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Assessment of the DCA Vantage and Atellica DCA HbA1c Dx Assays Compared to the European Reference Laboratory Method

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Background

The CDC National Diabetes Statistics Report states that over 38 million people have diabetes or 11.6% of the U.S. population.[1] Of the total number of people with diabetes, 29.7 million have been diagnosed, while around 8.7 million have gone undiagnosed. This suggests that 22.8% of adults with diabetes are undiagnosed. In 2008, the American Diabetes Association organized the International Expert Committee, the European Association for the Study of Diabetes, and the International Diabetes Federation; these groups worked on and developed criteria for the use of HbA1c in diagnosing diabetes.[2] After diagnosis of diabetes, HbA1c levels are monitored to best manage treatment and see how a plan works over time.[3] Maintaining optimal levels of HbA1c reduces risk of serious diabetes-related complications, including cardiovascular diseases, kidney failure, and neuropathy.[4]

Measurement of HbA1c point-of-care testing (POCT) provides rapid test results during patient/doctor office visits. This added convenience also has potential for broader reach to low-access populations. Siemens-Healthineers offers HbA1c POCT on both the Atellica DCA Analyzer and the DCA Vantage systems, providing measurement of hemoglobin A1c concentration that is recommended for monitoring the long-term care of persons with diabetes. To support the standardization of HbA1c measurement methods, the European Reference Laboratory for Glycohemoglobin (ERL) supplies value-assigned samples by using various reference methods based on different measurement principles, each calibrated with IFCC secondary reference material.

HbA1c is formed by the non-enzymatic glycation of the N-terminus of the β-chain of hemoglobin A. The HbA1c level reflects the mean glucose concentration over the previous period (approximately 8–12 weeks, depending on the individual) and provides better indication of long-term glycemic control than blood and urinary glucose determinations.[5] Studies have shown that long-term control of HbA1c levels can decrease the risk for development and progression of chronic complications caused by diabetes.[6,7]

The level of HbA1c is proportional to the level of glucose in the blood over a period of approximately 2–3 months. Hence, HbA1c is accepted as an indicator of the mean daily blood glucose concentration over the preceding 2–3 months.[8-11]

To evaluate the analytical performance of the Atellica DCA Analyzer and DCA Vantage systems for HbA1c testing, both systems were used to measure a set of ERL value-assigned samples. The results from each system were then individually compared to the ERL assigned values to assess accuracy and support standardization across POCT methods.

Figure 1. The Atellica DCA Analyzer

Principles of the Procedure

The Atellica DCA Analyzer and DCA Vantage systems, with use of the HbA1c Dx and DCA Systems Hemoglobin A1c reagent kit, respectively, automatically measure and calculate HbA1c using an inhibition of latex agglutination assay.[12,13] The concentration of hemoglobin A1c and the total hemoglobin are measured, and the ratio is reported.[10,14]

For the measurement of total hemoglobin, potassium ferricyanide is used to oxidize hemoglobin in the sample to methemoglobin. The methemoglobin then complexes with thiocyanate to form thiocyan-methemoglobin; the colored species that is measured. The extent of color development at 531 nm is proportional to the concentration of total hemoglobin in the sample.

For the measurement of specific HbA1c, an inhibition of latex agglutination assay is used. An agglutinator, synthetic polymer containing multiple copies of the immunoreactive portion of HbA1c, causes agglutination of latex coated with HbA1c specific mouse monoclonal antibody.
This agglutination reaction causes increased scattering of light, which is measured as an increase in absorbance at 531 nm. HbA1c in whole blood specimens competes for the limited number of antibody latex binding sites causing an inhibition of agglutination and a decreased scattering of light. The decreased scattering is measured as a decrease in absorbance at 531 nm. The HbA1c concentration is then quantified using a calibration curve of absorbance versus HbA1c concentration.

HbA1c in the sample is then calculated as follows:

$$\%HbA1c = [HbA1c] / [Total\ hemoglobin] \times 100$$

IFCC concentration in mmol/mol HbA1c is calculated as follows:

$$HbA1c\ mmol/mol = [HbA1c\ mmol] / [Total\ hemoglobin\ mol]$$

All reagents for performing these measurements are contained in the Atellica DCA Analyzer HbA1c Reagent Cartridge. All measurements and calculations are performed automatically by the Atellica DCA Analyzer, and the screen displays the HbA1c concentration at the end of the test. Values are in % HbA1c NGSP and where shown, in parentheses, as mmol/mol HbA1c IFCC.

Materials and Methods

Method Comparisons (CLSI EP09c-ED3)

- Method comparison (MC) studies compared the DCA Vantage systems HbA1c Cartridge's (CLIA-waived) and Atellica DCA HbA1c Dx (outside the United States) assay's performance to the ERL value-assigned samples.
- Samples (N=40, value-assigned by ERL) were assayed in duplicate on each analyzer. Value-assigned samples were reviewed using both IFCC units (mmol/mol) and NGSP units (%), which were derived from the former.
- Statistical analysis of DCA Vantage HbA1c vs ERL and Atellica DCA HbA1c vs ERL (multilevel means as outcomes linear least-squares) and DCA Vantage vs Atellica DCA HbA1c (Weighted Deming) were carried out and coefficients of determination (pseudo-R^2) calculated. Additionally, a method comparison of the DCA Vantage vs Atellica DCA HbA1c was performed (Weighted Deming) using the Replicate 1 results and then repeated using the Replicate 2 results.

Results

The following results are representative of the performance of the assay.

Both the Atellica DCA Analyzer and DCA Vantage systems exhibited similar performance characteristics, with results closely matching each other and showing strong agreement with the ERL-assigned reference values across the 40 tested samples.

Table 1. Summary of HbA1c (%) testing on Comparative Devices

Test Method	Reference Method	Regression Analysis model	N	Slope	Intercept	R^2
DCA Vantage systems	ERL Assigned	ML means as outcomes least squares*	40 paired replicates	0.9726	0.1766	0.9999
Atellica DCA Analyzer	ERL Assigned	ML means as outcomes least squares*	40 paired replicates	0.9970	0.0702	0.9983
Test Method 1	**Test Method 2**	**Regression Analysis model**	**N**	**Slope**	**Intercept**	**R^2**
Atellica DCA Analyzer	DCA Vantage systems	Weighted Deming	40 paired replicates	1.0251	-0.1103	0.9928

**Multilevel (ML) means-as-outcomes linear least squares model.*

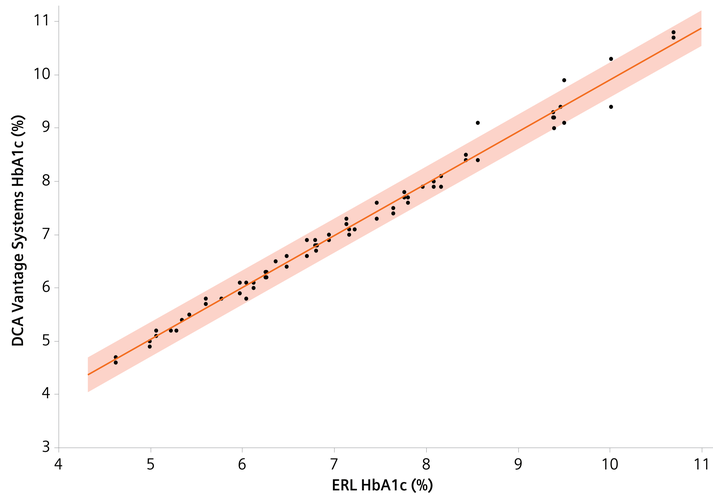

Figure 1. Comparison of the DCA Vantage systems to ERL HbA1c methods (*orange, band is a 95% prediction interval*). Samples ranged from 4.62% HbA1c to 10.69% HbA1c (27.00 to 93.34 mmol/mol). The comparison of the DCA Vantage systems to ERL methods of testing HbA1c level yielded y = 0.9726 x + 0.1766% HbA1c (y = 0.9726 x+ 1.3188 mmol/mol, with R^2=0.9999).

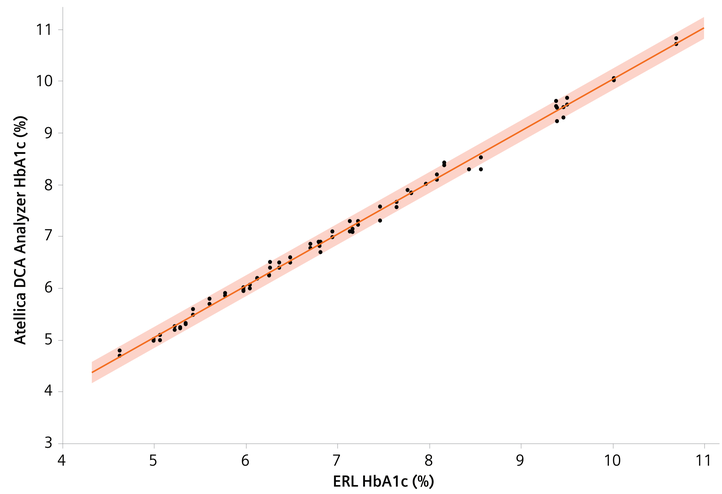

Figure 2. Comparison of the Atellica DCA Analyzer to ERL HbA1c methods (*orange, band is a 95% prediction interval*). Samples ranged from 4.62% HbA1c to 10.69% HbA1c (27.00 to 93.34 mmol/mol). The comparison of the Atellica DCA Analyzer to ERL method of testing HbA1c levels yielded y = 0.9970 x + 0.0702% (y = 0.9973 x+ 0.6967 mmol/mol, with R^2=0.9983).

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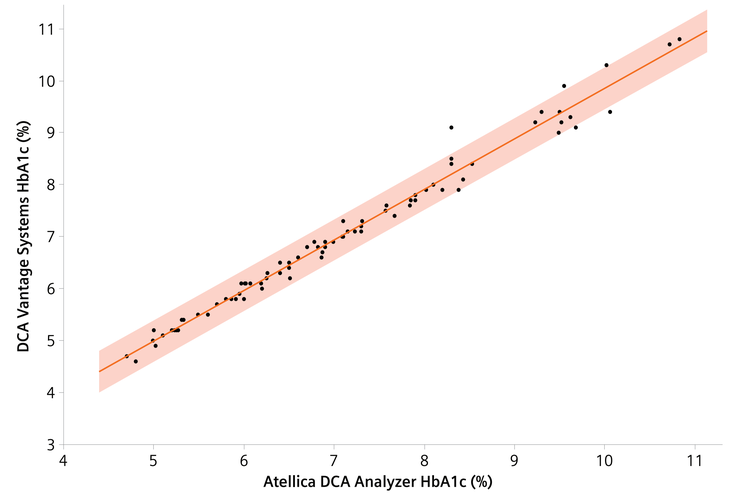

Figure 3. Comparison of the DCA Vantage systems to Atellica DCA Analyzer HbA1c methods (*orange, band is a 95% prediction interval*). Samples ranged from 4.62% HbA1c to 10.69% HbA1c (27.00 to 93.34 mmol/mol). The comparison of the Atellica DCA Analyzer to DCA Vantage systems of testing HbA1c levels yielded y = 1.0251 x + -0.1103% (y = 0.9756 x+ 0.6018 mmol/mol, with R^2=0.9929).

Samples ranged from 4.62% HbA1c to 10.69% HbA1c (27.00 to 93.34 mmol/mol). Using Weighted Deming regression for the HbA1c assays comparing the DCA Vantage systems HbA1c (y) to Atellica DCA Analyzer HbA1c (x) resulted in the following fits:

Replicate 1 vs Replicate 1:
y = 0.9612 x + 0.2135% (y = 0.9612 x + 1.4213 mmol/mol, with R^2 = 0.9852)
Replicate 2 vs Replicate 2:
y = 0.9890 x + 0.0083% (y = 0.9890 x – 0.1670 mmol/mol, with R^2 = 0.9802)

Medical Decision Levels

Medical decisions, based on American Diabetes Association, are made at 5.7%, marking the start of pre-diabetes, and up to 6.5% and higher, diagnosing Diabetes type 2 for most people.[15] Relative differences [100 x (assay – (ERL-assigned)) / (ERL-assigned)] at these medical decision levels comparing the ERL method results against the DCA Vantage systems and Atellica DCA Analyzer HbA1c methods, were determined: at 5.7% (ranges: 5.40% to 6.04% and 5.55% to 5.96% respectively) and 6.5% (ranges: 6.18% to 6.81% and 6.35% to 6.75%, respectively).

Table 2. Summary of Decision Level Comparability

Methods	HbA1c (%)	Relative Difference
Atellica DCA Analyzer vs ERL	5.7	0.7%
	6.5	0.6%
	8.0	0.6%
	12.0	0.6%
DCA Vantage systems vs ERL	5.7	0.8%
	6.5	0.2%
	8.0	-0.5%
	12.0	-1.6%
Atellica DCA Analyzer vs DCA Vantage systems	5.7	0.1%
	6.5	0.5%
	8.0	1.1%
	12.0	2.0%

Conclusions

The results from this study demonstrate that both the Atellica DCA Analyzer and the DCA Vantage systems provide HbA1c measurements that strongly correlate with those from the European Reference Laboratory (ERL), as evidenced by R^2 values exceeding 0.99 in method comparisons. These findings confirm the analytical robustness and clinical reliability of both Siemens Healthineers' point-of-care platforms in the measurement of HbA1c, across a clinically relevant range of concentrations.

Moreover, the close agreement between the two systems themselves (R^2 = 0.9928), and their consistent performance at key medical decision thresholds (5.7%, 6.5%, 8.0%, and 12.0% HbA1c), support their interchangeability for diabetes monitoring in various care settings. This high level of comparability to a global reference standard reinforces the role of these POCT systems in supporting timely, evidence-based diabetes management.

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