ESTIMATION OF OXYGEN SATURATION WITH LASER OPTICAL IMAGING METHOD

Arman JALALI PAHNVAR, Anıl ISIKHAN, Ibrahim AKKAYA*, Yusuf EFTELI, Mehmet ENGIN, Erkan Zeki ENGIN

Ege University, Electrical Electronics Engineering, Izmir, Turkey
{armanjalali35, aisikhan200}@gmail.com, {ibrahim.akkaya, yusuf.efteli mehmet.engin, erkan.zeki.engin}@ege.edu.tr

Abstract: *The aim of this study is to determine the estimation of hemoglobin concentration and oxygen saturation of tissue by non-invasively functional laser imaging for early skin cancer diagnosis. The early diagnosis of melanoma is a key factor that remarkably reduces the mortality rate. Diffuse reflectance spectroscopy is a very useful device for diagnosis and treatment purposes under in-vivo conditions. At this point, the aforementioned device, which takes into account the scattering of tissue, is to determine the concentration of chromophores (or optical absorbers) due to attenuated light strikes to the superficial layer of tissue. Laser-type light based imaging techniques in medical diagnosis substantially produce good results. Consequently, the aim of this study is to estimate HbO_2 (%) and Hb (%) concentrations by use of a single wavelength (680 nm).*

Keywords: *Melanoma; oxygen saturation; laser; non-invasive imaging.*

1. Introduction

The hemoglobin molecule in the red blood cells (RBC) serves to transport oxygen from the lungs to the tissues and binds to four oxygen atoms to form the oxygenated hemoglobin (HBO2) molecule [1]. Oxygen saturation (SO2) is the statistical mean of oxygenated hemoglobin (HBO2), depending on the total number of hemoglobin can be bound with the oxygen. Due to the fact that optical methods are non-invasive and allow the oxygen saturation to be continuously measured, the absorption of light by the blood due to oxygen saturation is an intensively studied subject [1 – 5]. Studies are concentrated at wavelength range between 250 – 1000 nm. Optical methods for measuring oxygen saturation in tissue are widespread in clinical conditions. These measurements are resulting from the absorption and scattering based losses along the path traveled by the light. Generally, the scattering losses are not often considered in data analysis.

On the other hand, in order to monitor the SO_2 value of whole circulation system of human, pulse oximetry is a non-invasive and widely used method [6, 7]. It depends on the light absorption changes of the arterial blood, while the absorption of the skin, muscle, bones and venous blood remain unchanged. Usually, the spectrophotometric method which uses multi-wavelength light source is used to monitor the arterial blood oxygen saturation [8, 9]. However, the accuracy of this method would be affected by opaque skin, irregular blood flow, motion of body, especially during hypo-perfusion. Moreover, it does not have the ability to monitor local changes of oxygen. The advantages of the proposed single-wavelength method contains less power consumption (only one wavelength needed), real-time monitoring (there is no need to switch wavelength) and simplicity (simple operational steps) for on-site and portable blood oxygenation monitoring applications.

Diffuse reflectance spectroscopy is a very useful device for diagnosis and treatment purposes under in-vivo conditions [10]. At this point, the aforementioned device, which takes into account the scattering of tissue, is to determine the concentration of chromophores (or optical absorbers) due to attenuated light strikes to the superficial layer of tissue. Non-invasive imaging and monitoring in biomedicine based on the developments in photonics for last three decades [11]. The imaging of subsurface of a skin emerges as a very important modality in terms of detection of the many optical properties of skin. Detection of skin cancer under in-vivo conditions based the investigation of non-invasive optical modalities has a capability that further increases the success of sensitivity and image magnification of visible optical window based methods [11]. However, several methods such as Optical Coherence Tomography - OCT, Confocal Scanning Light Microscopy - CSLM, and Magnetic Resonance Imaging – MRI are very expensive and are bulky systems. For this reason, in addition to the studying on visible optical region, at the same time, scanning near-infrared region as well, the developments of cheap and portable systems is becoming a more popular approach.

The aim of this study is to determine the estimation of hemoglobin concentration and oxygen saturation of tissue by non-invasively functional laser imaging for early skin

Received on: 14.03.2017
Accepted on: 21.03.2017

cancer diagnosis. The monitoring of absorption and scattering coefficients that are strongly related to the concentration of chromophores in a skin with light-skin interaction based models is very crucial and is still an open-ended problem.

2. Materials and Methods

2.1. Theoretical Approach

Oxygen saturation is related to the heart rate, the breathing rate, the blood pressure, and the body temperature. It is defined that as relative measure of oxygen amount of dissolved or carried in human body medium. It is important to determine whether a person has adequately supply oxygen. Also the continuous montioring of oxygen saturation is important for detecting hypoxemia condition [12]. For human body, estimation of arterial oxygen saturation at peripheral capillary is called SpO_2 which is primary focus of clinical conditions. SpO_2 is the percentage of oxygenated hemoglobin and expressed as follows,

$$SpO_2 = \frac{HbO_2}{HbO_2 + Hb} x100\% \quad (1)$$

where HbO_2 is the concentration of oxygenated hemoglobin and Hb is the concentration of deoxygenated hemoglobin [12]. Generally, in clincial conditions SpO_2 is measured depending on the selected two wavelengths; λ_1 and λ_2 such that absorbance by HbO_2 is more at at λ_2 than at λ_1 while the absorbance by Hb is more at λ_1 than at λ_2, as given in Figure 1.

Absorption of HbO_2 and Hb molecules depends on wavelength as seen in Figure 1 [13]. Absorption of Hb decreases in contrast to that absorption of HbO_2 increases, as wavelength increases in the range of between 680 nm to 800 nm. The determination of actual absorption coefficient is difficult due to the diffusive nature of light in tissue. A precise quantitative result is complicated by scattering in tissue and absorption of other chromophores in tissue like melanin.

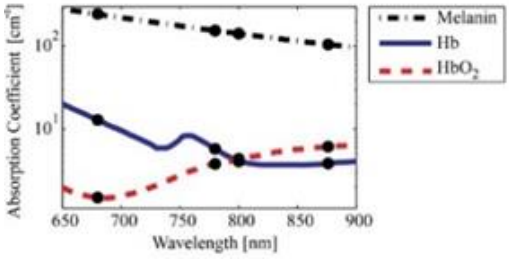

Figure 1. Changes in oxygenated hemoglobin and hemoglobin absorption coefficients according to wavelength

The chromophore distribution effects on backscattered light, so that there is a need a model of light transport in tissue to describe it. The diffusion equation for the absorption and scattering of light is described below for position and time t by [13]:

$$\frac{\partial\phi(\vec{r},t)}{c\partial t} + \mu_a\partial\phi(\vec{r},t) - \nabla\left[\frac{\nabla\partial\phi(\vec{r},t)}{3(\mu_a + \mu_s(1-g))}\right] = S(\vec{r},t) \quad (2)$$

In the equation above; Φ is fluence rate, μ_a and μ_s are absorption and scattering coefficients, g is the anisotropy factor, and S is an isotropic light source. In the diffusion equation that is given Eq. 2, light is generally attenuated exponentially in a medium for a given depth l, with the wavelength dependent absorption and scattering coefficients as $\mu_a(\lambda)$ and $\mu_s(\lambda)$. In addition, to simplify the problem of estimating absorption, μs is assumed constant on the related spectral bandwidth. If the reflectance data was acquired by a camera, the gray level value (intensity) of one imaged pixel can be described by the value of A(λ). The image which is obtained represents the total spatial (x, y) map of backscattered diffuse reflectance.

In our study, red and blue food dyes were used to mimic the oxygenated hemoglobin and hemoglobin chromophores respectively. Considering the variation of the absorbance coefficients of the oxygenated and hemoglobin in relation to the wavelength, it is seen that there is an important difference for the two kinds of hemoglobin at 680 nm as shown in Figure 1 [13].

2.2. Instrumental Setup

The illumination was done by a laser diode which had 680 nm center wavelength and 100 mW power, and the laser diode current was set by the driver circuit to prevent saturation. 1024x768 CCD camera (D223C; Thorlabs, USA) used as a detector. The camera exposure time was set approximately 8 ms and a glass diffuser (DG 100x100-600, Thorlabs, USA) was used in front of the laser to provide a homogeneous surface illumination. The work was performed in the dark room. The instrumental setup is given in the Figure 2.

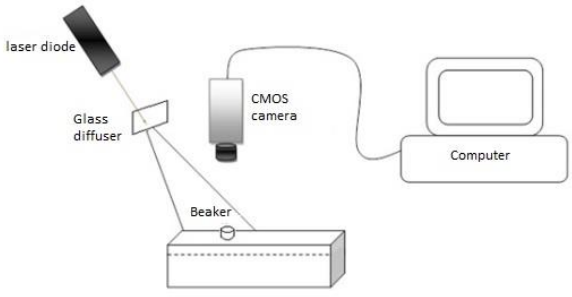

Figure 2. Instrumental setup

2.3. Measurements

The flowchart of the study steps is given and explained in the Figure 3.

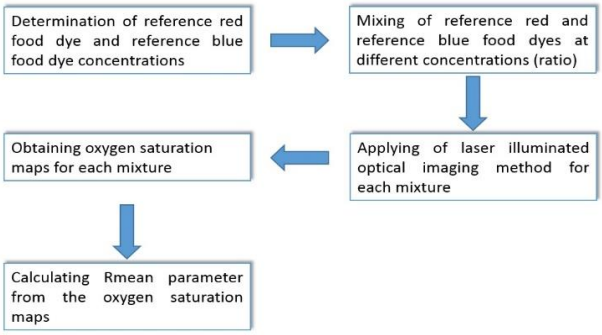

Figure 3. Changes in oxygenated hemoglobin and hemoglobin absorption coefficients according to wavelength

2.3.1. Determination of Reference Red and Reference Blue Dye Concentrations

As a reference material in the study, red food dye (Ponceau4R) and blue food dye (Brillant blue) were used for mimicking oxygenated hemoglobin and hemoglobin, respectively. Red and blue food dyes were put into two different beakers in varying amounts by trial and error. After then, it was mixed with distilled water. The solutions were prepared and poured into two separate regions on glass coverslips and imaged with the camera under ambient light.

Regions of red dye solution and blue dye solution were cropped separately and analyzed by RGB analysis, comparing the "R" and "B" components; histograms of the "R" and "B" components of the red and blue reference solutions in the two beakers were determined to be used in the study; 100 mg/dl and 5 mg/dl respectively. The actual dye mixtures are shown in Figure 4 as an example.

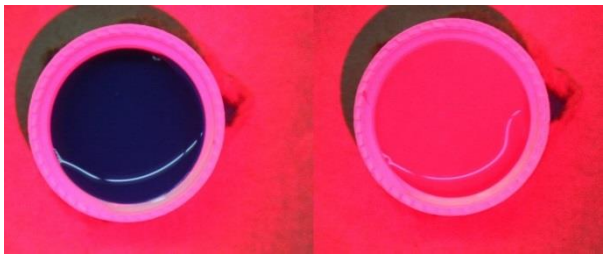

Figure 4. Reference red and reference blue concentrations images

2.3.2. Laser Illuminated Wide Field Imaging

The observation parameter is the average value of the pixel brightness and is essentially equal to the light absorption. Images were acquired from the phantom surface roughly. A rectangular sub-region was cropped for analysis. From the corresponding region image, the R maps (images) were obtained by estimating the "R" parameter corresponding to the oxygen saturation based on the pixel values. For a single pixel, this parameter can be calculated as [4]

$$R = \frac{I_1}{I_1 + I_2} \quad (3)$$

where I_1 refers to the pixel brightness in the reference red dye at 680 nm and I_2 refers to the pixel brightness in the reference blue dye at 680 nm. The R parameter was generated on a pixel-by-pixel basis for an entire image, thus the saturation map was generated from the "R" value of all pixels.

3. Results

Before the measurement of mixture of the dyes, the red and the blue dye concentraions were considered seperately. From this measurement, the output of the signal was obtained as pixel intensity values averages. The related results are given in Figure 5 and Figure 6 respectively. It is observed that there are inverse relationship between measured optical signal and concentrations.

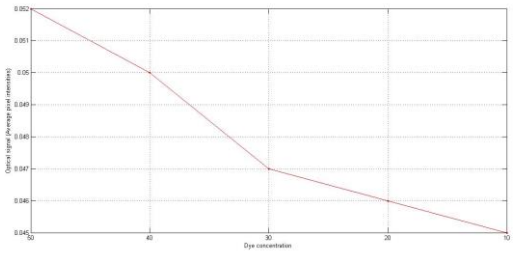

Figure 5. The investigation of the red dye

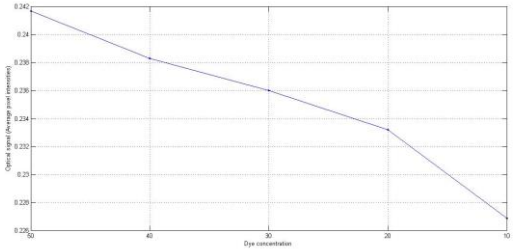

Figure 6. The investigation of the blue dye

The relative concentrations of HbO_2 and Hb were simulated by the dissolution of red and blue dyes in a certain amounts in distilled water respectively. Oxygen saturation (R) maps, produced for different concentrations are given below in Figure 7.

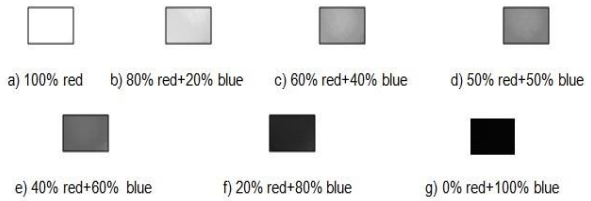

Figure 7. The R maps of the cropped region for different mixtures

In order to enhance the visual observation, the above R maps were subjected to pseudo – coloring which is given in Figure 8.

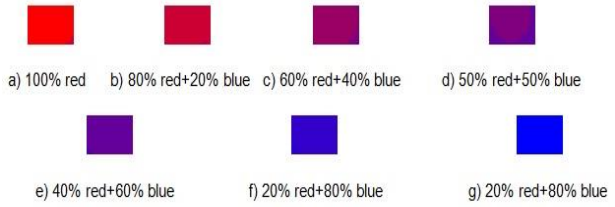

Figure 8. Pseudo – colored R maps

A representative parameter; R_{mean} is generated with calculating an average value from the estimates of oxygen saturation maps (images) which are mentioned above. The variation of the R_{mean} parameter is given in Figure 9. In the following figure, the horizontal axis represents the dye concentrations that corresponding to mixing percentage of HbO and HbO_2.

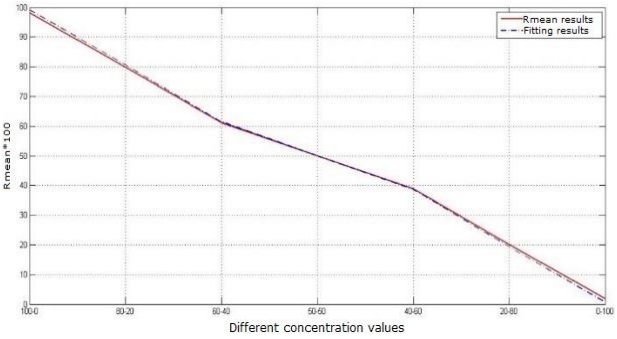

Figure 9. Changing of R_{mean} relating to mixture concentrations

As you can see from the graph; linear variation of the R_{mean} parameter depending on the combination of mixtures is observed. As stated in the literature, the use of 680 nm wavelength is suitable for this situation.

For the use of the behavior obtained for the artificial HbO_2 and Hb concentrations known above in the in-vivo and/or ex-vivo environments, calibration or classification learning stages will be provided by the numerical values produced by the above applications. For this purpose, variations were fitted to a linear equation and RMS fitting error for this equation is around 0.5137.

$$y = 1.0232x - 1.1606 \quad (4)$$

When the obtained results were investigated; it was observed that there was an approximated linear relationship between measured optical signal and dye concentrations. In the litrature like as declared in [6], the same relationship also was observed.

4. Conclusion

In this study, we investigated in-vitro based oxygen saturation measurements where the hemoglobin concentrations were simulated by different red and blue food dye mixing in the distilled water. In clinical conditions, the human tissue or arterial oxygen saturation is measured by two different optical wavelengths method and also photoacoustic technique. However, these methods cause hardware cost and have optical design limitations. Therefore, our proposed single wavelength based study would be promised method.

5. Acknowledge

This study was supported by the “The Scientific and Technological Research Council of Turkey (TUBITAK)” grant project (Tubitak-COST: 113E771).

6. References

[1] Faber D. J. et al. “Oxygen saturation-dependent absorption and scattering of blood”, *Physical Review Letters* 93, 028102, 2004.
[2] van Assendelft O.W., “Spectrophotometry of Hemoglobin Derivatives”, *Royal Vangorcum Assen*, Springfield, 1970.
[3] Zijlstra W.G., Buursma A., and Meeuwsen-van der Roest W. P., *Clin. Chem.* 37, 1633, 1991.
[4] Wray S. et al., *Biochim. Biophys.* Acta 933, 184, 1988.
[5] Tabulated data from various sources compiled by S. Prahl, 30/08/2016, Avaible: http://omlc.ogi.edu/spectra,.
[6] Gao F., Peng Q. W., Feng X. H., Gao B., and Zheng Y. J., “Single-Wavelength Blood Oxygen Saturation Sensing With Combined Optical Absorption and Scattering”, *IEEE Sensors Journal*, vol. 16, no. 7, pp. 1943-1948, Apr 1, 2016.
[7] Kiekkas P. et al., “Knowledge of pulse oximetry: Comparison among intensive care, anesthesiology and emergency nurses”, *J. Clin. Nursing*, vol. 22, nos. 5–6, pp. 828–837, Mar. 2013.
[8] Humphreys K., Ward T., and Markham C., “Noncontact simultaneous dual wavelength photoplethysmography: A further step toward noncontact pulse oximetry”, *Rev. Sci. Instrum.*, vol. 78, no. 4, p. 044304, Apr. 2007.
[9] Millikan G. A., “The oximeter, an instrument for measuring continuously the oxygen saturation of arterial blood in man”, *Rev. Sci. Instrum.*, vol. 13, no. 10, pp. 434–444, Oct. 1942.
[10] Hernández S. E., Rodríguez V. D., Pérez J., Martín F. A., Castellano M. A., and Gonzalez-Mora J. L., “Diffuse reflectance spectroscopy characterization of hemoglobin and intralipid solutions: in vitro measurements with continuous variation of absorption and scattering”, *J. Biomed. Opt.*14 (3), 034026, 2009.
[11] Memorandum of Understanding for the implementation of a European Concerted Research Action designated as COST Action BM1205: European Network for Skin Cancer Detection using Laser Imaging, 2012.
[12]Shao D., Liu C., Tsow F., Yang Y., Du Z., Iriya R., Yu H., Tao N., “Noncontact Monitoring of Blood Oxygen Saturaiton Using Camera and Dual-Wavelength Imaging Ssytem”, *IEEE Trans. On Biomed. Eng.*, 63 (6), 1091-1098, 2016.
[13] Dhawan A. P., D'Alessandro B., “Multispectral Transillumination Imaging of Skin Lesions for Oxygenated and Deoxygenated Hemoglobin Measurement”, *New Jersey Institute of Technology*, Newark, NJ, 2010.