Glucose Monitoring

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Glucose monitoring is essential to control diabetes and avoid long-term complications. Diabetics suffer on a daily basis with the traditional glucose monitors currently in use, which are invasive, painful, and cost-intensive. Therefore, the demand for non-invasive, painless, economical, and reliable approaches to monitor glucose levels is increasing.

Keywords: diabetes ; glucose ; non-invasive ; optics ; spectroscopy ; infrared ; Raman ; terahertz ; fluorescent ; photoacoustic

1. Introduction

As no cure has been found for diabetes yet, regular monitoring and control of glucose concentration in the blood is the only solution to optimize the lifestyle of diabetics and prevent them from experiencing severe complications [1]. Various glucose monitoring techniques have been developed recently. These technologies are classified based on their mechanism as invasive (IN), minimally invasive (MI), and non-invasive (NI). **Figure 1** maps most of the glucose-sensing technologies [2][3][4].

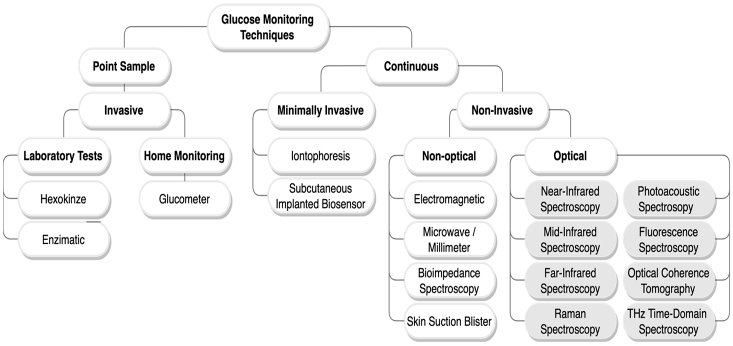

Figure 1. Glucose monitoring techniques classification chart. Herein, only the non-invasive optical methods with a grey background are reviewed.

The invasive methods are the gold standard and the most broadly employed for blood glucose measurements [2]. Conventional devices currently in use, such as the self-monitoring blood glucose (SMBG) devices, so-called glucometer, and the continuous-glucose-monitoring (CGM) devices, follow the invasive and minimally invasive methods, respectively [5][6][7]. They are both based on electrochemical biosensors. The SMBG sensors require drawing a drop of blood to be tested through finger-pricking, while the CGM sensors are based on a needle implanted subcutaneously. Although these techniques give high accuracy measurements, they have multiple drawbacks for being painful, promoting infection, using cost-intensive blood glucose testing supplies, and deterioration of accuracy over time. Accordingly, scientists have conducted studies on non-invasive glucose sensors that are reliable, fast, painless, and cost-effective for the convenience of patients to monitor their glucose level frequently; hence, reducing diabetes complications. Various types of non-invasive techniques have been proposed during the last two decades, including non-optical and optical techniques as illustrated in **Figure 1**. Among the non-invasive glucose monitoring techniques, the optical methods give the best measurements [8]. Optical technologies such as near-infrared, mid-infrared, or Raman spectroscopy have great selectivity for glucose sensing given the complexity of the blood/tissue properties. Furthermore, the targeted biological tissue in optical approaches is less exposed to irritation [8].

2. Comparison of Current Non-Invasive Optical Techniques

Despite the substantial development of glucose monitoring technologies, there is still a tremendous need for high accuracy, easy-to-use, and affordable techniques that can replace standard devices. The proposed methods face many challenges, such as system stability, sensitivity, specificity, and calibration. Among the non-invasive optical techniques discussed, PAS, fluorescence, and specifically NIR spectroscopy were the potential candidates for achieving the goal of obtaining optimal glucose sensing. **Table 1** summarizes various non-invasive optical techniques for blood glucose concertation estimation.

Table 1. Comparison of various non-invasive optical glucose sensing techniques [8][9][10][11][12][13][14][15].

Technology	Wavelength	Selectivity	Measurement Site	Merits	Drawbacks
NIR spectroscopy	**750–2500 nm**	**Good**	**Ear lobe, finger, forearm, cheek, lip mucosa, oral mucosa, and tongue**	-Low-cost -Easy to implement	-Glucose heterogeneous distributions affect accuracy. -Interferences by other chemical compounds
MIR spectroscopy	**2500–10,000 nm**	**Good, superior to NIR**	**Finger, skin, and oral mucosa**	-Quite accurate -Lightweight -Scattering is low	-Poor skin penetration depth -Expensive -High water abortion
FIR spectroscopy	**10–1000 μm**	**Good**	**ISF**	-Scattering is lower than NIR and MIR -Individual daily calibration is not required	-Difficulty in identifying other molecules than water due to strong water absorption
Raman spectroscopy	**Visible light**	**Excellent**	**Eye, human skin**	-Low sensitivity to water and temperature changes -Great specificity -Low-cost	-Lack of stability in the laser wavelength and intensity -Spectrum acquisition takes time
THz-TDS	**30 μm to 3 mm**	**Good**	**ISF**	-Not affected by background noise.	-Long measuring time -Low spatial and depth resolution
Fluorescence	**Ultraviolet light, visible light**	**Excellent**	**Tears, human skin**	-High sensitivity and specificity to glucose concentration -Not affected by light scattering	-Sensitive to changes in pH and oxygen levels -Susceptible to toxicity problems
PA spectroscopy	**Ultraviolet light, NIR, and MIR**	**Good**	**Finger, forearm, and aqueous humor**	-Unsusceptible to water distortion -Not affected by scattered particles	-Low signal-to-noise ratio -Affected by temperature changes, motion, pulsation, and acoustic noise

3. Conclusions

Over the past decades, there has been great interest in developing innovative methods of measuring blood glucose levels without the necessity for blood samples. Several non-invasive optical glucose measurement techniques have been introduced. These technologies still need improvement in order to meet the regulations to be released in the market. A summarized comparison was made on the advantages, disadvantages, and other specifications of the non-invasive optical methods. Although these methods show great potential, some challenges are facing them including sensitivity, stability, specificity, biological factors, and calibration issues. Therefore, an enhancement of these non-invasive optical methods is required to surmount their limitations and hopefully replace the conventional methods currently in use.

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