



**Final Report**

Group 201-16

Neil Jikaria

Zheng Lin

Lavanya Madhusudan

Alyssa Rosenzweig

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## Executive Summary

One of the most pressing consequences of the worldwide “plague” of obesity is prediabetes. Prediabetes is the condition experienced by patients who are highly susceptible to type 2 diabetes. If not addressed immediately, it can develop into type 2 diabetes, an illness with many undesired complications, ultimately leading to a lower quality of life or, at worst, a premature death. To combat this problem, we at DiaCure have developed the precise device that the world needs right now: The DiaBeater. Its functionalities will help improve the health of millions of prediabetics and delay the onset of type 2 diabetes.

The DiaBeater will measure blood glucose concentration, count calories burned during exercise and daily activities, record calories consumed, and administer a pancreatic Beta-cell enhancing drug using a wristwatch-like platform with an interactive, holographic interface. All of these features can be tailored to the individual patient’s needs and are easily managed. One common platform contains all of these specifications, with the variation of the method of glucose measurement. Three alternatives for measuring blood glucose will be discussed in the following pages (tympanic, optical coherence tomography, and ultrasound technology).

It has already been determined—using a unique prioritization system developed specifically for this problem—that the ultrasound technology is the best method. Initial results from proof of concept trials support this decision, but more testing and research will still need to be done in the future. A two-year research plan is included for the product development needed to bring this incredible device to the market, provided, of course, that the proper funding is supplied by generous donors.

Although not the largest by numbers, adolescents are the most important subset of this sizeable prediabetic population. The overlying goal of the DiaBeater is to initiate lifestyle changes, so we hope to prevent the disease in the earlier stages of life and educate as early as possible. They are a technology-savvy generation, and would be the most appropriate group to learn and use a new device.

Products on the market now do not specifically address the concerns of a prediabetic. Many will help with one aspect of the disease prevention, but none combine all the aspects into one coherent device like the DiaBeater does. The ultrasound technology used in the DiaBeater is extremely versatile, in that it can detect and administer a practically endless list of substances. It therefore has the power to benefit *every* person because universal substances (such as daily vitamins or short-term prescriptions) could be administered and detected (such as cholesterol levels). If successfully advertised and implemented, the technology of the DiaBeater could become the basis for a health aid that the whole world uses. Keep in mind that diabetes contributes a heavy monetary burden on many governments and societies, so prevention of it and improvement upon the overall health of users (and potential users of a modified version of the device) will lower health insurance costs for the individual and the proportion of the country’s spending on it.

Funding the DiaCure DiaBeater will be a wise investment choice. The investor has a huge potential for profit because the number of individuals the technology could potentially reach is significant, and none of the current options available for treatment of the prediabetes are as comprehensive and effective as this new device we propose to you in the following pages.

## I. Statement of the Problem

Prediabetes (also known as impaired glucose tolerance, impaired fasting glucose, and pre-clinical diabetes) is the precursor to diabetes. It has been shown that the best way to prevent the onset of type 2 diabetes is to follow a healthy meal plan, lose weight, and increase exercise (Diabetes Prevention Program). The prevention of diabetes is key, since over time, especially if blood sugar levels are not kept in check, diabetes can boost a person's risk of heart disease (cardiovascular disease), blindness (retinopathy), nerve damage (neuropathy), and kidney damage (nephropathy). According to the National Diabetes Fact Sheet, diabetes is the sixth leading cause of death in Americans (ADA). Based on studies conducted by National Diabetes Information Clearinghouse people with prediabetes tend to develop diabetes within 10 years unless they make lifestyle changes (NDIC). An important thing to note is that there are no apparent physical symptoms to prediabetes; one may have the condition for several years without noticing anything. Nevertheless, it is fairly easy to prevent prediabetes from evolving into more severe diabetes. The Diabetes Prevention Program study has found that people with prediabetes that walked or did other exercise for a half-hour at least five times a week and lost 5 to 7 percent of their total weight, cut their risk of developing full-fledged diabetes by nearly 60 percent. Therefore, educating people at risk is critical in reducing the chance of developing the disease.

In addition to the physical suffering of patients, diabetes related diseases also drained an enormous amount of our national wealth. In 2002, a report from National Institutes of Health and the Centers for Disease Control and Prevention has estimated that the total cost of diabetes in the US was as much as \$132 billion, or one out of every 10 health care dollars spent in the United States. According to the statistics provided by the American Diabetes Association, there are 13 million people in the United States, or 4.5% of the population, who already have been diagnosed with diabetes, with another estimated 5.2 million people (or nearly one-third) who are still unaware that they have the disease. However, this figure is not even including 41 million Americans who have prediabetes. Most disturbing of all, the complete cure for diabetes has not yet been found, so taking preventative measures before the actual onset of the disease is crucial in preventing diabetes (DPP).

Despite the potential problems posed by prediabetes, the most diabetic-related products currently on the market are only for treating diabetes, making it all the more necessary to design a device to assist people with prediabetes.

Since our device is the first of its kind, there aren't really any devices that are available currently that are directly comparable to the DiaBeater. The delivery aspect of our device can be compared to that of the insulin pump. It delivers a steady trickle of insulin, continuously to the patient's body throughout the day. One must keep in mind that insulin pumps are similar in one aspect of the function of the DiaBeater, but are meant for diabetics, not prediabetics. Our device, in order to prevent the patient from having to resort to the use of an insulin pump, serves to employ a new method of treatment specifically for prediabetics. A new type of medication is administered to the prediabetic instead of insulin. This new type of drug is called Thiazolidinedione (TZD), which functions by improving the way cells in the body respond to insulin by lowering their insulin resistance. In contrast, other diabetic medications, which just cause the pancreas to produce more insulin to compensate for the effect of cellular insulin

resistance, will provide no help at all in retaining the Beta-cell mass. In this case, TZD not only repairs the metabolic defects of insulin resistance and insulin deficiency, but also potentially preserves B-cell function and, therefore, prevents diabetes

In addition, the traditional ways of administering drugs like insulin also have been replaced by a more convenient and noninvasive method in the DiaBeater. Based on the severity, many people have to take insulin to control their blood sugar. However, insulin cannot be taken by mouth because it would be destroyed by digestion. Instead, most of the traditional method requires insulin to be delivered by injection through the skin and into the fatty tissue below. Hence, today's most common methods of drug delivering include injection, insulin pumps, insulin pens, and insulin jet injector. Insulin injection, insulin pump, and insulin pen all involved using a very fine needle to deliver insulin by breaking the outer layer of patient's skin, while jet injector is using high pressure air to send a fine spray of insulin through the skin. However, all of these traditional methods are either physically intrusive to human bodies, or are very difficult to maintain, such as you have to boil and sterilize the units of jet injector frequently. Therefore, a noninvasive, more reliable and user-friendly delivering method has been developed by our company to deliver TZD through the patient's skin. This method uses ultrasonic vibration to open up the pores on the skin and then allows the TZD or other type of drug to diffuse across the skin and be absorbed by the capillaries (Maione, 2002).

Additionally, the same method **is** used for detecting the blood glucose concentration, a method far more advanced than any that are currently in use. This method functions by allowing interstitial fluid to rise through the pore openings to the skin surface and, upon using certain chemical reactions within the device, the concentration of glucose would be computed (see Product Design below). Most important of all, when comparing to the other methods, the ultrasonic technology has proved to be extremely reliable, noninvasive, painless, and have minimal side effects (Malchoff, 2002). Bloomgarden, 2005).

Another aspect of our device is the calorie counting function, which can be compared to devices that are currently on the market, such as the Polar Heart Rate Monitors. By measuring the patient's heart rate during exercise, the Polar devices can measure the number of calories expended during exercise. That is the extent of the capabilities of the technology available today. The DiaBeater, however, will not only measure the amount of calories expended, but it will incorporate a computerized tracking system within our device to keep track of patient's total calorie intake by analyzing the different types of food that users have consumed and the total calories burned. From the data collected, our device will generate advice to users about a healthier diet or proper amount of exercise.

## II. Product Design

Our product takes a different approach to treating prediabetics. The overlying theme of the DiaBeater is to have the patients use it as a learning tool, so they can make the necessary lifestyle changes and prevent diabetes by being educated. The DiaBeater is unique in this aspect; it attempts to address a condition not only by

treatment, but by education, which is fundamental to the prevention and cure of any disease. To facilitate this, we had several design goals in mind for the DiaBeater.

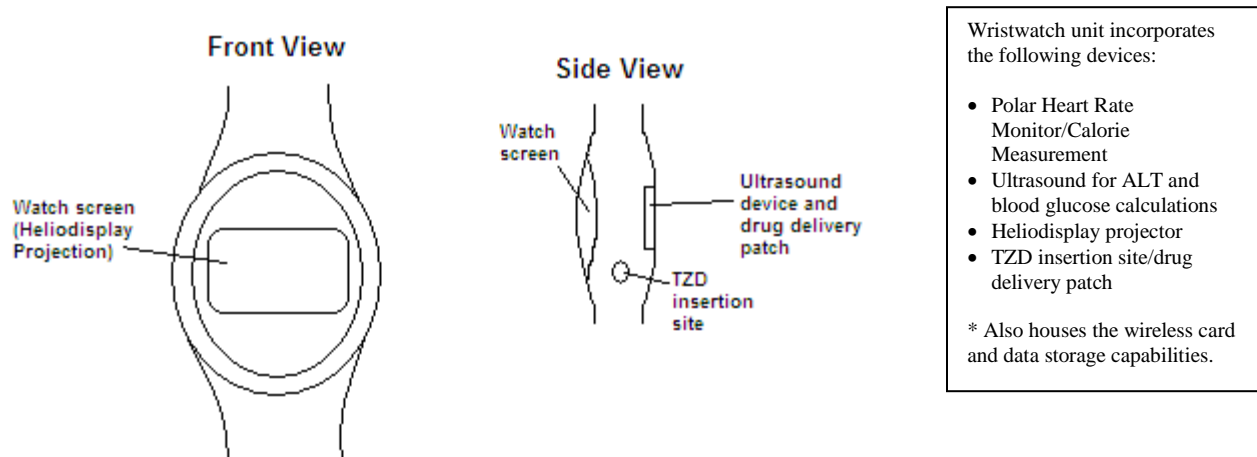
Our device had to include a blood glucose monitor, a calorie measurement device, a drug for prediabetics, and a way to administer it. We also wanted to make sure that our device was completely external; surgery was not something that we wanted to our prediabetic adolescent patients to deal with. Since our device is specifically targeted towards adolescents, it had to be minimally invasive, easy to use, safe, durable, and appealing to our target age group.

For our device specifications, we established that it had to be within the following limits:

- Dimensions within: .5 in L x 2 in W x 2 in D
- Withstand a force of 1250 N (275 lb)
- Function in the range of 40 F – 120 F
- Waterproof
- Watertight
- Internal power by lithium watch battery
- Cartridge capacity: One month's dose of TZD/ALT enzyme
- Monitor Blood glucose ranges from 40 mg/dL to 400 mg/dL
- Monitor ALT levels in the blood from 20 IU/L to 100 IU/L
- Real time blood glucose monitoring – every 1 second
- Based on user input, will provide analysis of meals (calories) in comparison to predetermined diet specifications
- Connectivity to external devices (Computers, Cell phone, PDA, etc.)
- Measures calories both while at rest and during activity through heart rate monitor
- Color, holographic display
- Weight: 2 oz – 5 oz.
- Can store up to six months worth of collected data
- Transcutaneous infusion set
- Material: plastic(impact resistant) and electrical components
- Shockproof (static electricity)
- Vibration mode, different sound levels (privacy/courtesy)

To incorporate these design goals and specifications into our device, we chose to use the wristwatch as our device interface (see **Figure 1**). The wristwatch is an extremely convenient and compact module to house all of the components of the DiaBeater.

**Figure 1 - 'Wristwatch' device platform**



Based upon the design goals mentioned above, there are several mechanisms that all of the device alternatives would have in common. These mechanisms are listed here in order of importance, and we will elaborate on how each mechanism functions.

First and foremost is the blood glucose monitor. This is the fundamental component of the DiaBeater. All of the other features of our device are based off of the data retrieved by the blood glucose monitor. The method of measuring the blood glucose is what differs between the three different design alternatives, and will be discussed further in the Design Alternatives section.

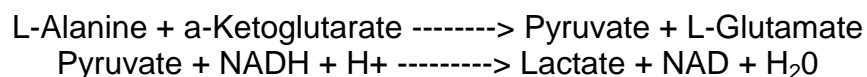
The second component of the DiaBeater is the Polar Heart Rate Monitor. Its primary function is to keep track of energy/calorie intake versus energy expenditure. The food intake amounts must be entered by the user and the device calculates how many calories are expended throughout the day. On the basis of food intake versus energy expenditure, it determines whether the user has gained/lost weight. The device generates food intake and exercise instructions based on input from the user, and most importantly, it allows the user to monitor their habits and learn which lifestyle changes need to be made. It is an essential component of our device since it serves as a learning tool for the patient (United States, 2005).

The third component of the DiaBeater has to do with drug delivery. This aspect of our device comes into play with the Thiazolidinedione drug (TZD). The TZD drug is meant to stimulate the B-cells in the pancreas to enhance insulin production. Thiazolidinediones improve glycemic control by targeting the metabolic defects of insulin resistance and insulin deficiency. They potentially preserve  $\beta$ -cell function and, therefore, prevent diabetes. They also function to decrease insulin resistance, prevent decline in  $\beta$ -cell mass, reduce glucose production in the liver, and help insulin work better in the muscle and fat. Studies conducted by the American Diabetes Association suggest that Thiazolidinediones decreased the risk of developing diabetes by 56%.

The DiaBeater will deliver the drug in routine installments. After extensive research, we have found that TZDs are the best option for prediabetics, as they have performed the best out of all of the other insulin replacement medicines. It is important to note that not all patients will be using this aspect of the device; it will be determined on a case by case basis, by the patient's physician. The TZD is stored in very small

vials, which **are** placed in the watch base of the device. The drug will then be released into the patch on the underside of the watch base and diffuse into the body through the skin pores. The drug delivery system of our device uses the cymbal array, a component of the ultrasound method, described in detail in the Device Alternatives section. The ultrasound waves open the pores of the skin. This increase in permeability allows the molecules of the drug to diffuse through the top layers of the skin and into the capillary system, where the drug can be distributed (Maione, 2002).

In very rare instances, however, patients who have used TZD have experienced liver problems (Bloomgarden, 2005). As a precautionary measure, we have included a feature in our device to detect if liver function is decreasing. An enzyme called Alanine Aminotransferase (ALT) is normally present in the blood, but when liver damage occurs, the levels of this enzyme in the blood increase. We have a reagent, called a-Ketoglutarate 13, which will react with the ALT in the blood using the following chemical reactions (Teco):



We use these reactions to determine the exact concentration, and the device deciphers whether it is within normal range (between 20 IU/L to 100 IU/L). The device uses the ultrasound method to detect the concentration of ALT in the blood. The ultrasound device will open the skin's pores and the compounds of the blood will diffuse through the skin and into the device. Once the compounds of the blood have diffused into the device, the chemical reaction will take place inside the watch base. The a-Ketoglutarate 13 reagent used in this reaction **is** stored in very small vials and inserted into the watch base. Although there are some very rare and minor risks associated with TZD, it is overall a very feasible option for decreasing blood glucose levels.

In order to display user feedback in a creative and user friendly way, we **use** holographic projection technology, called Heliodisplay, developed by IO<sub>2</sub> Technology. Feedback generated by the device **is** projected via the watch screen. The media **is** projected into the air space above the watch. A 3-D image, from 5 to 150 inches diagonally, will seem to float in midair above the watch base. The Heliodisplay works by agitating air to create a surface upon which it can project a 2-D image. Since the image does not appear on a physical object, the eye interprets it as a 3-D image. Heliodisplay is interactive; the image generated can serve as an input device, "a virtual touchscreen." Just as a user can manipulate an image on a computer screen with a mouse, a user can manipulate the floating image by touching the air into which the image is projected. The technology supports viewing from both the front and the back. Two people sitting on opposite sides may view the exact same image. It also has functions where the image can be made invisible from one side, for privacy purposes (Heliodisplay, 2005). This creative type of interface is a great way to add to the appeal of the product, especially since it is targeted towards adolescents. They **can** interact with a 3-dimensional character, and using their hands, they **are** able to move and manipulate the image. This is a major selling point of our device.

In addition to the key features mentioned above, all three of our device alternatives are be able to store data regarding food intake, energy expended, food



groups, and weight and blood glucose fluctuations. The device **is** able to store up to six months worth of data. It will also be able to wirelessly communicate with cellular phones, PDAs and computers in order to transfer data.

One of our design priorities was to make the DiaBeater non-invasive, in order to minimize the pain and maximize user acceptance and convenience. We also wanted the device to be an external for easy implementation, allowing patients to use it as needed. We wanted to ensure that this device would be well accepted by adolescents, so we kept the device simple and easy to use. This is why we chose the ‘watch’ as our platform. We also chose the watch design so that the device would be inconspicuous, and would not draw unwelcome attention.

As with any device, there are a few constraints associated with the DiaBeater. It is first and foremost meant to be an aid in the prevention of diabetes, not a cure. We cannot guarantee in any way that a person who uses the DiaBeater will not become diabetic; nor can we guarantee that the TZD drug that is delivered with the device will perform successfully in the body. There are always risks involved with fairly new drugs. The DiaBeater must be worn at all times. The fact that the device is external and visible poses a hindrance as well, but our choice of an watch interface (a commonplace accessory) minimizes any potential discomfort. The patient must also be willing to consult with their physician regularly so that their progress can be monitored. The wireless capabilities of the DiaBeater make this continual dialogue very simple, though. In addition, the DiaBeater requires regular maintenance and replacement of parts such as drug delivery patches and the drugs themselves, like TZD and the both the glucose and ALT detection reagents.

In order to choose the best method of glucose measurement, we developed the following priority system:

<b>Priority Number</b>	<b>Category Prioritized</b>	<b>Description of Category</b>
1	Safety	Most important thing; patients should not be presented with any unnecessary risks or hazardous situations because of their use of the DiaBeater
2	Side Effects	Patients should only have to experience minimal if any side effects due to an external device
3	Reliability	The device must be reliable and maintain working order so that the patient can get accurate feedback
4	Limitations	The device must not pose unnecessary constraints on the user or hinder them from performing their everyday duties
5	Durability	The device must maintain its function even in non-ideal environments

6	Maintenance	The device must require the minimum amount of maintenance possible
7	Inconspicuousness	The device must not be a physical hindrance and must not draw attention to itself due to its size

Based on the criteria described above, here are the ratings that the three device alternatives received (see below for more elaboration):

Category	Tympanic	OCT	Ultrasound	Maximum # of Points Possible
Safety	8	6	9	10
Side Effects	8	8	7	9
Reliability	4	7	7	8
Limitations	4	3	6	7
Durability	3	2	5	6
Maintenance	4	4	2	5
Inconspicuousness	1	1	3	4
<b>TOTAL</b>	<b>32</b>	<b>31</b>	<b>39</b>	<b>49</b>

### Device #1 – Noninvasive Tympanic Blood Glucose Monitor

The feasibility of this device is based on the principle of thermal emission spectroscopy for measuring the glucose concentration in the tympanic membrane. This technology is based on the discovery that human body naturally emits strong electromagnetic radiation in the micrometer wavelength region and its radiation contains spectral information about the tissue. Therefore, the intensity of radiation and its spectral characteristic are reflections of both the object's absolute temperature and its state and properties, such as glucose concentration.

The absorption and emission measurement from the glucose **is** detected by using a specially designed non-dispersive filter-based spectrometer (see **Figure 2**), because of its simplicity, a high signal-to-noise ratio, high throughput, and low cost. Moreover, in order to get a more precise reading, the device **is** placed on the tympanic membrane. It is an excellent position to measure body temperature due to the fact that it shares its blood supply with the hypothalamus, the center of core body temperature regulation. Therefore, a sensor **is** inserted into the ear canal to obtain a clear view of the membrane and its blood vessels and also to measure the amount of IR radiation the membrane emits. The spectral characteristics of various constituents of blood **are** separated by using the analytical chemistry spectroscopy method. That is, one filter will pass radiation through the thermal emission bands with glucose signatures and be placed in one of the IR detector windows, while the other IR detector window is covered

by a filter capable of passing radiation that does not include emission bands characteristic of the analyte at wavelengths in the range of interest. Then, the difference of the radiation intensity between the two radiation paths can be calculated and provides a measure proportional to the analyte concentration (Koshinsky, 2001).

**Figure 2: IR Spectroradiometer of Noninvasive Tympanic Blood Glucose Monitor**

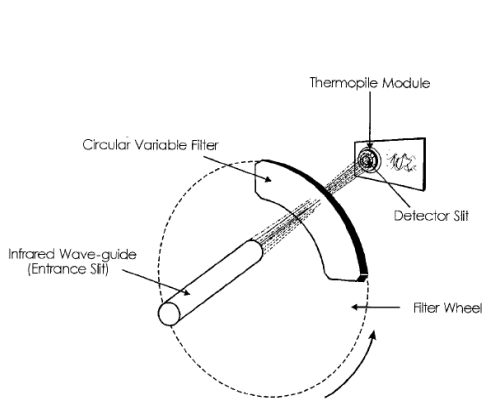


Figure 1—Schematic of the filter-based IR spectroradiometer.

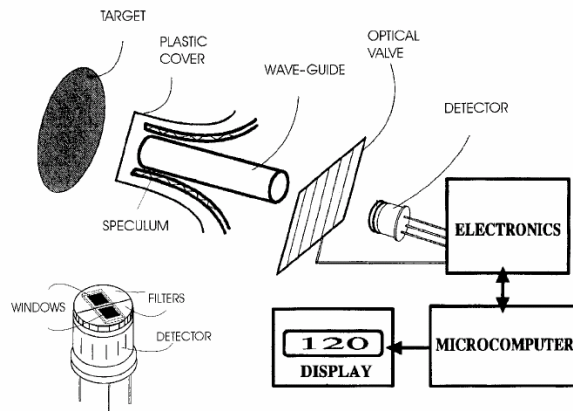
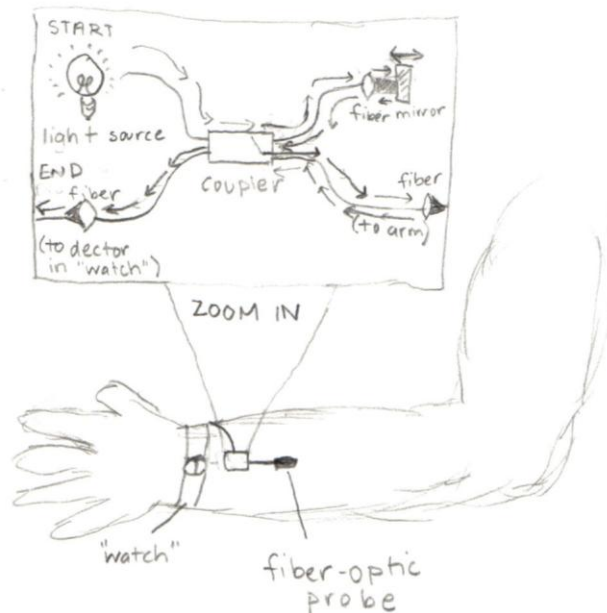


Figure 3—A simplified diagram of the glucose monitor.

## Device #2 - Noninvasive Blood Glucose Monitoring Through Optical Coherence Tomography

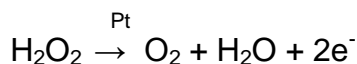
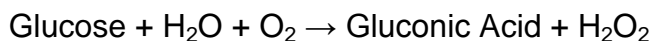
Fundamentally, OCT is based on the refraction of a light beam under the target surface (see **Figure 3**). Light is aimed into a fiber optic coupler where it splits paths, one beam leading into a moving reference mirror and the other focusing into the tissue. Both beams must pass through a fiber (defined by McGraw-Hill's AccessScience as a transparent threadlike object made of glass or clear plastic, used to conduct light along selected paths) before reaching their destination. It is this fiber that then channels the back-reflected light through the coupler to another fiber and detector to be processed and analyzed based on the interference between the tissue and reference signals. When, for example, glucose concentration or cell volume change, the light will bend due to the resultant differences in internal indexes of refraction. (Barton, 2000) When applying this technology to glucose monitoring, it is also important to note that the effect of the refractive index mismatch of glucose is approximately 8 to 40 times greater than that of other common bodily substances that would interfere, making it very easy to detect and attribute to for any changes (Larin et al., 2003).

**Figure 3 – OTC System Incorporated with wristwatch device platform**



**Device #3 – Noninvasive Blood Glucose Monitoring Through Ultrasound Technology**

This device alternative is the utilization of a glucose monitoring system uses ultrasound technology to allow glucose from the interstitial fluid below the surface of the skin to diffuse to the surface, where the glucose reacts with an electrochemical biosensor. The products of this reaction are measured, and are proportional to the amount of glucose. The chemical reaction is displayed below:



More details about the ultrasound technology, including the diagram can be found below, in the detailed design and product description section.

### *Compare and Contrast 3 Alternatives with Existing Technology and with each other*

#### **-Tympanic**

The tympanic technology is very new and is still in testing. It has not actually been included in a device that has been put to use for a specific purpose. We hope that by the year 2020, the technology will be fully developed and in use in many different types of biological devices. This first independent clinical study of an advanced noninvasive blood glucose prototype based on thermal emission in the mid-infrared spectral region has demonstrated glucose measurements with clinically acceptable accuracy but without the necessity of individual daily calibration. (Malchoff)

#### **-OCT**

The Optical Coherence Tomography technology too has only been tested in labs; it is not currently in use in actual devices. However the laboratory tests that have been run using the technology have been extremely successful, and the trends look promising. The pilot study demonstrated the capability of the OCT technique to monitor blood glucose concentration non-invasively in human subjects. Further studies with a larger number of subjects including diabetic subjects are planned to validate these preliminary results. (Larin)

#### **-Ultrasound**

The ultrasound technology is currently being utilized in a few devices. In fact, it is being used in a device called the GlucoWatch (GlucoWatch) which measures the blood glucose concentration using this ultrasound technology. This GlucoWatch is currently on the market and available for purchase. Thus far, the ultrasound technology has proven to be extremely effective and convenient, as per the results experienced both in the lab as well as out in the market.

### *Discussion of the Three Alternatives*

Out of the three design alternatives, the ultrasound device was the safest choice. The only major side effects of the ultrasound device were minor, while the considerations in this same category for the other two alternatives were much less safer. Use of the tympanic device presented risks in damaging the tympanic membrane, as well as hearing loss, while the OCT device presented the risk of burning the skin by scarring the cells with the laser technology. The side effects of all three alternatives were fairly minimal and about the same proportion. Since the tympanic device had much room for movement, and had to be positioned in a very specific place, the reliability of its readings was not very high. For the other two design prototypes however, the reliability factor was about the same. Both the tympanic and OCT devices presented the same problem when it came to physical characteristics; they both consisted of an additional piece of equipment which is far more inconvenient than just the wristwatch base. This is why they received lower markings on the priority system chart for limitations. The OCT and tympanic devices both are fairly fragile, since they do involve an additional component, one with the IR Spectroradiator while the other contains a laser. Maintenance was higher for the ultrasound device more so than the

others because the patch with the hydrogel layer requires regular replacement, whereas the other devices do not require regular change of parts. Once again, since both the tympanic and OCT models have that extra component, they rank very low in point value for their level of inconspicuousness.

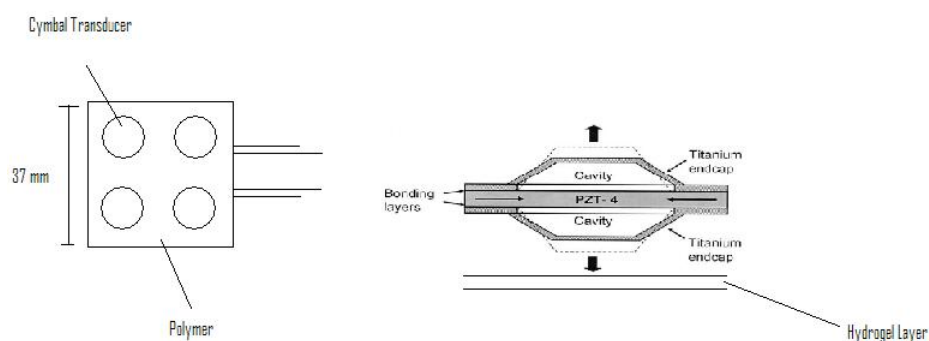
We used our priority system to select our optimal design choice. We assigned numbers in each category for each of the three models, and tallied the results. The device that received the highest number of points was the one we chose as our optimal design choice. Basically, the ultrasound device turned out to be the device with the least amount of complications for the user, as well as the safest alternative. Safety is a very important factor when it comes to medical devices, which is why it was worth the highest number of points on our prioritization scale.

The DiaCure DiaBeater model that we have chosen to present to you uses breakthrough ultrasound technology to monitor glucose and Alanine Aminotransferase levels in the blood, as well as to deliver the Thiazolidinedione drug via the bloodstream to the pancreas.

The device consists of an array of four cymbal transducers encased in a polymer (see **Figure 4**). Each cymbal is made of a 7 mm ceramic piezoelectric disk with two metal caps attached to the top and bottom. The ultrasound vibrations are caused by the radial motion of the disk, which causes the end caps to flex. The total frequency of the ultrasound vibrations is 20 kHz, which allows for the interstitial fluid to come to the skin surface.

Once at the surface, the glucose reacts with an electrochemical biosensor consisting of a hydrogel with the enzyme glucose oxidase. Glucose, water, and oxygen react with this enzyme to form gluconic acid and hydrogen peroxide. This hydrogen peroxide is then applied a positive electrical potential using a platinum electrode, which causes the hydrogen peroxide to be oxidized to oxygen, water, and two electrons. The current produced from this oxidation is proportional to the amount of hydrogen peroxide produced, which is one molecule for every one molecule of glucose. Thus, it is possible to determine the amount of glucose in the sample based on the current and the amount of hydrogen peroxide (Maione, 2002).

**Figure 4 – Cymbal Ultrasound Unit**



### III. Product Deve

#### *Proof of Concept Experiments*

## Objective

The objective of our proof of concept experiments was to compare the heart rates between subjects with differing BMIs before and after implementation of the device in the overweight subject's lifestyle

## Hypotheses

- The resting heart rate of a person with a high Body Mass Index (>25) will be higher than a control subject with normal Body Mass Index (18.5 <BMI< 25).
- The heart rate in a person with a high BMI will be higher than a person with a normal BMI during moderate physical activity (running in place).
- The time required for a person with higher BMI to return to their resting heart rate will be longer than that for a person with a normal BMI.

## Summary of Methods

BIOPAC Pulse Plethysmograph sensor was used to detect the heart rate. The Pulse Plethysmograph was placed on the right finger to record the heart rate of the subject. Two pre-diabetic 18 year old males (one subject with a high Body Mass Index (BMI), one with a normal BMI) were compared acknowledging the fact that the former will use the DiaCure device and lifestyle program, while the latter will not follow any preventative measures. The DiaCure device monitors blood glucose levels, measures calories ingested and expended, and administers Thiazolidinediones to stimulate Beta-cell production in the pancreas. It also provides the user with guidance regarding their lifestyle choices.

Before beginning this experiment, each subject's height (in) and weight (lb) was measured in order to calculate BMI ( $BMI = 703 * weight / (height)^2$ ). The purpose of the experiment was to compare the time to return to the resting rates between each subject, as well as the magnitude of the maximum and resting rates. Each subject's pulse rate was measured before, during, and after moderate physical activity (running in place for 2 minutes), terminating data collection after a total of 10 minutes had passed. The "cool down" period began after 2 minutes of exercise, and concluded at the end of 10 minutes. The heart rate was calculated after one minute of activity, at the beginning of the "cool down" period (the point when the subject sat down), and at 15-second intervals beginning at the fourth minute of data collection. The rate was calculated at these intervals until the heart rate reached the resting rate or a lower value. The number of intervals varies with subject.

This experiment will be repeated in four months to chart the progress of the subject using the device (high BMI) in comparison to the unrestricted plan for the control subject (normal BMI). The device will thus be evaluated by comparing the initial data with the new data in order to see if the hypotheses that overall physical fitness and health is represented by a test subject's heart rate were true.

## Results

### Table 1.1: Subjects' Physical Characteristics (Day 1 – 10/31/05)

<b>Subject</b>	<b>Control (Normal BMI)</b>	<b>Experimental (High BMI)</b>
Weight (lb)	132	135
Height (in)	68.5	67.5
Resting Heart Rate (Beats/15 seconds)	21 (88 Beats per minute)	14 (56 Beats per minute)

This table represents the initial collected data for each test subject. Before any type of data analysis could be performed, the data was converted into the proper units. The start of each 15-second time interval was converted into its respective time in minutes by dividing each number by 60. The number of beats per 15-second interval was converted to beats per minute by multiplying by a factor of 4:

$$\frac{35 \text{ beats}}{1 \text{ 15-second interval}} \times \frac{4 \text{ 15-second intervals}}{1 \text{ minute}} = \frac{140 \text{ beats}}{1 \text{ minute}}$$

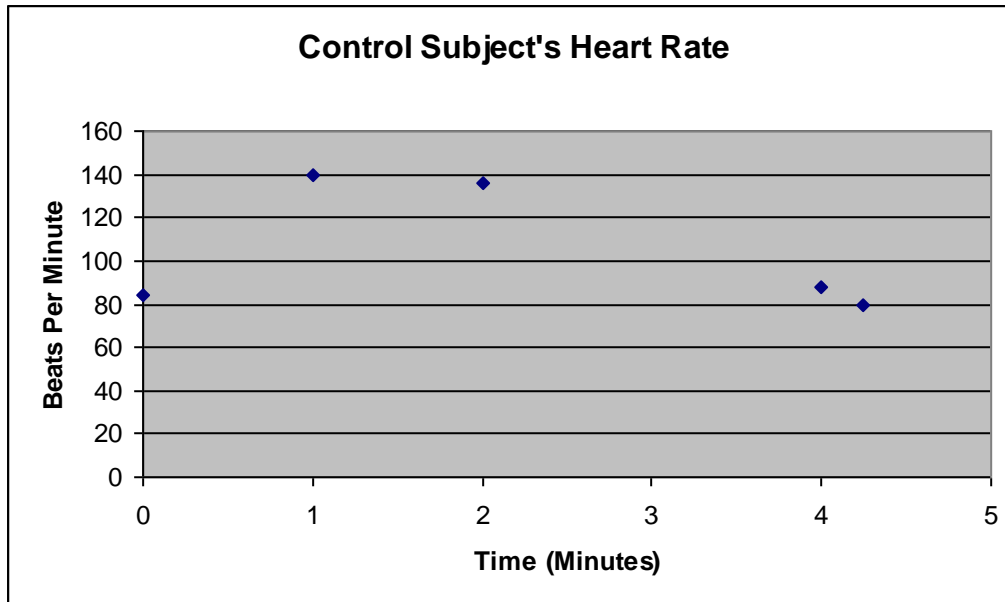
**Table 1.2: Control Subject's Heart Rate (Day 1 – 10/31/05)**

<b>Start of 15-Second Time Interval (s)</b>	<b>Number of Beats</b>	<b>Time (minutes)</b>	<b>Beats per minute</b>
0	21	0	84
60	35	1	140
120	34	2	136
240	22	4	88
255	20	4.25	80

This table contains the data collected for the control subject during trial 1 of the lab, on October 31, 2005.

**Figure 1.3: Plot of Control Subject's Heart Rate during Experiment (Day 1 – 10/31/05)**





Plot of Control Subject's heart rate during data collection.  
 Slope of regression line, beginning at t = 2 minutes, when subject stopped running:  
 $y = -24.5x + 185$

**Table 1.4: Control Subject's Heart Rate (Day 2, Trial 1 – 11/14/05)**

Start of 15-Second Time Interval (s)	Number of Beats	Time (minutes)	Beats per minute
0 (Resting)	22	0	88
90	33	1.5	132
150	31	2.5	124
180	28	3	112
210	26	3.5	104
240	23	4	92
270	22	4.5	88

**Table 1.5: Control Subject's Heart Rate (Day 2, Trial 2 – 11/14/05)**

Start of 15-Second Time Interval (s)	Number of Beats	Time (minutes)	Beats per minute
0 (Resting)	22	0	88
90	35	1.5	140
150	30	2.5	120
180	29	3	116
210	25	3.5	100
240	22	4	88

**Table 1.6: Test Subject's Heart Rate (Day 2, Trial 1 – 11/14/05)**

Start of 15-Second	Number of Beats	Time (minutes)	Beats per minute
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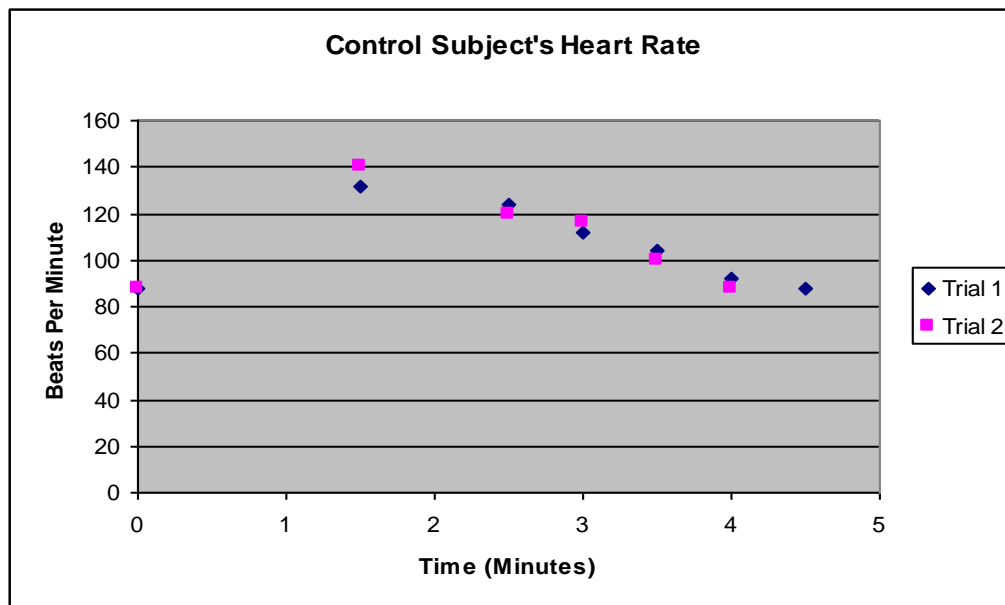
Time Interval (s)			
0 (Resting)	21	0	84
90	42	1.5	168
150	24	2.5	96
180	17	3	68

**Table 1.7: Test Subject's Heart Rate (Day 2, Trial 2 – 11/14/05)**

Start of 15-Second Time Interval (s)	Number of Beats	Time (minutes)	Beats per minute
0 (Resting)	13	0	52
90	36	1.5	144
150	22	2.5	88
180	17	3	68
210	14	3.5	56
240	15	4	60
270	14	4.5	56
300	14	5	56
330	13	5.5	52

The above data (**Tables 1.4 – 1.7**) represents the heart rate data collected on day 2 of the lab, on November 14, 2005.

**Figure 1.8: Plot of Control Subject's Heart Rate during Experiment (Day 2 – 11/14/05)**



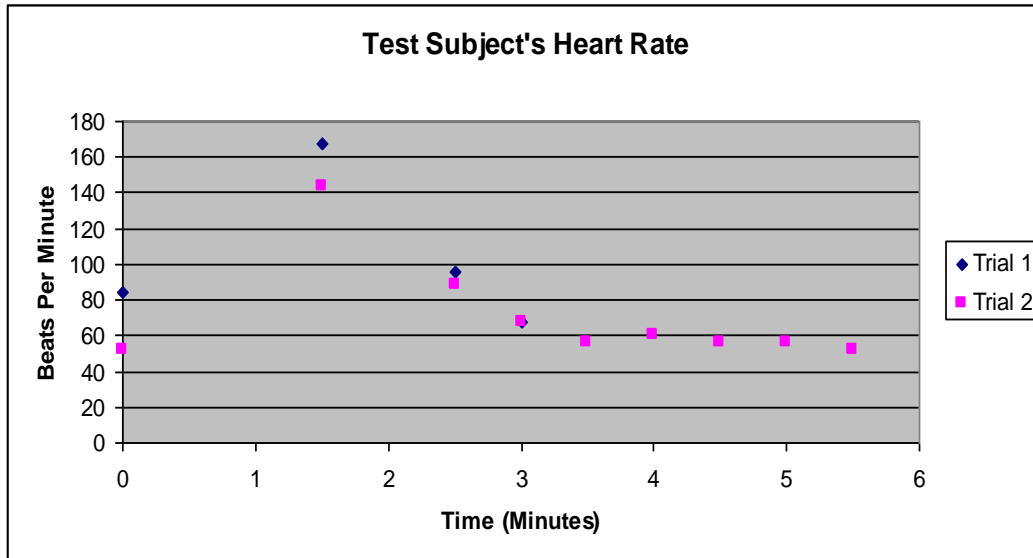
Plot of Control Subject's heart rate during data collection.

Slope of regression line, beginning at  $t = 2.5$  minutes, when subject stopped running:

$$\text{Trial 1: } y = -18.4x + 168$$

$$\text{Trial 2: } y = -22.4x + 179$$

**Figure 1.9: Plot of Control Subject's Heart Rate during Experiment (Day 2 – 11/14/05)**



Plot of Test Subject's heart rate during data collection.

Slope of regression line, beginning at t = 2.5 minutes, when subject stopped running:

Trial 1:  $y = -56.0x + 236$

Trial 2:  $y = -9.43x + 100$

### Data Analysis

t-Test: Two-Sample Assuming Unequal Variances

	<i>Control Subject</i>	<i>Test Subject</i>
<i>Trial 2 (11/14/05)</i>		
Mean	109	70.2
Variance	419	892
Observations	6	9
Hypothesized Mean Difference	0	
df	13	
t Stat	2.96	
P(T<=t) one-tail	0.00555	
t Critical one-tail	1.77	
P(T<=t) two-tail	0.0111	
t Critical two-tail	2.16	

### Interpretation

Using a t-Test for two samples assuming unequal variances, the probability that both samples were the same (the P value) was 0.00555. Since this value is significantly below 0.0500, it can be concluded that the two samples, the control subject and test subject, exhibit very different characteristics, as our hypotheses predicted.

### Discussion

With the converted data, a plot was made (see **Figures 1.8 and 1.9**) that illustrates the change in heart rate with respect to time (Beats/Minute<sup>2</sup>). Using a linear regression, the slope of the line that represents the “cool down” period was found for each subject. For the control subject, the average slope of the regression line was about -20 (Beats/Minute<sup>2</sup>). This means that the heart rate of the control subject declined by about 20 beats per minute per minute of rest. For the test subject, the slope was found to be about -32 (Beats/Minute<sup>2</sup>). The heart rate of the test subject declined by about 32 beats per minute per minute of rest. Therefore, the rate of change in heart rate was faster in the test subject than in the control subject, which does not agree with our hypothesis. However, this can be attributed to the fact that the actual test subjects used in the experiment did not exhibit all of the ideal characteristics of the intended test subjects.

In addition, several of our hypotheses that the heart rate in a person with a high BMI will be higher than a person with a normal BMI during moderate physical activity was proven to be correct using the data from the lab. The heart rate of the test subject during the peak of physical activity, at t=90 seconds, was significantly higher than the same measurement of the control subject (average 156 versus 136, see **Tables 1.4-1.7**). Our hypothesis that the time required for a person with higher BMI to return to their resting heart rate will be longer than that for a person with a normal BMI was not able to be proved correct using this data because the average time for both subjects was exactly 255 seconds. This inconclusive data may again be attributed to the fact that the actual test subjects used in the experiment did not exhibit all of the ideal characteristics of the intended test subjects

#### *Research Plan*

In order for the DiaBeater to be brought to market, it must first go through rigorous testing to ensure that it is safe and effective for use, particularly since it involves adolescents. Product testing must go on for one year, in several geographic locations, in order to sample a diverse population of prediabetic adolescents. Once this product has been tested and its safety confirmed, its marketing plan must be put into effect, which will take about one year to get the product ready to be distributed for use by the public. Production must be completed within six months of the completion of product testing. The data from the tests will then be used to analyze how well the device will work, and possibly indicate what changes must be made to the design.

#### IV. Market Potential

Even though the DiaBeater is a phenomenal device as is, there are still many ways to improve upon it in the future. Our goal at DiaCure is to make the most efficient and effective products. As a result of this, frequent updates will be done to maintain style and performance as the technology advances. Maintaining close contact with physicians and patients allows us to adjust the device when the individuals who most depend on it see reason for change.

Ideally, if the proper technology was available and approved, the DiaBeater would include many more features and functionalities. Solar rechargeable batteries are more advanced than lithium batteries and would prevent the need to ever purchase or replace the battery in the DiaBeater. As soon as the technology is further developed, a *continuous* wireless connection could also be made with a patient's health records or a

private database to store and share the collected data. The physician could always have access to this information as a means to help monitor his/her patient's progress and to compare with subsequent data.

The DiaBeater will be the first device on the market for prediabetics (already securing its success), yet it is still important to illustrate how much more powerful it is than the current options prediabetics have for prevention of type 2 diabetes. As already stated, following a healthy meal plan, weight loss, and increased exercise are the best ways to prevent the onset of diabetes (Diabetes Prevention Program). The following situations are improved upon with the technology of the DiaBeater.

Nutritionists often layout meal plans on paper for a prediabetic to follow, but the DiaBeater will have this all stored in memory and keep track of how closely the patient is following these guidelines. Internet services, such as GlucoMenu.com (Nutrition Click Inc.), provide menus tailored to the patient's specific needs (e.g. hypertension, high cholesterol, low sodium), but are dependent on a computer or wireless device and therefore not as convenient as the DiaBeater.

One of the most important challenges a prediabetic has is to healthfully lose weight. Currently, there are many studies on medications that could be used to help dissolve fat. As soon as one is brought to the market, DiaCure will be the first company to run trials incorporating its administration with the DiaBeater's versatile ultrasound technology. Eventually, it is also our goal to make the DiaBeater "smarter" so that less user input is needed (e.g. ability to sense the amount of calories consumed and for what food group), making the device even more convenient.

The Polar Electro (Polar Electro USA) heart rate monitors are very similar to our device (as the DiaBeater directly incorporates their technology), but they do not include the added features of drug administration or substance detection, lowering their appeal to prediabetics. Many weight loss and exercise aids are frustrating (especially for adolescents already coping with so many things during their teenage years), but not the DiaBeater. The fun and useful counseling provided by the Heliodisplay will attract adolescents more than any other medical device on the market. Because the biggest preventative measure that can be taken involves individual initiative, the power of the DiaBeater lies in its appeal to adolescents. If they were not impressed by a device's capabilities, they would not want to use it.

Some view the DiaBeater extension of the GlucoWatch (GlucoWatch), but do not overlook the power of incorporating so many technologies into one coherent device. The GlucoWatch does not offer counseling, record calories burned or administer any substance, all of which the DiaBeater does in an interactive and "cool" manner.

The DiaBeater is an extremely versatile device because of its ability to both administer and detect specific substances. This makes the range of consumers for the DiaBeater extremely broad. Ultrasound technology allows the device to potentially detect other substances besides glucose (providing the proper chemical reaction is known) and administer other medications besides TZD. For example, dopamine levels could be continuously detected in depressed or ADHD patients, in order to determine the prime time to take more medication and prevent undesired behavior. Lactose intolerant subjects could also use the ultrasound technology of the DiaBeater for the delivery of lactase, to aid in the digestion of lactose. There are countless substances

the device could potentially administer and detect, including many that every person can take (e.g. vitamins, short-term prescriptions, and cholesterol levels).

Type 1 and type 2 diabetics could also make use of the DiaBeater without having to modify the device as significantly as the former examples. By exchanging the TZD with insulin and modifying how the device responds to changes in blood glucose levels, diabetics could benefit from the technology of the DiaBeater. Athletes and dieters could also employ the nutrition and calculated exercise features to better monitor their progress towards individual goals. Hypoglycemic patients could take advantage of the non-invasive glucose monitoring system to be sure that their levels do not drop too low. Liver toxicity and failure in high-risk patients would also be simple to detect with the ALT feature, warning the patient before a serious problem arises.

## V. Bioethical Issues

### *Research Risks*

The fact that the device has been designed for use by adolescents poses a major risk in and of itself. Therefore, informed consent must be explicitly obtained from adults who care for the adolescent before any experimentation may begin. In addition, there is a possibility that test subjects may experience side effects of TZD, which may be as severe as liver failure.

### *Use and Misuse of the Device*

In addition to functioning to prevent the onset of diabetes in adolescents, several functions of the device may also be used by other groups of people. For athletes, the device has commercial applications that allow it to be used as a fitness and health training tool. Also, once the effectiveness of TZD in preventing diabetes is determined, the device may also be used for adults to control and treat type 2 diabetes. As for potential misuse of the device, no situation in particular can be seen. The goal of the device is to prevent diabetes, and therefore has no possible misuses that could harm the user.

### *Who May Benefit?*

As mentioned above, an additional use of the device may be for overall health and fitness. Therefore, many consumers, either athletes or those seeking to adopt a healthy lifestyle, may see potential uses from the device. Also, healthcare professionals and insurance companies will benefit from the implementation of the device because of the high costs attributed to treating diabetes today. Those costs will be virtually eliminated once the need for constant care is eliminated.

### *Resource Allocation*

During the testing phase, resources will be allocated to ensure that the device has been tested thoroughly and is ready for the market. Once the device is on the market, resource allocation will be shifted to maintaining proper operation and function of the device. During this phase, special attention will be paid to ensuring that progress is being made in the users of the device, as well as collaboration with healthcare professionals in order to determine any changes that must be made to the design after implementation.

## VI. Conclusions

As diabetes has become more and more prevalent in US, it has not only deterred people from living normal lifestyles, but has also exhausted our national wealth for treating this disease. Until today, there is no known medication that can effectively eliminate the disease completely; the only way to get rid of it is to prevent it before its actual onset occurs. Therefore, the DiaCure DiaBeater will be a great leap forward in preventing diabetes because it is the only device on the market that specifically aims to help prediabetics. The DiaBeater uses novel ultrasonic technology for both detecting the blood glucose levels and administering the Beta-cell stimulating drug (instead of insulin) within a single device, which potentially reduces the number of components needed. In addition, wireless communication technology is also incorporated within the DiaBeater to facilitate information transferring between the patient and physician. With this device, we are aiming to prevent diabetes by educating the patient, and a novel feature that we have incorporated into our device allows us to do so. Since a healthy lifestyle is crucial for preventing diabetes, a calorie calculator **is** another built-in feature of our device, which would not only calculate both calorie intake/expenditure, but would also generate advice for the patient to encourage them to pursue a healthier eating or exercising plan based on the data it has gathered. Accordingly, the main goal of our product is to help people with prediabetes and to prevent them from becoming diabetic, and therefore having to resort to later use of instruments such as insulin pumps and oral medication, Hence, our device is the only aid available to prediabetics in helping them to fight the battle against the raging disease we know as type 2 diabetes.

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