Real-time continuous glucose monitoring

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Purpose of review

To summarize the current literature on real-time continuous glucose monitors, focusing on devices that have been approved or are pending approval.

Recent findings

Real-time continuous glucose sensors are new tools to assist in diabetes management. Several devices are currently being sold and additional monitors are expected to be available shortly. These sensors measure interstitial glucose – a distinct physiologic space when compared with the blood glucose. The ability to recognize trends in blood glucose levels provides a new paradigm for making insulin dose decisions and treating hypo- and hyperglycemia.

Summary

Real-time continuous glucose monitoring systems are currently less accurate than home glucose meters, but provide information every 1–5 min throughout the day and night with alarms for hyper- and hypoglycemia, providing information on glucose trends and nocturnal glycemic excursions. Current real-time sensors are behavior modification tools. Thus, improvements in diabetes control depend on the willingness of patients to modify their diabetes management based on information provided by these devices.

Keywords

continuous glucose monitoring system, DexCom, glucose sensors, MiniMed Medtronic, Navigator

Curr Opin Endocrinol Diabetes Obes 14:288–295. © 2007 Lippincott Williams & Wilkins.

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Sponsorship: National Institutes of Health/National Institute of Child Health and Human Development grant HD041908 and General Clinical Research Center grant RR00070 JDRF.

Current Opinion in Endocrinology, Diabetes & Obesity 2007, 14:288–295

Abbreviations

ARD	absolute relative difference
FDA	Food and Drug Administration
Hb A1c	hemoglobin A1c

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1752-296X

Introduction

The major development in continuous glucose monitoring in the last several years has been the Food and Drug Administration (FDA) approval of several real-time continuous glucose sensors. These devices are now available to the public, but their cost is generally not covered by health insurance plans. Here, we will review the current literature on real-time monitoring and discuss issues that we believe are important considerations when using these devices.

Current and proposed sensor technology

A number of devices and technologies have been proposed for continuous glucose monitoring including the use of near-infrared and mid-infrared spectroscopy, erythrocyte scattering, photoacoustic phenomena, optical coherence tomography, thermo-optical techniques, Raman spectroscopy, and fluorescence measurements [1]. Currently commercially available continuous glucose sensors are based on measuring subcutaneous (interstitial) glucose levels. These are electrochemical sensors which utilize glucose oxidase and measure an electric current generated when glucose reacts with oxygen. They are coated with specialized membranes to make them biocompatible, generating almost no tissue reaction and providing a barrier to potential cross-reactants such as acetaminophen. These sensors are relatively stable and generally provide a good glucose signal for 3–7 days. As they pass through the skin, there is always the potential for an infection at the insertion site. Current sensors have a transmitter attached to them once they are inserted. The transmitter provides a source of energy to power the sensor, as well as allowing transmission of the glucose signal to a receiver using a radiofrequency signal. These sensors often take several hours to stabilize to the local interstitial environment before they generate a reasonably accurate signal. Some of this calibration time is related to the tissue reaction to the trauma of sensor insertion. As these sensors require a continuous source of power, the transmitter cannot be detached from the sensor for any length of time or the sensor must be recalibrated. One of the biggest user issues with these devices has been the adhesive required to secure the sensor and transmitter to the skin. The adhesives can be irritating to some wearers and others will develop a true tape allergy. For pump users, there are two insertion sites and two areas for potential tape-related issues. Wearing the tape repeatedly in the same area can temporarily disrupt the usual skin barriers to infection. Future devices may be able to combine a continuous glucose

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sensor with an insulin infusion set into one platform adhering to the skin.

One way to avoid the topical skin issues associated with adhesives is to implant the sensor. Implanted sensors are attractive to patients as they are not visible, they do not have to insert a needle-like sensor under their skin repeatedly and they would not interfere with daily activities such as showering, swimming or exercising. There is one published report of a long-term implanted subcutaneous continuous sensor [2]. The sensor was surgically implanted into the abdomen under local anesthesia. Two months after implantation 13 of the 15 implanted sensors were functioning and had a mean absolute relative difference (ARD) of 25% when compared with YSI glucose levels. For implanted devices to be acceptable they will probably need to function for at least 1 year once they are implanted, and ideally their insertion and removal could be performed in a physician's office and not require a surgical referral. Another approach would be an intravascular continuous glucose sensor. This technology was initially developed by Dr David Gough [3], and similar technology has been used in clinical trials conducted by MiniMed in France [4] and the USA. This sensor has about a 20-min delay in reported glucose levels, which has created difficulties when trying to integrate the sensor information into an artificial pancreas.

Continuous real-time glucose sensors reviewed in the paper

Tables 1 and 2 summarize the features of current real-time glucose sensors.

MiniMed-Medtronic REAL-Time Continuous Glucose Monitoring System

This FDA-approved system uses a glucose oxidase-based needle-like subcutaneous sensor, which is connected to a small transmitter that sends interstitial glucose levels by radiofrequency signal to an insulin infusion pump monitor. The insulin infusion pump can act as a monitor only (REAL-Time Continuous Glucose Monitoring System) or as a functioning insulin infusion pump (MiniMed Paradigm REAL-Time 522 or 722 systems). Calibration, recommended four times a day, can be achieved using any home glucose meter or by an transmission from the BD link meter. There are programmable alarms for hyper- and hypoglycemia. The sensor and transmitter unit that is attached to the subject, but not the receiver, is waterproof. The system measures glucose concentrations from 40 to 400 mg/dl.

DexCom STS

After manual insertion of the sensor, there is a 2-h initialization period and then the sensor is approved for 3 days of wear (DexCom has developed a 7-day sensor, which is pending FDA approval). It is calibrated twice a day by connecting the receiver to a Lifescan Ultra Meter after performing a blood glucose test. The data are displayed on a receiver, and provides 1-, 3- and 9-h trend grafts. There are programmable alarms for hyper- and hypoglycemia. The sensor and transmitter unit that is attached to the subject is waterproof. This FDA-approved sensor measures glucose in a range of 40 to 400 mg/dl.

TheraSense FreeStyle Navigator by Abbott Diabetes Care

This device is not yet FDA approved. After a spring-loaded device inserts the sensor, there is a 10-h initialization period and then the sensor can be worn for 5 days. Data are transmitted wirelessly from the sensor to a receiver which can display trends over 2-, 4-, 6-, 12- and 24-h. The receiver has an integrated FreeStyle blood glucose meter, which is used to calibrate the sensor. The sensor and transmitter unit that is attached to the subject is waterproof. Glucose is measured over a range of 20–500 mg/dl with results updated in the display every minute. There are programmable alarms for pending hyper- and hypoglycemia as well as for hyper- and hypoglycemic thresholds.

Issues with measuring interstitial glucose levels as compared with blood glucose levels

The current sensors measure interstitial glucose, which is a distinct physiologic space. When the blood glucose levels are changing rapidly, interstitial glucose levels will lag behind blood glucose levels by 8–18 min [5–7]. The temporal changes in interstitial blood glucose levels, however, correlate better with changes in central nervous system glucose when compared with changes in blood glucose [7]. The lag time between the blood glucose and sensor glucose can have a significant effect on calibrating a continuous glucose monitoring system. When the blood glucose is changing rapidly (above 1.5 mg/dl-min) there will be a greater difference in the sensor reading as compared with the blood glucose reading and this is an inappropriate time to calibrate the sensor [8]. In contrast, when glucose levels are stable, and there is equilibration between the interstitial and serum glucose levels, this error is reduced. Before a sensor is calibrated and providing data, it is difficult to know the rate of glucose change, so we recommend the initial calibration value be entered when it is anticipated there will be a low rate of change (fasting or preprandial). Subsequent calibration values can be entered when the rate of change is low by looking at the display of the real-time glucose sensor and using the graph or rate of change function. Although somewhat counter-intuitive, extra calibration values each day may actually decrease sensor accuracy if they are obtained when glucose values are changing rapidly (postprandial or with hypoglycemia).

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Table 1 Features for continuous glucose monitoring systems

	Abbott FreeStyle Navigator	DexCom STS 3- and 7-day systems	MiniMed Paradigm REAL-Time system (adult and pediatric models)	MiniMed Guardian REAL-Time system
FDA approval Status	Pending FDA approval	3-day system adults 18+; 7-day system pending FDA approval	Adults 18+ for the adult system; children 7–17 for the pediatric system	Children 7–17 and adults 18+
Communicates with an insulin pump	No	No	Yes – to the Paradigm 522 and 722 pumps	No
Calibration with a blood glucose meter	FreeStyle meter port integrated within receiver	3-day system calibration with Lifescan One Touch Ultra via a connection cable	BD Logic calibrations sent wirelessly; meter blood glucose can be entered manually	BD Logic calibrations sent wirelessly; meter blood glucose can be entered manually
Sensor life (h)	120 (pending approval)	72 (7-day sensor in development)	72	72
Length of sensor probe into the skin (mm)	5	13	16	16
Insertion device available	Each sensor has a disposable inserter, spring loaded	DexCom STS applicator, not spring loaded	Sen-serter, spring loaded	Sen-serter, spring loaded
Receiver size (inches)	3 × 2.5	4.5 × 2.3 × 0.85	Displays on 522 or 722 pump, no separate monitor	2.0 × 3.2 × 0.77
Transmitter size (inches)	2.05 × 1.23 rectangular	3-day sensor 1.8 × 1.2 × 0.4 attached to platform	1.38 × 1.63 with sensor attached	1.38 × 1.63 with sensor attached
Start-up initialization time (h)	10	2	2	2
Calibration Requirements	Calibrate at 10, 12, 24 and 72 h after insertion with no further calibration for the final 2 days of the 5-day wear, blood glucose must be between 60 and 300 mg/dl	Every 12 h	2 h, 6 h later after the first calibration, then every 12 h for the life of the sensor	2 h, 6 h later after the first calibration, then every 12 h for the life of the sensor
Range of glucose display (mg/dl)	20–500	40–400	40–400	40–400
Display updated	Every 1 min	Every 5 min	Every 5 min	Every 5 min
Trend arrows displaying the rate/ direction of change	Yes, past 15 min of data contributes to trend arrow	No	Yes, past 20 min of data contributes to trend arrow	Yes, past 20 min of data contributes to trend arrow
Graphs	Past 2-, 4-, 6-, 12- and 24-h glucose graphs	Past 1-, 3- and 9-h glucose graphs	Past 3-, 6-, 12- and 24-h glucose graphs	Past 3-, 6-, 12- and 24-h glucose graphs
Events that can be entered	Insulin, meals, exercise, health, other	None	Insulin, meals, exercise	Insulin, meals, exercise
Computer software	FreeStyle CoPilot Software	DexCom DM Consumer Data Manager; DM 2 Professional Data Manager	Carelink personal software integrates with Paradigm pump download	Carelink personal software

FDA, Food and Drug Administration.

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Table 2 Alarm features

	Abbott FreeStyle Navigator	DexCom STS 3- and 7-day systems	MiniMed Paradigm REAL-Time system (adult and pediatric models)	MiniMed Guardian REAL-Time system
Alarms on user-set low and high thresholds (mg/dl)	Low 60–139; high 140–300	Low 60–90; high 140–400	Low 40–400; high 40–'HI'; pediatric model low alarm cannot set *lower* than 90	Low 40–400; high 40–'HI'; pediatric model low alarm cannot set *lower* than 90
Predictive alarming	Yes – predictive alerts can be set for 10, 20, or 30 min before low alarm blood glucose level is reached	No	No	Yes – predictive alerts can be set for 5, 10, 15, 20, 25 or 30 min before glucose limits have been reached
Rate of change alarms	No	No	No	Yes
Alarm details	Alarm: beep or vibrate; stops alarming after 1 h if the alarms are ignored; alarms can be muted for 1 h or entirely turned off	Alarms: first alert is a vibration, if after 5 min no response, beep and vibrate, third alert beep and vibrate, if no response – no further alerts.	Alarm: beep or vibrate; alarms continue until cleared, if ignored for 10 min it goes into siren mode every minute until cleared; high and low snooze alarm option	Alarm: beep or vibrate; alarms continue until cleared, if ignored for 10 min it goes into siren mode every minute until cleared; high and low snooze alarm option

When sensors are assessed for accuracy, the rate of change of blood glucose levels will also have a significant impact on perceived accuracy of the sensor. In a study of Navigator accuracy the median ARD was 8.5% when the absolute rate of change was below 1 mg/dl, 11–11.8% when the absolute rate of change was 1–2 mg/dl-min and 16.9–17.4% when the absolute rate of change was above 2 mg/dl-min [9].

Understanding sensor lag-time is particularly important in the diagnosis and treatment of hypoglycemia in real-time. As the sensor may lag the blood glucose by 8–18 min (depending on the glucose rate of change), it is important for patients to check a blood glucose on their home glucose meter if they are having symptoms of hypoglycemia, even if their sensors are displaying normal glucose values. When treating their hypoglycemia, they should again use a glucose meter to recheck 15 min after treatment to confirm their blood glucose is above 70 mg/dl. As the sensor may delay showing an increase in the glucose level, the patient could overtreat their hypoglycemic episode with additional carbohydrates if they relied solely on the sensor glucose reading.

Accuracy of current real-time sensors

Real-time continuous glucose monitoring is not as accurate as discrete blood glucose monitoring using a glucose meter, but does provide additional information about the direction and rate of change of the glucose concentration. In one analogy, a discrete blood glucose has been compared with a digital photo and real-time monitoring to a digital video. Whereas there is less information in each video frame when compared with a digital picture, the video provides the added dimensions of the direction and rate of the glucose change. Real-time continuous glucose monitoring values are generally within 15% of the discrete blood glucose level (Table 3). In Table 3 we have chosen the median ARD as the primary measure of comparison. Real-time sensors are generally less accurate in the hypoglycemic range using these criteria, but this fact is partly a math issue, as a 10 mg/dl difference at 50 mg/dl is a 20% ARD, whereas a 10 mg/dl difference at 200 mg/dl is a 5% ARD. In a particular study, therefore, if there are few readings in the hypoglycemic range, the sensor may appear more accurate using median ARD criteria. As previously mentioned, sensors are generally less accurate when glucose levels are changing rapidly. Children with type 1 diabetes tend to have more rapid fluctuations in their glucose levels when compared with adults and particularly when compared to adults with type 2 diabetes. This may be one reason why the same sensor may appear less accurate in pediatric studies than in adult studies (see the two Navigator studies in Table 3). Another factor may be the conditions under which the sensor is studied. Inpatient studies that intentionally induce rapid changes in

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Table 3 Accuracy data

Device	Study population	Reference glucose	Median absolute relative difference			
			Overall	<70 mg/dl	70–180 mg/dl	>180 mg/dl
Guardian RT [10]	71 type 1 adults; ambulatory	Accu-Check Meter	17.3% ($n=4453$)			
Guardian RT [11•]	20 children <3 years old in cardiac intensive care unit	Laboratory (arterial blood)	Mean: 17.6% ($n=246$)			
DexCom STS [12] (3-day)	75 type 1 adults; 16 type 2 adults; ambulatory	Ultra Meter	15.9% ($n=6767$)			
DexCom STS [13] (7-day)	69 type 1 adults; 17 type 2 adults; ambulatory	Ultra Meter	11.4% ($n=6811$)			
Navigator [9]	85 type 1 adults; inpatient (insulin challenge and oral glucose tolerance test)	Laboratory (YSI)	9.3% ($n=20\,302$)	15.4%	~10.3%	~8%
Navigator [14]	30 type 1 children; inpatient (exercise and missed meal bolus)	Laboratory (hexokinase)	12% ($n=1811$)	21% ($n=83$)	13% ($n=1143$)	10% ($n=585$)
Navigator [14]	30 type 1 children; ambulatory	FreeStyle	14% ($n=8639$)	26% ($n=1094$)	15% ($n=4535$)	12% ($n=3010$)

the blood glucose will result in decreased sensor accuracy due to the lag time in interstitial glucose values.

Sensor function during hypoglycemia

From a patient perspective, one of the critical functions of a real-time continuous glucose sensor is the ability to detect clinically significant events, both hyper- and hypoglycemic. Avoidance of nocturnal hypoglycemic seizures is particularly important. Individuals vary in how long they can tolerate hypoglycemia before having a seizure. We are aware of three cases in which a patient was wearing a sensor and had a nocturnal hypoglycemic seizure, and in all cases the sensor was reading below 40 mg/dl for 3–4 h prior to the seizure. From these data, it would appear that, if a sensor detected hypoglycemia within 30 min and it was able to awaken the patient, most individuals would not have a seizure. The DirecNet study group has, therefore, evaluated hypoglycemic alarms using an event-based analysis allowing the sensor 30 min to recognize hypoglycemia [15]. In this study of the GlucoWatch, the value of using a predicted alarm (the trend of glucose values projects hypoglycemia) was compared with a threshold alarm (the measured glucose drops below the level set by the user). The predicted alarm detected significantly more hypoglycemic events, but also had a higher false-positive rate. Table 4 provides a summary of the incidence of true-positive and false-positive alarms using real-time sensors. There is substantial variability in the frequency of the alarms, which is mostly dependent on whether threshold and/or predicted alarms were used, and the definition of what constituted a true-positive alarm. Some definitions allow ±30 min for the sensor to recognize a hypoglycemic event and also allow a 10–15 mg/dl 'cushion' for the glucose threshold (i.e. if sensor was reading 78 mg/dl and alarm threshold was set to 70 mg/dl this value was considered a true-positive alarm). These various definitions make it difficult to compare the false-positive and true-positive rate of alarms in the current literature.

Results of published clinical studies using a real-time glucose sensor

The first randomized controlled trial using a real-time glucose sensor (the GlucoWatch) was conducted by the DirecNet study group [16]. In this 6-month randomized trial, 100 children were assigned to wear the GlucoWatch for 6 months and 100 children were assigned to the control group. There was no improvement in hemoglobin A1c (Hb A1c) levels nor any reduction in the incidence of hypoglycemia in the group using the GlucoWatch compared with the control group. Although subjects were encouraged to use the GlucoWatch frequently, there was a significant decline in GlucoWatch use during the study. Reasons given for declining use included: skin irritation (76%), skips too frequently (56%), alarms too frequently (47%) and does not provide accurate readings

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Table 4 True-positive and false-positive alarm rates for real-time sensors

Device	Alarm threshold	Sensitivity (true positive) (%)	False positive alarms (%)	Criteria
GlucoWatch [15]	Low (≤60 mg/dl)	23	51	Alarms in ±30 min
	Low (≤60 mg/dl)	88	78	With predicted low alarm and ±30 min window to detect a low
Guardian 1[10]	Low (≤70 mg/dl)	67	47	
DexCom STS [13] 7 day	Low (<70 mg/dl)	88		Low alarm set at 80 mg/dl
Navigator [9]	Low (<70 mg/dl)	80	7.2	Positive if <70 mg/dl in ±30 min with threshold or projected alarm; false positive if >85 mg/dl

(33%). The results of this study demonstrate that for a real-time sensor to have an impact on glycemic control, the device must be accepted by the patient and used frequently, and skin reactions can play a significant role in reducing patient acceptance of the device.

In a randomized trial using the MiniMed Guardian REAL-Time Continuous Glucose Monitoring System, 162 children, adolescents and adults were randomized into three groups [17•]. One group was instructed to wear the sensor continuously, another was instructed to wear the sensor for 3 days every 2 weeks and the third group did not wear a sensor (the control group). The Guardian sensor used in this study displayed the current interstitial glucose value, and had alarms for hyper- and hypoglycemia, but it did not display a graph of glucose values or have rate of change arrows. After 3 months there was a 1% decrease in Hb A1c levels in the group wearing the sensor continuously as compared with a 0.4% decrease in Hb A1c in the control group ($P = 0.003$). The group using the sensor for 3 days every 2 weeks had a 0.7% decrease in Hb A1c – not significantly different from the control group. This study demonstrates that real-time continuous glucose monitoring is most effective when it is used continuously.

There have been several small, uncontrolled studies of Guardian wear which have demonstrated an improvement in Hb A1c levels [18,19]. Larger, randomized trials of the Paradigm REAL-Time Continuous Glucose Monitoring System are currently being conducted by Medtronic MiniMed.

In a 9-day controlled study of the DexCom STS continuous glucose sensor, the group that was randomized to view their real-time data spent 21% less time in hypoglycemia and 23% less time in hyperglycemia as compared to the group that was blinded to their sensor readings [12].

In a 3-month feasibility study to assess the use and acceptance of the FreeStyle Navigator continuous glucose monitoring, 30 children using insulin pumps (mean age 11, range 4–17 years) were assigned to wear a Navigator daily [20•]. Mean Hb A1c improved from 7.1% at baseline to 6.8% at 13 weeks ($P = 0.02$), and the percentage of glucose values between 71 and 180 mg/dl increased from 52% to 60% ($P = 0.01$). There was no control group. Subjects and parents reported high satisfaction with the Navigator on the DirecNet Continuous Glucose Monitor Satisfaction Scale [21] and nearly all subjects chose to continue using the sensor in the subsequent extension phase of the study. They were not overwhelmed by the amount of information provided by real-time monitoring, and 70% thought the use of the Navigator made adjusting insulin doses easier, gave them more confidence in making diabetes decisions and showed them patterns in their blood glucose levels they had not previously been aware of. This study demonstrates that incorporating real-time continuous glucose monitoring into the daily management of type 1 diabetes in children is feasible, and the sensor was perceived as providing valuable information regarding glycemic control by parents and patients. The majority of subjects were using the sensor for at least 6 days a week throughout the duration of the study, indicating the device was well accepted.

The Juvenile Diabetes Research Foundation is currently sponsoring a large multicenter trial testing the use of MiniMed, DexCom and Navigator real-time continuous glucose sensors in children and adults with type 1 diabetes. This study is designed to test the concept that use of any continuous glucose monitoring system device will result in an improvement in metabolic control. There are two major groups: (1) subjects with an initial Hb A1c above 7%, for who the goal is to lower the Hb A1c; and (2) subjects with an Hb A1c below 7% where the goal is to decrease the time spent with glucose values below 70 mg/dl without increasing the Hb A1c. The study is not designed to compare the continuous glucose monitoring devices.

Clinical experiences with real-time continuous glucose monitoring

Real-time continuous glucose monitoring allows for insulin doses to be based not only on a single glucose value, but with knowledge of which direction the blood glucose is trending. Thus, the premeal dose of short-action insulin can be increased or decreased depending on the direction and speed of glucose changes at the time of

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the meal. Currently available insulin pumps utilize algorithms to incorporate current glucose levels and the expected carbohydrate intake into suggestions for bolus doses (the 'bolus calculator' or 'bolus wizard' features). With the availability of glucose trend information and rate of change arrows, more sophisticated algorithms can be developed. As an example, a patient might increase a premeal bolus by 20% if the glucose were rising faster than 2 mg/dl-min (this rate of change can be easily determined using trend arrows).

The use of predictive and threshold hypoglycemic alarms allows for treatment of possible hypoglycemia before it occurs. As an example, if the sensor alarms for hypoglycemia and a capillary glucose is 90 mg/dl, but the trend arrow shows a rapid downward rate of change (above 2 mg/dl-min), it would be predicted that the glucose would be less than 70 mg/dl in 20 min and it is appropriate to treat for pending hypoglycemia. In this situation we would recommend treating with 10 g of carbohydrate instead of the usual 15 g. This is a new paradigm for patients and healthcare providers. It remains to be determined if prospective treatment of pending hypoglycemia will result in an increase in Hb A1c levels.

There is a sense of security in wearing a continuous sensor when going to sleep, knowing that the sensor will generate alarms for severe or prolonged hypoglycemia. Unfortunately it has been our experience that patients do not always awaken to these nocturnal alarms, even when the alarms persist for several hours. When we videotaped the response of patients to nocturnal alarms, 40% awoke to the first alarm, but only 28% awoke to subsequent alarms [22]. We, therefore, recommend enhancing current sensors with a night time alarm system, which incorporates a bedside device that can receive the signal from the continuous glucose monitoring transmitter. When there is a hypoglycemic alarm, this bedside device could activate a bright light or transmits a stronger radiofrequency signal to an adjacent bedroom to awaken another member of the household.

One of the keys to achieving a significant benefit in glycemic control when using a real-time sensor is to look at sensor glucose levels and glucose trends frequently throughout the day. Patients who were most successful in using a real-time sensor were looking at the sensor 10–20 times a day and greatly missed the comfort of knowing their glucose levels when they were not wearing the sensor.

Some of the most common changes made to diabetes management as a result of real-time monitoring are based on meal related activities. Breakfast meals often result in the highest postprandial glucose levels. Many patients have changed the composition of breakfast by adding more protein and fat, and decreasing simple sugars. Other patients have started to give their insulin 10–20 min before eating a meal to decrease the postprandial glucose spike.

Real-time continuous glucose monitoring is a very powerful behavior modification tool, but it only works if someone is willing to modify their behavior. In using the continuous glucose monitoring in adolescents we have found some adolescents did not want to be bothered with frequent diabetes management decisions and the real-time continuous glucose monitoring is just a constant reminder that they have diabetes, when they wish their diabetes was nonexistent. These teenagers often did not achieve a significant benefit from wearing a real-time continuous glucose monitor.

There is a tremendous amount of information in the reports generated from real-time continuous glucose monitoring. As healthcare providers, we have found the reports generated by the CareLink software from MiniMed particularly helpful since these reports integrate the information from the insulin infusion pump with home glucose monitoring and their continuous glucose monitoring data. As it is known when a meal bolus is given, the software allows synchronization of blood glucose levels in the hours before and after a meal bolus, even if the meal is given at variable times over multiple days. The 'Daily Detail' report graphically shows continuous glucose monitoring data (including alarms), insulin pump data and carbohydrate intake. We have found this report particularly helpful in identifying problems with the carbohydrate to insulin ratio, a 'missed meal bolus', overtreatment of hypoglycemia and inappropriate suspension of the basal rate.

Uses outside of diabetes

Real-time continuous glucose monitors may play an increased role in diseases other than diabetes. One of the most promising uses for continuous glucose monitoring may be in the intensive care unit. Tight glycemic control in the intensive care unit has produced dramatic improvements in morbidity and mortality [23]. Real-time continuous glucose monitoring has functioned well in an intensive care unit setting even with variable changes in the core body temperature, use of inotropes and body-wall edema [11•,24]. When intravenous glucose infusions are provided at a steady rate, the blood glucose fluctuations associated with oral absorption of meals is avoided. In an intensive care unit setting insulin is delivered intravenously, which significantly improves the pharmacodynamics of insulin delivery in a closed-loop system. The intensive care unit may, therefore, be one of the initial settings in which closed-loop delivery of insulin using a continuous glucose sensor will be implemented.

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Conclusion

Real-time continuous glucose monitoring offers a great benefit to patients who want to actively manage their diabetes; however, widespread adoption of this technology will be delayed until insurance plans authorize this treatment. Continuous monitoring may be of particular benefit to patients with hypoglycemia unawareness, inpatients, athletes and pregnant women. Both patients and physicians need to learn how to best utilize the real-time data and pending hypo- and hyperglycemic alarms to make treatment decisions. Ongoing randomized controlled studies will help to determine if near-continuous use of real-time sensors over extended periods of time will result in significant improvements in Hb A1c levels, a decrease in the incidence of hypoglycemia and an improvement in the quality of life for people with diabetes.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 330).

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