PERSONALIZED NON-INVASIVE BLOOD GLUCOSE MONITOR

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Abstract - Non-Invasive Blood Glucose Monitor is developed for 4 decades but it is still clinically unacceptable in the market due to its poor accuracy. The main reasons for poor accuracy are sensor accuracy, within-patient and in between patient variation. Most of the inventions are done to improve the non-invasive sensor accuracy. This paper presents, the concept of "personalized non-invasive blood glucose monitor" to improve the accuracy by resolving both within and in between patient variations. Our concept consists of both invasive and non-invasive sensors on a single device. Initially, the patient monitors his/her blood glucose level using both invasive and non-invasive approaches. The device processor calculates the error in non-invasive measurements with respect to invasive glucose value. Based on collected data, software develops an error function model by best suitable regression analysis to reduce the sum of square error. Once the device is calibrated for a patient, the error function model compensates for the error in non-invasive measurement and gives accurate non-invasive blood glucose results. At this point, the patient measures blood glucose levels by non-invasive methods only. The personalized blood glucose monitoring concept is applied and accuracy is improved from -221% ~ 61% to -14% ~ 18% for a dataset.

Keywords - Blood Glucose Monitoring, Non-Invasive Blood Glucose Monitor, Personalized Glucose monitor, Non-Invasive Diabetic Care, Invasive Vs Non-Invasive Glucose Monitor.

I. INTRODUCTION

As per the world health organization (WHO), approximately 422 million people suffered from diabetes and approximately 1.6 million people died in the year 2014 [1]. It is growing every year with a ~8.5% rate and by 2030 more than a billion people will be suffering from diabetes [1]. Harmon-Boehm et al. [2] presented the result of Glucotrack, which consists of 3 sensors based on ultrasonic, electromagnetic and thermal technology. The test was performed on 91 subjects and absolute relative differences (ARDs) from invasive to non-invasive glucose values were 23.4% and 16.5% [2]. In reality, Glucotrack device accuracy was from -221% to 61% for non-invasive measurement. Malchoff et al. [3] presented the outcome of non-invasive glucose monitoring but the standard deviation found was 27mg/dl during the actual test [3]. Hence, this also has an accuracy issue. Vashist [4] has a test result from a single subject with 50 samples, but it has 8.3% of mean absolute relative differences (MARD). All these papers lack to address the non-invasive blood glucose accuracy issue due to variation within and in between patients entirely. The invention presented in this paper developed a "personalized non-invasive blood glucose monitoring device" exclusively for a patient. Device processor software builds an error function model based on invasive and non-invasive blood glucose values. The error function model compensates for the error in non-invasive measurement and gives accurate results for a patient. Source of variation in non-invasive measurements

To ensure the universal usage of a non-invasive blood glucose monitor, we analyzed the following sources of variation [5].

A. Within patient variation

1) Variation due to food intake
2) Variation due to physical activity
3) Variation due to stress or anxiety

B. In between patient variation

1) Heredity (Stem cell & reaction with pancreases)
2) Skin color
3) Skin thickness
4) Sensor accuracy

Our research addresses these sources of variation. The device is trained based on patient skin color, thickness, food intake, physical activity, stress, and other psychological patterns.

II. PERSONALIZED NON-INVASIVE MONITOR ARCHITECTURE

The architecture of our invention is shown in Figure 1. It has explained in the following 3 steps.

Step1: Training the device

Initially, data is acquired from both invasive and non-invasive sensors. Invasive blood glucose value is saved as a reference. Non-invasive blood glucose value is compared with respect to reference to calculate the initial error. A patient uses this device to generate multiple data for an initial period. The processor unit software program builds an "error function model" based on collected data by applying several curve fitting techniques to reduce the sum of square error (SSE) as explained in Figure 2.

For subsequent non-invasive glucose readings, the processor unit compensates the error in "non-invasive" glucose value as per the "error function model" and predicts "non-invasive predicted". The processor unit recalculates the error in "non-invasive predicted" with

respect to reference "invasive" value.

Step2: Monitoring glucose non-invasively only

Once the error in "non-invasive predicted" is within acceptable limit for subsequent readings, then the patient uses the device non-invasively only to monitor the blood glucose level. Now, the device becomes personalized for a user.

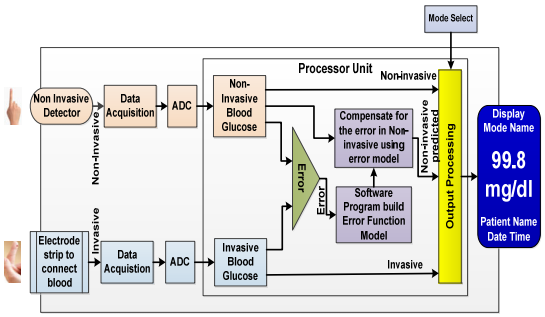


Fig. 1. Personalized Non-Invasive Blood Glucose Monitor Architecture.

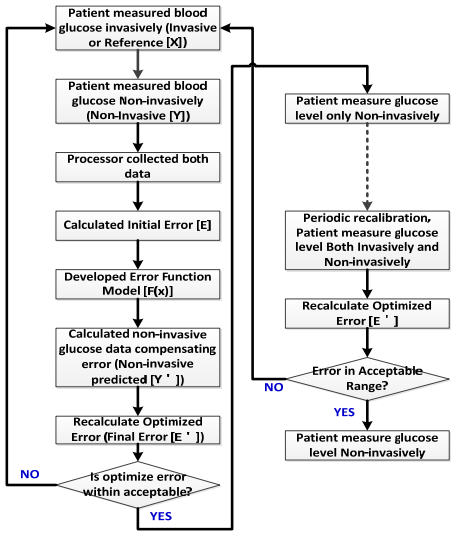


Fig. 2. Software flowchart of a personalized non-invasive glucose monitor.

Step 3: Periodic re-calibration of the device

As part of device periodic re-calibration, the patient measures both invasive and non-invasive glucose for the next few cases. If the predicted non-invasive value is within the acceptable error than the patient continues to use the device non-invasively. However, if it is outside the acceptable error limit than the device needs to be retrained as explained in step 1 and as shown in Figure 2.

Symbol	Description
n	Number of data
X	Invasive (reference) glucose value
Y	Non-invasive glucose value
Y'	Non-invasive predicted glucose value
E	Initial error in non-invasive glucose value
E'	Final error in non-invasive predicted glucose value
F(x)	Error function model between X & Y
SSE	Sum of square error

III. ALGORITHM AND ERROR FUNCTION MODEL

Table I represents the definition of the symbol used in this paper. Table II summarizes the error in the non-invasive glucose value of 804 data of 95 patients as referred from Harmon-Boehm *et al.* [2]. The absolute error is extremely high and varies from -221% ~ 61% as calculated per equation 1.

$$E = \frac{100\,x\,(Y - X)}{X} \tag{1}$$

Parameter	Unit	Minimum	Maximum	Mean
X	mg/dl	65	402	192
Y	mg/dl	80	352	196
E	%	-221	61	27

TABLE II
Non-invasive glucose monitor summary

The 804 data sets are further analyzed with various regression analyses to build an error function model. The goal is set to choose the types of a transfer function, which gives the least sum of square error (SSE). After several regression analyses both linear and non-linear on these data, the best suitable error function model is developed as in equation 2.

$$\begin{aligned} Y' = F(Y,E) = {} & a_0 + a_1 xY + a_2 x\,E + a_3 x\,Y^2 + a_4 x\,E^2 \\ & + a_5 xYxE + a_6 x\,Y^3 + a_7 x\,Y\,x\,E^2 + a_8 x\,E\,x\,Y^2 \\ & + a_9 x\,E^3 + a_{10} x\,Y^2 x\,E^2 + a_{11} x\,Y^3 x\,E + a_{12} x\,Y\,x\,E^3 \\ & + a_{13} x\,Y^3 x E^2 + a_{14} x\,Y^2 x\,E^3 + a_{15} x\,Y^3 x\,E^3 \end{aligned} \tag{2}$$

Here, a_0 to a_{15} are coefficients of the error function model.

Now, the error is re-calculated for the same data sets as per equation 3.

$$E' = \frac{100\,x\,(Y' - X)}{X} \tag{3}$$

Table III summarizes the "predicted non-invasive" blood glucose data and error with respect to the reference. The error is reduced to -14% ~ 18%. This improves the personalized blood glucose monitoring device accuracy to very high compare to initial error -221% ~ 61%.

parameter	unit	minimum	maximum	mean
X	mg/dl	65	402	192
Y'	mg/dl	57	399	192
E'	%	-14	18	15

TABLE III
Personalized non-invasive glucose monitor summary

IV. TEST RESULT AND GRAPH

Figure 3 shows the test result of glucose value for "invasive", "non-invasive" and "non-invasive predicted" graphically. It can be clearly seen that the non-invasive predicted curve is following an invasive (reference) glucose curve. The result will be much better if the personalized blood glucose monitoring concept will be applied to single patient blood glucose data.

Figure 4 interprets the initially non-invasive glucose monitor device accuracy is very wide -221% ~ 61%. After applying the personalized non-glucose monitor concept, accuracy improved remarkably to -14% ~ 18%.

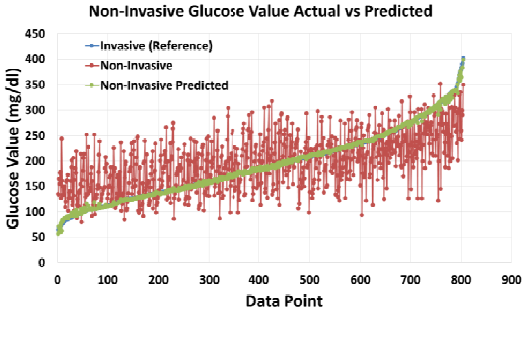


Fig. 3. Non-invasive glucose value actual vs predicted.

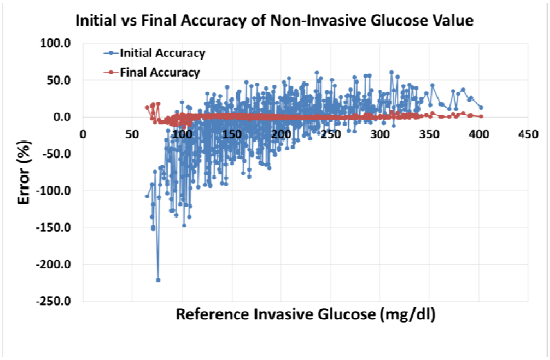


Fig. 4. Initial vs Final accuracy of a non-invasive glucose monitor.

V. CONCLUSION

Non-invasive blood glucose monitoring device accuracy improved from -221% ~ 61% to -14% ~ 18% by addressing within and in between patient variation using personalized non-invasive blood glucose monitor concept. As part of future work, this concept will be further applied to multiple sources of data using machine learning to improve the accuracy further.

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