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Robustness of Time-Domain Near-Infrared Spectroscopy Against Skin Pigmentation Differences

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Abstract: We systematically demonstrate skin pigmentation negligibly affects TD-NIRS results (optical properties, hemodynamic parameters) through in-vivo (static, dynamic, campaign on pediatric cohort) and phantom measurements, proving its robustness in retrieving tissue saturation in clinical settings.

1. Introduction

Time Domain Near InfraRed Spectroscopy (TD-NIRS) exploits the low extinction profile of tissues in the therapeutic window of 600 - 1100 nm, a wavelength range in which main chromophores thereby contained, e.g. hemoglobins, lipids and water, allow for up to a few centimeters of penetration depth [1]. TD-NIRS capability of easily decoupling absorption from reduced scattering coefficient and of encoding photon penetration depth in time of arrival allows it to retrieve with a single point measurement not only tissue oxygen saturation StO_2, but also absolute values of oxygenated (HbO_2) and de-oxygenated (HHb) hemoglobin, which constitute relevant physiological information in a clinical context [2]. As made evident by the COVID19 epidemic, pulse oximeters commonly employed in clinical scenarios provided severely underestimated saturation readings especially on patients with darker skin, particularly in low saturation regimes. The understanding of the influence of skin pigmentation tone, which can be sistematically evaluated via the Fitzpatrick scale or the Monk scale [3, 4], on the capability of light based oximeters of retrieving accurate values of StO_2 becomes of crucial importance. In this work, we wanted to assess the effect of skin pigmentation on the performance of TD-NIRS measurements by adopting a holistic approach encompassing: i. *in-vivo* measurements on voluntary subjects of different skin tones, both in static and dynamic (arterial occlusion) regimes; ii. measurements on calibrated bulk tissue phantoms, simulating specific saturation levels and respective concentrations of $HbO2$ and HHb; iii. measurement campaign on a large cohort of pediatric subjects covering the whole range of the Fitzpatrick scale, targeting both brain and peripheral muscle hemodynamics at rest.
For measurements i. and ii., we employed different calibrated thin phantoms superimposed on the skin and the phantoms respectively to simulate various degrees of skin tone in the sense of varying melanosome volume fractions (M_f).
Here we will mainly focus on the dynamic measurements of i. and the results related to muscle for the pediatric study (iii.)

2. Materials and methods

Thin tissue-mimicking phantoms (average thickness 270 ± 10 μm) with different skin pigmentation (and including a control phantom with no pigmentation), corresponding to M_f = 0, 2, 6, 14, 30, and 43% were prepared by

mixing silicone as matrix, TiO_2 powder as scattering agent, and a solution of alcohol-soluble nigrosine in ethanol as absorber (Fig.1).

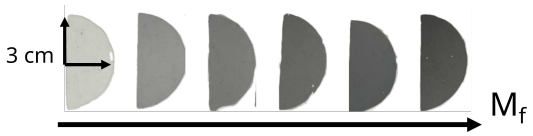

Fig. 1: Skin phantoms of varying equivalent melanosome concentration. From left to right, $M_f = 0$, 2, 6, 14, 30 and 43%.

As for i., six healthy volunteers underwent TD-NIRS acquisitions on the medial side of the right forearm's proximal third during a vascular occlusion test. The 8-minute protocol included three phases: (i) Baseline (1 min) at rest, (ii) Arterial occlusion (3 min) using a manual pneumatic cuff inflated to 250 mmHg on the right biceps, and (iii) Recovery (4 min) after cuff release. Subjects sat relaxed with the forearm resting at heart level. The setup featured two NIRSBOX (PIONIRS S.r.l., Milan, Italy) oximeters [5] and a custom probe with two injection and two detection fibers (2.5 cm source-detection distance). Four skin phantoms (melanin fractions $M_f = 0$, 2, 14, 43%) were used. For each subject, three acquisitions were performed, placing a control phantom ($M_f = 0$) proximally and a pigmented phantom ($M_f = 2\%$, 14%, or 43%) distally. The two optical probes where placed one next to the other, over the pigmented and control phantom respectively and measurements were synchronized and acquired in parallel.
For measurement campaign iii., we enrolled 352 pediatric participants (0–18 years) admitted to the Pediatric Department of Buzzi Children's Hospital, Milan, from March 2023 to February 2024. Eligible candidates were in stable clinical condition, meeting the following criteria: no fever, cardiac or pulmonary pathologies, chronic diseases, ongoing treatments, or wounds at the measurement site; stable vital parameters (heart rate, respiratory rate, SpO_2) and normal hematocrit levels confirmed via blood analysis. TD-NIRS measurements were conducted using the NIRSBOX oximeter with a G5 "Goccia" optical probe (2.5 cm source-detector distance) on the left frontotemporal cortex (Fp1, 10/20 EEG system) for cerebral hemodynamics and on the left mid-upper arm (below the deltoid) for peripheral muscle tissue hemodynamics.

3. Results and discussion

Results related to the arterial occlusion on one of the voluntary subjects are reported (Fig.2). As expected, StO_2 decreases during arterial occlusion and rapidly increases upon cuff release.

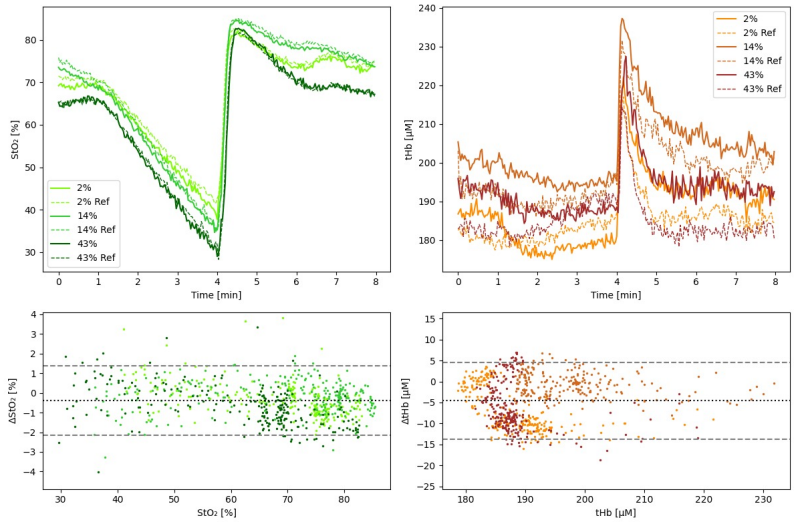

Fig. 2: StO_2 (top left) and tHb (top right) during arterial occlusion for a subject with various skin phantoms ($M_f = 2$, 14, and 43%, solid lines) against the simultaneous reference measurement (Ref, dashed lines). Bland-Altman plots for StO_2 (bottom left) and tHb (bottom right) are reported, taking into consideration all the data points of the protocol. Black horizontal dashed lines represent the upper and lower 95% limits of agreement (bias ± 1.96 × standard deviation of the difference).

The baseline difference observed for $M_f = 2\%$ compared to $M_f = 14\%$ and $M_f = 43\%$ likely stems from varying hemodynamic conditions, as various occlusion protocols were taken sequentially with time intervals. This is

further supported by the temporal evolution of tHb, which shows lower values for $M_f = 2\%$. The effect of arterial occlusion on tHb follows the expected pattern, remaining stable during cuff inflation and rising sharply after release. Unlike StO_2, tHb exhibits greater differences between control and pigmented measurements. The absolute StO_2 bias between pigmented and control phantoms remains $< 1\%$, indicating minimal systematic variation.The limits of agreement are relatively small compared to the measured scale, demonstrating good numerical consistency. In the Bland-Altman plot for tHb, data cluster around different mean values depending on pigmentation but remain mostly within the limits of agreement and temporal dynamics are shown to not be influenced by skin pigmentation level.

As for the pediatric measurement campaign, the cohort was clustered into different phototypes groups (using the Fitzpatrick scale as assessed by the clinicians), which resulted in six groups with population sizes of 17, 111, 129, 62, 26, and 7 subjects, corresponding to Fitzpatrick scores 1 through 6, respectively. Fig.3 shows StO_2 values obtained by TD-NIRS on the middle upper arm as a function of the Fitzpatrick scores.

The average values (dashed lines) are within the standard deviations of all groups. One-way ANOVA displays that there are no significant differences (p-value > 0.05) among the different Fitzpatrick group mean values in StO_2(f-value = 1.10, p-value = 0.36).

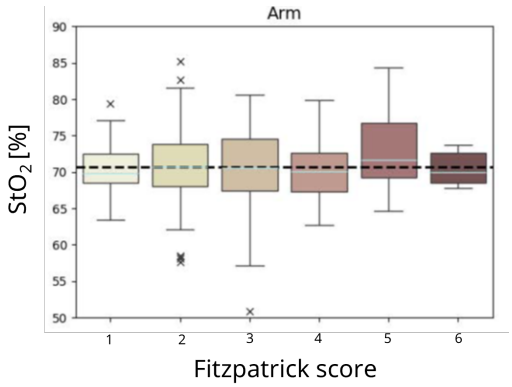

Fig. 3: Statistics of StO_2 of the middle upper arm for Fitzpatrick score-clustered pediatric patients. The solid line within each box plot represents the median value of each cluster; whiskers extend to $1.5 \cdot IQR$, where the Inter Quantilic Range (IQR) is defined by the solid edges of the boxplots; values marked with "x" represent outliers; the dashed line represents the global median.

4. Conclusion

We demonstrated that skin pigmentation do not significantly impact TD-NIRS estimates of optical properties, hemodynamic parameters and their temporal dynamics, highlighting the reliability and clinical potential of this technology.

5. Funding and disclosures

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