK is an employee of Boditech Med Inc. JB Consulting provided the funding for this study.

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