Impact of Skin Pigmentation On The Performance of Biomedical Optics Devices

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Abstract

Epidermal melanin can impact signals detected by a wide range of existing and emerging biomedical optics technologies used to perform trans-dermal measurements. We review the mechanisms and effects of melanin on six different clinical device types so as to enhance awareness of the need for additional research and regulatory practices to avoid racial disparities in medical devices.

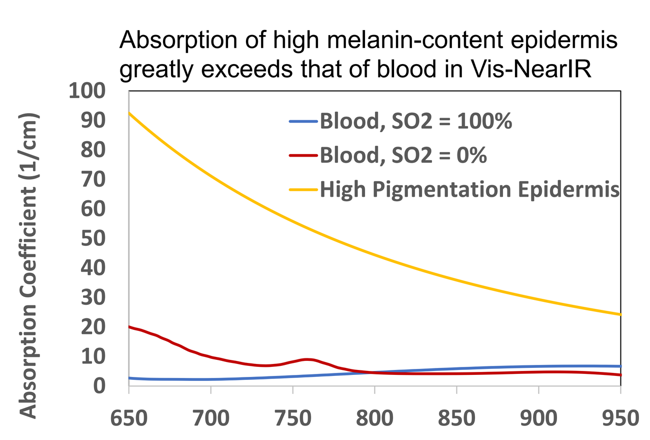
Introduction

Is there evidence that other infrared medical devices [besides pulse oximeters] that interact with a patient's skin pigment… also vary in efficacy by the patient's race and ethnicity?

--Sens. Warren and Wyden in Jan 25, 2021 Congressional Inquiry to FDA

We have performed an initial literature review on the impact of skin pigmentation in optical diagnostic devices. Epidermal melanin can be particularly challenging to device performance because:

- Absorption coefficient is much larger than any other dermal constituent
- Absorption level changes rapidly across the visible to near-infrared range
- Concentration can vary by more than an order of magnitude across the population
- Fluorescence yield is greater than most tissues



Methods

Top used search terms:

- [Device] AND Melanin
- [Device] AND Pigmentation
- [Device] AND Skin Pigmentation
- [Device] AND Pigmentation Influence OR Impact
- [Device] AND Melanin Correction
- [Device] AND Pigmentation Correction

Results and Discussion

Cerebral/Tissue Oximeters

Wavelengths: 675-950 nm (visible/near-infrared); 2-5 wavelengths

Applications

- Cerebral Oximeters are based on near-infrared spectroscopy (NIRS)
- Non-invasive monitor of bulk tissue oxygenation (StO_2) in ICUs/NICUs and during surgery, for rapid detection of hypoxia

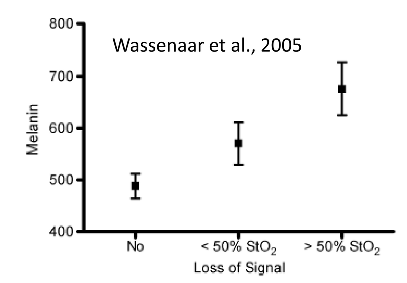
Impact of Pigmentation

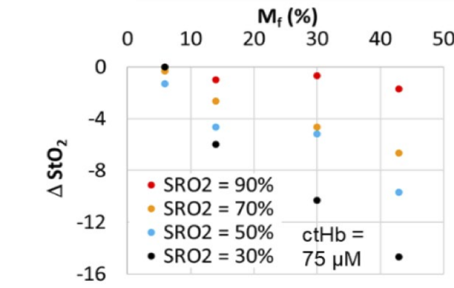
- With increasing pigmentation, Vis-NIR reflectance spectra show decrease in overall intensity, as well as reduced signals at shorter wavelengths (Mendenhall et al., 2015)
- Clinical study showed negative StO_2 bias in adults with high pigmentation in some commercial oximeters (P<0.001) (Bickler et al., 2013)
- African ethnicity / darker pigmentation is associated with lower preoperative intracerebral StO_2, yet this apparent bias did not worsen the ability to predict mortality (Sun et al., 2014)
- Tissue-simulating phantom testing in CDRH showed a negative bias of 5-10% with increasing pigmentation (Afshari et al., 2022)
- Not all cerebral oximeters show a significant pigmentation bias (Couch et al., 2015)
- High melanin levels increased loss of signal (Wassenaar et al., 2005)
- Mechanism of StO_2 negative bias is not well understood

Mitigation Procedures

- Stronger light sources, higher detector sensitivity and narrower probe spacing may be used to minimize the effect of attenuation from melanin and prevent signal loss (Wassenaar et al., 2005)
- Multiple source-detector separation distances and processing algorithms are used to minimize impact of superficial tissue layers

Mendenhall et al., 2015





Afshari et al., BOE 2022 (CDRH) – from phantom

Hyperspectral Imagers

Wavelengths: 400-1000 nm (Vis-NIR); Continuous (or Multi-spectral imaging, 4-5 wavelengths)

Applications

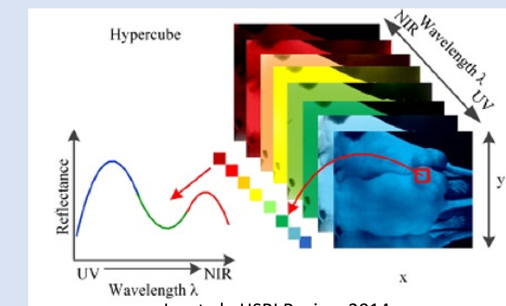
- Hyper/Multi-spectral reflectance imaging (HRI) has many clinical application: surgical guidance, detection of cancers, heart and circulatory pathologies, diabetic foot ulcers

Impact of Pigmentation

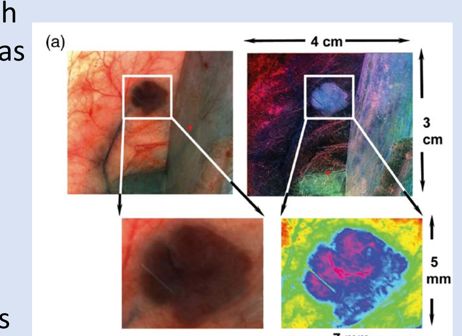
- Increased pigmentation levels is associated with increased absorbance (decreased reflectance) as well as spectral shifts in detected reflectance distributions (Tsai et al., 2020)
- HRI of highly pigmented patients may give a reading or give inaccurate readings of parameters such as oxygen saturation

Mitigation Procedures

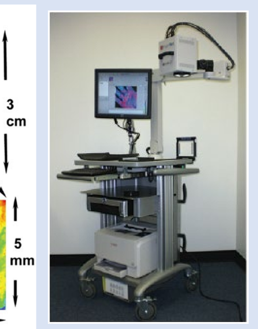
- Some HRI devices utilize weighted subtractions in order to minimize melanin content influence over the desired measurement
- Melanin content is assessed at 595-692 nm (red) and used to correct blood absorption measurements over 530-560 nm (green) to improve saturation measurements (He et al., 2019)



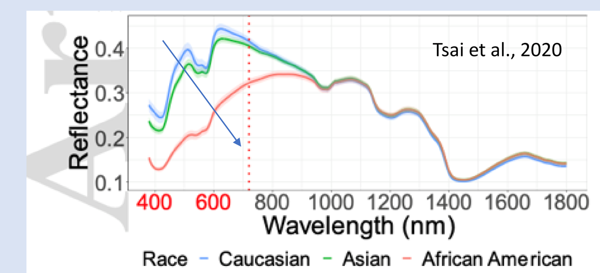
Lu et al., HSRI Review 2014



Lu et al., 2014



Yudovsky et al., 2010



Photoacoustic Imagers

Wavelengths: 550-900 nm (Vis-NIR); Single or multiple wavelengths

Applications

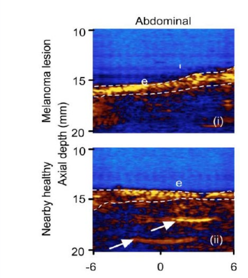
- Photoacoustic imaging (PAI), also known as optoacoustic imaging, has recently been cleared for breast cancer imaging and can visualize microvasculature and measure blood oxygenation. A wide range of applications are in clinical trials.

Impact of Pigmentation

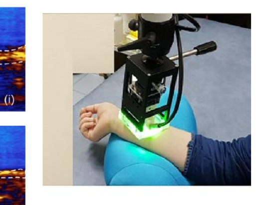
- Produces strong pressure transients in epidermis, increasing near-surface clutter/noise
- Lower signal to noise ratio in the dermis
- Alteration in blood oxygenation estimates via 'spectral coloring'

Mitigation Procedures

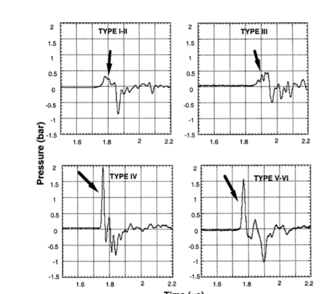
- Fluence correction algorithms may compensate for spectral coloring
- Revise illumination-detection design to minimize clutter



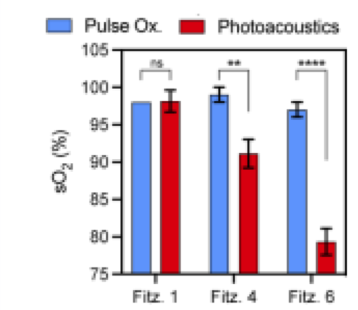
Kratkiewicz et al., 2019

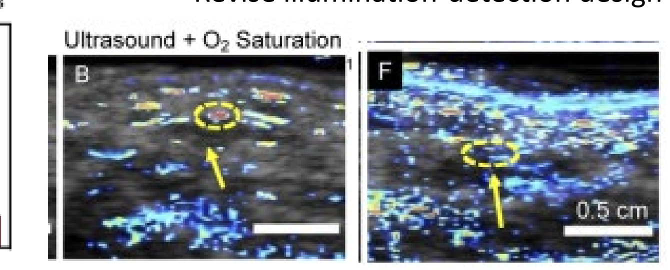


Li et al., 2018

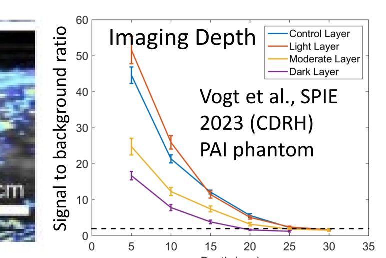


Viator et al., 2004





Mantri et al., BOE 2022



Wearables/PPGs (Photoplethysmography)

Wavelengths: 450-900 nm (Vis and NIR); 2 or more wavelengths

Applications

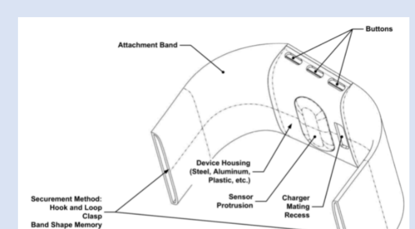
- Real time physiological monitoring of parameters such as heart rate and energy expenditure

Impact of Pigmentation

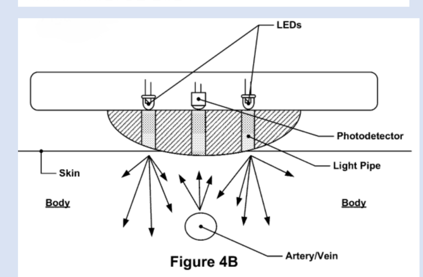
- Reduced modulation and waveform amplitude due to higher pigmentation levels may cause inaccurate pulse rate measurements.
- Fallow et al. (2013) reported that Type V (medium-dark) skin had lowest mean modulation.
- Manufacturer website: 'Skin tone can have an effect as the melanin in the skin absorbs some of the light…the sensor may have to work harder to find a pulse….'
- Some studies have found no significant correlation between skin type and device error/accuracy (Bent et al., 2020)

Mitigation Procedures

- No results found



Fitbit Inc., Patent US8945017B2 2014



Fitbit Inc.

Active green light sensors

Mean Modulation

Fitzpatrick skin type	Light wavelength Blue	Green	Red	Infrared
Type I/II	36.4 ± 16.1	81.2 ± 25.2*	19.4 ± 10.9	23.0 ± 17.6
Type III	37.2 ± 11.7	69.9 ± 32.3*	22.7 ± 14.8	32.9 ± 15.6
Type IV	31.8 ± 10.0	77.7 ± 22.7*	34.6 ± 12.3	34.9 ± 25.8
Type V#	23.6 ± 4.4	49.0 ± 46.8*	22.5 ± 5.7	18.1 ± 7.7

Data are expressed as mean modulation (×1,000) ± SD. Since mean modulation was calculated as the AC/DC ratio components and units are cancelled out, there is no unit to display

* $p < 0.001$ versus other wavelength; # $p < 0.05$ versus other skin types

Fallow et al., Skin Type Reflectance 2013

Transcutaneous Bilirubinometers

Wavelengths: 380-760 nm (Vis); continuous or 2+ wavelengths

Applications

- Detect and monitor hyperbilirubinemia in neonates by non-invasively measuring serum bilirubin values

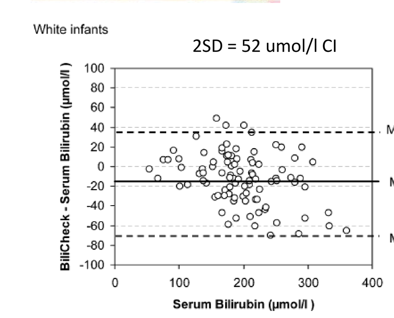
Impact of Pigmentation

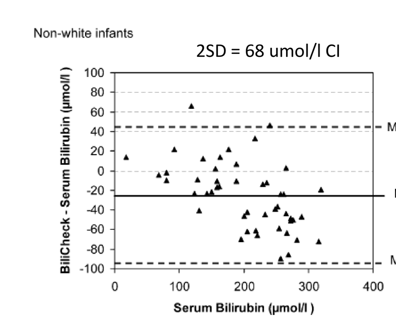
- Accuracy of the commercial bilirubinometer, Bilicheck, was significantly lower in non-white infants compared to white infant (P=0.02). (Szabo et al., 2004)

Mitigation Procedures

- Multiple wavelengths in 400 -760 nm used to correct for skin pigmentation (Cheng et al., BOE 2019)

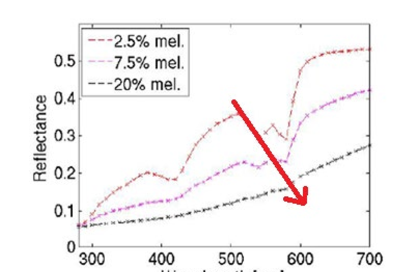
Verughese et al., Indian J Ped Derm 2018





Szabo et al., 2004

Impact of melanin on reflectance in visible region of spectrum



Raman Spectroscopy Devices

Wavelengths: 550-1100 nm (Vis-NIR); Single wavelength excitation, broadband detection

Applications

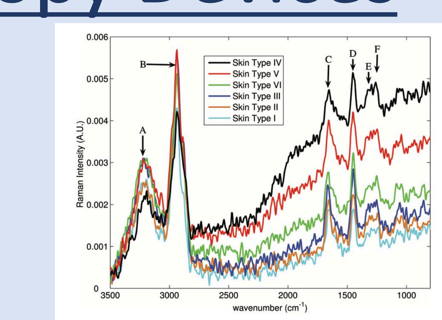
- Raman spectroscopy has been studied for non-invasive glucose sensing, cancer detection, psoriasis, atopic dermatitis, and other conditions

Impact of Pigmentation

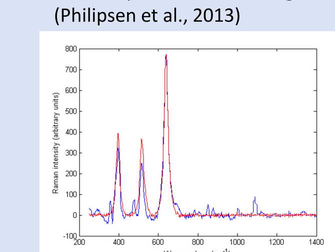
- Melanin has the potential to absorb both excitation light and Raman scattering
- Additionally, endogenous fluorescence from melanin produces high background compared to the weak Raman scattering signals (Knudsen et al., 2002; Philipsen et al., 2013)

Mitigation Procedures

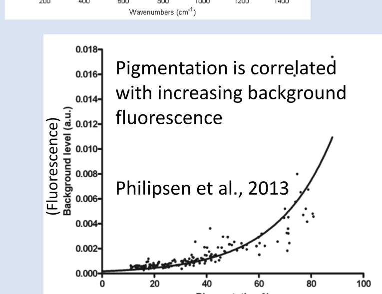
- Numerical background correction approaches are used to remove influence of melanin fluorescence
- Background correction approaches are typically highly effective at removing fluorescence contributions from detected Raman spectra



Raman Spectra Before Background Correction (Philipsen et al., 2013)



Raman Spectra After Background Correction (Assi et al., 2011)



References

Afshari et al. Biomedical Optics Express, 10 (8), 3731-3746, 2019
Bent et al., npj Digital Medicine, 3, 18, 2020
Bickler et al., Anesthesia and Analgesia, 117(4), 812-823, 2013
Couch et al., American Journal of Analytical Chemistry, 6, 911-916, 2015
Else et al., SPIE Poster, 2021
Fallow et al., Journal of Clinical Monitoring and Computing, 27(3), 313-317, 2013
Fitbit Inc., Patent US8945017B2, 2014
He et al., Biomedical Optics Express, 10(11), 5625-5638, 2019
Knudsen et al., Journal of Raman Spectroscopy, 33, 574-579, 2002
Kratkiewicz et al., Sensors, 19(12), 2815, 2019
Li et al., Journal of Biophotonics, 12(9), 2019
Lu et al., Journal of Biomedical Optics, 19(1), 010901, 2014
Maslov et al., Inverse Problems, 23, S113-S122, 2007
Philipsen et al., Photochemical and Photobiological Sciences, 12, 770-776, 2013
Smith et al., Ophthalmic Technologies XI, 4245, 2001
Sun et al., British Journal of Anesthesia, 114(2), 276-280, 2015
Szabo et al., European Journal of Pediatrics, 163, 722-727, 2004
Tsai et al., JEADV, 35, e306-e352, 2021
Viator et al., Journal of Investigative Dermatology, 122(6), 1432-1439, 2004
Wassenaar et al., Journal of Clinical Monitoring and Computing, 19, 195-199, 2005
Yudovsky et al., Journal of Diabetes Science and Technology, 4(5), 1099-1113, 2010

Conclusions

Although skin pigmentation may not be the only cause of disparities in device performance, melanin represents a significant confounding factor for many optical diagnostic technologies, through different physical mechanisms. Devices often employ approaches to mitigate the impact of pigmentation on final outputs, yet significant effects can remain. CDRH research scientists are developing regulatory science tools to evaluate device robustness to skin pigmentation.

This research was funded in part by **FDA's Office of Minority Health and Health Equity.**