

Analysis of an Electrochemical Blood Glucose Monitoring System with Hematocrit Compensation: Improved Accuracy by Design

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Abstract

The article entitled "Hematocrit Compensation in Electrochemical Blood Glucose Monitoring Systems" by Teodorczyk and colleagues in this issue of *Journal of Diabetes Science and Technology* demonstrates that the OneTouch® Verio™ glucose meter meets current regulatory expectations for glucose meter performance and is relatively free from interference by hematocrit. The lack of influence of hematocrit on whole blood glucose results is a valuable attribute for hospital applications, where greater variation of hematocrit among patients is anticipated. The choice of reference method for evaluation of glucose meters is an important consideration, and it is not clear to what extent reference methods used to evaluate glucose meters are also free from hematocrit interferences.

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The article by Teodorczyk and colleagues,¹ "Hematocrit Compensation in Electrochemical Blood Glucose Monitoring Systems," in this issue of *Journal of Diabetes Science and Technology* demonstrates an important progression in meter technology. Teodorczyk and colleagues have clearly demonstrated that the OneTouch® Verio™ Glucose meter meets International Organization for Standardization (ISO) standard ISO 15197:2003 accuracy performance expectations, even when challenged with specimens with a wide range of hematocrit levels.

Hematocrit is an important factor considered in the design of glucose meters and reagent test strips. All glucose meters use small volumes of whole blood for analysis, and by convention, results are reported as plasma-

equivalent glucose concentrations (e.g., mmol/liter or mg/dl of plasma).² Because "whole blood" is tested and "plasma-equivalent" results are reported, to ensure that the glucose results are accurate, either the glucose meter technologies are designed to be insensitive to the influence of red blood cells or biased-glucose measures are corrected for the effects of the red blood cells and the associated hematocrit prior to reporting. As long as there is a narrow range of hematocrit values in patients, such as that seen in ambulatory diabetes patients, then a constant correction factor can be used to convert results into plasma-equivalent glucose concentrations.^{2,3} However, there is a wide range of hematocrits among hospitalized patients (in neonates and patients in critical care, oncology, dialysis units, and surgical wards).⁴

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Abbreviations: (FDA) Food and Drug Administration, (ISO) International Organization for Standardization

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Through meter design innovation, such as reported by Teodorczyk and colleagues,¹ glucose meters will be less prone to bias associated with abnormal hematocrit, and will generate more accurate results.

Teodorczyk and colleagues¹ have described a sophisticated mechanism for hematocrit correction with the OneTouch Verio system.¹ In this system, hematocrit is indirectly estimated by measuring the oxidation of potassium ferrocyanide to an upper gold electrode. Increases in hematocrit cause a reduction in the apparent diffusion of reaction components between the cofacially arranged electrodes. This observation was noted to be consistent with the obstruction principle described by Fricke.⁵ An algorithm was then developed that utilizes estimates of glucose, hematocrit, temperature, and antioxidant status to compensate for hematocrit. Teodorczyk and colleagues¹ provide evidence that this hematocrit correction mechanism has reduced, but not eliminated, the impact of hematocrit on the measurement of glucose with the OneTouch Verio system when compared with the Food and Drug Administration (FDA)-preferred reference instrument, the YSI 2300 STAT PLUS™ glucose analyzer. The precise mechanism by which hematocrit influences the measurement of glucose with direct reading biosensors is unknown. Teodorczyk and colleagues¹ described the well-documented observation that negative biases are observed with glucose meter analysis of specimens with hematocrit levels > 42%; whereas positive biases (relative to the reference method) have been reported for specimens with hematocrit levels < 42%. The authors indicated that this phenomenon has been attributed to “diffusion due to increased sample viscosity or the action of red blood cells to impede plasma diffusion to the sensor reagent zone, and to pore blockage in membrane-based devices.”¹ This is a valid explanation for the hematocrit effect at the surface of the electrodes. The displacement of fluid volume by hemoglobin is the basis of the International Federation of Clinical Chemistry and Laboratory Medicine correction factor for reporting whole blood glucose in plasma-equivalent concentrations.² The manner in which this type of factor is used to correct for hematocrit is often considered proprietary by manufacturers, and it was not discussed by the authors in their report on the OneTouch Verio.

The FDA, the ISO, and the Clinical Laboratory Standards Institute are all currently reexamining performance expectations for glucose meters. Representation to these organizations includes specific government bodies, professional organizations, the diagnostic industry, health care professionals, and end users. Establishment

of performance expectations are achieved through consensus accounting for current technological limitations, different clinical needs for community versus hospitalized patients, and the balance between provision of a service and patient safety.

The choice of reference methodology to which glucose meter results will be compared by regulatory bodies establishing method performance is an extremely important issue. The vast majority of evaluations in peer-reviewed literature compare glucose meter results to whole blood analyzed by blood gas analyzers or the YSI analyzer or to various automated plasma glucose methods. A minority of studies have attempted to use more analytically rigorous isotope dilution mass spectrometry or acid-stabilized glucose reference methods. It has been well established that exogenous treatments/medications such as maltose, ascorbic acid, or acetaminophen as well as endogenous factors such as hematocrit can influence the quality of results obtained from glucose meters.^{4,6}

Reference methods have helped identify exogenous interferences, but it is often not well documented how these methods are influenced by endogenous and exogenous factors in patient samples. The goal has been to develop methods that are free from interference and that are capable of reliably hitting close to the target glucose values (**Figure 1**). Teodorczyk and colleagues¹ have demonstrated that the OneTouch Verio is relatively free from hematocrit interference. We wonder if the assignment of target values, the placing of the pin, would change should a new reference methodology be confirmed and how this will affect hitting the targets in the future for all devices.

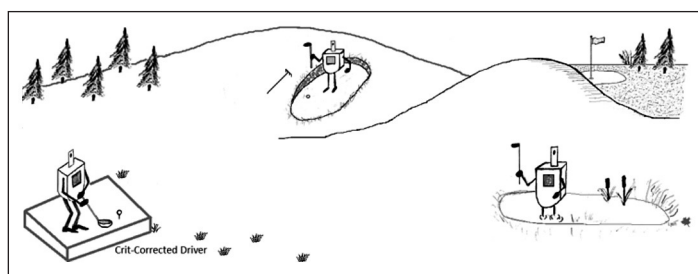


Figure 1. Improved glucose meter accuracy enables us to reliably hit close to the target, to consistently drive onto the green, technology with a bigger “sweet spot.” However, we are still uncertain about the placement of the pin on the green.

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