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Evaluation of the Analytical Performance of Three Sepsis Related Assays on the Atellica CI Analyzer

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Abstract

Background: The Atellica® CI Analyzer is an automated, high-throughput integrated chemistry and immunoassay analyzer utilizing both Atellica® CH and Atellica® IM assays. This study evaluated the analytical performance of the Atellica IM BRAHMS Procalcitonin (PCT) assay, and the Atellica CH Revised C-Reactive Protein (RCRP) and Lactate_3 (Lac_3) assays on the Atellica CI Analyzer.

Methods: Precision studies were performed according to CLSI EP05-A3 using native and contrived human serum (PCT, RCRP) or plasma and cerebrospinal fluid (Lac_3) samples. One aliquot of each sample pool was tested in duplicate in two runs per day ≥2 hours apart on each analyzer for ≥20 days. Precision studies were evaluated with one to three lots of reagent on one to two systems. Method comparison (MC) studies were performed using three reagent lots according to CLSI EP09c. Individual native and contrived human serum (PCT, RCRP) or plasma and cerebrospinal fluid (Lac_3) samples were analyzed using the Atellica IM PCT assay on the Atellica IM Analyzer, the Atellica CH RCRP, Lac_3 assays on the Atellica CH Analyzer and all three Atellica IM and CH assays listed above on the Atellica CI Analyzer.

Results: Representative precision and MC results for each assay are listed in the table. For the three assays tested, repeatability and within-lab %CVs were <5.1% and <8.9%, respectively. Slopes determined by the Deming linear regression model were approximately equal to 1.

Conclusion: Evaluation of the Atellica IM PCT and Atellica CH RCRP, Lac_3 assays using the Atellica CI Analyzer demonstrated good precision and equivalent performance compared to the same assays on their respective Atellica CH and Atellica IM Analyzers.

Analyte (Assay)	Precision				Method Comparison	
	Unit	Sample Range	Repeatability %CV Range	Within-laboratory %CV Range	Sample Range	Regression Equation for Comparative Assay
Procalcitonin (PCT)	ng/mL	0.08–36.09	1.1–5.0	1.7–8.8	0.06–45.55	y = 1.01x + 0.00 ng/mL
C-Reactive Protein (RCRP)	mg/dL	0.87–13.19	0.3–1.3	0.6–1.8	0.54–24.81	y = 0.99x - 0.06 mg/dL
Lactate (Lac_3)	mg/dL	13.7–116.3	0.6–2.0	1.1–2.1	6.7–138.2	y = 0.98x – 0.2 mg/dL

Background

Quantitative measurement of procalcitonin, C-reactive protein, and lactate in biological samples is performed in clinical laboratories as an aid in the diagnosis and treatment of sepsis.

Previously, three quantitative assays were developed and commercialized for use on the Atellica Analyzers: the Atellica IM BRAHMS Procalcitonin (PCT) assay,[1] and the Atellica CH Revised C-Reactive Protein (RCRP)[2] and Lactate_3 (Lac_3) assays.[3]

Recently, the Atellica CI Analyzer (Figure 1) was added to the Atellica Solution portfolio, with a reduced footprint of 1.9 square meters. It is an integrated clinical chemistry and immunoassay analyzer designed for low- to mid-volume laboratories and features the same reagents,* consumables,* and sophisticated user interface as the Atellica CH and IM Analyzers.[4]

Figure 1. The Atellica® CI Analyzer

To evaluate the analytical performance of the Atellica CH and IM assays using this new analyzer, precision, method comparison, limit of quantitation (LoQ), and linearity studies were assessed as performance indicators for the Atellica IM PCT and Atellica CH RCRP, Lac_3 assays on the Atellica CI Analyzer.

Material and Methods

Precision evaluation was performed according to CLSI EP05-A3. Two runs were performed each day for 20 nonconsecutive days, with a minimum of 2 hours between runs. Samples were tested in duplicate producing a total of n = 80 replicates for each system/lot combination. For each assay, one representative system/lot combination result across all lot and system combinations tested is shown. Precision studies included two calibration events per assay. A panel of human serum (PCT, RCRP) or plasma and cerebrospinal fluid (Lac_3) samples, and controls were tested as indicated in the precision table for each analyte (Tables 1-A to 1-C). Samples across the assay range were prepared using individual or combined native patient samples or normal samples spiked with positive stock made of purified recombinant human procalcitonin (PCT), concentrated C-reactive protein solution (RCRP), or concentrated lactate solution (Lac_3). Samples were frozen in aliquots and stored at ≤ –20°C prior to the start of the study. Each testing day, new aliquots were thawed and used for each run. Calibrators and QC materials were handled according to the manufacturer's instructions.

Method comparison (MC) studies were performed according to CLSI EP09c. Individual native and a few spiked human serum or plasma and cerebrospinal fluid (Lac_3) samples were tested on the Atellica CI Analyzer and Atellica IM (PCT) or CH Analyzer (RCRP, Lac_3). MC was evaluated by comparison to the parent analyzer, which is the Atellica CH or IM assay on the Atellica CH or IM Analyzer, using multiple reagent lots. One replicate was processed for each sample and each reagent lot on each analyzer. The total of native samples tested for each assay is indicated in Table 2. For each assay, one representative system/lot combination result across all lot and system combinations tested is shown in Table 2. Samples with a result outside the measuring interval of the assay were excluded from the analysis. MC studies for each assay were completed in more than 3 nonconsecutive days using a single calibration event. Slope and intercept were calculated using Deming and weighted Deming analysis as indicated in Figure 2.

LoQ studies were performed according to CLSI EP17-A2. Multiple independent low analyte level human serum or plasma and cerebrospinal fluid (Lac_3) samples were prepared and frozen in aliquots prior to the start of the LoQ study. Each testing day, fresh aliquots were thawed. The study was performed with three reagent lots. For the PCT assay, five samples were tested for 20 days, two runs per day with a minimum of 2 hours between runs, and two replicates per run on one analyzer for a total of 400 measurements per reagent lot. Calibration was performed on day 1 of the study. For each reagent lot, the within-laboratory precision for each sample, expressed as %CV, was calculated using a validated 20-day ANOVA Excel algorithm. For each reagent lot, the within-laboratory precision for each sample, expressed as %CV, was plotted against the mean concentration obtained for each sample. These data were then fitted using a power function to give a precision profile. LoQ for each reagent lot was determined as the analyte concentration corresponding to 20% within-lab CV. For the RCRP and Lac_3 assay, 12 and 5 samples were tested for 5 days, one run per day, and five replicates per run, on one analyzer for a total of 300 and 125 measurements per reagent lot, respectively. LoQ for each reagent lot was determined as the highest analyte concentration with an observed within-lab % CV≤20. For each assay, one representative system/lot combination result across all lot and system combinations tested is shown in Table 3. When the estimated LoQ was lower than the design requirement goal for the assay, a conservative value for LoQ was set and reported for the assay (Table 3).

For linearity studies, the linear intervals for the Atellica IM PCT, and Atellica CH RCRP and Lac_3 assays were established on the Atellica CI Analyzer according to CLSI EP06-ED2. High and low analyte samples, prepared from native patient samples, were mixed in various proportions to create a minimum of nine concentrations (Table 4) and assayed for each analyte using three reagent lots.

Results

Precision

Table 1. Precision for the Atellica IM PCT assay (A), and the Atellica CH RCRP (B), and Lac_3 (C) assays on the Atellica CI Analyzer

(A) Atellica IM PCT assay

Specimen Type	Mean (n=80) (ng/mL)	Repeatability		Within-laboratory Precision	
		SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)
Serum	0.08	0.004	5.0	0.007	8.8
Serum	0.26	0.007	2.7	0.011	4.2
Serum	1.92	0.021	1.1	0.038	2.0
Serum	36.09	0.413	1.1	0.598	1.7
Serum QC 1	0.41	0.009	2.2	0.013	3.2
Serum QC 2	10.31	0.129	1.3	0.196	1.9

The Atellica IM PCT assay on the Atellica CI Analyzer demonstrated ≤5.0% repeatability CV and ≤8.8% within-laboratory precision CV across the sample interval.

(B) Atellica CH RCRP assay

Specimen Type	Mean (n=80) (mg/dL)	Repeatability		Within-laboratory Precision	
		SD (mg/dL)	CV (%)	SD (mg/dL)	CV (%)
Serum	1.14	0.008	0.7	0.013	1.1
Serum	13.19	0.085	0.6	0.151	1.1
Serum QC 1	0.87	0.011	1.3	0.016	1.8
Serum QC 2	2.58	0.009	0.3	0.016	0.6
Serum QC 3	4.55	0.032	0.7	0.054	1.2

The Atellica CH RCRP assay on the Atellica CI Analyzer demonstrated ≤1.3% repeatability CV and ≤1.8% within-laboratory precision CV across the sample interval.

(C) Atellica CH Lac_3 assay

Specimen Type	Mean (n=80) (mg/dL)	Repeatability		Within-laboratory Precision	
		SD (mg/dL)	CV (%)	SD (mg/dL)	CV (%)
Plasma	13.7	0.27	2.0	0.29	2.1
Plasma QC	30.2	0.15	0.5	0.32	1.1
Plasma	107.1	0.63	0.6	1.74	1.6
CSF QC	16.7	0.21	1.3	0.32	1.9
CSF	66.5	0.67	1.0	0.99	1.5
CSF	116.3	0.68	0.6	1.56	1.3

CSF; cerebrospinal fluid

The Atellica CH Lac_3 assay on the Atellica CI Analyzer demonstrated ≤2.0% repeatability CV and ≤2.1% within-laboratory precision CV across the sample interval.

Method Comparison

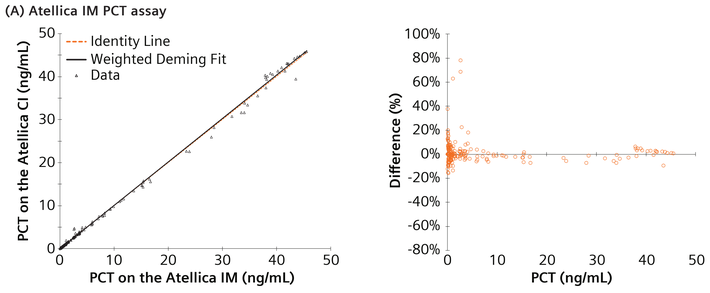
Table 2. Method comparison for the Atellica IM PCT assay, and the Atellica CH RCRP and Lac_3 assays on the Atellica IM (PCT) or Atellica CH (RCRP, Lac_3) and Atellica CI Analyzers

Specimen Type	Assay	Comparison Analyzer (X)	n	r	Regression Equation	Sample Range
Serum	Atellica IM PCT	Atellica IM	208	0.999	y = 1.01x + 0.00	0.06–45.55 ng/mL
Serum	Atellica CH RCRP	Atellica CH	111	0.999	y = 0.99x – 0.06	0.54–24.81 mg/dL
Plasma	Atellica CH Lac_3		100	1.00	y = 0.98x – 0.2 (y = 0.98x – 0.02)	6.7–138.2 mg/dL 0.74–15.34 mmol/L
CSF			100	1.00	y = 0.98x – 0.2 (y = 0.98x – 0.02)	2.0–139.9 mg/dL 0.22–15.53 mmol/L

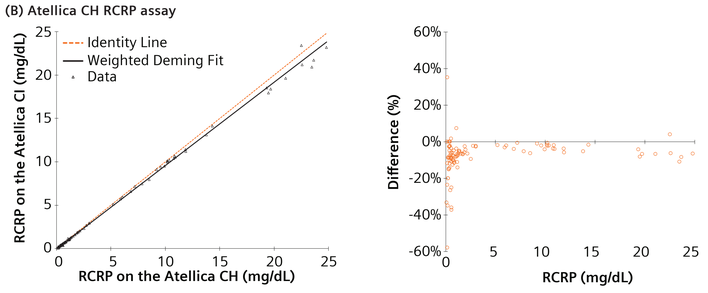
The design requirements for method comparison were met for the PCT, RCRP, and Lac_3 assays. When analyzed by regression, each Atellica CH or IM assay on the Atellica CI Analyzer recovered samples spanning the measuring interval, with a slope of 1.0 ± 0.1 and a correlation coefficient ≥ 0.95 (r) compared to the Atellica CH or IM Analyzer.

Weighted Deming or Deming fit and percent difference plots on the Atellica CI Analyzer for samples ranges indicated in Table 2 are shown for the Atellica IM PCT (Figure 2A) assay, and the Atellica CH RCRP (Figure 2B), and Lac_3 (plasma, Figure 2C; CSF, Figure 2D) assays.

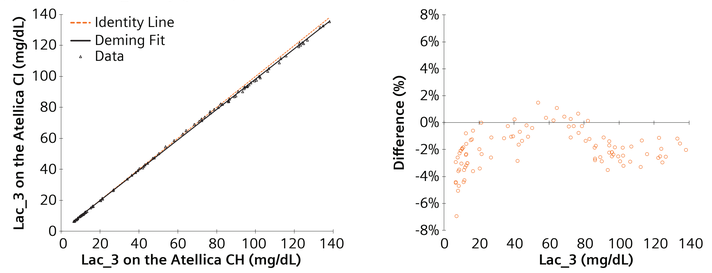
(A) Atellica IM PCT assay



(B) Atellica CH RCRP assay



(C) Atellica CH Lac_3 assay (plasma)



(D) Atellica CH Lac_3 assay (CSF)

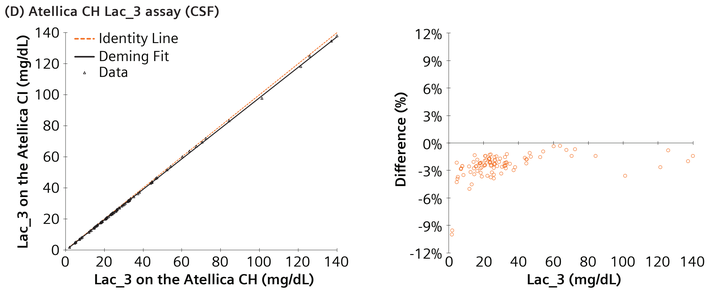


Figure 2. Weighted Deming or Deming linear regression and difference plots for the Atellica IM PCT assay (A), and the Atellica CH RCRP (B) and Lac_3 (plasma, (C); CSF, (D)) assays on the Atellica IM (PCT) or Atellica CH (RCRP, Lac_3) and Atellica CI Analyzers

Detection Capability

Table 3. LoQ for the Atellica IM PCT assay, and the Atellica CH RCRP and Lac_3 assays on the Atellica CI Analyzer

Specimen Type	Assay	Total Replicates per Reagent Lot	Lowest Concentration with CV ≤20%†	LoQ Reported
Serum	Atellica IM PCT	400	0.04 ng/mL*	0.04 ng/mL
Serum	Atellica CH RCRP	300	0.41 mg/dL	0.50 mg/dL
Plasma	Atellica CH Lac_3	125	1.1 mg/dL (0.12 mmol/L)	1.8 mg/dL (0.20 mmol/L)
CSF		125	1.4 mg/dL (0.16 mmol/L)	

**Lowest concentration at 20% CV using precision profile function.*
†Representative data obtained from one reagent lot using one Atellica CI analyzer, for each assay listed in the table.

For the PCT assay, the LoQ that corresponds to the lowest amount of procalcitonin in a sample at 20% within-laboratory CV resulted at 0.04 ng/mL. For the RCRP and Lac_3 assays, the highest analyte concentrations with observed within-lab % CVs ≤20 were 0.50 mg/dL and 1.8 mg/dL (0.20 mmol/L), respectively.

Linearity

Table 4. Linear interval of the Atellica IM PCT assay, and the Atellica CH RCRP and Lac_3 assays on the Atellica CI Analyzer

Specimen Type	Assay	# of Sample Combinations Tested	Linearity Reported
Serum	Atellica IM PCT	10	0.04–50.00 ng/mL
Serum	Atellica CH RCRP	11	0.50–25.00 mg/dL
Plasma	Atellica CH Lac_3	9	1.8–140.0 mg/dL (0.20–15.54 mmol/L)
CSF			

The Atellica IM PCT and the Atellica CH RCRP and Lac_3 assays are linear on the Atellica CI Analyzer across the intervals indicated in Table 4.

Conclusion

All results indicate that the Atellica IM PCT, and the Atellica CH RCRP and Lac_3 assays demonstrated analytical performance capable of measuring proclacitonin, C-reactive protein and lactate in serum or plasma and cerebrospinal fluid (Lac_3) samples with good accuracy and precision when run on the Atellica CI Analyzer. In addition, good concordance was observed between the assays on the Atellica CI Analyzer and the Atellica CH or Atellica IM Analyzer, depending on the analyte tested. Altogether, these results support that the Atellica CI Analyzer has performance capability comparable to the Atellica CH and Atellica IM Analyzers as a low- to mid-volume integrated clinical chemistry and immunoassay analyzer.

References

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Data/some data first presented at Worldlab IFCC 2024.

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