Proceeding Paper

Evaluation of a Continuous Blood Glucose Sensor's Performance for Hospitalized Patients †

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Abstract: Frequent blood glucose monitoring is crucial for managing blood glucose levels in critically ill hospitalized patients experiencing hyperglycemia or hypoglycemia. Existing blood glucose monitoring methods are often cumbersome, painful, and impractical for hourly testing. This work provides a solution for frequent glucose monitoring (less than 1 hour per test) for hospitalized patients, ensuring accuracy while minimizing discomfort from blood collection. The glucose sensor demonstrated accuracy within 10% across a range of 0-20 mM over 96 testing cycles. This meets the needs for hourly monitoring during an average 2-day hospital stay.

Keywords: Blood glucose; frequent monitoring; electrochemical glucose sensor; critical ill hospitalized patients; hyperosmolar hyperglycemia syndrome.

1. Introduction

Frequent blood glucose monitoring is crucial for managing blood glucose levels in critically ill hospitalized patients who experience hyperglycemia or hypoglycemia. Hyperosmolar hyperglycemic syndrome (HHS), an acute metabolic complication of diabetes mellitus, is often triggered by inadequate insulin therapy or infection. HHS is marked by high blood glucose levels, elevated serum osmolarity, and varying degrees of ketosis. Among the various therapeutic interventions for these patients, insulin therapy—particularly continuous intravenous (IV) insulin—is vital for achieving precise blood glucose control [1]. To optimize blood glucose regulation with continuous IV insulin, frequent blood glucose monitoring is essential [2].

Once continuous IV insulin is started, monitoring every hour is important, as dosage adjustments are based on these readings. The recommended target blood glucose level for critically ill patients is below 10 mmol/L, while for those with sepsis, the ideal range is between 7.8 mmol/L and 10 mmol/L. If a patient's blood glucose levels exceed 10 mmol/L in two consecutive readings monitoring should be conducted every 1-2 hours for the first 24 hours following admission [3-5].

Another group of patients who may need frequent blood glucose monitoring are those experiencing hypoglycemia (blood glucose < 4 mmol/L). Hospitalized patients might be at increased risk of hypoglycemia due to factors such as reduced caloric intake, poorly coordinated meal and medication schedules, or underlying health conditions [6]. When hypoglycemia is identified, rescue measures (such as oral glucose solutions or IV dextrose injections) will be administered, and blood glucose levels will need to be rechecked 15 minutes after these interventions. Rescue measures will be repeated as necessary until normal glucose levels are restored.

Current methods for blood glucose monitoring include venipuncture, arterial puncture, and bedside capillary blood collection. Samples from venipuncture or arterial

puncture can be analyzed using handheld glucometers, point-of-care testing (POCT) devices or sent to a central laboratory. These techniques generally yield more accurate results than capillary blood testing but involve repeated arterial punctures or the use of an invasive arterial line, and lab results can take longer to process. On the other hand, capillary blood testing can be less reliable in patients with conditions such as subcutaneous edema, shock, and hypoxemia, which are commonly encountered in ICU settings [4, 7]. Additionally, venipuncture, arterial puncture, and finger-pricking are not ideal for frequent monitoring due to the pain and skin alterations they cause, as well as the burden they place on nurses. This cumbersome process can lead to delays in glucose monitoring, affecting the timely adjustment of intravenous insulin, prompt rescue actions, and overall patient outcomes, making it impractical for frequent hourly monitoring. Additionally, recent advancements in glucose monitoring, such as wearable epidermal glucose sensors, have not yet been validated for use in critically ill patients.

Newer methods for continuous glucose monitoring measure glucose levels in interstitial fluid. However, there is a time lag of up to 20 minutes between glucose levels in the blood and interstitial fluid [8, 9]. Additionally, these methods are not clinically validated for use in critically ill patients, those on dialysis, pregnant individuals, and others [9].

To address the challenges of frequent blood glucose monitoring, a wearable blood glucose sensing system was developed. This system connects directly to the patient's intravenous (IV) cannula for automatic blood collection and glucose measurement. This setup allows for frequent, automated monitoring without causing additional discomfort to patients and simultaneously reduces the nurses' workload associated with blood collection procedures at every hour.

2. Design Overview and Fabrication

In this study, an enzyme-based glucose sensor has been combined with a fluidic system and circuit module for monitoring blood glucose levels. The fluidic system includes micropumps, microvalves, chemical reagents (such as saline and calibration solutions), and a waste compartment. The glucose sensor module is directly connected to the patient's existing IV cannula, enabling blood collection and glucose measurement at preprogrammed hourly intervals via the bi-directional pump module. The system is designed for automatic sensor self-calibration and cleaning after each test, ensuring measurement accuracy and enabling continuous use [11-15]. Compared to other blood glucose monitoring systems and research, this integrated sensor module offers a non-invasive, frequent venous blood monitoring solution. It eliminates the need for manual blood collection by nursing staff, reducing patient discomfort from repeated blood draws or finger pricking, while providing highly accurate and repeatable measurements suitable for critical care applications. Figure 1 illustrates a schematic of the blood glucose sensing module, which is designed to handle four key processes: sensor calibration, blood collection, glucose measurement, and system cleaning.

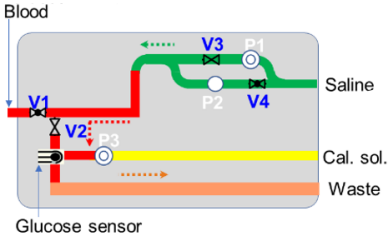

Figure 1. Schematic of blood glucose sensing module.

A commercial enzyme-based glucose sensor was chosen for its capability to provide continuous monitoring. The sensor was assembled with a polydimethylsiloxane (PDMS)-based fluidic channel on the top and a flat PDMS substrate on the bottom, creating a

sandwiched structure. Figure 2 depicts the fabrication and bonding process for the glucose sensing module. To manufacture the PDMS fluidic channel, a Teflon master mold was designed and produced, shaping the channel to accommodate a sensor sampling volume of 20 µL. PDMS was poured into the mold, and after curing for 24 hours at room temperature, the fluidic channel components were removed. Fluidic inlets and outlets were created by drilling into the PDMS channel. Both the top and bottom PDMS components were cleaned with isopropyl alcohol in an ultrasonic bath. The glucose sensor was then positioned on the PDMS fluidic channel components before plasma surface treatment. Following the treatment, the two PDMS components were aligned and bonded together using a sample bonding jig, with constant force applied uniformly. The assembled components were cured at 50°C for 12 hours and released from the bonding jig as shown in Figure 3. The glucose oxidase used in the glucose sensor maintains stable enzymatic activity at an accelerated temperature of 50°C for at least 4 months [16].

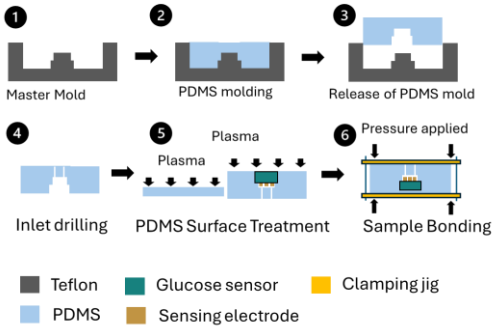

Figure 2. Fabrication and bonding process for glucose sensing module.

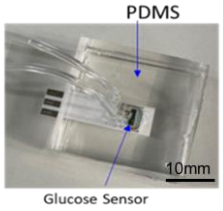

Figure 3. Assembled glucose sensing module.

3. Experimental Result and Discussion

After curing, the assembled samples (Figure 3) were subjected to fluidic leakage testing. A continuous flow of dyed fluid was injected into the assembled glucose sensing samples for one hour. Five samples were examined for leakage from the bonding interface, cracks in the PDMS components, and fluid flow issues. No abnormalities, fluid leakage, or blockages were detected. Consequently, the samples passed the fluidic leakage test and proceeded to further benchtop characterization.

Next, the glucose sensing module undergoes benchtop characterization. It has been validated to detect glucose concentrations ranging from 0 to 20 mM with a sensing volume of 20 µL. The current output corresponding to glucose concentration was measured. Each sensor was tested in 4 cycles to validate repeatability. The average current output, with a repeatability error of 7.2%, was recorded, consistent with other studies where the average current output typically falls within the nanoampere to microampere range [17]. This falls within the target acceptance criteria of ±10% when compared to the standard of commercial glucometers. Specifically, the criteria are 95% confidence level within ±12% for glucose levels greater than 4.17 mM, and within ±0.67 mM for glucose levels below 4.17 mM [18].

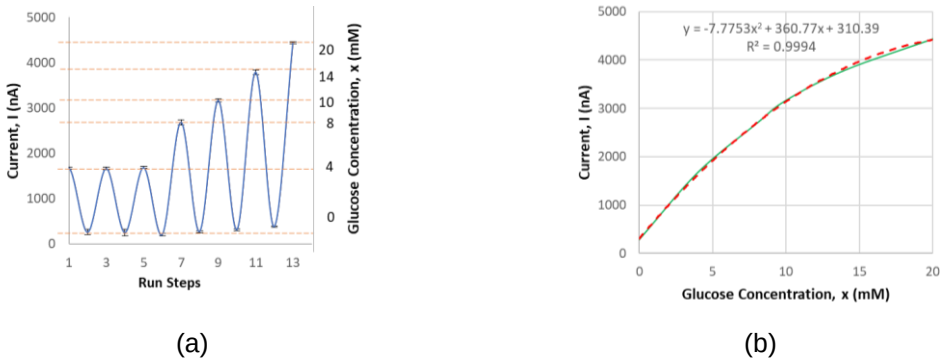

Figure 4. Glucose sensor benchtop characterization result (**a**) Current output related to glucose concentration based on the testing procedure steps; (**b**) Average current output Vs concentration.

The glucose sensor was further assessed for its durability and suitability for frequent monitoring. It has been observed that the sensor can endure 96 tests with a maximum repeatability error of 7.1% at a 14 mM glucose concentration, which is within the acceptable criterion of 10%. This performance meets the requirements for frequent monitoring, with up to one test per hour over an average hospital stay of 2 days.

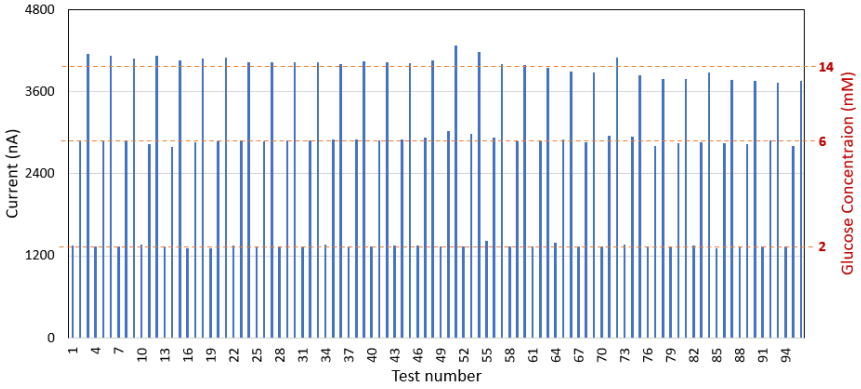

Figure 5. Glucose sensor durability testing result.

4. Conclusions

In this study, the enzyme-based glucose sensor was enclosed with a PDMS fluidic channel on top and a flat substrate. The assembled device was tested for fluid leakage during a 1-hour infusion, with no leaks detected. Additionally, the glucose sensing module was evaluated for its sensing range, repeatability, and durability for frequent use. It successfully detected glucose concentrations ranging from 0 to 20 mM, withstood 96 testing cycles, and maintained an accuracy within 10%, which meets the standard accuracy requirements for glucometers. These results satisfy the minimum criteria for blood glucose monitoring, allowing for a 1-hour test interval during a 2-day hospital stay.

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Conflicts of Interest: The authors declare no conflicts of interest.

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