SKIN-TONE INCLUSIVE MEASUREMENT OF BILIRUBIN IN NEWBORNS USING PHOTOTHERAPY

PATIENTS, PHYSICIANS, AND DESIGNERS CHANGE IN TRUST DUE TO BIAS FOUND IN PULSE OXIMETERS

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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General Research Problem: Ensuring Skin-tone Inclusive Optical Imaging Design

Optical imaging is affected by skin melanin content and can change medical outcomes.

Optical imaging is a clinical technology used by a broad range of medical devices to measure blood oxygen saturation, heart rate, and jaundice progression. These common measurements are used to guide decision-making for treatment plans and insurance approval. However, the optical measurement devices are affected by other pigments in the skin like melanin, which governs skin tone and is a potent light absorber. Thus less light can be used to measure the intended value, and the pigments reduce the penetration of the optical imagers (Mantri & Jokerst, 2022). For example, blood oximeters report significantly higher blood oxygen saturation levels in the dark-skinned population. This bias results in a 3.2-fold increased likelihood that dark-skinned subjects have undiagnosed hypoxia and potentially do not receive needed supplemental oxygen, which may lead to worse disease outcomes (Sjoding et al., 2020). The bias became widely known to the public during the 2019 COVID outbreak when several articles highlighted bias in pulse oximeters. Additionally, jaundice disease and or treatment progression is routinely measured through the skin. However, the absorbance spectrum of bilirubin, the pigment responsible for jaundice, overlaps with melanin, which causes the measurement devices to overestimate bilirubin concentration. Thus, dark-skinned newborns are subjected to unnecessary phototherapy and more skin pricks, which could lead to emotional distress, infection, and or bone disease (Okwundu et al., 2017).

These disparities in medical treatment illustrate the importance of creating skin tone-inclusive designs and investigating how trust in medical devices is affected by technical research

and the perception of physicians and patients. This research will be two-fold. First, the technical team will investigate alternate methods for measuring jaundice in newborns with high melanin content. Second, physician interviews, engineering students' assignments, and online readers' comments will provide insight into how these groups view and react to the skin-tone bias of pulse oximeters. Both research projects will help remedy bias and understand trust in medical devices.

Skin-tone Inclusive Measurement of Bilirubin in Newborns using Phototherapy

Can the properties of phototherapy be used to create an equitable jaundice measurement device?

Jaundice, or hyperbilirubinemia, is the yellow color in many newborns' skin due to high concentrations of bilirubin, a pigment from broken-down blood cells. Bilirubin accumulates in the skin due to poorly functioning livers, which is very common in newborns. Jaundice occurs in approximately 50% of term and 80% of preterm infants within the first week after birth. Phototherapy is completed in 10% of term and 25% of preterm neonates to treat severe hyperbilirubinemia by using light to break down bilirubin into lumirubin which the body can readily break down and excrete (Queensland Clinical Guidelines, 2019). The current gold standard measurement procedure is directly measuring bilirubin levels through blood serum samples from heel pricks, which is called Total Serum Bilirubin (TSB). These procedures are invasive and painful for the newborn and can lead to dangerous complications such as infection and bone or joint disease (Shah & Ohlsson, 2011). Noninvasive measurement methods have emerged by indirectly measuring bilirubin through the skin, like with Transcutaneous bilirubinometry (TcB). This is an easier, safer, and more convenient method to estimate blood

bilirubin concentration by optically measuring skin color, without requiring a skin prick (Dai et al., 1996). However, these TcB monitors tend to overestimate bilirubin concentration in neonates with high melanin content due to an overlap in absorption spectra of bilirubin and melanin, the dark pigment responsible for skin tone (Onks et al., 1993). This can result in dark-skinned newborns undergoing unnecessary phototherapy which needlessly separates the newborn from their mother and can disrupt their thermal environment (Okwundu et al., 2017). To remedy this issue, we will investigate alternate methods for accurately detecting TSB in neonates with high melanin content.

Our current solution will use the properties of phototherapy, which converts bilirubin to other molecules. Importantly, these molecules have the same chemical formula but different orientations at specific atoms and thus different properties. For example, lumirubin is the preferred orientation or configuration because it can be more easily removed from the skin and excreted from the body. Lumirubin has a different absorption spectrum than bilirubin due to the difference in configuration (Malhotra & Ennever, 1986). This property allows the conversation of bilirubin to lumirubin to be measured optically, the crux of our solution. Using concentrated phototherapy on a small area on the ear of a newborn, we hope to be able to measure the conversion from bilirubin over time, which we expect to follow an exponential decay curve. The initial concentration of bilirubin can be determined by fitting an exponential decay function to the curve. Since absolute absorbance is not used to measure bilirubin, this method will not be affected by skin-melanin concentration. We selected the ear as the site of testing because it is much easier to measure absorption when the amount of light that passes through the ear is known. Additionally, concentrated phototherapy in a small area allows for faster conversion and thus quicker test times.

We will first develop a computational model using known absorbances of skin pigments to determine the optimal wavelength for conversion to lumirubin. The wavelength of light used has been shown to significantly impact the proportion of lumirubin formed relative to other byproducts that are more difficult to excrete. The light intensity is also important because if too low, bilirubin degradation would occur too slowly for the device to work in a timescale similar to existing devices. Then we will adapt the computational model to predict the change in absorbance due to the conversion of bilirubin during phototherapy. This knowledge will guide our creation of a physical model by providing insight into the test duration, expected absorbance change, and optimal light wavelength. The physical model will measure the transmission of a blue LED array through a test cuvette with a spectrometer. Building a physical model that only accounts for melanin and bilirubin, while simple, is an important step; skin melanin concentration can be about 50 times greater in dark than fair skin tones (Karsten & Smith, 2011). This likely makes melanin the cutaneous component that is most likely to significantly impede the progression of our concept. We expect to have a working proof of concept that accurately measures bilirubin concentration in vitro across all physiological skin melanin concentrations.

Our research could be the foundation for a TcB device that is accurate for all skin tones. This could improve the quality of neonatal care, allow for the monitoring of jaundice in newborns, and reduce the number of newborns readmitted to the hospital for phototherapy or exchange transfusion. In addressing the dissonance in healthcare received by infants with higher melanin levels, the future applicability of our work provides an avenue for better tackling the mathematical and experimental intricacies of this problem.

Patients, Physicians, and Designers Change in Trust to Bias Found in Pulse Oximeters

How are skin-tone-inducted biases of optical pulse oximetry responded to by society, engineering students, physicians, and patients by their change in trust in the device?

Pulse oximeters are widely used in clinical and non-clinical settings to measure blood oxygenation levels of critically ill, perioperative, and chronically ill patients because they are quick, cheap, and easy to use (Bousfield et al., 2021; Jubran, 2015). Blood oxygen saturation levels provide knowledge about general patient health and thus are used to end respiratory treatment and as thresholds for insurance reimbursement (Jubran & Tobin, 1990). Low oxygen levels were a dangerous symptom of the SARS-CoV-2 virus, which lead to the increased use of pulse oximeters in households and patients' interaction with the device.

Pulse oximeters work by shining two wavelengths of light through someone's finger and measuring how much light is absorbed throughout a heartbeat. After a calculation, the absorption measurements are used to estimate blood saturation level using a calibration curve determined by the manufacturer. However, these absorption values are affected by the relative concentration of other skin pigments such as melanin. Researchers since the 1990s have observed an overestimation of blood oxygen saturation in darker-skinned patients (Jubran & Tobin, 1990). This bias could prevent darkly-skinned patients from access to supplemental oxygen or insurance reimbursement if those decisions are based on blood saturation levels read from pulse oximeters, which may put them at greater risk for dangerous complications.

The COVID-19 pandemic helped expand the use of pulse oximeters to the home and new research confirming the results from Jubran and Tobin has brought this bias into the publics' eye and onto their fingers. In 2020, Sjoding et al found that Black patients had an 11.4% chance of

having unknown low oxygen saturation compared to 3.6% in white patients (Sjoding et al., 2020). At the same time, Moran-Thomas and Rabin from Boston Review and The New York Times respectively published articles discussing the pulse oximeter "encoding racial bias" (Moran-Thomas, 2020; Rabin, 2020). This research and articles prompted responses from US Senators, the FDA, physicians, researchers, manufacturers, patients, and others. This sociotechnical research will explore how patients' perceptions and trust in the pulse oximeter change because of technical research, media articles, and government policies.

The FDA released a statement in February 2021 after a letter from Senator Warren, Wyden, and Booker in Jan 2021, asking for the FDA to review the accuracy of pulse oximeter devices. The FDA's statement starts with recommendations for patients and caregivers which includes being aware of factors like skin pigmentation. The statement reiterated that the FDA has recommended that every pulse oximeter clinical study must have two darkly pigmented participants or 15% of the participant pool, whichever is larger (FDA, 2022). The Anesthesia Patient Safety Foundation (APSF) first agrees with Sjoding et al. Then, they go on to say that the FDA's policy of at least 15% darkly pigmented subjects in the study group may reduce biases but not improve performance for the individual patient. Both the FDA's and APSF's statements point out that reduced confidence in pulse oximeters would be harmful to patient health because the devices can provide important biological estimates, which should be a piece of a patient's complete assessment leading to sound clinical decision-making (APSF, 2021). This is the argument for continuing to trust pulse oximeters as part of a holistic clinical diagnosis. The balance between trust and distrust in the eyes of patients, researchers, and physicians will determine new FDA policies, new medical devices, and new clinical procedures. This STS research will focus on how patients' trust in the pulse oximeter changes with differing responses

about the surfacing bias in pulse oximeters from physicians, the FDA, and the media because it has been largely unresearched.

Data Collection and Analysis

Initial thoughts about the trust in the pulse oximeters by healthcare professionals. Interviews with physicians and nurses at UVA Health will allow for more insight into the current usefulness of the pulse oximeter in a clinical setting, and how new research has affected the physician's trust in the device. These interviews will be transcribed and the sentiments from all the professionals will be compiled, which will be the clinical perspective of the device. Additionally, the healthcare professionals will be asked how they have dealt with their own and their patient's concerns with bias in measurement devices specifically the pulse oximeter. These stories and patient management techniques will provide insight into how provides navigate technological limitations in clinical care. Next, the comment sections of articles from the Washington Post, Wall Street Journal, and NPR will be similarly coded to understand what sentiments exist in the nonprofessional setting (Bajaj, 2022; LeMoult, 2022; Mosbergen, 2022). The professional and nonprofessional perspectives will be used to understand clinical trust in pulse oximeters and specific techniques professionals employ to gain patient trust while using biased measurement devices.

Conclusion

Medical devices that use optical imaging of the skin are not accurate across all skin tones due to the absorbance of light from melanin. This bias can cause worse outcomes for specific ethnic groups and decrease the trust and usefulness of certain medical devices. This research will

create a proof-of-concept for an equitable bilirubin measurement device for newborns, which if proven successful could turn into a commercial device. Additionally, the societal research will explore how measurement devices can be seen as trustworthy across skin tones, which could be used to create trust in our bilirubin measurement device and many other devices. Together, this research will progress equity in the healthcare system.

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