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# A Review of Noninvasive Techniques for Body Fluid Analysis

**Ammu Kripalal & Dr. Sukeshkumar A**

Assistant Professor, Vidya Academy of Science and Technology, Technical Campus
Associate Professor, Rajiv Gandhi Institute of Development Studies, Trivandrum

***Abstract:***

*Non invasive body fluid analysis is still an area to be further explored in the Biomedical engineering. As technology improves diagnostic techniques should be in such a way to provide a better and easy life for the mankind but the demanding of frequent piercing for the body fluid analysis is an awkward situation in this technologically advanced era. This review is to summarize the already explored methods for non invasive body fluid analysis. The principle behind each technology is described in this paper. The accuracy of existing technologies are not meeting the real expectations making it scope for a further study and development in this area. Hence the updated review of the previous works is mandatory.*

***Key words***

Noninvasive body fluid analysis, blood glucose analysis.

## 1. Introduction

Analysis of blood components remain an unpleasant experience to everyone attempted. It is always preferable to do the analysis in a more comfortable way "A non invasive method" which eliminates the usage of sharp objects, the main cause of all discomforts. This is mostly faced by patients suffering from diabetic, thyroid disorders and other hormonal imbalances as they need to do continuous monitoring of blood glucose, thyroid stimulating hormones and other blood components. This continuous monitoring is demanding frequent piercing.

The present lifestyle and food habits are in a way which will result a huge rise in the number of such patients. With the developing technologies it is high time to avoid such unpleasant experiences and to develop a non invasive body fluid monitoring technology which will provide a better understanding of body fluids and making the life healthier in the coming years.

## 2. Noninvasive glucose monitoring technologies

### 1. Near IR spectroscopy

This method makes use of light in the 750-2500 nm spectrum. The light which is allowed to penetrate 100 mm of depth in the tissues is partially transmitted, absorbed and reflected due to the interaction with the body tissue components. The glucose concentration will make corresponding changes to the absorption coefficients and the intensity of light gets scattered by the tissues. This can be analyzed with the aid of suitable optical detectors. Decreased absorption of glucose in this spectrum range results in a very weak spectral information.The spectral bands of some other components dominates in the 700 to 2500nm hence making it tough to distinguish the glucose spectral bands.

### 2.Mid IR spectroscopy

Mid IR spectroscopy also encorporates the same technology of near IR spectroscopy but with higher wavelength light than near IR ie 2500nm to 25000nm region.Due to the higher wavelength scattering is less and absorption is increased hence making the glucose spectrum more distinguishable.One of the additional

bottleneck is the poor penetration of this wavelength signal.

**Some of the disclosed early (before 1990) IR absorption methods are listed below.**

1. In PCT application WO No.81/00622 an IR absorption apparatus is mentioned in which absorption spectra of urine and serum are measured at two different wavelengths,one being at which the absorption of substance under the interest takesplace and the other wavelength at which the absorption of the substance is independent.Band used-10.54µm - 10.64µm and 19.13µm-19.17µm.Light source used-laser

2. In swiss Pat.No. CH-612.271 another method using an attenuated reflection prism is disclosed.In this method IR beams is passed through an ATR prism directly placed agaist lips or tongue.As the refractive index of the prism being larger than the medium of sample,beam experiences a total reflection.Attenuation of beam is according to the glucose concentration. This attenuation is processed into glucose determining data.

3. U.S Pat.No.3958560 published in 1976 discloses the use of contact lens sensor having IR source and detectors.When IR radiation is applied light is transmitted through cornea to the detector.The detected signal is processed to find the changes happened to the IR radiation which will indicate the concentration of glucose.

4. In U.S Pat,No.4 655225 published in 1987 discloses a method in which reflected or backscattered light from the body is collected along with a reference wavelength for the background absorption spectrum thus trying to eliminate the problem of dominating background spectrum.Used band 1000-2500nm.

## 3. Raman spectroscopy

Raman spectroscopy has enabled faster easier spectral analysis.This technology makes use of the band 200-1800 per cm.In this range glucose is easily distinguishable from other components spectra.In this technology laser light is used to introduce molecular vibrations.The scattering happens to light due to this vibration is analysed ,this will give the concentration of that vibrating molecule.This method provides less overlaping spectra.Traditional Raman spectroscopy is extended to terahetz Raman or low frequency raman.There is no reports available regarding the use of tera hertz raman in non invasive analysis.

## 4. Optical coherence tomography

This technique is making use of low coherence light from a super luminescent diode sourse.Light back scattered from tissuue is combined with light returned from the reference arm of interferometer and the resulting interferometric signal is detected using a photodetector.The delay correlation between the back scattered light in the sample arm and the reflected light in the reference arm is measured.OCT gave the concentration of glucose in intestitial fluid.This dualmode (depth 1mm and tangential) os tissue scanning gives images of 2D quality with good resolution property. But the value measured by OCT is similar to light scattering techniques mentoioned before. More over this technique is not claiming any avantages result than the exisiting light scattering techniques.

## 5. Fluroscence technology

This technology is making use of the property that human tissues genewrate fluroscence when exicited by lights at certain frequencies.It is said that if it was experimented with glucose solution the fluroscence intencity was dependent upon glucose concentration.The results are in terms of intensity as well as deccay time. Fluroscence of tears can also be measured as they reflect concetration in blood.

## 6. Bioimpedence spectroscopy

This technique is done by measuring the resistance of tissues to electric current flow. It is understood that increase in concentration of glucose leads to a decrease in sodium ion and increase in pottasium ion.This enable changes in potential and results a variationin electric flow. Measuring the

resistance to flow will give the gllucose concentration.

## 7. Electro magnetic sensing

This technology is done by taking the advantage of dielectric parameters of blood. Electro magnetic coupling between two inductors is used in electro magnetci sensing. The glucose concentration in blood will alter the di electri parameters of blood. Thus extracting the di electric parameteres will lead to an estimation of glucose concetration.The main bottle neck is that blood di electri depends not only on glucose but also on several other parameters.Temperatuire dependency of this technology is also a matter need to be taken into account.The frequiency used for the method is 2.4-2.9Mhz.

## 8. Polarisation technique

This technique is making use of the property of Chiral molecules in blood to change the polarisation of light bya particular angle which will indicate the concentration of such molecules which made this change in angle. In this method it is possible ot make use of the visible light whivh is easliy available. The main limiting factor in this method is the scattering due ot body tissues will depolarise the light hence leading to a false estimation.The preferred location for this technique is eye as it is haivng very less scattering.

## 9. Ocular spectroscopy

In this technology contact lens with hydrogel is used.In a reference paper it is stated that hydrogel wafer is with boric acid derivatives which will make bones with glucose.This will deppend on the concentration of glucose in tears.If a laser light is allowed to fall on the lens and the change in wave length of the reflected light depending on the bonding can be measured.Usage of contact lens is the difficult part in this technique.

## 10. Ultra sound technology

With the help of laser if the body fluid is excited thermal expansion takes place.Because of the energy of thermal expansion acoustic waves releases .This release of acoustic wave is a measure of required content in the fluid.This technique is named as photo acoustic spectroscopy.there is a chance to have interference from some other bilogical compounds,temperature change ,pressure change .

## 11. Chemical sensing in exhaled breath

This work depends on exhaled breath senses. Using an array of senses diabetics can simply be identified by examining the concentration of level of biomarker (Asetone) gases in exhaled breath.Variation in breath asetone can be manipulated as the concentration of glucose in blood.

## 12. Reverse Iontophoresis technology

This method is by makling the flow of sodium and chloride ion by applying an electri potential between as anode and cathode kept on skin surface.along with the movement of sodium ions uncharged molecules like gluocose are carried by electro osmosis.Thus transported glucose across the skin can be collected at the cathode using a traditional glucose sensor.Hnece this technology cannot be termed as non ivasive but minimally invasive.

## 13. Fluid harvesting

With the help fo laser light or utlra sounds some micro pores are created on human skin and thus making intestitial fluid migrate through the micro pores and allowing the direct mesurement of glucose using traditional glucose montoring techniques.Since there is a need for creating micro pores this technique can also be stated as minimally invasive.if it is utilising light(laser) then the technique is termed as Biophotonic techniques and it is called sonophoresius when it is done with ultra sound.

## 14. Thermal spectroscopy

The method is based on discovery that natural IR emission can happen from human body. It was found

that emission from glucose coould be dected from tympanic membrane.

### 15. Temperature modulated Localised reflectance

With the change in temperature refractive index of tissues also varies and this will make changes in scattering phenomena of light in scatter or reflection based technologies.in this method glucose concentration is estimated with some temperature modulated reflected signals.

### 16. Hair test mineral analysis

Hair test mineral analysis (HTMA) can be considered as a noninvasive method for the analysis of mineral content.HTMA has several advantages than serum blood test.By the analysis of zinc through HTMA can reveal the insulin glucose balance of body indirectly as zinc is involved in the production storage and secretion of insulin.

## 3. Non invasive glucose meters

There are various companies researching on this non invasive glucose meters. Companies are trying to introduce blood less glucose meters to the market in the near future. Some of the research or work by the companies is mentioned here:

### 1.Grove instruments -Bloodless glucose meter

Grove instruments latest research is a battery operated non invasive glucose meter. They used near infra red spectroscopy to measure the blood glucose. They claim that using this optical technology blood glucose can be measured in less than 20 seconds

### 2.Eco Therapeutics-Symphony tCGM

Eco Therapeutics developed the symphony tCGM Biosensor that monitors the blood glucose level. It uses a thersdermal sensor. This will transmit the blood glucose level to a remote monitor .It also provides alerts (audible and visual) if there is an unexpected rate of change of blood glucose.

### 3. OrSense Bloodless glucose meter

OrSense monitors blood glucose level using Occlusion spectroscopy Technology. It uses a ring shaped sensor which applies gentle pressure on the fingers in order to occlude blood flow.

### 4. Cnoga Medical Ltd-Non invasive glucose meter

Cnoga medical ltd a start up in Israel developed a non invasive glucose meters that uses optical sensors to track the skin color change. This technology has got approval from FDA (United States Food and Drug Administration) for other applications.This device is available in Europe but requires some more clinical trials.

### 5. Arriva Bloodless Glucose meter.

Arriva Medical an Alere Company has developed a glucose meter which uses interstitial fluid measurements. This meter doesn't require finger pricks but still requires some small blood sample. This meter cannot be considered as completely non invasive.

### 6. The non invasive Gluco-Track.

Gluco Track model DF-F glucose meter make use of different technologies like ultrasonic, electromagnetic and thermal to measure blood glucose .The battery operated device consists of a transmitter, receiver, processor and a personal ear clip which attaches to the earlobe.

### 7.GluCall Non invasive glucose meter

GluCall blood glucose monitoring meters are worn like a wrist watch and can store the continuous blood glucose reading via skin. They work on the principle of Iontophoresis.

### 8. C8 Medisensors

C8 Medicsensors uses the optical method to monitor the blood glucose non invasively .It uses

Bluetooth technology to connect Smartphone to C8 Medisensors.

### 9. Gluco(M)

Gluco(M) is a non invasive glucose monitoring meter which works on the principle of measuring glucose through bodily fluids using an electric flow. It can also store data and its previous readings.

### 10. Abbott-FreeStyle Libre

It is a new glucose monitoring concept by Abbott .it provides better data than continuous glucose monitoring (CGM). The readings are taken by scanning a sensor instead of pricking a finger. It provides a graph of how glucose levels are varying.

### 11. GlucoWise

GlucoWise measures blood glucose at the blood capillary level. GlucoWise transmit low power radio waves to the body such as earlobe or between the forefinger and thumb. The radio waves are received bya receiver that collects the data about the characteristics of blood.

### 12. Dexcom G5 CGM

Dexcom G5 is a continuous glucose monitoring system .its small sensors measure blood sugar level underneath the skin. The data can be send to remote device.

### 13. SugarBEAT®

SugarBEAT® is expected to be available in the market by mid of 2017.It is minimally invasive and offers real time glucose measurement. Connected to a small electronic sensor the SugarBEAT® patch can take measurement form the body's interstitial fluid from the skin

## 4. Conclusion

This paper presents the various techniques of noninvasive bodyfluid analysis and also mentions about the disclosed noninvasive bodyfluid monitoring meters.But it is understood that any of the above mentioned devices and many other meters which were proposed ten years back like Diasensor® BICO Inc. and SugarTrac, Life track Systems Inc. using near infrared spectroscopy,Pendra® ,Pendragon Medical Ltd. and Glucoband® Calisto Medical Inc. using Impedence spectroscopy have not yet arrived with fruitfull and accurate results. These understandings are providing ample scope for much more exploration inorder to implement an effective and accurate non invasive technique.

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