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News & Highlights

Advanced Devices Ease Burden of Glucose Monitoring for Diabetics

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For most of the world's many diabetics, monitoring blood sugar remains a time-consuming, inaccurate, and painful multiple-times-a-day, chemistry-laboratory-in-the-kitchen experience. Now, hope for easing this burden is being delivered by medical device manufacturers with striking advances in monitoring technology. The latest generation of glucose monitors are highly accurate, easy to use, and relatively painless. Applied directly to the skin for weeks at a time, these small sensors make tracking glucose levels as simple as glancing at a smartphone. They also take medical technology one step closer to the holy grail of fully automated, "closed-loop" delivery systems for insulin, which could go a long way to effectively freeing diabetics from the shackles—and perhaps worst health effects and risks—of their disease.

"Managing type 1 diabetes is a daunting task with patients expected to balance insulin doses based on more than 40 real-life factors that can affect glucose," said Viral Shah, an associate professor of pediatrics and medicine at the adult clinic of the Barbara Davis Center for Diabetes at the University of Colorado Anschutz Medical Campus in Aurora, CO, USA. "Closed-loop systems, where a pump delivers insulin based on glucose sensor readings every minute to every five minutes, hold the promise of improving glycemic control while reducing patient burden. This is the future of managing diabetes."

According to the World Health Organization, more than 400 million people worldwide have diabetes [1], a disease characterized by poorly controlled blood glucose levels. Chronically high glucose concentrations (hyperglycemia) can lead to stroke, heart attack, heart failure, kidney failure, blindness, and amputation. In addition, many patients also experience episodes of low blood glucose (hypoglycemia) that can result in coma and death. Currently, the most commonly used glucose-sensing technology is finger-prick-based glucose strips. This, however, involves taking multiple samples per day, making regular glucose monitoring a considerable challenge. In contrast, real-time continuous glucose monitoring (CGM) offers a much simpler and more accurate assessment of the large—and potentially dangerous—fluctuations in blood glucose that can occur daily in diabetics.

While CGM devices are being developed to monitor blood sugar levels in biological materials such as sweat [2] and tears [3], a handful of CGM devices—pioneered by companies such as Abbott (Chicago, IL, USA) and Dexcom (San Diego, CA, USA)—have been commercially available since 2016. These devices determine glucose levels from the interstitial fluid surrounding the cells of the tissue just below the skin; they are basically sticky patches with a short, embedded filament that punctures the skin. The filament is coated with the enzyme glucose oxidase that oxidizes glucose in the body's interstitial fluid. The electrons resulting from this reaction shuttle to an electrode within the filament, generating an electrical signal proportional to glucose levels. Onboard electronics transmit readings to an external device.

In September 2020, Abbott secured an European CE approval—awarded to products that conform to health, safety, and environmental standards of the European Economic Area—for the newest generation of its FreeStyle Libre continuous glucose monitors [4]. Worn on the back of the upper arm, the FreeStyle Libre 3 is rated for up to 14 days of constant use. At the size of two stacked pennies (2 cm diameter, 0.3 cm thick), the FreeStyle Libre 3 is the world's smallest and thinnest glucose sensor for commercial use (Fig. 1). "It is incredibly small," said Scott Harper, divisional vice president of Research and Development at Abbott's diabetes care business. "So small that you do not even really realize you are wearing it. This allows people to be very discreet."

The sensor's tiny size does more than just make it more comfortable and reduce the chance of scarring, though. Smaller sensors can also be more accurate. "Too big becomes a problem because you could knock it around or compress the skin, which may lead to motion artifacts and false readings," said Jason Heikenfeld, a professor of electrical engineering and materials science at the University of Cincinnati in Cincinnati, OH, USA.

While the new monitor's predecessor, the FreeStyle Libre 2, requires users to scan the sensor with an external reader or

Fig. 1. Compared to its predecessor, the FreeStyle Libre 2, Abbott's new FreeStyle Libre 3 glucose monitor is 70% smaller; it similarly requires no manual calibration, is just as accurate, and will cost about the same. Credit: Abbott laboratories (public domain).

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smartphone app to obtain their glucose result, the FreeStyle Libre 3 automatically sends minute-by-minute assessments to the wearer's smartphone via bluetooth. With both devices, apps on the wearer's phone can also display trends and trigger optional alarms when levels deviate from a healthy range. A separate app, called LibreLinkUp, can also alert the wearer's doctor or family member to potentially concerning readings [4]. Also, unlike some other CGM, the FreeStyle Libre monitors can be used right out of the box with no manual calibration.

The list price of the FreeStyle Libre 3 will be about 100 USD per month—the same as the FreeStyle Libre 2, which was 70% larger (3 cm diameter, 0.5 cm thick) [5]. Abbott plans to commercially launch the FreeStyle Libre 3 in Europe before the end of 2021 [4]. In its bid for US Food and Drug Administration (FDA) approval, the company recently completed a clinical trial comparing the accuracy of the FreeStyle Libre 3 to venous plasma measurements of glucose levels [6], though results have not yet been published.

Given how user-friendly it is, Abbott expects groups besides diabetics will use their technology to track glucose, including high-performance athletes. During high-intensity workouts, athletes typically see a rise in blood glucose. As exercise continues and glycogen stores are depleted, glucose levels begin to drop, especially in long-distance endurance events. Being able to check glucose levels in real time can help athletes boost performance [7]. In September 2020, Abbott announced the Libre Sense Glucose Sport Biosensor, designed specifically to provide athletes with data to know when and how to fuel and avoid fatigue [8]. Cyclists from some of the top-ranked cycling teams used the device during observation trials leading up to the 2020 Tour de France to determine the best times to refuel [8]. Ironman athletes are also using the device to boost performance in training sessions and races [9].

Abbott's closest competitor in the diabetic CGM market is Dexcom [10]. Dexcom's current offering, the G6, provides readings every five minutes, an accuracy comparable to the FreeStyle Libre 3, is rated for ten-day use, and can work with a reader, smartphone, or smartwatch. The company's next generation G7 monitor will have a lifespan of 14 days, be 60% smaller than the G6—but still bigger than the FreeStyle Libre 3 (Fig. 2)—and will also work with a smartphone or smartwatch; the company anticipates US FDA approval for the G7 in early 2021 and commercial launch in late 2021 [11]. Aside from their larger size (4 cm × 2.1 cm × 0.8 cm), the G6 sensors carry a 349 USD per month retail price tag—more than three times higher than that proposed for the FreeStyle Libre 3 [12]. The price of the G7 has not been revealed.

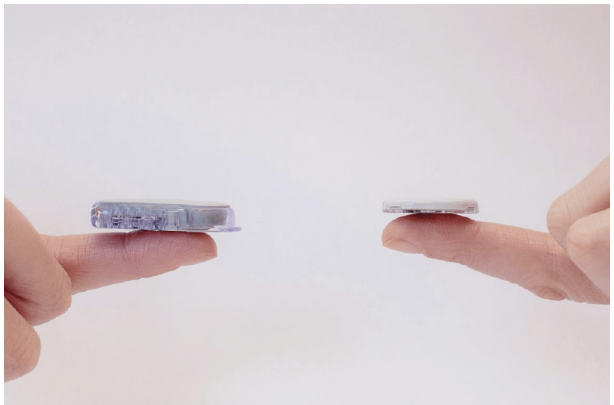

Fig. 2. Dexcom's G7 sensor (right) is 60% smaller than its predecessor, the G6 (left), but still larger than the FreeStyle Libre 3. While the G7 and Abbott FreeStyle Libre 3 are expected to gain approval for this application, the G6 is currently approved for use, integrated with Tandem's X2 insulin pump, as part of a closed-loop, automated insulin delivery system. Credit: Dexcom (public domain).

As mentioned above, Abbott and Dexcom have been working to integrate their glucose monitors with insulin-delivery devices, such as implantable pumps and prefilled insulin pens, to create automated insulin delivery systems. Such a system, sometimes referred to as an artificial pancreas, continuously transmits glucose level information from the sensor to a delivery device that increases or decreases insulin to maintain blood sugar as close as possible to a fixed target.

Dexcom currently has the inside track on such closed-loop delivery systems. The G6 was cleared by the US FDA in December 2019 to integrate with Tandem Diabetes Care's (San Diego, CA, USA) Control IQ technology, a software package that controls Tandem's X2 insulin pump, the only such device with an alternate controller enabled (ACE) designation from the US FDA [13].

In June 2020, the US FDA granted the FreeStyle Libre 2 an interoperable continuous glucose monitor (iCGM) designation [14], meaning it has the potential to work with other pieces of diabetes technology. However, unlike the similar designation granted to the Dexcom G6, the FreeStyle Libre 2 is not yet approved for use with automated insulin delivery systems. Most likely, though, the FreeStyle Libre 3 will receive the full iCGM designation soon after its launch in the United States. This will enable the sensor to be paired with Tandem's X2 insulin pump, as well as automated delivery systems from Bigfoot Biomedical (Milpitas, CA, USA); Abbott announced partnerships with both companies in 2020 [15].

The other major player in the diabetic CGM market is Medtronic. However, according to Shah, the medical device giant's latest technology, the MiniMed 780G system, lags behind Abbott's and Dexcom's monitors in terms of sensor size, lifespan, accuracy, and need for calibration. Yet Medtronic, which is still working to earn its own US FDA iCGM designation, builds both glucose sensors and insulin pumps, which may provide a more straightforward path to developing a truly automated insulin delivery system; the 780G system, which earned a CE mark in June 2020 and is available for purchase in Europe, integrates a glucose sensor and insulin pump to automate the delivery of both a basal dose of insulin and, as needed, correction doses every five minutes to keep people in a stable blood glucose range [16]. "The fact that they make both CGM and pump hardware is their major reason for still being in the market," Shah said.

As Abbott, Dexcom, and Medtronic keep competing to improve their glucose monitors, making them increasingly smaller and smarter, the companies are also working to develop ways to track additional molecules—including cardiac proteins and stress hormones—with wearable sensors. "The electronics, the form factor, the needle, all that stuff exists and can be leveraged for other analytes," Heikenfeld said.

"When we first introduced this technology, we knew that the FreeStyle Libre was not just a product," said Abbott's Harper, referring to the sensors' potential for monitoring biomolecules beyond glucose. "Rather, we knew it would really be a platform for future growth."

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