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Quantitative Analysis of Creatinine and HbA1c from Dried Microsamples as a Patient Centered Approach for Value Based Care Programs

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Background

Value based care (VBC) programs in the U.S. increasingly incentivize regular diabetes monitoring, supported by Centers for Medicare & Medicaid Services (CMS) policies that cover up to two diabetes screenings annually, including HbA1c testing without coinsurance. Clinical guidelines emphasize regular assessment of glycemic control and kidney function to prevent diabetes related complications. However, traditional venous blood collection can limit access and adherence, particularly for patients in rural settings or with mobility constraints. Dried blood microsampling offers a decentralized alternative by enabling convenient, at home capillary collection, reducing the need for clinic visits and improving patient participation. By facilitating more frequent monitoring, microsampling technology may help providers meet VBC quality metrics, including glycemic control and early detection of kidney disease, potentially supporting improved outcomes and reimbursement performance.[1-5]

Methods

A quantitative method comparison was performed between conventional venous samples and artificial dried blood microsamples derived from venous whole blood for HbA1c and creatinine measurement using the Siemens Healthineers Atellica CH Analyzer.

HbA1c was measured from dried Capitainer B microsamples using the Atellica CH Enzymatic Hemoglobin A1c (A1c_E) assay. Venous whole blood from healthy donors was applied to Capitainer B cards, generating two 10 µL spots per sample. In parallel, HbA1c was measured directly from whole blood as the reference. Prepared cards were air dried overnight at ambient temperature. For microsample processing, each spot was treated with 222 µL A1c_E Pretreatment solution (normally used for automated lysis), followed by incubation at 37°C for 1 hour with agitation. After centrifugation using spin filter columns, eluates were analyzed individually using a modified A1c_E assay protocol that bypassed the onboard lysis step. In total, 53 samples were analyzed in duplicates over 28 weeks.

Creatinine was measured using Capitainer B50 dried microsamples with the Atellica CH Enzymatic Creatinine_3 (ECre3) assay. Whole blood from healthy donors and disease control samples was applied to Capitainer B50 cards, generating two 50 µL spots per sample. Plasma obtained by centrifugation served as the reference measurement. Cards were dried overnight at ambient temperature and eluted using 500 µL of an 80:20 methanol:water solution to retain hemoglobin and reduce photometric interference. After incubation, eluates were collected and analyzed using a modified ECre3 assay that omitted the predilution step.

A total of 17 samples were measured in duplicates.

Figure 1 provides an overview of the standard workflow and the microsample workflow for both analytes.

Passing–Bablok (PB) regression was used to align microsample results to reference measurements. Linearity was assessed using the Cumulative Sum (CUSUM) test. Agreement after correction was evaluated using Bland Altman analysis and Median Absolute Deviation (MAD) standardized residuals to assess dispersion, outliers, and concentration dependent effects.

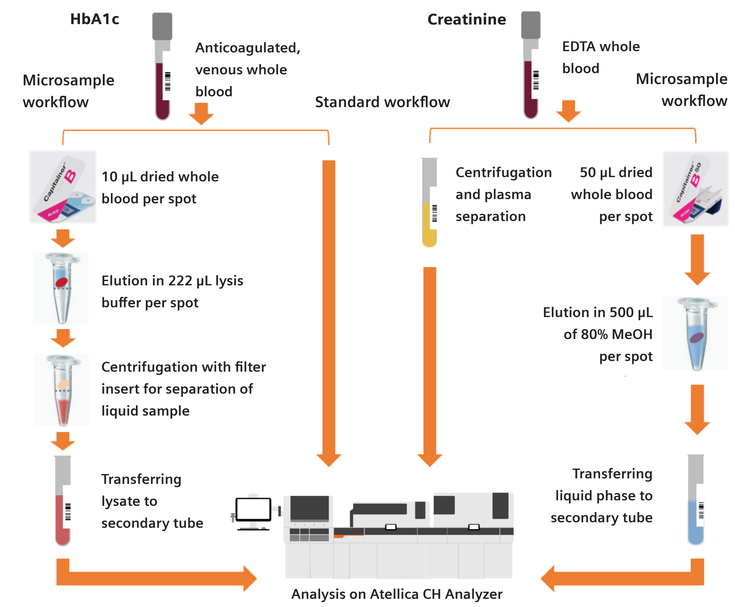

Figure 1. Comparative workflow overview of dried blood microsample preparation versus the standard workflow.

Results

For both analytes, mean values from duplicate microsample spots were used.

For HbA1c, PB regression showed a near proportional relationship between microsamples and whole blood (y = 1.000 x + 0.005). This equation was used to transform microsample results to the scale of the whole blood reference method (Figure 2). No deviation from linearity was detected (CUSUM p = 0.779). After PB based correction, Bland Altman analysis (Figure 3) demonstrated minimal bias (0.01% HbA1c) with narrow, symmetric limits of agreement (–0.176 to 0.197%). MAD residuals were centered around 0 with low dispersion, supporting strong agreement across the measurement range (Figure 4). A slight increase in HbA1c values with prolonged storage (>1 day) was observed for microsamples, suggesting a potential preanalytical effect.

For creatinine, PB regression revealed a consistent proportional bias (y = 3.051 x – 0.338), which was corrected using the regression equation. No deviation from linearity was detected (CUSUM p = 0.694). Post-correction Bland Altman analysis showed low residual bias (0.02 mg/dL creatinine) and symmetric limits of agreement (–0.243 and 0.286 mg/dL). MAD residuals were evenly distributed with minimal outliers, indicating reliable performance across concentrations (Figure 4).

Efficient hemoglobin retention in eluates was visually confirmed, supporting suitability for photometric analysis.

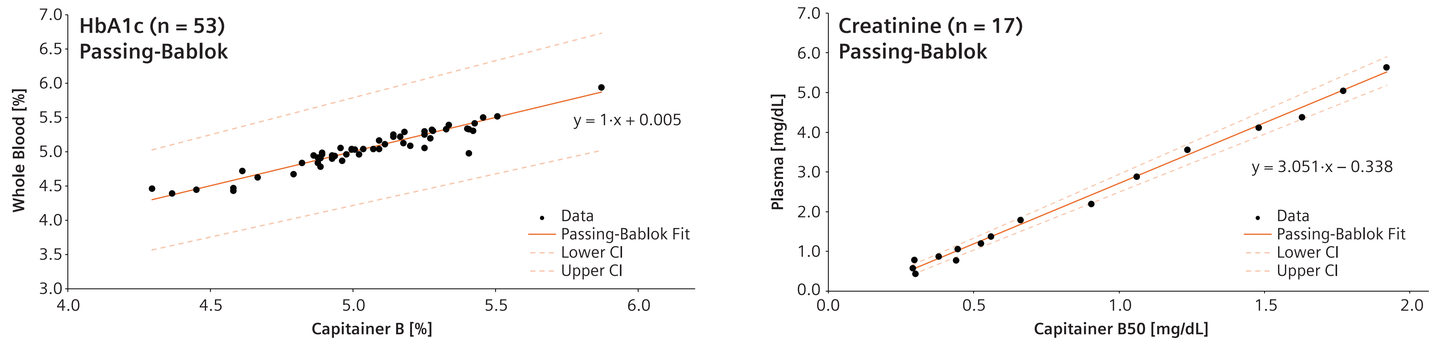

Figure 2. Passing Bablok regression analysis for HbA1c and creatinine, correlating microsample measurements with the corresponding liquid reference methods

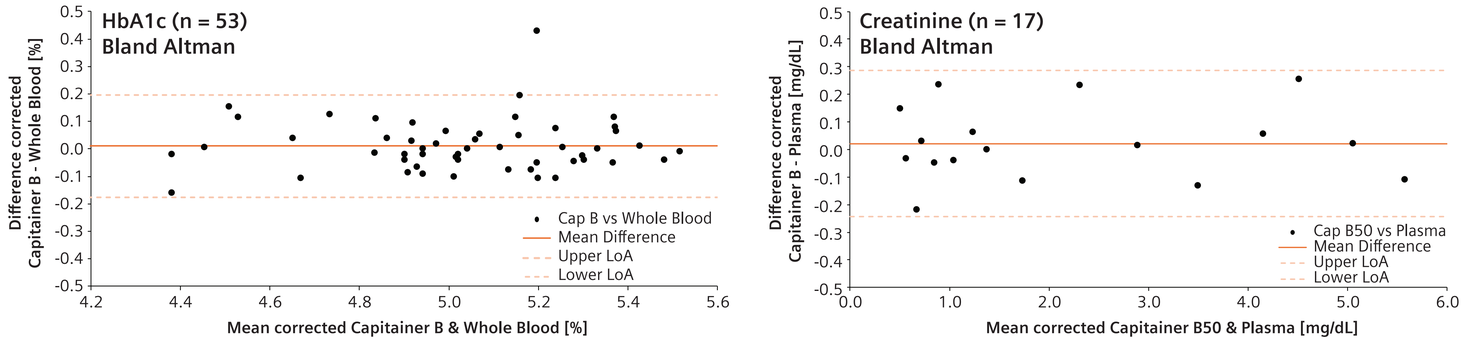

Figure 3. Bland Altman plots for HbA1c and creatinine showing agreement between Passing Bablok–corrected microsample results and corresponding liquid reference measurements. Mean difference and limits of agreement are indicated.

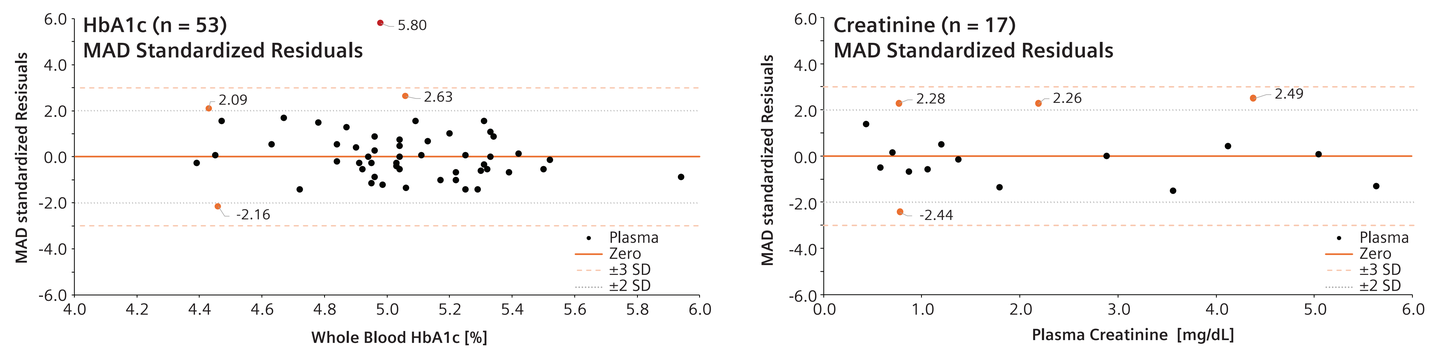

Figure 4. MAD standardized residuals following Passing Bablok correction for HbA1c and creatinine illustrating residual dispersion.

Conclusion

- Capitainer dried blood microsampling demonstrated strong analytical comparability to venous reference measurements for HbA1c and creatinine on the Atellica CH Analyzer after application of regression-based alignment under controlled study conditions.
- Linearity and low residual variability were observed, supporting the technical feasibility of evaluating microsamples using standard chemistry assays under controlled study conditions.
- Matrix-related differences were identified, indicating that microsample-derived results are not directly interchangeable with conventional measurements without appropriate correction.
- Further validation in capillary samples, broader concentration ranges, and real-world collection conditions is required to assess future applications.

References

1. *https://www.cms.gov/priorities/innovation/key-concepts/value-based-care*
2. *https://www.medicare.gov/coverage/diabetes-screenings*
3. *https://www.cms.gov/files/document/mm13487-diabetes-screening-definitions-update-cy-2024-physician-fee-schedule-final-rule.pdf*
4. *https://aspe.hhs.gov/sites/default/files/documents/6056484066506a8d4ba3dcd8d9322490/rural-health-rr-30-Oct-24.pdf*
5. *https://www.gao.gov/blog/why-health-care-harder-access-rural-america*

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