Technology

A new paradigm in continuous glucose monitoring technology?

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Over recent years, developments in continuous glucose monitoring (CGM) technology have largely been confined to the accuracy of the sensors, the sophistication of the related monitoring systems and the ability of the sensor to communicate with and, in some circumstances, control an associated insulin pump. Two studies highlighted in these pages describe a different type of sensing technology: a fluorescent glucose-responsive hydrogel. In this system, glucose binds reversibly to indicator boronic acid groups, and this increases the fluorescence intensity so that fluorescence increases as glucose levels in the interstitial fluid increase. The sensor is implanted subcutaneously and thus requires a minor surgical procedure both to insert and to remove it. This inconvenience is offset by the fact that the sensor life is at least 90 days. To complete the system, produced by Senseonics Inc (Germantown, MD, USA), the user wears a transmitter over the sensor implantation site, which picks up the fluorescent signal, converting it into a glucose concentration, and powers the sensor. The transmitter sends data wirelessly by Bluetooth to a smartphone-based software app, which displays the glucose levels. Alarms can be set and the alerts are delivered both by vibration of the transmitter and by a call from the smartphone.

Dehennnis and colleagues (their study summarised alongside) evaluated the system over 90 days in 24 people. The sensor continued to provide data for 90 days in 22 of the participants and, importantly, there was no significant change in sensor accuracy over the duration of its implantation. The sensor's mean absolute relative difference, the standard measure of CGM accuracy, was 11.4±2.7%, which is comparable with currently available CGM systems. This accuracy was similar across all ranges of glucose values, with the sensor performing well in the hypoglycaemic range.

In their study (summarised on the opposite page), Wang et al looked at the sensor's performance overnight and, in particular, sought to determine whether there was evidence of nocturnal sensor attenuation. This can occur with existing CGM systems when users lie on the sensor in bed and the pressure causes the sensor signal to drop off. Twelve people wore the sensor for 90 days, with hypoglycaemia alarms set to trigger at 3.9 mmol/L. On 13.6% of nights hypoglycaemia alarms were triggered for at least 10 minutes. The sensitivity of the sensor in alerting for hypoglycaemia was 77%, with a 4% false-positive alarm rate. Crucially, there was no evidence of nocturnal sensor attenuation.

These studies show the potential of this new glucose-sensing technology, with a good level of accuracy both in general and, specifically, in terms of nocturnal hypoglycaemia detection. It remains to be seen whether the need for a minor surgical procedure to implant and remove the sensor, as well as the need to continually wear the transmitter over the implantation site, limit the system's attractiveness for the CGM user, or whether the 90-day lifespan and potentially better overnight performance will prove effective selling points. This may depend on whether over 90% of sensors last at least 90 days in routine clinical practice. ■

J Diabetes Sci Technol

90-day accuracy of a new implantable CGM sensor

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 These authors evaluated the accuracy of a new continuous glucose monitoring (CGM) system over 90 days in 24 adults with T1D.

2 The CGM system, manufactured by Senseonics Inc (Germantown, MD, USA), uses a subcutaneously implanted sensor which measures glucose levels in the interstitial fluid via a non-enzymatic, fluorescent, glucose-indicating hydrogel, and which is linked to a transmitter worn over the implantation site.

3 Participants used the device for 90 days and were also issued with finger-stick tests to calibrate the device twice daily. The accuracy of the device was assessed every 2 weeks by comparison with venous blood glucose levels obtained in the clinic.

4 Of the 24 sensors evaluated, 22 remained functional for the full 90 days; the other two were stopped at days 55 and 84, respectively, when self-diagnostics reported inadequate sensor performance.

5 The mean absolute relative difference averaged across all 24 sensors was 11.4 ± 2.7% (range, 8.1–19.5%), comparable to other commercially available CGM systems.

6 The system also worked well at extreme blood glucose levels, with 91% of measurements falling within 20% of the reference range at blood glucose levels ≤3.9 mmol/L, and 88% within 20% of the reference range at levels >10.0 mmol/L.

7 There were no serious adverse events over the 90 days.

Dehennis A, Mortellaro MA, Ioacara S (2015) Multisite study of an implanted continuous glucose sensor over 90 days in patients with diabetes mellitus. *J Diabetes Sci Technol* **9**: 951–6

Diabetes Technol Ther

Nocturnal accuracy of the Senseonics CGM system

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 Many commercially available continuous glucose monitoring (CGM) systems can have poor accuracy at night, as pressure on the sensors when users lie on them can affect the readings.

2 With this in mind, these authors evaluated the Senseonics CGM system described on page 184 in the home setting in 12 adults with T1D, comparing CGM-derived glucose levels with those determined from the users' usual finger-stick routine.

3 Overall, the device was accurate, with a mean absolute relative difference of 12.3±0.7% at blood glucose levels of 2.2–22.2 mmol/L.

4 Hypoglycaemia alarms, which were set to trigger at glucose levels ≤3.9 mmol/L, occurred on an average of 13.6% of nights over the 90-day study, and the device showed a hypoglycaemia detection sensitivity and specificity of 77% and 96%, respectively, equating to a 4% rate of false alarms.

5 There was no evidence that the sensor failed overnight or had any pressure-induced inaccuracies.

Wang X, Ioacara S, Dehennis A (2015) Long-term home study on nocturnal hypoglycemic alarms using a new fully implantable continuous glucose monitoring system in type 1 diabetes. *Diabetes Technol Ther* **17**: 780–6

J Diabetes Sci Technol

In-hospital use of CGM in people with insulin-treated T2D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 The use of continuous glucose monitoring (CGM) in hospitalised people with T2D was evaluated.

2 CGM was compared with capillary point-of-care (POC) measurements taken before and after meals, at bedtime and at 03.00 in 38 inpatients receiving basal–bolus insulin treatment.

3 There was no difference in mean daily blood glucose levels between the groups; however, CGM detected 55 episodes of hypoglycaemia while POC detected only 12 (incidence rate ratio, 4.58; $P<0.001$).

4 CGM was accurate, with 91.9% of participants falling within the Clarke error grid A and B zones.

5 In conclusion, CGM is accurate in hospitalised people with T2D and is superior to POC for detecting hypoglycaemia.

Gómez AM, Umpierrez GE, Muñoz OM et al (2015) Continuous glucose monitoring versus capillary point-of-care testing for inpatient glycemic control in type 2 diabetes patients hospitalized in the general ward and treated with a basal bolus insulin regimen. *J Diabetes Sci Technol* 31 Aug [Epub ahead of print]

Diabet Med

Long-term benefits of CSII in T1D

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 The effects of continuous subcutaneous insulin infusion (CSII) over a follow-up of up to 12 years in a clinical population of 327 people with T1D were evaluated.

2 Compared with a mean baseline HbA_{1c} of 70 mmol/mol (8.6%), after 1 year of CSII this had reduced by 8 mmol/mol (0.7%), an improvement that was sustained at 2, 3, 4 and 5 years.

3 Over the study period, the proportion of participants with five or more mild-to-moderate hypoglycaemic episodes per week before initiating CSII fell from 29% to 12%, and the proportion of those with two or fewer episodes increased from 52% to 61%.

Beato-Víbora P, Yeoh E, Rogers H et al (2015) Sustained benefit of continuous subcutaneous insulin infusion on glycaemic control and hypoglycaemia in adults with type 1 diabetes. *Diabet Med* **32**: 1453–9

Lancet Diabetes Endocrinol

Dual-hormone artificial pancreas in children with T1D

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 In this open-label, crossover, randomised controlled trial, a dual-hormone (insulin plus glucagon) artificial pancreas (AP) was compared with an insulin-only AP and a conventional insulin pump in 33 children with T1D in a diabetes camp in Canada.

2 The participants wore each intervention for 3 nights (between 22.00 and 07.00) before switching, making a total study period of 9 nights. The allocation and order of devices was randomised.

3 The primary outcome, the proportion of time spent with blood glucose levels <4.0 mmol/L, was 3.4% with the conventional pump, 3.1% with the single-hormone AP ($P=0.032$ vs. the conventional pump) and 0% with the dual-homone AP ($P=0.032$ vs. single-hormone AP; $P=0.005$ vs. conventional pump).

4 The proportion of time spent in the target glycaemic range of 4.0–8.0 mmol/L was 29% with the conventional pump, 55% with the single-hormone AP and 63% with the dual-hormone AP.

5 In the pump group, 11 participants (33%) had 15 hypoglycaemic events requiring intervention according to camp protocol, compared with four events in four people in the single-hormone group and no events in the dual-hormone group.

6 The dual-hormone AP appears to improve nocturnal hypoglycaemia; however, questions remain as to whether its clinical benefit outweighs its increased complexity and potential cost.

Haidar A, Legault L, Matteau-Pelletier L et al (2015) Outpatient overnight glucose control with dual-hormone artificial pancreas, single-hormone artificial pancreas, or conventional insulin pump therapy in children and adolescents with type 1 diabetes: an open-label, randomised controlled trial. *Lancet Diabetes Endocrinol* **3**: 595–604

> *"The dual-hormone artificial pancreas appears to improve nocturnal hypoglycaemia; however, questions remain over whether its clinical benefit outweighs its increased complexity and potential cost."*