Point Spectroscopy System for Noncontact and Noninvasive Prediction of Transcutaneous Bilirubin Concentration

P.E. Ong, Audrey K.C Huong
Faculty of Electrical and Electronic Engineering, University Tun Hussein Onn Malaysia (UTHM)

Corresponding email: audrey@uthm.edu.my

Abstract. This paper presents the use of a point spectroscopy system to determine one’s transcutaneous bilirubin level using Modified Lambert Beer model and the developed fitting routine. This technique required a priori knowledge of extinction coefficient of bilirubin and hemoglobin components in the wavelength range of 440-500 nm for the prediction of the required parameter value. This work was conducted on different skin sites of six healthy Asians namely on the thenar region of the palm of their hand, back of the hand, posterior and anterior forearm. The obtained results revealed the lowest mean transcutaneous bilirubin concentration of 0.44±0.3 g/l predicted for palm site while the highest bilirubin level of 0.98±0.2 g/l was estimated for posterior forearm. These values were also compared with that presented in the literature. This study found considerably good consistency in the value predicted for different subjects especially at the thenar region of the palm. This work concluded that the proposed system and technique may be suitably served as an alternative means to noncontact and noninvasive measurement of one’s transcutaneous bilirubin level at palm site.

1. Introduction

Hyperbilirubinemia or more commonly known as Jaundice is a condition that occurred when liver is unable to remove the unwanted waste, which includes old red blood cells, from the system. The latter is then lead to an excessive bilirubin level in the bloodstream. The increase in the bilirubin level often resulted in the yellowish of white eyes and skin, which is used by medical practitioners as the prognosis for jaundice. The build-up of the bilirubin level in bloodstream usually caused nausea, fatigue and, in certain case, permanent brain damage due to the incomplete brain barrier[1]. The conventional clinical diagnosis of jaundice is based on invasive technique and laboratory test such as diazo and direct spectrophotometry technique. These laboratory tests required the drawing of blood, and the process is tedious and time consuming. This may sometimes lead to unnecessary blood loss and the risk of infection at the sampling site[2].

It must also be mentioned that several noninvasive systems for the prediction of transcutaneous bilirubin level (Tcb) are available in the market; these include Minolta, SpectRx and Bilichek[3-5]. There were, however, reported inconsistencies in the reported value depending on the skin properties of the subjects [6]. The predicted value was also reported to vary among individuals.

This work aims to investigate the consistency in the transcutaneous bilirubin concentration, $C_{bil}$ (in unit of g/l) value predicted using the Modified Lambert Beer model based on the reflected light intensity data collected using a point spectroscopy system. It is also the objective of this work to investigate variability in this value among different individuals and at different skin regions.
2. Materials and method

2.1. Reflectance spectroscopy and experimental procedure

The point reflectance spectroscopy system used in this study is shown in Figure 1. The employed light source in this research study is a white Light Emitting Diode (LED) (model no. SMD 5730), which emitted light with wavelengths in the range of 380-800 nm. The distance between light source and the skin sample is approximately 200 mm with the incident angle measured at 10° from normal. Meanwhile the distance between the skin sample and the tip of the probe of a commercial available spectrometer (USB4000-VIS-NIR, Ocean Optics Inc., Florida) is about 60 mm, the latter was placed at an angle of 30° from normal. The reflected light directed through an optical fiber before falling onto a built-in diffraction grating element mounted inside the spectrometer to produce an intensity spectrum. This intensity spectrum was detected by a line detector and signals were sent via Universal Serial Bus (USB) to a computer for further offline processing.

![Diagram of the point reflectance spectroscopy system](image)

**Figure 1.** Point reflectance spectroscopy system used for the measurement of the reflected signals.

In this study, experiments were conducted on six nonsmoking Asian volunteers; three males and three females (aged 24-27). All these volunteers gave their written consent to participate in the study, they declared no underlying illness such as kidney and liver diseases or malfunctions, and were not suffered from hepatitis. These volunteers were also asked about their caffeine (coffee and tea) consumption prior to the experiment as there were reports [7, 8] on the link between coffee and tea consumption and one’s bilirubin level. The measurement was taken from these volunteered at rest condition and three data were consecutively collected from each of the selected body regions, which include the thenar region of the palm, back of the hand, posterior and anterior forearm. These experiments were conducted in a dark room to prevent the detection of stray light.

The collected data were corrected by taking the white and dark reference data. The white reference was given by the signals reflected from Spectralon (Labsphere Inc.), while dark reference was by shutting the tip of the probe with a cap. Using these collected signals, the wavelength dependent light attenuation, $A_{corr}(\lambda)$, is calculated as:

$$A_{corr}(\lambda) = \log\left(\frac{I_w(\lambda) - I_s(\lambda)}{I_s(\lambda) - I_d(\lambda)}\right),$$

where $I_s$, $I_w$ and $I_d$ denote reflectance signals from the selected skin site, white and dark reference, respectively.
2.2. Modified Lambert Beer model and iterative fitting algorithm
In this work, Modified Lambert Beer (MLB) model shown in Equation (2) is used for the estimation of $C_{\text{bil}}$. This model was proposed by Pittman and Duling [9] to relate changes in light attenuation with the wavelength dependent total absorptivity, $\mu_aT$, of the medium.

$$A(\lambda) = G + \mu_a T d$$  \hspace{1cm} (2)

The symbol $G$ in Equation (2) denotes constant scattering dependent attenuation offset and $d$ is normally taken as the light pathlength. Even though absorptivity of chromophores such as melanin and dyshemoglobins is relatively dominant in the visible optical window, light absorption by these chromophores is only greatly enhanced for dark skinned and smoking individuals. For simplicity, this work assumed bilirubin (bil), oxyhemoglobin (OxyHB) and deoxyhemoglobin (dHb) are the only absorbers present. The wavelength dependent extinction coefficient of these absorbers is shown in Figure 2. The medium total absorptivity in Equation (2) is, therefore, given by the summation of absorptivity of bilirubin and hemoglobin as follows:

$$A(\lambda) = G + (\mu_{\text{bil}} + \mu_{\text{Hb}}) d$$  \hspace{1cm} (3)

where $\mu_{\text{bil}}$ and $\mu_{\text{Hb}}$ are the absorptivity of bilirubin and hemoglobin, respectively. The absorptivity is defined as the product of concentration ($C$) and extinction coefficient ($\varepsilon$) of the present absorber, so Equation (3) can also be written as

$$A(\lambda) = G + (\varepsilon_{\text{bil}} C_{\text{bil}} + \varepsilon_{\text{OxyHB}} C_{\text{OxyHB}} + \varepsilon_{\text{dHb}} C_{\text{dHb}}) d$$  \hspace{1cm} (4)

where the subscript in Equation (4) indicated that of the considered absorbers. Rearranging Equation (4) gives

$$A(\lambda) = G + \varepsilon_{\text{bil}} C_{\text{bil}} + \left(\varepsilon_{\text{OxyHB}} - \varepsilon_{\text{dHb}}\right) SO_2 + \varepsilon_{\text{dHb}} dT$$  \hspace{1cm} (5)

where $T$ is the total hemoglobin concentration and is taken as a constant value of 150 g/l. The $SO_2$ is percent blood saturation and is defined as the ratio of $C_{\text{OxyHB}}$ and $T$. This work considered only the extinction coefficients of the present absorbers in the range of 440 to 500 nm shown in Figure 2 owing to the peak absorptivity of the bilirubin and variability in the signatures of the hemoglobin absorbers across these wavelengths.

Figure 2. The absorptivity of the considered absorbers underneath the skin. The absorptivity of bilirubin was reported by Agati, G. and F. Fusli [10]. The absorptivity of deoxyhemoglobin and oxyhemoglobin is taken from Scott Prahl [11].
An iterative fitting routine was written in MATLAB to predict the required $C_{bil}$ value. The intensity data collected from the point spectroscopy system described in section 2.1 was used to calculate for the light attenuation in Equation (1); the data were then fit using the MLB shown in Equation (5). This fitting routine used the `fminsearch` function in MATLAB to find the value of the unknown parameters (i.e. $G$, $C_{bil}$, $SO_2$ and $d$) using the extinction coefficients of bilirubin and hemoglobin in the wavelength range of 440-500 nm as its *priori* knowledge. The fitting process began by initializing all the unknowns with the value ‘1’, the search of the optimal value was based on the absolute error between the value given by the MLB and the real attenuation, $ΔE$. This fitting process was terminated when either the $ΔE$ is less than $1 \times 10^{-20}$ or the number of iteration has reached 5000.

3. Results and discussion

In this work, spectroscopic data were collected from four different skin sites of the recruited volunteers (referred to as volunteer A to F); they are thenar region of the palm of the hand, back of the hand, posterior forearm and anterior forearm. Based on the data collected from these skin sites, the $C_{bil}$ was predicted using the MLB and tabulated in Table 1. The description of the caffeine intake of these recruits is also included in Table 1. The mean and standard deviation of $C_{bil}$ for each skin site is also calculated and plotted in Figure 3. These values were compared with that reported in the literature in Table 2.

Table 1. The transcutaneous bilirubin concentration, $C_{bil}$ (g/l) predicted for the recruited individuals (volunteer A to F) at different selected skin site.

| Volunteers | Description of caffeine consumption | Thenar region of the palm | Back of the hand | Posterior forearm | Anterior forearm |
|------------|-------------------------------------|---------------------------|------------------|------------------|-----------------|
| A          | Non-caffeine consumer               | 0.43±0.03                 | 0.72±0.07        | 0.92±0.09        | 0.78±0.05       |
| B          | Non-caffeine consumer               | 0.44±0.07                 | 0.92±0.05        | 1.32±0.09        | 1.03±0.08       |
| C          | Seasonal consumer                   | 0.49±0.07                 | 0.92±0.16        | 1.01±0.09        | 0.65±0.04       |
| D          | Seasonal consumer                   | 0.45±0.01                 | 1.12±0.15        | 0.72±0.08        | 0.64±0.06       |
| E          | Frequent (milk tea) tea consumer    | 0.44±0.06                 | 0.49±0.01        | 0.87±0.07        | 0.61±0.06       |
| F          | Heavy Coffee drinker                | 0.37±0.01                 | 0.43±0.12        | 1.03±0.10        | 0.78±0.03       |
The results shown in Table 1 revealed the variation in the transcutaneous bilirubin concentration, $C_{bil}$ across different individuals and skin regions. A lower and high consistency in the $C_{bil}$ value was observed at the thenar region of the palm with the predicted value given by $0.44\pm0.03$ g/l as shown in Figure 3. This is followed by the back of the hand and anterior forearm. This study predicted the highest $C_{bil}$ at the posterior forearm with the calculated value given by $0.98\pm0.20$ g/l. The observed higher mean and larger variability in the $C_{bil}$ value predicted for skin sites other than the palm of the hand is likely due to the effect of melanin, wherein it was reported that palm of the hand has the lowest melanin concentration compared to other sites [11]. Melanin is a skin pigment that is responsible for the skin color. Since the effects of melanin were not considered in this study, therefore, it is reasonable to hypothesize that the employed technique may predict an erroneous reading for dark-skinned individuals. This is supported by the relatively low $C_{bil}$ observed in volunteer C and D of approximately $0.64\pm0.002$ g/l in Table 1 for measurement performed at the sun-protected anterior forearm.

In addition, it is also interesting to note that an overall lowest transcutaneous bilirubin concentration was observed for Volunteer F shown in Table 1. This is likely related to the diet of the corresponding individual who is a frequent coffee consumer. This is followed by Volunteer E, who is a frequent tea consumer. This observation agreed considerably well with that reported in Moura-nunes et al [7] and Tanaka Maya et al [8].

Table 2. The comparison of the mean and standard deviation of transcutaneous bilirubin concentration ($C_{bil}$) predicted in this work and other similar works.

|                      | Overall mean±standard deviation ($\mu \pm \sigma$) of $C_{bil}$ (in g/l) |
|----------------------|--------------------------------------------------------------------------|
| Danaei N et al [4]   | 0.13±0.03                                                                |
| Danaei N et al [6]   | 0.12±0.03                                                                |
| Danaei N et al [6]   | 0.09±0.02                                                                |
| Grohmann K et al [6] | 0.08±0.01                                                                |
| Slusher, Tina M et al [12] | 0.16±0.04                        |
| Our works (Thenar region of the palm) | 0.44±0.03                                    |
| Our works (back of the hand)       | 0.77±0.27                                                                |
| Our works (posterior forearm)      | 0.98±0.20                                                                |
| Our works (anterior forearm)       | 0.75±0.15                                                                |

Figure 3. The calculated mean and standard deviation of transcutaneous bilirubin concentration, $C_{bil}$ predicted for different skin sites using the Modified Lambert Beer (MLB).
It must also be mentioned that this work predicted an overall higher $C_{bil}$ value compared to that reported in the literature as shown in Table 2. Several factors that might contribute to the observed discrepancies are such as differences in the selection of body region under investigation, human populations and the arrangement of the employed optical system. All the experiments conducted in the previous works listed in Table 2 are of the contact measurement whereas this work adopted a noncontact strategy in the monitoring of one’s skin bilirubin concentration. This may then result in the lowest $C_{bil}$ reading observed by Grohmann K et al [6] whose work was to predict the bilirubin level at lower end of the sternum, followed by Danaei N et al [4] and Slusher et al [12] for measurement at forehead, chest and thigh. Further works are currently underway to investigate the variability in the predicted value with the employed optical arrangement.

4. Conclusion
This work concluded that thenar region of the palm can suitably be used for noncontact and noninvasive prediction of transcutaneous bilirubin concentration using the employed optical system. This is largely owing to the high consistency in its predicted value. In addition, this work found an overall lower transcutaneous bilirubin concentration for a heavy coffee consumer recruited in this study. This study also suggested that the presence of melanin and the arrangement of the optical system could possibly affect the transcutaneous bilirubin concentration predicted using the adopted strategy.

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