**Spring 2005 MIDTERM PROGRESS REPORT**

**IPRO-331 Non-Invasive Blood Glucose Monitoring System**

**Professor:** Dr. Emmanuel Opara  
**Consultants:** Ray DeBoth

**TEAM MEMBERS:**  
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Ben Freemire  
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Prabhav Patil  
Vidya Shivakumar  
Yio-Fan (Deborah) Hsu  
Jude Kieltyka  
Stephen Mullins  
Veeral Oza  
Quratulann (Annie) Riaz  
Daniel Young

**REVISED OBJECTIVES:**

Our IPRO project is a continuation of the previous IPRO Fall 2004 team’s work. The main components of the original design have remained the same in which ultrasound is applied to disrupt the bio-lipid layer and reverse iontophoresis is applied to extract interstitial fluid. This is followed by suction of the fluid via a vacuum and measuring of glucose concentration in interstitial fluid using electrical impedance. While keeping the comfort of the patient in mind, this IPRO team has decided to improve the previous design by possibly adding heat to facilitate the extraction of interstitial fluid. Conjointly, unification of insulin delivery with this device will be investigated. Furthermore, it is the goal of this IPRO project to develop a prototype which integrates the various components into a single unit and apply for a patent for our device.

**RESULTS TO DATE:**

1. **Ultrasound**

We have decided to utilize the ultrasound technique to increase the permeability of the skin and facilitate the extraction of interstitial fluid. Ultrasound disrupts the lipid-bilayer of the stratus corneum (outermost layer of skin which has the most barrier properties) and creates microchannels where ISF can be extracted. (See Figure 1.)

![Image of ultrasound disrupting stratus corneum](image-url)  

Figure 1. Picture of how ultrasound disrupts the stratus corneum.
After researching various papers on experiments regarding the usage of ultrasound to extract interstitial fluid, the effects of this technique were:

1. **Low** frequency ultrasound (~20 kHz) increased the permeability of the skin by many orders of magnitude, much better than high frequency ultrasound

2. Ultrasound treatment at 20 kHz with intensity of 7W/cm\(^2\) for less than 1 minute increased skin permeability for up to 15 hrs.

2. No pain associated with the procedure

3. No damage to the skin

4. However, further studies assessing safety of ultrasound after repeated extractions are still required

5. Low vacuum strength for ~5 minutes needed to extract small amount of ISF

7. The use of ultrasound may slightly heat tissue

8. Studies showed that same low frequency ultrasound at 20 kHz can be used to deliver insulin (sonophoresis)

9. Power supply will be in the form of batteries, and a transducer and amplifier are needed ($25-$100).

2. **Iontophoresis and Reverse-Iontophoresis**

We did research on the mechanism involved in iontophoresis to determine if delivering insulin would be viable using this mechanism. Reverse-iontophoresis was studied in detail for the team to understand the mechanism involved, which can facilitate in making a prototype. Reverse-iontophoresis is used to extract interstitial fluid by applying a small electric current to transport charged and polar, neutral compounds across the skin. It was also determined that presence of sodium chloride is necessary in order to transport fluid out of the skin. In our research, we discovered that the initial extraction sample contains mostly information about the local reservoir, and a warm-up period is necessary before the interstitial fluid readings may be reflective of systemic levels. The proposed price range for an iontophoresis machine is about $850.

3. **Prototype**

We are making a prototype which can simulate the project design. In the device, a small speaker is used to provide ultrasound waves to disrupt the bio-lipid layer and a charge is applied. This is combined with a heated suction cup and a vacuum to extract the interstitial fluid. This should be followed by electrical impedance for glucose reading. Our progress so far is that we have
purchased a speaker and have combined it with the suction cup. A vacuum has been obtained which is connected to the cup to draw up interstitial fluid. Our prototype team is working diligently to find a way to apply a current to simulate reverse-iontophoresis and integrating all the components above mentioned into a single, workable unit.

4. Proposals and Sponsorship

Our IPRO predecessors faced some serious limitations due to lack of proper funding. Although the IPRO office does provide a limited amount of money, it is simply not enough for the goals and research objectives of our IPRO. We have decided to approach private and government institutions and market our idea of non-invasive blood glucose monitor in an attempt to receive grants. For instance, we have divided ourselves into groups of two and each group is pursuing one or two organizations and will be writing up grant proposals. Some organizations that are being targeted by our team include National Institutes of Health, National Science Foundation, Mini-Med, Genzyme, Bank of America, and American Diabetics Association.

5. Patent Research

Last semester our IPRO performed a patent disclosure, and we have decided to take it further and submit a patent (pending university approval). As we pursue our objectives, team members often come up with innovative ideas that are non-existent in the world today. Careful note is made of such ideas and included in the design of our final prototype. Concurrently, we plan to include such ideas into our patent disclosure and submit to the university for approval. Dr. Gottlieb has been of great assistance in helping us with this aspect of our IPRO. We further plan to approach Chicago Kent School of Law and request them for assistance with this objective.

6. Website

Our IPRO website has been initiated and is currently being updated. The website so far has a small JAVA based game, team pictures, background on the IPRO, and a Flash animation of what our final product will look like. Information regarding team members, diabetes, and our resources will also be added towards creation of the final website.

7. Jet-injectors

Another interesting aspect that we looked into was perhaps delivering insulin depending on the level of blood glucose. In order to study this possibility, we did a preliminary search on the different methods to successfully achieve this goal. Some companies have designed insulin-delivery systems which use a process known as jet-injection. Jet injection is a process which employs a jet injector to administer a high-pressure stream of medication. This method causes very little pain and affords great accuracy, ease of administration, and safety. The medication is more widely diffused in the body by jet injection than by the needle-and-syringe technique.
**REVISED TASK/EVENT SCHEDULE:**

<table>
<thead>
<tr>
<th>WEEK OF</th>
<th>TASKS</th>
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| 1/17    | o Introductions  
o Review of last semester’s work |
| 1/24    | o Dr. Opara’s lecture on diabetes  
o Set up group webpage |
| 1/31    | o iKNOW presentation  
o Split tasks into groups  
o Lecture on patents by Dr. Gottlieb |
| 2/7     | o Look into insulin delivery  
o Look into impedance spectroscopy frequencies |
| 2/14    | o Determine exact vacuum pressure for drawing up interstitial fluid and sweat  
o Work on prototype |
| 2/21    | o Study problems related to reverse iontophoresis  
o Determine ultrasound frequency and intensity needed to extract interstitial fluid |
| 2/28    | o Start work on website  
o Start work on prototype |
| 3/7     | o Look into sponsorships  
o Work on portfolio to present to companies |
| 3/14    | o Work on research project  
o Work on Midterm Report |
| 3/21    | o Look into patents  
o Submit midterm report |
| 3/28    | o Improve prototype  
o Look into sponsorships/grants |
| 4/04    | o Work on remaining drawbacks of prototype and interstitial fluid and sweat suction methods |
| 4/11    | o Work on poster  
o Work on abstract |
<table>
<thead>
<tr>
<th>Date</th>
<th>Task</th>
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<tbody>
<tr>
<td>4/18</td>
<td>- Work on IPRO presentation.</td>
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<tr>
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<td>- Work on final report</td>
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<tr>
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<td>- Submit abstract</td>
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<tr>
<td>4/29</td>
<td>- IPRO DAY</td>
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<tr>
<td>5/6</td>
<td>- Turn in Final Report and Comprehensive Deliverables CD</td>
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**UPDATED ASSIGNMENTS:**

**Website group**  
Stephen Mullins  
Daniel Young

**One-page Abstract**  
Veeral Oza  
Wadzanayi Maketiwa

**Comprehensive Deliverables CD**  
Stephen Mullins  
Daniel Young

**Sponsorship**  
whole team

**Midterm Report**  
Yio-Fan (Deborah) Hsu  
Quratulann (Annie) Riaz  
Veeral Oza

**Device Design**  
Yio-Fan (Deborah) Hsu  
Prabhav Patil  
Quratulann (Annie) Riaz  
Vidya Shivakumar

**Patent Work**  
Leland Barnard  
Daniel Young  
Stephen Mullins

**Prototype**  
Ben Freemire  
Wadzanayi (Wadzi) Maketiwa  
Daniel Young  
Leland Barnard
**Research**
Jude Kieltyka
Mehjabeen (Maje) Nazim
Veerai Oza
Quratulann (Annie) Riaz

**Project Plan Report**
Yio-Fan (Deborah) Hsu
Wadzanayi (Wadzi) Maketiwa
Mehjabeen (Maje) Nazim

**Oral Presentation**
Jude Kieltyka
Veerai Oza
Prabhav Patil

**Team Leader**
Jude Kieltyka

**Team Minutes**
Mehjabeen (Maje) Nazim

**Team Poster**
Leland Barnard
Vidya Shivakumar

**Final Report**
Leland Barnard
Ben Freemire
Vidya Shivakumar

**BARRIERS/OBSTACLES:**

The major obstacle encountered is that we currently have a limited amount of funding, but we are working on obtaining grants from various institutions for financial support. In addition, the integration of the prototype to incorporate ultrasound and iontophoresis will be difficult. Time constraints and the availability of lab space to test the prototype are also obstacles that need to be overcome.