Changes in oxygenation levels during moderate altitude simulation (hypoxia-induced): A pilot study investigating the impact of skin pigmentation in pulse oximetry.

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Abstract: The current COVID-19 pandemic has shown us that the pulse oximeter is a key medical device for monitoring blood-oxygen levels non-invasively in patients with chronic or acute illness. It has also emphasized limitations in accuracy for individuals with darker skin pigmentation, calling for new methods to provide better measurements. The aim of our study is to identify the impact of skin pigmentation on pulse oximeter measurements. We also explored the benefits of a multi-wavelength approach with an induced change of arterial oxygen saturation. A total of 20 healthy volunteers were recruited. We used Time Domain Diffuse Reflectance Spectroscopy (TDDRS) from a broad band light source, collecting spectra from the index finger along with three different pulse oximeters used simultaneously for monitoring purposes. Five acute hypoxic events were induced by administering 11% FiO_2 for 120 seconds, produced by a Hypoxico altitude training system, through a face mask with a one-way valve. Our multi-wavelength approach revealed a correlation between the signature of skin pigmentation and the dynamic range of oxygen saturation measurements. Principal Component Analysis (PCA) showed separation between a range of different pigmented volunteers (PC1 = 56.00%) and oxygen saturation (PC2 = 22.99%). This emphasizes the need to take into account skin pigmentation in oximeter measurements. This preliminary study serves to validate the need to better understand the impact of skin pigmentation absorption on optical readings in pulse oximeters. Multi-wavelength approaches have the potential to enable robust and accurate measurements across diverse populations.

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1 Introduction

Oxygen is required to sustain life and normal body function in humans; thus, an accurate measurement of arterial oxygen saturation (SaO_2) is an important physiological parameter to assess health status of an individual [13]. Altitude response can vary widely among individuals due to differences in ventilatory response to hypoxia. Multiple techniques for non-invasive oxygenation monitoring have been developed i.e. pulse oximetry. A number of blood properties can be measured non-invasively using optical techniques through the skin. Devices developed for these measurements have proved invaluable in both emergency situations and long-term monitoring of patients in critical conditions. However, they are limited to a narrow oxygen range (80% to 100%) and do not take skin pigmentation into consideration. Indeed Sjoding [15] and Dyer [7] identified that pulse oximeters can overestimate the blood oxygen level for people with pigmented skin and it is now officially recognized by The U.S. Food and Drug Administration (FDA) [4]. Pulse oximeters have become particularly widely used to remotely monitor patients with COVID-19, at home where the higher bias on measurements of oxygen level can result in undiagnosed hypoxemia, which can be fatal especially on patients with severe acute disease like COVID-19 infection. Therefore, the aim of our study is to identify the impact of skin pigmentation on pulse oximeter measurements and explore the benefits of a multi-wavelength approach during an induced acute change of SpO_2 (defined as SaO_2 quantified with a pulse oximetry) in healthy volunteers.

2 Material and Methods

Our cross-sectional study comprised of healthy non-smoking volunteers between 18 and 40 years old at the University of Glasgow (located 27 meters above sea level [1]). All participants provided written informed consent and subjects were excluded if they reported symptoms of flu or respiratory infections up to 10 days before the study, had a history of syncope or with possible pregnancy. The study was carried out in January to February 2020. Twenty volunteers were eligible, two were excluded for history of syncope, six were excluded due to unreadable data after the study, having twelve volunteers for data analysis. Skin pigmentation index was taken from volunteers' photographs (Figures 1B-2B) and classified in skin types I through VI according to the Fitzpatrick scale [9], in order to consider differences in the human skin optical properties due to melanin concentration [18]. Their height, weight, blood pressure, temperature, heart and respiratory rates were recorded. All study procedures were conducted in accordance with the Declaration of Helsinki and were approved by the Ethical Committee Review Board (approval number: 300180273). Volunteers were seated throughout the study, their left forearm and hand were placed over a platform in a table, the index finger was placed over

customized 3D printed holder or optical sensor connected to a multiple wavelength spectrophotometer Ocean Optics (Ocean Optics Inc., FL), a Mightysat Rx ® with Bluetooth LE (model P/N 9909, Masimo, Irvine, CA) was placed in the middle finger, in the ring finger a GO_2 Achieve ® (NONIN Medical Inc., Plymouth, MN) was placed, finally in the little finger a generic brand pulse oximeter was placed (Figures 1A-2A). After 30 seconds of recording at room air, five acute hypoxic events were induced by administration of 11% oxygen for 120 seconds by the Hypoxico altitude training system (Hypoxico Inc., New York, NY) which was previously warmed up for at least 20 minutes and was set using altitude pre-setting No. 12 (according to the manufacturer recommendation) [12]. For our study the oxygen percentage of the mixture was verified by the Handi®+ (Maxtec, Salt Lake City, UT). Administration was done through a face mask (Ambu ®, Ultraseal) connected to a circuit with a one way valve to allow exhalation and prevent mixture with room air during inspiration, administration lasted for 120 seconds while breathing normally, after this time the subjects could recover without the face mask for 5 minutes, at the end of each session, the blood pressure, heart rate, respiratory rate and modified Borg dyspnoea scale [5] were measured and recorded, the process was then repeated until five hypoxic events were recorded. Protocols to induce acute hypoxic events in healthy volunteers to asses accuracy of pulse oximeters are not standard [16, 12], the components of oxygen inspiratory are $PiO_2 = (PB – 47) \times FiO_2$; at Glasgow PB (barometric pressure) is 756 mmHg, 47 mmHg is water vapor partial pressure at 37 °C body temperature, and FiO_2 is the dry-gas fraction of oxygen in breathing gas at room air 20.9% [6], At room air, the inspiratory pressure of oxygen is 148 mmHg, the administration of FiO_2 of 11% created a sudden drop of inspiratory pressure to 78 mmHg; due to variability in lung clearance of the residual gas, acute hypoxic response [17] and cardiovascular response. The 120 seconds administration resulted in a drop to 72 % SaO_2 quantified with a pulse oximetry. The room temperature was kept constant at 24 °C. Data was processed and analyzed with in house MATLAB and Python 3.6 scripts.

3 Results

A spectral profile for all volunteers from different backgrounds and ethnicity was obtained (Figures 1C-2C). Skin types according the Fitzpatrick scale were as follows: Type I (n=3), Type II (n=1), Type III (n=4), Type IV (n=1), Type V (n=1), Type NA (Not defined n=2). To explore the impact of skin pigmentation on SaO_2, a Principal Components Analysis (PCA) was performed. The analysis showed clusters relating to skin pigmentation and oxygenation status. PC2 = 22.99%, scores split into normoxia and hypoxia (Figure 3A) and PC1 = 56.00%, scores divided in skin pigmentation Type I-V according to Fitzpatrick (Figure 3B). There is a difference between subjects with Type I, II and III, compared subjects Type IV and V,

especially subject ID: 019 which diverge the most. Moreover, normoxia and hypoxia cluster are well defined between the samples.

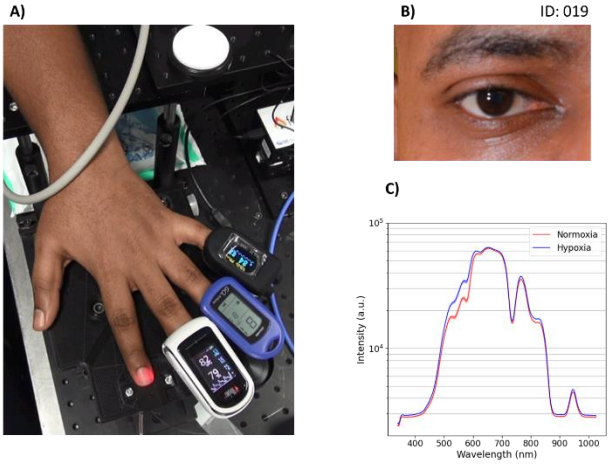

Fig. 1 Volunteer No. 019, high skin pigmentation, Type V. A) left hand volunteer, commercial pulse oximeters placed and reading, index finger optical set-up. B) photo of the volunteer's eye, which shows the presence of melanin in iris coloration, C) averaged spectra HbO_2 (Normoxia) vs HbO_2 (Hypoxia) and standard deviation (shaded).

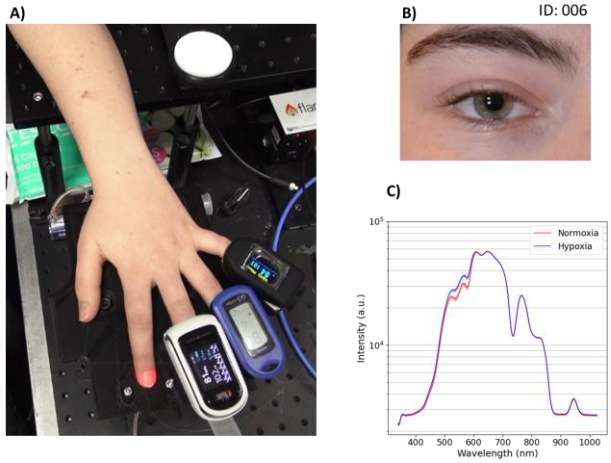

Fig. 2 Volunteer No. 006, low skin pigmentation, Type I. A) left hand volunteer, commercial pulse oximeters placed and reading, index finger optical set-up. B) photo of volunteer's eye, which shows the presence of low melanin in iris coloration, C) averaged spectra HbO_2 (Normoxia) vs HbO_2 (Hypoxia) and standard deviation (shaded).

4 Discussion and Conclusions

This preliminary study using PCA serves to validate the need to better understand the impact of skin pigmentation absorption on optical readings in pulse oximeters. We saw differences in oxygen saturation, which was related to skin pigmentation, especially in Type V volunteer. However, due to the limited sample size of Type V volunteer, future work with a larger sample size is needed to confirm these findings. Initial observation for Type III, IV and V spectral distance between normoxia and hypoxia is closer compared to Type I which is larger. This phenomenon might impact the sensibility of SaO_2 detection on commercial devices. Future work should use melanin quantification expressed as a percentage, to avoid possible color skin misinterpretations (akin to the color scales). Regulatory calibration (ISO) [2] and validation (FDA) [3] procedures mentioned the inclusion of people of color. However, the percentage of inclusion (13% of darkly pigmented subjects) does not reflect the diversity of the population. There is also a need to acknowledge the variability of skin pigmentation inside within ethnicities (i.e. Type I skin pigmentation can change by sun exposure over time for example). To avoid race bias in equipment accuracy would alleviate the subsequent health risks associated with the lack of detection of hypoxemia. In conclusion our multi-wavelength approach was able to detect hypoxia events, but also emphasized the need to take into account skin pigmentation in oximeter measurements.

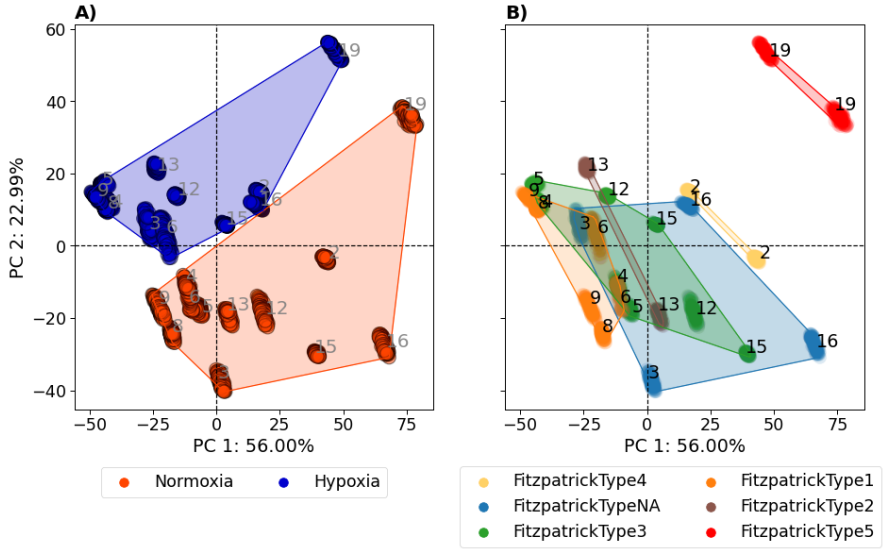

Fig. 3 PCA scatter plots of hyper-spectral measurements (350nm-1000nm; VIS-nIRS) form 12 volunteers. Every dot represents *n* spectral measurement. A) Data colored by oxygenation status. B) Skin pigmentation according Fitzpatrick scale types from I-V.

Acknowledgments We acknowledge support provided by INER and The University of Glasgow, especially to INER's Principal Dr. Jorge Salas-Hernandez and Dr. Laura Gochicoa-Rangel. V. Ochoa-Gutierrez acknowledges financial support from the Mexican National Science and Technology Council and the Ministry of Energy (CONACyT - SENER) through scholarship No. 593603 and the Secretariat of Public Education (SEP) through scholarship BC-9517/36248.

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