Summary
The Nellcor™ N-600x pulse oximeter from Medtronic has shown motion tolerance and compliance with recently introduced specifications and recommendations of the International Standards Organization and the United States Food and Drug Administration. Novel use of monitoring equipment and metrics has provided a chain of evidence that demonstrates compliance to the test protocol and industry recommendations.

Oxygen saturation and pulse rate accuracies were evaluated over a saturation range of 70% to 100% during a protocol consisting of periods of random rubbing and tapping movements. A study size analysis was carried out to ensure the study was adequately powered. Fourteen subjects generated 1,240 data points for SpO2 accuracy evaluation and 1,300 data points for pulse rate accuracy evaluation. An improved methodology was employed to aid adherence to new international standards and FDA guidelines for oximeter motion testing.

Methods
Introduction of Artifact
The means of inducing artifact in the photoplethysmogram (PPG) for testing has been a matter of debate for several years.9-12 Some advocate the use of machine-generated noise, where a motion table moves the hand under test, tapping or rubbing the fingertips periodically (or piece-wise periodically) against a smooth surface.11 Others suggest that voluntary motion (rub, tap and scratch) of the hand in a prescribed aperiodic manner provides artifact more likely to be encountered in the clinical setting12 and is therefore more realistic than “simple repetitive sine waves.”13 To more realistically simulate motion under clinical conditions, artifact in this study was created by periods of volunteer-generated tapping and rubbing against a solid surface. Additional equipment was used to confirm that all digits of the test hand were fulfilling protocol requirements and participating in the motion.

Measurement of Artifact
One of the more important introductions to recent ISO and FDA guidelines is the recommendation to provide data indicating the degree of artifact introduced to the PPG during motion. The example of percent modulation (ratio of the AC pulse to DC signal as a percentage) is given as a potentially useful metric for this task since it typically increases during motion.4 However, some have shown that pulse amplitude is poorly correlated with amount of signal artifact.4
An additional estimate of signal distortion can be derived from changes in the PPG’s signal-to-noise ratio, or SNR, shown in Equation 1:

$$SNR = 10 \times \log_{10} \left( \frac{\text{Signal Energy}}{\text{Noise Energy}} \right)$$

Equation 1

Figure 1 illustrates the percent modulation and SNR values during a motion breathe-down study of a single subject. The drop in SNR during periods of motion can be clearly seen, while changes in percent modulation appear less obvious. The SNR metric eliminates some of the potential issues with changes in vasotone that can confound the measurement of percent modulation because it is a local ratio, taken over a short window of time, and self-normalizing during changes in vasotone.

**MATERIALS**

An often cited issue with volunteer-generated motion is the variation observed across the study; voluntary motions are not consistent between subjects or from one lab to another. This study incorporated a closed-loop feedback arrangement to improve consistency during voluntary motion studies (see figure 2).

- A calibrated pressure mat provided measurable contact during tapping and rubbing.
- A visual cue (a line drawn on a clear plastic sheet) was placed adjacent to the hand under test on the surface being tapped and rubbed to aid subjects in generating the proper motion.
- A standard web camera (Logitech 9000 pro Webcam, Logitech Inc.) was used to video the hand under test, providing a close-up view of the finger tips and visual cue. This video was relayed to a personal computer for immediate, real-time feedback for the subject and study personnel.

Signals were processed and recorded using proprietary data acquisition and computer software tools. Neither SpO2 nor pulse rate data were made available to the subject undergoing the test at any time.

**STUDY SIZE ANALYSIS**

One of the goals in properly powering a study is to reduce to an acceptable level the likelihood that a truly poor-performing system will by chance ”pass” these tests. In order to ensure an appropriate power in the current study sample size, an analysis of previous motion studies from the Medtronic database was carried out. The analysis used a legacy dataset consisting of 11 historic studies, including 68 subjects and 156 digits, and 3,914 [SaO2, SpO2] sample pairs. This data was restricted to invasive motion studies employing Nellcor™ oximeters and sensors with OxiMax™ technology. It was further filtered so that only traces containing demonstrable artifact on the PPG were included in the analysis.

The true system accuracy was taken to be the root mean square error (A_{true}) computed from the data set described above. The results of this analysis confirmed that for a study powered at around 97%, 12–14 subjects are required if two systems per subject are tested and 19–21 subjects are required if one system per subject is tested.

**STUDY PROCEDURE**

Two disposable, adhesive-type sensors were tested in this study: the Nellcor™ Max-A, an adult sensor, and the Max-N, a neonatal sensor also labeled for adult use (Medtronic, Boulder, CO, USA). Two sensors of each type were tested on each subject and the fingers upon which they were placed rotated for successive subjects. As is customary, visible and infrared light blocking material was used to prevent sensor cross-talk.

The invasive controlled desaturation study followed the guidelines described in industry standards. Oxygen saturation of the tested subjects was varied by adjusting their fractional inspired O2 delivered via mask. Desaturation manifested as four saturation plateaus: in room air, and at SpO2 = 90%, 80% and 70%. During each plateau, the subject performed two motion behaviors: rubbing and tapping. The subject tapped for at least 90 seconds and rubbed for at least 90 seconds. The order of signal interference type was rotated on a subject-by-subject basis. Movements were cued every 0.25–1 seconds, thus coinciding with the likely subject pulse rate (and its harmonics) and making the artifact more challenging for the pulse oximeter to exclude.

Data from the pressure pad were used to provide real-time feedback and also post processed to ensure that the appropriate motion was executed during the study. When a subject’s pressure pad trace indicated fewer than three points of contact occurred for more than 25% of the motion periods, the entire subject’s data were excluded as inconsistent with protocol requirements. The video stream was also reviewed to ensure the motion amplitude was within the prescribed range.

**RESULTS**

The study was conducted at the Medtronic Clinical Laboratory (Boulder, Colorado, USA). Seventeen healthy volunteers were selected randomly from the available subject pool. The enrolled subjects included 10 men and 7 women, aged 23 to 43 years (mean = 31.6; standard deviation = 6.6), and spanning a range of light to dark skin pigmentation.

The tables and figures on the following pages summarize the results of the testing. Of the 17 subjects enrolled into the study, three were excluded according to the clinical protocol because they had less than three points of finger contact for more than 25% of the motion intervals over the course of the study. The resulting data set produced 1,240 saturation data pairs and 1,300 pulse rate data pairs for assessing accuracy.

The performance metrics for saturation and pulse rate during motion are provided in Table 1. They reflect the data shown in the modified Bland-Altman plot of figure 3 (with an abscissa...
axis of SaO₂, rather than the mean of SaO₂ and SpO₂). These results meet the system’s specified accuracy values (A<sub>rms</sub> < 3 % SpO₂), without significant systemic deviation or outliers. Similarly, the performance metric for pulse rate accuracy is within device specification limits (A<sub>rms</sub> < 5 BPM).

Table 2 shows the changes in percent modulation and SNR metrics from baseline to periods of motion for the 14 subjects analyzed. The SNR and percent modulation metrics confirm a significant change in both during periods of motion (p<0.05; Wilcoxon Rank Sum, single tail).

**DISCUSSION**

The materials and procedures introduced above seek to create a clinically relevant and repeatable test, thus enhancing existing desaturation study designs. Using the new procedures and an appropriately powered sample size, we validated that the Nellcor™ N-600x pulse oximeter (Medtronic, Boulder, CO, USA) is motion tolerant to the accuracy levels specified, and meets the requirements and recommendations of the new FDA guidelines. Additionally, the protocol and analysis extend beyond the recent recommendations of the ISO Standard to ensure protocol compliance.

None of the publications referenced above appear to describe a rationale for the number of subjects included in their studies, another requirement of the recent ISO Standard. In carrying out our study size analysis, we recognized that special care should be taken during oximeter testing, where longitudinal (or serial) correlation from multiple observations of the same subjects can bias results even when compensations are applied. By taking a non-parametric, empirical, approach to sample size analysis it is intended that the effects of the many potentially confounding covariates (digit perfusion, artifact level, sensor placement, etc.) are minimized and that a robust estimate of sample size is generated.

**CONCLUSIONS**

The Nellcor™ N-600x pulse oximeter from Medtronic has demonstrated motion tolerance according to the recently introduced specifications and recommendations of the International Organization for Standardization (ISO) and the United States Food and Drug Administration (FDA). The introduction of additional monitoring equipment to that of the standard breathe-down test protocol has provided a chain of evidence that extends beyond the recent recommendations of the ISO Standard to ensure that the system performance evaluation is protocol compliant.

A study size analysis has been conducted and the adopted study size is powered to 97%.

Conventional (percent modulation) and new (signal to noise) metrics have been employed to quantify artifact introduced into the PPG signal during pulse oximetry motion testing. Both percent modulation and the new SNR metric indicated a significant (p<0.05; single tail) change in signal noise content during motion.
Table 1: SpO2 and PR accuracy results during motion

<table>
<thead>
<tr>
<th>Sensor</th>
<th># of Data Points</th>
<th>Bias (%)</th>
<th>Std Dev (errors)</th>
<th>R^2</th>
<th>A_max(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpO2</td>
<td>1240</td>
<td>-0.31</td>
<td>1.50</td>
<td>0.98</td>
<td>1.53</td>
</tr>
<tr>
<td>PR</td>
<td>1300</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.64</td>
</tr>
</tbody>
</table>

Table 2: Changes in percent modulation and SNR metrics between quiescent and motion periods.

<table>
<thead>
<tr>
<th>Percent Modulation</th>
<th>SNR (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quiescent</td>
<td>Motion</td>
</tr>
<tr>
<td>4.3</td>
<td>6.9</td>
</tr>
</tbody>
</table>

p < 0.05; Wilcoxon Rank Sum, single tail


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