Journal of Diabetes Science and Technology
Volume 5, Issue 2, March 2011

ORIGINAL ARTICLES

Accuracy Performance of the Medtronic NexSensor™ for 6 Days in an Inpatient Setting Using Abdomen and Buttocks Insertion Sites

Tim Peoples, M.A., E.L.S.,[1] Timothy Bailey, M.D., FACE, FACP,[2,3] Ronald Brazg, M.D., FACE,[4] Howard C. Zisser, M.D.,[5] Bob Janowski, B.A.,[6] Suiying Huang, M.S.,[6] Cary Talbot, B.S.E.E,[6] Qingqing Yang, M.S.[6]

Abstract

Background:

Users of continuous glucose monitoring are concerned with product accuracy and choice of insertion site. The Medtronic NexSensor™ was evaluated for accuracy during 6 days of wear when inserted in the abdomen and buttocks areas.

Methods:

Adults (ages 18–75) with type 1 diabetes wore two sensors simultaneously for 6 days, one each inserted in the abdomen and buttocks. Subjects underwent a frequent blood sampling study for 12 hours, during which time reference blood glucose values were obtained every 15 minutes and compared to sensor values.

Results:

Sixty-three subjects were enrolled, and 61 subjects completed the study. The mean agreement rate between sensor and blood glucose values was 75.5% [95% confidence interval (CI), 69.5, 81.4] at the abdomen site, 73.8% (95% CI, 68.8, 78.8) at the buttocks site, and 75.6% (95% CI, 70.8, 80.4) when sensor and reference data were combined between sites. Over 90% of paired sensor-reference values on Clarke error grids were within the A and B ranges. The mean absolute relative differences were 17.1% at the abdomen site, 16.5% at the buttocks site, and 16.8% when sites were combined.

Conclusion:

The NexSensor was accurate for inpatient, frequent-sample testing for 6 days when inserted into the abdomen and buttocks. The results of this study also provide evidence that both the abdomen and buttocks are suitable as sensor insertion sites.

J Diabetes Sci Technol 2011;5(2):358-364

Author Affiliations: [1]Medtronic, Inc., Goleta, California; [2]Advanced Metabolic Care + Research, Inc., Escondido, California; [3]University of California, San Diego School of Medicine, San Diego, California; [4]Rainier Clinical Research Center, Inc., Renton, Washington; [5]Sansum Diabetes Research Institute, Santa Barbara, California; and [6]Medtronic, Inc., Northridge, California

Abbreviations: (A1C) glycated hemoglobin, (ARD) absolute relative difference, (CEG) Clarke error grid, (CGM) continuous glucose monitoring, (CI) confidence interval

Keywords: accuracy, blood glucose, continuous glucose monitoring, subcutaneous glucose sensor

Corresponding Author: Tim Peoples, Medtronic, Inc., Surgical Technologies, 125 Cremona Dr., Goleta, CA 93117; email address tim.peoples@medtronic.com

Introduction

In published studies, continuous glucose monitoring (CGM) reduced glycated hemoglobin (A1C) levels in people with type 1 diabetes by 0.53% (CGM versus self-monitoring of blood glucose) and 0.6% (sensor-augmented insulin-pump therapy versus multiple daily injections with self-monitoring of blood glucose).[1,2] Frequent sensor wear has been consistently associated with reduction in A1C,[1–3] but obstacles to frequent CGM use include concerns about accuracy and discomfort related to sensor placement. Improvements in sensor accuracy and greater flexibility in sensor placement may help promote CGM sensor use and, therefore, improve clinical outcomes. Such improvements may also help to expand reimbursement for CGM systems by insurance companies and other payers.

The NexSensor™ subcutaneous glucose sensor has a form factor that is identical to—and can use the same insertion device and CGM receiver as—the commercially available Sof-Sensor® (all Medtronic, Inc., Northridge, CA). Both NexSensor and Sof-Sensor are composed of a microelectrode with a thin coating of glucose oxidase beneath several layers of biocompatible membrane. The NexSensor features a number of manufacturing and sensor chemistry enhancements over the Sof-Sensor that are intended to improve operating life reliability and consistency between sensors. Current labeling for Sof-Sensor allows for a maximum of 3 days of continuous use in the United States and 6 days in Europe. This labeling also indicates Sof-Sensor insertion only in the abdomen.

The present study was conducted to assess whether NexSensor was accurate for 6 days in the abdomen and buttocks insertion sites.

Methods

Study Conduct

This study was conducted according to Good Clinical Practices. Written informed consent was obtained from all subjects in accordance with U.S. regulations. The study was conducted at three clinical sites in the United States (Escondido and Santa Barbara, CA, and Renton, WA). The NexSensor was an investigational device at the time of the study but was not conducted under an investigational device exemption owing to its nonsignificant risk profile. This study was registered on *ClinicalTrials.gov* (NCT00865345).

Subjects were 18 to 75 years of age and had type 1 diabetes treated with an insulin pump or multiple daily injections of insulin for at least 3 months. Subjects wore the NexSensor on the abdomen and buttocks simultaneously. Sensors inserted at the abdomen site were connected to a real-time CGM system (Guardian® REAL-Time System, Medtronic, Inc.), and sensors inserted on the buttocks site were connected to a CGM recorder (CGMS *i*Pro™, Medtronic, Inc.).

All subjects were randomized to a single 12 h frequent blood sampling test on 1 of the 6 days of sensor use. Sensor values collected during these visits were compared to plasma glucose values drawn every 15 min and processed using a laboratory analyzer (YSI 2300 STAT Plus™, YSI, Inc., Yellow Springs, OH). The subjects' glucose was allowed to fall below 70 mg/dl as measured by the laboratory analyzer. At the discretion of the investigator, insulin was used to induce this value. A meal was then given. At the same meal or a subsequent meal, the subjects' glucose value was allowed to rise above 250 mg/dl, as measured by the laboratory analyzer.

Statistical Analyses

The accuracy analysis was derived from a data set of paired sensor and reference values obtained during the frequent-sampling visits. Sensor and reference values were restricted to 40–400 mg/dl to correspond to the sensor's performance range. Sensor and reference values were adjusted between 10 and 15 min later, in time to approximate the physiologic delay between interstitial fluid and blood as well as the delay between glucose and the sensor's displayed value.[4–6] Sensor values collected at the buttocks site using the retrospective professional CGM recorder were postprocessed using the calibration algorithm of the real-time CGM system used for collecting sensor values at the abdomen site.

The proportion of sensor values that were within 20% (or 20 mg/dl in the 40–80 mg/dl range) of corresponding reference values (i.e., the mean agreement rate) and corresponding 95% confidence interval (CI) were obtained by performing an analysis of variance model. Clarke error grid (CEG) analyses were conducted according to published criteria.[7] Mean absolute relative difference (ARD) and median ARD were calculated between the sensor and reference values relative to the reference

value. Differences between sites in mean agreement, mean ARD, and CEG zones were compared using a repeated measures analysis of variance.

Statistical analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC).

Results

Subjects

Sixty-three subjects were enrolled. Sixty-one subjects completed the study. No subjects discontinued the study owing to an adverse event. Two subjects withdrew because the subject or legal representative requested withdrawal from the study. Subjects were randomized to participate in frequent sampling on days 1, 2, and 4 (3 groups of 11 subjects each) or on days 3, 5, and 6 (3 groups of 10 subjects each). Demographic and other baseline characteristics are displayed in **Table 1**.

Table 1.
Demographic and Other Baseline Characteristics[a]

Characteristics of subjects (n = 63)	Value
Mean age, mean (SD), years	38.7 (13.7)
Sex, number of subjects	
Female	25
Male	38
Race, number of subjects	
White	59
Asian	2
Native Hawaiian/other Pacific Islander	1
Other	1
Ethnicity, number of subjects	
Hispanic/Latino	3
Non-Hispanic/Latino	60
Body mass index, mean (SD), kg/m^2	25.9 (6.2)
A1C, % (SD)	7.3 (1.12)

[a]SD, standard deviation

Precision Analysis

A precision analysis compared the values derived from the abdomen and buttocks sensors using the abdomen sensor as the reference. The mean agreement rate within 20% (or 20 mg/dl in the 40–80 mg/dl range) was 72.48%.

Accuracy Performance

The mean agreement rate within 20% (or 20 mg/dl in the 40–80 mg/dl range) was 75.5% (95% CI, 69.5, 81.4) at the abdomen site and 73.8% (68.8, 78.8) at the buttocks site. The mean agreement rates were similar between sites (p = .78). The mean agreement rate was 75.6% (95% CI, 70.8, 80.4) when the sensor and reference data from both sites were combined.

The overall median ARD was 12.3% at the abdomen site, 11.5% at the buttocks site, and 11.8% when sites were combined. The overall mean ARD was 17.1% at the abdomen site, 16.5% at the buttocks site, and 16.8% when sites were combined (**Table 2**). The overall mean ARD was similar between sites (p = .54). The buttocks site had a higher absolute difference than the abdomen site in the 40–80 mg/dl range, and the abdomen site had a higher ARD than the buttocks site in the >240–400 mg/dl range. These differences between sites were not statistically

Table 2.
Absolute Relative Difference by Glucose Range[a]

Site	40–400 mg/dl %	40–80 mg/dl[b]	>80–120 mg/dl %	>120–240 mg/dl %	>240–400 mg/dl %
Abdomen mean ARD (SD)	17.1 (16.9)	17.6 (14.1)	16.5 (15.7)	14.0 (13.7)	18.1 (17.1)
Abdomen median ARD	12.3	14.3	13.4	10	12.6
Buttocks mean ARD (SD)	16.5 (16.1)	21.8 (14.6)	16.8 (14.5)	13.7 (13.7)	12.4 (9.5)
Buttocks median ARD	11.5	22.1	12.7	9.6	10.5
Combined mean ARD (SD)	16.8 (16.5)	19.5 (14.3)	16.7 (15.2)	13.9 (13.7)	15.3 (14.1)
Combined median ARD	11.8	16.8	13.1	9.8	11.3

[a] SD, standard deviation
[b] For the 40–80 mg/dl range, mean and median ARD are given in mg/dl.

significant (respectively, $p = .36$ and $p = .16$). The ARD was consistent from days 2 through 6 of sensor wear. Day 1 of sensor wear had a higher ARD than other days (**Table 3**). Tracings representative of good and poor agreement between sensor and reference glucose values are shown in **Figure 1**.

Over 90% of paired sensor-reference values were in the A and B zones of the CEGs at the abdomen, buttocks, and combined sites (respectively, 93%, 94%, and 94%; **Figure 2**). The proportion of values in CEG zones A+B was not statistically different between sites ($p = .62$). The abdomen site had more values in zone D than the buttocks site, but this difference was not statistically significant ($p = .53$). The number of paired values in each CEG zone for each day of wear is given in **Table 4**.

Safety

One adverse event was reported but was unrelated to the study device or procedures.

Table 3.
Absolute Relative Difference by Day of Wear[a]

Site	All days	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Abdomen mean ARD (SD)	17.1 (16.9)	24.2 (22.9)	14.3 (13.5)	16.5 (14.1)	13.6 (12.2)	19.1 (17.7)	15.2 (16.8)
Abdomen median ARD	12.3	18.3	10.8	14.2	10.4	13.5	8.8
Buttocks mean ARD (SD)	16.5 (16.1)	21.2 (20.2)	14.3 (12.6)	20.9 (19.1)	11.5 (9.0)	16.5 (17.0)	14.5 (13.6)
Buttocks median ARD	11.5	16.9	10.6	14.1	9.4	10.4	10.6
Combined mean ARD (SD)	16.8 (16.5)	22.8 (21.7)	14.3 (13.1)	18.8 (17.1)	12.4 (10.5)	18.0 (17.5)	14.9 (15.4)
Combined median ARD	11.8	17.6	10.6	14.1	9.8	11.8	9.8

[a] SD, standard deviation

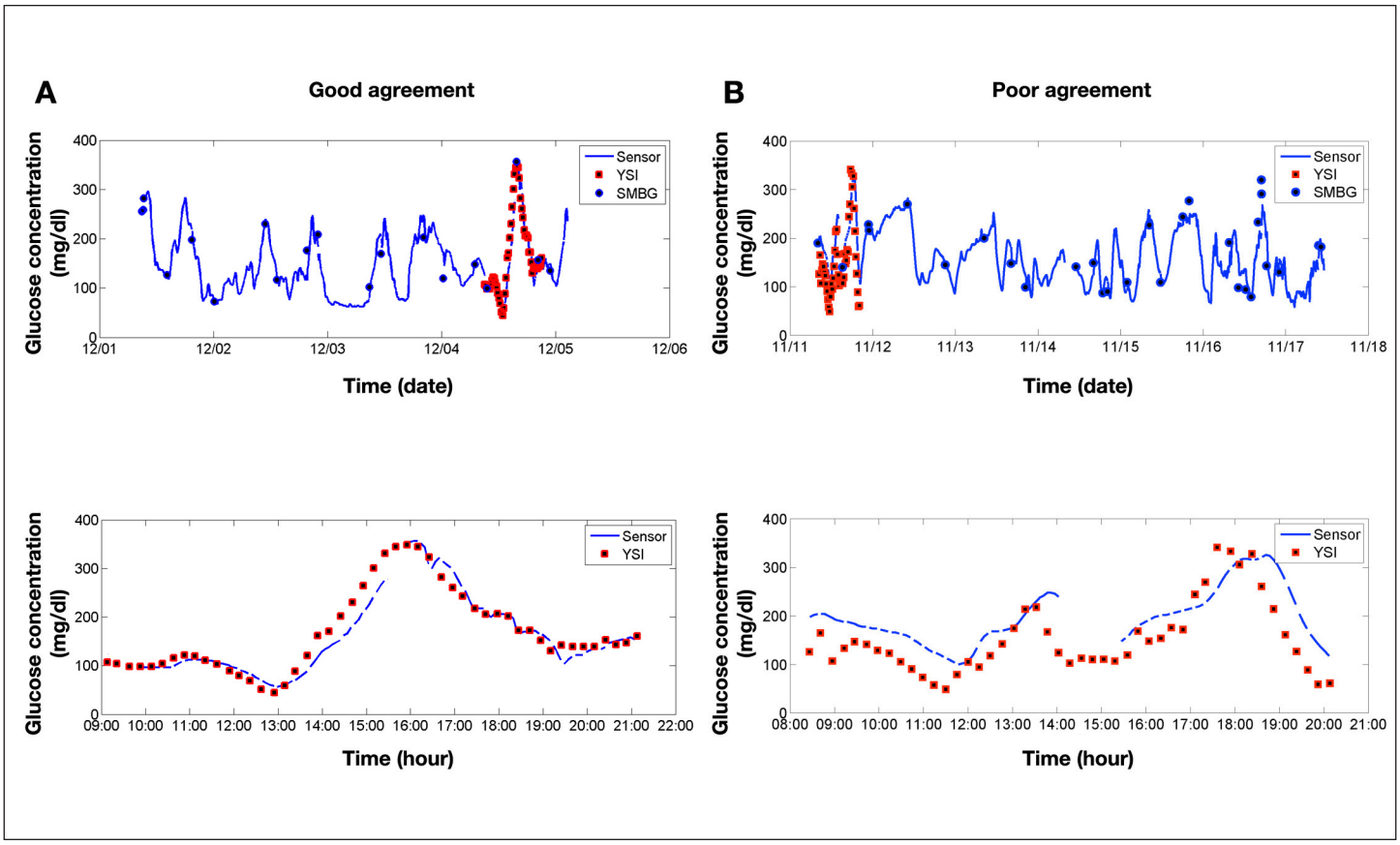


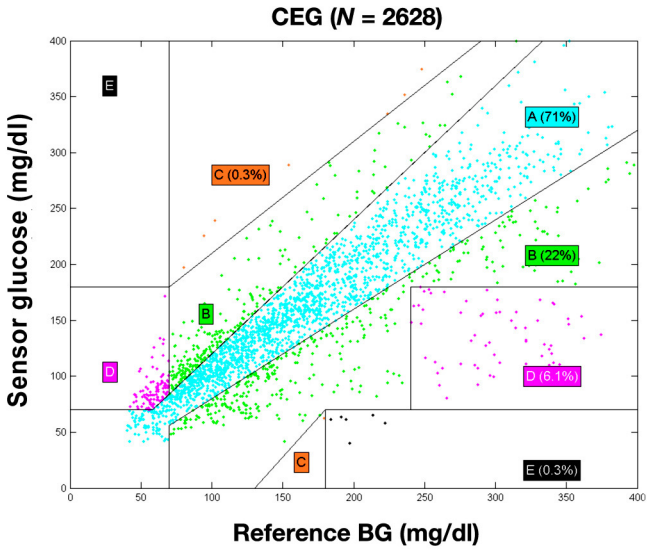
Figure 1. Tracings of NexSensor and reference values: **(A)** good agreement and **(B)** poor agreement. SMBG, self-monitoring of blood glucose.

A. Abdomen site, Clarke error grid

A zone = 71%

B zone = 22%

A+B zones = 93%

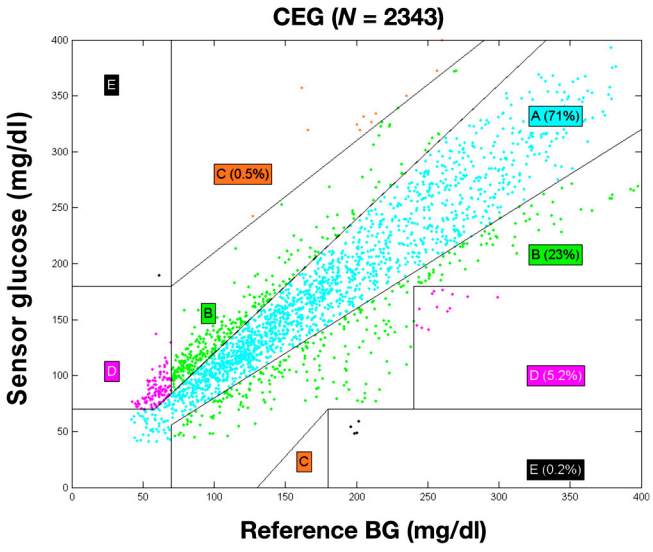


B. Buttocks site, Clarke error grid

A zone = 71%

B zone = 23%

A+B zones = 94%



C. Combined sites, Clarke error grid

A zone = 71%

B zone = 23%

A+B zones = 94%

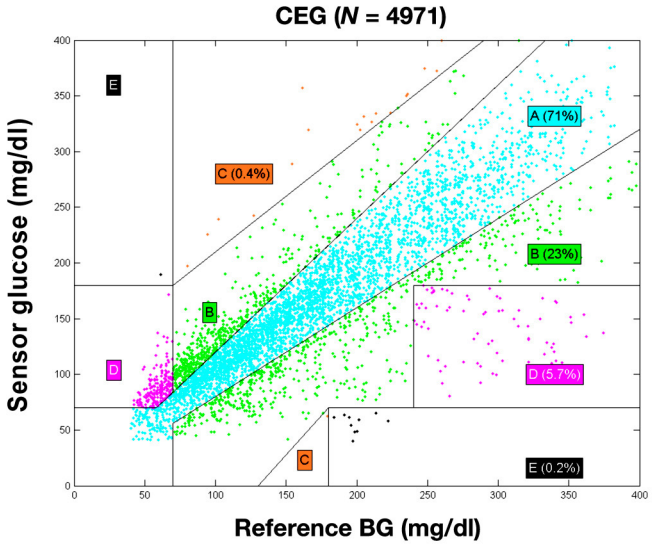


Figure 2. Clarke error grids. CEG, Clarke error grid; BG, blood glucose.

Table 4.
Clarke Error Grid Zones by Day of Wear for Combined Abdomen and Buttocks Sites[a]

Zones	All days	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
A+B	93.66 (4656)	92.72 (675)	96.40 (992)	89.41 (726)	97.48 (620)	93.62 (939)	92.27 (704)
A	71.03 (3531)	56.18 (409)	75.70 (779)	66.63 (541)	81.76 (520)	69.29 (695)	76.93 (587)
B	22.63 (1125)	36.54 (266)	20.70 (213)	22.78 (185)	15.72 (100)	24.33 (244)	15.33 (117)
C	0.38 (19)	0.82 (6)	0	1.11 (9)	0.31 (2)	0.20 (2)	0
D	5.71 (284)	6.18 (45)	3.40 (35)	8.99 (73)	2.20 (14)	5.78 (58)	7.73 (59)
E	0.24 (12)	0.27 (2)	0.19 (2)	0.49 (4)	0	0.40 (4)	0

[a] Results presented as % (paired values).

Discussion

This study demonstrated that NexSensor was accurate for 6 days at both insertion sites, individually and combined. The NexSensor also had a low mean ARD and median ARD, and >90% of paired values were within the A and B ranges of CEGs at both sites.

The results of our study, which had a design similar to several previous investigations of CGM sensors,[8–10] are discussed here. The study[8] for regulatory approval of Sof-Sensor found a mean ARD of 19.7%. The mean ARD for NexSensor in our study was 16.8% using combined site data, 17.1% using abdomen site data, and 16.5% using buttocks site data. The difference in mean ARD between Sof-Sensor and NexSensor was nearly 3% in favor of the sensor used in our study. Furthermore, there was substantial consistency of ARD values from days 2 through 6 of sensor wear. Day 1 of sensor wear had higher ARD values than other days, perhaps owing to calibration issues. The sensor does not display values until after the initial calibration at 2 h; thereafter, the system must be calibrated once every 12 h.

The CEG analysis provides further details about the accuracy of NexSensor in our study. The proportion of paired values in CEG zones A+B was slightly lower in our study of NexSensor (94%, combined sites) than in the regulatory study[8] of Sof-Sensor (96.0%). Values in zone A, however, were higher in our study (71%, combined sites) than in the Sof-Sensor regulatory study (62%). In our study, CEG values of the combined sites, like ARD values, were mostly consistent when stratified by day. A slightly higher proportion of values were in zone D (and slightly fewer values in zones A+B) on days 3 and 6, a finding that was not consistent with ARD values. The raw number of paired values in zone D on days 3 and 6 (respectively, 73 and 59), however, were similar to days 1, 2, and 5 (45, 35, and 58). Day 4 had only 14 paired values in zone D and had a higher proportion of values in zones A+B (97.48%) than the total of all days (93.66%) or for any other day individually.

Our study showed that NexSensor was safe and accurate when placed in either the abdomen or buttocks site for 6 days of use. Mean agreement rates, overall ARD, and error grid A+B zone rates were statistically similar between sites. The mean agreement rate and ARD values suggest a potential advantage to the abdomen site in the hypoglycemic range and the buttocks site in the hyperglycemic range. However, the differences between sites in mean agreement rate and mean ARD were not statistically significant, and mechanical disturbances were not assessed for possible effects on accuracy. Published accuracy studies[11–13] of Sof-Sensor attached to the Guardian REAL-Time System in adult subjects do not specify which site was used. We are, therefore, reporting the first published study to investigate whether the Sof-Sensor/NexSensor form factor is safe and accurate for use in the abdomen and buttocks sites. This is an important finding because patients frequently use current sensors in locations other than those specified on the labeling.

Conclusions

The NexSensor was accurate and safe to wear for 6 days at the abdomen and buttocks sites. The improvements in accuracy shown in our study demonstrated that NexSensor is an advancement in the management of diabetes via CGM technology.

Funding:

This study was sponsored by Medtronic, Inc.

Disclosures:

Tim Peoples, Bob Janowski, Suiying Huang, Cary Talbot, and Qingqing Yang are employees of Medtronic, Inc. Tim Peoples, Bob Janowski, and Cary Talbot are stockholders of Medtronic, Inc. Timothy Bailey has received consulting fees from Animas, Becton Dickinson, Medtronic, and Roche; speaking honoraria from Amylin, DexCom, Eli Lilly, and Novo Nordisk; and research support from Animas, Bayer, Becton Dickinson, DexCom, LifeScan, Medtronic, Novo Nordisk, Roche, and sanofi-aventis. Ronald Brazg has received research support from Medtronic. Howard C. Zisser has received consulting fees from Animas, Roche, MannKind, and Insulet; he has also received grant support from Eli Lilly, Medtronic, DexCom, Insulet, Glumetrics, and Roche.

Acknowledgments:

We acknowledge and thank Rajiv Shah, M.S., for creating much of the technology used in the Medtronic NexSensor and for ensuring that this clinical study came to fruition.

References:

1. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane WV, Beck RW, Bode BW, Buckingham B, Chase HP, Clemons R, Fiallo-Scharer R, Fox LA, Gilliam LK, Hirsch IB, Huang ES, Kollman C, Kowalski AJ, Laffel L, Lawrence JM, Lee J, Mauras N, O'Grady M, Ruedy KJ, Tansey M, Tsalikian E, Weinzimer S, Wilson DM, Wolpert H, Wysocki T, Xing D. Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med. 2008;359(14):1464–76.
2. Bergenstal RM, Tamborlane WV, Ahmann A, Buse JB, Dailey G, Davis SN, Joyce C, Peoples T, Perkins BA, Welsh JB, Willi SM, Wood MA, STAR 3 Study Group. Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. N Engl J Med. 2010;363(4):311–20.
3. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck RW, Buckingham B, Miller K, Wolpert H, Xing D, Block JM, Chase HP, Hirsch I, Kollman C, Laffel L, Lawrence JM, Milaszewski K, Ruedy KJ, Tamborlane WV. Factors predictive of use and of benefit from continuous glucose monitoring in type 1 diabetes. Diabetes Care. 2009;32(11):1947–53.
4. Voskanyan G, Barry Keenan D, Mastrototaro JJ, Steil GM. Putative delays in interstitial fluid (ISF) glucose kinetics can be attributed to the glucose sensing systems used to measure them rather than the delay in ISF glucose itself. J Diabetes Sci Technol. 2007;1(5):639–44.
5. Keenan DB, Mastrototaro JJ, Voskanyan G, Steil GM. Delays in minimally invasive continuous glucose monitoring devices: a review of current technology. J Diabetes Sci Technol. 2009;3(5):1207–14.
6. Davey RJ, Low C, Jones TW, Fournier PA. Contribution of an intrinsic lag of continuous glucose monitoring systems to differences in measured and actual glucose concentrations changing at variable rates *in vitro*. J Diabetes Sci Technol. 2010;4(6):1393–9.
7. Clarke WL, Cox D, Gonder-Frederick LA, Carter W, Pohl SL. Evaluating clinical accuracy of systems for self-monitoring of blood glucose. Diabetes Care. 1987;10(5):622–8.
8. Medtronic MiniMed, Inc. Guardian® REAL-Time Continuous Glucose Monitoring System User Guide. Northridge: Medtronic MiniMed, Inc.; 2006. http://www.minimed.com/pdf/guardian_real_time_user_guide.pdf. Accessed September 15, 2010.
9. Zisser HC, Bailey TS, Schwartz S, Ratner RE, Wise J. Accuracy of the SEVEN continuous glucose monitoring system: comparison with frequently sampled venous glucose measurements. J Diabetes Sci Technol. 2009;3(5):1146–54.
10. Garg SK, Smith J, Beatson C, Lopez-Baca B, Voelmle M, Gottlieb PA. Comparison of accuracy and safety of the SEVEN and the Navigator continuous glucose monitoring systems. Diabetes Technol Ther. 2009;11(2):65–72.
11. Kovatchev B, Anderson S, Heinemann L, Clarke W. Comparison of the numerical and clinical accuracy of four continuous glucose monitors. Diabetes Care. 2008;31(6):1160–4.
12. Mader JK, Weinhandl H, Köhler G, Plank J, Bock G, Korsatko S, Ratzer M, Ikeoka D, Köhler H, Pieber TR, Ellmerer M. Assessment of different techniques for subcutaneous glucose monitoring in type 1 diabetic patients during 'real-life' glucose excursions. Diabet Med. 2010;27(3):332–8.
13. Bode B, Gross K, Rikalo N, Schwartz S, Wahl T, Page C, Gross T, Mastrototaro J. Alarms based on real-time sensor glucose values alert patients to hypo- and hyperglycemia: the Guardian continuous monitoring system. Diabetes Technol Ther. 2004;6(2):105–13.