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Rapid and nondestructive measurement of glucose in a skin tissue phantom by near-infrared spectroscopy

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ABSTRACT

Diabetes is one of the most serious metabolic diseases worldwide, and frequent monitoring of blood glucose is an essential part of diabetic management. However, a significant drawback of current monitoring methods was destructive and time-consuming. To meet this need, this study was to develop a method for rapid and noninvasive blood glucose assay in a skin tissue phantom by Near-Infrared spectroscopy (NIRS) and Raman spectroscopy. With partial least-squares (PLS) regression method, the multivariate calibration models of NIRS were generated and optimized individually by considering spectral region, spectral pretreatment methods and latent variables (LVs). The optimal NIR model was established with root mean square error of cross-validation (RMSECV) of 0.114, root mean square error of validation (RMSEP) of 0.061, correlation coefficient (*R*) of 0.9933, and residual predictive deviation (RPD) of 12.2, respectively. The validation results demonstrated that NIRS could be applied for rapid and noninvasive blood glucose assay.

1. Introduction

As declared by World Health Organization (WHO), Diabetes has become one of the most serious global metabolic diseases due to its rapidly increasing incidence. As well known, Diabetes was a disorder in the control of the blood-glucose level as the pancreas of diabetes underproduces or does not produce insulin for cells to absorb blood glucose [1,2]. According to the study of WHO, more than 3.4 million deaths were caused by unregulated blood glucose concentration every year, as persistent high blood glucose concentration may lead to complications including heart disease, stroke, kidney failure, blindness and nerve damage [1–4]. The Diabetes Care and Complications Trial (DCCT) demonstrated that frequent monitoring of blood glucose is an essential part of diabetic management for avoiding diabetic complications and having good and healthy life [1].

However, a significant drawback of current blood glucose monitoring methods was destructive and time-consuming that requires a finger prick for blood sample and complex analysis process. The frequent blood glucose monitoring can induce substantial pain to the patient and increase the risk of infection, as well as incurring significant cost due to the number of test strips required [4–6]. For this purpose, a reliable rad and nondestructive analysis methodology for blood glucose monitoring is highly desired. Most non-invasive systems had been investigated extensively for many years by using various spectroscopy and optic methods. Among the various optical spectroscopic techniques for continuous glucose monitoring, NIRS and Raman spectroscopy have received the most attention [1,5,6].

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Table 1
The distribution of 100 samples.

		N	Range (mg ml^{-1})	Mean (mg ml^{-1})
Intralipid concentration	1.9%	25	0.1025 ~ 4.939	2.521
	2.0%	50	0.1018 ~ 5.053	2.577
	2.1%	25	0.2030 ~ 5.075	2.639
Total set		100	0.1018 ~ 5.075	2.579
Calibration set		82	0.1018 ~ 5.075	2.561
Validation set		18	0.2953 ~ 4.858	2.658

Among the investigated technologies, NIRS with chemometrics has proven to be one of the most promising techniques for clinical blood glucose assay on the basis of its measurement in tissues in the range of 1–100 mm of depths, with a decrease in penetration depth for increasing wavelength values [7–9]. However, the main holdback is that, the relatively low absorbance of glucose and the relatively high overlapping and strong absorption of interferences such as water, protein and fats, and the variations of physiological status and measurement conditions at different time [2,5,10]. As Raman scattering of water is weak, and Raman spectroscopy usually provides more distinct and sensitive absorption, and less overlapped spectra, Raman spectroscopy has the advantage to provide rich information about the molecular structure of the sample. However, it has been relatively less exploited due to several drawbacks, such as weak scattering signals, matrix background interference, fluorescence from biological samples, the instability of the laser intensity, and the photo-thermal damage to samples [11–13].

Intralipid solution is usually used as a scattering model of the biological tissue. A 2% Intralipid solution provides the similar spectral characteristics of skin tissue for the skin tissue phantom in our research [10,14]. In this paper, NIRS and Raman spectroscopy were used to realize a rapid and noninvasive glucose assay in a skin tissue phantom. The PLS Calibration models are generated and optimized individually by considering spectral region, spectral pretreatment methods and LVs. Due to the noise and matrix background interference cannot be eliminated simultaneously [10–13,15], Raman spectroscopy is inappropriate to describe the underlying data structure for glucose noninvasive measurement. However NIR model was efficient and successful for the determination of glucose. The results show the NIR model established is robust, accurate and repeatable.

2. Experimental

2.1. Samples and reagents

A 2% Intralipid solution was used as the skin tissue phantom. As show in Table 1, The affection of the variation of the individual skin properties was simulated by three different concentration of Intralipid solution (1.9%, 2.0% and 2.1% Intralipid solution), and 100 samples was got with glucose concentration range of 0.1 ~ 5.0 mg ml^{-1} (10 ~ 500 mg dl^{-1}) to cover the variation range of blood glucose in normal man and the diabites.

2.2. Data collection and processing

The NIR spectra were recorded by a Fourier transform near infrared (FT-NIR) spectrometer (Bruker Optick, Ettlingen, Germany) equipped with a PbS detector and a fiber optic probe. The spectra were collected with OPUS spectral acquisition and processing software (Bruker Optick, Ettlingen, Germany). As shown in Fig. 1, each spectrum was obtained in an average of 32 scans at a resolution of 8 cm^{-1} over the wavelength range of 12,000 cm^{-1} to 4000 cm^{-1}, and air absorbance was recorded firstly as the reference standard.

As shown in Fig. 1, The Raman spectra in the 3200 ~ 90 cm^{-1} range were acquired with a Metage OPAL Portable Raman System (ProRoman L-785, EVWAVE Optronics. lnc) equipped with thermoelectrically controlled CCD detector (cooled to -50°C), stander laser excitation at 785 nm diode laser and a fiber optic probe. The spectra for each sample were recorded in an average of 10 scans at a resolution of 4 cm^{-1} by the eFTIR spectral acquisition and processing software (Essential FTIR V3.00.047 from Operant LLC Licensed to MTG).

The NIR and Raman calibration models were established respectively by the OPUS software. The optimal spectral region, spectral pretreatment methods and LVs were assessed according to the model parameters of RMSECV, RPD, *R* and RMSEP. The best model should have the highest *R* and RPD with lowest RMSECV and RMSEP. The statistical test was analyzed by SPSS (the SPSS for windows version 12.0, SPSS Inc., Chicago, USA).

3. Results and discussion

3.1. Division of calibration and validation set

As shown in Table 1 and Fig. 1, the total data set consisted of 100 samples, then this set was split into the calibration set and the validation set. In order to develop a robust NIR model, the content range of the calibration set must be wide enough to cover the range of the validation set, so the samples with maximum and minimum concentrations were selected in the calibration set, then 18