REVIEW OF LITERATURE
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HISTORY

As with any new techniques, many people contributed to the development of usable in vivo oximeters. Two early researchers who stand out are Carl Madsen and Glen Milliken. Madsen is often considered the father of oximetry. Between 1934 and 1944 he published a series of articles investigating oxygen transport to tissue by light transmission techniques.

In 1935 Kramer also demonstrated that the transmission of red light through tissue was dependent on oxygen saturation but since he employed only one wavelength of light, this method only measured trends in saturation.

In 1935 Madsen built the first device that continuously measured human blood oxygen saturation in vivo by transilluminating tissue. He used two wavelengths of light, one that was sensitive to changes in oxygenation and another that was not. The second wavelength, in the impaired range, was used to compensate for changes in tissue thickness, hemoglobin content and light intensity. This device could follow trends in saturation but was difficult to calibrate.
J. R. Squire, in Great Britain, developed a similar device that was calibrated by compressing the tissue to eliminate the blood. This same calibration technique was later adopted in the first oximeters used in the operating room.

In the early 1940s, Glen Millikan coined the term "oximeter" to describe a light-weight device he developed for aviation research.

Later in the 1940s, oximeters similar to Millikan's were used by Earl Wood and others in the operating room, where they were noted to detect significant desaturations even during routine anaesthetics.

In the United States in 1942, Glen Millikan and colleagues developed a small ear oximeter for use in aviation research.

A paper published as early as 1951 in ANESTHESIOLOGY concluded prophetically that "on many occasions this instrument has detected anoxemia when observations of pulse, blood pressure and color of the patient, and peripheral vascular tone have shown no abnormalities". These findings were consistent with the classic work of Comroe et al (1947) documenting the unreliability of cyanosis for the detection of anoxemia.

In its initial clinical development, the ear oximeter had several limitations. It was a delicate
instrument that required a technician to operate and maintain. The ear-piece was large, difficult to position and produced enough heat to cause second degree burns on the pinna. Furthermore, it required calibration on each patient prior to use.

During the 1950s, Karl Wood devised a modification of the Millikan ear piece that was used in many clinical and laboratory investigations. Although the ear oximeter showed promise in some settings, it was still considered a research tool.

In the 1960s, Robert Shaw developed a self-calibrating eight-wavelength ear oximeter that was produced by Hewlett-Packard. Although cumbersome and expensive, this device became the standard for oximetry because of its accuracy.

In the 1970s, Hewlett-Packard marketed the first self-calibrating ear oximeter. This device used eight wavelengths of light to determine hemoglobin saturation. Hewlett-Packard's oximeter also used the method of heating the ear to "arterialize" the capillary blood. This oximeter quickly became a standard clinical and laboratory tool in pulmonary medicine.

In the mid 1970s, Takuo Aoyagi, an engineer working for Nihon Kohden Corporation, made an ingenious discovery regarding oximetry. He was developing a method
to estimate cardiac output semi non-invasively by detecting the wash-out curve of dye injected into a peripheral vein as it perfused the ear. This washout curve was measured in the ear with a red and infra-red light densitometer similar to the Millikan ear oximeter. He noticed that his washout curves contained pulsations due to the arterial pulse in the ear. To more easily analyze the dye washout curve, he subtracted these pulsations from the curve, and in doing so he discovered that the absorbance ratio of the pulsations at the two wavelengths changed with arterial hemoglobin saturation. He soon realized that he could build an ear oximeter that measured arterial hemoglobin saturation without heating the ear by analyzing pulsatile light absorbances. This first pulse oximeter, developed by Nihon Kohden, used filtered light sources similar to Millikan's ear oximeter. The device was evaluated clinically in the mid 1970s, and marketed with little success.

In the late 1970s, Scott Wilber in Boulder, Colorado, developed the first clinically accepted pulse oximeter by making two modifications of the Nihon Kohden method. First, he produced a light-weight sensor by using light emitting diodes (LEDs) as light sources and photo diodes as detectors.

In the year 1975 Nakajima and colleagues introduced the pulse oximeter. By analyzing the ratio of the pulse-added absorbances of the red and infra-red light,
this method allowed accurate determination of hemoglobin saturation with only two wave-lengths of light on various tissue thicknesses and skin colors. This device, developed by Minolta, used fiberoptics to transmit the light signals to and from a finger sensor.

In the early 1980s, these fiberoptics were cumbersome, and Minolta's monitor was quickly replaced by pulse oximeters developed by BTL, Biox Corporation of Boulder, Colorado, and was successfully marketed to pulmonary function laboratories.

The clinical utility of the non-invasive oximeter in the operating room was re-discovered in the 1980s by William New, an anaesthesiologist at Stanford University. Realizing that a continuous, non-invasive monitor of oxygenation would be useful to anaesthesiologists, New developed and marketed a pulse oximeter to this group. The Nellcor model N-105 had by 1985 become almost synonymous with the term "pulse oximeter".

THE PHYSICS AND PHYSIOLOGY OF PULSE OXIMETRY

BEER'S LAW:

In the 1930s, Matthew used spectrophotometry to determine hemoglobin oxygen saturation. This method is based on the Beer-Lambert Law, which relates the concentration of a solute to the intensity of light transmitted through a solution.
\[ I_{\text{trans}} = I_{\text{in}} e^{-\alpha} \]  \hspace{1cm} (1)

\[ \alpha = DC \]  \hspace{1cm} (1a)

where

- \( I_{\text{trans}} \) = intensity of transmitted light
- \( I_{\text{in}} \) = intensity of incident light
- \( \alpha \) = absorption
- \( D \) = distance light is transmitted through the liquid (path length)
- \( C \) = concentration of solute (hemoglobin)
- \( \alpha \) = extinction coefficient of the solute (a constant for a given solute at a specified wavelength).

Thus, if a known solute is in a clear solution in a cuvette of known dimensions, the solute concentration can be calculated from measurements of the incident and transmitted light intensity at a known wavelength. The extinction coefficient \( \alpha \) is a property of light absorption for a specific substance at a specified wavelength. In a one-component system, the absorption \( \alpha \) is the product of the path-length, the concentration and the extinction coefficient, equation 1a. If multiple solutes are present, \( \alpha \) is the sum of similar expressions for each solute. The extinction coefficient can vary dramatically with the wavelength of the light (Fig. 1).
Fig. 1: Transmitted light absorbance spectra of four hemoglobin species: oxyhemoglobin, reduced hemoglobin, carboxyhemoglobin, and methemoglobin. Adapted from Barker SJ and Tremper KK: Pulse Oximetry: Applications and limitations, Advances in Oxygen Monitoring, International Anesthesiology Clinics Boston, Little, Brown and Company, 1987, pp. 155-175.
Laboratory oximeters use this principle to determine hemoglobin concentration by measuring the intensity of light transmitted through a cuvette filled with a hemoglobin solution produced from lysed red blood cells. For Beer's law to be valid, both the solvent and the cuvette must be transparent at the wavelength used, the light path length must be known exactly, and no absorbing species can be present in the solution other than the known solute. It is difficult to fulfill these requirements in clinical devices, therefore, each instrument theoretically based on Beer's law also requires empirical corrections to improve accuracy.

**Hemoglobin Saturation Definitions**

Adult blood usually contains four species of hemoglobin: oxyhemoglobin (O₂Mbh), reduced hemoglobin (Hb), methemoglobin (Met Mbh) and carboxyhemoglobin (CO Mbh) (Fig. 1). The last two species are in small concentrations, except in pathologic condition. There are several definitions of hemoglobin saturation. Historically, "oxygen saturation" was first defined as the oxygen content expressed as a percentage of the oxygen capacity. The oxygen content (cc of oxygen per 100 cc of blood) was measured volumetrically by the method of Van Slyke and Keil (1924). The oxygen capacity was defined as the oxygen content after the blood sample had been equilibrated
with room air (133 mm Hg oxygen at sea level). By the above definition of oxygen saturation, the two form of hemoglobin that do not bind oxygen (CO Hb and Met Hb) are not included. This is the origin of what is now referred to as "functional hemoglobin saturation", defined as (Severinghaus, J.H., personal communication):

$$\text{Functional } \% \text{SaO}_2 = \frac{\text{O}_2 \text{ Hb}}{\text{O}_2 \text{ Hb} + \text{Mb}} \times 100\% \quad (2)$$

with the advent of multi-wavelength oximeters that can measure all four species of hemoglobin, "fractional saturation" has been defined as the ratio of oxyhemoglobin to total hemoglobin:

$$\text{Fractional } \% \text{SaO}_2 = \frac{\text{O}_2 \text{ Hb}}{\text{O}_2 \text{ Hb} + \text{Mb} + \text{CO Hb} + \text{Met Hb}} \times 100\% \quad (3)$$

The fractional hemoglobin saturation is also called the "oxyhemoglobin fraction" or "oxyhemoglobin %".

When oximetry is used to measure hemoglobin saturation, Beer's Law must be applied to a solution containing four unknown species: O₂ Hb, Mb, CO Hb, and Met Hb. Expanding equation in to a four-component system results in an absorption given by:

$$A = D_1 C_1 E_1 + D_2 C_2 E_2 + D_3 C_3 E_3 + D_4 C_4 E_4 \quad (4(b))$$

The subscripts 1 through 4 correspond to the four hemoglobin species. If the path lengths are the same, then 0 can be factored out:
The extinction coefficients $k_1$ through $k_4$ are constants at a given wavelength (Fig. 1). The absorption defined in equation 1c is determined from equation 1 by measuring the incident and transmitted light intensities. From equation 1c, we see that four wavelengths of light are needed to produce four equations to solve for the unknown concentrations $C_1$ through $C_4$. If CO Mb and Met Mb were not present their contributions to the absorption would be zero and functional hemoglobin saturation could be determined by a two-wavelength oximeter (two equations and two unknowns). If two wavelengths existed for which the extinction coefficients for CO Mb and Met Mb were zero, then these absorption terms would again be zero and a two wavelength oximeter could measure functional saturation. Unfortunately, as illustrated in Fig. 1, the extinction coefficients for CO Mb and Met Mb are not zero in the red and infra-red range, and their presence will, therefore, contribute to the absorption. Even though the definition of functional hemoglobin saturation involves only two hemoglobin species (O$_2$ Mb and Mb), when Met Mb and CO Mb are present, four wavelengths are required to determine either functional or fractional hemoglobin saturation.

**SUMMARY**

Non-invasive oximeters measure red and infra-red light transmitted through a tissue bed, effectively using
Fig. 2: This figure schematically illustrates the light absorption through living tissue. Note that the AC signal is due to the pulsatile component of the arterial blood while the DC signal is comprised of all the nonpulsatile absorbers in the tissue: nonpulsatile arterial blood, venous and capillary blood, and all other tissues. Adapted from Ohmeda Pulse Oximeter Model 3700 Service Manual, 1986, p. 22.
the finger or ear as a cuvette containing hemoglobin. There are several technical problems in accurately estimating $\text{SO}_2$ by this method. First, there are many absorbers in the light path other than arterial hemoglobin, including skin, soft tissue, and venous and capillary blood. The early oximeters subtracted the tissue absorbance by compressing the tissue during calibration to eliminate all the blood, and using the absorbance of bloodless tissue as the base-line. These oximeters also heated the tissue to obtain a signal related to arterial blood with minimum influence of venous and capillary blood.

Pulse oximeters deal with the effects of tissue and venous blood absorbances in a completely different way. (Fig. 3). Schematically illustrates the series of absorbers in a living tissue sample. At the top of the figure is the pulsatile or AC component, which is attributed to the pulsating arterial blood. The baseline or DC component represents the absorbances of the tissue bed, including venous blood, capillary blood, and non-pulsatile arterial blood. The pulsatile expansion of the arteriolar bed produces an increase in path length (equation 1b), thereby increasing the absorbance. All pulse oximeters assume that the only pulsatile absorbance between the light source and the photodetector is that of arterial blood. They use two wavelengths of light: 660 nanometers (red) and 940 nanometers (near infra-red). The pulse oximeter first determines the AC component of absorbance at each wavelength.
Fig. 3: This is a typical pulse oximeter calibration curve. Note that the \( SaO_2 \) estimate is determined from the ratio \( R \) of the pulse-added red absorbance at 660 nanometres to pulse-added infrared absorbance at 940 nanometers. The ratios of red to infrared absorbance vary from approximately 0.4 at 100% saturation to 3.4 at 0% saturation. Note that the ratio of red to infrared absorbance is one at a saturation of approximately 35%. This curve can be approximately determined on a theoretical basis but for accurate predictions of \( SaO_2 \), experimental data are required. Adapted from JA Pologe; Pulse oximetry: Technical aspects of machine design, International Anaesthesiology Clinics, Advances in Oxygen Monitoring. Edited by Tremper KK, Breuer SJ. Boston, Little, Brown and Company, 1987, p. 142.
and divides this by the corresponding DC component to obtain a "pulse-added" absorbance that is independent of the incident light intensity. It then calculates the ratio (\( a \)) of these pulse-added absorbances, which is empirically related to \( \text{HbO}_2 \):

\[
    a = \frac{\frac{AC_{660}}{DC_{660}}}{\frac{AC_{940}}{DC_{940}}}
\]  

(4)

Fig. 3 is an example of a pulse oximeter calibration curve. The actual curves used in commercial devices are based on experimental studies in human volunteers. Note that when the ratio of red to infra-red absorbance is one, the saturation is approximately 85%. This fact has clinical implications to be discussed later.

It is a fortuitous coincidence of technology and physiology that allowed the development of solid-state pulse oximeter sensors. Light emitting diodes (LEDs) are available over a relatively narrow range of the electromagnetic spectrum. Among the available wavelengths are some that not only pass through skin but also are absorbed by both oxyhemoglobin and reduced hemoglobin. For best sensitivity, the difference between the ratios of the absorbances of \( \text{O}_2 \text{Hb} \) and \( \text{Hb} \) at the two wavelengths should be maximized. As we see in Fig. 1, at 660 nm, reduced hemoglobin absorbs about ten times as much light as oxyhemoglobin (Note that the estimation coefficients are
plotted on a logarithmic axis. At the infra-red wavelength of 940 nm, the absorption coefficient of O2Hb is greater than that of Hb.

**Engineering Design and Physiologic Limitations**

Although the theory on which pulse oximetry is based is relatively straightforward, the application of this theory to the production of a clinically useful device involves a significant engineering effort. This section will present in general terms the clinical and physiologic problems of oximeter design and their engineering solutions. This discussion is divided into four areas:

- Dyshemoglobins and dyes,
- LED center wavelength variability,
- Signal artifact management, and
- Accuracy and response.

**Dyshemoglobins and Dyes**

Being two-wavelength devices, pulse oximeters can deal with only two hemoglobin species. As noted above, this would be adequate to measure functional SaO2 if Met Hb and CO Hb did not absorb red or infra-red light at the wavelengths used. Unfortunately, this is not the case, and therefore both Met Hb and CO Hb will cause errors in the pulse oximeter reading. It is not intuitively obvious how a pulse oximeter will behave in the presence of
dyshemoglobinemia. With respect to carboxyhemoglobin, we can
gain some insight from the extinction curves of Fig. 1.
In the infra-red range (940 nm), CO Hb absorbs very little
light; whereas, in the red range (660 nm), it absorbs as
much light as does O₂ Hb. This is clinically illustrated
by the fact that patients with carboxyhemoglobinemia appear
red. Therefore, to the pulse oximeter, CO Hb looks like
O₂ Hb at 660 nm while, at 940 nm CO Hb is relatively
transparent. The effect of CO Hb on pulse oximeter values
has been evaluated experimentally in dogs. In this study,
the pulse oximeter saturation (Sp O₂) was found to be given
approximately by:

\[
SpO_{2} = \frac{O_{2}Hb + 0.9 \times CO Hb}{Total Hb} \times 100\%
\]

(5)

The effects of methemoglobinemia on pulse oximetry are
also partially predictable from the extinction curves
(Fig. 1). Met Hb has nearly the same absorbance as reduced
hemoglobin at 660 nm, while it has a greater absorbance
than the other hemoglobins at 940 nm. This is consistent
with the clinical observation that methemoglobinemia
produces very dark, brownish blood. Thus, it would be
expected to produce a large pulsatile absorbance signal at
both wavelengths. The effect of Met Hb on pulse oximeter
readings has also been measured in dogs. As methemoglobin
levels increased, the pulse oximeter saturation (Sp O₂)
tended towards 85% and eventually became almost independent
of the actual \( \text{SaO}_2 \). In other words, in the presence of high levels of Met Hb, \( \text{SpO}_2 \) is erroneously low when \( \text{SaO}_2 \) is above 85% and erroneously high when \( \text{SaO}_2 \) is below 85%. This may be explained by the fact that Met Hb causes a large pulsatile absorbance at both wavelengths, thereby adding to both the numerator and denominator of the absorbance ratio \( A \) (equation 4) and forcing this ratio towards unity. As shown in Fig. 3, an absorbance ratio of one corresponds to a saturation of 85% on the calibration curve. Pulse oximeter error during methemoglobinemia has also been confirmed in a clinical report.

In neonatal blood, a fifth type of hemoglobin is present, fetal hemoglobin (Hbf). Hbf differs from adult Hb in the amino acid sequences of two of the four globin sub-units. Adult Hb has two alpha and two beta-globin chains, while Hbf has two alpha and two \( \beta \) chains. This difference in globin chains has little effect on the extinction curves and therefore should not affect pulse oximeter readings. This is indeed fortunate because the fraction of Hbf present in neonatal blood is a function of gestational age and can not be accurately predicted. Hbf does produce a small error in (in vitro) laboratory oximeters; \( O_2 \) Hbf may be interpreted as consisting partially of \( CO_2 \) Hb.

The absorbance ratio \( A \) (equation 4) may be affected by any substance present in the pulsatile blood that absorbs light at 650 or 940 nm and was not present
In the same concentration in the volunteers used to
generate the calibration curve (Fig. 1). Intravenous
dyes provide a good example of this principle. Schaller
et al (1986) evaluated the effects of bolus doses of
methylene blue, indigo carmine, and indocyanine green
on pulse oximeters in human volunteers. They found that
methylene blue caused a fall in \( \text{SpO}_2 \) to approximately 65% for
1-2 min. Indigo carmine produced a very small drop in
saturation, while indocyanine green had an intermediate
effect. The detection of intravenous dyes by pulse
oximeters should not be surprising, because it was this
effect that led Noguchi to the invention of pulse oximetry.

**LED center wavelength variability:**

The LEDs used in pulse oximeter sensors are not
ideal monochromatic light sources; there is a narrow
spectral range over which they emit light. The center
wavelength of the emission spectrum varies even among
diodes of the same type from the same manufacturer. This
variation can be \( \pm 15 \) nanometers. As seen in Fig. 1,
a shift in LED center wavelength will change the measured
extinction coefficient and thus produce an error in the
saturation estimate. This source wavelength effect will
be greatest for the red (660 nm) wavelength, because the
extinction curves have a steeper slope at this wavelength.
Manufacturers have found two approaches to this problem:
some test all the LEDs and reject those that are out of
those specified wavelength range, e.g. 660 ± 3 nanometers. This is expensive due to the number of LEDs rejected; i.e. narrower acceptable range yields improved accuracy but also more rejected LEDs. Alternatively, other manufacturers program the pulse oximeter to accept several ranges of LED center wavelengths for both the red and infra-red, allowing the device to correct internally for different wavelengths. This permits the manufacturer to use more of the available LEDs, but also requires a more sophisticated device with a mechanism for identifying the sensor LED wavelengths to the pulse oximeter. Incompletely compensated LED frequency variation will not change the pulse oximeter's ability to trend saturation changes, but will produce probe to probe variability in the absolute measurement of \( \text{SpO}_2 \).

**Signal Artifact Management**

Probably the most difficult engineering problem in pulse oximeter design is the identification of the "ripple" absorbance pattern of the arterial blood in a "sea" of electromagnetic artifact. Artifact has three major sources: ambient, light, low perfusion (low AC/DC signal), and motion (large AC/DC signal). All of these result in poor signal-to-noise ratio.

The photodiodes used in the sensor as light detectors cannot discriminate one wavelength of light from another. Therefore, the detector does not know whether received light originates from the red LED, the infra-red
LED, or the room lights. This problem is solved by alternating the red and infra-red LED. The red LED is turned on first and the photodiode detector produces a current resulting from the red LED plus the room lights. Next, the red LED is turned off and the infra-red LED is turned on, and the photodiode signal represents the infra-red LED plus the room lights. Finally, both LEDs are turned off and the photodiode generates a signal from the room lights alone. This sequence is repeated hundreds of times per second. In this way, the oximeter attempts to eliminate light interference even in a quickly changing background of room light. Some fluctuating light sources can cause problems in spite of this clever design. Clinically, ambient light artifact can be minimized by covering the sensor with an opaque shield.

Another engineering problem is that of low A/D-to-dc signal ratio. When a small pulsatile absorbance signal is detected the pulse oximeter will amplify that signal and estimate the saturation from the ratio of the amplified absorbances. The pulse oximeter can thereby estimate saturation values for a wide range of patients with differing pulsatile absorbance amplitudes. Unfortunately, as with a radio receiver, when a weak signal is amplified, the background noise (static) is also amplified. At the highest amplifications (which can be as much as a billion times), the pulse oximeter may analyze this noise signal and generate an sp O₂ value from it. This problem could
be demonstrated in early pulse oximeters by placing a piece of paper in the sensor between the photodiode and the LED. Most early models would amplify the background noise in searching for a pulse until they eventually displayed a pulse and saturation value. To prevent this type of artifact, manufacturers have now incorporated minimum values for signal-to-noise ratio, below which the device will display no 
\(SpO_2\) value. Some oximeters also display a low signal strength error message, and some display a plethysmographic wave for visual identification of noise.

Several studies have examined the effect of low perfusion on pulse oximeter estimates. Animal experiments have demonstrated that, during hemorrhagic shock, pulse oximeters may under-estimate saturation or lose signal altogether. In one clinical study of pulse oximeter accuracy in the critically ill under a wide range of hemodynamic conditions, extremes in systemic vascular resistance were associated with loss of signal or decreased accuracy. In these and most other studies of pulse oximeter accuracy, data were collected only when the pulse oximeter heart rate equaled the EKG heart rate. It has been assumed that this is a necessary condition for accuracy because it implies that the pulse oximeter is detecting pulses produced by heart-beats.
Since the device automatically increases its amplification as the pulse signal decreases, the pulse oximeter display should be relatively insensitive to changes in perfusion. Nevertheless, several clinical studies have used the pulse oximeter to assess the adequacy of peripheral perfusion. One study even employed this device to evaluate perfusion in reimplanted extremities. As with any plethysmograph, the pulse oximeter will detect a complete loss of peripheral blood flow, as has been illustrated by Lawson et al (1987). They determined the peripheral blood flow lower limit at which a pulse oximeter ceased detecting pulses. The blood flow was assessed at the finger by a laser-doppler flow probe as a blood pressure cuff was inflated. The pulse oximeter stopped detecting pulses when blood flow had decreased to 3.6% of its control value, which occurred when the pressure cuff was inflated to 96% of the control systolic pressure. When the tourniquet was slowly released from full occlusion, the pulse oximeter regained a pulse and saturation value when blood flow was only 4% of the baseline. This experiment demonstrates the effectiveness of the pulse oximeter in detecting and amplifying small pulse signals to estimate arterial hemoglobin saturation. This experimental model is not analogous to clinical shock, for as the blood pressure cuff is progressively inflated, there is a progressive increase in the venous blood volume. Theoretically, this increase in venous blood should not influence the pulse oximeter because it is non-pulsatile.
Patient motion (large AC/DC signal) may be the most difficult artifact to eliminate. Motion artifact rarely causes difficulties in the operating room, but in the recovery room and intensive care unit, it can make the pulse oximeter nearly useless. Engineers have tried several approaches to this problem, beginning with the signal averaging time. If the device averages its measurements over a longer time period, the effect of an intermittent artifact will be lessened. This also shows the response time to an acute change in $Sp\text{O}_2$. Most pulse oximeters allow the user to select one of several time averaging modes. In addition, the designer can use sophisticated algorithms to identify and reject spurious signals. These algorithms may assess the AC-to-DC signal ratio, or they may check the validity of the saturation estimate by calculating its rate of change. For example, if the saturation estimate changes from 95% to 90% in one-tenth of a second, this sudden change may not be averaged into the displayed $Sp\text{O}_2$, or it may be given a lower weighting factor. As stated earlier, these artifact rejection schemes may also affect the accuracy and response time of the pulse oximeter.

ACCURACY AND ASSESSMENT

There are both technological and physiological limitation to the accuracy of a pulse oximeter. The $Sp\text{O}_2$
value is only as accurate as the empirical calibration curve programmed into the device, which, in turn is only as accurate as the in vitro laboratory oximeter used to generate it. The instrumentation laboratories model 282 Co-oximeter claims an accuracy of ± 1% for fractional saturation (± 2 standard deviations) when the pH is 7.0 - 7.4, hematocrit is 20 - 10% and the total hemoglobin is 12 - 16 gms/dl.

Before reviewing studies that are intended to determine pulse oximeter accuracy, we should discuss some problems in the statistical interpretation of accuracy data. These studies are referred to by statisticians as "methods comparison studies". A methods-comparison study was two methods to measure the same variable. One method is usually a new technique (in this case, pulse oximetry), and the other is a "gold standard" (in this case, in vitro saturation measurements from arterial blood samples). Bearing in mind that both methods have uncertainty, we wish to know what error to expect if the new method is compared to the standard. In the medical literature, the data analysis usually includes a correlation coefficient (r) with a P value, and a linear regression slope and intercept. Unfortunately, this is not the most informative statistical analysis for methods-comparison studies. The correlation coefficient is not a measure of agreement; it is a measure of association. We know that
pulse oximeter $SpO_2$ values and $SaO_2$ values are highly associated and we therefore expect a correlation coefficient that is significant. This does not tell us whether one measure of saturation can be used in place of the other, or what degree of confidence we should have in the new measure.

As an alternative, Altman recommends calculating the mean and standard deviation of the difference between the two methods of measurement. The mean of the difference is called the 'bias' and the standard deviation is often referred to as the "precision". The bias will show a systematic over-estimate or under-estimate of one method relative to the other, while the precision will represent the variability of "random error". If these systematic and random errors are clinically accepted table, then one method can be replaced by the other.

Unfortunately, in the pulse oximetry literature, many authors provide only correlation coefficient and linear regression analysis. It is difficult to compare their results in terms of measurement accuracy without bias and precision values. Most manufacturers claim that their pulse oximeters are accurate to within ± 2% (39) from 70% to 100% saturation and ± 3% (39) from 50% to 70% saturation, with no specified accuracy below 50% saturation. This implies that, for $SaO_2$ above 70%, approximately 48%
of the data will fall within $+3\%$ of a line of identity, and $95\%$ of data will fall within $+4\%$ ($+2.5\%$).

In reviewing the pulse oximetry literature, two additional points should be kept in mind. First, some of these studies were carried out in the healthy adult volunteer subjects, while others were conducted on patients in a variety of clinical settings. The studies using healthy volunteers were performed under optimal conditions, while the clinical studies were done in a variety of less than optimal conditions. Second, since these devices are empirically calibrated, the algorithm programmed into each oximeter undergoes a series of revisions that affect the accuracy and response characteristics. Table I summarizes the results from twelve studies: five in adult volunteers, three in adult patients, and two each in pediatric and neonatal patients. The data from each of these studies were analyzed differently by the authors. Most consistently presented are correlation coefficients and regression slopes and intercepts. This is sometimes accompanied by a standard error of the estimate ($\hat{e}xy$ or $\hat{e}yx$), which is the standard deviation of $Y$ values about the regression line.

Experimental studies on early models of the Nellcor N-100 and the Ohmeda Bias II showed good agreement under steady state conditions when the saturation was 75% or greater (Table I). Chapman et al noted that in this range the bias was only 0.09%. For $S_{\text{O}_2}$ less than 75%,
they found increasing over-estimation by the pulse oximeter. Between 50% and 60% \( \text{SaO}_2 \), there was a positive bias of 11.2% whereas between 70% and 75% the bias was 3.88%.

Two recent studies are of particular interest because they evaluated pulse oximeter accuracy during deep desaturation and also measured response times to rapid desaturation and resaturation. Both studies revealed errors in some manufacturers’ calibration algorithms. This prompted these manufacturers to revise their algorithms and their devices were subsequently reevaluated. This emphasize again the importance of specifying the software revision employed in any pulse oximeter study.

Unfortunately, most reports do not specify the software revision (Table 1). Eagle et al (1987) evaluated the Ohmeda 1700 (KJ1 software) and the Nellcor N 100 in a volunteer study and found 99% prediction limits of ± 4% over a saturation range of 60 - 100%. Since 99% prediction limits are ± 3 SD, this implies a standard deviation of ± 2.7%, not far from manufacturers specifications. These authors also measured the time for 50% recovery of resaturation from a hypoxic state. With the pulse oximeter set on the “fast” (3 s) averaging mode, the ear probe showed resaturation more quickly than the finger probe (6 s versus 24 s).
Severinghaus and Seifert (1987) published an interesting volunteer study comparing seven different pulse oximeters during severe desaturation. They also measured response times for both ear and finger probe desaturation and resaturation. This study did not determine accuracy over a range of steady-state saturation, but rather during a sudden, brief desaturation to an $\text{SaO}_2$ of 40 - 70% (Table 1). The authors noted significant variations in bias and precision among manufacturers as well as among subjects. The bias varied from 11% to 9%, with a precision as high as 10%. They also found that ear sensors were usually more accurate than finger sensors. This difference in accuracy could be a result of the unsteady nature of this experiment. The $\text{SaO}_2$ response times were again much faster for ear probes than for finger probes. The $T_{1/2}$ for the ear probe during desaturation ranged from 24 to 35 s. This differing response time is presumably due to different perfusion time constants for the ear and finger circulation. The response to resaturation was faster than to desaturation. One problem with this study that may limit the comparison of the devices is that the signal averaging times of the monitors were not the same. This would affect their response time to transients, and may also affect their accuracy during brief, deep desaturation. The $\text{SaO}_2$ values from the finger probes were still falling when the expired oxygen level and ear sensor $\text{SaO}_2$ had already shown resaturation. Therefore, some oximeters may
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<td>.96</td>
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<td>48</td>
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$r$ = Correlation coefficients. $s$ = Linear regression slopes. $b$ = intercepts. $n$ = No. of data pairs. SEE% (sys) = Standard error. Bias = mean difference between $SpO_2$ and $SaO_2$. Prec. = standard deviation of the differences.
All manufacturers specified accuracy are similar. 1 SD = ± 1%, 100% to 70-80%.
1 SD = ± 3%, 70-80% to 50%, and unspecified ≤ 50%. Manufacturers: N-100 and N-200 (Nellcor); Biox II, Biox III, and Ohmeda 3700 (Ohmeda); CR (Criticon); PC 1600 (Physio Control); NO (Novametrix); NC (Marquest); and Datex. The software revision is in parenthesis following the manufacturer abbreviation when this information was provided in the referenced study. (Nellcor N-100 Technical Manual. Nellcor Corporation, Hayward, CA; Ohmeda 3700 Pulse Oximeter Technical Manual. Ohmeda Division of ROC, Boulder, CO; Novametrix 500 Pulse Oximeter Technical Manual. Novametrix Medical Equipment, Wallingford, CT).

* These values of σy± are determined from the authors 95% confidence intervals.

† The SpO₂ data were collected in patients with pulmonary artery catheters for simultaneous cardiac output determinations. Therefore, these patients were probably more critically ill than those in the other studies.
have not reached equilibrium at steady-state desaturated \(S\text{po}_2\) values due to their longer averaging time.

The most recent volunteer study examined the accuracy of four pulse oximeters over a range of saturation from 65 to 100% (Table 1). This study also compared the results of three bench oximeters and \(S\text{ao}_2\) calculated from a blood gas analyser using the multi-wavelength IL 383 co-oximeter as the reference. Two of the bench oximeters (which employed two wavelengths) yielded bias and precision values of \(-0.1 \pm 2.5\%\) and \(+1.8 \pm 0.7\%\). The calculated \(S\text{ao}_2\) values from the blood gas machine were of similar accuracy \(-1.9 \pm 2.4\%\). The accuracies of the pulse oximeters compared favourably to these values (Table 1).

Among the clinical studies on adult patients, Trumper et al (1985) found a low correlation coefficient of \(r = 0.57\), but a bias of precision of \(1.4 \pm 1.1\%\). These bias and precision values are similar to those of volunteer studies and the two other adult clinical studies presented in Table 1. The clinical studies of Abell et al (1985) and Ceci et al obtained the values of \(r\) to \(r = 0.9\) which were higher than those of Trumper due to the wider saturation range over which the data were collected. Comparing these results demonstrates how the correlation coefficient alone can be a misleading index of accuracy in methods-comparison studies.
The accuracy of pulse oximeters is impressive, considering the many possible sources of error. We should remember that the specified uncertainty of ±2% to 3% is for one SD, or a 68% confidence interval. If we desire 95% (2 SD) or 99% (3 SD) confidence, then the uncertainty is two or three times as large, respectively.

**Experimental Studies**

The pulse oximeter is an excellent monitor for transport from the operating room to recovery because of its portability and ease of use. In a study of American Society of Anesthesiologists Class I and II patients being transported while breathing room air, Tyler and associates found that 35% of their patients exhibited \( \text{SpO}_2 \) values below 90% during transport. This hypoxemia correlated with obesity and a preoperative history of asthma.

In a related study, Graham and colleagues found that 15 patients transported while breathing room air desaturated to an average \( \text{SpO}_2 \) of 80%, whereas 19 similar patients transported with supplemental oxygen experienced no major desaturations. In these two studies, the pulse oximeter firmly established the value of supplemental oxygen during transport to the recovery room.

Choi and associates used \( \text{SpO}_2 \) to monitor postcesarean section patients who were being treated with either epidural or parenteral narcotics. Each patient was
monitored for approximately 1,000 minutes. Both groups exhibited an average of 3 to 4 minutes of desaturations below 90%, with no significant difference between the groups. The work of Nakatsuka and Rollin (Departments of Anesthesiology and Nursing, Medical College of Virginia, Richmond, Virginia) on the "Incidence of post-operative hypoxemia in the recovery room detected by the pulse oximeter" has revealed the important findings of their study. In the 101 post-surgical patients, 12 patients (11.9%) developed moderate hypoxemia (\(S\bar{a}O_2 \leq 90\%\), \(77.3\%\)) and 6 patients (5.9%) suffered severe hypoxemia (\(S\bar{a}O_2 \leq 85\%\)). Smoking habit was significantly associated with post-operative hypoxemia (\(P \leq 0.05\)). Supplemental \(O_2\) inhalation decreased the incidence of hypoxemia significantly (\(P \leq 0.05\)). There was a trend toward a higher incidence of post-operative hypoxemia in patients with AAA III, chest surgery and ventilator support. Supine head down position and lateral position in the recovery room seemed to have higher incidence of hypoxemia.

New applications for the pulse oximeter are being discovered on a regular basis. A pulse oximeter placed on the great toe has been used as an aid in cannulating the femoral artery in obese patients. The pulse oximeter is now accepted as the primary indicator for and monitor of home oxygen therapy in patients with severe obstructive lung disease.
Clinical Consequences of Pulse Oximetry

As any new technique becomes standard of care, there is a time window during which it is ethically feasible to perform randomized, controlled studies of its effectiveness. A recent clinical study by Cote et al (1988) has confirmed the necessity of \( \text{SpO}_2 \) monitoring during pediatric anesthesia. One hundred and fifty-two patients were continuously monitored with \( \text{SpO}_2 \) during anesthesia. In half of these patients, the \( \text{SpO}_2 \) data were "unavailable" to the anesthetic team. A major desaturation event was defined as \( \text{SpO}_2 \) less than 85% for 30 s or longer. There were 24 major events in 74 cases when \( \text{SpO}_2 \) data were "unavailable", and only 11 when the \( \text{SpO}_2 \) data were "available". The majority of these events occurred in patients below 3 yr of age in both groups. Smaller pediatric patients have a greater tendency to desaturate due to their relatively high oxygen consumption, smaller functional residual capacity and possible fetal circulatory pattern. Asmar et al (1987) blindly collected \( \text{SpO}_2 \) data from 108 out-patients during gynecologic surgery. They found episodes of moderate desaturation (\( \text{SpO}_2 \leq 90\% \)) in 10% of the cases and severe hypoxemia (\( \text{SpO}_2 \leq 85\% \)) in 5% of the cases. Under current recommended standards for anesthetic monitoring, it may be difficult to conduct further controlled studies on intra-operative \( \text{SpO}_2 \) monitoring.
Monitoring during transport to the recovery room has also been examined in children and adults. Fullerite et al monitored 71 healthy pediatric patients during transport and found that 28.1% had \( \text{SpO}_2 \) values \( \leq 90\% \), while only 45% of these desaturated patients had observable cyanosis. In a similar study of adult patients, Tyler et al found that 35% had \( \text{SpO}_2 \) values \( \leq 90\% \), and 12% had \( \text{SpO}_2 \) falls to 85% or less. Both studies conclude that due to the high incidence of desaturation and the inability to clinically recognize it, all patients should receive supplemental oxygen during transport from the operating room to the recovery room.

The oxygenation of adult and pediatric patients in the recovery room has been evaluated with interesting results. Soliman et al compared \( \text{SpO}_2 \) to a post-anesthesia recovery score in children. The post-anesthesia recovery (PAR) score is a system based on motor activity, respiratory effort, blood pressure, consciousness, and color. An \( \text{SpO}_2 \geq 95\% \) was considered adequate oxygenation for a healthy pediatric patient. They found no correlation between the PAR score and the patients' oxygenation. They concluded that pediatric patients in the recovery room should be monitored continuously with pulse oximetry or at least treated with supplemental oxygen regardless of their apparent wakefulness, and that an \( \text{SpO}_2 \) value should be included among the recovery room discharge criteria.
Norriss et al (1986) studied 241 adult patients in the recovery room, measuring $\text{SpO}_2$ values upon arrival, 5 min after arrival, 10 min after arrival and just prior to discharge. The recovery room personnel were blinded to the $\text{SpO}_2$ data. Of the 249 inpatients studied, 14% had episodes of desaturation to below 90%. As might be expected, the factors associated with desaturation were obesity, extensive surgery, age, and ASA physical status. Most surprising is the fact that more patients were found to be hypoxic at the time of discharge than at any of the other measurement times. These results demonstrate our present lack of knowledge as to what saturation levels imply immediate danger or a poor prognosis in post-operative patients under various clinical circumstances.

In examining the clinical consequences of pulse oximetry, we must be aware of the pulse oximeter's limitations. Arterial oxygen tension can vary over a wide range during general anesthesia, but $\text{SpO}_2$ will reflect none of this variation until desaturation occurs as $\text{PaO}_2$ decreases below 100 mmHg. The pulse oximeter is effectively a sentry standing at the edge of the "cliff" of desaturation.