B-012 Preliminary Performance of Access hsTnI, PCT, and TSH 3rd IS Assays on a Next-generation Prototype Analyzer†

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Abstract

Beckman Coulter's next-generation, high-volume immunoassay analyzer is currently under development. The analyzer is designed to achieve a higher throughput, employ an enhanced chemiluminescent substrate (LUMI-PHOS PRO), deliver shorter turnaround times, increase tests run per reagent pack, and provide high-quality patient results with improved user workflows when compared to the legacy Access UniCel DxI 800 Immunoassay System.

Assay data generated on the prototype analyzer demonstrates a strong correlation and similar imprecision to Beckman's predicate platform, the Access 2 Immunoassay System (A2).

Highlighted here are three example assays from the current portfolio, thyroid stimulating hormone (TSH), troponin (hsTnI), and procalcitonin (PCT), demonstrating improvements in sensitivity and precision achieved by the prototype analyzer.

INTRODUCTION & METHODS

As advances in automated immunoassay testing have allowed for improved sensitivity, specificity and shortened time to first result of diagnostic assays, expectations have also become more discerning. With product improvements, workforce shortages and consolidations, many diagnostic laboratories are adopting increased automation with higher throughput testing, while maintaining or improving their quality. Beckman Coulter is developing a new immunoassay system to address these needs while transferring the assay menu currently available on its Access 2 Immunoassay System. The new prototype system employs improved precision pipetting and an enhanced chemiluminescent substrate that allows for increased tests per reagent pack, increased sensitivity, improved precision, and shortened time to first result

A comprehensive assay menu was characterized on the prototype analyzer and all data is compared to Access 2 performance. The three assays represented were selected based upon their clinical importance and frequency of use. Procalcitonin (PCT) is used as an early indicator of sepsis and/or sepsis risk and troponin (hsTnI) aids in the diagnosis of myocardial infarction ; both are used in critical care settings. Thyroid stimulating hormone (TSH) is used to assess thyroid status and has applications for both screening and monitoring in individuals with hyper- or hypothyroidism, as well as other thyroid disorders.

For each assay, a panel of residual samples spanning assay analytical measuring ranges and commercially available quality controls were tested across three reagent lots, two calibrator lots, over multiple days of testing on three prototype analyzers and three Access 2 systems. Accuracy[1], imprecision[2], and sensitivity[3] were calculated and compared to the Access 2 following procedures based on CLSI guidelines. PCT and TSH were evaluated and compared the increased tests per pack on the prototype to the standard tests per pack on the Access 2.

RESULTS SUMMARY

A subset of preliminary data for the Access TSH 3rd IS, Access hsTnI, and Access PCT assays generated on the prototype analyzer is presented here. Each of these assays exhibit a strong correlation to Access 2, similar imprecision, and improved sensitivity as measured by limit of quantitation (LoQ). In addition to achieving quality results, an increase in number of tests per reagent pack is realized for both TSH and PCT assays. All data within this poster was generated by Beckman Coulter Diagnostics[4].

RESULTS - ACCURACY

A method comparison study was performed to evaluate the prototype's accuracy when compared to the predicate platform, Access 2, for PCT, hsTnI and TSH. Assay-specific controls and sample types were evaluated and analyzed using a Passing-Bablok regression. All three assays yielded passing method comparison results with slopes meeting the required specification of 1.00 ±0.1.

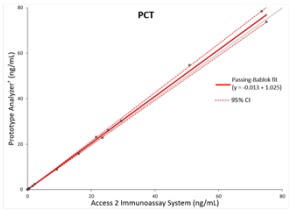

Figure 1a. Passing-Bablok analysis of PCT platform method comparison

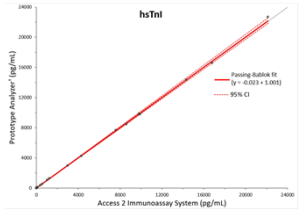

Figure 1b. Passing-Bablok analysis of hsTnI platform method comparison

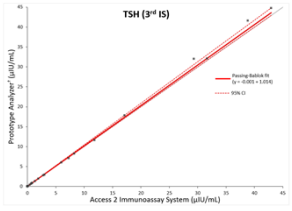

Figure 1c. Passing-Bablok analysis of TSH platform method comparison

	Accuracy (Passing-Bablok slope) Access 2 vs Prototype Analyzer†
PCT	1.025
hsTnI	1.001
TSH (3rd IS)	1.014

RESULTS - PRECISION

A three-day precision study was completed on three prototype analyzers and three Access 2 analyzers. Samples included commercially available quality controls and residual samples and were distributed across the assay's measuring range. Estimates of total imprecision presented herein are inclusive of variability attributed to within-run, between-day, instrument-to-instrument, calibration-to-calibration, reagent lot-to-lot, and calibrator lot-to-lot. Quality control materials used were assay specific with PCT, hsTnI and TSH (3rd IS) using Bio-Rad Lyphochek Specialty, MORE Diagnostics' Cardiac Markers and Bio-Rad Lyphochek Immunoassay Plus, respectively. Control concentration results on the Access 2 and prototype were compared to acceptable concentration ranges as determined by the manufacturer.

	PCT						hsTnI						TSH (3rd IS)					
	Concentration (µIU/mL)		SD		%CV		Concentration (ng/mL)		SD		%CV		Concentration (pg/mL)		SD		%CV	
	Access 2	Prototype†	Access 2	Prototype†	Access 2	Prototype†	Access 2	Prototype†	Access 2	Prototype†	Access 2	Prototype†	Access 2	Prototype†	Access 2	Prototype†	Access 2	Prototype†
Low Sample	0.03	0.03	0.003	0.002	13%	6%	5.69	5.31	0.646	0.495	11.4%	9.3%	0.02	0.02	0.003	0.001	14.7%	4.5%
Assay-Specific Controls Levels 1-3	0.61	0.69	0.030	0.034	5.0%	4.9%	48.8	52.8	2.17	1.47	4.5%	2.8%	0.67	0.71	0.039	0.026	5.9%	3.7%
	2.24	2.42	0.111	0.099	4.9%	4.1%	1242	1280	50.54	51.64	4.1%	4.0%	5.88	5.74	0.369	0.245	6.3%	4.3%
	21.6	23.6	0.747	0.683	3.5%	2.9%	16779	16582	805.4	664.9	4.8%	4.0%	29.49	30.72	1.70	1.54	5.8%	5.0%
Total Imprecision					6.4%	4.3%					8.3%	6.8%					6.6%	6.1%

RESULTS - SENSITIVITY

Samples were tested across each assay's measuring range and sensitivity capabilities of LoB, LoD and LoQ were calculated for the prototype and predicate platforms. The calculated conservative surrogate estimates are shown below. Testing was completed across multiple pack lots and calibrator lots to also evaluate lot-to-lot variation.

Limit of Blank (LoB)

	PCT (ng/mL)	hsTnI (pg/mL)	TSH (3rd IS) (µIU/mL)
Claim	≤ 0.005	≤ 4.0	≤ 0.005
Access 2	0.002	1.23	< 0.001
Prototype†	< 0.001	0.52	< 0.001

Limit of Detection (LoD)

	PCT (ng/mL)	hsTnI (pg/mL)	TSH (3rd IS) (µIU/mL)
Claim	≤ 0.01	≤ 4.0	≤ 0.005
Access 2	0.004	1.56	0.003
Prototype†	0.002	0.63	0.001

Limit of Quantitation (LoQ)

	PCT (ng/mL) 20% CV	hsTnI (pg/mL)	TSH (3rd IS) (µIU/mL) 20% CV
Claim	≤ 0.02	≤ 11.5 (10% CV) ≤ 5.0 (20%CV)	≤ 0.01
Access 2	0.007	2.9 (10% CV) 1.1 (20% CV)	0.004
Prototype†	0.003	0.75 (10% CV) 0.33 (20% CV)	0.001

CONCLUSION

Preliminary assay data generated on the next-generation, high-volume immunoassay analyzer prototype system demonstrates a strong correlation to Access 2 and enhanced performance with regards to precision. Accuracy analyses showed there is minimal (<5%) dose difference between the prototype and predicate platforms.

Additionally, characterization data demonstrates the opportunity to achieve improved sensitivity for assays including Access TSH 3rd IS, Access hsTnI, and Access PCT while increasing tests available from each individual pack for TSH and PCT assays.

References

1. CLSI. Approved Guideline – Measurement Procedure Comparison and Bias Estimation Using Patient Samples, EP9C-ED3. Clinical and Laboratory Standards Institute.
2. CLSI. Approved Guideline – Evaluation of Precision of Quantitative Measurement Procedures, EP5-A3. 2014. Clinical and Laboratory Standards Institute.
3. CLSI. Approved Guideline – Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, EP17-A2. 2012. Clinical and Laboratory Standards Institute.
4. Soller, et al. (2018-2020). Prototype analyzer evaluation [Unpublished raw data]. Beckman Coulter.

† The prototype is not cleared or approved for commercial use is any geography