Skin Pigmentation Impacts in Established and Emerging Optical Diagnostic Devices: A Review of Mechanisms and Effects

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Abstract

Melanin has long been recognized as a major dermal chromophore, and the same optical characteristics that make melanin the chief determinant of visually identifiable pigmentation also have the potential to adversely impact the performance of medical devices based on light. This work encompasses an extensive review of literature of the impact of skin pigmentation on optical diagnostic technologies including pulse oximeters, PPG wearables, cerebral oximeters, photoacoustic imagers, bilirubinometers, hyperspectral imaging systems, and Raman spectroscopy devices.

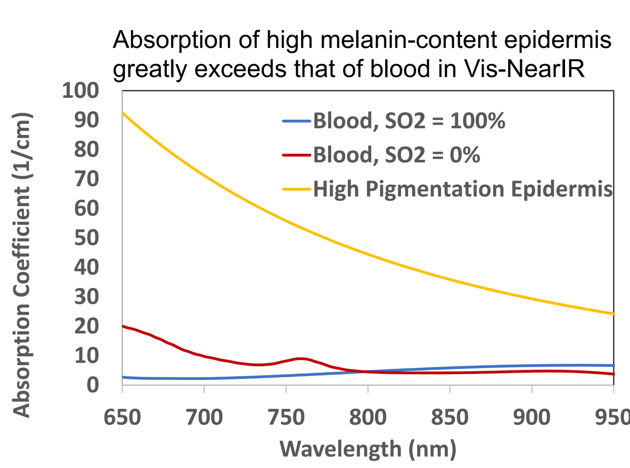
Introduction

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

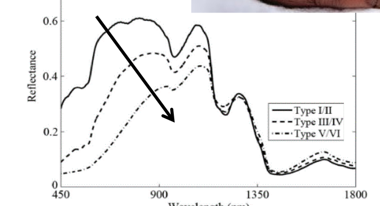
- Cerebral Oximeters are based on near-infrared spectroscopy (NIRS)
- Non-invasive monitor of bulk tissue oxygenation (StO_2) in ICUs/NICUs and during surgery, for rapid detection of hypoxia

Impact of Pigmentation

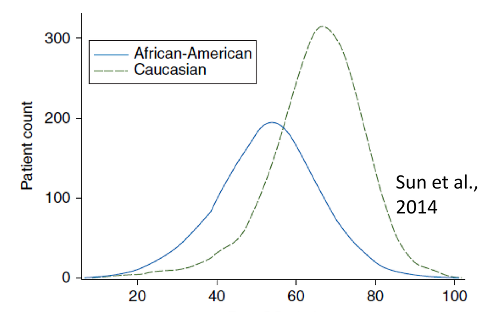
- With increasing pigmentation, Vis-NIR reflectance spectra show decrease in overall intensity, as well as reduced signals at shorter wavelengths (Mendenhall et al., 2015)
- Clinical study showed negative StO_2 bias in adults with high pigmentation in some commercial oximeters (P<0.001) (Bickler et al., 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., 2019)
- Not all cerebral oximeters show a significant pigmentation bias (Couch et al., 2015)
- Mechanism of StO_2 negative bias is not well understood
- High melanin levels increased loss of signal (Wassenaar et al., 2005)

Mitigation Procedures

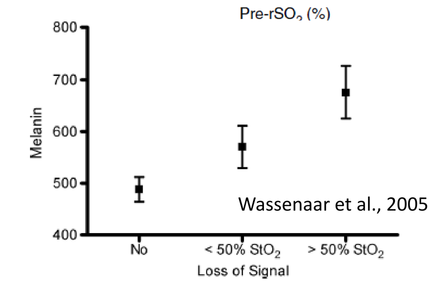
- Stronger light sources, higher detector sensitivity and narrower probe spacing may be used to minimize the effect of attenuation from melanin and prevent signal loss (Wassenaar et al., 2005)
- Multiple source-detector separation distances and processing algorithms are used to minimize impact of superficial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



Mendenhall et al., 2015



Sun et al., 2014



Wassenaar et al., 2005

Hyperspectral Imagers

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

Applications

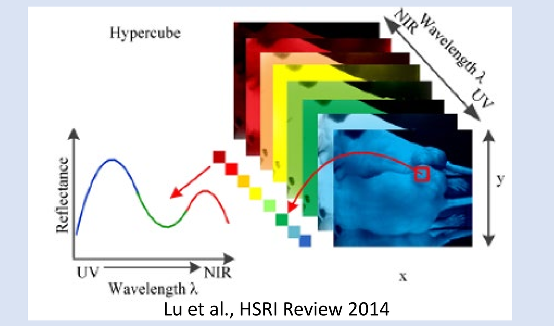
- Hyper/Multi-spectral reflectance imaging (HRI) has many clinical application: surgical guidance, detection of cancers, heart and circulatory pathologies, diabetic foot ulcers

Impact of Pigmentation

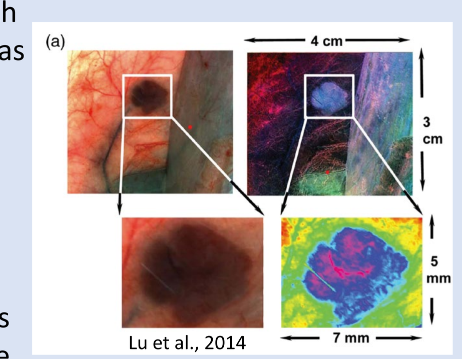
- Increased pigmentation levels is associated with increased absorbance (decreased reflectance) as well as spectral shifts in detected reflectance distributions (Tsai et al., 2020)
- HRI of highly pigmented patients may give a reading or give inaccurate readings of parameters such as oxygen saturation

Mitigation Procedures

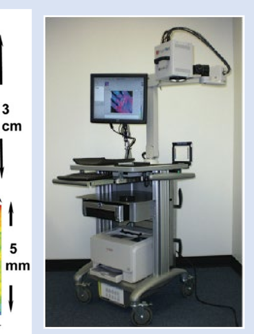
- Some HRI devices utilize weighted subtractions in order to minimize melanin content influence over the desired measurement
- Melanin content is assessed at 595-692 nm (red) and used to correct blood absorption measurements over 530-560 nm (green) to improve saturation measurements (He et al., 2019)

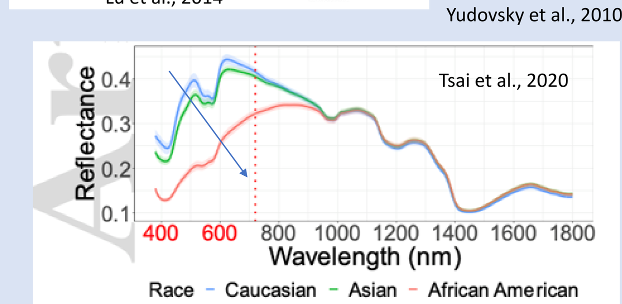


Lu et al., HSRI Review 2014



Lu et al., 2014


Yudovsky et al., 2010



Tsai et al., 2020

Photoacoustic Imagers

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

Applications

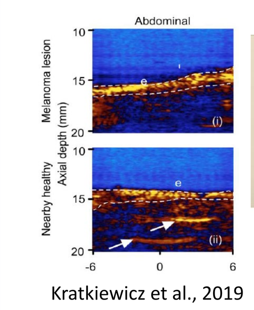
- Photoacoustic imaging (PAI), also known as optoacoustic imaging, has recently been cleared for breast cancer imaging and can visualize microvasculature and measure blood oxygenation. A wide range of applications are in clinical trials.

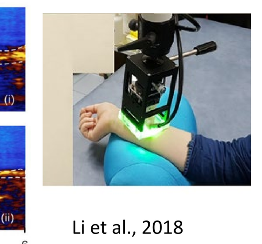
Impact of Pigmentation

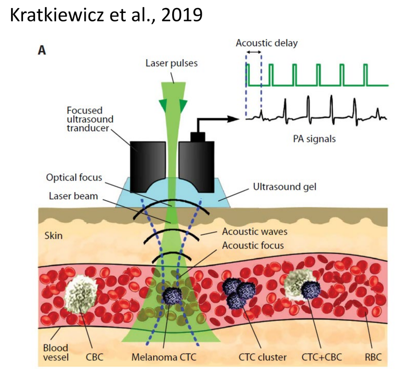
- Increasing melanin content is associated with higher pressure amplitudes near surface, which may increase superficial clutter/noise
- Darker pigmentation results in lower signal to noise ratio in the dermis
- Epidermal melanin absorption can alter saturation estimates via 'spectral coloring' (based on simulations)

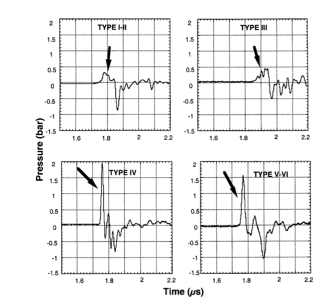
Mitigation Procedures

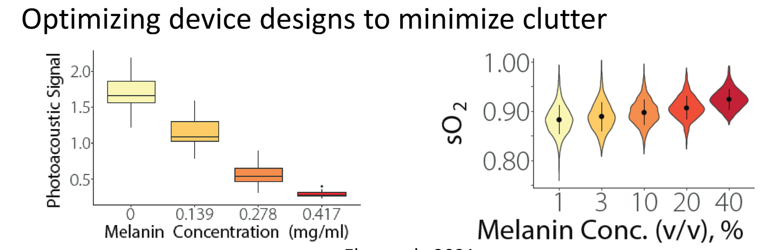
- Fluence correction algorithms may compensate for spectral coloring
- Optimizing device designs to minimize clutter


Kratkiewicz et al., 2019


Li et al., 2018


Galanzha et al., Science Trans Med 2019


Viator et al., 2004



Else et al., 2021

Wearables/PPGs (Photoplethysmography)

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

Applications

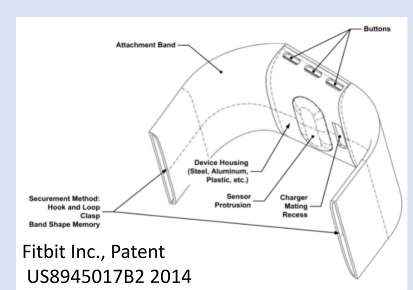
- Real time physiological monitoring of parameters such as heart rate and energy expenditure

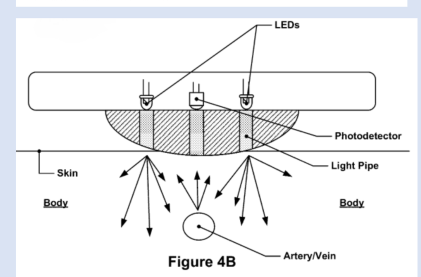
Impact of Pigmentation

- 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

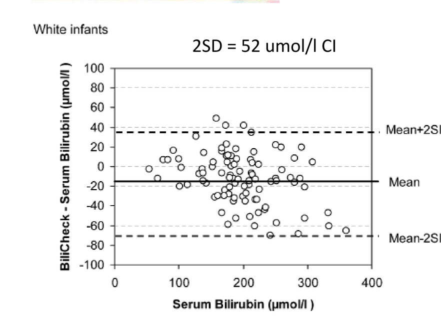
Impact of Pigmentation

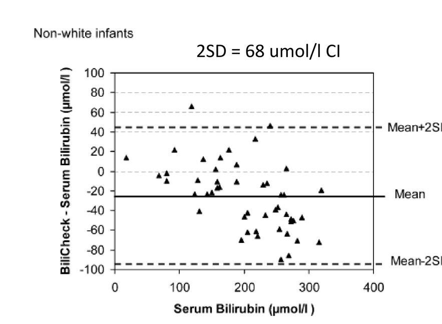
- Accuracy of the commercial bilirubinometer, Bilicheck, was significantly lower in non-white infants compared to white infant (P=0.02). (Szabo et al., 2004)

Mitigation Procedures

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

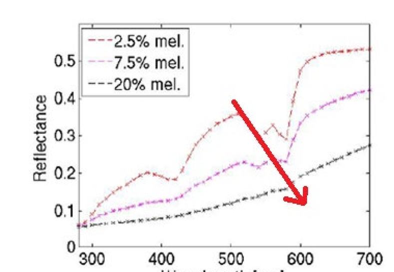

Verughese et al., Indian J Ped Derm 2018





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

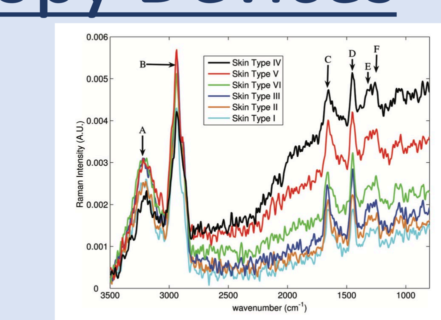
- Raman spectroscopy has been studied for non-invasive glucose sensing, cancer detection, psoriasis, atopic dermatitis, and other conditions

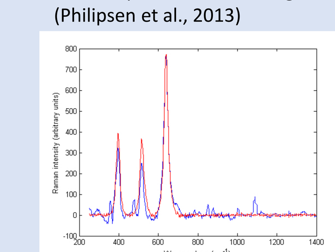
Impact of Pigmentation

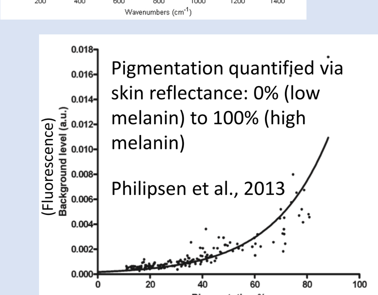
- Primary mechanism is optically distinct from reflectance and absorption based technologies.
- Endogenous fluorescence from melanin produces high background compared to the weak Raman scattering signals (Knudsen et al., 2002; Philipsen et al., 2013)
- Background correction approaches are typically very effective at removing fluorescence contributions, so there is typically minimal effect on major Raman peaks

Mitigation Procedures

- Numerical background correction approaches are used to remove influence of melanin fluorescence


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


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



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Conclusions

Although skin pigmentation may not be the only cause of disparities in device performance, it is a significant confounding factor for many optical diagnostic technologies. Signals detected by all of the device types reviewed were reported to be impacted by melanin concentration through several different mechanisms. Devices often employ approaches to mitigate the impact of pigmentation on final outputs, yet significant disparities remain.

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