Midterm Report Fall 2004
IPRO 331: Non-invasive Blood Glucose Monitoring

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Revised Objectives:

The objective of this Interprofessional Project is to develop a Non-Invasive blood glucose monitoring technique. Currently, invasive techniques such as venepuncture are being used to monitor blood glucose levels in patients. Unfortunately, because diabetics must constantly monitor their blood sugar level venepuncture is a very undesirable procedure because it requires multiple needle punctures a day. It is no surprise that this process is uncomfortable for the patient and therefore a better solution must be developed.

Over the course of the semester we split up into different groups. Each group researched topics that were necessary for developing a non-invasive technique. These topics included determining skin permeability, ionic properties of glucose, iontophoresis and impedance as methods of measuring glucose concentration. Through these research groups we mapped out areas which will help us in developing a non-invasive method. We have decided to use ultrasonic energy and a two-way vacuum to extract the interstitial fluid, and then the glucose concentration would be determined using impedance. The results of each area and group are shown below:

Results to Date:

Vacuum

The 'vacuum' group looked into non-invasive methods of extracting interstitial fluid from the body. Interstitial fluid can be removed non-invasively, and the concentration of glucose in interstitial fluid can be correlated with that of the blood, it can therefore serve as a substitute to blood. They looked into various methods such as ultrasound, and iontophoresis.

Iontophoresis

Iontophoresis is a procedure that requires a small electrical current to be sent through the skin. The drawbacks of this process include long duration of measurement time and cracking of the skin in the treated area. Most patients reported a tingling sensation and mild pain especially at the beginning of the treatments. Weighing the setbacks of this

method, the group agreed on using an alternate technique to pull interstitial fluid from the skin. Therefore we decided to choose ultrasound.

Ultrasound

Ultrasonic energy applied on the skin disorganizes the lipid-bilayer of the stratum corneum, and creates reversible microchannels in the skin through which fluids and analytes can be extracted and large molecules delivered. The transport permeability of the skin increases 100 fold after ultrasonic skin permeation. The skin is then left permeable for approximately 15 hours. Ultrasound thus presents a non-invasive way of obtaining interstitial fluid.

The next issue to address was how to draw up the interstitial fluid above skin level. Since interstitial fluid comes up via the microchannels created by the ultrasound, we decided to use a vacuum to draw it up.

An airtight seal would be formed on the skin. There will be an internal piston within the device that will be controlled by a button. Once activated it will cause the piston to draw back, thus increasing the volume and reducing the pressure in the sealed space. This will cause the interstitial fluid (ISF) to be drawn out of the microchannels and fill the space within the sealed area. The ISF will be directed in a collection device for glucose measurement.

The previous IPRO group determined that residual sweat on the skin interferes with accurate glucose measurement. The issue of getting rid of the residual sweat on the skin was addressed by researching the following methods:

a) Evaporating the water from sweat
b) Reacting the salt with some agents and then evaporating the water
c) Using alcohol rub to remove the sweat
d) Vacuum- to pull up both sweat and interstitial fluid.

After researching the above options, the team decided that the best solution would be to use the vacuum to pull both the sweat and interstitial fluid through the skin. The concept was to use pressure to pull up the sweat first, and then apply greater pressure to pull up the interstitial fluid.

Self-Cleaning Sensors

After deciding to use the vacuum option the next step was to determine how to clean out the vacuum chamber after a sample was taken. As a result, the group looked into cleaning the vacuum chamber through self-cleaning sensors. Self-cleaning sensors are produced by the company TOTO. They are working on a film made of titanium oxide (TiO_2) which oxidizes organic compounds when illuminated with UV light. Another great feature of the titanium oxide film is that it is super hydrophilic. This means that when water is added to the TiO_2 and it is exposed to UV light, the water spreads to form a very thin layer because of its high affinity for water. If a contaminant is present on the surface of

the TiO_2, and water and UV are added, the water replaces the contaminants' positions on the film and the contaminants are oxidized. There is no need for detergents to clean the film.

Determining Glucose Concentration

Impedance Spectroscopy

The last step in the process is to measure the glucose concentration. Various methods of measuring glucose concentration were researched such as Near Infrared Spectroscopy (NIR), Far Infrared Spectroscopy (FIR), and impedance spectroscopy. It was determined that dielectric impedance spectroscopy is the most favorable.

Radio wave impedance spectroscopy measures how changes in blood composition affect the impedance pattern of the skin and underlying tissue. The device itself is the size of a wrist watch and is fixed with an open resonant circuit which lies against the skin. This circuit performs the impedance measurement. The device is optimized to measure the affects of glucose molecules on the impedance pattern, these measurements are then calculated into glucose concentrations. In turn indirectly monitors the changes in blood glucose.

The components for a device using this technology will be inexpensive because they will be off-the-shelf and not custom-miniaturized versions of bench-top equipment.
There are some problems that could arise using this technology. First, impedance is also affected by factors other than glucose, which must be accounted for to determine the relationship between impedance and blood glucose concentration. These factors include the concentration of electrolytes in the blood, finger width, and body temperature. Second, an inexpensive disposable finger clip may be necessary to conduct the radio waves.

Updated Assignments/ Revised Calendar:

Week #	Tuesday	Thursday
1	Introduction	Background Lecture
2	Background Lecture	Brainstorming
3	Work in Groups	Work in Groups
4	Work in Groups	Work in Groups
5	Work in Groups	Work in Groups
6	Work in Groups	Work in Groups
7	Work in Groups	Work in Groups
8	Work in Groups	Work in Groups
9	Work in Groups	Work in Groups
10	Work in Groups	Fall Break
11	Work in Groups	Work in Groups
12	Work in Groups	Work in Groups
13	Work in Groups	Work in Groups

14	Prepare for Presentation	Prepare for Presentation
15	Prepare for Presentation	Prepare for Presentation
16	Finish Final Report	Finish Final Report

For the remaining portion of the semester, the group aims to develop a prototype by bringing together various components of the research that has been completed. In addition to developing a prototype, the team will be preparing for the presentation, poster session, and website development for IPRO Day.

Website: Brogan Dexter and Jon Young
Design: Adeseye Adekeye, Sangeeta Bookseller, Jude Kieltyka
Aesthetics: Chad Nishizuka, Daisy Rathod, Shivani Shah, Anupama Topgi

Barriers/Obstacles:

We could face obstacles using impedance to measure glucose concentration due to the electrolytes and other components of the interstitial fluid. Another barrier is that we need financial support to make the prototype a reality.