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Noninvasive measurement of relative blood oxygen saturation in human retina by using 1µm Fourier Domain Optical Coherence Tomography

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Abstract: The relative blood oxygen saturation measurement has been done in human retina by using Fourier Domain Optical Coherence Tomography (FDOCT) data. A broadband (120 nm bandwidth) light source with central wavelength, 1060 nm was used in FDOCT for deeper penetration in retina. A least squares method was implemented to extract oxy and de-oxy haemoglobin concentrations from the FDOCT data. The measured blood oxygen saturation levels in an artery and veins are comparable with existing methods. Thus, this technique can be used to measure *in-vivo* relative blood oxygen saturation non-invasive way.

Keywords: Optical Coherence Tomography (OCT), Blood oxygen saturation, FDOCT, Retina.

I.INTRODUCTION

Hemoglobin is a protein presents in the blood, which is responsible for carrying oxygen to all organs in the human body. When Hemoglobin charged with oxygen in lungs it forms as Oxy-Hemoglobin (HbO_2) or oxygenated blood. After delivering oxygen to cells it becomes as de-oxygenated blood (Hb). The amount of oxygen actually present in the blood compared to maximum amount it can hold is called blood oxygen saturation (sO_2). In clinics, local, non invasive and non contact measurement of sO_2 has great importance. The eye deceases like Diabetic Retinopathy (DR), neovasularisation are directly related to the blood flow and retinal hypoxia this would leads to low vision or vision loss[1, 2]. It can be used for diagnosing deceases like Peripheral Vascular Diseases (PVD), Compartment syndrome, perfusion [3]. Furthermore, some studies are suggesting that by measuring tumours hypoxia one can predict the carcinogenic nature of cells, thus it would be useful for determining metastases state of carcinoma tumour [4]. Blood has different absorption properties at different wavelengths of the light. This is the main key feature for measuring sO_2 levels in blood. Pulse oximetry is also works on the same principle but with it, it is not possible to measure local or depth dependent sO_2 levels in blood.

Optical Coherence Tomography (OCT) works on low coherence interferometry and useful for studying high resolution cross sectional images of biological objects [5]. In OCT, another modality called Spectroscopic Optical Coherence Tomography (SOCT) which is used for extracting local spectroscopic properties of biological samples [6]. Measuring sO_2 with OCT has several advantages over conventional sO_2 measurement techniques. It's high spatial resolution would enable us to resolve different layers of the sample, extract it's local spectroscopic properties, due to its non invasive, high speed it can be used to measure bloods flow velocity and generates enface images, cross sectional images [7]. For studying spectroscopic properties of an eye with OCT, the wavelength band selection is the most important since it contains 90% water molecules. Hence it is important to choose central wavelength whose absorption coefficients and scattering effects are lowest. In OCT for ophthalmology purpose, 800 nm, 1060 nm, 1300 nm central wavelengths are most popular. In case of spectroscopic study of retina and choroid, 1060 nm is the optimum central wavelength. It has been experimentally proved that, at 1060 nm water molecules absorption spectrum shows local minima and scattering effects of blood above 800 nm decreases approximately with $\lambda^{-1.7}$ [8]. Also, the depth dependent broadening of the axial

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point spread function of OCT has suppressed and water shows very less percent of dispersion effects [9,10]. The water molecules absorption is very high at 1300 nm wavelength, whereas 1060 nm central wavelength shows less absorption by Retinal Pigment Epithelium (RPE), hence deeper penetration depth can be achieved by it and also, this enables us clear visualization of choroidal vessels below the choroid capillary layer [9-11] .

Few people has attempted to study spectroscopic properties of blood with the OCT. SOCT was used to study the absorption properties of HbO_2 and Hb samples [12]. Also 780 nm, 810 nm central wavelength bands has been used in OCT for measuring absorption coefficients of diluted 100% oxygenated or deoxygenated samples [13]. *In vivo* 575 nm as central wavelength band was also implemented for extracting sO_2 levels in normal mouse dorsal skin [14], 840 nm as central wavelength band used for measuring the sO_2 levels in human eye [15]. But, these central wavelength bands have several constraints. Our study will be the first attempt to measure sO_2 in retina with OCT using 1060 nm as central wavelength.

The main objective of this work is to explore measurement of sO_2 levels in human retinal blood by using FDOCT with 1060 nm as central wavelength and having a 120 nm spectral bandwidth which is optimized wavelength band for extracting spectroscopic properties of deep retina and choroid[16-19].

II.THEORY

LIGHT TRAVELLING THROUGH ANY SAMPLE FOLLOWS THE BEER LAW IT CAN BE EXPRESSED AS

$$I_t = I_0 \exp(\alpha_a d) \tag{1}$$

Where, I_t and I_0 represents transmitted and incident intensities of light, α_a represents absorption coefficient, d length travelled by light in sample.

The above formula is for transmitted light, but Spectral Domain Optical Coherence tomography (SDOCT) works on backscattered light thus it can be can express as [14]

$$I_b(\lambda, d) = rI_0 \exp(-\alpha_a(\lambda)2d) \tag{2}$$

Where, I_b, I_0 represents backscattered and incident intensities of light, r is the reflectivity or scattering cross section of sample, α_a represents absorption coefficient, λ represents the wavelength of incident light, the multiplier 2 represents bidirectional passing of light through the sample, d is the thickness of the sample. The absorption coefficient $\alpha_a(\lambda)$ can be expressed as concentration (C) times of its molar extinction coefficient $\varepsilon(\lambda)$.

$$\alpha_a(\lambda) = C * \varepsilon(\lambda) \tag{3}$$

The interference signal collected from eye by using SDOCT can be expressed as

$$I = I_r + I_s + 2\sqrt{I_r I_s}\cos(k.2\Delta L) \tag{4}$$

Where, I_r, I_s are the intensities from reference mirror and sample, $k\left(=\frac{1}{2\pi}\right)$ is wavenumber, $2\Delta L$ is the optical path delay between the sample and reference mirror in the interferometer. After removing DC part in the equation (4) can be equated to (2). From eq (2) and (3) can be used to estimate the concentration of chromophores. Partial oxygen saturation of blood can be defined as the amount of HbO_2 present in the total blood or in other words the ratio of HbO_2's concentration to sum of HbO_2 and Hb's concentrations, this can be expressed as [11, 19]

$$sO_2 = \frac{C_{HbO_2}}{C_{HbO_2} + C_{Hb}} \tag{5}$$

Where, C_{HbO_2} is the concentration of HbO_2, C_{Hb} is the concentration of Hb .

III.METHOD

FDOCT spectral data from normal human eye (Asian, 24 yrs) was collected and used in this study. The FDOCT system has penetration depth about 2.5 mm. Then data was analysed by custom made codes written using Labview (National Instruments, Inc., Austin, Texas). In order to estimate the levels of sO2 in retinal capillaries, capillary portions in retina

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was identified from B-scan image which comprises of 512 x 1500 pixels. A volume (512x1500x128) projection image was presented Fig.1.

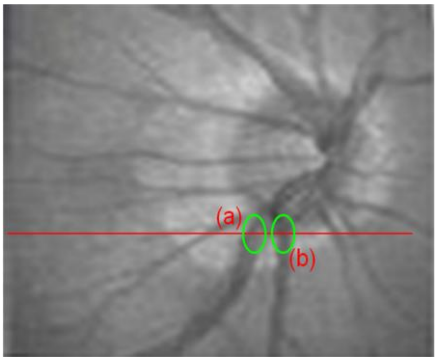

Fig.1. SDOCT volume projection image. Red color line showed in the above figure is 76th (slice) extracted for B-scan image as shown in Fig.2. Green circles represent vein and artery portions.

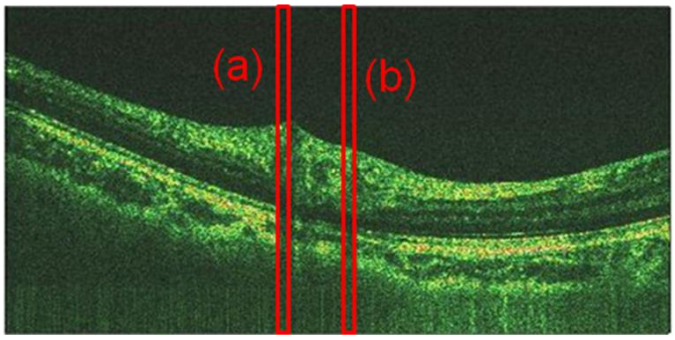

Fig.2. Extracted B-scan image of human retina from Fig 1 marked as red line. The portions (a) and (b) is the vein and artery vessel respectively, from where the data was extracted.

The vein and an artery portions have been identified by visual inspection of the SDOCT fundus image [12, 20] it can be seen in fig.1 and fig.2. In present study, four fringe patterns from the edges of the vein, artery and its adjacent tissues, as shown in Fig. 2(a) and (b) was sampled. These fringes were averaged in order to avoid specular reflections [15]. In blood, concentration of HbO_2 and Hb can be calculated by assuming light absorption depends only on concentration state of HbO_2 and Hb. Intensity of SDOCT A-line can be expressed as [14]

$$I_b(\lambda,d) = rI_0 \exp\left(-2d\left[\varepsilon_{HbO_2}(\lambda)C_{HbO_2}+\varepsilon_{Hb}(\lambda)C_{Hb}\right]\right) \quad (6)$$

Where, $\varepsilon_{HbO_2}, \varepsilon_{Hb}$ are the extinction coefficients and C_{HbO_2}, C_{Hb} are concentrations of HbO_2 and Hb in blood respectively.

The above equation (eq.6) can rewrite in the form of linear equation as follows

$$\frac{-1}{2d}\ln\left(\frac{I(\lambda,d)}{I_0}\right) = \varepsilon_{HbO_2}(\lambda)C_{HbO_2} + \varepsilon_{Hb}(\lambda)C_{Hb} - \frac{1}{2d}\ln(r) \quad (7)$$

Where, $\ln\left(\frac{I(\lambda,d)}{I_0}\right)$ is called as Optical Density (OD) at wavelength λ. For n number of wave lengths eq (7) can be written as follows [14]

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$$\frac{-1}{2d}\begin{bmatrix} \frac{I(\lambda_1)}{I_0} \\ \frac{I(\lambda_2)}{I_0} \\ . \\ . \\ \frac{I(\lambda_n)}{I_0} \end{bmatrix} = \begin{bmatrix} \varepsilon_{HbO_2}(\lambda_1) & \varepsilon_{Hb}(\lambda_1) & \frac{-1}{2d} \\ \varepsilon_{HbO_2}(\lambda_2) & \varepsilon_{Hb}(\lambda_2) & \frac{-1}{2d} \\ . & . & . \\ . & . & . \\ \varepsilon_{HbO_2}(\lambda_n) & \varepsilon_{Hb}(\lambda_n) & \frac{-1}{2d} \end{bmatrix} \begin{bmatrix} C_{HbO_2} \\ C_{Hb} \\ . \\ . \\ \ln(r) \end{bmatrix} \quad (8)$$

Where, $\lambda_i, 1 \le i \le n$ are discretely measured wavelengths in band width.

Here the number of known equations is more than unknown parameters this is over determined case, the solutions of the eq. (8) can be obtained by using the least-squares method [14].

The theoretical values of ε_{HbO_2} for 100% oxygenated blood and ε_{Hb} for 0% oxygenated or deoxygenated blood by using, absorption coefficients [8, 21] as mention below.

$$\varepsilon(\lambda)\left[\frac{liter}{molesmm}\right] = \frac{\alpha_a(\lambda)[mm^{-1}] * 64{,}500\left[\frac{g}{mole}\right]}{x\left[\frac{g}{liter}\right]} \quad (9)$$

Where, $\alpha_a(\lambda)$ is absorption coefficients, 64,500 is the gram molecular weight of the hemoglobin, *x* is concentration.

The calculated values of extinction coefficients have been used in eq. (8). Its solutions will be C_{HbO_2}, C_{Hb}. The partial blood oxygen saturation values can be estimated by using above concentration values and eq. (5).

IV. Results and Discussion

In this work, C_{HbO_2}, C_{Hb} values for vein and artery were estimated at 0.5 mm depth. The values are 15.4 g/L-mm, 75.5 g/L-mm for vein and 43.8 g/L-mm, 14.4 g/L-mm for artery respectively. According to Robles *et al.*, [18, 20] , the lowest feasible C_{Hb} value was 1.2 g/L-mm, which is supporting our calculated values. Within this method the maximum depth limitation was up to 1 mm, however in our work we used 0.5 mm depth range. The measured sO_2 level in the vein was 16.8% and for an artery it was 75.3%. Accuracy of our measurement of sO_2 level may be influenced by wavelength band due to some portion of radiation also absorbed by water molecules [8].

V. Conclusion

In summary, the sO_2 level in retinal layer was measured by using FDOCT data with 1060 nm wavelength band and least squares method. The obtained results are well comparable with existing results. So, we can conclude that 1060 nm wavelength band is optimal for measuring sO_2 levels in retino-choroidal complex. We successfully implemented least squares method for measuring concentrations of Hb and HbO_2. We also observed sO_2 levels of the vein are less than an artery.

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