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ORIGINAL ARTICLE

Continuous Monitoring of Glucose in Subcutaneous Tissue Using Microfabricated Differential Affinity Sensors

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Abstract

Objective:

We describe miniaturized differential glucose sensors based on affinity binding between glucose and a synthetic polymer. The sensors possess excellent resistance to environmental disturbances and can potentially allow wireless measurements of glucose concentrations within interstitial fluid in subcutaneous tissue for long-term, stable continuous glucose monitoring (CGM).

Methods:

The sensors are constructed using microelectromechanical systems (MEMS) technology and exploit poly(N-hydroxyethyl acrylamide-*ran*-3-acrylamidophenylboronic acid) (PHEAA-*ran*-PAAPBA), a glucose-binding polymer with excellent specificity, reversibility, and stability. Two sensing approaches have been investigated, which respectively, use a pair of magnetically actuated diaphragms and perforated electrodes to differentially measure the glucose-binding-induced changes in the viscosity and permittivity of the PHEAA-*ran*-PAAPBA solution with respect to a reference, glucose-unresponsive polymer solution.

Results:

In vivo characterization of the MEMS affinity sensors were performed by controlling blood glucose concentrations of laboratory mice by exogenous glucose and insulin administration. The sensors experienced an 8–30 min initialization period after implantation and then closely tracked commercial capillary glucose meter readings with time lags ranging from 0–15 min during rapid glucose concentration changes. Clarke error grid plots obtained from sensor calibration suggest that, for the viscometric and dielectric sensors, respectively, approximately 95% (in the hyperglycemic range) and 84% (ranging from hypoglycemic to hyperglycemic glucose concentrations) of measurement points were clinically accurate, while 5% and 16% of the points were clinically acceptable.

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Abbreviations: (AC) alternating current, (CGM) continuous glucose monitoring, (IP) intraperitoneal, (ISF) interstitial fluid, (MEMS) microelectromechanical systems, (PAA) poly(acrylamide), (PAAPBA) poly(acrylamidophenylboronic acid), (PBS) phosphate-buffered saline, (PHEAA) poly(N-hydroxyethyl acrylamide), (PHEAA-*ran*-PAAPBA) poly(N-hydroxyethyl acrylamide-ran-3-acrylamidophenylboronic acid)

Keywords: animal experiment, capacitive detection, continuous glucose monitoring, dielectric sensor, differential measurement, viscometric sensor

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Abstract cont.

Conclusions:

The miniaturized MEMS sensors explore differential measurements of affinity glucose recognition. *In vivo* testing demonstrated excellent accuracy and stability, suggesting that the devices hold the potential to enable long-term and reliable CGM in clinical applications.

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