Everything You Wanted to Know About Continuous Glucose Monitoring

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***Abstract*—Diabetes occurs due to lack of insulin generation inside the human body. The continuous glucose monitoring using noninvasive measurement in smart healthcare can be effective for the diabetes people. The conventional method for glucose measurement requires pricking the blood samples which may not be advisable for frequent measurement specially for old age people and children. The paper provides brief review about various approaches of continuous glucose measurement with non-invasive manner. This article covers the state of the art glucose measurement methods and its control mechanism. The study of various consumer products have also been discussed along with the open challenges.**

I. Introduction

The glucose is produced through food intake inside the human body which provides the energy for daily activities. The ideal range for glucose varies from 80 to 150 mg/dl. However, the higher value of glucose is considered as Diabetes Mellitus (DM) (see Figure 1). The main reason for DM is insufficient insulin generation inside the human body [1]. The probability of death after DM may increase upto 50% in comparison with non-diabetic person. DM is one of the chronic disease which would build up over the time and could be controlled easily with frequent blood glucose monitoring. Traditionally, the blood glucose is measured either in well-equipped laboratory tool or through self-measurement device which are invasive in nature and also measure the intermittent glucose value. DM may lead to long term complication in case of glycemic profile remains unnoticed over the period of time. There are mainly three types of diabetes as: Type 1 Diabetes, Type 2 Diabetes and Gestational Diabetes [2]. Type 1 diabetes is a condition where body does not able to produce insulin to have the proper insulin-glucose balance. In case of type 2 diabetes, the body does not generate adequate insulin to maintain proper glycemic profile. Whereas, Gestational Diabetes occurs during the pregnancy of the women where body is unable to generate insulin for glucose regulation.

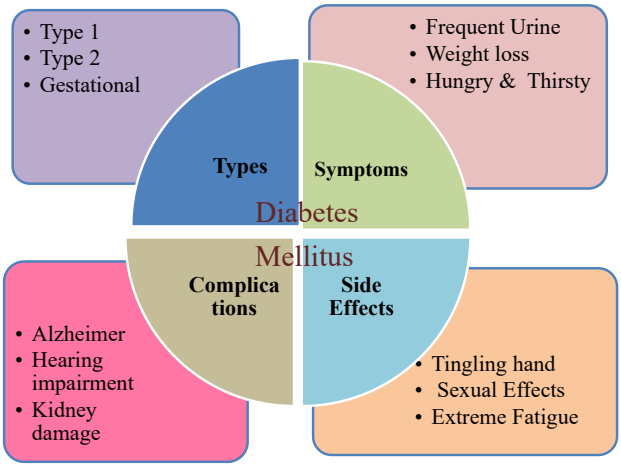

Fig. 1: Diabetes Overview.

II. Diabetes as Health Crisis and Need for Glucose Measurement

A. The Health Crisis due to Diabetes

The number of diabetic persons has grown in exponential manner from past few years. The prevalence rate of diabetes patients was around 9.3% in 2019 with overall 463 million population in the world which is expected to move around 700 millions over next two decade (See Figure 2) [3]. Almost 1 out of 2 diabetes patients is unaware about their situation and don't have adequate knowledge

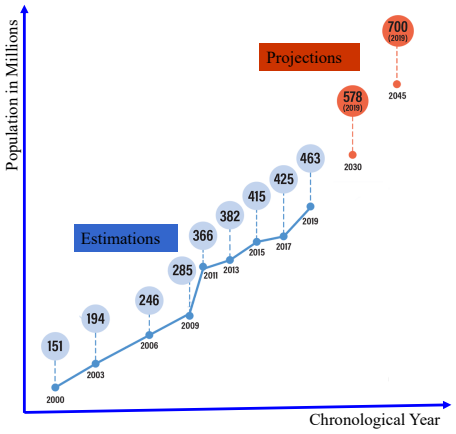

Fig. 2: Global Trends of Diabetes [3].

about their glucose profile. It is essential to track the blood glucose values in daily life for avoiding the long term complication of DM. The control of glycemic profile for diabetes persons lead to reduce in other associated risk factors such as high systolic, diastolic blood pressure and cardiovascular disease such as lipid profile. DM may lead to failure of heart & kidney and may lead to blindness. It mainly affects the people of Type-1 Diabetes patient because they find difficult to control the blood sugar due to inadequate generation of insulin. Moreover, most common people are of type 2 diabetes cases where the limited insulin is produced by body.

B. Need of Continuous Glucose Measurement

The blood glucose measurement may be possible through invasive, minimal invasive and non-invasive techniques. The invasive approach is not used for frequent/Continuous Glucose Measurement (CGM) whereas non-invasive is ideal for CGM where blood glucose is measured without any blood pricking. CGM allows to have proper blood glucose analysis over the period and also helps to provide personalized health solution for better glucose control. The proper control of glycemic profile is achieved with appropriate diet plan with recurrent glucose monitoring. The database of the glucose values could be stored at cloud for long time observation. The CGM is helpful to observe the glucose value for longer duration and is also useful to get the average blood glucose for 3 months which is equal to glycated hemoglobin (HbA1c) test.

III. Overview of Glucose-Level Measurement

Typically the glucose measurement is carried out either laboratory based technique or home based monitoring. They are invasive in nature which require the blood pricking and it helps to measure the glucose value at that point of time only. It is inconvenient to measure the body glucose by taking the blood samples frequently. Hence, there would every chance of change in glycemic profile remains unnoticed which may lead to have improper insulin dosage for type 1 diabetes patients.

The noninvasive CGM would provide reliable, convenient, and cost effective solution for glucose measurement. They noninvasive methods helps to measure the glucose from interstitial fluid (ISF). There were several non-invasive efforts to have glucose measurement from skin surface, saliva, sweat, tears and retina [4]. Some of the selected work are defined in Table I [2]. However, there is still research is going on for precision, reliability and higher sensitivity. These would useful to measure glucose multiple times in a day to have the necessary preventive steps for hypoglycemia and hyperglycemia patients. These could be really helpful for the dietitian and healthcare professionals to propose the better diet plan as per patient's glucose fluctuation [1], [5], [6].

IV. Smart Healthcare for Glucose Management

The smart healthcare for diabetes requires CGM, intelligent mechanism for glycemic profile management and quality point of care mechanism. Internet-of-Medical-Things (IoMT) would provide the remote connection for glucose-insulin control with closed loop system (See Figure 3) [5]. The serum glucose monitoring would allow the accurate glucose monitoring for appropriate control mechanism [7]. The integrated IoMT framework with continuous serum glucose measurement and insulin pump is helpful to provide proper insulin delivery with closed-loop automated insulin control.

A. Glucose Measurement Consumer Products

Various types of non-invasive Glucometers are available in the market for invasive, non-invasive

TABLE I: Qualitative comparison of various noninvasive glucose-level monitoring methods [2].

Technique	Advantages	Disadvantages
Near Infra-Red (NIR)	Easier & Accurate Measurement	High Scattering
Mid Infra-Red (MIR)	Low scattering & Strong absorption	Limited light penetration
Thermal Emission Spectroscopy	Low sensitive towards scattering	Sensitivities for temperature and substance thickness
Raman Spectroscopy	High specificity & less sensitivity	Susceptible for noise interference
Photo Acoustic	Effective and not harmful for the tissue	Vulnerable towards acoustic noise, temperature, motion
Polarimetry	Stable method for glucose measurement	sensitive for the change in pH and temperature
Reverse Iontophoresis	Highly accurate as it measure glucose from interstitial fluid	Difficult to have proper calibration
Fluorescence	Good sensitivity because of distinctive optical properties	Sensitive for local pH and/or oxygen
Bio impedance spectroscopy	Best for CGM	Large calibration requirement
Millimetre and Microwave Sensing	Deep skin penetration depth	Poor selectivity
Optical Coherence Tomography	High SNR	Glucose value may change as per skin and motion Suffers from tissue inhomogeneity
Surface Plasma Resonance	high sensitivity	Bulky and Long calibration process
Time of flight and THz Time domain Spectroscopy	strong absorption and dispersion	longer time for measurement
Metabolic Heat Conformation	Easy captured physiological parameters for glucose prediction	Sensitive towards temperature & sweat
Electromagnetic Sensing	low-cost and No risk	Low selectivity
Ultrasound Technology	Long penetration below the skin or tissue	costly and not useful for CGM
Sonophoresis	Reliable & no side-effect to skin	Error prone due to environmental parameters

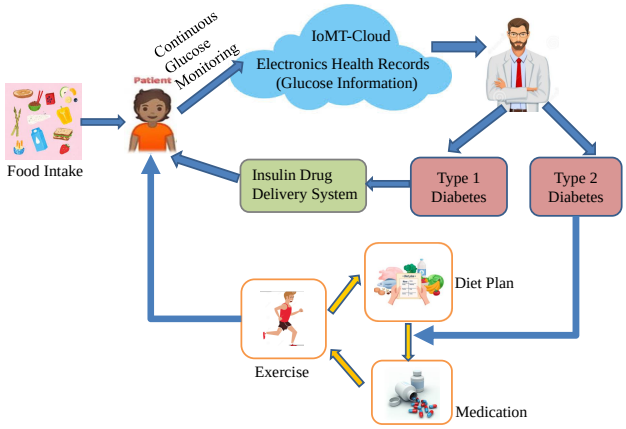

Fig. 3: Diabetes Management through Glucose Monitoring.

and minimal invasive types. The CGM approaches are either semi-invasive or non-invasive in nature. The implantable devices are minimal (or semi) invasive type based on bio-sensing glucose principal. Smart contact lenses, sweat patches and Glucowatch are wearable types of sensors based on spectroscopic in nature. The wearable devices would provide frequent glucose measurement with state of art solutions. The comparative study of few selected non-invasive glucose measurement consumer products have been reported in Table II.

B. Glucose Sensing Approaches and Its Control

The development of glucose-insulin control model includes various parameters such as glucose absorption rate, renal excretion rate, glucose consumption, net hepatic balance etc. The glucose control model has been designed to balance the glycemic profile of diabetic person [5]. There are few mathematical models were developed for insulin drug delivery for type-2 diabetes patients. One of most popular FDA approved simulator ”Uva/Pendova” was used with virtual patients database of type-1 diabetes [8]. The glucose control model was explored for glucose tolerance test using Hovorka maximum model with non-diabetic persons [9]. The model of T1DM patient with frequent glucose measurement was developed for

TABLE II: Noninvasive Glucose Measurement Consumer products [2].

Company	Device	Technology	Object
Abott Ltd.	Free Style Libre	Glucose oxidase method	Fore-arm skin
Cygus Inc.	GlucoWatch G2 Biographer	Reverse iontophoresis	Wrist skin
C8 Medisensors	C8 Medisensor Glucose detector	Raman Spectroscopy	Fingertip skin
Tech4Life Enterprises	Non invasive glucometer	Infra red Spectroscopy	Finger
C8 Medisensor	Non invasive glucose monitor	Raman Spectroscopy	Fore arm skin
MediWise Ltd.	Glucowise	Radio Wave Spectroscopy	Forefinger skin/Earlobe
Nemaura Medical	SugarBeat	Reverse iontophoresis	Arm,Leg and adbomen
Pendragon Medical	Pendra	Impedance Spectroscopy	Wrist Skin
CNOGA	Combo glucometer	Tissue photography analysis	Finger
OrSense Ltd.	OrSense NBM-200G	Occlusion Spectroscopy	Fingertip skin
Integrity Applications	Glucotrack	Combination of Electromagnetic, ultrasonic and Thermal	Earlobe tissue

insulin delivery using meal detection concept. An intelligent PID controller was designed to examine the glycemic profile in absense of diet schedule for type-1 diabetic patients.

V. Research Gaps and Open Challenges

Most of the noninvasive glucose measurement approaches are not validated on real subjects. They work on artificial samples and fail to perform for human samples. These have issues of glucose measurement for all range glucose reading specifically hyperglycemia and hypoglycemia cases. The environmental parameters and subject parameters such as temperature, blood pressure and humidity have not been considered for noninvasive glucose measurement. The available solutions are costly and is not suitable for reliable glucose measurement in smart healthcare. The glucometer with IoMT framework has not been explored much for insulin delivery mechanism. The glucose-insulin mathematical model for automatic insulin delivery has not addressed properly with continuous monitoring concept. The security and privacy issues of IoT network and glucose and insulin pump is really an important open issue which is very critical because security vulnerabilities of medical devices and personalized health records could lead serious health complicacies of the patients [6].

VI. Conclusions and Future Research

There are several glucose measurement techniques have been proposed in past with proof of concept which was able to estimate blood glucose in non-invasive manner. However, they are unable to provide precise measurement in full glucose range and was not provide cost effective solution hence they are not popular as consumer product around the world. The NIR based optical detection is a potential candidate which could mitigate all the drawbacks. The precision in estimation could be improved using multi-model approaches and also with consideration of environmental parameters. The device should provide the effective solution for CGM to all kinds of people.

Acknowledgment

A longer version of this work is available at [2].

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TABLE III: A comparative perspective of a selected state of art approaches for glucose measurement [2].

Work	Technology	Object	Remarks
Monte-Moreno 2011 [10]	Photoplethysmography (PPG)	Finger	The features extracted using machine learning model to estimate blood glucose along with blood pressure
Song et al. 2015 [11]	Impedance Spectroscopy and multi-wavelength NIR Spectroscopy	Left Handed Wrist Hand	The indirect dielectric characteristics of surrounding blood tissue helps to measure glucose with optical scattering using Multi-model approach
Kino et al. 2016 [12]	Mid-Infrared Attenuated Total Reflection (ATR)	Oral Muscosa inner lips	The blood glucose is measured using multi-reflection prism with higher sensitivity and flat contact surface
Chen et al. 2018 [13]	Optical Coherence Tomography	Fingertip	Uses optical rotation angle and depolarization index concept where angle increases with glucose increase and depolarization index decreases
Singh et al. 2019 [14]	Transmission Spectroscopy	Saliva	Glucose detection by changing the pH level using color strips
Rachim et al. 2019 [15]	Visible NIR	Wrist	Biosensor for pulsation of arterial blood volume is used to estimate blood glucose.
Xiao et al. 2020 [16]	Microwave sensing	Earlobe	Improved Neural Network model and Hybrid Optimization (INNHO) is developed where ultra-band microwave is used to find the glucose concentration with S-parameter relation using back prorogation neural network.
Jain et al. 2020 [1]	NIR Spectroscopy	Fingertip	Short NIR waves with absorption and reflectance for glucose measurement

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