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Review

Current development in non-invasive glucose monitoring

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Abstract

Painless control of blood glycemic levels could improve life quality of diabetes patients, enabling a better regulation of hyper- and hypoglycaemia episodes and thereby avoiding physiological complications. Although research groups have been trying for decades to separate non-invasive glucose information from interference compounds, none of the available commercial devices offers enough precision to replace lancet approaches.Many reviews have already been published on this topic, but the great amount of information available and the fast development of technologies require a continuous update in the research status. Besides the description of current in-vivo methods and the analysis of devices available commercially, one also explains treatment algorithms useful for multivariate analysis.

Keywords: Blood glucose monitoring; Diabetes mellitus; Non-invasive measurement; Transcutaneous sensors

Contents

1. Introduction

Glucose is the main carrier of energy in the human organism, with recommended levels between 4.9 mmol/L and 6.9 mmol/L in whole or capillary blood [1]. The sugar concentration in blood is controlled by the islet cells in the pancreas through the production of the glucagon hormone This hormone raises the level of blood sugar, and insulin, responsible for helping the body to change glucose into

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energy [2]. World wide, 150 million people suffer from disturbances in the endocrine metabolic regulation, called diabetes. Approximately 10% of cases result from insulin deficiency (type 1), which often starts during childhood and requires giving this hormone usually many times a day. Insulin resistance (type 2) corresponds to 90%, occurring more in people over 40 years old. Additional cases also are related to pregnancy, where 2% of women have gestational diabetes [3]. Any kind of diabetes can be dangerous because long-term excess of glucose (hyperglycemia) can cause blindness, damaged nerves and kidneys (renal failure), or even increase the risk of heart diseases, strokes, and birth defects. Low levels (hypoglycemia), however, can result in confusion, coma and even death [4].

Fig. 1 shows different classifications of blood glucose monitoring: invasive, minimally invasive and non-invasive. Fully invasive systems can be either bedside clinical devices or self-monitoring meters. Bedside monitors are suitable for intensive care units and use sensors with an accuracy of approximately 1% [5]. Such systems allow continuous monitoring, therefore increasing the amount of clinical information.

Systems which puncture the skin are still standard techniques for home monitoring (6–7% accuracy) reading glucose concentrations through electrochemical, colorimetric or optical disposable strips for finger-prick blood samples [6]. Efforts have been made in order to reduce the level of invasiveness by decreasing the blood sample volume to a few microlitres, and measuring areas of the body less sensitive to pain than fingertips, such as the forearm, upper arm, or thigh. Drawbacks of such systems area lack of control during sleeping or manual activities, undiscovered episodes of hyper- or hypoglycaemia, risks of infection, nerve damage and the discomfort of pricking the finger several times a day, which painful activity often leads to non-compliance [7].

Minimally invasive measurements sample the interstitial fluid (ISF) with subcutaneous sensors [8]. Even in this method the discomfort causes difficulties to the patient's therapy. Therefore, research groups are working to develop non-invasive glucose control devices [9]. Unfortunately, so far there are no reports or patents which show that such non-invasive methods have the same accuracy as invasive procedures.

Although there are many complete reviews of painless blood glucose techniques [10–12], the great volume of recent research results in this field requires a constant update. Therefore, besides the description of important measurement approaches, this work also shows available devices on the market with their technologies and measurement sites. Because absorption spectroscopy is a widely sensing method, the wavelengths used in non-invasive tests will also be described. In addition, algorithms for multivariate analysis will be presented, showing that recent improvements in technologies and multiparameter measurements may still enable improved accuracy of the predictions.

2. Non-invasive glucose monitoring

One option to painless intermittent glucose control is the substitution of blood with other fluids that could contain glucose, like saliva, urine, sweat or tears [13,14]. But continuous monitoring could only be accomplished through direct

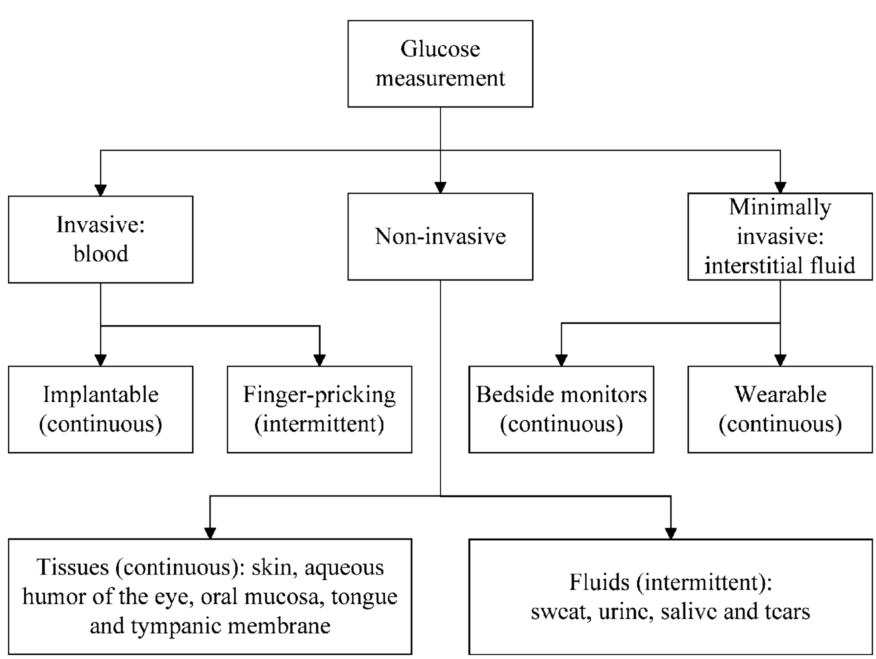

Fig. 1. Overview of technologies for non-invasive blood glucose control.