Analytical Performance Evaluation of Infopia Element™ Auto-coding Blood Glucose Monitoring System for Self-Monitoring of Blood Glucose

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Background: Element™ Auto-coding Blood Glucose Monitoring System (BGMS; Infopia Co., Ltd., Anyang-si, Korea) was developed for self-monitoring of blood glucose (SMBG). **Methods:** Precision, linearity, and interference were tested. Eighty-four capillary blood samples measured by Element™ BGMS were compared with central laboratory method (CLM) results in venous serum. Accuracy was evaluated using ISO 15197:2013 criteria. **Results:** Coefficients of variation (CVs; mean) were 2.4% (44.2 mg/dl), 3.7% (100.6 mg/dl), and 2.1% (259.8 mg/dl). Linearity was shown at concentrations 39.25–456.25 mg/l ($y = 0.989 + 0.984x$, SE = 17.63). Up to 15 mg/dl of galactose, ascorbic acid, and ac-

etaminophen, interference > 10.4% was not observed. Element™ BGMS glucose was higher than CLM levels by 3.2 mg/dl (at 200 mg/dl) to 8.2 mg/dl (at 100 mg/dl). The minimum specification for bias (3.3%) was met at 140 and 200 mg/l glucose. In the Clarke and consensus error grids, 100% of specimens were within zone A and B. For Element™ BGMS values, 92.9% (78/84) to 94.0% (79/84) were within a 15 mg/dl (< 100 mg/dl) or 15% (> 100 mg/dl) of the average CLM value. **Conclusion:** Element™ BGMS was considered an appropriate SMBG for home use; however, the positive bias at low-to-mid glucose levels requires further improvement. J. Clin. Lab. Anal. 30:849–858, 2016. © 2016 Wiley Periodicals, Inc.

Key words: blood glucose monitoring system; self-monitoring of blood glucose; accuracy; evaluation

INTRODUCTION

Self-monitoring of blood glucose (SMBG) is considered to be an effective tool in glycemic control in patients with diabetes mellitus (1). Patients can test for and obtain their blood glucose level at home as well as the hospital without venous blood collection. About 70% of diabetes patients practice SMBG (2). In a hospital setting, blood glucose monitoring systems (BGMS) are widely used as these methods do not require centrifugation, and availability of whole blood from capillaries enables a rapid turnaround time for the results (3). As whole blood has lower water content, the glucose

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concentration of whole blood samples is 10–18%, lower than that of plasma or serum (4,5). The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) recommends the use of plasma-calibrated values for reporting glucose levels and an adjustment factor of 1.11 for converting concentrations in whole blood to the equivalent concentrations in plasma, assuming a normal hematocrit (5).

The analytical performance of BGMS is important because their accuracy can affect decisions regarding glycemic control, such as insulin dosage (6). For comparison of methods, a central laboratory method (CLM) is used, which should have analytical imprecision $\leq 2.9\%$, bias $\leq 2.2\%$, and total error (TE) $\leq 6.9\%$ (7). The Clinical and Laboratory Standards Institute (CLSI) POCT12-A3 guideline recommends that 95% of results of BGMS from at least 100 patients lie within ± 12 mg/dl of the average reference value for concentrations below 100 mg/dl and within $\pm 12.5\%$ for those at or above 100 mg/dl as acceptable criteria for hospital use (7). The International Organization for Standardization (ISO) 15197:2013 standard recommends that two minimum criteria are fulfilled in order to hold acceptable system accuracy. One criterion is that the overall difference in 95% of values shall be within ± 15 mg/dl for concentrations < 100 mg/dl and $\pm 15\%$ for those ≥ 100 mg/dl. The other is that 99% of measured values fall within zones A and B of the consensus error grid (CEG) (8).

In recent years, the ElementTM Auto-coding BGMS (Infopia Co., Ltd., Anyang-si, Republic of Korea) has been developed for SMBG. It is composed of an ElementTM Auto-coding Blood Glucose Test Strip and ElementTM Auto-coding Blood Glucose Test Meter and adopts the glucose oxidase method and biosensor technology with electrochemical components for the determination of glucose levels. It was designed to give plasma-calibrated glucose values to patients in self-testing. It is stated that a relatively small volume of whole blood, 0.3 μ l, is required for analysis and it takes about 3 sec to obtain a result.

The purpose of this study is to assess the performance of the ElementTM Auto-coding BGMS for SMBG in home use. The precision, linearity, interference, and methods comparison were evaluated.

MATERIALS AND METHODS

Precision

Glucose levels were measured in duplicate in each run, and two runs per day for 20 days from the three concentrations of control materials. For this, ElementTM glucose control solution was supplied by the manufacturer.

The calculated total coefficients of variation (CVs) were compared with the desirable (2.9%) and minimum (4.35%) specification for imprecision for serum glucose derived from biologic variation (9). Results were also compared with the manufacturer's claims for precision in the package insert sheet.

Linearity

During the period of the linearity test, specimens with the highest and lowest glucose concentrations were selected from lithium heparin containing whole blood specimens that were left over after routine testing (elapsed time after completion of test < 1 hr). The two specimens were mixed at ratios of 5:0, 4:1, 3:2, 2:3, 1:4, and 0:5 and these six concentration levels were then measured in quadruplicate. The desirable specification for TE from biologic variation of serum glucose, 6.9% (9), was used as the criterion for allowable nonlinearity.

Interference Test

The effects of galactose, ascorbic acid, and acetaminophen spiked into patient specimens with three glucose concentrations were evaluated. Specimens were selected in the same way as for linearity test. Specimens were prepared to interferent concentrations of 0, 3.75, 7.5, 11.25, and 15 mg/dl. Each was measured five times. The minimum specification for TE from biologic variation of serum glucose, 10.4% (9), was used as the criterion for significant difference.

Methods Comparison

As comparative methods, one of the most widely used SMBG systems, OneTouch Ultra[®]2 (LifeScan, Inc., Milpitas, CA, USA), and a CLM, Gluco-quant Glucose/HK assay (hexokinase method) on a Roche Modular D analyzer (Roche Diagnostics, Mannheim, Germany), were used. OneTouch Ultra[®]2 was also compared with the CLM. The target population was ambulant diabetic patients who were not hospitalized. Consecutive patients with diabetes who were ≥ 18 years old and visiting the Diabetes Center of the Bucheon St. Mary's Hospital from July to August 2013 were potential participants. Bucheon St. Mary's Hospital is a 600-bed university hospital near to Seoul. Eligible criterion was the latest hematocrit measured within a week of sample-taking, which should be in the range of 20 to 60. Glucose measurement of ElementTM Auto-coding BGMS was claimed to be valid in this hematocrit range. Hematocrit was measured from EDTA whole blood specimens with Sysmex XE-2100TM Automated Hematology System (Sysmex Co., Kobe, Japan). After a

TABLE 1. Precision of the Element™ Auto-coding BGMS Using Three Levels of Control Material

Mean (mg/dl)	Test result (<i>n</i> = 80)				Claim of manufacturer (<i>n</i> = 600)			Specification for imprecision ^a			
	Within-run imprecision		Total imprecision		Mean (mg/dl)	Total imprecision		Desirable		Minimum	
	SD (95% CI)	CV (%)	SD (95% CI)	CV (%)		SD (95% CI)	CV (%)	SD	CV (%)	SD	CV (%)
44.2	1.1 (0.9, 1.4)	2.4	2.2 (1.8, 3.0)	5.1	37.0	1.7 (1.66, 1.74)	4.6	1.3	2.9	1.95	4.35
100.6	3.7 (3.0, 4.7)	3.7	4.2 (3.6, 5.0)	4.2	104.0	3.1 (3.02, 3.15)	3.0	2.9		4.35	
259.8	5.3 (4.4, 6.8)	2.1	6.8 (5.8, 8.3)	2.6	316.0	6.8 (6.71, 6.95)	2.2	7.5		11.25	

SD, standard deviation; CI, confidence interval; CV, coefficient of variation.

^aSpecification for imprecision of glucose from biological variation (9).

full explanation about this study, only patients who gave written informed consent were enrolled as participants to donate blood specimens for methods comparison. First, the glucose level was measured once by each system: two Element™ Auto-coding BGMS and two OneTouch Ultra®2 BGMS, in capillary whole blood collected from a fingertip with the Element™ lancing device. The order of measurement by the four devices was random. Tests using the BGMS were performed by a well-trained technician to minimize user errors and interuser variance. Immediately after skin prick on the finger (interval < 1.0 min), venous blood was collected from an antecubital vein into serum separation tubes. This blood was then given 15 min to clot and centrifuged at $1,942 \times g$ for 10 min. Glucose levels were measured by CLM in duplicate. Estimated differences at 100, 126, 140, and 200 mg/l of medical decision points (MDPs) were compared to the desirable (2.2%) and minimum (3.3%) specifications for bias from biologic variation for serum glucose (9). In addition, for each duplicated measurement of the BGMS and the mean values for CLM, we performed Clarke error grid (CEG) analysis and evaluated system accuracy using criteria from ISO 15197:2013 (8) and CLSI POCT12A3 (7).

During the period when methods comparison was performed, the ranges of monthly CV (mean) of the CLM from internal quality control were 1.8–2.2% (62.35–62.83 mg/dl) for level 1 control material and 1.3–2.4% (360.1–363.2 mg/dl) for level 3. The standard deviation index (SDI; CV ratio) was 0.28–0.55 (0.6–0.8) for level 1 and 0.13–0.50 (0.50–0.80) for level 3. They were obtained from the control materials Bio-Rad MultiQual levels 1 and 3 (Lot 45640) and Unity™ Interlab Report available at <http://www.qcnet.com> (Bio-Rad Laboratories Ltd., Hemel Hempstead, UK). The CLM underwent proficiency testing run by the Korean Association of Quality Assurance for Clinical Laboratory (KAQACL) (10) on August 8, 2013, a day falling in the period when methods comparison for this study was performed. The SDI and variance index score from three levels (94.2, 112.7, and 285.5 mg/dl) of proficiency test specimens were –0.6 to –0.9 and 20–31, respectively. So, CLM

in this study could be considered reliable as a reference method.

Statistical Analysis

StatisPro version 2.53.00 (CLSI, Wayne, PA, USA) and EP Evaluator release 10 (Data Innovations, South Burlington, VT, USA) were used for data analysis.

This study was approved by the Institutional Review Board (IRB) of the Catholic Medical Center at the Catholic University of Korea (HC12DSSE0113).

RESULTS

Precision

The range for total CVs was 2.6–5.1%. At a high concentration (mean = 259.8 mg/dl), both the desirable specification and manufacturer's claim for imprecision were fulfilled. Imprecision at lower levels of glucose (mean = 44.2 mg/dl) and mid-levels (mean = 100.6 mg/dl) did not meet the desirable specification for imprecision of 2.9%. Imprecision in these cases was also larger than that claimed at similar levels of 37 mg/dl and 104 mg/dl. However, the total CVs at all three levels were not significantly different from the minimum specification of 4.35% (Table 1).

Linearity

Linearity was observed in the concentration ranges of 39.3–456.3 mg/dl (Table 2 and Fig. 1). Neither second nor third order polynomial fits showed statistical significance. The obtained linear equation was $y = 0.989 + 0.984x$ (SE = 17.63).

Interference Test

In specimens including galactose, ascorbic acid, or acetaminophen up to 15 mg/dl, no differences larger than the minimum specification for TE, 10.4%, from those not containing the potential interfering substance were

TABLE 2. Linearity of Element™ Auto-coding Blood Glucose Measuring System Results From Dilutions of Patient Whole Blood Samples

Tested range (mg/dl)		Linear fit			Measuring interval claimed by manufacturer (mg/dl)		Allowable
Lower limit	Upper limit	Slope	y-Intercept	SE of fit	Lower limit	Upper limit	nonlinearity ^a
39.25	456.25	0.984	0.989	17.63	10	600	6.9%

SE, standard error.

^aDesirable specification for TE of serum glucose from biological variation was used as the allowable nonlinearity (9).

observed. However, difference up to -10.4% was observed in a specimen with 77.8 ± 3.5 mg/dl of glucose when adding acetaminophen to a concentration of 15.0 mg/dl (Table 3).

Methods Comparison

A total of 84 patients were enrolled as blood specimen donors. The number of male and female participants was 36 and 48, respectively. The average age (mean $\pm$ SD) of the group was 59.4 ± 13.2 and the mean hematocrit was 39.5 ± 4.6 . Minimum and maximum values of

hematocrit were 28.5 and 52.3, respectively. Element™ Auto-coding glucose levels were higher than those for CLM, with a difference of 3.2 mg/dl (at 200 mg/dl) to 8.2 mg/dl (at 100 mg/dl). The desirable specification for bias of 2.2% was met only at 200 mg/l of glucose and minimum specification was met at 140 and 200 mg/l. One-Touch Ultra®2 glucose level results were also higher than those for CLM. A difference of 3.2 mg/dl (at 200 mg/dl) to 8.7 mg/dl (at 100 mg/dl) was observed and fulfillment of specification of biological variation was the same as the Element™ Auto-coding BGMS. Differences between Element™ Auto-coding BGMS and OneTouch Ultra®2

Fig. 1. Scatter plot of expected and measured glucose levels from linearity testing of Element™ Auto-coding BGMS. The obtained linear equation was $y = 0.989 + 0.984x$ (SE = 17.63).

TABLE 3. Interference Test

Potential interfering substance	Concentration of interfering substance (mg/dl)	0			3.75			7.5			11.25			15			Significant difference (mg/dl) ^a
		Mean ± SD	Mean ± SD	Difference (mg/dl [%])	Mean ± SD	Mean ± SD	Difference (mg/dl [%])	Mean ± SD	Mean ± SD	Difference (mg/dl [%])	Mean ± SD	Mean ± SD	Difference (mg/dl [%])	Mean ± SD	Mean ± SD	Difference (mg/dl [%])	
Galactose	Low	83.0 ± 4.9	84.0 ± 2.0	1.0 (1.2%)	78.6 ± 4.6	78.6 ± 4.6	-4.4 (-5.3%)	78.6 ± 4.6	78.6 ± 4.6	-4.4 (-5.3%)	79.6 ± 5.2	79.6 ± 5.2	-3.4 (-4.1%)	79.6 ± 5.2	79.6 ± 5.2	-3.4 (-4.1%)	8.6
	Mid	149.8 ± 2.6	146.6 ± 5.0	-3.2 (-2.1%)	146.6 ± 6.8	146.6 ± 6.8	-3.2 (-2.1%)	146.6 ± 6.8	146.6 ± 6.8	-3.2 (-2.1%)	147.4 ± 2.7	147.4 ± 2.7	-2.4 (-1.6%)	143.8 ± 3.3	143.8 ± 3.3	-6.0 (-4.0%)	15.5
	High	315.2 ± 10.2	293.2 ± 5.0	-22.0 (-7.0%)	290.8 ± 7.5	290.8 ± 7.5	-24.4 (-7.7%)	290.8 ± 7.5	290.8 ± 7.5	-24.4 (-7.7%)	301.6 ± 2.9	301.6 ± 2.9	-13.6 (-4.3%)	307.8 ± 12.0	307.8 ± 12.0	-7.4 (-2.3%)	32.6
Ascorbic acid	Low	99.2 ± 2.0	90.0 ± 3.5	-9.2 (-9.3%)	90.4 ± 2.6	90.4 ± 2.6	-8.8 (-8.9%)	90.4 ± 2.6	90.4 ± 2.6	-8.8 (-8.9%)	92.4 ± 1.1	92.4 ± 1.1	-6.8 (-6.9%)	95.4 ± 1.5	95.4 ± 1.5	-3.8 (-3.8%)	10.3
	Mid	153.6 ± 4.6	149.4 ± 3.0	-4.2 (-2.7%)	144.0 ± 1.9	144.0 ± 1.9	-9.6 (-6.3%)	144.0 ± 1.9	144.0 ± 1.9	-9.6 (-6.3%)	149.2 ± 4.5	149.2 ± 4.5	-4.4 (-2.9%)	156.6 ± 2.9	156.6 ± 2.9	3.0 (2.0%)	15.9
	High	302.4 ± 6.2	293.4 ± 3.2	-9.0 (-3.0%)	292.4 ± 6.8	292.4 ± 6.8	-10.0 (-3.3%)	292.4 ± 6.8	292.4 ± 6.8	-10.0 (-3.3%)	298.2 ± 12.3	298.2 ± 12.3	-4.2 (-1.4%)	294.4 ± 12.4	294.4 ± 12.4	-8.0 (-2.6%)	31.3
Acetaminophen	Low	86.8 ± 4.4	84.6 ± 4.7	-2.2 (-2.5%)	83.2 ± 5.9	83.2 ± 5.9	-3.6 (-4.1%)	83.2 ± 5.9	83.2 ± 5.9	-3.6 (-4.1%)	80.2 ± 4.8	80.2 ± 4.8	-6.6 (-7.6%)	77.8 ± 3.5	77.8 ± 3.5	-9.0 (-10.4%)	9.0
	Mid	145.2 ± 3.3	142.6 ± 2.3	-2.6 (-1.8%)	142.8 ± 3.8	142.8 ± 3.8	-2.4 (-1.7%)	142.8 ± 3.8	142.8 ± 3.8	-2.4 (-1.7%)	142.6 ± 2.7	142.6 ± 2.7	-2.6 (-1.8%)	142.0 ± 2.6	142.0 ± 2.6	-3.2 (-2.2%)	15.0
	High	283.2 ± 5.7	274.2 ± 16.7	-9.0 (-3.2%)	268.6 ± 12.4	268.6 ± 12.4	-14.6 (-5.2%)	268.6 ± 12.4	268.6 ± 12.4	-14.6 (-5.2%)	257.8 ± 9.1	257.8 ± 9.1	-25.4 (-9.0%)	257.0 ± 9.4	257.0 ± 9.4	-26.2 (-9.3%)	29.3

Comparison of blood glucose levels measured using Element™ Auto-coding Blood Measuring System in blood samples containing various concentrations of interfering substance with normal blood samples.

^aThe minimum specification for TE of serum glucose from biologic variation, 10.4%, was used as criteria for clinically significant difference (9).

TABLE 4. Methods Comparison Between Element™ Auto-coding BGMS, OneTouch Ultra®2 BGMS, and Roche Modular Analyzer (n = 84)

Test method	Comparative method	Concentration range (mg/dl)	r	y-intercept		S _{y,x}	MDP (mg/dl)	Difference		Allowable bias ^a	
				Slope (95% CI)	(95% CI)			(mg/dl [95% CI])	(%)	Desirable (mg/dl)	Minimum (mg/dl)
Element™ Autocoding BGMS	Roche Modular analyzer	72–374	0.990	0.95 (0.920, 0.981)	13.15 (7.99, 18.30)	9.1	100	8.2 (5.6, 10.8)	2.2	2.2	3.3
								6.9 (4.7, 9.1)	2.8	2.8	4.2
								6.2 (4.2, 8.2)	3.1	3.1	4.6
OneTouch Ultra®2 BGMS	Roche Modular analyzer	72–374	0.991	0.945 (0.917, 0.973)	14.25 (9.52, 18.97)	8.3	100	3.2 (0.9, 5.6)	4.4	4.4	6.6
								8.7 (6.3, 11.1)	2.2	2.2	3.3
								7.3 (5.3, 9.3)	2.8	2.8	4.2
Element™ Autocoding BGMS	OneTouch Ultra®2 BGMS	86–371.5	0.982	0.989 (0.947, 1.031)	1.54 (-5.76, 8.84)	12.0	100	6.5 (4.6, 8.4)	3.1	3.1	4.6
								3.2 (1.0, 5.4)	4.4	4.4	6.6
								0.5 (-3.2, 4.2)	2.2	2.2	3.3
							126	0.2 (-2.8, 3.2)	2.8	2.8	4.2
								0 (-2.7, 2.8)	3.1	3.1	4.6
								-0.6 (-3.7, 2.4)	4.4	4.4	6.6

MDP, medical decision point; CI, confidence interval.

^aDesirable and minimum specifications for bias of serum glucose from biological variation was used as the allowable bias (9).

Fig. 2. Scatter plot (A) of Element™ Auto-coding BGMS and the CLM, (B) of OneTouch Ultra®2 BGMS and CLM, and (C) of Element™ Auto-coding BGMS and OneTouch Ultra®2 BGMS.

BGMS at 100, 126, 140, and 200 mg/dl of glucose ranged from -0.6 to 0.5 mg/dl and were within the limits of desirable specification, 2.2% (Table 4, Figs. 2 and 3). In Clarke and CEG analyses, 100% of specimens were within zone A or B for both Element™ Auto-coding BGMS and OneTouch Ultra®2 BGMS (Table 5 and Figs. 4).

When applying the system accuracy criteria of ISO 15197:2013, 63.6% (7/11)–72.7% (8/11) of Element™ Auto-coding BGMS values were within ± 15 mg/dl (<100 mg/dl) and 95.9% (70/73)–98.6% (72/73) were within $\pm 15\%$ (≥ 100 mg/dl) of the average reference value. Across the overall concentrations, 92.9% (78/84)–94.0% (79/84) of specimens met these criteria (Table 6). For the OneTouch Ultra®2 BGMS, 90.9% (10/11) of values were within ± 15 mg/dl (<100 mg/dl) and 94.5% (69/73)–95.9% (70/73) were within $\pm 15\%$ (≥ 100 mg/dl) of the average reference value. As a whole, 94.0% (79/84)–95.2% (80/84) of values were within the limits (Table 6). The results obtained according to the accuracy criteria of CLSI POCT12A3 are also presented in Table 6.

DISCUSSION

The analytical performance of Element™ Auto-coding BGMS was concluded to be of a good level for SMBG for home use. Although it did not meet the ISO 15197:2013 and CLSI POCT12A3 acceptability criteria, its system accuracy corresponded to an intermediate-level among BGMS on the market (derived from the capillary blood specimen). Element™ Auto-coding BGMS passed error grid analysis even with different types of specimen. However, the concentration range around 100–126 mg/dl should be observed with caution, and to further improve its accuracy, the BGMS may require recalibration for this low- to mid-level of glucose.

The imprecision observed at three levels (44.2, 100.6, and 259.8 mg/dl) of glucose met the minimum specification for imprecision and linearity was shown in the concentration range of 39.3–456.3 mg/dl. The differences in Element™ Auto-coding BGMS from CLM at two of four MDPs (140 and 200 mg/dl) were not larger than the minimum specification of biological variation for bias (3.3%) with statistical significance. A similar pattern of difference was observed in the comparison between the OneTouch Ultra®2 BGMS and CLM. In both BGMS, 100% of 84 specimens fell in zone A or B in both types of error grid. This meant that the difference in results would lead to no effect on clinical action (for zone A) or little or no effect on clinical outcome even with altered clinical action (for zone B) (8). In 92.9% (78/84)–94.0% (79/84) of specimens, the difference across all the measured concentrations was within ± 15 mg/dl or $\pm 15\%$ of the reference value. This value was a little less than that obtained for OneTouch Ultra®2 BGMS and the ISO 15197:2013 criteria. Although immediately collected from subjects, using different types of specimen in methods comparison was considered as a factor contributing to the observed difference. The difference was more likely to be smaller if the same specimen capillary blood had been used for methods comparison. This could be supported by finding that estimated difference between the two BGMS used in this study was very small at four MDPs (-0.6 mg/dl at 200 mg/dl to 0.5 mg/dl at 100 mg/dl).

Among the BGMS currently on the market, 15 mg/dl of galactose, 6.6 mg/dl of ascorbic acid, and 8 mg/dl of acetaminophen have been described as the highest levels of interfering substance that do not interfere with glucose measurement by BGMS, according to the research of Tirimacco et al. (11). The interference test result of Element™ Auto-coding BGMS was considered equal to or better than these previous results. In several studies

Fig. 3. Bland–Altman plot of (A) Element™ Auto-coding BGMS and (B) OneTouch Ultra®2 BGMS against the CLM and (C) Element™ Auto-coding BGMS against OneTouch Ultra®2 BGMS. The x-axis represents the average of the measurements by the two methods. The y-axis shows the difference between them.

TABLE 5. Error Grid Analysis of Glucose Levels Measured by Element™ Auto-coding Blood Glucose Measuring System (BGMS) and OneTouch Ultra®2 BGMS Against Roche Modular Analyzer (n = 84)

Test method	Comparative method	Replicate	Error grid method	Zone A	Zone B	Zone C	Zone D	Zone E	Mean % error	95th Percentile
Element™ Auto-coding BGMS	Roche Modular analyzer	1	Clarke	96% (81)	4% (3)	0% (0)	0% (0)	0% (0)	6.7%	18.9%
			Consensus	100% (84)	0% (0)	0% (0)	0% (0)	0% (0)		
		2	Clarke	95% (80)	5% (4)	0% (0)	0% (0)	0% (0)	6.9%	21.3%
			Consensus	98% (82)	2% (2)	0% (0)	0% (0)	0% (0)		
OneTouch Ultra®2 BGMS	Roche Modular analyzer	1	Clarke	98% (82)	2% (2)	0% (0)	0% (0)	0% (0)	6.6%	16.1%
			Consensus	99% (83)	1% (1)	0% (0)	0% (0)	0% (0)		
		2	Clarke	96% (81)	4% (3)	0% (0)	0% (0)	0% (0)	7.0%	18.8%
			Consensus	98% (82)	2% (2)	0% (0)	0% (0)	0% (0)		

with various settings, venous plasma or serum glucose has been compared with capillary blood glucose measured by BGMS (12–16). Although the size of the difference varied (+2.7 mg/dl at 111.0 mg/dl to +12.6 mg/dl at 127.9 mg/dl) depending on the BGMS and CLM used, characteristics of the test population, fasting status, and study design, the direction of the difference obtained from the present study was consistent with those from the previous studies (12–16). One of them showed similar-sized difference to that in the present article (+7 mg/dl at 115 mg/dl vs. +6.9–8.2 mg/dl with Element™ Auto-coding BGMS, and +7.3–8.7 mg/dl with OneTouch Ultra®2 BGMS at 100–126 mg/dl) (16). Underestimation of hypoglycemia (17, 18) and overestimation of hyperglycemia

(18) due to positive bias of BGMS was highlighted by some researchers. Likewise, users should be aware of possible positive bias of Element™ Auto-coding BGMS, especially at lower glucose levels. This requires improvement by the manufacturer.

The system accuracy of Element™ Auto-coding BGMS was mid-level among those presented in Robinson’s paper (91.7–95.2% vs. 89.0–100% according to ISO criteria; 84.5–89.3% vs. 83.0–98.0% according to CLSI criteria; Table 6) (19). Element™ Auto-coding BGMS was thought to have a good accuracy level even with different types of specimen. However, if more patients with glucose levels <100 mg/dl had been enrolled, the overall system accuracy may have been lower.

Fig. 4. Clarke (upper row) and consensus (lower row) error grid plot of (A) Element™ Auto-coding BGMS and (B) OneTouch Ultra®2 BGMS. Each specimen was measured in duplicate by each method (replicates 1 and 2).

TABLE 6. Comparison of System Accuracy Between BGMS and OneTouch Ultra®2 BGMS ($n = 84$)

Test method	Comparative method	Glucose concentration	Replicate	ISO 15197:2013 criteria	CLSI POCT12A3 criteria
Element™ Auto-coding BGMS	Roche Modular analyzer	<100 mg/dl	1	Within ±15 mg/dl	Within ±12 mg/dl
			2	63.6% (7/11)	54.5% (6/11)
		≥100 mg/dl	1	72.7% (8/11)	54.5% (6/11)
			2	Within ±15%	Within ±12.5%
		Total	1	95.9% (70/73)	89.0% (65/73)
			2	98.6% (72/73)	94.5% (69/73)
		Total	1	Within ±15 mg/dl or ±15%	Within ±12 mg/dl or ±12.5%
OneTouch Ultra®2 BGMS	Roche Modular analyzer	<100 mg/dl	1	91.7% (77/84)	84.5% (71/84)
			2	95.2% (80/84)	89.3% (75/84)
		≥100 mg/dl	1	Within ±15 mg/dl	Within ±12 mg/dl
			2	90.9% (10/11)	63.6% (7/11)
		Total	1	90.9% (10/11)	72.7% (8/11)
			2	Within ±15%	Within ±12.5%
		Total	1	95.9% (70/73)	91.8% (67/73)
			2	94.5% (69/73)	86.3% (63/73)
		Total	1	Within ±15 mg/dl or ±15%	Within ±12 mg/dl or ±12.5%
			2	95.2% (80/84)	88.1% (74/84)
		Total	1	94.0% (79/84)	84.5% (71/84)
			2		

CLSI POCT12A3 and ISO 15197:2013 recommended capillary blood for central laboratory measurement (7, 8) and using the same specimen in the methods comparison could give information about analytical aspects to personnel who decide whether BGMS are accepted for use. However, it may not reflect the real situation that SMBG-system users are confronted with in practice and could not provide practical information that they may wonder. Therefore, in this study, serum samples from venous blood were used for CLM in methods comparison, as this specimen is commonly used in hospital settings. Preanalytical factors such as specimen difference and glucose metabolism for ~15 min during clotting before centrifugation should be considered when determining its acceptability with the results of this article. Although each blood donor's hematocrit results from less than seven days prior to the blood drawings that were within the operational limit claimed by the manufacturer were used for the methods comparison study, the omission of hematocrit sensitivity tests is a major limitation of this article.

In conclusion, Element™ Auto-coding BGMS seemed to demonstrate good performance in terms of precision, linearity, and interference. Even using different types of specimen in a methods comparison with CLM, an intermediate level of accuracy among BGMS currently on the market was shown. This system could be considered an appropriate BGMS for SMBG for home use; however, positive bias at low- to mid-levels of glucose should be observed with caution and requires improvement.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

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