COMMENTARY

Advances in Subcutaneous Glucose Sensing

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CONTINUOUS GLUCOSE MONITORING has forever changed diabetes management. In the past year, the Dexcom G5 sensor was approved by the Food and Drug Administration to make diabetes-related treatment decisions, and the Medtronic 670G using the Guardian 3 sensor became the first hybrid closed-loop system to be commercially available in the United States.¹ The accompanying article² “Accuracy of a Fourth-Generation Subcutaneous Continuous Glucose Sensor” describes the design of the Guardian 3 sensor and accuracy results from a study of 88 subjects with type 1 or type 2 diabetes. The advanced sensor design includes an 80% reduction in implanted sensor volume, distribution of the working and counter electrodes across the sensor surface, focused application of enzyme over only the working electrode, and the use of electrochemical impedance spectroscopy (EIS) for fault detection.

Logically, a smaller sensor would be expected to cause less scarring, and indeed use of a smaller diameter has been shown to reduce fibrous capsule formation in animals.³ The distance over which the working and counter electrodes are distributed has been increased on the Guardian 3, which addresses subcutaneous tissue heterogeneity, such as differences in capillary density. Application of enzyme over only the working electrode functions to help reduce sensor delay by minimizing the distance that hydrogen peroxide (produced by the reaction of glucose with oxygen in the presence of glucose oxidase) needs to diffuse to reach the working electrode. In addition, the use of EIS enables the detection of the sensor being pulled out of the subcutaneous tissue.

This enhanced sensor design allowed for a mean absolute relative difference (MARD) of 9.1%–10.6% when calibrated every 12 h and 8.7%–9.6% when calibrated 3–4 times per day. The assessment of accuracy appropriately included evaluations across days 1, 3, and 7 after insertion and hyper- and hypoglycemic challenges. As seen with Guardian 3, accuracy on the same day as sensor insertion (day 1) has been historically lower than subsequent days likely because of transient bleeding and the inflammatory response to the small wound inflicted by sensor insertion.⁴ The data show that overall there were a limited number of serious accuracy errors exceeding 30 mg/dL for reference glucose values ≤ 80 mg/dL or exceeding 30% for glucose values > 80 mg/dL. Less than 1% of evaluation points were observed in Zone D or Zone E for either the Consensus error grid or Clarke error grid.

The results presented in the accompanying article demonstrate a significant improvement over earlier-generation Medtronic sensors.⁵ However, the accompanying article does not directly address compression artifact,⁶ which may occur when a person lies on the sensor site while sleeping, which could result in artificially low values or acetaminophen interference,⁷ which could result in artificially high values. Both providers and users should note that the Medtronic 670G user guide⁸ indicates that patients should not use the automated insulin delivery mode while taking acetaminophen, which is a concern given how commonly acetaminophen is used. It is also notable that accuracy results obtained during in-clinic assessments are far superior than those obtained during home use. A study by Kropff et al.⁹ reported for the Medtronic Paradigm Veo Enlite system an MARD of 16.6% in clinic as compared with 19.9% at home. Differences between in-clinic and home results may be related to suboptimal insertion or calibration technique.

The exciting results presented by Christiansen et al. demonstrate a substantial improvement of the Medtronic sensor technology. Depending on the sensor site and the frequency of calibration, the presented accuracy results meet or approach the MARD cut-off of 10% for nonadjunctive use proposed by Kovatchev et al.¹⁰ This advanced sensor is now available as a component of the long-awaited first commercially available hybrid closed-loop system. Future advancements are still required to reduce the burden associated with calibrating devices and to address the possible issue of acetaminophen interference.

Author Disclosure Statement

J.R.C. has a financial interest in Pacific Diabetes Technologies, Inc., a company that may have a commercial interest in the results of this type of research and technology. This potential conflict of interest has been reviewed and managed by Oregon Health and Science University. In addition, J.R.C. reports research support from Dexcom and Tandem Diabetes Care outside of the submitted work. The time for J.R.C. to prepare this article was supported by Grant No. 1DP3DK101044-01 from NIH/NIDDK. J.R.C. would like to thank Dr. Ken Ward of Pacific Diabetes Technologies for discussions on the topic of sensor design.

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