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ORIGINAL ARTICLE

Pilot Study of a Prototype Minimally Invasive Intradermal Continuous Glucose Monitor

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Abstract

Introduction:

The purpose of this study was to assess point accuracy, rate-of-change accuracy, and safety of a prototype, minimally invasive continuous glucose monitoring (CGM) device over a 12 h in-clinic study. The CGM system consisted of a wireless electronics module with a disposable glucose sensor attached to the bottom. The electronics module was affixed to the abdomen using an adhesive pad on the bottom of the disposable sensor housing.

Methods:

Two CGM sensors were inserted into the abdominal tissue (left and right) of 15 adults aged 26–67 years, 5 with normoglycemia, 5 with type 1 diabetes, and 5 with type 2 diabetes. Over a 12 h period, each participant was fed three meals. Reference venous blood samples were drawn at periodic intervals (12.4 ± 5.3 min), and glucose was measured at the bedside using a laboratory reference method. For each participant, a single plasma equivalent glucose concentration was used for retrospective sensor calibration.

Results:

A total of 1082 paired data points were obtained from 15 subjects and 25 of 30 sensors. Statistical analysis yielded a mean absolute relative difference of 12.6% and a mean absolute difference of 16.0 mg/dl. Continuous glucose error grid analysis showed the combined point and rate-of-change accuracy was 97.4% in zone A and 1.5% in zone B (98.9% A+B), with 1.1% erroneous readings.

Conclusions:

The prototype CGM system provided clinically accurate results 98.9% of the time and was well tolerated by participants, with little or no pain and no adverse events.

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Abbreviations: (CG-EGA) continuous glucose error grid analysis, (CGM) continuous glucose monitoring, (CRU) clinical research unit, (FDA) Food and Drug Administration, (HbA1c) hemoglobin A1c, (ISF) interstitial fluid, (MARD) mean absolute relative difference, (MAD) mean absolute difference, (P-EGA) point error grid analysis, (R-EGA) rate-of-change error grid analysis, (SMBG) self-monitoring of blood glucose, (YSI) Yellow Springs Instruments

Keywords: continuous glucose, error grid, interstitial, intradermal, minimally invasive

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Introduction

For the majority of people with diabetes, self-monitoring of blood glucose (SMBG) levels is performed using finger stick BG meters. Due to cost, discomfort, and inconvenience, SMBG is performed too infrequently to allow for accurate assessment of glycemic variability. These limitations are major obstacles to reducing and preventing serious complications due to hypoglycemia and hyperglycemia.[1]

Continuous glucose monitoring (CGM) devices are attached to the skin and utilize a needle-like sensor inserted into the subcutaneous tissue to measure glucose within interstitial fluid (ISF).[2–4] This revolutionary technology facilitates better management of BG levels by providing a continuous data stream, with user feedback, that can reduce postprandial glucose excursions and the incidence of hypoglycemia and hyperglycemia.[5–8]

It has been 10 years since the commercial introduction of the first minimally invasive CGM device.[9,10] The availability of this technology has given people with diabetes a new tool for achieving better glycemic control. Frequent readings and trend information coupled with built-in alarms, to warn of impending hyperglycemia and hypoglycemia, promise to revolutionize the management of diabetes. Accuracy, reliability, and user comfort need to be improved in order for CGM technology to reach its full potential.[11] Although accuracy issues have limited their Food and Drug Administration (FDA) approval to adjunctive therapy to finger stick monitoring, studies have demonstrated the benefit of CGM in lowering hemoglobin A1c (HbA1c) levels and reducing time spent in hypoglycemia.[12–14]

In the future, the use of CGM will undoubtedly expand, and enhanced devices that offer better performance, reliability, and ease of use will be available. The greatest benefit to people with insulin-requiring diabetes will be realized through the integration of CGM technology with an insulin pump to form an artificial pancreas.[15–20] In this article, we describe the use of a prototype CGM sensor inserted 4 mm into the skin. The small size of the sensor eliminates pain and reduces the inflammatory response.

Methods

Study Subjects

Prior to commencing this study, biocompatibility and toxicology testing was conducted on the components of the disposable sensor by NAMSA (Northwood, OH). Test results showed the device to be biocompatible and nontoxic. A sterilization protocol was optimized to provide a sterile sensor for the pilot study (SteriPro Labs, Itasca, IL, and NUTEK Corp., Hayward, CA). Following a determination by the FDA that the prototype CGM device was a nonsignificant risk to humans, the study protocol was approved by the Institutional Review Board for the Protection of Human Subjects at the State University of New York Upstate Medical University in Syracuse, NY. All study participants provided written, informed consent prior to enrollment.

Fifteen subjects (4 female, 11 male, 87% Caucasian, 13% black/African-American) were enrolled and studied in the Clinical Research Unit (CRU). Participants were 52.1 ± 13.6 years old (range 26–67 years) with a body mass index of 30.8 ± 7.8 kg/m^2. Of the volunteers, 5 had normal glucose levels, 5 had type 1 diabetes, and 5 had type 2 diabetes.

Three to five days prior to placement of the CGM device, participants reported to the CRU at State University of New York Upstate Medical University for a review of their medical history and laboratory testing, including a comprehensive metabolic panel and complete blood count with platelets. Inclusion criteria were males and females ages ≥21 years without diabetes, with type 1 diabetes using insulin therapy for at least one year, or with type 2 diabetes and those willing to give informed consent, capable of following the protocol and instructions of study staff, and available for scheduled visits. Exclusion criteria were age <21 years, HbA1c > 9%, uncontrolled hypertension and/or hyperlipidemia, renal disease, liver disease, low or abnormal hemoglobin level, inability to follow the protocol, inability to read and write English, skin abnormalities near potential insertion sites, or a history of allergy to adhesives. Volunteers with chemistry and hematology laboratory values outside of established norms were excluded from the study at the discretion of the study physician.

Data Analysis

Data analyses were performed according to guidelines proposed by the Clinical and Laboratory Standards Institute.[21] Three types of error grid analysis were used to characterize the performance of the prototype CGM device. The first is the original Clarke or point error

grid analysis (P-EGA),[22] the rate-of-change error grid analysis (R-EGA),[23] and the continuous glucose error grid analysis (CG-EGA), which combines both point and rate-of-change accuracy.[24]

Sensor Design

In this pilot study, the working electrode consisted of a glucose-oxidase-coated platinum needle working electrode with a skin contact, planar silver–silver chloride reference electrode and a skin contact, planar silver–silver chloride counter electrode. Each skin contact electrode had a conductive adhesive on the surface to facilitate good electrical contact with the skin. The glucose needle sensor consisted of a 4.0 × 0.35 mm (28 G) platinum wire dip coated with glucose oxidase dissolved in phosphate-buffered saline followed by crosslinking with glutaraldehyde. Following the cross-linking step, the enzyme-coated sensor was dipped into a solution of polyurethane dissolved in solvent. The polyurethane-coated sensor was oven cured to remove the solvent. The sensors were stored in ambient air at room temperature until assembled into the disposable sensor housings. The disposable sensor housings were sealed in foil pouches and sent out for electron beam sterilization (NUTEK Corp., Hayward, CA). The packaged, sterilized sensors were stored at room temperature until use.

There are three components to the sensor system: (1) an injection-molded disposable sensor housing having an adhesive pad on the bottom along with the two skin contact, silver–silver chloride button-type planar electrodes for the reference and counter electrodes, respectively (in the center of the disposable sensor housing, a platinum needle-type glucose oxidase sensor was mounted within a spring); (2) a wireless electronics module to which the disposable sensor is attached and adhered to the skin; and (3) a remote wireless receiver that stores, analyzes, and displays data sent from the electronics module. Using a button on the top of the electronics module, the glucose sensor (0.35 mm diameter, 28 G) was inserted vertically 4 mm into the skin.

High-frequency ultrasound studies have shown that the combined thickness of the epidermis and dermis in the abdominal area is approximately 2.0 mm.[25] Other studies have shown that dermal thickness can vary between 1 and 4 mm,[26] whereas subcutaneous adipose tissue thickness can vary between 1 and 12 mm.[27] A paper by Groenendaal and coauthors[28] showed that the ISF content of the dermis was 35–45% while that for adipose tissue was 10–30%. Their study indicated the dermis shows the least amount of glucose variability among subjects and is closer to BG concentration than the adipose tissue. The relative concentration of glucose within the range of 1–3 mm within the dermis remains constant while, in the adipose tissue, glucose concentration decreases significantly below a depth of 1 mm within the subcutaneous tissue. Glucose uptake within the adipose tissue increases in the presence of insulin versus no insulin effect in the dermis.

The glucose sensor in this study has an active length of 4 mm, because the full length of the needle has glucose oxidase immobilized on its surface. Depending on the depth of penetration, a mixed sensor response is possible if the sensor resides partly in the dermis and partly in adipose tissue; however, a study of lag time and accuracy versus depth of penetration was beyond the scope of this pilot study.

Study Design

This was a single-center study that relied on meal-induced glucose excursions to determine the point and rate-of-change accuracy of a prototype CGM device compared with periodic venous BG reference samples measured with a standard laboratory reference method. Participants were admitted to the CRU in the morning, having fasted overnight. Each was fitted with an intravenous angiocatheter in the forearm for venous blood sampling. Following catheterization, each subject had two CGM sensors attached, one on the left side and one on the right side of the abdomen. Data were collected at a frequency of 0.2 Hz and transmitted wirelessly, at regular intervals, to a receiver (laptop computer) where the data were stored and displayed. The display was not visible to study participants.

Post sensor insertion, reference venous blood samples were drawn at 60, 90, and 120 min intervals. Reference glucose measurements were performed at the bedside using a Yellow Springs Instruments (YSI; YSI Life Sciences, Yellow Springs, OH) Model 2300 glucose analyzer. The YSI whole blood results were converted to plasma equivalents using the YSI conversion algorithm and the measured hematocrit: Plasma Equivalent YSI = YSI WB × [1 / (1 - (Hct × 0.0024)],[29] where WB is the whole blood result reported by the YSI and Hct is the measured hematocrit on the morning of the test day.

At 120 min post sensor insertion, each participant was fed breakfast, followed later by lunch and dinner. The average time between breakfast and lunch was 3.5 ± 0.3 h, and

the average time between lunch and dinner was 4.0 ± 0.3 h. The average carbohydrate content of the meals was 61.6 ± 10.3 g (mean ± standard deviation) for breakfast, 76.1 ± 34.3 g for lunch, and 74.3 ± 39.4 g for dinner. Following each meal, reference BG samples were drawn at 15 min intervals, unless the rate-of-change exceeded 1 mg/dl/min when blood samples were drawn at 5 min intervals until peak or nadir. For all participants, the average time between reference blood samples was 12.4 ± 5.3 min. Those subjects with type 1 diabetes followed their usual premeal insulin bolus procedure, and those with type 2 diabetes followed their usual oral and/or insulin medication schedule. At the end of the testing period, the sensor was retracted from beneath the skin by rotating the button on top of the sensor module.

Break-In Period and Calibration

The data collected consisted of raw sensor output current readings that were low-pass filtered and transformed into calibrated glucose concentrations, retrospectively.[30] To determine the actual sensor break-in period, a time point beyond the expected break-in period was chosen (in this case, 4 h). Using the filtered sensor current and plasma equivalent reference glucose concentration at this time point, a single-point calibration was used to calculate past and future CGM glucose concentrations from the filtered sensor output currents coinciding with YSI reference glucose concentrations.[31] The percentage bias between the calculated CGM glucose and the reference YSI glucose measurements was determined at each venous blood sample time point before and after the preselected time point. A plot of percentage bias (CGM versus YSI) versus time produced a graph similar to **Figure 1**. The first time point at which the bias was within ±20% was used as the actual break-in period. The 20% bias limit was chosen because it corresponds to the clinically accurate A zone of the Clarke error grid. This procedure was repeated for each of the sensor data sets. The mean break-in period for all 25 sensors was determined to be 2.3 ± 0.9 h. The average break-in period of the sensors used in this study is similar to those reported for other CGM devices.[32–34]

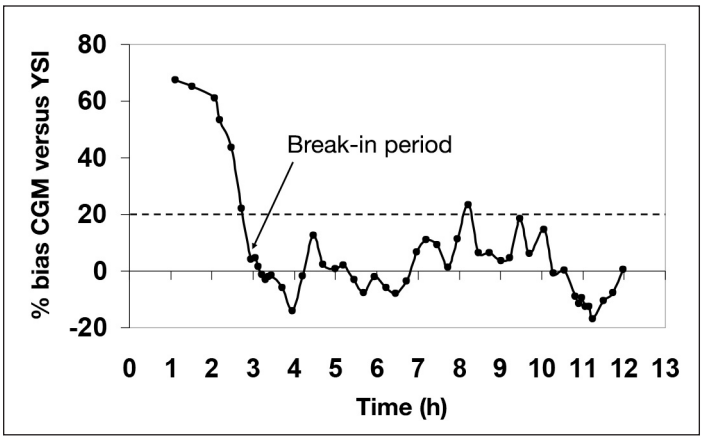

Figure 1. Analysis of *in vivo* sensor break-in period.

Lag Time

Each data set was analyzed for lag by determining the maximum of the Pearson correlation coefficient when the filtered sensor currents were moved forward in time by 1 min increments (0 to +20 min) versus the YSI glucose data.[35–38]

The average lag time, for all sensors, was 10.1 min; therefore, a fixed time of 10 min was used to correct individual data sets for lag.

Safety

Pain was assessed using an analog scale [0 (no pain) to 10 (worst pain you can imagine)] as well as a visual scale that consisted of a 10 cm line [0 (no pain) to 10 (worst pain you can imagine)]. Assessments of pain were performed just after insertion of the sensor into the skin and again following removal of the electronics module from the skin at the end of the 12 h study.

The clinical staff was asked to rate the strength required to remove the adhered electronics module from the skin at the end of the study. A 5 cm line with 1 (easy) on left-hand side, 3 (moderate) in the middle, and 5 (difficult) on the right-hand side of the line was used.

An assessment of skin irritation (Draize Dermal Irritation Scoring System[39]) was used by the clinical staff at a 48–72 h follow-up visit to assess erythema and edema. The clinical staff was asked to rate both erythema and edema. (Erythema scale: 0, no erythema; 1, very slight, barely perceptible erythema; 2, well-defined erythema; 3, moderate to severe erythema; 4, severe erythema, beet redness. Edema scale: 0, no edema; 1, very slight edema, barely perceptible; 2, slight edema, slight raising of skin; 3, moderate edema, raised about 1 mm; 4, severe erythema, raised more than 1 mm.)

Results

A primary end point of this study was evaluation of point and rate-of-change accuracy of a prototype CGM device compared with periodic venous BG measurements analyzed by a standard laboratory reference method.

Figure 2 shows examples of glucose versus time profiles for each of two study subjects, one with type 1 diabetes (upper graph) and one with type 2 diabetes (lower graph). The error bars around the YSI reference measurements are ±20%, which correspond to the clinically accurate A zone of the Clarke error grid. The study utilized data from each of 15 participants, from 25 of 30 sensors, resulting in 1082 paired YSI–CGM device data points. Mean calculated glucose concentration was 157 ± 55 mg/dl, with a range of 59 to 311 mg/dl.

The 1082 paired points were subjected to P-EGA and plotted in **Figure 3**. The results from each individual sensor were used for the analysis in **Figure 3**. The dual sensor readings from each study participant were not averaged. Analysis showed that 90.8% of the CGM glucose concentrations fell within the clinically accurate zone A, 8.8% in the benign error zone B (99.6% A+B), 0% in zone C, 0.4% in zone D, and 0% in zone E. The stratified data, by glucose concentration, from **Figure 3** is shown in **Table 1**. The combined mean absolute difference (MAD) was 16.0 mg/dl, and although the combined mean absolute relative difference (MARD) was 12.6%, the CGM device was most accurate in the euglycemic and hyperglycemic ranges, with an average MARD of 9.6% and average MAD of 16.4 mg/dl.

A CG-EGA was conducted on the non-lag-corrected data using software available from the Epsilon Group (Charlottesville, VA). The CGM data for CG-EGA was not corrected for lag, because the algorithm has a built-in lag correction of 7 min. For CG-EGA, consecutive paired data points having at least a 12 min difference between them were utilized (735/1082). Mean time difference between paired points was 15.5 ± 2.5 min. The CG-EGA data stratified by glucose concentration are shown in **Table 2**. The data show that, within the hypoglycemia range (6 paired points), 88.9% were in zone A, 0% in zone B, and 11.1% in erroneous zones; in the euglycemic range (498 paired points), 98.6% were in zone A, 1.4% in zone B, and 0% in the erroneous zones; in the hyperglycemic range (230 paired points), 95.2% were in zone A, 1.8% in zone B, and 3% in the erroneous zones. The CG-EGA combined point and rate-of-change accuracy was 97.4% in zone A and 1.5% in zone B (98.9% A+B), with 1.1% erroneous results. The glucose

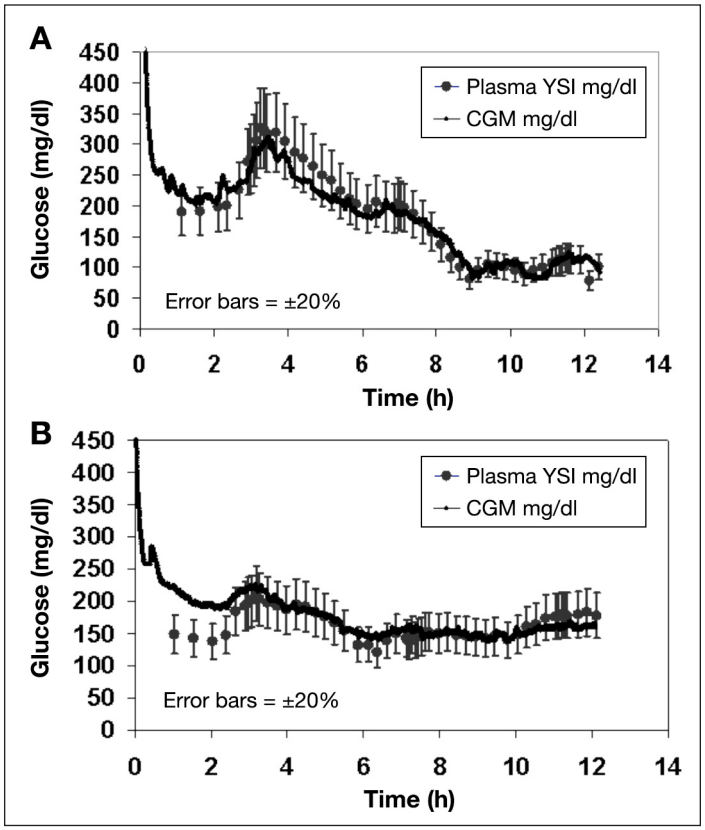

Figure 2. Examples of CGM glucose versus time and YSI reference measurements for **(A)** a patient with type 1 diabetes and **(B)** a patient with type 2 diabetes.

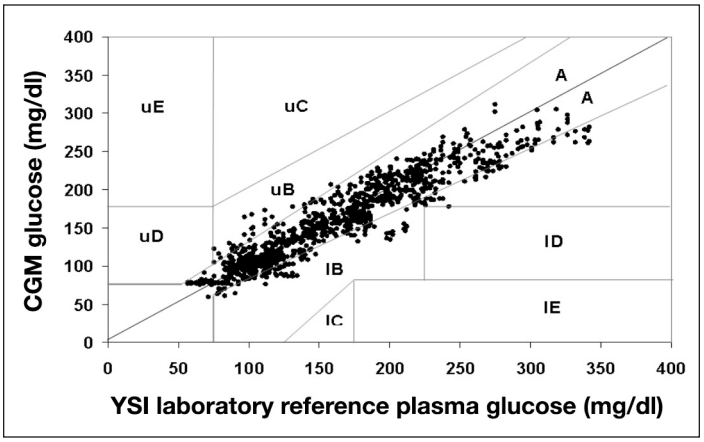

Figure 3. Point error grid analysis of 1082 paired data points. $Y = 0.85X + 20.3$; $r = 0.942$.

Table 1.
Stratified Continuous Glucose Monitoring Response Data from Point Error Grid Analysis in Figure 3

Range md/dl	*N*	%		MAD mg/dl	MARD %
BG < 70	8	0.7		15.2	18.7
70 ≤ BG ≤ 180	690	63.8		12.6	10.3
BG > 180	384	35.5		20.2	8.8
Total	1082	100.0	Mean	16.0	12.6

Table 2.
Continuous Glucose Error Grid Analysis of 735 Paired Data Points with a Mean Time Period of 15.5 Min

		Point error-grid zones										
		Hypoglycemia BG ≤ 70 mg/dl			Euglycemia 70 < BG ≤ 180 mg/dl			Hyperglycemia BG > 180 mg/dl				
Rate error-grid zones		A	D	E	A	B	C	A	B	C	D	E
	A	0.6%	0.0%	0.0%	45.1%	11.8%	0.0%	21.9%	1.8%	0.0%	0.0%	0.0%
	B	0.1%	0.0%	0.0%	7.9%	2.8%	0.0%	4.1%	0.6%	0.0%	0.0%	0.0%
	uC	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	0.1%	0.0%	0.0%	0.0%
	IC	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%	0.0%	0.0%	0.0%	0.0%
	uD	0.1%	0.0%	0.0%	0.1%	0.3%	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%
	ID	0.0%	0.0%	0.0%	0.3%	0.1%	0.0%	1.0%	0.1%	0.0%	0.0%	0.0%
	uE	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	IE	0.0%	0.0%	0.0%	0.3%	0.1%	0.0%	0.0%	0.1%	0.0%	0.0%	0.0%

Zone	Hypoglycemia BG ≤ 70 mg/dl 0.8% of data		Euglycemia 70 < BG ≤ 180 mg/dl 67.8% of data		Hyperglycemia BG > 180 mg/dl 31.3% of data	
	%	*N*	%	*N*	%	*N*
Accurate	88.9	5	98.6	491	95.2	219
Benign	0.0	0	1.4	7	1.8	4
Erroneous	11.1	1	0.0	0	3.0	7
Total	100.0	6	100.0	498	100.0	230

readings in zone A, obtained from CG-EGA (97.4%), were an improvement over zone A readings from P-EGA (90.8%), which is used to define point accuracy only. The CG-EGA accuracy was highest in the euglycemic range (100% A+B).

To determine the rate-of-change accuracy, the 735 paired data points from the CG-EGA were used. Point-to-point rate of change for each paired data set (YSI and CGM) was calculated by taking the difference between consecutive glucose (G_{n+1}, G_n) measurements divided by the difference in time, (t_{n+1}-t_n), where Rate (R) = [(G_{n+1} - G_n)/(t_{n+1} - t_n)]. The rate-of-change data for each paired set is shown in **Figure 4**, where the rate of the CGM glucose data (*y* axis) is compared with the rate of the YSI glucose data (*x* axis). The R-EGA showed that 85.7% of the CGM data fell within zone A, 11.3% in zone B (97% A+B), 0.4% in zone C, 2.6% in zone D, and 0% zone E.

The data in **Figure 4** were further analyzed for rate of change deviation (RD) and absolute rate of change deviation (ARD). The RD is calculated as follows: RD = (dR-dS)/dt, where dR and dS are the YSI (R) and CGM (S) glucose differences over a time period, dt. The MARD was 0.58 ± 0.65 mg/dl/min, and as shown in **Table 3**, 83.9% of the data fell within 1 mg/dl/min, 12.7% within 1–2 mg/dl/min, 2.4% within 2–3 mg/dl/min, and 1% within 3–4 mg/dl/min.

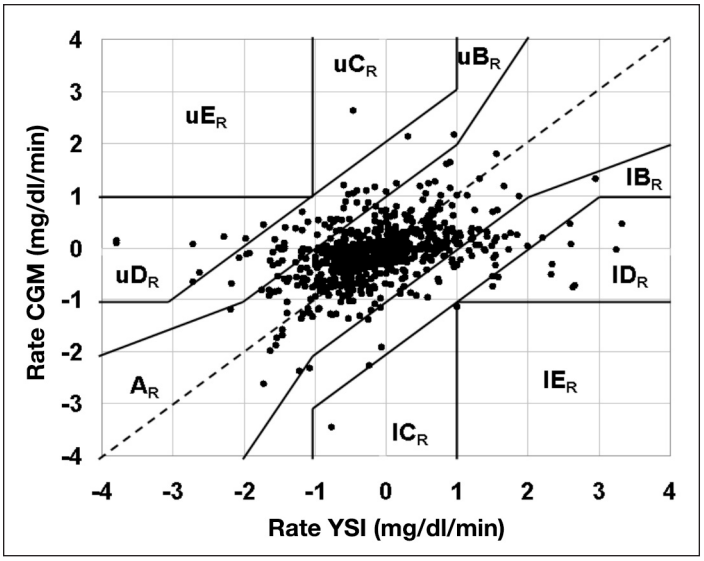

Figure 4. Rate-of-change error grid.

Pain, Adhesive Strength, Erythema, and Edema Assessment

Pain was assessed immediately following sensor insertion using the previously described analog scale [0 (no pain) to 10 (worst pain you can imagine)]. The average score was 1.1, indicating very low pain. Similarly, using the visual scale [0 (no pain) to 10 (worst pain you can imagine)], the average score was 0.9, indicating very low pain. The two scoring systems produced nearly the same average result, with a Pearson coefficient $r = 0.457$.

Pain was also assessed immediately following removal of the electronics module using the analog and visual pain scales described earlier. This pain assessment is related to the physical act of peeling the adhered electronics module from the skin surface. The average analog score was 1.6, indicating low pain. Using the visual scale, the average score was 1.7, indicating low pain. The two pain scales produced nearly the same average score, with a Pearson coefficient $r = 0.960$. The average pain on removal of the electronics module from the skin was greater (1.7/10) than the average pain upon insertion (1.0/10) of the sensor into the skin.

An assessment by the clinical staff of the strength required to remove the adhered sensor module from the subject's skin was performed using the 5 cm line scale. The average score was 1.9, indicating easy removal.

A 48–72 h follow-up visit was scheduled to evaluate the site where the sensor had been attached to the skin. The clinical staff was asked to rate both erythema and edema. The average score for erythema was 0.5, indicating none to very slight erythema, and the average score for edema was 0, indicating no edema was observed.

The above data show the CGM prototype was nearly painless to wear; the adhesive had adequate holding strength, and at the 48–72 h follow-up visit, there was no erythema or edema observed.

Technical Difficulties

From the total of 30 sensors placed on 15 participants, 5 sensors did not provide data. The primary reason was malfunction of the mechanical/electrical interface between the disposable sensor housing and the electronics module. Given that the device was an early prototype, the choice of electrical connector was based on readily available off-the-shelf components. In future versions, a custom electrical interface will be designed to assure robust electrical contact between the sensors and electronics module.

Table 3.
Rate-of-Change Deviation

R-deviation			Absolute R-deviation		
mg/dl/min	*N*	%	mg/dl/min	*N*	%
<-3	4	0.5			
-3 to -2	6	0.8			
-2 to -1	51	6.9			
-1 to 1	617	83.9	0 to 1	617	83.9
1 to 2	42	5.7	1 to 2	89	12.7
2 to 3	12	1.6	2 to 3	14	2.4
>3	3	0.4	>3	7	1.0
Total	735	100.0		735	100.0

Discussion

This study utilized a prototype CGM device for the measurement of glucose within ISF. The measurement technology uses an amperometric electrochemical sensor consisting of glucose oxidase immobilized on a platinum electrode. So far, three CGM devices have been approved by the FDA as adjunctive therapy to finger stick glucose monitoring, and all three use amperometric glucose oxidase biosensors.[40–42] The present CGM system differs from those commercially available in that the glucose sensor is inserted vertically into the skin rather than subcutaneously within the adipose tissue. Its small size causes less pain, resulting in a reduced inflammatory response. Overall, the sensor equilibrates with its environment in a relatively short period of time (<3 h),[32–34] and a single-point calibration was sufficient for the 12 h wear period.

In 2009, Zisser and coauthors[43] published a study on the accuracy of the DexCom Seven system. The MARD compared with the YSI was 13.3%, which may suggest nearing an upper limit to needle-type sensor accuracy.[44] In addition, analysis using P-EGA resulted in 70.4% of results within zone A, 27.5% in zone B (97.9% A+B), 0.6% in zone C, 1.5% in zone D, and 0.0% in zone E. In this same study, using CG-EGA, 95.9% of results were accurate readings, 1.6% were benign errors, and 2.5% were erroneous readings.

In 2012, Keenan and coauthors[45] published a study of the accuracy of the Medtronic Enlite Veo 6-day glucose sensor. The reported MARD was 13.89% versus the YSI. Analysis using P-EGA resulted in 78.4% of results within zone A, 18.9% in zone B (97.3% A+B), 0.4% in zone C, 2.2% in zone D, and 0.1% in zone E. In this same study,

using CG-EGA, 80.3% of results were accurate readings, 17.2% were benign errors (97.5% A+B), and 2.4% were erroneous readings.

In 2008, Kovatchev and coauthors[34] published their studies comparing the accuracy of four CGM devices. Three of the CGM devices were minimally invasive subcutaneous glucose sensors[40–42] while the fourth was a microdialysis probe. Considering only the minimally invasive subcutaneous glucose sensors, P-EGA of the combined (unstratified) data for the three sensors showed that the percentage of data in zone A was 76.3% for the Medtronic Guardian, 55.4% for the DexCom STS, and 76.3% for the Abbott Navigator (overall mean = 69.3%). The combined A+B zones for P-EGA were 97.5%, 100%, and 99.7%, respectively, for an overall mean of 99.0%. Similarly, R-EGA of the combined (unstratified) data showed that the percentage of data in zone A was 73.4% for the Medtronic Guardian, 70.7% for the DexCom STS, and 74.4% for the Abbott Navigator (mean = 72.8%). The combined A+B zones for the R-EGA were 92.1%, 91.7%, and 94.3%, respectively, for an overall mean of 92.7%.

In comparison with the published data, the data obtained from the CGM device used in this study yielded a MARD of 12.6% compared with the YSI. Analysis using P-EGA showed 90.8% of results were in zone A, 8.8% in zone B (99.6% A+B), 0% in zone C, 0.4% in the zone D, and 0% in the zone E. For CG-EGA, 85.7% of results were in zone A, 11.3% in zone B (97.0% A+B), 0.4% in zone C, 2.6% in zone D, and 0% in zone E. These comparisons demonstrate the prototype CGM device used in this study compares favorably with data published for three FDA-approved CGM devices.

Ramchandani and coauthors[11] assessed problems associated with CGM, focusing on users' likes and dislikes. The most disliked aspect of using CGM devices was associated pain and discomfort. In the current report, pain assessment was one of the primary outcomes. By using a small-diameter sensor (0.35 mm, 28 G), it was hypothesized there would be a reduction in the pain associated with initial insertion into the skin and the resulting inflammatory response.[46] Our analysis showed that the sensor was nearly pain-free, and over the 12 h period of the study, there were no adverse reactions and no sensor drift was observed.

Conclusions

A new CGM device that measures ISF glucose was tested on 15 participants, and the results showed the calculated interstitial glucose concentrations were well correlated with YSI reference venous BG measurements. The CGM device was well tolerated without problems, and pain assessment indicated the device was not associated with significant discomfort and did not cause irritation over the period of use.

Additional clinical studies are required over longer time periods and with more participants. Studies using different lengths of the glucose sensor will be conducted to determine whether the lag time and/or accuracy is dependent on depth of penetration. The disadvantages of the present prototype sensor module include its size (2 in. diameter, 0.5 in. high) and lack of waterproofing. The next-generation device will be smaller and waterproof. In addition, the electrode and connector layout will be improved to reduce noise and movement artifacts. Lag correction, calibration, and alarm algorithms will be incorporated into a handheld monitor to be tested in a larger, prospective, multiday study, with the goal of making available a well-tolerated and accurate device that will help people with diabetes better manage their disease.

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