ANALYTICAL PERFORMANCE CHARACTERISTICS OF THE NEW BECKMAN COULTER ACCESS PCT IMMUNOASSAY

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BACKGROUND

Procalcitonin is a peptide of 116 amino acids with a molecular weight of ~13 kDa. PCT is produced in thyroid C-cells where it is converted to calcitonin in healthy individuals with less than 0.1 ng/mL PCT normally in circulation. PCT is a useful biomarker for diagnosis of sepsis and systemic inflammation because PCT levels increase in response to bacterial endotoxins and inflammatory cytokines.

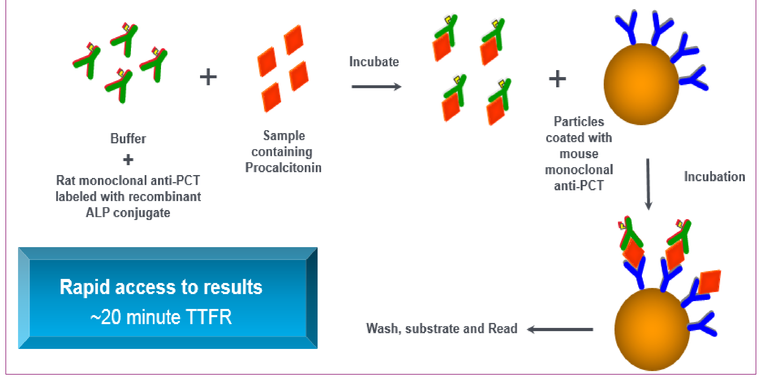
Beckman Coulter recently developed a highly sensitive procalcitonin (PCT) immunoassay for use on the Access Immunoassay Systems†. The study results described here are from prototype studies of the assay and may not represent final product claims in all geographies.

METHODS

The Access PCT assay is a sequential two-step sandwich assay. Monoclonal anti-PCT antibody alkaline phosphatase conjugate is added with sample to a reaction vessel and incubated. Paramagnetic particles* coated with a different monoclonal anti-PCT antibody are then added and incubated. After washing, a chemiluminescent substrate is added and light is generated which is directly proportional to the PCT concentration in the sample. The assay time to first result is ~20 minutes.

*The Access PCT assay does not utilize biotin-streptavidin particle chemistry; as a result, it is not susceptible to biotin interference.

ACCESS PCT: SEQUENTIAL TWO-STEP 'SANDWICH' ASSAY



RESULTS

Assay Characteristic	Access PCT Assay
Analytical Measuring Range	~ 0.02 to 100 ng/mL Up to 1000 ng/mL with automated dilution
Sample Volume	35 µL
Tests per Pack	50
Calibrators S0-S6	Lyophilized Reconstituted Stability: 4 Hours at 20 to 25˚C 90 Days at -30 to -15˚C 3 freeze/thaws
Open-Pack/Stored Curve Stability	42 Days
Sample Types	Serum (gel or no gel) Lithium Heparin Plasma EDTA Plasma
Hook Effect	No hook effect up to 5,000 ng/mL

		Within-Run (Repeatability)		Between-Run		Between-Day		Within Lab (Total Imprecision)	
Sample	Grand Mean (ng/mL) (n=80)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)
QC 1	**0.68**	0.013	1.9	0.014	2.1	0.015	2.2	0.024	**3.6**
QC 2	**2.15**	0.040	1.9	0.056	2.6	0*	N/A	0.069	**3.2**
QC 3	**20.65**	0.333	1.6	0.531	2.6	0.228	1.1	0.667	**3.2**
Sample 1	**0.090**	0.003	3.2	0.002	2.7	0.005	5.8	0.006	**7.2**
Sample 2	**0.18**	0.006	3.2	0.003	1.7	0.008	4.3	0.010	**5.6**
Sample 3	**0.27**	0.008	2.8	0.003	1.0	0.009	3.2	0.012	**4.4**
Sample 4	**0.43**	0.011	2.6	0.014	3.3	0.016	3.8	0.024	**5.7**
Sample 5	**1.41**	0.039	2.8	0.034	2.4	0.048	3.4	0.070	**5.0**
Sample 6	**7.59**	0.175	2.3	0.121	1.6	0.239	3.2	0.320	**4.2**
Sample 7	**76.31**	1.753	2.3	1.773	2.3	1.452	1.9	2.885	**3.8**

*Default value when estimated variance was negative

Figure 1 A precision study was performed according to CLSI EP05-A3[1] using serum samples run over 20 days. The total imprecision for serum sample mean PCT concentrations from 0.090 to 76.31 ng/mL resulted in %CV values of 3.8 to 7.2.

		Within-Run		Between-Run		Between-Day		Between Site		Between Lot		Reproducibility	
Sample	Grand Mean (ng/mL) (n=176)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)
QC 1	**0.68**	0.015	2.2	0.009	1.3	0.013	1.9	0.008	1.2	0.006	0.9	0.024	**3.5**
QC 2	**2.20**	0.046	2.1	0.039	1.7	0*	N/A	0.049	2.2	0.019	0.9	0.079	**3.6**
QC 3	**21.01**	0.418	2.0	0.308	1.5	0.368	1.8	0.652	3.1	0*	N/A	0.911	**4.3**
Sample 1	**0.090**	0.003	3.2	0.002	2.6	0.003	2.9	0.001	1.6	0.002	2.2	0.005	**5.7**
Sample 2	**0.18**	0.005	2.8	0.004	2.3	0.003	1.7	0.003	1.5	0.004	2.0	0.008	**4.7**
Sample 3	**0.27**	0.008	2.8	0.005	1.8	0.006	2.1	0*	N/A	0.004	1.4	0.011	**4.2**
Sample 4	**0.43**	0.011	2.6	0.009	2.2	0.006	1.4	0.005	1.1	0.007	1.7	0.018	**4.1**
Sample 5	**1.41**	0.039	2.8	0.026	1.8	0*	N/A	0.028	2.0	0.024	1.7	0.060	**4.2**
Sample 6	**7.79**	0.195	2.5	0.135	1.7	0.096	1.2	0.321	4.1	0.124	1.6	0.429	**5.5**
Sample 7	**77.03**	2.218	2.9	1.157	1.5	0.284	0.4	1.529	2.0	1.412	1.8	3.266	**4.2**

*Default value when estimated variance was negative

Figure 2 A reproducibility precision study was performed at three external sites using serum samples run in duplicate with two runs per day over five days. The reproducibility across sites for serum sample mean PCT concentrations from 0.090 to 77.03 ng/mL resulted in %CV values of 3.5 to 5.7.

Parameter	Criteria (ng/mL)	Maximum Observed Result (ng/mL)
LoB	**≤0.005**	**0.001**
LoD	**≤0.01**	**0.002-0.003**
Serum		**0.002**
Lithium Heparin Plasma		**0.002**
EDTA Plasma		**0.003**
LoQ 20% CV	**≤0.02**	**0.002-0.003**
Serum		**0.002**
Lithium Heparin Plasma		**0.002**
EDTA Plasma		**0.003**

Figure 3 Studies performed based on CLSI EP17-A2[2], the Access PCT assay exhibited a Limit of Blank of 0.001 ng/mL, and a Limit of Detection (LoD) and Limit of Quantitation (LoQ) of 0.002 ng/mL in Serum and Lithium Heparin Plasma, and 0.003 ng/mL in EDTA Plasma.

Sample Size	Median (ng/mL)	95% Upper Reference Interval (ng/mL)
202	**0.025**	**0.065**

Figure 4 PCT reference interval testing was performed at one external site on an Access 2 immunoassay system using 202 serum samples from approximately equal numbers of apparently healthy male and female subjects ≥21 years of age.

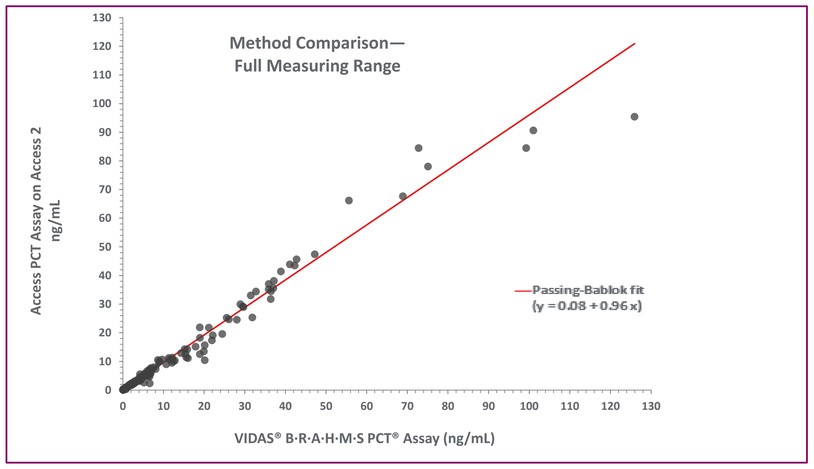


Figure 5 Method Comparison with 229 patient samples using the Access PCT assay and the VIDAS® B·R·A·H·M·S PCT® assay gave a Passing-Bablok Slope of 0.96 and Intercept of 0.08 ng/mL. The Pearson correlation coefficient was 0.99.

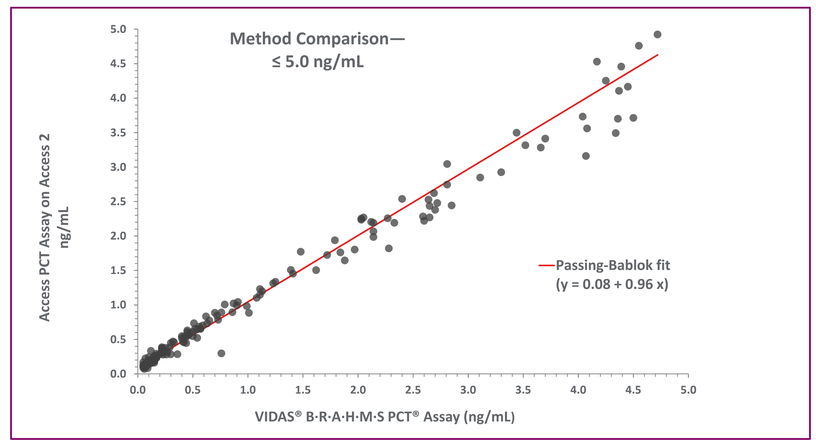


Figure 6 Method Comparison with patient samples ≤ 5 ng/mL using the Access PCT assay and the VIDAS® B·R·A·H·M·S PCT® assay gave a Passing-Bablok Slope of 0.96 and Intercept of 0.08 ng/mL. The Pearson correlation coefficient was 0.99.

	Access 2		
Platform	Correlation (r)	Overall agreement @ 0.5ng/mL	Overall agreement @ 2.0ng/mL
VIDAS® B·R·A·H·M·S PCT®	0.99	95.8%	99.2%
ARCHITECT® B·R·A·H·M·S PCT®	1.0	96.9%	96.1%
ELECSYS® B·R·A·H·M·S PCT®	0.99	97.3%	92.7%

Figure 7 The correlation and analytical concordance between the Access PCT assay and the VIDAS® B·R·A·H·M·S PCT® assay, the ARCHITECT® B·R·A·H·M·S PCT® assay and the ELECSYS® B·R·A·H·M·S PCT® assay at the PCT levels of 0.5 and 2.0 ng/mL.

CONCLUSIONS

The Access PCT prototype assay is highly sensitive and precise, demonstrating strong correlation and concordance to several well-established predicate PCT methods at clinically relevant levels.

REFERENCES

1. CLSI EP05-A3:2014 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition.
2. CLSI EP17-A2:2012 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, Second Edition.

†CE Marked. Pending submission and clearance by the United States Food and Drug Administration; not yet available for *in vitro* diagnostic use in the U.S.

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