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Initial Validation of the NOL Nociception Level Index® Monitoring System in Black and Multiracial People

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Abstract: The NOL-Nociception Level Index® is a multiparameter index, based on artificial intelligence for the monitoring of nociception (physiological pain response) during anesthesia that has recently been authorized by the FDA. The monitor utilizes continuous streams of information from a finger probe comprising four sensors, including photoplethysmography, to provide a personalized nociception score on a scale of 0–100. Recent studies have suggested racial bias in pulse oximeter measurements due to the effect of melanin levels on photoplethysmography measurements. Therefore, there is a need to clinically validate new monitoring technologies in patients of all skin tones. The performance of the NOL scale in 8 patients that self-identified as Black or multiracial was compared to a database of 447 consented patients, assessing the response to surgical events at different levels of intensity. The descriptive, pilot data suggest that NOL performance in Black and multiracial patients is not different from the performance shown for the large database. Larger studies utilizing recognized skin tone scales to ensure accurate assessment of skin pigmentation are planned for the future.

Keywords: nociception monitoring, pain management, inequity in healthcare, patient monitoring

Introduction

Recent studies have shown that despite improvements in overall health in the US, racial and ethnic minorities experience a lower quality of health care, are less likely to receive routine medical care and face higher rates of morbidity and mortality than non-minorities. A recently published report by the AHRQ (Agency for Healthcare Research & Quality) [1] noted that substantial disparities in life expectancy exist among people of different racial and ethnic backgrounds. A report published by the IOM (Institute of Medicine) concluded that a comprehensive, multilevel strategy is needed to eliminate these disparities.[2] A well-published example is the racial bias in pulse oximeters - demonstrated by higher frequency of occult hypoxemia in Black patients.[3] In response, the FDA (Food & Drug Administration) published a safety alert concerning the use of pulse oximeters and recently proposed a new approach for the validation of pulse oximeter devices that takes skin pigmentation, race, and ethnicity into consideration.[4] The FDA has started assessing innovative devices submitted for pre-market review to ensure that performance is validated in patients representative of the general population, including different racial and ethnic backgrounds, in order to decrease disparities in healthcare. A recent study[5] demonstrated that limited differences exist between pigment groups in pulse oximetry measurements.

The PMD-200™ monitor (Medasense Biometrics, Ramat Gan, Israel) is a nociception monitor that was recently authorized by the FDA as an innovative device through the De Novo pathway. The monitor makes use of an algorithm based on advanced machine learning technologies; it combines photoplethysmograph (PPG) amplitude, skin conductance, heart rate, heart rate variability and their time derivatives into a single index - The NOL index.[6] Machine learning was used to create the optimal algorithm to translate input (predictors) into output (NOL index) without the need of an a-priori specified stochastic model. The index ranges from 0 (absence of nociception) to 100 (extreme nociception) (Figure 1). The algorithm was validated in multiple studies[6–8] with a NOL value of 25

Received: 22 August 2024
Accepted: 30 October 2024
Published: 13 November 2024

Figure 1 The PMD-200 Monitor.

identified by the manufacturer as the `best fit` cut-off score to discriminate between nociceptive and non-nociceptive response.[9] The algorithm furthermore 'personalizes' its nociception reading to the individual patient by "learning" the magnitude of the physiologic responses to surgical stimuli as the case progresses and normalizing its output to the accumulated data accordingly.

In this report, we will describe the technical design considerations of the device and the initial clinical validation performed to demonstrate the generalizability of the device performance in black and multiracial people. This study complies with the declaration of Helsinki.

Materials and Methods

The photoplethysmograph (PPG) signal and derived measurements in the PMD-200 are used for assessing volumetric changes during pulsatile flow in the vascular bed of the patient's finger. The PPG sensor measures the light reflectance of incident light of a single wavelength (940 nm). In contrast, PPG sensors used to derive arterial oxygen saturation (SpO2) shine light through the skin and measure the difference in light absorbance at two wavelengths (660 nm and 940 nm).

The predominant skin pigment in humans, melanin, is a major absorber of light. The absorption of epidermal melanin is much higher in the visible region of the spectrum (660 nm) and much lower in the near infra-red region of the spectrum (940 nm). Therefore, concerns relating to effects of skin pigmentation on the accuracy of the PPG are most pertinent to the measurement of SpO2, as it relies on absorbance of 660 nm light, and not to volumetric measurement, which relies on the reflectance of a single, infrared wavelength of light (940 nm).[10] As the wavelength of 660 nm is not used to derive the PPG signal used as input to the NOL index, concerns about artifacts caused by higher melanin levels in patients with darker skin pigmentation are greatly reduced.

In addition, PPG measurements implemented in the NOL algorithm are relative and not absolute. Thus, any potential offset introduced by skin pigmentation or other differences in patient characteristics[9] would be mitigated by the normalization process of the algorithm where the NOL output is normalized to the patient's own data, offering a personalized measure.

In summary, although both SpO2 and NOL derive a physiologic measurement from photoplethysmograph (PPG), they do so using different wavelengths and properties of light and extract and interpret different features from the

signal. NOL uses a wavelength that is not affected by skin tone (near IR). Moreover, NOL is a personalized measurement normalizing the data to the patient's own accumulated physiological data as analyzed by the algorithm. Therefore, by design, the NOL index is not susceptible to potential offsets from varying amounts of skin pigmentation.

In order to perform an initial assessment of the influence of skin pigmentation on NOL performance, 8 fully annotated adult patient datasets denoted as Black (n=5) or multiracial (n=3) through patient self-reporting, gathered during clinical pilot studies conducted in the USA, were identified. No quantitative scales were used to assess skin pigmentation levels.

The eight adult patient sets selected for the analysis were gathered from two IRB approved pilot studies performed in the US, one of which was published.[11] IRB approval numbers were 2020–00581 at Stony Brook University Hospital, New York and 19–1646 at Cleveland Clinic, Ohio. In both pilot studies, datasets were shared with the device manufacturer for further research. All patients signed written informed consents.

These datasets were compared to a clinical database comprised of eight prospective NOL validation studies. All eight studies were individually approved by the relevant Institutional Review Boards, and all patients enrolled signed written informed consents. Data were shared with the manufacturer in a compliant manner and with permission for the current use.

We compared the NOL response in those 8 patient datasets to the database of 447 patients, evaluating the response to surgical events at different levels of intensity that had already been studied in an assessment of the generalizability of the algorithm performance in patients undergoing surgery under general anesthesia across different patient subgroups. The subgroups included sex, ASA risk score, BMI, age, anesthesia regimen and analgesia regimen.[9] Based on the technical explanation above, we expected the data from the 8 patient datasets to be no different from the general cohort.

For each patient, the same analysis performed on the database cohort was repeated, and the annotated events with the respective NOL values for non-nociception, mild nociception, moderate nociception and intense nociception were added to the box-plot presentation for the general population for each type of event.

Thirty-two datapoints were identified and highlighted in the analysis. The results are presented in Figure 2.

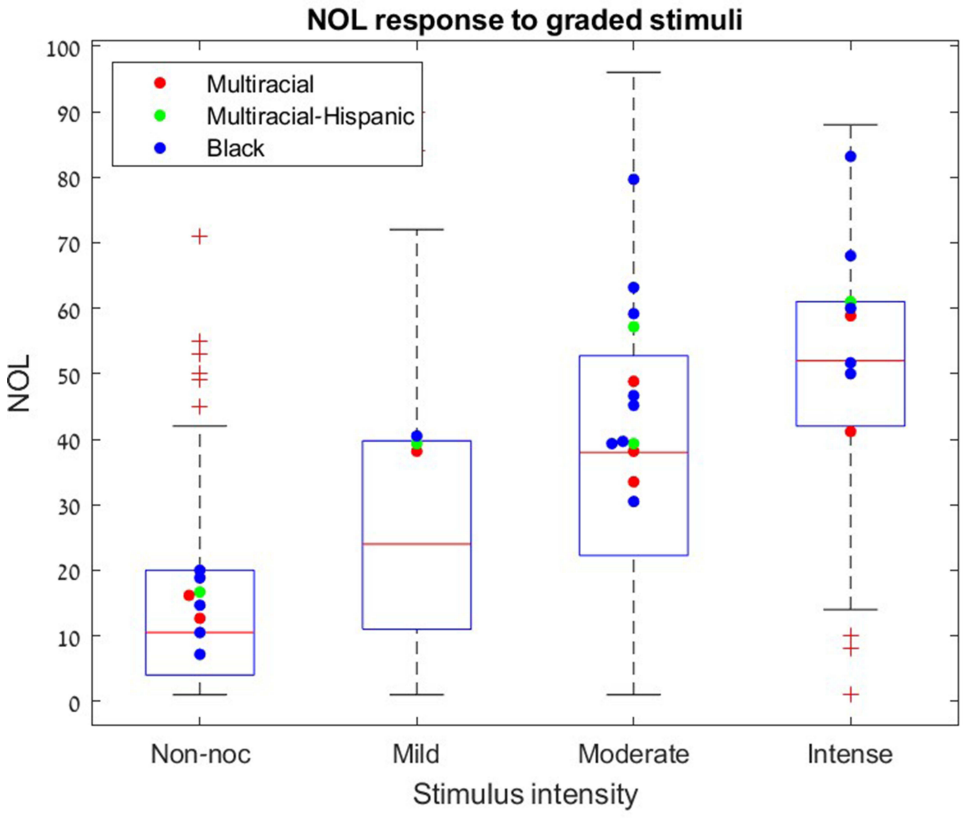

Figure 2 NOL response to graded stimuli – compared to general population.

Results

The results demonstrate that all datapoints from Black and multiracial patients fell within the range of the general population box plots with no outliers. Although the sample size did not allow for statistical analysis, the descriptive data suggests that NOL performance in Black and multiracial patients is not different from the performance shown for the large, general database. Based on these initial results, a sample size calculation was performed in order to power a future study comparing the response of NOL to different levels of nociceptive stimuli in multi-racial and Black patients to that of the general population. Assuming a Type I error of 0.05 and Type II error of 0.2 and an acceptance criterion of 3 NOL units between means to demonstrate a meaningful difference between the groups, a sample size of 1440 patients (720 in each group) is required.

Discussion

The personalized nature of the machine learning algorithm achieved through normalizing the data to the patient's own data patterns over time, and the use of a wavelength of 940 nm, which is not affected by melanin, mitigate the risk of racial disparities in the use of NOL technology. Initial clinical data from a small sample size suggest that the NOL readings of Black and multiracial patients in response to different levels of nociceptive stimuli were valid. Larger powered studies utilizing recognized skin tone scales such as the Monk scale[12] to ensure accurate assessment of different skin pigmentation levels are planned for the future.

Over time, it is expected that nociception/pain monitors will continue to evolve and be used outside the operating room. Therefore, the contribution to decreasing racial bias may be more pronounced in clinical settings in which objective quantification of pain may be challenging. Relevant examples include patients with sickle cell anemia or other chronic diseases with pain as a hallmark, obstetrics, pain management in opioid tolerant patients, and perioperative pain management. As there are long-term ramifications to the undertreatment of perioperative pain (ie, atelectasis from respiratory splinting, tachycardia and hypertension with potential for demand ischemia, the development of chronic pain, etc.) as well as the overtreatment of pain (ie, sedation, respiratory depression, constipation, nausea, dependence, etc), use of pain monitoring technologies to help execute personalized analgesia that is well validated across a wide range of skin tones may be of value in reducing racial bias in the treatment and management of pain. To determine the statistical significance of data across the skin tone spectrum, further research with larger numbers of volunteers with medium and darker skin tones is needed.

Disclosure

Ms Rachel Weissbrod reports personal fees from Medasense Biometrics, during the conduct of the study. The authors report no other conflicts of interest in this work.

References

1. 2023 National Healthcare Quality and Disparities Report. Content last reviewed January 2024. Rockville, MD: Agency for Healthcare Research and Quality. Available from:.https://www.ahrq.gov/research/findings/nhqrdr/nhqdr23/index.html. Accessed November 01, 2024.
2. Institute of Medicine Findings & Recommendations. Institute of Medicine Findings and Recommendations on Health Disparities. Available from: https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/public-health/iom_1.pdf. Accessed November 01, 2024.
3. Sjoding M, Dickson RP, Iwashyna TJ, et al. Racial bias in pulse oximetry measurement. *N Engl J Med*. 2020;383:2477–2478. doi:10.1056/NEJMc2029240
4. Approach for improving the performance evaluation of pulse oximeter devices taking into consideration skin pigmentation, race and ethnicity. Available from: https://www.fda.gov/media/173905/download. Accessed November 01, 2024.
5. Khanna AK, Beard J, Lamminmäki S, Närväinen J, Antaki N, Yapici HO. Assessment of skin pigmentation-related bias in pulse oximetry readings among adults. *J Clin Monit Comput*. 2024;38(1):113–120. doi:10.1007/s10877-023-01095-1
6. Ben-Israel N, Kliger M, Zuckerman G, Katz Y, Edry R. Monitoring the nociception level: a multi-parameter approach. *J Clin Monit Comput*. 2013;27(6):659–68.doi10.1007/s10877–9. doi:10.1007/s10877-013-9487-9
7. Meijer FS, Martini CH, Broens S, et al. Nociception-guided versus standard care during remifentanil–propofol anesthesia: a randomized controlled trial. *Anesthesiology*. 2019;130:745–755. doi:10.1097/ALN.0000000000002634
8. Fuica R, Krochek C, Weissbrod R, et al. Reduced postoperative pain in patients receiving nociception monitor guided analgesia during elective major abdominal surgery: a randomized, controlled trial. *J Clin Monit Comput*. 2023;37:481–491. doi:10.1007/s10877-022-00906-1

9. Ruetzler K, Montalvo M, Rotem OM, et al. Generalizability of nociception level as a measure of intraoperative nociceptive stimulation: a retrospective analysis. *Acta Anaesthesiol Scand*. 2023;67(9):1187–1193. doi:10.1111/aas.14286
10. Fine J, Branan KL, Rodriguez AJ, et al. Sources of inaccuracy in photoplethysmography for continuous cardiovascular monitoring. *Biosensors*. 2021;11:126. doi:10.3390/bios11040126
11. Ruetzler K, Montalvo M, Bakal O, et al. Nociception level index-guided intraoperative analgesia for improved postoperative recovery: a randomized trial. *Anesth Analg*. 2023;136(4):761–771. doi:10.1213/ANE.0000000000006351
12. The Monk Skin Tone Scale (MST) Dr. Ellis P. Monk, Jr Harvard University. Available from: https://osf.io/preprints/socarxiv/pdf4c. Accessed November 01, 2024.