In Vivo Pulse Oximeter Validation Study

Test Protocol

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Hypoxia Lab

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The Hypoxia Research Laboratory at UCSF laboratory has developed methods that permit the performance testing of pulse oximeters, enabling collection of data for submission to the FDA for device clearance or for engineering development of the devices. The basics of the protocol involve brief stable arterial oxygen desaturation in healthy volunteers and sampling arterial blood when a stable level of hypoxia has been attained. The blood sample is analyzed for oxygen saturation with a gold standard bench CO-oximeter, currently a Radiometer ABL-90. This document describes the program and arrangements. 6 to 8 subjects can be studied in a single day, with 20-25 arterial blood samples from each subject.

Subjects

Ten to 12 subjects can be studied over two days, also with 20-25 arterial blood samples each. This protocol is aligned with the latest ISO and FDA guidance documents for pulse oximeter testing. 10 subjects can be studied in one day if no blood draws are planned.

Methods

The key to obtaining stable, safe and controlled hypoxia is breath-by breath by breath respiratory gas analysis and a computer program that permits the inspired gas mixture to be adjusted to achieve a level of lung alveolar gas that will achieve the desired degree of hypoxia. Typically, saturation is determined once with air breathing and then at one of 6 levels, e.g. 94%, 90%, 85%, 80%, 75% and 70% saturation for about 30-60 seconds at each level. During Aim 1 and aim 2, an arterial blood sample is obtained from an indwelling catheter at the end of each hypoxic plateau. The operator changes the inspired oxygen concentration at the end of each blood sampling to attain the next desired stead-state conditions hypoxia. A "run" takes 10-15 minutes, and each run is terminated by a breath of 100% O2 followed by room air. Two runs together enable obtaining a total of 20-25 blood samples, 2 samples at each different plateau. Saturation of each arterial blood sample is determined by direct oximetry in a Radiometer ABL-90 multi-wavelength oximeter. The precise target levels of saturation can be adjusted to suit the sponsor, but typical testing is done to satisfy ISO and FDA standards for testing, which is 70% to 100%.

Data from test pulse oximeters for comparison to blood values can be obtained in several ways. In every case, the goal is to obtain a reading from the oximeter that corresponds to the associated blood sample or a reference oximeter. Because of circulation delays and instrument averaging time, we attempt to create steady state conditions at each level of oxygenation. Therefore, a means should be provided to record the instrument reading at each blood sample. This instrument reading may be obtained with several different approaches. Some instruments have no digital or analog output and the instrument reading may be recorded manually or recorded by a video of the instrument display. Other instruments may have an analog output. The laboratory can record analog data by use of LabView. Digital recording of output can also be obtained via LabView but his requires information from the sponsor concerning the structure of the digital signal. Consultation with us is recommended.

If a manufacturer prefers to collect and analyze the data, the continuous digital signal of each oximeter should be read, for comparison with the blood sample, 9 seconds before the record shows a sudden fall or rise in oxygen saturation, not at the time of blood sampling. This procedure accounts for the delays of finger circulation and uses the estimated delay from the lung to the sample site. There is no useful correlation between the actual time of blood sampling and the oximeter recording because of the variability of tissue blood flow lag. As mentioned, steady-state hypoxia avoids the concern that oximeter reading is not aligned with a blood sample reading.

We enroll only healthy subjects between the ages of 18 and 55 in the studies. The study takes about 1 hour of each subject's time. Analysis of the data requires several days. We encourage manufacturer’s

representatives to be present for these tests, and to mount the probes. An extra charge is made if no representative is present, requiring us to mount the probes and record data.

Sites for affixing pulse oximeter probes may include the fingers, wrist, ears, forehead or other flat body surfaces and the nose. Special testing, with various conditions or with special subject populations can also be arranged, at extra charge.

We also offer testing for performance during controlled subject hand motion. Three types of motion are typically used: tapping, rubbing and random motion. Tapping and random motion are done with a computer-controlled motion machine.

Testing during low perfusion conditions is also available at an extra charge. In all cases, the blood analysis data are provided, including the SaO2, MetHb, COHb and Hgb concentration.

Data Analysis:

The data analysis report will consist of the following:

- A Table of the oximeter readings versus corresponding blood SaO2 values.
- Graphic plots of the bias between the oximeter reading and the SaO2 measured by the hemoximeter (on the blood sample, i.e Modified Bland -Altman plots for each instrument or instrument probe combination.
- Regression equations for the bias of each instrument.
- Tables of the mean error or bias, its standard deviation, standard error, 95% confidence interval, maximum and minimum and root mean square error, all computed both overall and by several sub-ranges of desaturation.
- A table of the demographics of the subject population is provided.

These studies are done with approval of the UCSF Committee on Human Research. Informed consent is obtained from each subject. The UCSF Hypoxia Laboratory conforms to Good Clinical Practice Standards for the involvement of human subjects and handling of test data.

Manufacturers must provide their own pulse oximeters and probes. Each individual manufacturer is charged an amount determined by the number of subjects, the number of samples per subject, and the number of oximeters plus the departmental and UCSF overhead charges.

Statistics

The number of subjects and the number of comparisons (paired pulse oximeter readings and arterial saturation values) is determined by current FDA guidance requirements (*Pulse Oximeters - Premarket Notification, 2013).* This is a minimum of 200 data points and 10 subjects. During this type of study, some subjects may drop out, some readings can be lost due to motion or other interference and occasionally some do not consent.

The following demographic data will be collected on the subjects:

- gender
- age
- skin tone (dark/medium/light and Fitzpatrick scale)
- height (cm)
- weight (kg)