Original

Assessment of Photoplethysmography Method in Extraction of Hemoglobin Concentration

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ABSTRACT

Background: The importance of continuous monitoring along with rapid and accurate notification of changes in blood components such as hemoglobin concentration, especially in acute situations, encourages researchers to use non-invasive methods for measuring.

Objective: This study was aimed to investigate the correlation between hemoglobin concentration and photoplethysmogram (PPG) and the possibility of measuring it by an optical method.

Material and Methods: In this applied study, a PPG signal was simultaneously recorded at four different wavelengths for thirty subjects who were referred to the laboratory for a hemoglobin concentration test. After calibrating the special recording probe with a standard pulse oximeter system and applying the required preprocessing on the obtained signals, the peak-to-peak value of PPG signals was extracted. Finally, the correlation between the peak-to-peak value of the signal at a certain wavelength and hemoglobin concentration was analyzed using Spearman and Pearson correlation for determining the process of changes in the data.

Results: The results demonstrated that based on the normal distribution of data at 590 nm wavelength, there is a significantly negative correlation between a function of the signal peak slope and the hemoglobin concentration, with a Pearson coefficient of -0.787 ($p<0.01$). In addition, the investigation of rank correlation indicated a significantly negative correlation of -0.842 ($p<0.01$) using Spearman correlation analysis.

Conclusion: Considering the high correlation between hemoglobin concentration and PPG signal characteristics, optical methods can be used to develop a rapid, precise, clean and inexpensive method to measure hemoglobin concentration.

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Keywords

Hematologic Tests; Hemoglobinometry; Photoplethysmography; Correlation of Data

Introduction

Blood test is one of the most efficient ways to evaluate an individual's health. An increase or decrease in blood components can lead to different diseases and even death in some acute situations. One of the disadvantages of this method is that it is invasive, which causes not only unwanted problems for the patient, but also a long delay between blood sampling and learning the results. This delay in cases such as surgery, may jeopardize the life of the patient or lead to death

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due to untimely diagnosis. Hemoglobin is the most vital component of blood. Hemoglobin concentration in blood is an important parameter in evaluating the physiological conditions of an individual. Knowing the hemoglobin concentration, one can diagnose hyperemia or anemia. Anemia is a condition in which the hemoglobin concentration is lower than the defined level and results in a decrease in the oxygen-carrying ability of red blood cells. In most cases, the individual suffers from fatigue, weakness, drowsiness and may even face death [1]. One situation where the hemoglobin concentration should be measured is to diagnose the probability of hemorrhage after surgery. Currently, this is performed using invasive methods. First, blood sampling is performed and then the blood is analyzed to determine the hemoglobin concentration level. The disadvantage of this method is the long interval between blood sampling, its analysis and the results which prevents continuous monitoring of the patient in acute situations [1, 2].

The optical technique is one of the most important tools in non-invasive diagnosis of human blood components. It not only provides continuous monitoring, but also prevents possible infections from blood sampling. The light absorption of blood at visible wavelengths and close to infrared depends on hemoglobin and its derivatives and blood plasma, which mainly contains water. Pulsatile blood volume changes in tissue are measured using radiation and reflection of light on the tissue; this process is called photoplethysmography (PPG). The ratio between the peak-to-peak amplitude of the PPG signal at different wavelengths depends on the light absorption characteristics of human blood, thus gives appropriate information about blood components [2-4]. The absorption and scattering for hematocrit (volume of red blood cells in the blood) are other clinically important parameters influenced by the total concentration of hemoglobin [5-7].

The blood hematocrit has been measured using two wavelengths of near infrared ranges of 810 and 1300 nm in 1992 [8]. Later, from 2005 to 2009 according to this method, a lot of work was performed to determine the concentration of hemoglobin by Timm et al. [1, 3]. Doshi et al. did it with two red and infrared wavelengths in 2013 [2]. Kratil et al. determined the concentration of hemoglobin in the blood using 5 high wavelengths [6, 9]. The paramount importance of diagnosing blood components using non-invasive and optical methods leads to numerous international patents, including the diagnosis of hematocrit and hemoglobin with optical methods in the United States [10-12]. The initial reports of Aldrich et al. indicated that the relationship between the normalized PPG signal and the hemoglobin concentration is in the range of 905 nm wavelengths [10]. In addition it has been shown that the AC proportion of some visible lights to infrared wavelengths is dependent on the concentration of hemoglobin [11]. None of the mentioned research results were used clinically as a reliable method.

It is important to find reliable wavelength to have the highest correlation with hemoglobin concentration variation and evaluate it clinically. In the present research, when taking the blood sample, the PPG signal was recorded simultaneously at four different wavelengths; accordingly, the hemoglobin concentration was extracted, analyzed and compared with the blood sample data at laboratory. All the processes were performed offline in MATLAB.

Material and Methods

In this applied study, the subjects of this study were 30 individuals (6 male and 24 female) 15-65 years old. Each subject's PPG signal was recorded at four different wavelengths, infrared (950 nm), red (660 nm), orange (590 nm) and green (560 nm), while taking a blood sample at the laboratory. Signals were recorded at the laboratory using PowerLab system and special probe as seen in Figure 1. Sampling frequency in recording

Figure 1: PPG probe designed in this project for recording in four wavelengths

signals was 10 KHz. In order to compare the hemoglobin concentration obtained through direct optical method and by invasive method in the same laboratory conditions, the recording protocol was the same as for the standard hemoglobin test. The signals at the aforementioned wavelengths were recorded for 60 seconds while a blood sample was taken from the subject's opposite-hand index finger. Figure 2 shows the simultaneous recording of the PPG signal at each wavelength and taking of the blood sample at the laboratory.

The original signal Contatined data from different wavelengths in the form of time multiplex; therefore, separating them was necessary. Since PowerLab system did not have that ability and the signal recording probe had been made especially for this research (for synchronizing probe and PowerLab), three notification pulses were sent and then the PPG signals were recorded at each wavelength. However, before separation and to omit the unwanted noise on the main signal, the signal was passed through a band pass filter with a low cutoff frequency of 0.5 Hz and a high cutoff frequency of 20 Hz. Figure 3 depicts the

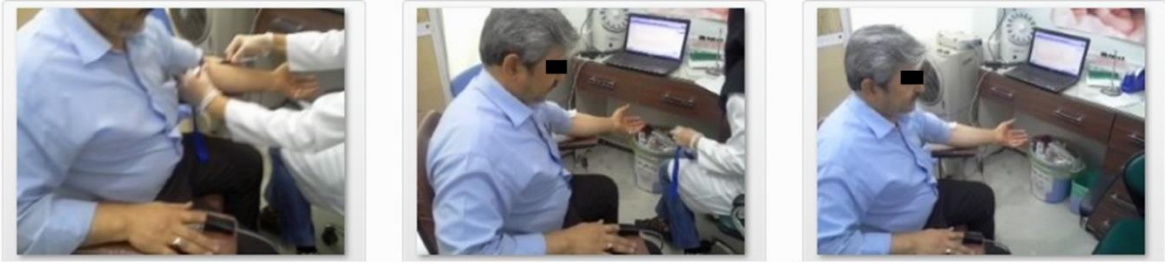

Figure 2: The blood sample and recording PPG signal from a subject simultaneously

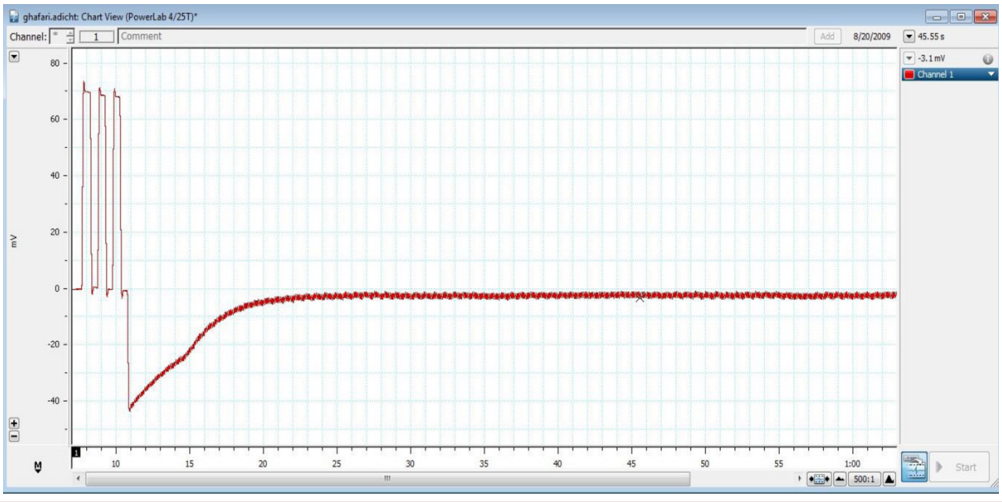

Figure 3: Original PPG signal saved in the Lab Chart software. Three synchronization pulses for the probe and the PowerLab are shown at the start of the recording.

multi-wavelength PPG signal of a subject that was recorded using the PowerLab system and Lab Chart software. At the beginning of the signal, three synchronization pulses between the probe and the PowerLab system are visible.

The frequency of the sampling signal was then reduced to 1 kHz. Afterwards, the PPG signals were separated based on certain time intervals that were previously designed by the software. For a simpler analysis and omission of negative values, the signals were standardized based on equation 1 and the minimum value for all signals was considered one.

$$X(t) = x(t) - \min(x(t)) + 1 \qquad (1)$$

To validate the results, blood oxygen saturation was calculated for 5 subjects using 2 infrared and red wavelengths, which was then calibrated with a standard pulse oximeter system in Pasteur Hospital, Mashhad. Figure 4 shows the PPG signal of a subject at different wavelengths.

The PPG signal is logarithmically proportional to light intensity: the maximum of light intensity occurs at peak systole and the minimum occurs when the volume of blood in the arteries is at its lowest value. Thus, equation 2 can be used to calculate the ratio of peak-to-peak PPG signal at different wavelengths [13]. Since the minimum value of the signals was set to one in the initial processing, it is just enough to calculate the maximum value of two signals in equation 2. Since the bioelectric signals are non-stationary, it is necessary to consider it as a stationary signal at a specified time interval. The calculation of relation peak-to-peak PPG signal was performed in windows with a length of 10 heartbeats [14].

$$R = \frac{\max(x_1)}{\min(x_1)} \Big/ \frac{\max(x_2)}{\min(x_2)} \qquad (2)$$

At next level, the correlation among the ratio peak-to-peak PPG signals in a special wavelength was investigated with hemoglobin concentration. In this research, the Pearson correlation coefficient was used to determine the criterion and the relation between two varia-

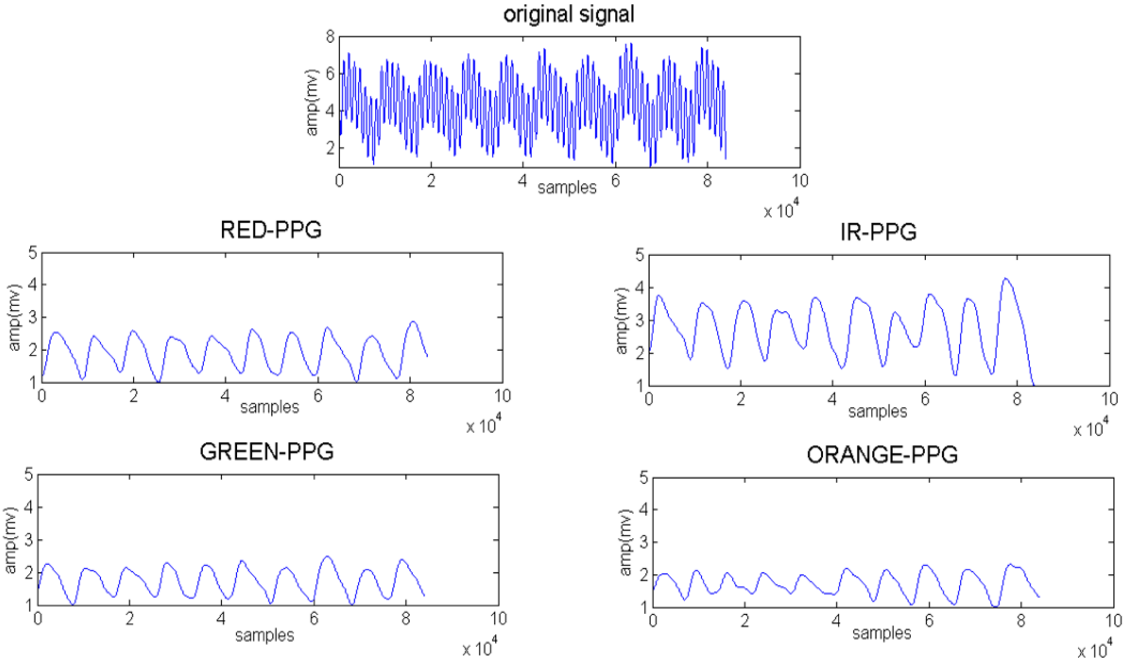

Figure 4: The original signal contains four different wavelengths-Red, Infrared, Green, Orange-in the form of time multiplex and four extracted PPG signals of it for a subject.

tions.

To use this ratio, the data must be normal. Before the correlation coefficient calculation, the Kolmogorov-Smirnov test was used to assess the normal distribution of data. In this test, the null hypothesis is the assumption of normal distribution of data and the other is the lack of normal distribution. In the Pearson correlation test, the relation between two quantified variables is reported between -1 and +1, and the positive and negative indicate the direction or indirection to the trend in two variables; if the absolute value is greater than zero, it shows the completion of this relationship. Also, the Spearman correlation was used to investigate the correlation between variation trends of two variables. It is a nonparametric test, so the normality of data is not needed. The null hypothesis is the uniformity distribution and independence of the data, while the opposed hypothesis is the increasing or decreasing trend of data where the Spearman correlation coefficient is reported between -1 and +1.

Results

Figure 5 shows the results of extracted hemoglobin concentration in blood laboratory. After calculating peak-to-peak PPG signal, the hemoglobin concentration had the highest correlation with the ratio of orange (590 nm) wavelength to infrared wavelength which was called H (equation 3). It should be noted that the wavelength was obtained from the combination of two green and red wavelengths. The ratio of peak-to-peak PPG signals in orange wavelength to infrared wavelength is shown in Figure 6 for all subjects.

$$H = \frac{\frac{AC_{590}}{DC_{590}}}{\frac{AC_{950}}{DC_{950}}} = \frac{\frac{\max(PPG_{590})}{\min(PPG_{590})}}{\frac{\max(PPG_{950})}{\min(PPG_{950})}} \quad (3)$$

F(H) was constructed as a function of H and the slope of primary and secondary PPG peaks. This function had shown a negative correlation with hemoglobin concentration. It means as the hemoglobin concentration decreases, F(H) increases. F(H) variations based on changes in blood hemoglobin concentration are shown in Figure 7. Table 1 shows the significantly negative correlation between F(H)

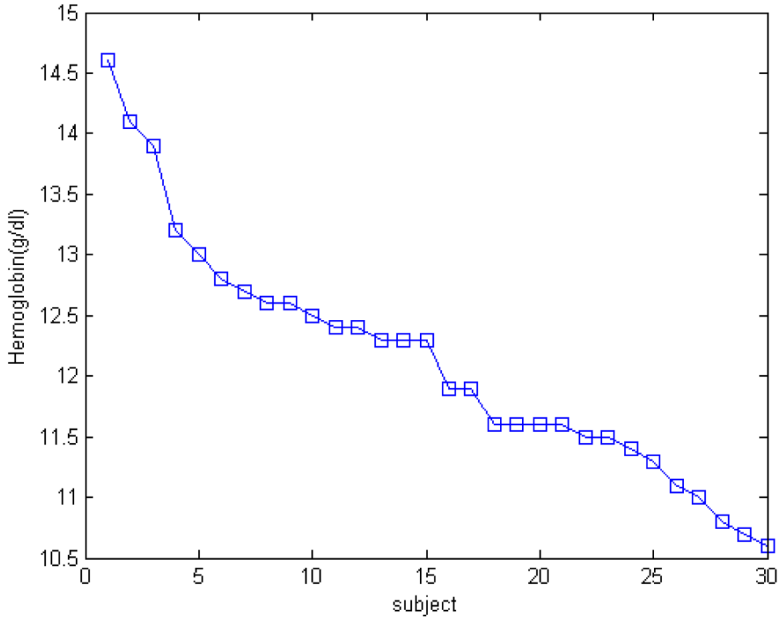

Figure 5: Measured hemoglobin concentration from blood sample for all subjects. Subjects are arranged in descending order in terms of hemoglobin concentration.

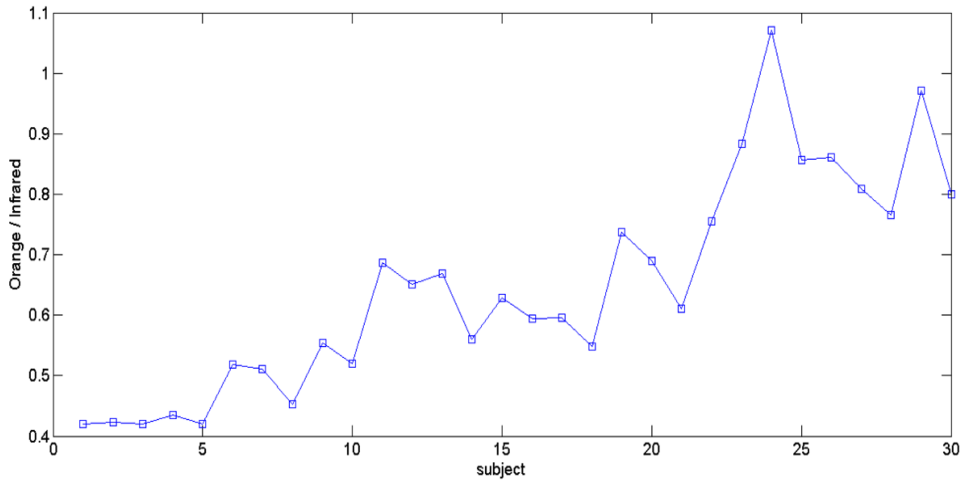

Figure 6: Peak-to-peak ratio of PPG signals in orange wavelength to infrared wavelength for all subjects.

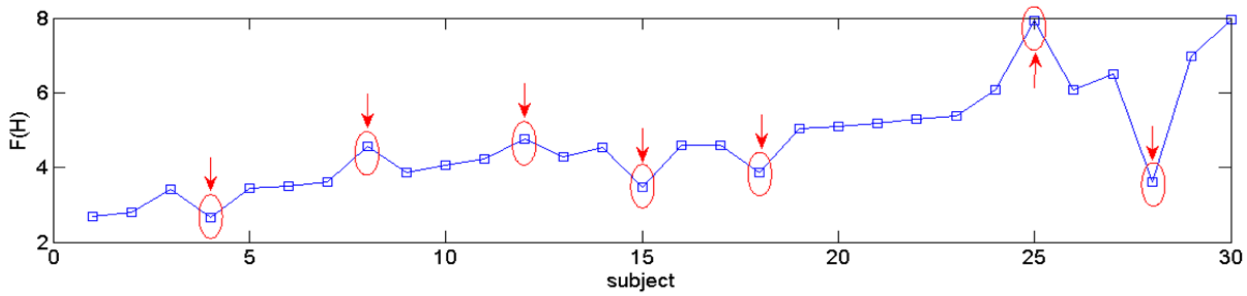

Figure 7: Variations in F(H) by reducing the amount of hemoglobin in subjects. Arrows are related to subjects that their data didn't match the other.

and the changes of hemoglobin concentration using non-parametric Spearman and parametric Pearson correlation analysis ($p<0.01$). These analyses were done using SPSS18 software. The normality of distribution of hemoglobin concentration and F(H) data were studied by Kolmogorov-Smirnov, and the results indicated normal distribution of data.

However, as seen in Figure 7, the data for seven subjects did not match others. Two of them were higher than 100, but the absolute value of the slope between the PPG peak and its secondary peak was higher than 2. It means that secondary PPG peak was very small and moved. Second decreased PPG peak and its displacement are related to increase the resistance and inertance along with decreased vascular compliance [15]. Figure 8 shows the PPG signal of 3 subjects who experienced unusual changes and a subject with F(H) changes that are proportional to the concentration of hemoglobin in the infrared wavelengths.

Discussion

Due to the significance and applicability of optical and non-invasive methods to detect human blood components, a relatively large amount of research has been conducted in this area. Blood hemoglobin concentration and hematocrit were measured using optical methods with different wavelengths from red [1-3] to infrared ranges as previously mentioned [6, 8-12]. A more advanced technique was used which compares a reflection of polarized light to a small vessel under the tongue [16]. In addition, a similar technique has been used based

Table 1: Correlation of F(H) and hemoglobin concentration by Pearson and Spearman Methods

Method	Subjects	Correlation Coefficient	p-value
Pearson	30	-0.787	0
Spearman	30	-0.842	0

on imaging of the finger [17]. These two techniques yielded acceptable results, but because of the limits, complexity of calculation and the expense of the required equipment, they are not justified.

Reflection and scattering of light are related to light wavelength, hemoglobin of red blood cells and oxygen in the bloodstream. In addition, the light transmission depends on wrapping artifacts and the deformation of red blood cells [18, 19]. Artifacts may also be related to pulsatile blood flow. Other errors in the data can be ascribed to abnormal hemoglobin concentrations and related diseases [20, 21].

In this study, the hemoglobin concentration of subjects was evaluated with peak-to-peak of their PPGs at different wavelengths and then compared to the laboratory outcomes. The results showed that the ratio of peak-to-peak PPG signal at a wavelength of 590 nm obtained by combining red and green wavelengths has a significantly negative correlation with the infrared wavelength (H). The peak-to-peak signal variation at two mentioned wavelengths in 7 subjects, and the results were not consistent with others. There were two major differences in their data which was related to the high heart rate and the reduction of amplitude and displacement of the second peak of PPG. The amplitude and displacement of the second peak of the signal are related to aging and associated with resistance, vascular compliance and inertance and it appeared as interference in the data. The result of this initial report is related to the start of this study in Islamic Azad University, Mashhad Branch. The results showed progress compared to other similar studies, particularly in correlation of selected wavelength with hemoglobin concentration. The authors hope to achieve high accuracy in extracting the hemoglobin concentration in non-invasive optical access, which is a clean, cheap and fast method for detecting the concentration of hemoglobin and has many clinical applications mentioned in the article.

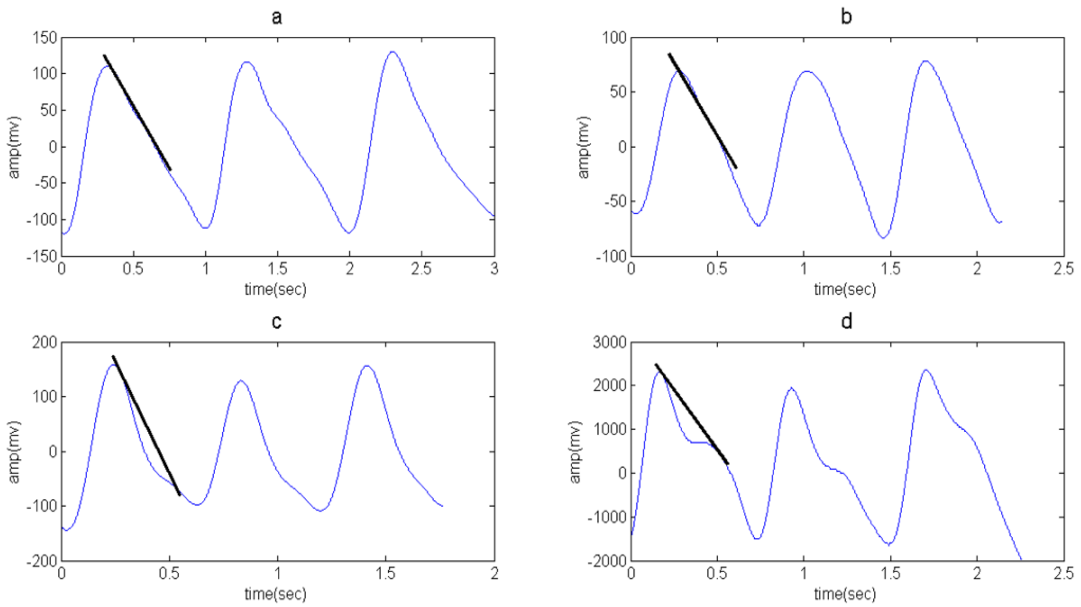

Figure 8: Infrared PPG signals in four subjects: (a-c) Amplitude and displacement of second peak is changed, lead in increasing slope; (d) a normal slope.

Conclusion

Measuring the hemoglobin concentration by non-invasive, rapid, precise, clean and inexpensive methods is important and useful in many clinical applications. The result of this study showed that according to the high and significant correlation between hemoglobin concentration and characteristics of PPG signal, selecting appropriate wavelengths and characteristics of optical signals can lead to precise extracting of hematologic parameters.

Acknowledgment

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Conflict of Interest

None

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