Noninvasive Blood Glucose Monitoring with Optical Coherence Tomography

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Abstract
In recent years, continuous glucose monitoring (CGM), a noninvasive and accurate measurement of blood sugar, has been developed. Although the traditional finger-prick method is accurate, it is not suitable for multiple daily use because it is very painful and the test strips are expensive. Although minimally invasive and noninvasive CGM systems have been introduced, they are quite expensive and require blood to be drawn from a fingertip. Given the prevalence of diabetes in low- and middle-income countries, there is an urgent need for accessible, noninvasive blood glucose monitoring devices. This article briefly reviews noninvasive blood glucose monitoring technology and related research. The communication media are optical, transdermal and enzymatic. This present study evaluates the system in an experimental form for blood glucose measurement are discussed. The review concludes with key points and insights for the future development of diabetes testing.
Keywords: Noninvasive Blood Glucose, Optical Coherence Tomography, Diabetes

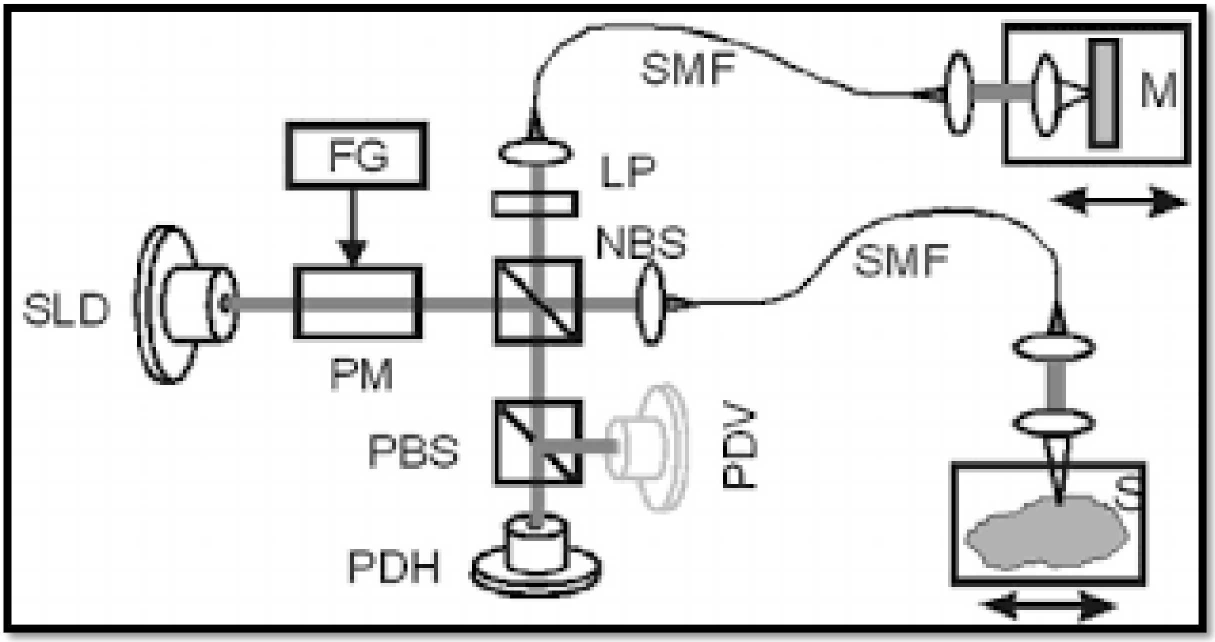
Introduction

Glycemic control of people with diabetes is considered the foundation of their care. Outcome assessments are used to evaluate treatment outcomes and recommend changes in diet, exercise, and medications to achieve optimal diabetes control. Currently, the most commonly used method of self-monitoring blood glucose (SMBG) involves the chemical analysis of blood collected from a finger or forehead device to determine blood glucose concentration. Although SMBG has revolutionized diabetes management, the discomfort and inconvenience of this invasive procedure often hinders its effectiveness and quality of control. These disadvantages limit the number of blood glucose tests that diabetics can perform, which can lead to poor control. Continuous technology that can continuously monitor blood sugar levels with accuracy equal to or better than existing blood glucose meters can improve blood sugar monitoring.

Over the past few years, many research groups and companies have made efforts to develop biosensors for noninvasive blood glucose measurement. Various optical methods have been proposed to achieve this goal. These techniques include polarimetry, Raman spectroscopy, near-infrared (NIR) absorption and scattering, and photoacoustics. Although promising, these methods have limitations related to low sensitivity and accuracy, and are not specific for measuring glucose at physiologically relevant levels.

In this study, researchers tested a new optical coherence tomography (OCT) technology for noninvasive blood glucose measurement in a clinical study on healthy volunteers. OCT technology was first developed by Fujimoto et al. in 1991 and has since been widely used in diagnosis and treatment. The OCT system uses a low-coherence light interferometer (coherence length: lc = 10–15μm), a movable mirror arm, a standard arm, and a photodetector to measure the interference signal. The light backscattered from the tissue combines with the light returned by the interferometer using the arm, resulting in a reflected signal that is detected by the photodetector. Signal interference is only effectively produced in the wavelength range of light; The mirror in the movable interferometer arm allows scanning to a depth of ~10 μm in tissue. The addition of a second mirror to the sample arm allows the light beam to be scanned across the tissue. Therefore, the new OCT technology has a unique depth and lateral scanning capability to obtain good two-dimensional (2D) images.

According to the Beer-Lambert law,light attenuation inside tissues is exponential. The slope of this exponential attenuation is proportional to the totalattenuation coefficient of ballistic photons ($\mu_t=\mu_s+\mu_a$, where μ_s is the scattering and $\mu_a$is the absorption coefficients, respectively). Because $\mu_a << \mu_s$ for tissues in the NIR, the exponential attenuation is proportional to thescattering coefficient. Only ballistic photons backscattered to the OCT systemcontribute to the OCT image; therefore,by analyzing the exponential profile oflight attenuation detected by the OCTsystem, one can obtain information on tissue scattering properties.



Source: Jiao et al (2005)

Figure 1: Experimental Setup, superluminescent diode

Tissue scattering properties arehighly dependent on the ratio of the refractive index of scattering centers (cell membranes, cellular components, andprotein aggregates), ns, to the refractiveindex of the interstitial fluid (ISF), n_{ISF}: Raising the tissue glucose concentrationincreases nISF by 1.52 x 10^{-5} per each 10mg/dl, decreases the scattering coefficient (μ_s) of tissues, and decreases therefractive index mismatch:

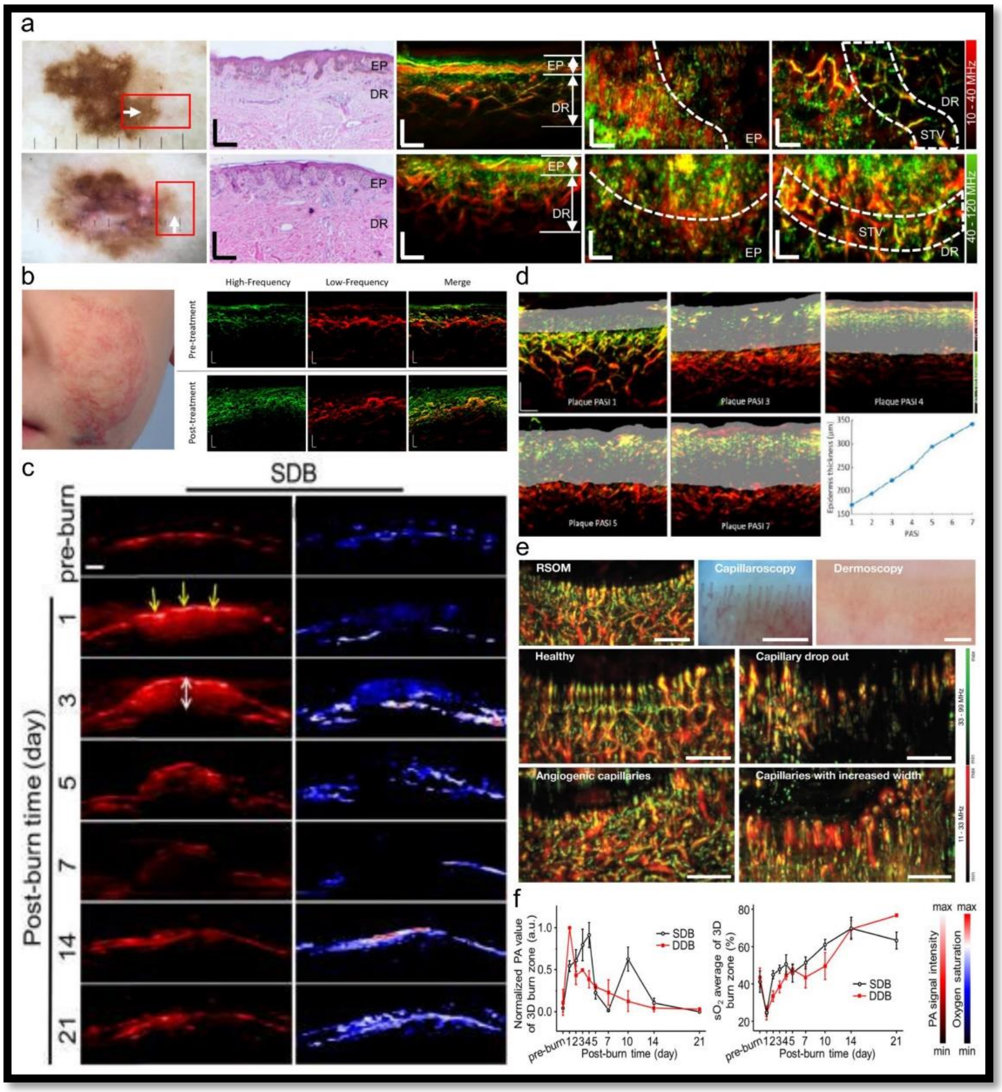
According to the Beer-Lambert law, the attenuation of light in tissue is exponential. The slope of the exponential decay is proportional to the total attenuation coefficient of the ballistic photon ($\mu_t=\mu_s+\mu_a$, where μ_s is the scattering and $\mu_a$is the absorption coefficients, respectively). Since μa << μs for tissues in the NIR, the exponential decay is proportional to the scattering coefficient. Only ballistic photons scattered back to the OCT system have an effect on the OCT image; therefore, the information of the fractured tissue can be obtained by analyzing the distribution of light reflected from the OCT system. , ns, is the refractive index (ISF) of the interstitial fluid, nISF: Increase the tissue glucose concentration by increasing nISF by 1.52 x 10^{-5} per 10 mg/dl, reduce the soft tissue scattering coefficient (μ_s), and reduce the refractive index mismatch.

$$\Delta n \equiv \frac{n_s}{n_{1SF} + 1.52\, X \frac{10^{-5}}{10mg}/dl}$$

Changes in glucose in fractured tissue can be detected with OCT systems. The high resolution of OCT technology and the measurement depth of up to 1 mm allow the measurement of tissue breakdown in the dermal layer. For example, human skin has three main layers: the dead keratinized squamous layer (epidermal stratum corneum), the spiny cell layer (epidermis) and the dermal connective tissue, which is the only layer with good blood. Since the glucose concentration in the ISF is very close to the blood glucose concentration, glucose changes can be expected in the OCT signal seen from the dermal region of the skin. The high resolution and integrated optical light in OCT technology can see the tissue directly in the dermis without the OCT red affecting the other tissue layers. In contrast, the signal obtained by optical techniques such as diffuse reflectance spectroscopy is the integration of the entire photon path involving many tissues. the accuracy of measuring the coefficient of variation in tissue samples and the relationship between glucose concentration changes and animal OCT signal slope. In this study, we tested the feasibility of using the OCT system for noninvasive blood glucose monitoring in healthy individuals.

Experimental setup

In this study, researcher used an OCT systemwith a wavelength of 1,300 nm, outputpower of~0.3 mW, and in-depth andlateral resolution of 10 and 14 µm, respectively. Schematics of our experimental setup used in this study is depicted in below given figure. Light from the OCT system wasdelivered to the skin using a single-modeoptical fiber. A specially designed optical fiber holder was attached to thesubject's forearm using medical double-sided adhesive tape. Lateral and in-depth scanning was~5 and 1 mm,respectively. In-depth scans were averaged five to seven times. Single lateralscans were accomplished every 15–25 s.The operation of the OCT scanner wascompletely automated and controlled bya portable personal computer (PC). Altogether,~500 2-D OCT images were obtained in each experiment and stored inthe PC for further processing.



Source: Zafar et al (2024)

Figure 2: Typical OCT image obtained from skin of a Sample Unit

In this study, the researchers used an OCT system with a wavelength of 1,300 nm, an output power of~0.3 mW, and depth and resolution of 10 and 14 µm, respectively. The schematic diagram of the experimental setup used in this study is shown below. The same type of optical fiber is used to transmit light from the OCT system to the skin. A specially designed fiber optic stent is fixed to the patient's forehead using double-sided medical tape. Lateral and depth scans are 5 mm and 1 mm, respectively. Deep scans are performed on average five to seven times. A single test is performed every 15–25 seconds. The operation of the OCT scanner is fully automatic and controlled by a portable computer (PC). A total of 500 2D OCT images were acquired for each experiment and stored on a PC for further processing.

Sample of Study

A total of 15 healthy subjects (8 males and 7 females), aged 18 years and older (mean age 49 years), participated in 18 clinical studies. Subjects were healthy, drug-naive, and of mixed backgrounds. This study was approved by the Institutional Review Board of the University of Texas Medical Branch. All subjects signed informed consent.

Experimental Process

Starting from 08:00 in the morning, all volunteers underwent oral glucose tolerance test (OGTT) using 75 g glucose. (Duration = 0) After overnight fasting. The duration of each test was 190 - 200 minutes (10 - 20 minutes for baseline data and 180 minutes after glucose administration). OCT images were obtained from the left forearm. During the measurement, volunteers were asked to remain calm and not to eat or drink to reduce the amount of artificial energy. Two subjects were excluded from the study because they could not complete the test without intervention. During the experiment, all blood tests were continued on the right side of the forehead at 5 or 15-minute intervals using a catheter inserted into a vein. Measure blood sugar concentration in a plasma glucometer.

Results

During this trial, a total of 426 blood glucose measurements were made via blood chemistry tests, and 8,437 OCT images and corresponding markers were recorded and processed. The figure below shows a typical 2D OCT image obtained from a volunteer's skin and the corresponding OCT signal shown on a logarithmic scale as a function of depth. Large layers are easily distinguished and labeled on both the image and the OCT markers. The figure below shows two representative individuals from our study. The slope of the OCT signal is plotted on the calibration curve. Blood glucose concentration was measured every 15 and 5 min throughout the experiment. The OCT signal decreases and increases with changes in blood glucose concentration. Slopes were calculated at depths of 550 - 600 μm and 380 - 500 μm. The slope of one volunteer changed significantly by 17% as glucose varied from 90 to 140 mg/dl, while the slope for another volunteer changed by 15% as glucose varied from 100 to 200 mg/dl. The relationship between the OCT signal and the measured blood glucose concentration is shown in the following figure, respectively. Blood glucose concentration was measured 12 and 35 times over 3 h and included the OCT signal slope. In these experiments, OCT slope changes of 2% and 1.2% were observed at 10 mg/dL The correlation coefficients were 0.8 and 0.95, respectively, and the calculated P values were >1% and 0.1%, respectively. Data from another volunteer (not shown) showed a mean change in OCT slope of 1.9% at 10 mg/dL.

Conclusions

This study is the study of healthy volunteers to show a correlation between unmeasured OCT signal slope changes during the OGTT period and normal blood glucose content. In these studies, the mean slope change per 10 mg/dl was 1.9%. The results of these tests are similar to those obtained in our animal studies. The main advantages of OCT technology for blood glucose monitoring compared to previous optical methods are:

a. high resolution,
b. consistent detection of radiographs.

This unique product allows optical tissues to be measured with accuracy, precision and resolution. The changes in the OCT slope in glucose obtained in our experiment are due to the following: 1) OCT technology has the ability to monitor the optical texture of the specific process in the tissue without creating unwanted traces from other layers; . Clinical studies in normal subjects have shown a relationship between the OCT signal slope and the blood glucose concentration at a depth of 200 - 600 μm during OGTT. Measurements performed on the skin and upper dermis revealed no or weak changes in the OCT signal slope as a function of blood glucose concentration (data not shown). This is most likely due to the glucose concentration gradient from the dermal microvessels to the stratum corneum. Therefore, the sensitivity and accuracy of OCT in measuring blood glucose concentration are highest in the subdermal region. The differences in the content of the data obtained in these three experiments are mainly due to the artificial devices and tissue inhomogeneities. Our next research will focus on developing new methods for OCT image registration, averaging and signal processing to improve the accuracy of blood glucose monitoring using the old urine OCT technology. Physical and environmental differences can change tissue scattering and thus the slope of the OCT signal. Our future studies will evaluate the effects of glucose as an osmotic agent that can change tissue mass, tissue heterogeneity, artifacts, temperature drift, blood pressure and heart rate of the OCT signal slope. Our preliminary investigation of the effects of other dietary osmolytes on the specificity of OCT-based glucose sensors shows that the maximum change in the partition coefficient caused by these substances is lower than that of products made from sugar. Although OCT systems require calibration using invasive glucose sensors, they will reduce the number of invasive measurements and provide continuous monitoring of blood glucose concentration. The results of this study suggest that OCT technology can be noninvasive, instantaneous, and can monitor blood glucose concentrations of subjects during the OGTT. Additional studies with a variety of subjects, including diabetic patients, are planned to test these preliminary results.

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