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Quantitative evaluation of human's hepatic functional reserve by indicator pharmacokinetics method

Xiaofeng Zhang[a,b,*], Guangda Liu[a], Guozhong Xu[b], Rundong Zhou[a], Yutong Zha[a]

[a] College of Instrumentation and Electrical Engineering, Jilin University, Changchun 130061, China
[b] School of Life Science and Technology, Changchun University of Science and Technology, Changchun 130022, China

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ABSTRACT

After liver surgery, the most common cause of death is hepatic failure; therefore, the preoperative evaluation of hepatic functional reserves is of great significance. Thus, a method has been applied to an optical measurement from the artery in a patient's finger. The indicator indocyanine green (ICG) was intravenously injected. Afterwards, the optical signals which were picked up from the sensor were measured with the signal conditioning module, and then collected to the PC by Lab-VIEW acquisition system. The ICG spectral signal is analyzed by the methods of delta absorption model, so the dilution and excretion curve of ICG concentration can be attained. The parameters reflecting the hepatic functional reserves can be calculated, including the mean transit time, the ICG 15 min retention rate, the EHBF (effective hepatic blood flow). Compared with the clinical "gold standard" methods of blood sampling to measure these two parameters by clinical controlled trials, 30 sets of data were obtained. About the 15 min retention rate of ICG, the two groups of data have fine linear relationship (coefficient of determination $R^2 = 0.9738$, $P < 0.001$); and the EHBF, the coefficient of determination R^2, $P < 0.001$. Through the analysis of the test data by Bland–Altman method, the two group results are consistent. Therefore, a simple and minimal invasive method for liver functional reserves was realized more practicability in clinic and relatively precision.

1. Introduction

The liver has a remarkable capacity to carry out a wide variety of synthetic, storage, excretory, and metabolic activities [1]. Timely and accurate assessment of liver function is critically important for treating liver disease and many other diseases. The traditional clinical method of detecting liver function is a static test including bilirubin (TBIL), albumin (ALB), cholinesterase (CHE), and the prothrombin time (PT). The Child–Pugh scoring system uses all of these routine biochemical examinations combined with clinical signs to evaluate liver function [2,3]. Unfortunately, the predictive value of the Child score for liver resections has been shown to be quite variable. An accurate and noninvasive dynamic measurement of the hepatic functional reserve is the best method of liver function and cardiovascular assessment. The noninvasive measurement method described might be applicable to clinical applications in which an invasive method is undesirable or inconvenient [4].

After indocyanine green (ICG) was introduced by Fox et al. in 1957, it soon came into general use for recording dye dilution curves as a diagnostic aid for blood volume determination, cardiac output, or hepatic function. ICG is a water-soluble and relatively unstable 755-kDa tricarbocyanine dye. When ICG is added to blood plasma, it rapidly binds to proteins in the serum. The principal advantages leading to rapid acceptance of the dye are the presence of an absorption maximum near the isobestic point of hemoglobin and oxy-hemoglobin around 804 nm, confinement to the vascular compartment by binding to plasma proteins, very low toxicity, and rapid excretion, almost exclusively into bile [5]. ICG was found to be a safe, accurate, and precise tracer for liver function measurements [6].

In 2002, Aoyagi studied a new modification called pulse spectrophotometry based on pulse oximetry, which is a reliable noninvasive method to measure arterial blood oxygen saturation [7]. In 2003, this method was used to measure the ICG concentration in an artery [8]. From then on, the application of non-invasive ICG retention test is more and more used in clinical practice. The ICG-r15 test is an effective tool for assessment of portal hypertension

* Corresponding author at: College of Instrumentation and Electrical Engineering, Jilin University. The No. 938 of western democratic street, Changchun 130061, China. Tel.: +86 13504321580.
E-mail address: zhangxf@cust.edu.cn (X. Zhang).

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in patients with compensated cirrhosis [9]. ICG15 retention test is more effective to predict and avoid liver failure for patients with hepatolithiasis after hepatectomy than Child–Pugh scoring system. It may also decrease the morbidity and mortality rate through strict selection, thus increasing operative safety [10]. And indocyanine green (ICG) clearance test is also used for assessment of hepatic function of patients before cardiac surgery [11].

Here, we design a new optical device to measure the hepatic blood flow parameters noninvasively and continuously by. The system mainly consists of the acquisition of spectral signals, the measurement of the ICG concentration spectral curve, and the determination of the hepatic function parameters.

2. Design of the measurement device

The entire system mainly consists of lower and upper computer parts. The main component of the lower computer part (Fig. 1) is a high-performance ARM processor system; another contains the three-wavelength sensor probe and data acquisition electronics. Data viewing and storage is achieved via an NI acquisition card connected to a personal computer.

The measurement of the laser-diode drive circuit is time-sharing driven by two square waves with mutually inverted phases. The sensor contains three center wavelengths of 660, 805, and 940 nm from a light-emitting-diode source (Fig. 2), and the optical receiver wavelength range is 600–1000 nm. The principle of the sensor probe is shown in Fig. 3.

The signal acquisition system includes the signal separation circuit, signal amplifier, and NI data acquisition card PCI6228. In the signal separation circuit, mixed signals with wavelengths of 660, 805, and 940 nm can be separated in order to calculate the absorbance ratio and to prepare for the measurement of oxygen saturation and the dye concentration graph. In the signal amplifier, weak signals obtained from the finger-clip sensor are filtered and amplified for the data acquisition card.

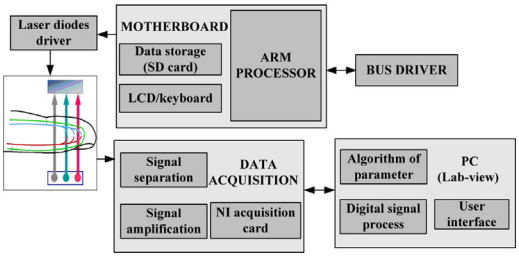

Fig. 1. It is the block diagram of the measurement system. It contains four modules, the three-wavelength sensor probe, high-performance ARM processor system, and data acquisition circuits; data processing and storage is achieved via the NI instrument.

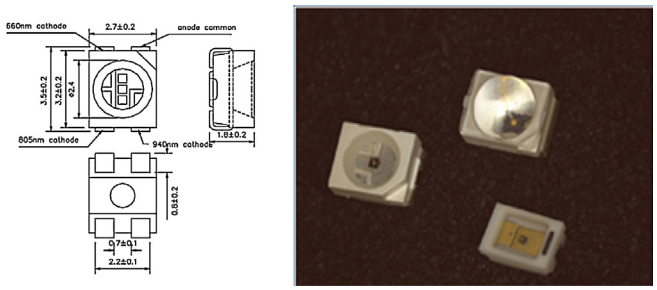

Fig. 2. Physical size and control diagram. The sensor contains three center wavelengths of 660, 805, and 940 nm from a light-emitting-diode source, and the optical receiver wavelength range is 600–1000 nm.

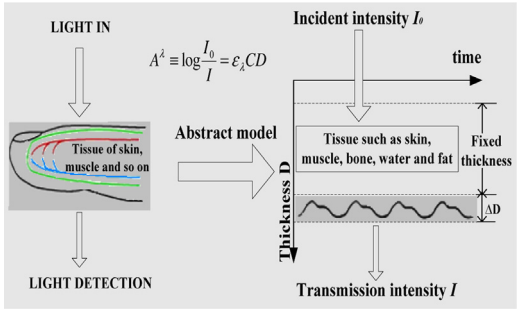

Fig. 3. Principle diagram of the sensor probe. According to the Lambert–Beer Law, the incident intensity and the transmission intensity have the relationship with the substances in the blood.

The upper computer part contains the mathematical algorithms for data preprocessing, digital filtering, and parameter calculation along with the user interface. They are achieved by using LabVIEW application software. In the LabVIEW software platform, spectrum signals are processed and analyzed in order to separate the dye concentration graph, and then, the parameters are calculated. The friendly human–computer interface is very easy to use.

3. Determination of the ICG concentration

3.1. Principle

The ICG concentration dilution procedure should assess liver function. Therefore, determination of the ICG concentration curve is equivalent to building a dilute model curve. It is based on the intensity fluctuations caused by the pulse wave. Thus, the method makes use of photoplethysmography with NIRS techniques for monitoring the ICG concentration in an artery.

It is well known that pulsatile changes in the blood volume in tissue can be observed by measuring the transmission or reflection of light. Therefore, this method is an indirect measurement technique based on the detection and analysis of the NIRS. Thus, a device that measures the hepatic functional reserve and cardiac hemodynamic parameters by the acquisition and analysis of near-infrared pulse dye signals is studied.

The spectral sensitivity range of 600–1300 nm is called the optical window in biological tissue. By the method, the major optical measuring materials are the hemoglobin and ICG. Among them, the ICG participated in blood circulation by intravenous injection. Before determination of the unknown ICG concentrations, the system must be calibrated by measuring two samples containing known ICG concentrations. Therefore, it is necessary to subtract the basal extinction at 940 nm (no ICG extinction) from the extinction at 805 nm (peak ICG extinction) in each sample (Fig. 4: The spectral characteristic curves of the hemoglobin and oxy-hemoglobin and

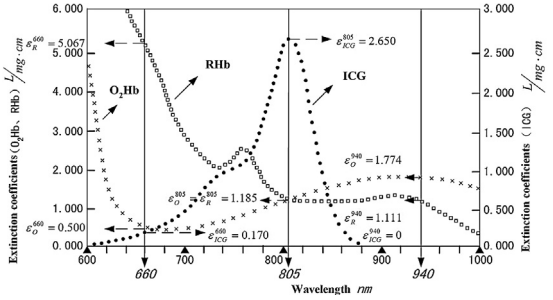

Fig. 4. Spectral characteristic curves of the hemoglobin and oxy-hemoglobin and the ICG. It is necessary to analyze the extinction coefficient quantitatively of the main material at each characteristic wavelength.