Investigation of gender and prandial state as factors affecting skin bilirubin level

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Abstract. This paper demonstrates the use of the developed non-invasive optical system to measure differences in the mean concentration of skin bilirubin $C_{bil(m)}$ among individuals of different gender and at different prandial state. This system employed the use of color filters to allow an illumination of the selected skin site using light beams of centre wavelength 420 nm, 440 nm and 460 nm. The prediction of the required skin bilirubin concentration value is via Modified Lambert Beer law. This study conducted experiments on the back of the hand of twelve recruits. The results revealed a higher mean $C_{bil(m)}$ value of 0.25 ± 0.007 µmol/L for males as compared to 0.14 ± 0.0086 µmol/L measured for females. In addition, this work observed a decrease in the mean $C_{bil(m)}$ value for the ten recruits of mixed gender from 0.23 ± 0.06 µmol/L at preprandial phase to 0.18 ± 0.04 µmol/L during the postprandial period. This study concluded that the developed system is able to detect changes in the skin bilirubin concentration level with one’s gender and prandial state as reported in literature. However, this system may be further improved for future clinical application on jaundiced patients.

1. Introduction

In the medical arena, non-invasive devices able to provide comprehensive information of one’s health status are highly sought after. This includes information of one’s bilirubin concentration, which is a waste product produced during the breakdown of aged red blood cells. This orange-yellow pigment yields yellow stains in skin and other tissues (jaundice) if its concentration in blood is high. The poor functional efficiency of one’s liver in eliminating aged or damaged red blood cells would lead to the accumulation of the latter, and hence an excessive production of bilirubin. This medical condition is often found either in individuals with liver diseases or newborns whose liver have yet fully developed.

In addition to the underlying health status, previous research revealed that one’s blood bilirubin concentration would also be affected by the change in their dietary intake [1]. The corresponding work showed a decrease in this value for populations who consumed either carbohydrate and calorie-rich foods or diet containing high fat and carbohydrate as compared with the standard normal diet ($\rho < 0.001$) [1, 2]. This same pattern of results was also reported by [3] for frequent caffeine consumers. Meanwhile other study concluded that gender is a factor that may contribute to the differences in the bilirubin concentration level [4].

Many types of bilirubin detector are commercially available in the market; they can be categorized as invasive and non-invasive approach. The former is a laboratory blood test that required the drawing
of a small amount of blood in the measurement of total and direct bilirubin concentration value. This process is time consuming, laborious and there may also be a risk of infection at the sampling site; hence it is not a preference for many. In view of this, non-invasive technique is often considered as the more favourable approach to use. This technique measured the reflected light signals upon interaction of light with the investigated skin site. The required value would then be translated from the measured signals using a lookup table. The existing non-invasive devices include Bilirubinometer and Bilitec [5]. These devices provide harmless and quick prediction of the required transcutaneous bilirubin concentration value. Nonetheless there were reports on inconsistency in the predicted value depending on the measured site and skin pigmentation [6]. This is likely owing to the fact that the good performance of the employed lookup table may be limited to certain groups of population.

For this reason, other work [7] reported the use of an analytical model as a more suitable approach in the estimation of the required health parameter value. The operating principle of this technique is based on analysis of the measured light spectrum to interpret the variation in light absorptivity underneath skin. Therefore, it is the aim of this study to develop and propose a multi-color filter system to provide non-invasive measurement of one’s skin bilirubin level without the use of a look-up table. It is also the objective of this study to investigate the variation in this value predicted for individuals of different gender and at different prandial state.

2. Material and Method

2.1. Experimental system and subjects

The optical system developed for non-contact monitoring of skin bilirubin concentration value is shown in Figure 1. The employed light source in the system is a white Light Emitting Diode (model no. SMD 5730). Light reflected from the selected skin site would pass through a color filter to allow only the detection of light of the chosen wavelength by a Complementary Metal Oxide Semiconductor (CMOS part no. CW835). The latter was located at a distance of 400 mm and an angle of approximately 30° from normal. In this work, light balancing filter (model no. LB120 from Hoya Optics), blue filter (B-440, Hoya Optics) and green filter (G-533, Hoya Optics) were used as the color filter to pass light of centre wavelength 420 nm, 440 nm, and 460 nm, respectively, through them. The reason of the selection of these wavelengths is due to the high bilirubin absorptivity across wavelength range of 400 – 500 nm [8]. These color filters were mounted on a makeshift rotating filter wheel controlled by a stepper motor (17PM-J).

In this study, experiments were conducted on twelve non-smoking Asian volunteers (six males and six females) aged between 23 and 27 years. All volunteers gave their consent to participate in the study, they declared healthy and were not suffered from hepatitis. Experiments were conducted at the back of the right hand of these individuals seated in a chair. The same procedure was repeated for a group ten volunteers of mixed gender during pre-meal (fasting for over 12 hours) and post-meal (postprandial) session. The validation of the obtained value is via a comparison study among volunteers of different genders, and during pre and post-meal intake. This is following the previous reports [2,4], which cited these as the factors to the differences in the bilirubin concentration value. Meanwhile the reason of the choice of this skin site is to investigate the consistency in the pattern of results for individuals with different skin tone using the proposed quantification strategy.
2.2 Modified Lambert Beer model

In this work, Modified Lambert Beer (MLB) model shown equation (1) is used in the estimation of the skin bilirubin concentration. This model is commonly used to relate changes in light attenuation, $A$, with the wavelength dependent total absorptivity, $\mu_a$, of the medium as follows:

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

The $A$ is given from the measurement of reflected light intensity and is defined as:

$$A(\lambda) = \log \frac{I_W}{I_S}$$  \hspace{1cm} (2)

where $I_W$ and $I_S$ represent average light reflectance from a white sheet and from the selected skin site, respectively. The wavelength dependent $\mu_a$ is given by:

$$\mu_a(\lambda) = \varepsilon_{bil}(\lambda)C_{bil}.$$  \hspace{1cm} (3)

where $\varepsilon_{bil}(\lambda)$ and $C_{bil}$ denote wavelength dependent extinction coefficient and concentration of skin bilirubin, respectively. The symbol $d$ in equation (1) represents light mean pathlength, and is taken here as the reciprocal of the medium’s reduced scattering coefficient, $\mu_s'$. Since the tissues $\mu_s'$ value is approximately 10 cm$^{-1}$ at light wavelength of 450 nm [9], the parameter $d$ is calculated as 1 mm. The effects of light scattering on light attenuation is notably dominant at the shorter wavelength, so the scattering dependent attenuation offset, $G$, is assumed here as $A(\lambda = 420 \text{ nm})$. Therefore, substituting equation (3) into (1), and rearranging the equation gives

$$C_{bil} = \frac{A(\lambda_2)-A(\lambda = 420 \text{ nm})}{\varepsilon_{bil}(\lambda_2)d}$$  \hspace{1cm} (4)

where $\lambda_2$ represents light wavelength of 440 nm and 460 nm. The $\varepsilon_{bil}(\lambda_2)$ at these wavelengths is given by 52109 cm$^{-1}$M$^{-1}$ and 53869 cm$^{-1}$M$^{-1}$, respectively [10]. The $C_{bil}$ calculated from equation (4) for light wavelength 440 nm and 460 nm is then averaged to give the mean bilirubin concentration, $C_{bil(m)}$.

3. Results and Discussion

Figure 2 showed the boxplot of skin bilirubin concentration value, $C_{bil(m)}$, predicted for the recruited females and males. The results revealed a mean and standard deviation of $C_{bil(m)}$ given by 0.25 ± 0.007 µmol/L and 0.14 ± 0.0086 µmol/L for males and females, respectively. Meanwhile a comparison in the $C_{bil(m)}$ value estimated for volunteers during pre and post-meal session, which changes one’s blood glucose level, is shown in Figure 3. A test of correlation between the value predicted for volunteers
during fasting and postprandial period was via a paired, two tailed sample $t$-test in SPSS software (SPSS 22, Inc., Chicago, Illinois). This statistical test revealed significant value, $\rho = 0.000$, using the confidence level of 95%.

The results shown in Figure 2 for the two genders revealed a mean difference of 0.11 µmol/L in the calculated $C_{bil(m)}$, wherein the value estimated for males is predominantly higher than that of its counterpart gender. This observation is agreeable in the work reported by Zucker et al. [4], who observed a mean difference of 0.2 mg/dL in the value measured using in-vitro laboratories technique. This discrepancy may be contributed by factors such as differences in physical activities, body mass index and diet between females and the males as discussed in the work of Tanaka et al. [11]. The relatively low standard deviation in the values predicted for males and females given by 0.007 µmol/L.
and 0.0086 µmol/L, respectively, may indicate the robustness of the proposed quantification approach towards differences in skin pigmentation.

In addition, this work found a decrease in the predicted skin bilirubin concentration value following glucose load as shown in Figure 3. This value dropped from mean value of 0.23 ± 0.06 µmol/L measured during fasting state to 0.18 ± 0.04 µmol/L after meal. The notable difference between these values was further confirmed with the calculated $\rho = 0.000$. This decrease in the value was likely to be contributed by an increase in the liver stiffness after food intake [12]. These changes in the liver function would, therefore, modify one’s bilirubin concentration in blood. These preliminary findings showed that the developed optical system that used light beam of wavelength 420 nm, 440 nm and 460 nm is able to detect changes in the predicted $C_{bil}$ in the same pattern as that reported in the literature. However, this system may be further improved via the use of diffused laser beams as the light source to allow illumination of the selected skin site using a narrower light spectrum, and hence a more precise measurement of light attenuation value at each wavelength.

4. Conclusion

This study demonstrated the use of the developed multi-color filter system to provide a non-invasive and non-contact monitoring of one’s skin bilirubin level without the use of a look-up table. This work found a variation in the predicted $C_{bil}$ value depending on genders, and a negative association between the estimated value and the blood glucose level. The results revealed a small variation in the value predicted for individuals of the same gender, which may suggest the robustness of the employed strategy towards differences in the skin pigmentation. This work concluded that the reasonable good performance of this system may imply the possibility of its application in clinical settings for the diagnosis of neonates jaundice.

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