Minimally Invasive Glucose Sensing Device

Medina Alogba, Kyran Gibson, Mike Mistretta, Alex Paskal, Cynthia Uzoukwu

Advisor(s): Dr. Edward Eisenstein, Fischell Department of Bioengineering, University of Maryland, Dr. Johana Diaz, University of Maryland School of Medicine

Motivation

It is estimated that **~15 million** babies are born preterm. Preterm birth complications are the **leading cause of death** in children under the age of 5. There are degrees of severity of preterm birth depending on the amount of gestation, which ranges from extremely preterm: < 28 weeks, very preterm: 28-32 weeks, and moderate to late preterm: 32-37 weeks

Series of tests are performed on infants in the NICU to varying degrees which depend on the severity of their preterm birth. One tests performed consistently on infants in the NICU is the **blood glucose test**, blood is obtained from the infants via heel pricks or arterial lines in order to measure their glucose level.

Neonates are faced with potential issues such as **anemia due to immense drawing of blood** and **abnormal gate when the infants begin to walk** as a result of the pain from heel pricking. Heel pricks have been observed to cause swelling, redness, neonatal staphylococcal, and inguinal adenitis.

Objective

The project goal is to create a minimally-invasive medical device that can be used to measure blood glucose concentration using interstitial fluid. This device is a necessity in the neonatal intensive care unit (NICU) as the device will be able to:

- **Decrease amount of blood drawn** from neonates to reduce instances of anemia
- **Reduce use of heel pricking** to decrease amounts of infection and possible abnormal gaits when the infants begin walking

Additionally we hope that future work can help to reduce the amount of leads that are placed on neonattes which can cause discomfort for both neonates and nurses.

Methods

Concept Design

Concept Choice → Market Research → Preliminary Brainstorming → CAD Design → Proof of Concept & Prototype Planning

Proof of Concept

- Hollow microneedles have been empirically demonstrated to be collecting a sufficient quantity (>2μL) of interstitial fluid for glucose strip saturation over a clinically acceptable period (<30s)

Prototype Design

- **SolidWorks** was used to create the sampling component and microneedle patch
- The prototype was printed using **PLA** material on the **FDM 3D printing machine**
- Microneedle patch to be 3D-printed using **NanoScribe** 3D printer

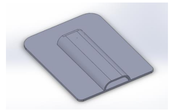
Prototype Testing

- Powdered glucose was incubated in 8 varying concentrations of 2 mmol to 20 mml for a period of 2 weeks prior to testing
- Glucose strips were saturated with the various concentrations and **Rodeostat potentiostat** was used to apply a voltage to the electrodes on the glucose strips to **induce current**
- Triplicate measurements of current vs. time were collected for each glucose concentration
- Current at time t=4s was extrapolated for each glucose concentration, to create a **look-up table for calibration** of the analytical component of the device

Results

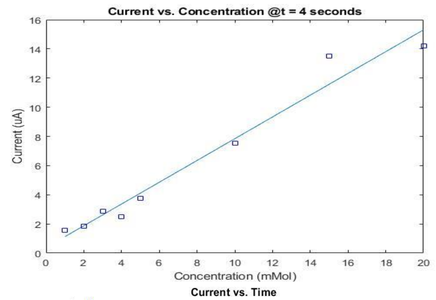
Sampling Component

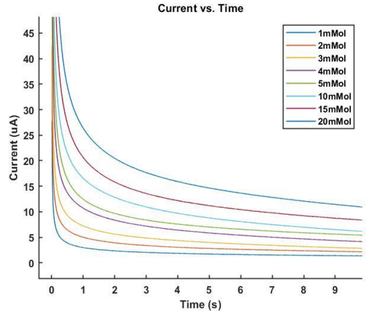
- Sampling component FEA proved difficult in SolidWorks
- Material would be changed to an FDA approved medical device material



Analytical Component

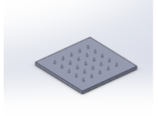
A linear regression was performed at time t = 4 to estimate a function relating current and concentration. This linear relationship allows us to estimate the concentration of glucose corresponding to a measured current.



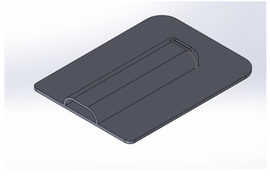


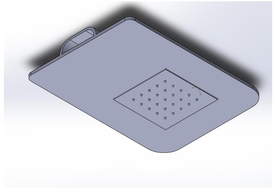
Microneedle

- Difficulties in printing abilities of Terrapin Works
- FEA of CAD was used to prove the feasibility of the patch
- Future work consists of new printing strategy



Finished Prototype Design





Ethical Implications

Neonatal safety and comfort were of top priority when designing the sampling component and microneedle patch. During the design process, these ethical criteria were considered:

- Material constraints to minimize any possible negative impacts on the neonate's health or comfort
- Materials considered are bioinert or biocompatible
- Whether nurses and doctors would be positively affected by our device by being able to conduct tests in a timely manner
- Parents would be able to watch their baby undergo a less invasive method of testing
- No person (neonate, nurse, doctor) could undergo any significant risk from our device

Future Work & Conclusion

Microneedle

- The microneedle patch ideally will be 3D printed for performance efficiency using the polymer **PEEK** due to its chemical inertness and biocompatibility. However, constraints such as price, printability and manufacturing time may require us to make use of other materials such as PLA, PLGA, or silicon
- Remaining design criteria and constraints will be considered to **optimize flow through the microneedles**

Collection Component

- To prevent any form of accident that may occur, we are suggesting that the sampling component, should be printed using the **M6000 printer Stratasys Object 500 with a printing material Connex3**
- A biocompatible adhesive, **Cyberbond 5000**, will be used to adhere the microneedle patch to the sampling component. This adhesive is commonly used for medical devices and is provided by the company H.B. Fuller
- Experiments determining collection capacity will be performed

Point-of-Care

The major impact this device can lead to is it potential to be used to **analyze other analytes found in interstitial fluid**. Its application can be a foundation to create a **point-of-care glucose measuring device** in not only neonates but children ranging two years old and younger as it may be used to diagnose hyperglycemia and hypoglycemia similar to an adult glucose meter.

Conclusion

Glucose concentrations within the clinically relevant range (5-10 mmol) can be measured accurately and reliably using chronoamperometric methods in conjunction with standard glucose strips saturated with glucose water. Provided hollow microneedles can be reliably and affordably manufactured and can produce sufficient volume of ISF, the ease of fabrication and convenience of our device makes it an excellent alternative to existing minimally-invasive and non-invasive glucose monitoring devices.

References

1. Katzer, A., Marquardt, H., Westendorf, J., Wening, J., & Von Foerster, G. (2002). Polyetheretherketone—cytotoxicity and mutagenicity in vitro. *Biomaterials, 23*(8), 1749-1759. doi:10.1016/S0142-9612(01)00300-3
2. Kurtz, S. M., & Devine, J. N. (2007). PEEK biomaterials in trauma, orthopedic, and spinal implants. *Biomaterials*, *28*(32), 4845–4869. doi:10.1016/j.biomaterials.2007.07.013
3. Waghule, T., Singhvi, G., & Dubey, S. (2018, November 09). Microneedles: A smart approach and increasing potential for transdermal drug delivery system. Retrieved from https://www.sciencedirect.com/science/article/pii/S0753332218348091
4. Wenz, L., Merritt, K., Brown, S., Moet, A., & Steffee, A. (1990). In vitro biocompatibility of polyetheretherketone and polysulfone composites. *Journal of Biomedical Materials Research, 24*(2), 207-15.