Longitudinal Oxygen Gradients Affect Corrections for Vessel Diameter Sensitivity in Retinal Oximetry

EUGENE AND MARILYN GLICK EYE INSTITUTE
INDIANA UNIVERSITY
School of Medicine

Program 5035 Poster A176

James M. Beach[1], Alon Harris[2], Brent A. Siesky[2], Yoel Arieli[2], Aaron Pickrell[2].

[1]CytoViva, Inc. Auburn, Al, [2]Glick Eye Institute, Indiana University School of Medicine, Indianapolis, IN.

Introduction

The use of imaging to measure oxygen saturation (OS) in retinal blood vessels has developed in many forms since the first measurements using dual-wavelength film recordings were published in 1959 [1]. One of the significant advances has been in capturing vessels over larger areas of retina in single images, allowing examination of oxygen status using fewer images and a shorter session with the subject. With this improvement has come a realization that the smaller vessels systematically show higher OS than larger vessels, even though analysis is performed by exactly the same means on every vessel. The expectation is opposite. Arterial OS is expected to fall along the vessel tree as oxygen diffuses from the smaller vessels. A higher OS in veins near the disc has been suggested, where the source of oxygen is high, however higher OS in the smaller distal veins is not expected to be a prevalent finding. While retinal background surrounding vessels can locally perturb measurements of OS through optical effects that include variation in pigment density and presence of choroidal reflections, these conditions do not systematically increase measured OS in smaller vessels. In fact, the sensitivity of the calculated OS to vessel diameter (D) was shown to be significantly greater in veins than in arteries, and thus correction for the effect may be dependent on vessel type [2]. In this report we provide new measurements across a range of D and consider possible causes that could explain an effect of the vessel diameter on the measured OS.

Methods

OS and D were measured along artery and vein networks (Fig. 1) containing vessels sizes between 30 and 180 µm using Oxymap Retinal Analyzer (N=6 subjects). Vessel diameter sensitivity (DS) was evaluated by linear least squares regression. Regression slopes were used to correct OS values. Dual-wavelength oximetry images obtained with the Oxymap T1 Retinal Oximeter were analyzed to show %OS with a calibrated color saturation map using ImageJ processing. Diameter corrections were performed using morphology plugins (local thickness, B Dougherty; tubeness, J Longair).

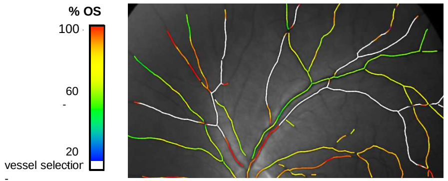

Fig. 1. Retinal oximetry image recorded with 50 degree field of view. Measured vessels have a white overlay.

Vessel Type	% OS 150 µm	% OS 40 µm	% OS difference	DS (%OS/µm)
Artery	92.1	100.4	8.3	-0.14
Vein	61.2	80.0	18.8	-0.43

Table I. % OS and Diameter Sensitivity (DS) in large and small vessels. Values of DS are equal to the slopes of line fits in Figure 2 multiplied by 100.

Results

In both artery and vein, the calculated OS is greater for smaller diameter vessels (D = 40 µm), with the relative increase being approximately 3 times greater in veins (Table I). Vessels greater than 90 um showed no effect of D on calculated OS in either vessel type (Fig. 2). Below 90 um, calculated OS increases with reduction in vessel diameter. Regression slopes (x 100) are taken from Fig. 2 and labeled as the Diameter Sensitivity (DS) in Table I. DS in vein was approximately 3X greater than in artery.

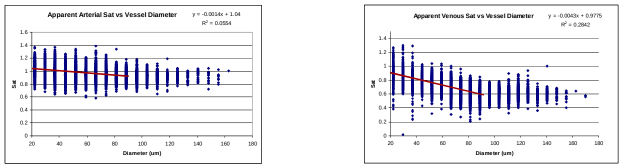

Fig. 2. OS plotted against vessel diameter with line fits applied below D = 90 µm . Left: arterial networks. Right: venous networks.

These findings suggest that additional factors may be involved which influence the calculated OS. Two models are proposed:

1. OS measurements may be parametric

1A. Light scatter from red cells back to the imaging system is relatively greater in larger vessels [3]. A change in the contribution of scattering may explain the presence of DS in the smaller vessels where single and double-pass light transmissions contribute more to the image of the vessel.

1B. The optical density ratio (ODR), a linear function of OS, is itself larger in veins, where greater deoxyhemoglobin concentration raises optical density. If relative amounts of absorption and scatter differ between the oxygen-sensitive and insensitive wavelengths used in dual-wavelength oximetry, this could cause DS to differ in the smaller vessels that transport higher and lower amounts of oxygen.

2. Longitudinal oxygen gradient

2. Diffusion of oxygen from smaller arteries may counteract the effect of DS. This can explain different apparent DS in artery and vein. Here we look to diffusion to explain the difference.

Supported by an unrestricted grant from Research to prevent blindness and Pfizer Pharmaceuticals.

SUPPORTED BY Research to Prevent Blindness

Oxygen Diffusion Model

Diffusion of oxygen into tissue during transport has been reported in small arteries [4-5] and simulated in retinal vessels [6]. We assume that longitudinal OS gradients are present in retinal vessels and that the arterial gradients are large compared to those in veins. The OS gradient along small arteries from diffusion would oppose the apparent changes in OS caused by DS. Table II compares the difference between apparent OS increases from DS and the OS difference found from the diffusion simulation of Liu et al. (2009).

Source	% OS	% OS	OS Difference
Dual wavelength measurement	18.8 increase in vein	8.3 increase in artery	10.5
Diffusion-convection simulation	93.1 artery > 50 µm	82.2 artery < 50 µm	10.9

Table II. Comparison of the difference between saturation increases in vein and artery networks with the drop in arterial saturation found by simulation.

Diameter correction for OS

In oximetry images (Fig. 3) the vessel color is calibrated to % OS. Arteries appear red and veins appear green according to their normal range of OS. The corrected image (right) used the Diameter Sensitivity (Table I) obtained from veins of D < 90 µm.

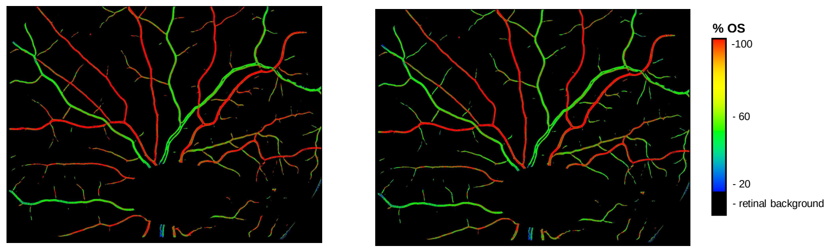

Fig. 3. Retinal arterial and venular networks from dual-wavelength oximetry image before and after correction for DS. This is the same image from Fig. 1 after recalculation of vessel saturations and diameters (ImageJ plugin). Left: Before correction, calculated OS is relatively higher in small diameter segments of veins. This increase is too small to readily observe in arteries. Right: After correction, calculated OS is relatively constant over large and small vein segments. Smaller arterial segments show reduced OS. In this image the correction is based solely on vessel diameter and does not show the saturation gradient along the vessel that would be obtained by convection-diffusion simulation.

Conclusions

Below a vessel diameter of ~90 mm, values of oxygen saturation calculated from dual-wavelength images are inversely related to the vessel diameter. This effect causes artificially high values in the small vessels, more so in veins than arteries. The effect could arise from different optical paths through the large and smaller vessels. We show that if the diameter sensitivity (DS) for calculated saturation is actually the same in both vessel types, the relatively higher values for veins in uncorrected images can be explained by a longitudinal saturation gradient along smaller arteries, due to oxygen diffusion out of the vessel, which counteracts the effect of DS.

References

1. J.B. Hickam, H.O. Sieker, R. Frayser. Studies of retinal circulation and A-V oxygen difference in man. Tr. Am. Clin. & Climatol. A. 71: 34, 1959.
2. M. Hammer, W.Vilser, T. Riemer, D. Schweitzer. Retinal vessel oximetry-calibration, compensation for vessel diameter and fundus pigmentation, and reproducibility, Journal of Biomedical Optics, 13(5), 054015, 1-7, 2008.
3. M.H. Smith, K.R. Denninghoff, A. Lompado, and L.W. Hillman. Effect of Multiple Light Paths on Retinal Vessel Oximetry, Applied Optics, Vol. 39, Issue 7, 1183-1193, 2000.
4. R.N. Pittman. Influence of microvascular architecture on oxygen exchange in skeletal muscle. *Microcirculation*. 1995;2:1–18.
5. M. Sharan, A.S Popel. A mathematical model of countercurrent exchange of oxygen between paired arterioles and venules. *Math Biosci*. 1988;91:17–34.
6. D. Liu, N B. Wood, N. Witt, A.D. Hughes, S.A. Thom, and X.Y. Xu. Computational Analysis of Oxygen Transport in the Retinal Arterial Network, Current Eye Research, 34(11), 945–956, 2009