WaveSense Algorithms Account for Hematocrit Variations while Determining Blood Glucose

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Introduction

Studies have shown that controlling blood glucose can reduce the onset and progression of the long-term microvascular and neuropathic complications associated with the chronic course of *diabetes mellitus*[1-3]. Episodic blood glucose monitoring has long been considered a very useful method for improving glycemic control[1]. Effective interpretation of readings is dependent on obtaining frequent and accurate glucose readings. While frequency of testing depends on patient motivation, measurement accuracy may be influenced by a variety of known factors. System errors attributable to sample characteristics such as hematocrit, testing environment (ambient temperature and humidity) or manufacturing variability (lot-to-lot differences in test strips) can all affect the accuracy of blood glucose readings[4,5].

In electrochemical blood glucose monitoring systems (BGMS), varying hematocrit levels may affect the accuracy of blood glucose testing by several mechanisms[6]:

- the erythrocytes may physically obstruct and impede the diffusion of plasma into the test strip reagent layer, thereby slowing the rate of reagent dissolution upon sample application
- the diffusion of glucose and reagent components within the plasma may be slowed down by increased erythrocyte levels, thereby reducing the measured electrochemical signal

Electrochemical BGMS typically tend to underestimate blood glucose levels at higher hematocrit and overestimate the levels at lower hematocrit as compared to normal hematocrit levels. The positive and negative bias are relevant because hematocrit variations are quite common in the diabetic population. Renal dysfunction can cause anemia, while smoking or living at high altitudes can lead to an increase in red blood cells[7]. Technologies which are able to compensate and correct for hematocrit variations would enable more accurate BGMS and allow end users to manage their blood glucose levels with tighter control.

Aims

The aims of this study were as follows:

- to evaluate the ability of WaveSense Dynamic Electrochemistry technology to compensate and correct for the bias effects of hematocrit on BGMS accuracy
- to quantify the distribution of hematocrit levels seen in real-world clinical settings
- to investigate the efficacy of WaveSense technology to correct for hematocrit bias across multiple test strip production lots

Methods

Glucose concentrations were measured from fresh capillary whole blood fingerstick samples from both WaveSense brand BGMS and the YSI 2300 STAT Plus (reference method) as follows:

- Codeless WaveSense brand BGMS were used
- Data were gathered from four clinical sites with a range of temperatures (20.1° to 27.9°C), humidity (<15% to 50%), and altitudes (8 meters to 2311 meters).
- A total of 416 study participants with either Type I or Type II Diabetes were sampled
- 1,143 test strips were used (across eleven unique strip lots)

For each patient sample, the hematocrit was measured and tabulated. The bias due to hematocrit was calculated for each whole unit hematocrit level as the percent deviation of the WaveSense brand BGMS reading from the YSI reference value, as described below.

Results

Accuracy Analysis

The overall BGMS accuracy was assessed by Parkes Consensus Error Grid analysis[8]. Figure 1 shows all individual meter readings plotted versus the YSI reference value (n=1143). In summary, 99.6% of readings fell within Zone A (no effect on clinical outcome) and the remaining 0.4% of readings fell within Zone B (altered clinical action with little or no effect on clinical outcome). The bias of the meter readings from the YSI value was also tabulated in the ISO 15197[9] format (Table 1). Overall, 98.9% of the results fell within the ISO acceptability criteria (95% of the results must be within ± 0.83 mM of the reference value at concentrations < 4.2 mM and within ± 20% of the reference value at concentrations ≥ 4.2 mM).

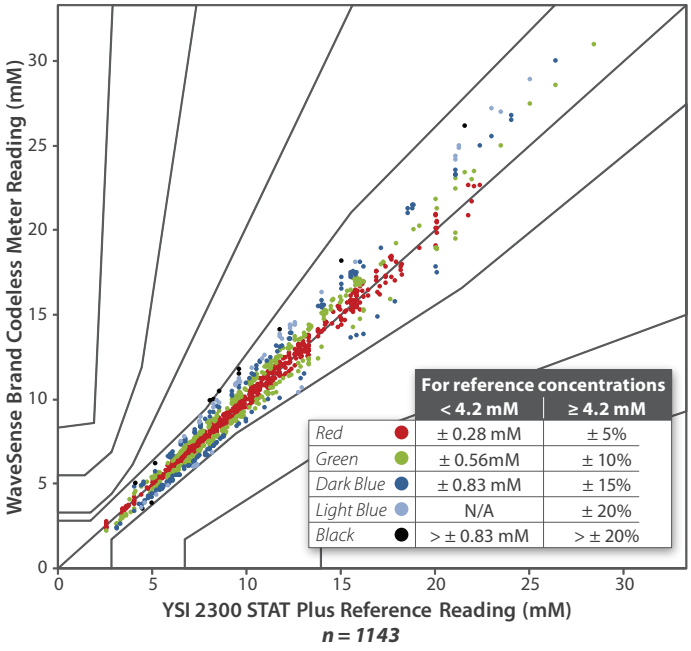

Figure 1. *Parkes Consensus Error Grid analysis of WaveSense brand codeless BGMS readings vs. the YSI reference readings.*

Table 1. *Accuracy of the codeless BGMS powered by WaveSense.*

For reference concentrations < 4.2 mM		
Within ± 0.28 mM	Within ± 0.56 mM	Within ± 0.83 mM
47.7%	**86.4%**	**97.7%**

For reference concentrations ≥ 4.2 mM			
Within ± 5%	Within ± 10%	Within ± 15%	Within ± 20%
49.8%	**79.4%**	**94.6%**	**99.0%**

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Effect of Hematocrit

The systematic effect of hematocrit variation on the accuracy of the BGMS readings was investigated by analyzing the bias of the BGMS readings from the YSI as a function of hematocrit. Figure 2 shows the distribution of hematocrit levels observed in this study. Hematocrit levels with less than 20 readings were omitted from the analysis. Data from hematocrit levels between 35% to 52% were therefore considered.

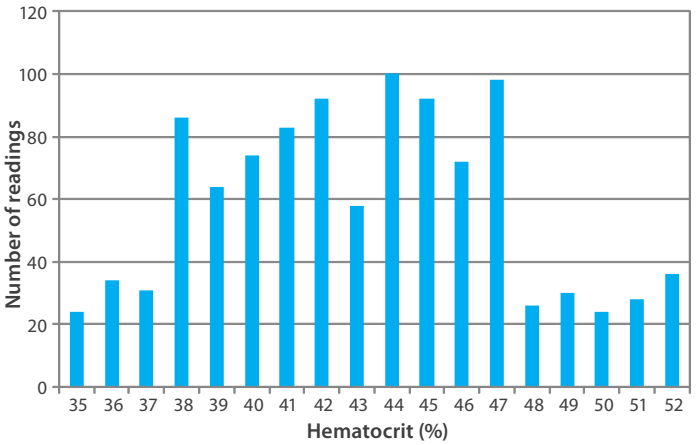

Figure 2. *Hematocrit level distribution of samples (n=1052).*

The mean bias (MB_h) at each hematocrit level (h) was calculated as follows:

$$MB_h = \frac{\sum_{n=1}^{k_h}\left(\frac{(\text{BGMS reading})_n - (\text{YSI reading})_n}{(\text{YSI reading})_n}\right)}{k_h} \times 100\%$$

where:

- k_h is the number of data points at each hematocrit level h , (where $k_h \geq 20$)
- $(\text{BGMS reading})_n$ is the n^{th} individual WaveSense brand BGMS reading for a given sample
- $(\text{YSI reading})_n$ is the YSI reading corresponding to the same given n^{th} sample

Figure 3 shows the mean bias of the codeless WaveSense BGMS across the measured hematocrit range of 35% to 52%.

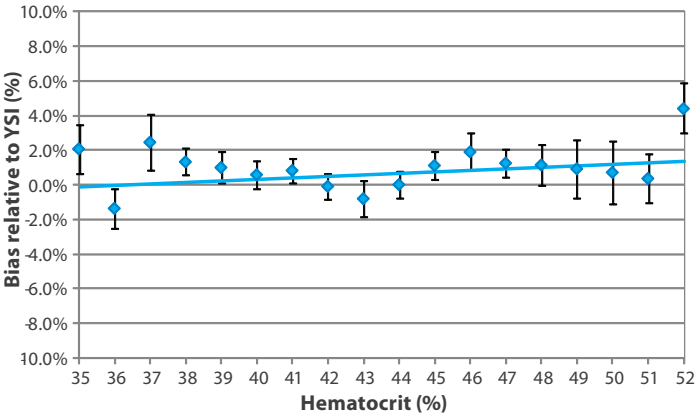

Figure 3. Effect of Hematocrit. The mean bias and its standard error are shown as a function of hematocrit.

The effect of hematocrit on the readings obtained by the codeless WaveSense brand BGMS was determined by least squares linear regression of the bias (in %) versus hematocrit. The slope of the regression line was 0.09% per hematocrit unit. Based on this regression analysis, samples with a hematocrit of 52 are predicted to give readings 1.5% higher than those with a hematocrit of 35 (95% confidence interval is -1.1% to +4.1%). This difference is of minimal clinical significance.

Conclusion

The results from this study indicate there is no significant systematic effect of hematocrit on the accuracy of WaveSense brand BGMS.

The WaveSense Dynamic Electrochemistry algorithms compensate and correct for the variations in hematocrit that may alter blood glucose readings. The WaveSense brand of codeless BGMS provide highly accurate blood glucose readings across a broad range of hematocrit levels, which can be helpful in achieving tighter glycemic control in the management of diabetes.

References

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